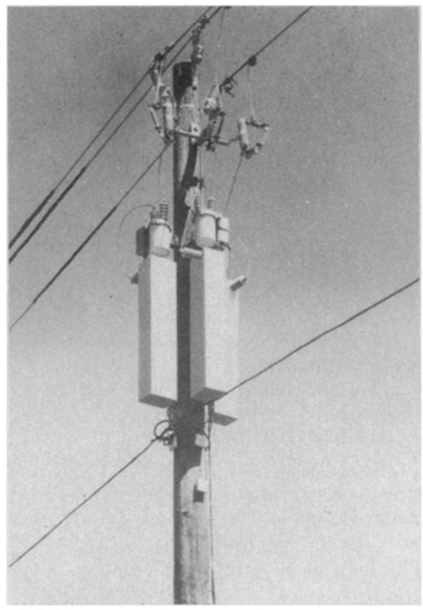
Puzzled Over PCBs

A symposium beset by controversy looked at some industrial chemicals turned environmental contaminants

By LINDA GARMON



A PCB-containing capacitor.

The intense, two-day symposium on a once-popular class of industrial chemicals called PCBs was running behind schedule. "We have a slight time problem," the chairman said before the final discussion period; he proceeded to suggest that the remainder of the session be limited only to those "questions that can be easily answered." The audience laughed. "Well," the chairman acknowledged, "this of course is impossible." Indeed, precious few easy-to-answer questions had been posed during this U.S. Environmental Protection Agency meeting, held May 12 and 13 in Bethesda, Md. The meeting, billed as a forum for the exchange of the latest scientific information, rekindled the debate on the health effects of PCBs, or polychlorinated biphenyls.

PCBs — oily or waxy substances that have been shown to cause cancer in animals — were manufactured in the United States from 1929 to 1977. Because of their particular physical properties, these chlorine-containing hydrocarbons were sort of jack-of-all-chemical trades. They were used — and continue to be used — as cooling liquids in electrical transformers and capacitors. They also were used as heat transfer and hydraulic fluids, dye carriers in carbonless copy paper, additives in paints, adhesives and caulking compounds, sealant and dust-control road covering and pesticide extenders.

Although EPA years ago banned the manufacture, processing, distribution in commerce and use of these chemicals in "non-totally enclosed systems," PCBs — among the most stable substances known — still are ubiquitous. EPA estimates that 150 million pounds of PCBs are dispersed throughout the United States — in air and water supplies, for example. An additional 290 million pounds are located in landfills. And an estimated 750 million pounds still are in use in various pieces of equipment, ranging from voltage regulators to electromagnets.

Because of the stability and ubiquity of PCBs, various organisms have accumulated levels of these chemicals, and those concentrations in turn have "biomagnified" in the food chain. For instance, fish from Indian Creek in Triana, Ala. — which collects drainage from Redstone Arsenal and Huntsville — contain 0.36 to 3.32 milligrams of PCBs per kilogram of body weight, says Renate D. Kimbrough of the Centers for Disease Control in Atlanta, Ga. And persons living in the fish-eating Triana community have an average level of 17.2 micrograms of PCBs per liter of blood serum, Kimbrough reported at the recent EPA symposium. While numerous studies have reported PCB levels in various other groups, no comparable published data exist for the general population, Kimbrough says. Still, it is the consensus of the scientific community that PCBs probably have accumulated in varying concentrations in all persons in at least the industrialized countries.

In 1968, a tragic accident in one such industrialized country demonstrated the acute health effects of PCB exposure. That year, at least 1,000 persons in Yusho, Japan, became ill after eating rice oil contaminated with Kanechlor 400 — a mixture of PCBs and some impurities. The most common symptoms observed among the victims of this accident included acne-like skin lesions, called chloracne, disorders of the peripheral nervous systems, eye discharges and hyperpigmentation of the skin, nails and mucous membranes. Moreover, although precise data are not yet available, statistics suggest an increased rate of cancers — particularly those of the stomach and liver — among Yusho victims.

The Yusho incident resulted in worldwide notoriety for PCBs and an increased concern about the potential health effects that could result from low-level, long-term exposure to the chemicals. But various industries and companies — including those that might somehow be negatively affected financially by further decisions about, or regulations of, PCBs — feel that the concern has mushroomed into needless hysteria. Monsanto, once the major U.S. producer of PCBs, is one of those companies.

While Monsanto voluntarily stopped production of PCBs before the EPA ban, it continues to be bound to the PCB issue by lawsuits. One major suit stems from a 1979 accident at the Pierce Packing Co. in Billings, Mont. There, PCB-containing fluid leaked from a transformer, contaminated an animal feed process and eventually led to a massive destruction of hens, eggs, chicken meat and egg-containing products. Persons whose property was destroyed sued Pierce Packing Co., who in turn sued Monsanto (and General Electric Co., which manufactures transformers). The entire consolidated lawsuit is scheduled to be tried in November in the U.S. District Court in Billings.

Because 25 to 50 such consolidated suits have precluded Monsanto Co. from shaking its connection with the PCB issue, company employees keep an eye out for published health effects studies. Recently, several of these employees pointed out to EPA Assistant Administrator John A. Todhunter that numerous studies had been published since EPA's last review, in 1978, of the PCB data. "They [Monsanto officials] thought that PCBs were being treated very emotionally by the media, and they felt that there were some more scientific facts that should be brought out," EPA's Bill Gunter told SCIENCE NEWS. "Todhunter said that he would consider sponsoring a symposium as a way of providing a forum for people to air information about these

Gaffey Speaks...

At the recent PCB symposium, Monsanto's William Gaffey presented this interpretation of several independent studies looking at whether blood levels of PCBs are linked to specific health effects. While evidence suggests PCBs can cause skin problems, said Gaffey, the data on other possible adverse health effects – liver malfunction and increased cholesterol concentrations, for example – are so inconsistent as to suggest no relationship.

Study	Dermatologic effects					Liver function		Fat metabolism		
	Chloracne?	Other dermatitis?	Dose related?	Adjusted for other variables?	Abnormalities?	Dose related?	Adjusted for covariables?	Total cholesterol?	Triglycerides?	Adjusted for covariables?
A. Fischbein, et al. Annals of the New York Academy of Sciences, Vol. 320, page 203, 1979.	N	Y	Y	N	N		N	N	N	N
E.L. Baker, et al. American Journal of Epidemiology, Vol. 112, page 553, 1980.	N	N		N	N		N	N	Y	N
A.M. Maroni, et al. British Journal of Industrial Medicine, Vol. 38, page 55, 1981.	Y	Y	?	N	Y	Y	N	•	•	•
K.H. Chase, et al. Journal of Occupational Medicine, Vol. 24, page 109, 1982.	Y	Y	?	N	Y	Y	Y	N	Y	Y
A.B. Smith, et al. British Journal of Industrial Medicine (accepted for publication)	N	Y	N	N	Y	Y	Y	N	N	Y
K. Kreiss, et al. Journal of the American Medical Association, Vol. 245, page 2505, 1981	•	•	•	•	N		Y	Y	N	Y

From Gaffey's "Recent Epidemiologic Studies of PCBs."

And Others React

- *"What he [Gaffey] did was very simplistic," says Renate D. Kimbrough of the Centers for Disease Control in Atlanta, Ga.*
- *"We only presented a very brief summary in that ANNALS article," says Alf Fischbein of the Mount Sinai School of Medicine in New York City. "For many of the aspects of our work which he [Gaffey] classified as 'not found,' we stated that these would be subject to further analysis." Upon further analysis, Fischbein did find, for example, an association between blood levels of PCBs and chloracne. Still, he says, Gaffey's overall presentation was "basically correct."*
- *The studies Gaffey compared involved different groups "exposed to different mixtures of PCBs, and the kind of PCBs involved is important," says Mary S. Wolff of Mount Sinai School of Medicine.*

Key:
N = not found/no
Y = found/yes
no entry = not reported
• = not applicable
? = unclear

most recent studies."

The seeds for the recent EPA symposium had been planted. But when word got out of the meeting and its scheduled speakers, the Natural Resources Defense Council suggested that it be canceled. In a May 4 letter to EPA Administrator Anne M. Gorsuch, NRDC attorney Jacqueline Warren expressed "serious concern" about the timing of the symposium, coupled with the "strong pro-industry bias of the majority of speakers scheduled to make presentations."

Warren charged that the symposium was timed to coincide with, "and presumably to influence," the agency's re-write of regulations that detail exemptions to the PCB ban (see p. 359). In addition, she noted, two of the scheduled speakers represented firms that previously had been hired by two different major industry groups — the Chemical Manufacturers Association and the Edison Electric Institute — to review published studies on the health effects of PCBs. "Not unexpectedly, the consultants for both industries reached the predictable conclusion that PCBs are not hazardous," Warren said. "This self-serving conclusion flies in the face of an extensive body of evidence documenting the hazards of PCBs," she wrote. "EPA has acted improperly in hastily assembling such a biased set of hand-picked industry speakers and presenting them to the public as a group of impartial scientists."

Despite Warren's protests, the symposium proceeded, with roughly half of the invited speakers presenting original data and half reviewing the work of others.

One of the "reviewers" was William Gaffey of the Monsanto Co. in St. Louis, Mo. Gaffey began his overview by stating that the Yusho incident is not really a straightforward example of PCB ingestion. Recent analyses by Japanese researchers, he explained, show that the Yusho victims "had in fact ingested about the same amount of polychlorinated dibenzofurans (PCDFs) as of PCBs." PCDFs are toxic impurities normally found in PCB mixtures in only trace amounts. "It therefore appears that the epidemiologic findings in the Yusho incident should properly be attributed to ... PCDF[s] rather than to PCBs," Gaffey said.

Reaction to labeling PCDFs the culprit in the Yusho incident was mixed. Alf Fischbein of Mount Sinai School of Medicine in New York City told SCIENCE NEWS it is a possibility. (He and colleagues are looking for concentrations of these impurities in the oil to which a particular group of capacitor manufacturers once were exposed.) On the other hand, Stephen Safe of Texas A&M University at College Station says, "You can't blame everything on PCDFs." Indeed, research published last year in the March JOURNAL OF THE NATIONAL CANCER INSTITUTE suggests that PCBs possess at least one form of potentially toxic activity in their own right. Bradley D. Preston and colleagues of the University of Wisconsin at Madison showed that a PCB mixture dubbed Aroclor (AR) 1254 promotes — that is, enhances — the ability of another chemical to induce liver cancers in rats. "This promoting ability is not compromised by removal of the PCDF components from the commercial AR 1254 mixture," the researchers discovered.

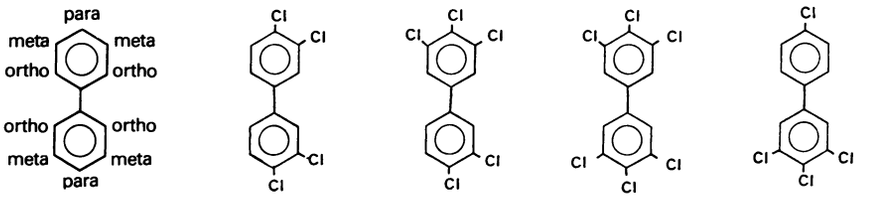
Next, Gaffey reviewed numerous published studies that have investigated whether certain health effects can be linked to measured blood levels of PCBs. Most of the studies involved occupationally exposed workers — capacitor manufacturers and utility company employees, for example. All of the health effects the various research groups searched for — chloracne, liver abnormalities and changes in cholesterol or triglyceride levels in the blood — "were the kinds of things that turned up in the Yusho incident," Gaffey said. The Monsanto scientist noted whether specific health effects were found in each study, whether they were "dose related" (whether higher blood levels of PCBs caused more of a particular effect than lower levels) and whether the

findings had been statistically adjusted for other variables that could have influenced the results. Taking all this information into account (see the table p. 362), Gaffey concluded that while there is some agreement that PCB exposure can cause various skin problems, results regarding any other health effects are so inconsistent as to suggest no association.

Again, Gaffey's conclusion met with mixed reviews. Kimbrough said she "had a lot of problems" with his "simplistic" interpretation. For instance, she explained, in one of the studies that Gaffey included, the researchers discovered that the experimental and control groups they were comparing actually had similar PCB blood levels. "You can't use that study to say, 'PCBs don't cause any effects,'" she said. Also, for the study by Alexander B. Smith of the National Institute for Occupational Safety and Health and colleagues, Gaffey reported that no association was found between PCB and triglyceride levels. In actuality, the report — to be published in the BRITISH JOURNAL OF INDUSTRIAL MEDICINE — states that increased levels of blood PCBs were associated with increased levels of plasma triglycerides in two (electrical equipment manufacturers and public utility employees) of the three occupationally exposed groups studied. "The consistent positive association of a serum PCB with plasma triglyceride ... may have long-term cardiovascular consequences," Smith and colleagues reported. Fischbein pointed out similar inaccuracies in Gaffey's interpretation of his study. Despite these misinterpretations, Fischbein more or less agreed with Gaffey's bottom line: The data are inconsistent.

Inconsistent data also plague three recent cancer mortality studies that find, for the most part, non-statistically significant increased rates of cancer among different occupational groups that were exposed to PCBs, Gaffey said. (None of the authors of these studies were invited symposium participants.) "Excess cancer of the liver, rectum, stomach, pancreas, biliary tract and lung are each found in one of the studies but in none of the others," he said. Kimbrough and others countered, however, that inconsistent data are not reason to discount potential adverse health effects when it comes to PCBs: There are 209 different structures that fall under that chemical heading; the inconsistency may be because different studies involve groups of persons exposed to different mixtues of those structures.

Identifying precisely which structures persist in human tissues must necessarily precede evaluation of their potential health effects. Thus far, researchers have been content to quote total PCB blood and fat tissue levels in health effect studies. Now, however, several scientists in the field are encouraging their colleagues to separate the structural components with a sophisticated analytical procedure that involves a glass capillary column.



A model PCB structure identifying the possible positions for chlorine, left, and the four most potent AHH-inducing PCBs, right. Safe, et al.

The conventional analysis for PCBs involves gas-pushing the "unknown" through a 2- to 3-meter-long column that is packed with specific material to separate the sample's components, E. D. Pellizzari of Research Triangle Institute in North Carolina reported at the meeting. The glass capillary column, on the other hand, is about 50 meters long and specially packed to enable it to more clearly separate individual PCB components, Pellizzari said.

Mary S. Wolff and colleagues of Mount Sinai School of Medicine have used the glass capillary column to analyze the PCB components in the fat tissue and plasma of capacitor manufacture workers. Their results — published in the February TOXICOLOGY AND APPLIED PHARMACOLOGY — show that even certain PCBs with relatively lower numbers of chlorine atoms do persist in the environment and accumulate in living organisms. (The hydrocarbon rings of PCBs have spaces for one to 10 chlorine atoms.) "There is a dictum in the field that the higher chlorinated PCBs are the persistent ones," Wolff explained. "Apparently, it doesn't matter how many chlorine atoms the compound has," she said; "it depends where they are on the ring."

Probing even more specific relationships between structure and activity is a group under the direction of Safe. This group has used capillary glass columns to ensure pure PCB components that in turn are used in the search for structural definitions of PCB toxicity.

In this case, a PCB is considered toxic if, when placed in cell cultures, it can increase the concentration of and "turn on" AHH — an enzyme found in most organs of the body. "Inducing AHH previously has been associated with enhancing the carcinogenicity of other chemicals," Safe reported. Therefore, the AHH induction test is "a biochemical screen" for potential toxic activity, he said.

Thus far, Safe and colleagues have found that the most potent AHH inducers among PCBs have chlorine atoms at both "para" positions and at least two "meta" positions (see the diagram above). The occupied "meta" positions do not need to be on the same "phenyl" ring of the biphenyl compounds. The four PCBs that meet these structural requirements (shown in the diagram above) are presumed to be the most toxic members of their chemical class. Fortunately, they are rarely found in commercial PCB mixtures and human tissues, Safe reported.

However, he and colleagues have discovered that chlorine added at one or two "ortho" positions of the "presumed toxic four" may tend to diminish but not eliminate the AHH-inducing activity. Some of the PCBs that meet these structural requirements are present in commercial mixtures and human tissues. Wolff and colleagues found several in their blood and fat tissue samples of capacitor manufacture workers; Safe and colleagues have found several in samples of breast milk.

The discovery of these AHH inducers in both occupationally exposed workers and in breast milk samples is especially significant in light of the symposium report by Mary Jo Vodicnik of the Medical College of Wisconsin. Vodicnik and colleagues have found that ^{14}C-labeled PCB-treated mice eliminated "essentially their entire body burden of the chemical to offspring" by nursing. These findings raise the question of whether mothers occupationally exposed to PCBs should nurse their children.

It was hoped by several meeting attendees — representatives of companies where employees once were exposed to PCBs, for example — that such questions would be addressed in the final session on risk assessment. But some participants already had left — Kimbrough, annoyed with the way data were being interpreted, said she saw no reason to stay for a risk assessment discussion — and the final discussion period consisted largely of exchanges between angry attorney Warren and an employee of a firm that has consulted for the Chemical Manufacturers Association. Chairman Otto Hutzinger of the University of Amsterdam in the Netherlands later would write in his summary document of the meeting, "No meaningful and scientifically sound discussion took place on [risk assessment] during the symposium."

Addressing that issue after the meeting, Safe told SCIENCE NEWS, "I don't think we really understand enough about what they [PCBs] are doing." Kimbrough agreed and added that specific issues such as the potential carcinogenicity of PCBs cannot be resolved until a sufficient latency period has passed.

"I know it's a typical scientist thing to say that 'more work needs to be done,'" Safe said, "but ... more work needs to be done." □