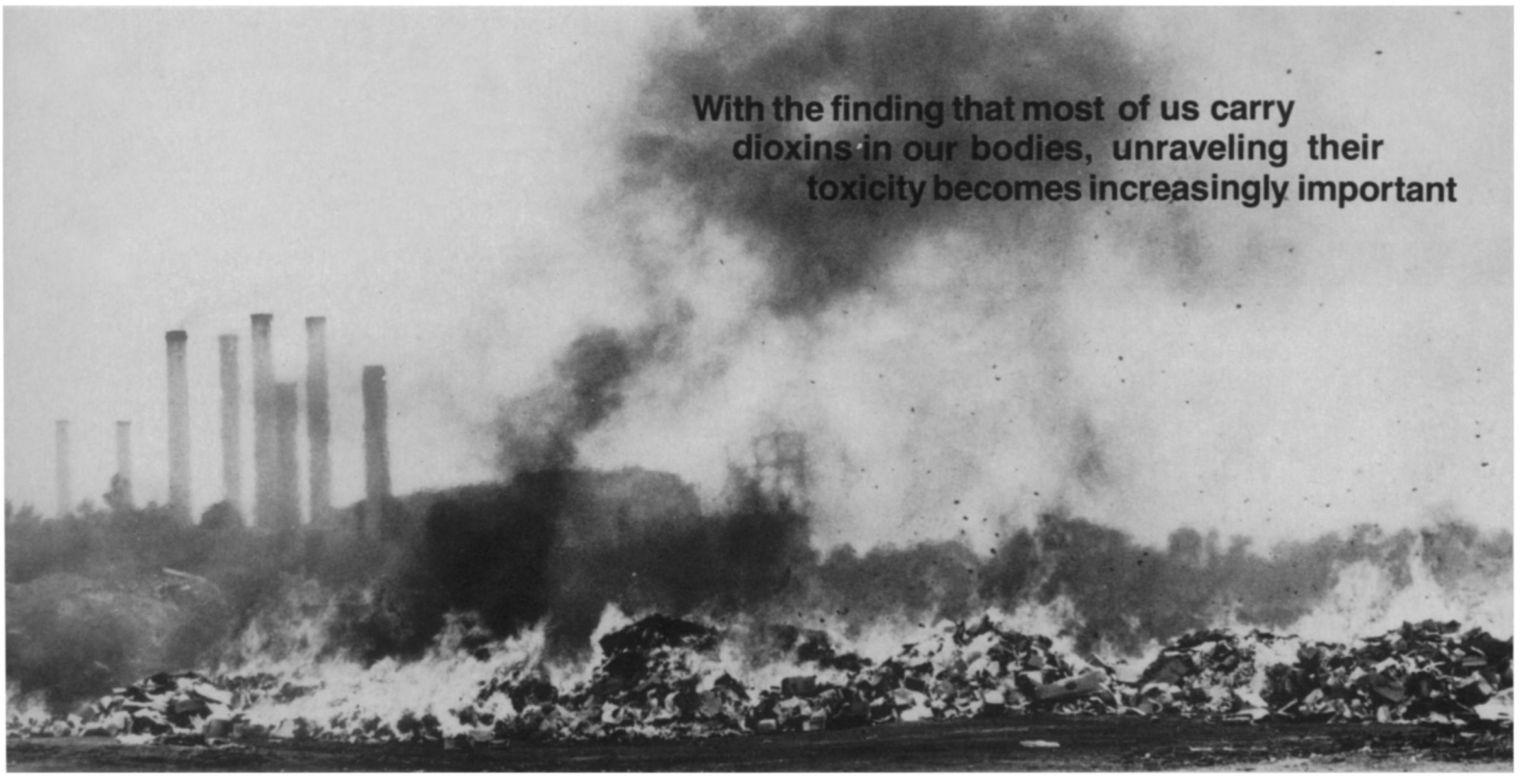


Dioxin: Is Everyone Contaminated?

By JANET RALOFF

Dioxin: Most people know it as the extremely toxic contaminant in Agent Orange, or the pollutant that transformed Times Beach, Mo., into a virtual ghost town. The Environmental Protection Agency has called it "one of the most perplexing and potentially dangerous chemicals ever to pollute the environment." What most people don't realize is that, according to recent studies, a body burden of dioxin and its chemical cousins has become a price humanity pays for its industrial culture.

"In the United States we've found that everyone's got dioxin in them," says Arnold Schecter, a professor of preventive medicine at State University of New York in Binghamton. Because the same appears to be true of Canadians and Europeans, dioxin researchers are now coming to the conclusion that these industrial pollutants, along with furans and PCBs, contaminate the bodies of all individuals living in developed countries — and potentially in many lesser-developed countries as well.

Says Schecter, "This is powerful, new data that is just overwhelming in what it suggests." At a minimum, he says, the finding calls into question the validity of all published and ongoing epidemiology investigating the human health effects of these toxic chemicals. "The American numbers suggest very strongly," he says, "that current epidemiologic studies are very seriously flawed because they're probably not comparing exposed with nonexposed populations — as they originally thought they were." And any good epidemiologic study, he says, must be able to distinguish between those exposed and those not.

One implication of all this, he says, is that many of the cancer incidence figures now treated as normal for the general population may be due in part to society's low-dose exposure to these toxic chemicals. In other words, these pollutants may be exerting a subtle but deleterious effect on the health of the world's most industrialized societies.

Right now the extent of that effect is not known for certain, Schecter acknowledges. However, the best-known and most toxic of dioxin's 75 different species—2,3,-7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) — has been shown to cause cancer in animals, has been linked with an increased incidence of certain rare cancers in humans and can cause a disfiguring human skin disease, chloracne. Moreover, TCDD exposures in animals have been linked with weight loss, liver disorders, gastric ulcers, birth defects, reproductive failure and immune system abnormalities. Knowing this, and knowing the extent to which the industrial world is contaminated, scientists should put increased emphasis on identifying precisely how toxic to humans this family of chemicals really is, Schecter believes.

Together with John J. Ryan of Health and Welfare Canada, in Ottawa, Schecter presented several papers in May at the national meeting of the American Chemical Society (ACS) in Miami, detailing human dioxin levels in both North American and Vietnamese populations. At an ACS meeting two years ago, Ryan had reported finding TCDD in a small sample of Canadians (SN: 9/3/83, p. 156). This year, he and Schecter described results of a follow-up analysis of tissues from more than 100 presumably unexposed individuals in Canada and the United States. Within these people, the researchers again found a general low, or "background," level of contamination with dioxins and furans — related toxic chemicals often found in association with one another. Although all the tissues they examined contained the chemicals, Ryan says, "we found the highest levels of dioxins and furans in fat." Moreover, the levels found in any tissue tended to reflect its relative amount of fat.

In this group of Canadians and Americans, TCDD was measured at background levels of between 5 and 10 parts per trillion (ppt) in fat. Furans that similarly contained four chlorine atoms per molecule were found in somewhat smaller concen-

trations. The more highly chlorinated dioxin and furan species — which are less toxic but not necessarily benign — were measured at concentrations of up to 1,000 ppt in fat.

As a rule, dioxin concentrations were somewhat higher than furan concentrations. There also seemed to be an unwritten rule that as one progressed from 8-chlorinated molecules to 7-chlorinated, and on down successively to 4-chlorinated ones like TCDD, the concentrations of each particular species of dioxin or furan decreased.

Schecter and Ryan point out that the levels they measured in these members of the general population "are two or three orders of magnitude lower than those known to cause acute effects in humans, although the [chronic] long-term effects of these residues are not clear."

Fish, they suggest, could be one dietary source of 2,3,7,8-TCDD, which enters the environment as an industrial contaminant in the antiseptic hexachlorophene and in the bactericide 2,4,5-trichlorophenol. (Products made from the latter include 2,4,5-T, a popular herbicide that was a component of Agent Orange.) Bodily residues of the more highly chlorinated dioxins, say Schecter and Ryan, could come from exposure to pentachlorophenol, a chemical extensively used as a wood preservative, general bactericide and fungicide.

Scientists last year reported similar TCDD levels among the controls of a preliminary study investigating the likelihood of finding dioxin residues in the tissues of Vietnam veterans. Writing in ENVIRONMENTAL RESEARCH (Vol. 33, p. 261), Michael Gross and his colleagues from the University of Nebraska in Lincoln and two Environmental Protection Agency laboratories reported that it appeared that here too were signs of a "baseline accumulation of TCDD in some members of the general U.S. population."

In a second paper, Schecter and Ryan reported on the first measurements of dioxins and furans in the adipose tissues (fat) of Vietnamese. The researchers see northern Vietnam, where Agent Orange was not used, as a control for the population in southern Vietnam, onto which the U.S. military dropped some 19 million gallons of TCDD-contaminated herbicides, mainly Agent Orange. For this study, Schecter obtained the fat samples of 18 patients in hospitals awaiting surgery and two from autopsies while he was visiting the country last year as a guest lecturer. Vietnamese physicians and scientists studying Agent Orange and dioxin asked him to take the fat samples back for analysis in the West, where techniques are available to measure minute quantities of these toxic chemicals.

The five patients and two autopsies chosen for Schecter from Hanoi's Viet Duc Hospital are from what was formerly North Vietnam. Able to detect dioxin levels as low as 2 ppt, Ryan's analysis of their fat showed no discernible TCDD, and little or no evidence of other dioxins and furans. According to Schecter, this makes them, with regard to these chemicals, "the cleanest tissues seen in the world anywhere to date."

By contrast, tissues from 13 people hospitalized in Ho Chi Minh City (formerly Saigon), to the south, "showed the same types of dioxins and furans as are found in North Americans." Moreover, the levels of dioxins and furans identified in them were similar to those in North Americans except for TCDD—where "the mean, on a net weight basis, was 22.1 ppt, or about three times the value we were getting in the United States," Schecter says.

Based on the pattern of more highly chlorinated contaminants — those having between five and eight chlorine atoms in each molecule — Schecter and Ryan see what looks to be the same pentachlorophenol "fingerprint" of dioxin and furan contamination in the people from southern Vietnam that exists in North Americans. And that's not surprising, they say, since pentachlorophenol has been widely used in South Vietnam, probably from the days when the French ruled. However, since TCDD is not among the many dioxins that contaminate pentachlorophenol, the researchers suspect that the high TCDD levels they detected in the fat from 10 of the 13 southern Vietnamese most likely represent a residual contamination from the heavy use of Agent Orange there during the war.

In light of these findings, Schecter and Ryan suggest that Vietnam would be the ideal place to conduct a major epidemiologic study of dioxin's health effects. "We're talking about a potential sample population of exposed and controls here of 60 million people," Schecter says.

Schecter also points out that the longer researchers wait to conduct a Vietnamese study, the weaker its potential results would be. Unless replenished, body burdens of dioxins can slowly dissipate. If the high levels of TCDD found in some of the southern Vietnamese are due to high wartime and postwar exposures to Agent Orange, eventually their body burdens may fall back to background levels, whatever those might be.

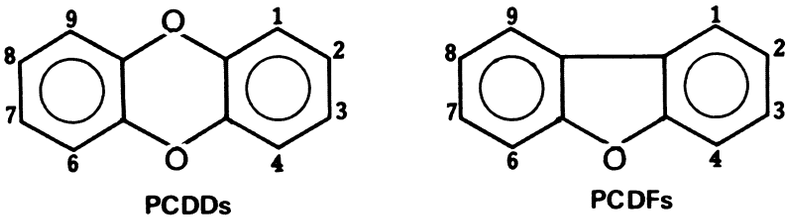
That appears to have happened to Swedish forestry and agricultural workers exposed to chlorophenols and TCDD-contaminated herbicides during the 1950s and 1960s. In a paper given at the same meeting, Lennart Hardell reported on fat biopsies taken from seven such workers who had presumably received brief (two-week to 10-month) but substantial exposures to 2,4,5-T between 20 and 30 years ago, and who now have sarcomas. Three have soft-tissue sarcomas, the cancer type now most suspected of being caused by dioxin. All the workers' biopsies showed background levels of dioxin and furan contamination that were virtually identical to those in the 18 controls.

Hardell, a cancer epidemiologist with University Hospital in Umeå, Sweden, decided to look at adipose tissue from these herbicide sprayers because their work history and illness fit the profile of a potential dioxin-induced cancer — a profile he has helped elucidate over the past 10 years.

In one of his earlier studies, he found a fivefold increased risk of soft-tissue sarcoma associated with TCDD-contaminated herbicides and a sixfold increased risk of this cancer associated with chlorophenols.

From these and other data Hardell cal-

Polychlorinated dibenzo-*p*-dioxins (PCDDS) and dibenzofurans (PCDFs)



Of the 210 chemicals that make up the dioxin/furan family, 75 are dioxins. The long strings of numbers used to identify individual species, or isomers, within this family refer to the positions of their chlorine atoms. In 2,3,7,8- varieties, chlorines bond to the outermost left and right positions. Tetra-chlorinated isomers contain a total of 4 chlorines, pentas have 5, hexas 6, heptas 7 and octas a full complement of 8. Though the tetras are believed most toxic, many of the more prevalent, higher-chlorinated forms are not considered benign. And among higher-chlorinated isomers, those with chlorines at the 2, 3, 7 and 8 positions are considered most toxic, Schecter says. Fat biopsies indicate that most of the higher-chlorinated species found in humans contain such "2,3,7,8-substituted" dioxins and furans.

Peasant transports rice harvest in southern Vietnam, where Agent Orange residues may still be contaminating river sediments and soil.

culated a crude latency period for the onset of the cancer: 15 to 20 years for exposure to the herbicides, and 21 to 25 years for exposure to chlorophenols. He says that for Vietnam veterans, if these cancers are going to develop, "they should begin appearing in the 1980s and continue on through the end of the decade." However, his research also suggests that by the time such a cancer is diagnosed, it will probably be long after any fingerprint of Agent Orange exposure is visible in the form of elevated levels of dioxins and furans in their fat.

Hardell and Schecter see in this an important lesson for dioxin epidemiologists: that they risk losing validation of potential dose-effect evidence if fat biopsies of American Vietnam veterans and southern Vietnamese residents are not collected as soon as possible and correlated with what is known about these individuals' estimated exposure to dioxins and furans. In fact, Schecter believes the Vietnamese population offers to yield the stronger data. Because residues of the defoliating herbicides that rained over South Vietnam may still be present in river sediments and soil, contaminating fish and other foods, southern Vietnamese exposures to these chemicals may be more recent, if not higher, than those experienced by American servicemen, he notes.

That's one reason Schecter has decided to go back to Vietnam, probably within the next two months, for a small follow-up survey of adipose tissue. Not only does he want to see if an additional 100 samples show the same striking north/south differential in exposures to TCDD, but he also plans to collect fish and breast milk as possible sources of TCDD contamination in the diet.

Alvin Young, formerly a dioxin researcher and now a policy analyst with the President's Office of Science and Technology Policy, is less sanguine about the value of such surveys. Citing confounding variables such as poor nutrition, infectious disease and drugs, he says it "would be impossible to try and control for all these in Vietnam." Moreover, he says, "Although [Schecter] says you have a very pure population of those exposed to dioxin, you also have two populations who experienced totally different war situations." Among other differences, he notes, the South was heavily bombed. In fact, Young believes any major federally funded dioxin study involving fat biopsies would be premature until results come in from a new Veterans Administration study of 500 human fat tissues collected between 1970 and 1980; many of the tissues come from Vietnam veterans.

"Frankly, we [in the Reagan administration] are concerned about continuing to call wolf," he says. "There are so many important health issues in this country that we're very concerned that we now begin to put our dollars in places where there are actual data of significance on people dying of cancer. In the case of dioxins, we don't have records of a single person dying from a dose of TCDD."

However, Hardell and Schecter say there is a growing body of data linking dioxins to cancer. In addition to his soft-tissue sarcoma studies, Hardell notes a Danish study, soon to be published in the British JOURNAL OF CANCER, showing an increased risk of those cancers linked with exposure to TCDD-contaminated herbicides. He also cites studies by himself and others linking nasal cancers to chlorophenols and reporting a two- to threefold increased risk of liver cancer in Vietnamese exposed to Agent Orange.

Most U.S. attention on the consequences of human dioxin exposure has focused on health risks to Vietnam veterans. But the finding that civilians have also sustained inadvertent dioxin exposures brings the importance of dioxin toxicology results much closer to home.

Where do the civilian exposures come from? At the Miami meeting, David Firestone and colleagues from three Food and Drug Administration (FDA) laboratories described their analyses of dioxin residues in fish and other foods. Though they found trace residues in the edible portion of fish from certain regions in the Great Lakes and elsewhere, they said, "the presence of 2,3,7,8-TCDD in fish does not appear to be widespread, but rather is localized in areas near 2,4,5-TCP and 2,4,5-T production sites." FDA analyses since 1979 for more highly chlorinated dioxins have turned up hepta- and octa-chlorinated species in eggs, bacon, chicken, pork chops and beef liver—contamination that the researchers say appears to be related to agricultural use of pentachlorophenol.

Christoffer Rappe and co-workers from the University of Umeå reported in a series of papers on another source of dioxin and furan contamination of the diet: air pollution from municipal, industrial and hazardous-waste incinerators. Dioxins and furans can be generated during the combustion of organic chemicals, polyvinyl chloride and some chlorinated solvents. In fact, in Scandinavia, these incinerators are the best-known source of dioxins. Rappe, an organic chemist whose work has focused on dioxins for many years, has more than a passing interest in the subject. Living only 100 yards from such an incinerator in Umeå, he decided "I had to do a risk calculation on whether to sell my house."

For these calculations, Rappe's team measured dioxins and furans in the air pollution plume downwind of the Umeå incinerator. Measured quantities of the furans and dioxins were then converted, based on what is known about the relative acute toxicity of each, into TCDD equivalents. The result was a finding of 55 femptograms of TCDD equivalent per cubic meter of air. (A femptogram is 10^{-15} gram.) Assuming his 50-kilogram wife inhaled 20 cubic meters of air daily, he calculated a daily dose for her of 0.02 picogram (a picogram is 10^{-12} gram) per kg of body weight per day — well below the 1 to 5 pg/kg body weight that he says is being discussed by some scientists as a possible

"allowable daily intake" value for TCDD. He decided not to sell his house.

However, Rappe's research shows, inhalation is probably not the primary route by which these incineration pollutants enter the body. Milk from dairy cows grazing under the incinerator's plume exhibits 10-fold higher dioxin and furan contamination than milk from cows grazing elsewhere, his data show. More important, he says, "We found the cows pick up only the most-toxic 2,3,7,8-substituted dioxins and furans." The Umeå researchers have also measured levels of these chlorinated chemicals in Baltic seals, salmon and human breast milk (see chart).

Rappe says that based on his data, Sweden's EPA decided to enact a moratorium on all new incinerators beginning last February, during which time his group will begin monitoring for trends in dioxin levels in the diet — particularly in breast milk, because of its potential relationship to child health. His research already suggests that nursing infants can get very high doses (measured in TCDD equivalents) — 20 to 100 times the amount being discussed as an allowable daily intake value.

Ironically, Rappe's group has found, incinerators needn't be potent polluters. When one incinerator that they had monitored emitting 80 nanograms of TCDD equivalent per cubic meter of exhaust gases was inspected six months later — after it had been "tightened up" to limit air leakage — it emitted a mere 6 ng/m^3. Combustion turbulence, which can vary dramatically depending on how well the combustion chamber is sealed, seems to be the most important factor in determining dioxin/furan emissions, explains Rappe.

While analytical techniques resolve in ever-clearer detail the extent to which dioxins and furans contaminate our environment and ourselves, there is one vital piece of the dioxin picture that remains fuzzy — the human toxicity of each of the chemicals that make up this large family. Though few people would suggest that these chemicals are harmless, what data exist on them currently defy any solid quantification of their risks. And that is what makes deciding how to respond to the newfound low-level population exposures such a dilemma for environmental policymakers today. □

HUMAN DIETARY DIOXIN AND FURAN SOURCES IN UMEÅ, SWEDEN

Source	Daily Amount (picograms*/kilogram body weight)
Inhalation of air (contaminated with 55 femptograms of TCDD equiv/meter^3)	0.02
Liter of cow's milk	0.5 to 5
Baltic salmon (roughly 100 grams)	20
Nursing (5 kg) child drinking 850 milliliters breast milk	20 to 100

*Though a wide range of dioxins and furans have been measured in these sources, the values given portray the sum — based on estimates of their relative toxicity — calculated in TCDD equivalents.

Although an allowable daily intake (ADI) value being discussed within the dioxin-research community is only 1 to 5 picograms of TCDD equivalent per day, work in Rappe's lab suggests a bioaccumulation of these pollutants can lead to human dietary exposures well in excess of the proposed ADI.

Rappe