**Testimony Presented to the Committee
on Science and Technology's Subcommittee
on Environment and the Atmosphere**

Chester R. Richmond

MASTER

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TESTIMONY PRESENTED TO THE
COMMITTEE ON SCIENCE AND TECHNOLOGY'S
SUBCOMMITTEE ON ENVIRONMENT AND THE ATMOSPHERE

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MARCH 1976

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TESTIMONY PRESENTED TO THE
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ABSTRACT

This report contains the basis for oral testimony to the House Committee on Science and Technology's Subcommittee on Environment and the Atmosphere in November 1975. The subject of the hearings was "Effects and Costs of Long-term Exposure to Low Levels of Manmade Pollutants" and the purpose of the hearings was to increase the awareness of low-level pollution and its impacts on human health, agriculture and climate.

This report contains information related to impacts of low-level pollutants on human health. I have attempted to point out the major adverse health effects (e.g., carcinogenic, mutagenic and teratogenic) that may result from chronic exposure to low-level pollutants.

Also addressed are important questions such as what do we know about dose-response relations for chronic exposure to pollutants and how can we establish comparisons with knowledge obtained from exposure to ionizing radiations. The report also considers the wisdom of extrapolating from health effects data obtained from acute, high-level exposures to chronic, low-level exposure conditions. Lastly, a few examples of the societal costs related to low-level pollutant exposure are presented.

INTRODUCTION

These hearings, conducted by the Honorable George E. Brown, Jr., are very timely because of the growing interest, both in Congress and throughout the United States, concerning the magnitude of health effects associated with exposure to low-levels of pollutants and the attendant societal costs. Virtually everyone is interested in or concerned about this important issue, and almost daily we hear or read about the importance of the environmental etiology of cancer. We know that acute exposure to high-levels of pollutants are damaging and costly, but we are only beginning to better understand the situation as regards chronic exposure of the general public to lower levels of pollutants in our environment.

My testimony will deal with the question of what are the major kinds of adverse health effects as regards exposure to chronic low-level pollutants. In addition, I will discuss briefly the relation between exposure level and severity of response (dose-response) borrowing heavily from our experience in the radiation field.

To begin with, we must appreciate the simple fact that man has evolved from simpler forms and learned to efficiently perform work, communicate, think and record his efforts from generation to generation. Whatever man does results in changes both good and bad in his surroundings. It also follows that the overall potential for increased environmental and health damage has increased as industrialization, urbanization, science and technology, and--perhaps most importantly--population increase. Some of these factors, such as science and technology, may be our strongest weapons against further environmental and human health degradation from chronic low-level exposure to pollutants.

Man has manipulated and exploited his environment in an attempt to increase his standard of living and decrease human misery and suffering while his numbers have increased dramatically as the result of the dark side of the Malthusian growth curve. We must now collectively act responsibly to put our house in order and learn how to strike a balance between the relative benefit and cost of exploiting our environment. Dr. Barry Commoner's fourth law of ecology cautions us that there is no such thing as a free lunch (1). Put simply, this means that we pay a price for everything we do and nothing is gotten free. We are only now learning what we have actually been paying in health costs resulting from chronic low-level exposure to an ever-increasing number of pollutants, or, as I prefer, biological stressing agents.

Man's efforts are not new in this area although, granted, they have not been spectacular over the years. For example, England appointed its first Commissioner of Sewers over 300 years ago. Even earlier during the 13th century, the English authorities worried about smoke from coal fires. By the 14th century, the first clean air legislation had been passed and one man was actually hanged for violating the law. We have not always recognized what has been obvious to some. For example, the mid-16th century Spanish explorers visiting what is now the Los Angeles, California area noted layers of smoke from Indian fires hanging over the area. Smog, unfortunately, did not become an important issue for the Los Angeles area until several decades ago.

A current problem, but certainly not a new one, stems from the arguments of prohibitionists and nihilists exhorting us to retreat from technological advances or to impose moratoria on specific technologies or on science and technology in general so that we may protect man and his environment from further abuse. In fact, a commonly stated cause of our environmental problems is the overuse of technology. However, in taking exception to this view, Buckminster Fuller, inventor of the geodesic dome, said that more--not less--technology is needed to overcome environmental ills. He concluded, "It's an ignorance crisis we face, not a pollution crisis or an energy crisis... But, above all, I think nature is really trying to make a success of man despite his ignorance."

We must also meet head-on the question of cost. Again, the real question is "how much will it cost not to do something" rather than what is the "cost of doing something" to reduce the ultimate external costs to man and his environment from exposure to chronic low-level pollutants. Actually, the words "ecology" and "economics" come from the same Greek

root "ecos" meaning house and are not incompatible or antithetical. Economics is the management of the house whereas ecology is the study of the house.

MORTALITY-MORBIDITY-DEGENERATIVE DISEASE

The widely discussed acute episodes of severe pollution that occurred in London, Donora, Osaka, New York, the Meuse Valley in Belgium, and other locations demonstrated quite convincingly that severe air pollution could cause both illness and death. In October 1948, the deaths of 19 of Donora's 13,800 residents were blamed on smog as were 6,000 cases of illness (2). Actually a similar incident occurred in 1945, according to a review of Donora's health statistics (3). Atmospheric pollution was also the cause of the December 1952 London incident when the normal death rate during and following a four-day period of heavy pollution increased by 4,000 persons. In the following two months, an additional 8,000 persons were to die prematurely in London. A decade later, New York suffered a similar, but less severe, increase in death rate during a period of heavy atmospheric pollution. Some of these acute incidents are given in Table I of the Summary Report of the National Academy of Sciences-National Academy of Engineering report on air quality prepared for the Senate Committee on Public Works (4) and in a publication of the World Health Organization (5). Deaths from bronchitis, pneumonia, and other respiratory and cardiac diseases increased and people over 45 years of age were mainly affected in the London incident. Although increase in bronchitis deaths was the largest single contributor to the increased deaths, diseases involving impairment of respiratory function added to the death toll. In addition to the increase in heart disease

related deaths, perhaps from stresses related to impairment of respiratory function, there was also observed a substantial increase in deaths from all other causes. Although there was a close correlation between excess mortality and atmospheric concentrations of smoke and sulfur dioxide, it is still not clear what the toxic components of the London incident were, as components other than smoke and sulfur dioxide were not measured.

There have been other instances of mortality and morbidity from exposure to pollutants. For example, the widely publicized case of poisoning from the toxic material mercury in Minamata, Japan (6) which paralyzed or killed about 115 people, or the 1965 episode of water pollution in Riverside, California that resulted in several deaths and 18,000 cases of gastroenteritis (inflammation of the digestive tract).

Mercury is but one of several toxic metals such as lead and cadmium which have caused human health effects via environmental pollution. Cases of lead poisoning date back to antiquity. It has been said that in the second century B.C. the wealthy inhabitants of Rome were drastically affected by sterility, child mortality, and permanent mental impairment (the less wealthy could not afford lead eating and drinking utensils) (7). It has been estimated that 180,000 tons of lead were emitted from the combustion of lead-containing gasoline in 1968. This source, the largest of all environmental sources, represented about 14% of all the lead consumed that year in the U.S. (7). Even though the acute toxicity of lead has been known for over 2,000 years, we do not know the health effects from current ambient levels of lead in air and water. Our knowledge of the toxicity of low-levels of lead is contained in an excellent review in Environmental Health Perspectives (8).

Serious health effects from cadmium related "itai-itai" disease have occurred in Toyama City, Japan (9). Exposure to cadmium dioxide or cadmium dust is known to produce acute pulmonary edema. Chronic inhalation exposure results in chronic emphysema and renal disturbance. However, in the Japanese incident, cadmium released from a smelter was concentrated by rice plants to levels much higher than those in the general environment. The health effects differed from those observed in industrial exposures in that most of the affected were females over 50 years who had borne several children. The disease was characterized by bone and kidney damage that suggests severe disturbances of calcium metabolism. These data suggest that a segment of the population may be sensitive to adverse health effects of environmental levels of cadmium because of dietary deficiencies.

There exists very extensive literature on the biological effects of cadmium which has been summarized in several recent reviews (10, 11). However, as pointed out in a recent review on the environmental impact of cadmium, much of the information has come from studies of acute toxicity rather than from studies directed toward the evaluation of low-level environmental effects. In 1965, another poisoning incident resulting in serious neurological damage was reported in Niigata, Japan. Friberg et al. (12) estimate that about 100 deaths have occurred from this disease.

Beryllium, in addition to posing a serious potential industrial health problem, must also be considered from the standpoint of the general public. Hardy reports that 30% of the 60 people with non-occupational berylliosis on file with the Beryllium Registry were exposed to air containing beryllium in the vicinity of beryllium plants (13).

WHAT ABOUT THE EFFECT OF CHRONIC LOW-LEVEL EXPOSURE TO POLLUTANTS
ON MORTALITY AND MORBIDITY?

Acute episodes of air pollution for the most part produce exposures to unusually high concentrations of pollutants with the subsequent production of obvious health effects. Our problem under discussion during these hearings relates specifically to the question of health effects which may result from prolonged exposure to chronic low-levels of pollutants and whether or not these exposures produce morbidity, mortality, cancer, genetic defects, or decreased life span in individuals in the community. It is quite obvious that the toxic health effects related to acute exposure to pollutants alert the community and others to the situation and need for action. However, this is not the case for chronic low-level exposure. For lower exposure levels, the latent period (time required for the effect, such as cancer, to become apparent in an individual) increases, therefore the effects are delayed and may be difficult to detect from the normal incidence of a given disease. An often-cited example is lung cancer which has a latent period of the order of 20-30 years. The list of materials now identified as environmental pollutants known or believed capable of producing health effects, including cancer, at least in experimental animals, includes but is not limited to such diverse materials as benzo(a)pyrene, radioactive materials, asbestos, nickel, chromates, arsenic, vanadium, numerous polynuclear organic compounds (that can occur in a variety of sources including tobacco smoke, smoked fish and meat), coal products, exhaust gases (from gasoline and diesel engines, and increasingly in the atmosphere of urban and rural areas), aromatic amines, chlorinated hydrocarbons, and n-nitroso compounds.

It might be useful at this point to consider the conclusions and recommendations of the National Academy of Sciences-National Academy of Engineering report entitled "Man, Materials, and Environment" (14).

The report states:

"At least three factors are operating to make it possible, even likely, that some environmental disruption will be experienced as sudden catastrophe rather than as a slowly moving and predictably growing shadow. One is the long time lag that often intervenes between an environmental insult and the appearance of harm--e.g., carcinogens and mutagens. The second factor is the irreversibility of some kinds of damage--e.g., the loss of genetic variability. The third is the apparent existence of environmental thresholds in some processes, wherein a small increment of some input to the environment generates a disproportionate response--e.g., triggering of climatic change by natural processes."

Other pollutants must also be considered both from the standpoint of acute and long-acting effects. Some of these materials occur in nature, yet they must be considered along with the "man-made" variety. Among these are carbon monoxide, sulfur oxide and particulates, nitrogen oxides, hydrocarbons, and oxidants, including ozone, which are associated with air pollution arising from numerous sources including automobile emissions and electrical energy production.

Carbon monoxide in low concentrations is known to have physiological effects because of its affinity for the blood pigment hemoglobin, almost 250 times greater than that for oxygen and hemoglobin, resulting in less oxygenation of body tissues. Heart muscle requires large amounts of oxygen so adverse effects of high carbon monoxide levels are expected

for coronary disease patients. Carbon monoxide is also suspected to have an effect on fetal development because of the observed association between smoking mothers and smaller baby size. Increased CO levels may also affect reaction time, visual thresholds and work performances.

Sulfur has been released by human activity to the air we breathe for at least 5,000 years from mining and smelting activities. Early descriptions of Roman smelters by Strabo in 7 B.C. mentions furnaces with chimneys "so that the gas (sulfur dioxide) from the ore may be carried high into the air for it is heavy and deadly." Currently, in the U.S. about half of the SO_2 released to the air appears to come from only about 10% of our land area. Therefore, concentrations tend to be higher in large Eastern urban areas. Figure 1 shows both geographic variations for SO_2 emissions and air concentrations for the U.S. (15).

Exposure to sulfur oxides, especially at high concentrations, causes a constriction of the trachea and larger bronchi. Apparently, small but statistically significant effects can be observed following a one-hour exposure to air containing SO_2 at levels as low as 0.62 ppm. Following chronic exposure, rats exposed to 10 ppm for six weeks developed thickening of the mucosal layer in the bronchi of the upper respiratory tract. Higher exposure levels in rats led to "chronic bronchitis-like" effects. However, no effects on the respiratory tract (including histological) were observed in experiments involving lower exposure levels (0.13-5.72 ppm) suggesting a tolerance to lower SO_2 concentrations. Chronic exposure of subhuman primates to SO_2 (0.14-1.28 ppm) has also yielded negative results (16).

In 1969, the man-produced quantity of sulfur oxides amounted to about 33,000,000 tons, most of which (24,000,000 tons) came from burning

Nationwide geographic variation in annual SO₂ emission density

Geographical distribution of typical annual urban ambient sulfur dioxide concentrations

Fig. 1

sulfur-containing fuels at stationary power plants (17). The concentration of SO_2 in the air of large industrialized cities (e.g., New York, Chicago, St. Louis, Philadelphia) often was larger than the concentrations that are thought to increase both illness and death rate.

Oxidation of SO_2 in air results in sulfuric acid salts which probably are present as aerosol droplets. Work in experimental animals including subhuman primates shows that the biological effects of the acid sulfates are considerably greater than SO_2 per se.

Recently obtained epidemiological information from the Environmental Protection Agency's Community of Health Environmental Surveillance System (CHESS) and other studies suggests that health effects may be related more closely to particulate sulfate concentrations than to SO_2 concentrations (18). These works suggest that a primary standard as low as 0.003 ppm ($8 \mu\text{g}/\text{m}^3$) as a daily average (not to be exceeded more than once a year) may be required to prevent mortality, aggravation of heart and lung disease, and asthma in elderly patients (15).

The primary national ambient air quality standard for SO_2 specifies that the 24-hour average concentration shall not exceed 0.14 ppm ($365 \mu\text{g}/\text{m}^3$) more than one time per year and that the yearly arithmetic mean shall not exceed 0.03 ppm ($80 \mu\text{g}/\text{m}^3$).

Nitrogen oxides are known to be highly toxic to experimental animals and man. Short-term exposures to air containing NO_2 above 25 ppm results in serious or fatal pulmonary edema. At exposure levels of 2-5 ppm, abnormal pulmonary function changes have been observed in human subjects. Reduced resistance to bacterial and viral infection has been observed in animals exposed intermittently or chronically (for a year) to air containing nitrogen dioxide at levels ranging from 0.5 to 1 ppm. Some slight

histological changes were seen at concentration of only 1 ppm. There are suggestions of synergistic response (more than an additive response) when NO_2 and viral insults are given together. Also, we know very little about possible interactions between NO_2 and particulates on human health although preliminary work suggests adverse lung effects from NO_2 and carbon-containing particulates when no effects were seen when either agent was administered alone. In general, it appears that our knowledge of the adverse health effects of nitrogen oxides is considerably less than that for CO and sulfur oxides or oxidants such as ozone.

Ozone accounts for about 90% of the measured oxidants in urban air. It has caused irritation of the nose and throat at concentrations above 0.3 ppm in both experimental animal studies and in occupational exposure situations. Occupational exposures to ozone suggest that even short exposures to air containing about 10 ppm ozone may have severe effects on the mechanical properties of the lung which affect exhalation. Recent observations in non-occupational settings suggest episodes of respiratory difficulty for people performing work (cyclists) during periods when the ozone and SO_2 concentrations were only approximately 0.2 ppm; again an effect which is greater than additive is suggested. Similar effects were observed for human subjects exposed to ozone plus SO_2 . Detailed information and health effects of air pollution were documented in the National Academy of Sciences Summary of Proceedings on the 1973 Conference on Health Effects of Air Pollution (16). A recent source of information concerning the health effects resulting from combustion products of fossil fuels is the proceedings of a workshop held in late 1974 by the Electric Power Research Institute (19). Another fairly comprehensive review of the health effects of selected

atmospheric pollutants exists in the National Academy of Sciences-National Academy of Engineering's Report on Air Quality and Automobile Emission Control (17).

The quantities of pollutants available in the environment to cause health effects are staggering. For example, Table I, taken from a Council on Environmental Quality report (20) shows the estimates for U.S. air pollution emissions for 1969. Note that the units are millions of tons per year. The nationwide trends for selected air pollutants as given in Table II (17) indicate the general increasing severity of the problem with time.

Table III, modified from L. D. Hamilton (21), lends additional perspective to the magnitude of pollutant release related to the generation of electrical energy from various power plants (a 1,000 MWe power plant operating at 75 percent load is assumed in each case). Thus for each 1,000 MWe coal fired plant, over 40,000 tons of particulates and approximately 100 tons of CO are generated each year.

Hydrogen sulfide also enters the air through the natural decay of organic materials and oxidized to SO_2 . Volcanoes also contribute to the "natural" background of SO_2 . Although natural sources may account for about 80% of the atmospheric SO_2 , these sources seldom produce concentrations that would be regarded as pollution (22).

In October 1973, the National Academy of Sciences convened a conference on the Health Effects of Air Pollution (16). The conclusions of this conference are of interest to our topic as they are virtually unchanged today. One conclusion was that the exposure of human beings and animals to automobile exhaust pollutants or to SO_2 and the associated small particles in certain stack gases has been associated with the occurrence of adverse

TABLE I

ESTIMATED NATIONAL AIR POLLUTION EMISSIONS - 1969Millions of Tons Per Year

Source	Carbon Monoxide	Sulfur Oxides	Hydro- Carbon	Nitrogen Oxides	Particulates
Transportation*	111.5	1.1	19.8	11.2	0.8
Fuel Combustion** from Stationary Sources	1.8	24.4	0.9	10.0	7.2
Industrial Processes	12.0	7.5	4.8	0.2	14.4
Solid Waste Disposal	7.9	0.2	2.0	0.4	1.4
Miscellaneous	18.2	0.2	9.2	2.0	11.4
Total	151.4	33.4	36.7	23.8	35.2

*Mainly from automobiles

**Mainly from power plants

TABLE II

ESTIMATED NATIONWIDE AIR POLLUTANT EMISSION TRENDS 1940-1970

(Millions of Tons per Year for Continental U.S.A.)

YEAR	SO ₂	TSP*	CO	HC	NO _x
1940	22.8	44.9	72.5	16.6	6.5
1950	24.9	33.2	82.9	21.8	8.8
1960	23.2	29.9	98.6	25.8	11.4
1968	31.1	28.4	111	29.7	19.5
1969	32.1	35.0	115	28.7	21.1
1970	33.4	25.5	101	27.3	22.1

*Total Suspended Particulates

TABLE III

Estimated environmental impacts of generating 6.57×10^6 MWh/year by coal, oil, natural gas, and light water reactor methods. A 1000 MWe power plant operating at 75 percent load is assumed in each case.

<u>CHARACTERISTIC</u>	<u>COAL</u>	<u>OIL</u>	<u>NATURAL GAS</u>	<u>LIGHT WATER REACTOR (LWR)</u>
Impacts to Air				
Emissions (Tons)				
Dusts	$3.2 - 4.2 \times 10^4$			
Particulates	4.2×10^4	1.1×10^3		
SO _x	1.5×10^5	2.9×10^4		18
NO _x	3.5×10^4	1.3×10^4	3.5×10^4	25
CO	101	312		
HC	72	479		
Organics	11	122		
Ammonia		280		8
SO ₂				0.2
NO ₃				19
Fluorides				1
CO ₂	$7.5 - 10.5 \times 10^6$	5.3×10^6	4.5×10^6	

pathological and clinical sequelae. However, no data were presented that would allow a statement of the actual incidence of the adverse effects, either in the general population or in specific subsets. Also, assignment of any specific adverse effect to a specific pollutant is prevented, since the same adverse effects are also known to be produced by other causes. It is not presently possible to diagnose and attribute the illness of a particular person as the result of exposure to a specific pollutant or pollutant mixtures at atmospheric concentrations.

The second major conclusion stated the impossibility, because of limitations of knowledge, of establishing an ambient concentration of any pollutant--other than zero--below which it is certain that no person would be adversely affected.

The third conclusion was the "safety factors" afforded by present standards were modest and probably less than a factor of ten if avoidance of adverse physiological change is used as the criterion. The "safety factor" is much greater for lethality as the criterion, and unknown for those individuals with preexisting disease except for the effects of carbon monoxide on persons with heart disease.

CANCER PRODUCTION (CARCINOGENESIS)

Carcinogens are chemical, physical or natural agents, both naturally occurring and man-made, which under proper exposure conditions will produce cancer in man. It is well known that exposure of human subjects to various radiations (ionizing and non-ionizing), and both inorganic and organic pollutants can in some instances, depending on the exact exposure conditions, result in carcinogenesis (cancer production). As regards public health hazards, Hueper (23) relates the highest cancer risk to the following exposure conditions:

"Carcinogens which are stable and are not rapidly destroyed in the tissues by metabolic action and are not quickly excreted from the body with the urine, feces or respiratory air but are retained in the body over long periods and act as carcinogenic depots.

Carcinogens, which are capable of penetrating the placental barrier or are excreted in the milk begin their exposure with the fetus or infant who have the optimal chance to outlast carcinogenic latent periods by years or even decades. These carcinogens also have the chance to accumulate over the individual's total lifetime.

Carcinogens, which are introduced into the body often and over long periods of time from multiple sources and for various reasons (food additives and contaminants, drugs, air and water pollutants, pesticides, etc.), may create during the course of years a total carcinogenic burden of considerable and significant degree through accumulation and summation. Often these individually small doses of carcinogens display a syncarcinogenic action."

Hueper also points out that considering the long latent period (decades) that often elapses between the time of contact with a carcinogen and the development or manifestation of a cancer, it is likely that the progressive rise in cancer frequency with advancing age reflects the action of carcinogens operating at a rather low level over decades or the entire lifespan.

Among the metals and minerals that can cause cancer under certain exposure conditions are arsenic, chromium, nickel, asbestos, selenium, cobalt, cadmium, lead and zinc. Also on the list of cancer-producing materials are the incomplete combustion products of carbonaceous matter, including numerous polycyclic aromatic hydrocarbons which arise from

several environment sources including energy production. Specific fractions containing polynuclear aromatic hydrocarbons (PAH) have been isolated from polluted air and tested for carcinogenicity in mice by skin painting experiments. When tested in this way, the fractions have been shown to be carcinogenic. Another large group of carcinogenic chemicals represent organic products resulting from our many industries and including lubricants, fuels, fuel additives, plastics, rubber products and dyes.

Some of the recognized human carcinogens include benzol, chlorobenzols, benzidine, naphthylamine, xenylamine, coal tar, pitch, creosote, anthracene, chlornaphazin, oil, paraffin oils, asbestos, shale oil, paraffin, lignite oils, carbon black and soot (one of the first known causes of occupationally related cancer of the scrotum and skin in chimney sweeps).

About 365,000 residents of the U.S. will die from cancer this year. Thus, about one out of six Americans dies from this cause. The overall incidence has increased each decade this century and there currently are suggestions that 75% or more of all cancer may be environmentally related (23). Obviously, it is not known at this time if this is indeed a fact. We do know, however, that certain associations do exist between exposure to specific pollutants and cancers of a specific kind; for example, observations of cancer of the lung among persons living near asbestos plants or along roads on which the material is transported by truck (24).

Berylliosis of the lung, presumably resulting from beryllium exposure, has been reported for some persons living near beryllium plants (25) and it is known that carcinoma of the lung has been found together with berylliosis in beryllium workers (26). This observation plus the knowledge that lung carcinoma can be induced in rodents and subhuman primates

exposed to beryllium dust by inhalation has led some to predict that lung cancer can be expected to exist in persons living near beryllium plants. One can also infer from occupational exposures that non-occupational exposures to numerous chemical agents may result in cancer production as a late biological effect. This, of course, depends on numerous factors such as the shape of the dose response curve for the material in question and the route of environmental exposure.

Recent vital statistics data from a National Cancer Institute report on the distribution of various kinds of cancer by county throughout the U.S. (27) suggest that increases in specific kinds of cancer in certain parts of the U.S. may be related to industrialization. We do not yet know what fractions of the total increases are related to non-occupational exposure to given pollutants. These observations, however, do give us cause for concern as regards the probable importance of man-generated pollutants in producing "naturally occurring" cancer.

Ultraviolet solar radiation and ionizing radiations, either naturally occurring or man-made, are known to be carcinogenic under certain exposure regimes. There is also clinical and epidemiological evidence which argues for a causal relation between solar radiation and several kinds of human skin cancer that are usually nonfatal. These data are not absolutely conclusive. For example, there is a doubling of skin cancer (non-melanoma) incidence for approximately each 10° decrease in latitude which presumably is related to the concomitant increase in the amount of UV radiation reaching the earth's surface. Recent estimates based upon observed changes in skin cancer incidence with variations in latitude for each percent reduction in ozone concentration range from about 2,000 to 15,000 new cases of skin cancer (non-melanoma) per year

for light skinned persons in the U.S. at equilibrium conditions (28). Thus, there is much concern about the effects of man-made fluorocarbon compounds commonly used as refrigerants and as propellants in aerosol products on the earth's stratospheric layer of ozone which shields us from solar UV radiation. These chemicals diffuse upwards and are decomposed by solar UV radiation in the stratosphere releasing free chlorine in the process. In turn, the chlorine atoms decrease the ozone concentration through a series of catalytic reactions. Oxides of nitrogen also destroy ozone, but with considerably less efficiency (about threefold). The reduction of the average stratospheric concentration of ozone leads to an increase in the amount of harmful solar UV radiation reaching man and consequently a postulated increase in the number of skin cancers. Of special significance is the fact that the first technical paper to postulate this chain of events was published in 1974. Also, the proposed sequence of events indicates the exceedingly complex route whereby a chemical might "cause" cancer through a remote complex chemical reaction.

GENETIC EFFECTS (MUTAGENESIS)

Technological and industrial activities create a large number of chemical pollutants, some of which enter the environment each day at low levels and some of which find their way to man at times following considerable environmental concentration. These chemicals, plus agents such as ionizing radiation, can effect changes in the genes of human reproductive cells that will persist and survive as long as their bearers survive. Generally, the first generation containing the mutated reproductive cells is not directly affected. Mutations for the most part are damaging, yet they produce little effect in the first generation offspring, especially

if inherited from only one parent. However, the mildly deleterious mutations can accumulate and produce an accumulated genetic burden for many generations. Thus, each individual during his life may accumulate several mutations to add ultimately to those which were contributed by predecessors.

Mutations can also affect non-reproductive cells (somatic) and produce cancer, but these somatic mutations are not inherited and affect only the person carrying the mutation. We know, however, that some chemicals have both carcinogenic and mutagenic properties. Included in this list are: 3, 4-benzpyrene, 20-methylcholanthrene, sulfur mustard, p-dimethylaminobenzene, cyclohexylamine, nitrogen mustard, ethyl carbonate, methylnitrosourea, ethylnitrosourea, and dimethylnitrosomine. Not all chemicals that are carcinogenic produce mutagenic changes. Several examples of this category include 2-acetyl-amino-fluorene, nitrosopiperazine, diethylstilbestrol, and chromium salts.

Two years ago at a conference on the Evaluation of Chemical Mutagenicity Data in Relation to Population Risk, Dr. A. Hollaender recounted the problems he had experienced in attempting to convince people of the significance of chemically produced mutagens (29). His efforts were successful and since then the Environmental Mutagen Society was formed and several important workshops were held. Hollaender pointed out the need for a protection standard for chemical hazards perhaps similar to those that have evolved in the radiation field. He emphasized that "it (the standard) will no doubt be a crude measurement and quite limited in its application, but it will at least be a 'statement' and a starting point that can be altered and adjusted as more data become available." Hollaender also urged that there would be a need for cooperative effort

among people in industry, the medical profession, government laboratories, and universities for "otherwise we won't get anywhere." To Dr. Hollaender's list, in the interest of speeding up the process, I would add those government agencies which have varying degrees of responsibility for the overall problem of real and suspected environmental mutagens.

It is important to identify potential mutagens before they can accumulate in man and produce genetic damage. We must learn a great deal about what levels of pollutants can get into gonadal tissue where they may produce genetic mutations in germ cells. We need to ask if there are special mechanisms which concentrate materials in gonadal tissue (30). Also needed are sensitive and reliable test systems to screen the large number of potential mutagens and also a human monitoring system to help detect genetic abnormalities that might not be detected by screening systems (31). Screening systems now used in numerous laboratories include the use of bacteria, fungi, plants, insects, mammalian cell cultures and intact animals.

Based upon laboratory experiments, potential mutagenic agents produced by fossil fuel combustion include sulfate and nitrate in the chemical transformation of SO_2 and NO_2 , benzo(a)pyrene, and trace metals (e.g., arsenic and chromium) in particulates, radionuclides, and ozone (19).

Some materials that are found in polluted air are capable of producing mutagenic or carcinogenic effects in experimental animals, but generally the concentrations required are much higher than those normally found in the environment. Of the large number of pollutants available, relatively few have been tested for carcinogenicity and fewer still for mutagenicity.

BIRTH DEFECTS (TERATOGENESIS)

Some chemicals can effect abnormal changes in the developing embryo resulting in an effect in the offspring of the individual originally contaminated. For extreme cases, the conceptus or embryo may be killed and the effect not transmitted to a living offspring. Less extreme deviations may result in various degrees of abnormal development ranging up to gross structural or functional alteration of the embryo, which are more commonly known as congenital malformations. Probably the most widely known example of a health effect resulting from a teratogen is the large number of congenital malformations produced by the drug thalidomide.

A number of chemicals are known to produce teratogenic effects under laboratory conditions (5,32,33). Although the Laboratory data indicate a teratogenic potential for a wide variety of environmental factors in animals, very few are known or strongly suspected to be capable of producing embryopathic effects in man (5). Hypoxia, which can result from increased levels of carbon monoxide can produce teratologic changes. Teratogenic effects of cadmium have been observed in animals, yet very little is known about its teratogenic effects in man (11). Cadmium is also known to be present in the first trimester of human embryo development, which is an important period when organs are developing and the fetus is very sensitive (also to physical agents such as radiation).

DOSE-RESPONSE CHARACTERISTICS FOR CHRONIC LOW-LEVEL EXPOSURES

The adverse effects of ionizing radiation were observed around the start of this century and since then much knowledge has been accrued on the effects of radiation on man and experimental animals. It has been stated that "despite the existing gaps in our knowledge, it is abundantly

clear that radiation is by far the best understood environmental hazard" (34). Also abundantly clear is the fact that despite the years of investigation and favorable state of knowledge concerning health effects of radiation, we still have serious problems in a critical area of application of this knowledge--that is, in the establishment of dose-response curves which allow us to relate mathematically or quantitatively the exposure (or dose) to the biological effect. Much has been said and written on this subject, at times emotionally, in many forums including Congressional hearings. Although a linear dose-response function often is assumed for planning purposes, we know that for many end points and for exposure conditions involving low dose or dose rates, the linear relationship is conservative and not representative of the true risk. Storer has recently reviewed the question of dose-response functions in the field of radiobiology (35).

I'd like to say a few words about risk evaluation because it has become increasingly popular for individuals and organizations to perform risk analyses based upon the man-rem concept. In this scheme, the product of the dose (rem) and the number of people assumed to be exposed are calculated and related to a risk estimator obtained from a dose-response curve which expresses, for example, the theoretical number of cancers expected per million man-rem. A recent National Academy of Sciences report (36) is often interpreted as follows for whole body exposure: continuous exposure of a population of one million persons to one rem per year could result in 150-200 cancer deaths per year. A dose of 100 rem to 10^4 people would yield the same cancer incidence as would 10^{-3} rem to 10^9 people.

The concept has been misused and abused to the point where the National Council on Radiation Protection and Measurements has in its 15 January 1975 NCRP Report No. 43 (37) reviewed the current state of radiation protection philosophy. The following statements from NCRP 43 are of considerable interest.

"Numerical radiation protection guides or dose limits for the exposure of radiation workers or the general public are provided only as upper limits; all exposures should be kept to a practicable minimum. The NCRP has always assumed that its admonitions in this regard would be interpreted in a reasonable way. The application of this principle involves value judgements based upon perception of compensatory benefits commensurate with risks, preferably in the form of realistic numerical estimates of both benefits and risks from activities involving radiation and alternative means to the same benefits.

"The linear dose-effect hypothesis has been coming into frequent use in analyses in which population exposures are expressed in the form of person-rem, including doses of one millirem per year or less to population groups and doses to individual organs, with linear extrapolation to damage estimates through the use of the NAS-BEIR Committee Report values. The indications of a significant dose rate influence on radiation effects would make completely inappropriate the current practice of summing of doses at all levels of dose and dose rate in the form of total person-rem for purposes of calculating risks to the population on the basis of extrapolation of risk estimates derived from data at high doses and dose rates.

"The NCRP wishes to caution governmental policy-making agencies of the unreasonableness of interpreting or assuming 'upper limit' estimates

of carcinogenic risks at low radiation levels, derived by linear extrapolation from data obtained at high doses and dose rates, as actual risks, and of basing unduly restrictive policies on such an interpretation or assumption. The NCRP has always endeavored to insure public awareness of the hazards of ionizing radiation, but it has been equally determined to insure that such hazards are not greatly overestimated. Undue concern, as well as carelessness with regard to radiation hazards, is considered detrimental to the public interest."

Hopefully, we will not repeat this error in treating the health effects of non-nuclear pollutants. However as Santayana stated, "Those who cannot remember the past are condemned to repeat it."

Our state of knowledge as regards health effects in general and dose-response relations in particular for non-nuclear pollutants is primitive as compared with that for nuclear pollutants. To compound the problem, we are faced with a staggering number of known and potential pollutants, many of which can act together additively, synergistically, or as promoters, or in ways that are not currently known. One view currently held by many researchers is that although thresholds probably do not exist for carcinogens at the molecular or cellular level, there may be concentrations for even the most potent carcinogens that will not produce cancer in the intact animal or under natural exposure conditions.

We must not underestimate the complexity or magnitude of the problem. We must endeavor to combine our total national resources, particularly in the important planning stages, so that we increase the odds that we are addressing the most important problems and using the most cost-effective approaches (e.g., screening tests for groups of related compounds). I personally hope that the government agencies charged with various

health and safety responsibilities will increase their interactions both in planning and implementing national environmental health programs. The magnitude of the problem virtually demands this type of integrated approach if we are only to qualitatively understand the dose-response relations for chronic low-level exposure to the more important non-nuclear pollutants. Neither should we delude ourselves into thinking that we will be able to quantitatively measure the dose-response relation and estimates of risk for very low exposure levels of a pollutant; a wealth of experience with radiation has taught us otherwise.

I have discussed earlier the problems inherent in extrapolating downward from acute high-level exposures to the lower dose and dose-rate domain. This is one of the remaining problem areas in radiation protection and one for which we have virtually no experience in the non-nuclear pollutant area, as we are still in many instances learning about the health effects resulting from high or relatively high exposure levels. Another real complication stems from the fact that much of our experience, including that in the radiation effects area, comes from acute rather than chronic experiments. Thus, we are often faced with the problem of extrapolating from acute high-level exposure situations to conditions of chronic low-level exposure. Again, we should not delude ourselves; this may be a problem that is virtually insoluble and we may never know the real risk resulting from chronic low-level exposure to the vast number of environmental pollutants to which we are or could be exposed. On the brighter side, almost any new knowledge in this area increases our storehouse by large factors.

It is virtually an impossible task to attempt to quantify the range of cost estimates for health effects (health care, premature aging, loss

of work days or inefficiency) one could infer from the range of possible dose response curves simply because we do not have the necessary information.

We can only generalize, again from the radiation dose-response analogy, where one can invoke the use of the man-rem concept, assign a "cost" per man-rem, and derive dollar values which in theory allow us to relate health cost to dollars.

The cost that society now pays for health effects produced by environmental pollutants is huge. For example, we still experience a high rate of lung cancer, mesothelioma and asbestosis in asbestos workers. Large numbers of workers and some non-workers have developed disease from exposure to beryllium. Coal miners develop pneumoconiosis (black lung) and other lung disease. The annual cost to U.S. taxpayers for black lung payments to coal miners and their families is over \$1,000,000,000 per year. (Interestingly, black lung benefits are now linked by law to pay of Federal employees in terms of periodic adjustments.) I have no idea what the related cost is for lung disease suffered by the general population, except that it is huge.

Chronic bronchitis and emphysema are among our fastest growing diseases and have doubled every five years since the 1940's; they account for the second highest number of disabilities under social security. Respiratory diseases account for more days lost from work and school than all other diseases combined and cause more than 1,000,000,000 lost work days per year (14)--this is equivalent to 3.8 million man-years productivity lost per year.

According to the EPA, auto pollution is responsible for 4,000 deaths and 4,000,000 sick days per year. This is in addition to the acceptable risk (and cost) associated with the 40,000 or so deaths and many more injuries from auto accidents.

NATURAL BACKGROUND LEVELS, MANMADE EXPOSURES
AND HEALTH EFFECTS

Figure 2 is a comparison of pollutant standards, background levels and health effects for whole body radiation, SO_2 and NO_2 (38). It is clear that for the radiation case, both the standard value and the actual exposure level from nuclear reactors in 1970 represent small fractions of the natural background radiation level. Risk-benefit and as low as practicable (for release) philosophies have been closely allied to standards development in the nuclear area. This situation is not the same for non-nuclear pollutants as shown in Figure 2. Federal air standards and measured exposure levels (at some locations) are higher than estimates of background levels for SO_2 and NO_2 . One must also consider the large number of chemical pollutants for which we have insufficient information as regards exposure levels and background levels and, in many instances, no exposure standards.

Fig. 2. Comparison of pollutant standards, background levels, manmade exposures and health effects

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