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Message: The articles sum up current divvix research (gosh, it's
bad for you after all!). The Forests Deadlock memo is to
spread wherever it might do some good.
Love, to Liz, to Jay, & to the incipient Infant Phenomenon!

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Concerns Broaden over Chlorine and Chlorinated Hydrocarbons

Calls for gradual phaseout of classes of chlorinated organics are being made in response to evidence of adverse health effects on humans and wildlife

Bette Hileman, C&EN Washington

Concerns are growing that chlorinated organics are causing cancer in adults and adverse health and reproductive effects in the offspring of both humans and wildlife.

Evidence of such a connection between chlorinated organics as a class and human health—and, hence, of the need for sweeping reductions in the production and use of chlorine and many chlorine-containing products—is still patchy. It ranges from the essentially certain, to the suggestive, to the circumstantial.

But, whatever the merits of the scientific evidence, public concern over the health and environmental impacts of chlorine is an issue that is not going to go away. It has already brought regulations and the banning of selected products as well as calls from highly responsible groups for an eventual phaseout of at least some sectors of the chlorine industry. It is something chemical makers are having to treat with increasing seriousness.

Today there are about 15,000 chlorinated compounds in commerce. They include pesticides, pharmaceuticals, disinfectants for drinking water, and many modern consumer products such as items made of polyvinyl chloride (PVC) that have improved the quality of life in both developed and developing countries. In addition, chlorine intermediates are very useful in reaction pathways leading to many nonchlorinated products, such as silicon for electronic chips or epoxy resins. Almost 85% of the pharmaceuticals manufactured in the world require chlorine at some stage of production. Therefore, a broad-based ban on chlorine would have enormous practical and economic implications.

How did chlorinated compounds come to be portrayed in such a bad light, almost cast as environmental villains? In the case of chlorofluorocarbons (CFCs), the answer is simple. Their phaseout is mandated under the Montreal Protocol on Substances That Deplete the Ozone Layer. For chlorinated solvents, the explanation also is fairly straight-

forward. Some of these solvents are ozone depleters and must be phased out under the Montreal protocol. All of them are skin and eye irritants and may produce adverse effects on the central nervous systems of workers. There also is concern that several of them are carcinogenic.

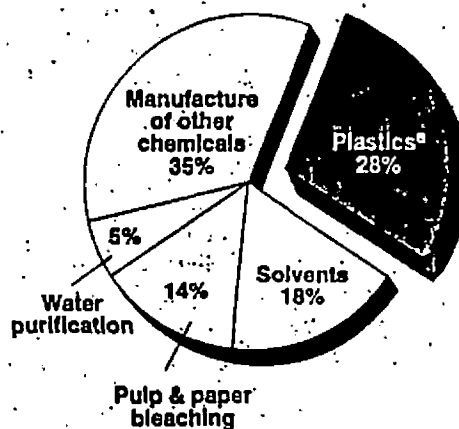
The arguments against the continued use and production of other chlorinated compounds and chlorine as bleach in the pulp and paper industry are less clear and more complicated. One is that some of the compounds are believed to cause cancer in humans. Another is that both the chlorine bleaching process and production of many chlorinated hydrocarbons, such as PVC, inadvertently produce 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) and hexachlorobenzene (HCB), which are considered mildly carcinogenic. Also, fires in buildings constructed with PVC materials may produce dioxins and furans, similar to what happens when PVC is destroyed in incinerators that are not operating properly. But an increasingly prominent element of the argument against use of chlorinated hydrocarbons is that many of these compounds cause noncancer health effects—endocrine, immune, and neurological problems—principally in the offspring of exposed humans and wildlife, and seem to create these problems at extremely low exposure levels.

Governmental bodies and industries, particularly the chemical industry, are responding to these health concerns.

One year ago, the International Joint Commission (IJC), the U.S.-Canadian agency that is the environmental watchdog for the Great Lakes, called for a gradual phaseout of the use of chlorine and chlorine-containing compounds as industrial feedstocks. Similarly, last September, the Paris Commission, the European equivalent of IJC that oversees emissions of pollutants into the northeast Atlantic Ocean, recommended that discharges of organochlorines be reduced, while programs are initiated to phase out their use.

In addition to the broad phaseout advocated by the IJC and the Paris Commission, new regulations have been introduced in various countries that would restrict specific uses of chlorine or ban certain

Largest single use of chlorine is in plastics



a Polyvinyl chloride makes up the bulk of chlorinated plastics.
Source: Chlorine Institute

Pulp and paper industry cuts its chlorine use

The U.S. pulp and paper industry, which uses chlorine to produce white paper, has sharply reduced its use of the chemical and plans to curtail use further during the next few years. In part, this reduction can be traced to the increased sophistication of pulp and paper plants during the past decade. The cooking and bleaching operations have been fine-tuned. Wood chips are cooked more before they go to the bleach plant, so less bleaching is required. Also, in some plants other bleaching compounds, such as chlorine dioxide, have been substituted for chlorine. When chlorine dioxide is used, less dioxin is produced.

These changes have resulted in an 80% reduction in the amount of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) associated with bleaching, says Matthew Van Hook, senior environmental counsel with the American Forest Products & Paper Institute. When EPA surveyed 104 mills in 1988-89, it found that all the mills generated a total of 25 lb of 2,3,7,8-TCDD during that period. Now, that total is below 8 oz per year.

According to some estimates, the amount of chlorine used for pulp and paper bleaching in the U.S. will fall from 1.4 million tons in 1990 to 920,000 tons by 1995, while the amount of sodium chlorate used to generate chlorine dioxide for bleaching will rise from 670,000 tons to 975,000 tons. During the same time period, more hydrogen peroxide and oxygen will be used as bleaching agents.

At least one plant in the U.S. will soon be producing white paper without the use of chlorine: Louisiana Pacific in Portland, Ore. However, Van Hook contends that mills using different bleaching sequences, including those that use some chlorine, "are able to achieve comparable environmental performance overall." But, he cautions: "You cannot make the entire range of products that require bleaching without using some sort of chlorine compound." And he says effluent from modern mills is quite benign.

However, a report prepared by John H. Carey at Environment Canada (the Canadian Environmental Protection Agency) and coworkers says:

"The physiological disruptions in fish near pulp mills are associated with significant effects on their reproductive development." These effects occur from the effluent from all types of pulp and paper mills and seem to have no relation to the level of 2,3,7,8-TCDD or total chlorinated organics in the receiving water. Carey's report, however, is highly controversial and is not yet published in the scientific literature.

Gord Perks of Greenpeace in Toronto says the important issue surrounding chlorine is that it is very corrosive, so plants that use chlorine cannot easily recycle process water, and must produce liquid effluents. In plants that do not use chlorine, it is easier to eliminate effluent production. He predicts that in 10 years or so, pulp and paper mills will have very little liquid effluent.

In contrast, Van Hook contends that it is almost impossible to operate a pulp and paper plant so it produces no liquid effluents. There is no plant in the world today, he notes, that does not produce liquid effluents.

types of chlorinated organics. The Canadian province of British Columbia has decided to reduce the chlorine content of the waste from its pulp and paper mills to 1.5 kg per ton of pulp manufactured by 1995 and to 0 kg per ton of pulp by 2002. The provinces of Quebec and Ontario have established similar standards for 1995 and goals of 0.8 kg of chlorine per ton of pulp by 1999 or 2000. Sweden also is committed to eliminating chlorine use in its pulp and paper mills.

A number of cities and towns in Germany and Austria have decided not to use PVC materials for any of their new public buildings. Four of the nine regional capitals in Austria—Vienna, Linz, Salzburg, and Innsbruck—have PVC-free construction policies for public buildings, and two entire Austrian states have followed suit. More than 100 German communities will no longer use PVC in their new public buildings. The German state of Lower Saxony banned purchase of PVC products by the government for any purpose, unless no substitutes can be found.

The use of chlorinated herbicides is also under pressure in Europe. Application of atrazine, one of the most heavily used herbicides in the U.S., is restricted in Germany, the Netherlands, several Nordic countries, and northern Italy. Use of a number of specific chlorinated organics has been severely restricted and in some cases banned in the U.S. over the past 20 years; DDT was restricted in 1972, polychlorinated biphenyls (PCBs) in 1976.

What is new today concerning global efforts to curtail use of chlorinated organics is that the IJC and several environmental groups, such as Greenpeace and the Sierra Club, are

calling for a very broad-based phaseout in the production and use of chlorinated organics. They base their call for drastic changes in industrial production on a weight-of-evidence approach. "Even though many of the [chlorinated organics] have not been proven to be individually toxic," the IJC says in its sixth biennial report, "there is a growing body of evidence that these compounds are at best foreign to maintaining ecosystem integrity and quite probably persistent and toxic and harmful to health. . . . Thus, it is prudent, sensible, and indeed necessary to treat these substances as a class rather than as a series of isolated individual chemicals."

Several large chemical firms in the U.S. have responded to such concerns by developing long-range strategic plans to cut back on their use and production of chlorine and chlorinated organics. Vehicle manufacturers in both Europe and the U.S. are now trying to move away from the use of chlorinated solvents in their paints.

Such actions do not mean that industry would support a chlorine phaseout nor that it thinks one is necessary. According to a Washington, D.C.-based industry association, the Chlorine Institute, phaseouts and bans are "neither scientifically supportable nor a socially responsible policy for dealing with chlorinated organic compounds used by society at the present time." The group charges that the reasons advocates present for such a ban "are of questionable scientific significance as well as misleading."

In fact, none of the efforts to phase out chlorine and chlorinated organics focus on all uses. None of them are directed at pharmaceuticals nor are any directed at chlorine use

for producing inorganic chemicals. Furthermore, in the U.S. at least, little effort is being made to ban chlorine as a drinking water disinfectant, which accounts for a very small part (1%) of this nation's chlorine use. Most of the phaseout moves are aimed at organochlorines such as pesticides, PVC, CFCs, and solvents; and at the use of chlorine in the pulp and paper industry.

Trends in human and animal health

Some disturbing trends in the health of both humans and wildlife have been observed during the past few years, health effects that many researchers theorize may be caused in part by environmental exposures to organochlorines. Devra Lee Davis, senior scientist at the National Research Council (NRC), and colleagues from 20 countries have reported "increases in cancer that cannot be explained solely in terms of aging, changes in coding [for individual diseases], or access to care." Increased mortality from multiple myeloma, prostate cancer, breast cancer, brain cancer, non-Hodgkin's lymphoma, kidney cancer, and testicular cancer have been observed.

Breast cancer increases are particularly puzzling. Thirty years ago, an American woman had a one in 20 chance of developing breast cancer by the age of 85. Now her chances are one in nine.

Another trend is that sperm counts in men throughout the developed world appear to have fallen 42% since 1940. During the same period, the rates of birth defects in the reproductive tract of males, such as undescended testicles, have increased. Because these same effects are produced in the offspring of lab animals exposed to very small amounts of organochlorines, such as 2,3,7,8-TCDD, during pregnancy, researchers are considering the possibility that these human health problems are caused by exposure of the male fetus to organochlorines that cross the placental barrier.

In related studies on women, Joseph and Sandra Jacobson, psychologists at Wayne State University, Detroit, found that women who ate as few as two or three meals a month of Lake Michigan fish for at least six years preceding their pregnancies gave birth to babies who weighed less, had smaller crania, and experienced shorter gestation than babies born in the same communities of mothers who did not eat fish. The major contaminant in the Lake Michigan fish is PCBs, compounds that cross the placental barrier. In addition, these PCB-exposed babies had behavioral, motor, and cognitive problems at birth and, even at age four, had reduced memory skills.

Since 1987, communities of marine mammals such as dolphin, seal, and whale have experienced wide-scale die-offs in various parts of the world. Although common viruses and bac-

teria seem to be the immediate cause of death, some researchers hypothesize that organochlorines in the animals' tissues depressed their immune systems and made them more susceptible to ordinary infectious agents. In some areas, researchers found that the dead animals had higher levels of PCBs in their tissues than did animals in the general population.

In the Great Lakes, 100% of the sexually mature pink, coho, and chinook salmon have vastly enlarged thyroids that do not appear to be caused by an iodine deficiency. (Thyroid enlargement is an indication of a disturbed endocrine system.) Some of these salmon species also experience a variety of reproductive problems, thus waters must be restocked with hatchery-bred fish.

Although no one trend can be linked with certainty to organochlorines, many researchers think that most of these health problems may be caused by persistent exposure to organochlorines that are widely distributed in the environment. They note that levels of some very persistent toxic organochlorines, which peaked in the early 1970s, have either now leveled off at a recalcitrant plateau or have begun to rise again, which means that exposure continues even for those compounds that have been restricted in the U.S.

After falling from a peak in 1972, DDT levels have begun to rise again in Great Lakes fish—probably from long-range atmospheric transport of the chemical. Levels of mirex, which was used as a fire retardant and to kill fire ants, have also be-

Variety of health effects have been observed in creatures in the Great Lakes Basin

Species	Reproductive effects	Eggshell thinning	Generational effects	Deformities	Organ damage	Behavioral changes	Hormonal changes	Metabolic changes	Immune suppression	Tumors
Bald eagle	●	●	●			●				
Beluga whale	●			●	●		●		●	●
Black-crowned night heron	●	●								
Caspian tern	●		●		●					
Chinook-coho salmon	●				●		●			●
Common tern	●				●	●			●	
Double-crested cormorant	●	●	●		●	●				
Forster's tern	●		●		●	●				
Herring gull	●	●	●		●	●	●		●	
Lake trout	●		●		●	●				
Mink	●		●		●					
Osprey	●	●								
Otter										
Ring-billed gull	●								●	
Snapping turtle	●	●	●		●					

Note: Effects listed have been in scientific literature published during the past decade.

gun to increase. The concentrations of several other persistent pesticides, although down from high points reached in the mid-1970s, are no longer declining. Concentrations of these same pesticides in human adipose tissue have plateaued as well.

At the same time, researchers realize that the health problems seen in Great Lakes fish, marine mammals, and humans could be due to some other nonchlorinated bioaccumulative chemical like mercury, which is elevated in fish tissue, or some substance that is not being monitored.

Organochlorines and endocrine disruption

Evidence that organochlorines can cause cancer and can have adverse effects on the endocrine, immune, and nervous systems of exposed fetuses has grown during the past few years. For example, one study found that if pregnant female rats are fed one meal containing a dose of 2,3,7,8-TCDD as small as 0.16 µg per kg of rat weight on day 15 of pregnancy, the sex organ weights in the male offspring are reduced. In addition, when the affected male pups reach adulthood, their sexual behavior is both demasculinized and feminized and their sperm counts are reduced.

However, only since mid-1991 has a diverse group of researchers studying humans and a broad range of wildlife begun to realize that certain organochlorines, as well as a number of other chemicals like tributyltin, may cause alterations in sexual and functional development in exposed fetuses, even at the low levels usually found in the environment.

In summer 1991, Theo Colborn, senior fellow at the W. Alton Jones Foundation, Charlottesville, Va., and the World Wildlife Fund, convened 21 scientists at the Wingspread Center in Racine, Wis. Participants included experts in a variety of fields, including reproductive physiology, ecology, comparative endocrinology, histopathology, immunology, and zoology. Few of the scientists who attended the meeting knew about each other's work beforehand. Each was surprised to learn that the adverse health effects being observed in his or her object of study, such as Great Lakes salmon, were being seen across a broad range of species (C&EN, Nov. 16, 1992, page 5).

At the end of the meeting, the scientists concluded: "A large number of man-made chemicals that have been released into the environment, as well as a few natural ones, have the potential to disrupt the endocrine systems of animals, including humans. Among these are the persistent bioaccumulative organohalogen compounds that include some pesticides (fungicides, herbicides, and insecticides) and industrial chemicals, other synthetic products, and some metals.

"Many wildlife populations are already affected by these compounds. The impacts include thyroid dysfunction in birds and fish; decreased fertility in birds, fish, shellfish, and mam-

mals; decreased hatching success in birds, fish, and turtles; gross birth deformities in birds, fish, and turtles; metabolic abnormalities in birds, fish, and mammals; behavioral abnormalities in birds; demasculinization and feminization of male fish, birds, and mammals; defeminization and masculinization of female fish and birds; and compromised immune systems in birds and mammals."

The scientists who attended the Wingspread meeting also came to a consensus on a number of other issues. They decided that chemicals that disrupt endocrine systems often have entirely different effects on the embryo and developing fetus than they have on an adult, and the effects are most often seen in the offspring. Very low dose exposures during fetal development can be damaging to embryos, whereas large dose exposures may have no effect on adults. They pointed out that the timing of exposure is critically important for determining its final outcome. The effects of exposure may not become ob-

vious until the exposed offspring reach adulthood. The offspring at birth often have no visible defects, but some organ systems may be undeveloped or deformed and never function properly.

Although less is known about the effects on humans of endocrine disrupters, humans, too, have probably been affected by some of the same chemicals that are known to harm wildlife, the Wingspread researchers say. They believe this because, as Leon E. Gray Jr., of the Environmental Protection Agency's Health Effects Research Laboratory, Research Triangle Park, N.C., describes it, "Many of the basic mechanisms underlying the [fetal] developmental process are homologous in all mammals, although the timing of certain events varies." Thus, "chemicals that have adverse effects on reproductive development in rodents should be considered potential human reproductive toxicants as well," he explains.

The effects of a strong synthetic estrogen in humans can be seen in the daughters and sons of the 3 million to 4 million women who, between 1948 and 1971, took diethylstilbestrol (DES) to prevent miscarriage. The daughters have increased rates of vaginal cancer, abnormalities of the genital tract, and higher rates of autoimmune diseases. The sons show high rates of abnormalities in their reproductive systems. Other endocrine disrupters are expected to have effects on humans that are similar to those observed from DES. "In humans," Gray says, "exposure to DES... during gestational development provides us with grim examples of the potential for environmental chemicals to induce morphological and pathological alteration of the reproductive tract of both men and women."

How can minuscule amounts of endocrine-disrupting chemicals cause such havoc for the developing embryo or fetus? The compounds, which are usually lipophilic (fat loving) and have low water solubility, accumulate in the mother's fat



Davis: cancer increases cannot be explained solely in terms of aging

throughout her lifetime. Some portion of what is in the mother's fat then passes through the placental barrier into the fetus, or, in birds and fish, passes from the mother into the egg. There, according to John A. McLachlan, director of intramural research at the National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park, N.C., these chemicals are believed to interfere with endocrine function in five possible ways.

They may recognize the binding sites of natural hormones and mimic the effect of natural hormones, especially estrogen. They may block the effect of natural hormones by keeping them from binding to their natural binding sites. They may react with a hormone directly or indirectly. They may alter the pattern of hormone synthesis. Or they may change the number of hormone receptors. However, says McLachlan, because cellular endocrinology is undergoing a revolution, the ways in which these chemicals act is still partly theoretical. "What the receptors are and how they work is an evolving moving target."

Interfering with natural hormones in a developing fetus can have devastating effects on the offspring because it is the balance of male to female hormones that causes the sexual organs in the fetus to develop normally. In the early developmental stages, the mammalian fetus has rudimentary ducts for the genital tracts of both sexes called Wolffian and Müllerian ducts. If the fetus is genetically male, the normal amount and normal ratio of male to female hormones will cause the Wolffian duct to persist and develop while the female Müllerian duct withers away. A similar, though opposite, progression takes place in the female fetus. Chemicals that mimic female hormones (estrogen mimics) or interfere with them can upset this delicate balance and cause the offspring to be born with both sets of sex organs or faulty or incomplete development of one set of organs, such as undescended testicles. If DES is given to pregnant mice, for example, the male mice are born with both sets of sex organs.

Interfering with the endocrine system in a fetus can also damage the nervous and immune systems because the endocrine system exerts some control over them. It can affect the sexual behavior of the offspring—feminization of male rat behavior, for example.

Animals in the Great Lakes Basin have been studied more extensively than those of any other region. Scientific papers indicate at least 14 animal species that depend on Great Lakes fish "are suffering severe health problems," says Colborn, who edited a recently published book titled, "Chemically Induced Alterations in Sexual and Functional Development: The Wildlife/Human Connection" (Princeton Scientific Publishing, Princeton, N.J.). For each species, the research shows "strong associations" between chemi-

cals that are known endocrine disrupters "and the health of the offspring of exposed animals," she adds.

For example, herring gulls usually lay two to three eggs per nest. DDE (a metabolite of DDT), mirex, and 2,3,7,8-TCDD residues in herring gull eggs on Lake Ontario shores peaked in about 1972. By 1977, herring gull clutches with five to six eggs were prevalent. Each of these nests resulted from two females engaging in a shared breeding attempt. However, the number of eggs per nest declined rapidly during the next four years as levels of DDT and other persistent organochlorines declined. Glen A. Fox of the Canadian Wildlife Service speculates that female-female pairings, which almost never produce offspring, probably result from male mortality or feminization of the male embryo by endocrine disrupters, such as DDT. Feminized male birds would be incapable of reproduction.

Studies of great blue heron exposed to pulp mill effluent in British Columbia's Georgia Strait found growth retardation in chicks that correlated with levels of 2,3,7,8-TCDD, Fox says. The Georgia Strait receives the greatest concentration of wastes from forest products industries in Canada. The most contaminated colony of blue herons did not produce any young. Lab evidence shows, however, that some of the wildlife effects may result from unidentified substances in wood pulp, such as plant sterols, rather than from 2,3,7,8-TCDD.

The emerging research on endocrine disrupters is so new that it really isn't a major reason some groups have been advocating a phaseout of organochlorines. However, this research is becoming an increasingly prominent part of the discussion. IJC cited findings on endocrine disruption as one of its chief arguments for advocating a gradual broad phaseout of organochlorines. EPA's proposed Great Lakes guidance, announced March

31, also mentions the effects of certain organochlorines (and other chemicals) on the developing fetus as one important reason for controlling pollutants that bioaccumulate in fish (C&EN, April 12, page 22). The guidance proposes water quality criteria for 28 chemicals with a bioaccumulation factor greater than 1000. Fifteen of these are organochlorines.

The cancer question

The suspected carcinogenicity of many of the chlorinated organics was, and probably still is, the primary reason driving most phaseout efforts. In general, however, chlorinated organics are not strong carcinogens in rodents. In animal tests for cancer, the majority of organochlorines are negative. Those chlorinated organics that show a positive response are usually mild or moderate carcinogens in animals, producing modest elevations in tumors in only one sex of one species.

Recent research, however, points to organochlorines as one possible cause of cancers whose rates are rising in the



Colborn: EPA should revise cancer-testing protocols to reflect effects of extremely low exposures

C&EN staff photo

general population. The occurrence of several of these cancers is also rising among farmers, but at a faster rate. Cancers occurring in excess among farmers include non-Hodgkin's lymphoma, multiple myeloma, leukemia, and cancers of the skin, prostate, brain, and kidney.

To NRC's Davis, this increase in certain cancers in farmers points to a common cause, some agents that farmers and the general population are exposed to, but that farmers come into contact with to a greater degree. "Of special concern to my colleagues and me is the fact that the same types of cancer that kill farmers in increasing rates are also killing people in the general population," Davis says. "We do not know the reasons for these changes. But we sure had better find out."

Aaron Blair and Sheila H. Zahm, cancer epidemiologists at the National Cancer Institute (NCI), speculate that exposure to pesticides, solvents, engine exhausts and fuel, fumes from molten metals, sunlight, viruses, microbes, and fungi may be responsible for the increased cancer rates among farmers. Pesticides may cause lymphoma, leukemia, brain cancer, and non-Hodgkin's lymphoma, they say. Several studies show a strong link between non-Hodgkin's lymphoma and (2,4-dichlorophenoxy)acetic acid (2,4-D). Also, dogs whose owners use 2,4-D, a herbicide commonly applied to lawns, have higher cancer rates than dogs without such exposures. According to Kenneth P. Cantor, also a cancer epidemiologist at NCI, farmers who have used the insecticide lindane have increased rates of lymphoma. In another study, children who used a lindane-containing shampoo to kill lice were found to have increased rates of brain cancer.

Some researchers believe the rising rates of breast cancer in industrialized countries may be caused by chlorinated organics accumulated in fat tissue. They cite several reasons for this theory. Fat tissue in women with breast cancer has been found to have higher levels of DDE than fat tissue from healthy women. Also, blood from patients with breast cancer has been found to contain four times as much DDE and about 50% more of the insecticide hexachlorocyclohexane (HCH) as blood from healthy women. Researchers believe the levels of DDE are important for breast cancer because DDE is both an estrogen mimic and a tumor promoter.

Industrialized nations with more severe pollution also tend to have much higher breast cancer rates than nonindustrialized countries. However, when exposure to organochlorines declined sharply in Israel between 1976 and 1986, breast cancer rates went down 8%. In other industrialized nations where exposures did not decrease, breast cancer rates rose. Lindane, DDT, and α -HCB were banned from Israeli dairy farms in 1978, causing insecticide levels in dairy products to drop as much as 98%. If pesticide cutbacks were indeed responsible for the fall in Israeli breast cancer incidence, the pesticides were obviously behaving as promoters, rather than initiators, because the cancer rates fell almost immediately after the pesticide levels dropped. Initiators take decades to act.

Researchers suggest several mechanisms by which organochlorines could play a role in breast cancer. Estrogen is virtually essential for the initiation of mammary gland tumors in animals and humans and also promotes such tumors. High natural estrogen levels and sustained levels during a longer-than-normal period of time are known risk factors for breast cancer. Organochlorines that mimic estrogen could bind to estrogen receptors and thereby increase the body's effective estrogen level. Or by mimicking estrogen,

they could artificially extend the time during which a woman is subject to high estrogen levels. In this way they could elevate two of the risk factors for breast cancer.

Endocrine disrupters that cross the placental barrier could also program a fetus to be more susceptible to environmental toxicants by creating in it an abnormally high number of estrogen receptors, hence increasing the number of receptors that could bind to man-made estrogen mimics during the offspring's lifetime. So there may be some similarities in the mechanisms by which chemical endocrine disrupters cause reproductive and other problems in the developing fetus and possibly promote subsequent breast cancer.

The triazine herbicides, especially atrazine, are coming under increasing scrutiny as a possible cause of breast cancer. Atrazine is the most heavily used pesticide in the U.S. However, except for farm workers and people who drink water from contaminated wells, exposure to atrazine is generally low. But exposure is actually very widespread because atrazine is found in rain, in groundwater, and in 98% of streams in the Midwest during the growing season. Atrazine is considered a possible animal carcinogen. In several bioassays, it is linked to mammary tumors in one species of female rat (Sprague-Dawley) and, in one experiment, it caused mammary tumors in male Sprague-Dawley rats.

Atrazine may play a role in human breast, prostate, ovarian, and endometrial cancer by inducing some hormones, but inhibiting others, NCI's Zahm says. "A study in Italy showed an increase in ovarian cancer among women exposed to atrazine," she explains. "It seems possible that other hormonally related cancers may also be affected by atrazine." EPA, along with the producers of atrazine and other triazine herbicides, are now engaged in a series of workshops to consider whether the Sprague-Dawley rat is a good model for humans and whether there is a threshold for atrazine's production of mammary tumors. Darrell Sumner, environmental issues manager for Ciba Geigy, says the "mechanism [of atrazine's action] supports a threshold, which, when compared to environmental concentrations, shows very comfortable margins of safety. The risk to humans in such a situation is thus minimal."

Health & Welfare, Canada, the equivalent of the U.S.'s National Institutes of Health, is embarking on a study to elucidate the role of organochlorines, among other factors, in breast cancer. NCI and NIEHS are supporting similar investigations.

NRC's Davis points out that it is extremely important to tease out the causes of what seems to be a cancer epidemic in the industrialized world. From 1973 to 1987, for instance, cancer mortality in the U.S. decreased in younger people, but cancer incidence increased in all age groups. In Sweden, people born in the 1950s are two to three times as likely to develop cancer during their lifetimes as people born between 1873 and 1882. "Increases in new cancer cases are especially troubling, as they must stem from factors other than smoking and augur increased demand for health care and treatment," Davis says. Cancer increases cannot be linked to smoking, she adds. In fact, lung cancer in men in some countries has begun to decline.

Government responses

Even though organochlorines may be partly responsible for the rising incidence of cancer, there is emerging evidence that the effects they have on the developing fetus may have broader, more pervasive impacts on society.

On a weight basis, more than half the pesticides and a

About half of known endocrine disrupters are chlorinated hydrocarbons

Herbicides

Alachlor
Amitrole
Atrazine
(2,4-Dichlorophenoxy)
acetic acid (2,4-D)
Metribuzin
Nitrofen^a
(2,4,5-Trichlorophenoxy)
acetic acid^a (2,4,5-T)
Trifluralin

Fungicides

Benomyl^a
Hexachlorobenzene^a
Mancozeb^a
Maneb^a
Metiram complex^a
Tributyltin^a
Zineb^a
Ziram^a

Insecticides

Carbaryl
Chlordane^a
Dicofol
Dieldrin^a
DDT and metabolites^a

Endosulfan^a

β-Hexachlorocyclohexane^a
(β-HCH)
Heptachlor and H-epoxide^a
Lindane (γ-HCH)^a
Methomyl
Methoxychlor^a
Mirex^a
Oxychlordane
Parathion^a
Synthetic pyrethroids
Toxaphene^a

Nematocides

Aldicarb^a
Dibromochloropropane^a

Industrial chemicals

Cadmium
Lead
Mercury
Polybrominated biphenyls
Polychlorinated biphenyls
Pentachlorophenol
Penta- to nonylphenols
Phthalates
Styrenes
2,3,7,8-Tetrachlorodibenzo-
p-dioxin (2,3,7,8-TCDD)

■ = Chlorinated products

^a Restricted, cancelled, or unregistered pesticide. All these chemicals were exported from the U.S. in 1991 except for 2,4,5-T, hexachlorobenzene, metiram complex, β-HCH, toxaphene, and dibromochloropropane, according to U.S. customs records analyzed by the Foundation for Advancement in Science & Education.

wide range of other industrial chemicals now used are capable of causing endocrine disruption. How should government respond to this issue? An immediate ban on all these products is not likely. Such a step would cause widespread economic hardship for farmers, lessen food availability at least for a few years, and adversely affect many other sectors of society.

"It will be very difficult to craft legislative language that takes endocrine effects of pesticides into account without placing a large fraction of currently registered pesticides in jeopardy," says Charles M. Benbrook, a consultant in Washington, D.C., and former head of the NRC's Board on Agriculture. However, he suggests a possible solution to the dilemma.

Of the nearly 270 old pesticides that must be reregistered by EPA, only 19 have so far reached the end of the process, and about 250 active ingredients are in various phases of reregistration and review. Instead of immediately trying to test all 250 or so active ingredients for endocrine disruption, Benbrook says, EPA might consider testing known endocrine disrupters that bioaccumulate and cross the placental barrier and are applied heavily to crops or consumed in large quantities by infants. High priority should be given to major chemicals now under active review by EPA.

Colborn says in future toxicological testing, EPA should revise its chronic feeding protocols used to test for carcinogenicity. One or two groups of animals that receive very low doses of the pesticide would have to be added to the usual experiment because endocrine effects often occur at extremely low exposure levels. In addition to examining the offspring of the exposed females for gross birth defects, while the animals mature they should be tested for subtle defects such as shifts in hormone balance, lower than normal sperm counts, reduced sex organ weights, and minor behavioral changes. Also, the offspring would have to be bred to test their fertility. These tests are not now required in most animal bioassays.

Persistence should be another major criterion in deciding whether to restrict a pesticide, Benbrook says. In general, persistent pesticides that are also endocrine disrupters are probably more harmful to humans and wildlife than nonpersistent ones. They usually tend to accumulate in wildlife and humans. But, Colborn points out, nonpersistence may not mean a chemical is safe. Because timing is so important, a woman who is exposed to a nonpersistent endocrine-disrupting pesticide at a critical time during her pregnancy might endanger her offspring, she says. The same criteria that are applied to pesticides could be applied to other industrial chemicals, intermediates, and by-products before they are released to the environment.

Currently, Congressional staff who are rewriting the Kennedy-Waxman food safety bill (Pesticide Food Safety Act of 1993) are trying to incorporate endocrine effects into the legislative language concerning pesticides. It is a difficult task because standard testing protocols and quantitative risk assessment methodology for endocrine effects have not yet been codified by EPA, though such methods are in the process of development.

"Given that such a significant percentage of pesticides may at least potentially cause these endocrine effects, one rational near-term response is to reduce total pounds of use while we do the science needed to reduce our uncertainty," Benbrook says. "The best way to accomplish this goal quickly would be for EPA to comprehensively review and adjust tolerances downward to safe, health-based levels."

EPA has already banned some chlorinated organics, but only a small fraction of the 15,000 or so that are in commerce. In the 1970s, the agency restricted most of the persistent heavily chlorinated insecticides, such as DDT, aldrin, dieldrin, kepone, lindane, chlordane, mirex, and toxaphene. Although these insecticides were known to be persistent and to cause adverse effects in wildlife, they were regulated on the basis of their possible carcinogenicity in humans.

A few chlorinated insecticides, such as methoxychlor, are still used widely, and some of the restricted insecticides are used for minor purposes in the U.S. Dieldrin is employed as a moth repellent in rugs, and lindane is used in a preparation for killing head lice in children.

Unfortunately, even products that have been banned in the U.S. still present problems for the nation's environment. PCBs are especially troublesome because, though they are not being produced, they are being used in closed transformers. They are also stored in warehouses and are present in contaminated sediments and many landfills. Peter J. H. Reijnders of the Research Institute for Nature Management,

Den Burg, the Netherlands, estimates that more than 70% of the global production of PCBs is still in use or in stock and could reach the environment in the future. "Unless adequate retrieval and disposal of remaining PCBs in use is enforced, these noxious compounds will in the near future become an even larger global environmental problem than at present," he says.

Most of the persistent insecticides that were banned or restricted in the U.S. are still being used in developing countries. According to Landell Mills, a market research firm in Bath, England, 15 million lb of lindane was used on crops in India in 1991, and aldrin and dieldrin are still being used in India and Pakistan. In addition, the Foundation for Advancement in Science & Education in Los Angeles, reports that almost 4.1 million lb of banned, canceled, or voluntarily suspended pesticides were exported from the U.S. in 1991, including almost 96 tons of DDT. About half of these pesticides went to developing countries. Some fraction of these products return to the U.S. via airborne transport, migratory fish, and, to some extent, on crops. Eggshell thinning from DDT has recently been reported in bald eagle eggs on the Columbia River.

The PVC quandary

Many people find it hard to understand why anyone could be opposed to PVC. It is cheap to manufacture, it has hundreds of uses, and it is inert.

However, Greenpeace and many groups in Germany and Austria want to phase out the use of PVC for a variety of reasons. PVC manufacture produces emissions of 2,3,7,8-TCDD and HCB, Greenpeace spokesmen say. When accidental fires occur in buildings that contain large amounts of PVC building materials, they produce dioxin and furan contamination, Greenpeace says.

Because useful products can't be made of pure PVC, it is mixed with different additives to make hundreds of varieties, depending on the use. Therefore, it is very difficult to recycle PVC back to its original use because it would have to be separated into hundreds of categories for recycling. As a result, only a fraction of total PVC production can be easily recycled, and that fraction is usually down-cycled, that is, recycled into something like rug backing, a commodity that is less valuable than the original product. And incinerating PVC waste, according to Greenpeace, produces dioxin. In addition, Greenpeace says, the vinyl chloride used to make PVC is highly explosive and therefore dangerous to transport. The monomer has caused a number of serious accidents that have required thousands of people to be evacuated. For most uses of PVC, it is easy to find substitutes, though sometimes they are more expensive.

Robert Burnette, executive director of the Vinyl Institute, Akron, Ohio, says the institute has no data on 2,3,7,8-TCDD

and HCB emissions from the manufacture of vinyl chloride in the U.S. "But my understanding is that with current detection techniques, the plants can't detect any [such emissions]," he adds.

Some PVC can be recycled easily, Burnette says. In the U.S., about 1% of total vinyl production is being recovered in the form of packaging. The institute is aiming for a goal of recovering 25%, "but the economics will be difficult to overcome," he says. His institute is also looking into projects to recycle durable goods. However, Burnette agrees that recycling some kinds of PVC back to their original uses is difficult because there are so many varieties.

Burnette also claims that 2,3,7,8-TCDD emissions from properly controlled and operated municipal incinerators have no relationship to the amount of PVC being burned. "Incinerator operating conditions are the key to controlling dioxin formation," he says.

Fires involving PVC are not unusually hazardous, Burnette says. Carbon monoxide is the main killer in fires and it is present in all fires. Following two fires that recently took place in German warehouses where postconsumer PVC waste and other plastic waste were being stored, the dioxin and furan levels were measured and found to be less than background after the fire. "So Greenpeace seems to have jumped off of that issue," he says. "In the U.S. there really have been no serious accidents involving vinyl chloride for many years."

Chlorine reduction strategies in industry

Several large U.S. chemical companies have taken steps to reduce their use of chlorine and their production of chlorinated products. They are also trying to limit the generation of chlorinated wastes when they do use chlorine. Du Pont does not sell a lot of chlorinat-

ed products, but those it does sell are "involved in strategic business review," says John Carberry, director of process and environmental R&D. In its review, Du Pont tries to predict regulatory and customer expectations and what effect these will have on the product. "Environmental considerations and the fit of that product in the environmental expectations of the world" play a major role in the strategic review, he says. "There is little doubt that all products with chlorine in them will undergo modification," Carberry adds.

For products that are not chlorinated, but are produced with chlorinated intermediates, Du Pont "is looking for different ways to manipulate chemical molecules without using chlorine as an operator," Carberry says. The company is doing this to avoid producing waste hydrochloric acid, which is expensive to dispose of. Du Pont is also trying to find an economical way to convert waste hydrochloric acid back into chlorine. This conversion would reduce Du Pont's overall use of chlorine.



Benbrook: legislating to account for endocrine effects jeopardizes registered pesticides

Monsanto also is working on a number of ways to reduce its production of chlorinated wastes and to treat those wastes that are generated in the best possible way, says Michael W. Berezo, director of environmental strategy. If Monsanto is consuming a chlorinated product or producing a chlorinated product, "the first thing we do is make sure we have handling and treatment systems that are really in a class with best demonstrated technology," he says. Monsanto tries to reduce the generation of chlorinated wastes by using substitute material in its processes.

In the development of new products, Monsanto is designing processes with the ultimate goal of not producing waste in the first place by recycling streams and eliminating the use of toxics, Berezo says. For products that will not capture a large market, he adds, it is particularly important not to produce toxic waste because the best available control technology would be relatively too expensive to install for such products.

Dow Chemical, a large manufacturer of chlorine, vinyl chloride, and PVC, has no plans to curtail these businesses. However, the company is currently involved in performing risk-benefit analyses of its products and applications, says W. Joseph Stearns, director of environmental health and government affairs. "If the benefit isn't greater than the risk, then we recognize those products or applications should be phased out," he says.

To help reduce the use of chlorinated solvents and assist customers with the safe handling of these solvents, Dow has formed an advanced cleaning systems business, Stearns says. This business has developed technologies to capture vapors from chlorinated solvents. It is also aiding customers, like dry cleaners, in the proper use of existing control technologies. As a part of this enterprise, Dow has developed a number of aqueous and semiaqueous cleaning products to use as substitutes for chlorinated solvents.

Even though some U.S. companies are working to cut back on their uses of chlorine and especially on their production of chlorinated wastes, David H. Marks, director of Massachusetts Institute of Technology's program in environmental engineering, education, and research, thinks U.S. industries are moving somewhat too slowly "in widening their dialogue outside the industry. I think there is a big tidal wave coming here. Industry is making a major proactive swing, but the question is: Can it do it fast enough and efficiently enough and with enough gusto to protect itself?"

Chlorine Institute's response

Robert G. Smerko, president of the Chlorine Institute, maintains that evidence used to support a broad-based chlorine ban—endocrine disruption, developmental impairment, reproductive dysfunction, and cancer—is based

on effects of a few selected organochlorines, such as PCBs, DDT, mirex, and lindane, "that have been phased out of use." Historical data should not be extrapolated to the whole class of existing organochlorines, he says. The compounds now in use in the U.S.—alkanes, alkenes, and lower chlorinated monoaromatics, most of which have half-lives of hours or days—"do not accumulate in the environment and therefore do not reach environmental concentrations that would result in adverse impacts," he points out. Most of these compounds have high water solubilities and high vapor pressures in contrast to persistent ones, which generally have low water solubilities and low vapor pressures.

Smerko also opposes the idea of zero discharge of chlorinated organics. This "implies that any level of chlorinated organic material would have an adverse impact on the biosphere," he says. Instead of "zero discharge a no adverse

impact" policy should be implemented," he argues. The concentration of a chemical has to reach a critical level to have an adverse impact. For example, the fact that some bird populations in the Great Lakes area have shown improved reproductive success indicates there are some concentrations of chlorinated organic compounds that do not have an impact on these birds, he claims.

Risk assessment, Smerko says, can be applied to determine environmental concentrations of chemicals that have no adverse impact. And new technologies can be used to ensure that environmental loading rates remain below the level that would have adverse effects.

Smerko maintains that the Great Lakes ecosystem "has shown a remarkable recovery and that chlorinated organic compound concentrations in this environment are no longer inducing widespread adverse effects in wildlife popula-

tions." He also says the Jacobson and other studies that indicate the effects of PCBs on the offspring of women who ate Great Lakes fish are inconsistent.

Phasing out the use of chlorine in the pulp and paper industry would not improve environmental quality, Smerko says, because 2,3,7,8-TCDD and furans have largely been eliminated from pulp mill effluent. For all of these reasons, he advocates considering chlorinated compounds on a case-by-case basis.

The Chlorine Institute commissioned a report on the economic benefits of chlorine, which was published recently. It has also commissioned "an in-depth review and interpretation of the critical scientific literature on chlorine chemistry related to environmental and human health," which will be released in about two months.

Chlorine provides great benefits to society, says Brad Lienhart, head of the Chlorine Coordinating Council, a Chlorine Institute-Chemical Manufacturers Association



Smerko: evidence used to support broad chlorine ban based on few selected organochlorines

Caustic soda can be produced without making chlorine

Caustic soda (NaOH) is an important industrial commodity used in a variety of industries, including pulp and paper, organic compounds, inorganic compounds, water treatment, alumina, and soap and detergents. Because chlorine inevitably is produced during the electrolytic reaction commonly used to produce caustic, some observers argue that chlorine production cannot decline. However, there are a number of ways to make less chlorine and still supply enough caustic—or suitable substitutes—for industry.

Recycling caustic within industrial processes is one way to help meet the demand for the compound. In the paper industry, much of the caustic used is already recycled, but more of it could be recycled if chlorine were eliminated from the paper bleaching process. In aluminum oxide manufacture, caustic can also be recycled.

In many processes, other chemicals can be substituted for caustic. Carbonates, lime, and magnesium hydroxide can often be used in applications requiring alkalinity. Dow, for example, is planning to substitute lime for caustic in its U.S. propylene oxide production. In processes that require sodium ions, sodium carbonate or sodium sulfate can often be used.

Caustic also can be made by three other processes. One process is causticization of sodium carbonate produced from lime and salt using the Solvay process. Another process is causticization of sodium carbonate mined as trona ore. Huge deposits of trona ore exist in Wyoming and Turkey, and in Africa and Asia. In Wyoming, several companies with a combined production capacity of 290,000 tons per year are already producing caustic from trona ore. Caustic can also be made by elec-

trolysis of sodium sulfate from natural ores or electrolysis of the sodium sulfate in waste streams from many industries.

The Washington, D.C.-based industry group, the Chlorine Institute, maintains, however, that alternative methods of producing caustic are more expensive than caustic production using the standard chlor-alkali process. And the association adds that mining trona ore in Wyoming causes serious environmental problems.

Joe Thornton of the environmental organization Greenpeace in Seattle, Wash., disagrees, saying there are no major environmental threats involved with mining trona. He says Greenpeace suggests a surcharge be placed on caustic produced by the chlor-alkali process, so that caustic users would have an incentive to use alternative manufacturing processes that do not produce chlorine.

venture to communicate to the public about chlorine. "Over half of chlorine chemistry practiced goes into public health and human health applications. Ninety-five percent of all crop protection chemicals are based on chlorine. In the U.S. through chlorination of drinking water and sewage we are saving 25,000 lives a year."

Two philosophies concerning regulation

There are basically two philosophies concerning the regulation of organochlorines. Some people and organizations, like the Chlorine Institute, prefer to take a compound-by-compound approach. They demand strong evidence of harm before an individual compound is phased out. "It is ludicrous to suggest that all ... organochlorine compounds should be banned. There is a spectrum of organochlorine chemicals ranging from thoroughly nasty candidates for banning to relatively innocuous degradable substances," says Dori Mackay of the Institute for Environmental Studies at the University of Toronto.

Other people and institutions require only indications of harm before advocating phasing out a compound or a whole class of compounds. They say it is not possible to evaluate each compound individually. It will take much longer than our lifetimes to thoroughly test all of them. And if one chlorinated hydrocarbon is phased out, another chlorinated hydrocarbon with equally bad or worse health or ecological effects will be invented to take its place. It will take even longer to test the various permutations and combinations of chlorinated hydrocarbons. John R. Vallentyne, research scientist emeritus at the Canada Center for Inland Waters, expresses this point of view succinctly. "Because of overlapping and interactive effects among persistent toxic substances, causality and proof of harm are elusive, if not

impossible to obtain. That is why a preventive approach to harm is needed based on weight of evidence rather than on absolute proof of harm."

Scientists who have been following the trail of epidemiological data believe there is now clear evidence from both basic and epidemiologic studies that some chlorinated compounds are risk factors for several types of cancer. But there is also a new wave of information emerging from studies of animals and humans that raises concerns about exposures at even lower levels than have been thought important for cancer. The evidence that endocrine-disrupting organochlorines at the levels found in the environment cause adverse health effects in the offspring of wildlife is strong. Even though humans have in their tissues about the same levels found in the tissues of wildlife, the evidence is not as strong that organochlorines are causing similar problems in human offspring.

However, the concerns about humans and wildlife are definitely going to affect the regulations taking shape. Such concerns have already influenced EPA's new Great Lakes guidance and will probably affect many more regulations and laws that will be written during the next few years.

These "ongoing pressures are forcing action on many diverse fronts [of chlorine phaseout] ... and these actions are not likely to abate," says John R. Erhenfeld, research associate at MIT's Center for Technology, Policy & Industrial Development, who has recently completed a report on chlorine phaseout for the Norwegian government and industry. "Although unprecedented, this call for a ban on chlorine must be taken seriously. To government policymakers and industry decisionmakers alike, this call presents both opportunities and challenges," he adds. □

DIOXIN TOXICITY RESEARCH

Studies show cancer, reproductive risks

Two new studies have found evidence for cancer and reproductive risks from exposure to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD).*

A study of the effects of the chemical plant explosion that occurred in Seveso, Italy, 17 years ago indicates that exposure to 2,3,7,8-TCDD increases the risk of cancer in humans. This is the first scientific study to show increased cancer rates in people exposed to the dioxin in the accident [*Epidemiology*, 4, 398 (1993)]. Previously, the only adverse health effect reported from the accident was chloracne, an acnelike skin condition that is often permanent.

In addition, a study by Environmental Protection Agency (EPA) scientists has found that a single low dose of 2,3,7,8-TCDD in pregnant laboratory animals causes reproductive abnormalities in their offspring. The EPA results have not yet been published, but they will be presented this month at a meeting in Vienna.

These results and other similar laboratory studies may affect the way EPA writes its protocols for testing pesticides and toxic substances. The agency's Office of Prevention, Pesticides & Toxic Substances is in the process of developing new guidelines for testing pesticides and toxic substances that will require looking for subtle reproductive endpoints in the multigenerational studies.

In the Seveso study, Italian researchers led by Pier Alberto Bertazzi of the University of Milan found higher than normal rates of several types of cancer in people exposed to a cloud of 2,3,7,8-TCDD from the plant explosion. The exposed population was divided into three categories according to the degree of contamination in their area of residence—heavily exposed, moderately exposed, and lightly exposed.



Rat receives 2,3,7,8-TCDD to test effects on offspring

Researchers then compared the cancer rates in the more than 36,000 exposed people with the rates in 180,000 people living close by in uncontaminated areas. No conclusions could be drawn about the heavily exposed group because it contained so few people. In the moderate-exposure group, liver cancer incidence was about three times higher than in the control population. Men showed an increase in a cancer of the lymph nodes called lymphoreticulosarcoma, and women had an increased incidence of multiple myeloma and leukemia. The group with the lightest exposure had elevated incidences of soft tissue sarcoma and non-Hodgkin's lymphoma.

Three previous studies of people exposed to 2,3,7,8-TCDD in the workplace have linked elevated blood levels of the compound to increased cancer mortality.

In the animal study, researchers led by L. Earl Gray Jr. of EPA's Health Effects Research Laboratory, Research Triangle Park, N.C. gave pregnant rats and

hamsters one minuscule dose of 2,3,7,8-TCDD (1 µg per kg of animal weight). Preliminary results show that about two thirds of the male rat offspring had reduced sperm counts, Gray says. And male pups in both rats and hamsters experienced delayed puberty.

In female rat and hamster offspring, the results are even more striking. About 30% of the female rat offspring show structural abnormalities in the reproductive and external urinary tract, Gray says. The defects include delayed or complete absence of vaginal opening, clefting of the clitoris, and hypospadias—a condition in which the urethra empties into the vagina rather than into a separate opening. The dose of chemical was about one 500th of that which would cause adverse effects, such as cancer, in an adult animal.

Most of the abnormalities are not "the kind of thing that an untrained observer might notice," and many cannot be seen until the animal reaches puberty, says Linda Birnbaum, who works with Gray and is the director of the environmental toxicology division of the Health Effects Research Laboratory. Dioxinlike polychlorinated biphenyls and furans would be expected to produce effects similar to dioxins, Gray says. But none of these have been tested in lab mammals for more subtle reproductive abnormalities in offspring.

2,3,7,8-TCDD is not simply an anti-androgen or antiestrogen agent, Gray adds. It is much more complicated. "Dioxin is unlike anything we've seen anywhere in the literature. It disrupts multiple endocrine systems."

A panel of experts convened by EPA reviewed the dioxin literature last September and decided that the content of dioxins and dioxinlike compounds already found in humans is at or near a level where adverse responses would

be expected to occur, Birnbaum says. She and Gray both stress, however, that more work needs to be done to determine the levels of dioxins and dioxinlike compounds that the human fetus is exposed to, and to assess what effects these are likely to have.

The new research is one component of the information that is coming together on dioxin toxicology that will be used in the overall reassessment of 2,3,7,8-TCDD, says Dwain L. Winters, director of EPA's dioxin policy project. One of the questions EPA will ask is over what range do these effects occur in humans.

Peter de Fur, senior scientist at the Environmental Defense Fund, says these experimental results indicate that EPA should move away from the cancer paradigm. Until now, EPA has assumed that if it set a standard stringent enough to protect against cancer, the standard would protect against other adverse health effects. These results show that "fairly low concentrations over a very short and critical period, levels too low to cause cancer, can have profound effects in the developing embryo that don't show up until adulthood," he says.

Bette Hileman

Dry ice detected in a natural diamond

Diamond thieves have long referred to their heists as "ice." That argot seems closer to the mark since two geochemists reported last week detection of the unmistakable spectral signature of dry ice—solid carbon dioxide—inside a natural diamond.

The surprising discovery provides direct evidence that carbon dioxide-containing fluids exist under great pressure at depths of 220 to 270 km beneath Earth's surface. It also demonstrates that diamonds can trap and carry such fluids to the surface. Most minerals aren't strong enough to do this.

The infrared spectra that revealed the diamond's icy deposit were recorded by assistant professor Oded Navon and graduate student Marcus Schrauder at Hebrew University's Institute of Earth Sciences in Jerusalem. They describe their findings in the Sept. 2 issue of *Nature* [365, 42 (1993)].

Navon and Schrauder purchased the diamond—a very small, unpolished,

brownish-yellow stone weighing some 10 or 15 mg—at a diamond exchange in a Tel Aviv suburb. They have no idea where it came from. Schrauder "picked it for its strange color," hoping to find out why it has that color, Navon tells C&EN.

On examining its infrared spectrum, they discovered prominent bands that closely fit the spectrum of solid carbon dioxide at a pressure of 5 gigapascals, or almost 50,000 times atmospheric pressure. That amount of pressure is enough to keep the trapped gas in the solid state, even at room temperature. At atmospheric pressure, carbon dioxide sublimates at -78°C .

Navon believes that the carbon dioxide must have been trapped inside the diamond at even greater pressures—about 70,000 to 85,000 atm, corresponding to depths of about 220 to 270 km. At these pressures, he says, free carbon dioxide would be expected to react quickly with metal silicates, which are common in Earth's mantle, to produce metal carbonates. But the survival of carbon dioxide suggests that scientists may have to rethink what they know about the mineralogy of this hot environment.

The source of the trapped carbon dioxide remains a matter of speculation. Navon says it might have originated from limestone or other carbonate-containing surface rocks that were pushed deep into the mantle in a process known as subduction. If carbonate rocks were involved, it could have many implications for carbon cycles on Earth, he says.

A more likely possibility is that the carbon dioxide was released from highly pressurized fluids as they ascended through the mantle—say from a depth of 300 km—to regions of lower pressure. Such carbon-containing fluids are involved in volcanic phenomena and are important in the formation of kimberlites, igneous rocks that erupt explosively through the crust, sometimes bringing diamonds to the surface. If free carbon dioxide really is present at those depths, Navon says, it would have to be considered in any mechanism of kimberlite formation, and in many other processes that are important to mantle evolution.

Geochemist David R. Bell of the Geophysical Laboratory of Carnegie Institution of Washington (D.C.) points out that "direct samples of the deeper interior of the Earth, particularly fluids, are very, very difficult to come by. And [Navon's diamond] is one of the deepest [samples] we have." The scarcity of

such samples makes it very difficult to piece together the puzzle of mantle chemistry, he says.

Edwin W. Roedder, a geochemist at Harvard University, echoes this view: "Diamond is sort of the window to the mantle, but it's a difficult window to see through. . . . Any new revelation about the nature of inclusions in diamond is useful."

The infrared spectral bands observed imply that the diamond's carbon dioxide is present in a crystalline form. But even under high magnification, the Hebrew University researchers can see no solid inclusions in the specimen. Therefore, they assume the carbon dioxide resides in sub-microscopic inclusions. If that is true, they say, "the internal pressure of 5 gigapascals is the highest pressure ever measured in any inclusion at room temperature."

Although the most intensely colored regions of the diamond show the strongest carbon dioxide infrared bands, the brownish-yellow hue cannot be due to carbon dioxide itself because it doesn't absorb visible light. The color probably is due to microscopic pressure-induced strains on the diamond lattice, Navon concludes.

Carbonates and water previously have been found in fluid inclusions in fibrous diamonds. And carbon dioxide, water, carbon monoxide, methane, hydrogen, and nitrogen have been detected in gases released from crushed or heated diamonds—but their origin from inside the diamond could not be confirmed beyond doubt.

However, the carbon dioxide spectrum of Navon's diamond is clean, revealing no impurities other than gaseous nitrogen and hydrogen.

Ron Dagani

Ohio plant explosions stir calls for shutdown

Starting at 12:10 AM on Friday, Aug. 27, two massive and several minor explosions rocked an Aztec Catalyst organic peroxides plant in Elyria, Ohio.

There were no serious injuries. But the explosions resulted in extensive damage to two plant buildings, and sent a cloud of hydrochloric acid drifting toward residential areas, causing evacuation. Coming in