

Dioxin's Peril to Humans: Proof Is Elusive

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By WAYNE BIDDLE

The deadly chemical dioxin, an unwanted byproduct of herbicides, pesticides and other industrial products, is raising increasing concern among government agencies, scientific researchers and people who may come in contact with it.

Communities from New York to Oregon have reported human health problems that they fear are linked to exposure to dioxin, although the links have not been proved scientifically.

Officials in Missouri say the number of sites there believed contaminated by the chemical has risen to about 100, and Gov. Christopher S. Bond has asked his Legislature to set up a special fund to help clean them up. Dioxin, he said, could lead to "public hysteria" if not handled properly.

Research biologists and environmental scientists generally agree that in laboratory experiments on animals, dioxin has more harmful effects, and in smaller doses, than any chemical man has produced. Twenty-five millionths of a gram is known to be potent enough to kill a two-pound animal. There are 28 grams in an ounce.

But scientific proof of the effect on humans has been elusive. Conducting tests of toxic chemicals on people is ethically unacceptable, and establishing epidemiological proof by looking for correlations between exposure and effect on a given population is not always possible. In some cases, cancer may not

develop for 30 years after exposure to a chemical carcinogen.

Among the other unknowns about dioxin is how much of it there is in the country and how much is being produced.

Dioxin is nearly insoluble in water, but it clings tightly to soil particles and dissolves in organic solvents like alcohol or oil. It can enter the body by direct skin contact, ingestion or inhalation.

Dioxin was contained in oil sprayed almost a decade ago as a dust-control measure at horse stables and along roadsides throughout eastern Missouri. In recent months, concern has arisen about dioxin's long-lasting effects on residents of Times Beach, Mo., and other areas, and state and Federal officials have been finding more and more

sites at which the chemical was dumped.

Dioxin was among the hazardous chemicals found in 1978 at the Love Canal near a residential neighborhood of Niagara Falls, N.Y., and it has been found at individual dump sites elsewhere in the country. It was also a chemical contaminant of the defoliant Agent Orange, used in Vietnam. Humans who have been exposed to it near Love Canal, in Vietnam or in situations such as train wrecks or factory explosions have suffered a variety of severe health problems, including kidney and liver ailments, birth defects and cancer.

But whether it was the dioxin that caused the ailments among the humans exposed to it has not been determined to the satisfaction of medical researchers. The Veterans Administration, which has said it will seek to determine whether a link exists among Vietnam veterans, has relinquished control of the project to the Federal Centers for Disease Control.

Scientists Are Progressing

Only in recent months have scientists begun to make what they now regard as an important breakthrough. They believe a clearer understanding of the effect of dioxin on health is emerging.

Not until recent years were many physicians even trained to recognize symptoms of so-called chemical diseases. Moreover, scientists, underscoring the frequent difficulty in proving cause and effect in medicine, emphasize that it took 40 years to establish a link between cigarette smoking and lung cancer, even though the evidence seemed to point that way all along.

Now, in a series of experiments reported most recently in last November's issue of the scientific journal *Nature*, a member of the dioxin group of compounds, one called 2,3,7,8-Tetrachlorodibenzene-p-dioxin, or TCDD, has been shown to be what is called a potent "tumor promoter" in rats and mice.

According to the paper, by Dr. Alan Poland and others at the University of Wisconsin's McArdle Laboratory for Cancer Research, the model of tumor production derived from these experiments is relevant to humans because the excessive multiplication of cells in the skin of mice is strikingly similar to that evoked by TCDD in human skin.

Dr. Poland said TCDD did not appear to be a complete carcinogen by itself. But he said it enhanced morbid growth in cells already exposed to potential cancer-causing agents; that is, exposure to TCDD, in conspiracy with other environmental factors, brings on the cancer.

"There is no question that dioxin plays a role in tumor formation in animals, and almost certainly has the same action on human cells," said Dr. Howard Eisen, a medical officer at the National Institutes of Health. "The

basic mechanism is the same."

TCDD is the variety of dioxin found in Agent Orange, which is a mixture of 2,4-D and 2,4,5-T herbicides, and the variety confirmed in Missouri soil by the Environmental Protection Agency. Members of the dioxin family, known as polychlorinated dibenzodioxins, or PCDD's, are byproducts not only of herbicides and pesticides but also of dyes, pharmaceuticals, wood preservatives and other products known generally as chlorinated phenols.

In general, these synthetic organic compounds are formed by adding chlorine to hydrocarbon molecules that are derived from petroleum.

Two decades ago commercial 2,4,5-T often contained as much as 70,000 parts per billion of TCDD and sometimes more. But manufacturers say current techniques can reduce it to a level of less than 10 parts per billion. The industry maintains that it can assure safe products, especially since the material sprayed on fields is heavily diluted.

If the TCDD content of commercial 2,4,5-T is 100 parts per billion, for example, a single spraying might cause surface soil concentrations of 0.02 parts per trillion. Estimates of TCDD soil contamination from Agent Orange in Vietnam are about 0.08 parts per billion.

Spokesmen at the Dow Chemical Corporation said that by testing their output of the dichlorophenol herbicide 2,4-D nine times every 24 hours, they make sure dioxin contamination never exceeds 1 part per billion. Although 2,4-D

is closely related to 2,4,5-T, it is not generally contaminated with TCDD. It does contain other less toxic dioxins, though there has been almost no research on the effects of these substances.

The possible risk posed by even that level of dioxin must be weighed, industry spokesmen say, against the enormous economic value of the products.

Industry specialists say they believe, further, that the risk is not so high as to require special precautions other than those always taken in handling hazardous substances like herbicides and pesticides.

Advice From Disease Agency

Assessing that risk is, of course, part of the problem. Researchers say the risk begins to appear in animals with exposure in the parts-per-1,000-billion range. The Centers for Disease Control have advised Missouri officials that materials containing more than one part per billion of TCDD should be removed from residential areas.

But that figure itself has caused some confusion. Dr. Renate D. Kimbrough of the Federal disease agency expressed annoyance with some news accounts that reported, incorrectly, that the agency considered dioxin concentrations below 1 part per billion in soil to be "safe." Although this is the detection limit being used in soil tests at residential areas in Missouri, she said, it represents a compromise between health concerns and cleanup practicalities.

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Dioxin's Effects in Italy Are Less Than Feared 3

By JON NORDHEIMER

Special to The New York Times

SEVESO, Italy, Jan. 28 — On a clear July day seven summers ago, a quiet Saturday in the Lombardy region of northern Italy just an hour's drive from the Alps, a soft explosion at a small chemical plant at Seveso sent a column of smoke and particles of debris mushrooming into the afternoon sky.

The cloud trailed south over the town and nearby villages before slowly dissipating against the horizon. Children reported playing in the snow-like crystals that filtered down from the sky.

Within weeks, Seveso was known to scientists around the world as "the poisoned city" and some compared its inhabitants to the victims of Hiroshima and Nagasaki, fatally exposed to a frightening man-made element.

A byproduct of the production of fertilizers at the chemical plant was dioxin, one of the most toxic substances known to science, so powerful, it was reported, that a few drops in a water reservoir could kill all the inhabitants of a large metropolis. It is the same substance that contaminates at least 15 sites, and perhaps as many as 100, in Missouri.

Children Developed Rash

It was said here that at least 22 pounds and perhaps as much as 132 pounds of dioxin had escaped in the explosion's cloud. Children who had frolicked in the poison crystals developed an ugly red rash, chloracne. Pregnant women were counseled to have abortions. The center of town was evacuated. Seveso, it was said, was a valley of death and would become a desert.

None of the worst predictions have come true. The city looks no worse for wear than other aging northern Italian communities that have made uneasy accommodations with industry. Nearly everyone agrees that the original estimates of how much dioxin escaped into

the environment was exaggerated. Hoffmann-La Roche, the Swiss company that operated the plant, places the figure at less than one-half pound. Others believe it was higher, but nowhere near the amount, perhaps more than 50 pounds, that was part of waste oil sprayed to contain dust at the Missouri sites a decayed age.

No new cases of chloracne have been recorded here since 1979, according to a group of scientists who continue to monitor the aftereffects of the explosion.

Little Evidence Found

This study has produced evidence that there was a slightly elevated incidence in birth defects in the two years after the explosion, but Italy lacks reliable data on birth defects and scientists are not sure that a similar investigation

of new births in any other urban-industrial population in northern Italy would not produce the same deviation.

Lancet, the respected medical science publication, last fall reported that with the exception of chloracne, there was no evidence of substantial dioxin poisoning at Seveso. And, the publication also reported, the established cases of chloracne were relatively mild ones, suggesting at most a low level of dioxin poisoning instead of a catastrophic one. It said that only a few patches of ground close to the explosion site ever registered dioxin levels approaching those at the contaminated sites in Missouri.

These findings have reduced, but not eliminated, the sense of doom in Seveso. The cloud's shadow still lingers in the minds of scientists and townsfolk.

"I trust in God the worst is over and we can go on with our lives and not worry anymore," said Vittorio Chiapinini, a factory worker who lives inside the monitored danger zone. "We are tired of doctors and technicians invading our homes and inspecting us like laboratory animals. What will happen has happened."

Still Unanswered Questions

The future, however, holds the biggest unanswered questions.

"In terms of chronic disease, like cancer or cirrhosis of the liver, we still don't know if something important has happened at Seveso," said Dr. Ercaldo Stringini of the Istituto Tumori in Genoa. "We will have to wait another ten or 20 years."

There is also concern that the authorities do not know how much dioxin has been concentrating in fields where produce is now being grown for Italian markets, and how much of the substance has collected in waterways.

Only One Autopsy

While such fears are discounted by the Government, a 1980 incident shows

that the dread of dioxin is never far away. A local farmer discovered one morning that his flock of 200 sheep died after grazing in a field that had been barred to livestock since the contamination. A chill went through the people. But it was proven to nearly everyone's satisfaction that the flock died from eating

ing a grass that is known to be fatal to sheep, and no "unusual" traces of dioxin were found by autopsies, according to Franco Nelo, a biologist.

But there is no clear understanding of how much dioxin may be collecting in the tissues of the living residents. Only one autopsy has been performed on a

human being exposed to the fallout from the explosion, an elderly woman who had already been suffering from cancer of the pancreas. The autopsy found significant levels of dioxin in her organ tissues, according to Mr. Nelo.

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Dr. Kimbrough said exposure to lower concentrations over extended periods could still present health risk.

In one area of Missouri, the Environmental Protection Agency said, dioxin was found last fall in surface soil concentrations of 300 parts per billion. The Federal agency calculates that exposure to this soil presents an added cancer risk, for children who ingest it regularly, of as much as 35 percent. That is, these children have a 35 percent greater chance of contracting cancer in their lifetime than those who do not ingest the soil. This is regarded as above the approximately 30 percent risk of cancer that all Americans face.

The special properties of chlorinated phenols, of which dioxins can be a byproduct, are what make them so useful to an industrial society. But those properties, such as heat resistance and electrical resistance, insolubility in water, and chemical durability, are also what make the phenols biologically threatening. Among other things, the substances may collect in living organisms at higher concentrations than in the surrounding ecosystem, a process known as bioaccumulation.

In virtually all types of tissue in every animal species tested, Dr. Poland of the University of Wisconsin's laboratory said in an interview, TCDD induces the production of enzymes that are the organism's attempt to metabolize, or render harmless, the chemical irritant. But the enzymes are now often thought of as a double-edged sword, because organisms that have a high capacity for producing them are more susceptible to tumors at the spot where a carcinogen is administered, while those with a low capacity show distant cancers such as leukemia or lymphomas.

Dr. Daniel Nebert, the branch chief of developmental pharmacology at the National Institutes of Health, who is also active in dioxin research, con-

curred with Dr. Poland's findings, calling them a "major breakthrough." Other scientists generally agreed with that assessment.

According to Dr. Nancy Kim of the New York State Department of Health's toxic substances assessment unit, TCDD fits into one of two major cancer theories. In the first, the hypothesis is that merely one foreign molecule attaching to DNA can set off the cancer process. Because TCDD does not bind appreciably to DNA, it does not match this scheme. But its ability to cause excessive cell multiplication, known as hyperplasia, does fit the second theory, that cancer is caused by repeated irritation of tissues.

Although scientists believe that current laboratory work showing the similarities in animal and human cancer mechanisms has taken the research a crucial step forward, such theoretical work is only half the puzzle-solving process. The other half is human epidemiology, a tedious, time-consuming matter hindered by all the real-world ambiguities that laboratory work can filter out.

Study of Chemical Plant Workers

Scientists at the National Institute of Occupational Safety and Health are studying an unusually high incidence of soft-tissue sarcomas among workers exposed to dioxin at two chemical companies in Michigan and West Virginia. In a letter to the medical journal *Lancet* for the January 1981 issue, the researchers reported that three of 105 workers who died suffered from the rare cancer. This was 2.9 percent of the deaths in the group; the general population would be expected to show only seven one-hundredths of one percent.

The study might provide the first international confirmation of a 1977 report from Sweden suggesting that for-

estry workers exposed to 2,4-D and 2,4,5-T have a roughly fivefold higher incidence of soft-tissue sarcomas. In addition, several studies have revealed an increased incidence of Hodgkin's disease in lumberjacks and woodworkers. A *Lancet* editorial noted last year that any change in the pattern of sarcomas, "even in small numbers of cases," might strengthen the causative association with dioxin.

Studies by Dr. Bertram Carnow, an occupational health consultant and editor of the *Journal of Occupational Medicine*, examined a group of 47 men from 1980 to 1982 who had been exposed to dioxin after a railroad accident in 1979. In an interview, Dr. Carnow said the exposure varied from 8 hours to 90 days at concentrations in soil or liquid runoff of about 30 parts per billion. Five of the men, or 10.6 percent, have developed skin cancers; the expected incidence in the general population is about 0.17 percent a year. A significant number of other disorders was also observed.

"The only safe level of dioxin is non-detectable," said Dr. Carnow, whose medical practice in Chicago has treated nearly 300 cases of dioxin exposure.

Besides the role of TCDD in causing cancer, the other great area of medical concern regards apparently related fetus damage and other reproductive problems. For animals, the evidence is straightforward and overwhelming. TCDD injures or kills animal embryos at doses as low as one billionth of a gram administered per kilogram of body weight per day. For humans, however, the record so far is circumstantial.

The Environmental Protection Agency used emergency powers in 1979 to ban virtually all use of 2,4,5-T in the United States after discovering a higher than normal rate of spontaneous abortions in an Oregon region that had been sprayed.

Estimated Risk of Chemical Pollutants

Percentage of increased risk of cancer, calculated on the basis of animal experiments and human epidemiologic studies, to a person weighing 150 pounds who, over a 70-year lifespan, breathes air containing one microgram of substance per cubic meter.

SUBSTANCE	USE	PERCENT RISK OF CANCER
Acrylonitrile	Manufacturing of plastics, rubber, and fibers	.031
Allyl chloride	Manufacturing of plastics, rubber, and fibers	.000099
Arsenic	Manufacturing of chemicals, pigments, and dyes	.34
Benzene	Manufacturing of chemicals, pigments, and dyes	.00076
Beryllium	Manufacturing of chemicals, pigments, and dyes	27.0
Cadmium	Manufacturing of chemicals, pigments, and dyes	.2
Dimethylnitrosamine	Manufacturing of chemicals, pigments, and dyes	.29
Dioxin	Manufacturing of chemicals, pigments, and dyes	100.0

Source: U.S. Environmental Protection Agency

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The chart shows the projected percentage of increased risk of cancer, based on animal studies, calculated to occur among people who weigh 150 pounds and who, in a 70-year life span, breathe air containing one microgram of chemical particulate per cubic meter of air.