another tortuous cancellation proceeding. But EPA has cited heptachlor as an alternative—though not a recommended one—that will be available next year to many farmers who have depended on aldrin and dieldrin. Early suspension of the production of this pesticide is therefore unlikely.

Quite aside from the availability of heptachlor, Train concluded that aldrin and dieldrin could be eliminated without major losses on the part of corn growers or other farmers—a finding that has been derided by Shell and its devoted ally, the U.S. Department of Agriculture (USDA). The 9.7 million pounds of aldrin used this past crop season was just half the amount used as recently as 1966, and aldrin is applied now on only about 8 percent of the nation's cotton acreage. A variety of factors have contributed to aldrin's decline—the development of resistance in some pests, changes in cultural practices, the use of post-emergent baits and sprays that kill the mature insect after it leaves the soil, and so forth. The EPA administrator concluded that neither from the standpoint of the farm economy as a whole nor from that of individual farmers was there much to fear from a suspension of aldrin and dieldrin production.

In truth, aldrin and dieldrin never should have been registered without extensive prior testing of animals exposed to low, nontoxic dosages. The only such testing required was that done ex post facto for the setting of tolerances for residues in food—tolerances that have never been set, although the matter has been pending ever since 1957, first before the FDA, then before EPA. According to John C. Kolojeski of the EPA general counsel's office, the test results that were forthcoming from Shell—beginning in the late 1960's—remained virtually unnoticed until the cancellation proceeding in 1971. Some within EPA simply regard the tolerance-setting program as a bad joke.

To make matters worse, EDF, which has spent nearly $300,000 in its fight against DDT and aldrin and dieldrin over the past several years, is operating at a deficit and will face a dilemma should it become necessary to campaign for the suspension of heptachlor and chlordane. Such a commitment might be made only at some sacrifice of the organization's other objectives, such as reform of energy policy and public works programs.

For some time now, there has been a deepening awareness within EPA and among its allies that existing laws for the regulation of pesticides and industrial chemicals must be supplemented by a Toxic Substances Control Act to require chemical companies to do adequate testing of new compounds *before* they are registered for use. Although time is rapidly running out in this Congress, legislation that could establish such a requirement is far enough along to become law this year—given sufficient priority. With or without such a law, the government clearly has an obligation to see that adequate test programs are conducted for all persistent pesticides. NCI will soon organize a new interagency task force that will have this as one of its objectives. In view of the millions of pounds of these chemicals that already have gone into the environment, the NCI knows the hour is late.—LUTHER J. CARTER

Cancer and the Environment (II): Groping for New Remedies

Arduous as the fight over aldrin and dieldrin has been, turning thumbs down on these two pesticides was a relatively easy decision for the Environmental Protection Agency to make compared with others the agency now faces. For the EPA has only begun to grapple with the larger problems of regulating man-made carcinogens, some of which —like vinyl chloride, the raw material of plastic products as diverse as floor tiles and phonograph records—are used so pervasively, in so many ways, as to be an almost inescapable part of American life.

Aldrin and dieldrin, after all, were used in only one way—as pesticides—and on a limited number of crops. Substitutes existed, although their adequacy is in debate. But at least the EPA was able to conclude intuitively, if not by precise calculation, that any risk of cancer these two pesticides might pose thoroughly overwhelmed their limited benefits. Hence the simple remedy of an outright ban.

But for hundreds of other known or suspected carcinogens that crop up in industrial processes and consumer products, an outright ban may not be practical. Accordingly, the EPA is moving tentatively toward setting environmental standards that will limit, but not eliminate, the general public's exposure to some of the more potent and clearly established carcinogens. In a pioneering step last December, the EPA proposed a water effluent standard for benzidine, a chemical widely used by the dye industry and linked unmistakably to bladder cancer among workers more than a decade ago. And by next spring the agency expects to issue an emission standard for vinyl chloride, an industrial gas used by the billions of pounds that was thought to be biologically "benign" until it was linked last January to 21 fatal cases of angiosarcoma, a rare liver cancer, among workers subjected to large repeated exposures.

Last month the EPA estimated that 200 million pounds of vinyl chloride are lost to the environment each year in the process of converting it to polyvinyl chloride plastic (about 5 billion pounds of PVC plastics were produced in the United States last year). Still more vinyl chloride was spread about as a propellant in aerosol cans of hair spray, pesticides, and other consumer products until last spring, when such uses were banned by the EPA and the Food and Drug Administration. The EPA, however, appears to be giving no thought to an absolute ban on vinyl chloride emissions, a move the plastics industry says would cost the nation $90 billion in industrial output and sacrifice 2.2 million jobs.

In trying to set standards for environmental carcinogens, the EPA finds itself in the difficult position of deciding, in effect, what number of human cancer cases constitutes an "acceptable risk" —a potential toll presumably balanced by a carcinogen's economic benefits to society. In the case of benzidine and

vinyl chloride, and probably in the case of most other carcinogens the government may eventually decide to regulate, this momentous decision is made all the more difficult by having to translate skimpy experiments on animals into a standard that will hold up in court.

The formidable technical problems of this translation process were the subject of a spirited meeting organized last month by the National Institute of Environmental Health Sciences. Convened at a seaside resort 150 miles from the North Carolina headquarters of the NIEHS, the meeting was in some ways an informal summit conference for three dozen statisticians, cancer specialists, toxicologists, and epidemiologists from the United States and Britain. The conference coincided with the EPA's final decision on aldrin and dieldrin, but foremost on the participants' minds were the more complex technical and regulatory issues raised by vinyl chloride and a host of other alleged and confirmed industrial carcinogens. (Between 60 and 90 percent of all human malignancies are believed to be caused by environmental factors, ranging from ultraviolet light to synthetic chemicals.)

"The chemical industry has really only grown up in the last 20 or 30 years," NIEHS director David Rall observed. "We have an enormous number of new, unique synthetic chemicals, and with a latency period of 20 or 30 years [before the appearance of malignancies] there is little reason to be confident that the dimensions of the problem have been revealed.

"Society has largely ignored the problem of delayed, irreversible effects of chemicals, swept it under the rug. We are still terribly uncertain about the risk these chemicals entail for the population in general and for individual members of the population. There is still no clear way of determining this risk."

The major sticking point for limits on carcinogens is summed up in one word: extrapolation. It's actually a two-part problem. In the first place, virtually all the information available about the potency of chemical carcinogens comes from experiments with rats, mice, and other conventional test animals that are subjected to doses much higher than humans usually experience. Higher test doses mean swifter results with fewer animals, and at lower cost. But how should dose-and-effect relationships seen at these higher levels be extrapolated downward to levels comparable to human exposure?

Over the last 15 years biostatisticians have developed and refined an assortment of mathematical models for doing this. But each model has its own advantages and disadvantages, there are disagreements over how accurately they reflect biological reality, and at lower and lower doses their predictions of cancer incidence tend to diverge.

The second difficulty might be called the "mouse-to-man problem." Useful as they are, mice are not little men. In many ways yet to be quantified, their metabolism differs dramatically from that of humans, a point that industry traditionally has made in arguing against the significance of animal tests for carcinogenicity. The uncertain differences in species sensitivity work both ways, however, and it can be argued no less effectively that men are more susceptible than mice to carcinogens, if only because the greater variety of human cell types provides more targets of opportunity.

In any case, there is, as Rall expressed it, a "massive lack of proper knowledge" standing between animal experiments and environmental standards. But the challenge is "how do we set standards on the basis of what we know? And then how do we improve our knowledge?"

Three days of talks in a room only slightly filled with smoke produced no consensus on the best method for estimating the "risk" or incidence of cancer from low doses of carcinogens. But there was general agreement on several points of relevance to the regulators:

► Chronic exposure to carcinogens should be assumed to pose some risk of cancer in a large population, no matter how low the "dose" allowed by the standards.

► Some carcinogens, like the chlorinated pesticides, can be avoided and should be. But for others, such as vinyl chloride, the only practical policy may be to limit their release to the environment and, if necessary, their production and use.

"Obviously we should avoid these things when we can," said Umberto Saffiotti, the National Cancer Institute's associate director for carcinogenesis. "But in those cases where we cannot remove them, or where well documented benefits exist, we must set limits so as to balance risks and benefits."

► Despite the imperfections of extrapolation models, regulatory agencies should begin to use them in setting standards on environmental carcinogens. The models can at least indicate the incidence of cancer that may result from exposures allowed under a standard, and thereby provide a measure of the risk against which a chemical's benefits may be weighed.

The EPA, in fact, is taking this risk-prediction approach in developing its standards for benzidine and, to a lesser extent, for vinyl chloride.

For benzidine, officials in the agency's Office of Toxic Substances began by selecting a risk that seemed acceptable—a chance of one in a million that people drinking water contaminated with benzidine would develop cancer—and then calculated a "dose" or exposure limit that would pose a risk of cancer no greater than this. The EPA based its calculations on small-scale rat experiments, done in the late 1950's, that showed benzidine to be a carcinogen in mammals. To account for the differences between rats and men, and for a number of other imponderables, the EPA threw in a safety factor of 100 and ended up with a standard that—if formally adopted—would allow dye manufacturers to dispose of no more than a pound of benzidine a day in a moderately large river flowing at 10,000 cubic feet per second.

Last summer some EPA officials urged the agency to take the same course in setting an emission standard for vinyl chloride. But the EPA has since been unable to decided how large a "mouse-to-man" safety factor to include in its standard and has therefore retreated to a more conventional approach. The EPA is now looking toward the "best available control technology" as the basis for its standard, an approach that portends no great economic hardships for the plastics industry, but one which EPA officials believe will reduce emissions by 75 to 90 percent.

The next step will be to estimate the cancer risk associated with the "best available technology" for persons living near the 15 plants making vinyl chloride and the 37 others using the gas to make polyvinyl chloride resin.

"If you find that the risk of using the best technology is unreasonably high," one EPA official explained, then you're faced with several options, such as developing better technology, finding substitutes, shutting plants down, or some combination of these."

It would have been preferable, of course, to discover the drawbacks of vinyl chloride in the 1950's, before polyvinyl chloride plastics became the basis for 1 percent of the gross national product.

But the belated discovery of carcin-

ogens in industrial processes and consumer products is likely to be a recurrent problem until the thousands of industrial chemicals now in use can be tested for safety and until some systematic way is found to screen hundreds of new chemicals synthesized each year.

According to the Chemical Abstracts Service, about 1.8 million different chemicals have been formulated. The list grows by about 250,000 new compounds annually, and 300 to 500 of these go into major commercial use each year. A great many of these are new synthetic organic chemicals, more than 9000 of which are currently produced in amounts greater than half

Briefing

Justice Joins in Appeal on Taconite Pollution

The U.S. Department of Justice, after deliberating several weeks, has now joined Minnesota, Wisconsin, and Michigan in asking the Supreme Court to allow District Judge Miles W. Lord to close the taconite plant on Lake Superior that is contaminating public water supplies with possibly carcinogenic, asbestos-like fibers (*Science*, 4 October).

After a 139-day trial, Judge Lord last April ordered the Reserve Mining Company to close the taconite plant, holding that the 200,000 people who live along the western arm of Lake Superior were threatened by the plant's daily discharge of 67,000 tons of tailings into the lake and 100 tons of particulates into the air. The plant had been shut down for only 2 days, however, when a three-judge panel of the U.S. Court of Appeals for the Eighth Circuit stayed the district court order. The panel had concluded that Judge Lord's finding of a compelling public health hazard probably was not supported by the evidence. This gave rise to speculation that the appeals court would not accept any form of proof less definitive than a "body count," and that a dangerous precedent for future environmental health cases might have been set.

The three states and the environmental groups who were suing Reserve Mining then made their first appeal to the Supreme Court, only to have it rejected by an eight to one vote (Justice Douglas dissenting). The Justice Department did not take part in that appeal. The case continued to drag along, leading to the new round of appeals by the states, with Justice now joining in.

In mid-July, Russell W. Peterson, chairman of the Council on Environmental Quality, had urged Justice to "aggressively pursue all means to eliminate this unwarranted public health menace." Then, in early September, Assistant Attorney General Wallace Johnson, in charge of Justice's land and natural resources division, recommended to Solicitor General Robert H. Bork that the department join in the new appeal. Bork, known for his conservatism and his dismissal of Eliot Richardson and William Ruckelshaus in the "Saturday night massacre," took the matter under advisement.

Prior to his decision, Bork came under growing pressure. Jutice Harry Blackmun, a Minnesotan formerly on the 8th circuit court, asked the department to take a position on the appeal. Also, members of the Michigan congressional delegation were calling on Justice to lend its weight to the states' appeal for Supreme Court review.—L.J.C.

Air Force Tries Again On Agent Orange

The U.S. Air Force is trying to revive a moribund plan to market its stocks of the herbicide known as Agent Orange for use by farmers in the United States and possibly abroad. Past Air Force attempts to give away or sell the 2.3 million gallons of the herbicide, which was withdrawn from use in South Vietnam in 1970, have run into opposition because one compound in the herbicide, 2,4,5-T, contains a teratogenic impurity known as dioxin which is one of the most harmful chemicals known (*Science*, 6 April 1973).

The Air Force has been meeting with the Registration Division of the Office of Pesticide Programs of the Environmental Protection Agency (EPA) to find out how it can register its stockpile, which is stored on Johnston Island in the mid-Pacific, and at Gulfport, Mississippi. Registration by the EPA is required by law before herbicides can be marketed. In a letter sent to the EPA before the talks, Assistant Secretary of the Air Force Frank A. Shrontz announced the Air Force's intention to have the stocks registered by the EPA for domestic use, and said that their market value could be as much as $80 million, although previous estimates put their worth at $15 million.

When the Air Force first tried to register the stockpile last year, the EPA turned back the application because cancellation proceedings were under way for 2,4,5-T. However, in a move which brought objections from environmentalists, the EPA this summer ended those proceedings and thus opened the way for anyone who owns or makes products containing 2,4,5-T to register and market them. The EPA permits the use of these products on rangelands, forests, rights-of-way, and rice crops, but all other uses are prohibited.

Part of the impetus for the original Air Force attempt to get the herbicide registered was that some business entrepreneurs had offered to market the material in Latin America. The plan was killed when the EPA decided not to permit the material to be registered. However, if the EPA allows registration now, the Air Force will be able to proceed with foreign as well as domestic sales.

But the problem of what to do with the huge stockpile of what was once considered a military weapon will remain knotty at best, and at worst, insoluble. For one thing, to register the stockpile, EPA will have to come up with a scientifically defensible standard for dioxin levels in the herbicide—which will not be easy in light of recent findings that dioxin is even more teratogenic than previously believed.—D.S.

Shuttle Pollution Study Sought

Senator William Proxmire (D–Wis.) has asked the National Academy of Sciences—National Academy of Engineering (NAS-NAE) to do a further study of the environmental impact of the space shuttle, with emphasis on the effects of its solid rocket propellants on

a ton; by 1968 production of synthetic organic chemicals (including vinyl chloride) had reached 120 billion pounds a year, an increase of more than 160 percent in a single decade.

Umberto Saffiotti, of the National Cancer Institute (NCI), estimates that of all the nearly 2 million chemicals known, no more than 6000 have been tested for carcinogenicity. Of this number, he believes, only half have been adequately tested. Altogether, about 1000 have shown some sign of being carcinogenic. And out of the thousand no more than a few hundred have been "clearly established" as carcinogens.

The NCI, working mainly through outside contracts, manages to screen about 200 chemicals a year for carcinogenicity. But as yet there is no systematic way to screen new chemicals before they become part of industrial processes and escape to the environment; indeed, federal regulators have no way of knowing which of the quarter million new substances synthesized each year will go into production.

It happens that the House and Senate have passed legislation that would require the chemical industry to test new chemicals and notify the EPA before producing them in commercial amounts. The Toxic Substances Control Act of 1973 would empower the EPA to set up a system of pre-market screening of new chemicals before they became pollutants, and the Act would give the EPA administrator new powers to restrict or prohibit production of dangerous new substances if laws already on the books did not suffice.

This legislation, however, has been stalled in a House-Senate conference committee for more than a year, partly because committee members have been preoccupied with energy legislation and mostly because they have been unable to resolve wide differences between the House and Senate versions.

The major disagreement involves the number of chemicals to be screened prior to production. Both House and Senate versions require the EPA to list classes of chemicals considered to be dangerous; new members of these classes could not be produced until a company submits data to the EPA (90 days before production begins) demonstrating their safety. The difference concerns chemicals that are *not* specifically listed by the EPA as dangerous. The Senate bill would require companies to submit a notice of impending production—though not test data—for all new chemicals, thus giving EPA a chance to determine whether testing is needed. The House version requires no such notification.

In addition, the two versions differ sharply on the matter of jurisdiction. The Senate bill would let the EPA use the new Act's powers at its discretion; the House bill downgrades the legislation to a last resort supplement to a dozen other laws already on the books, from the Atomic Energy Act to the Egg Products Inspection Act.

Not surprisingly the chemical industry vigorously opposed passage of any new toxic substances controls (although the American Chemical Society, most of whose members are in industry, supported it). Environmental and consumer groups have lined up behind the legislation, and so has an impressive list of health researchers. Among them is Irving J. Selikoff of New York's Mount Sinai School of Medicine, who told a Senate subcommittee in August that the vinyl chloride disaster might have been prevented had such legislation been in effect 20 years ago.

"More than a Prayer"

Amid renewed interest in environmental carcinogens, the staffs of the House and Senate conferees have started negotiating again. Adjournment is fast approaching, but one Senate staffer predicts that the Toxic Substances Control Act "might have more than a prayer" of passage in this session.

Even with pre-market testing for new chemicals, however, a good many man-made carcinogens are likely to slip through the net. Some, which probably act directly on the DNA in human cells to produce cancer, are relatively easy to detect. But others become carcinogens only after they are metabolized in animals (and metabolism varies greatly not only from mice to men but among individual humans as well). Still other chemicals are not carcinogens themselves but enhance the potency of substances that are.

And even with mountains of new information from the chemical industry there is no guarantee that government will act to regulate the spread of a carcinogen before it is proved harmful to humans beyond all doubt. Vinyl chloride, again, is a case in point. The first report that it had caused cancer in laboratory animals (liver tumors in mice) appeared in the May 1971 issue of *Cancer Research*, nearly 2½ years before the first human malignancies were found and reported.

Saffiotti notes that animal experiments in recent years have produced similarly worrisome evidence about dozens of other chemicals. Says Saffiotti: "The flags are up and waving for anyone who walks by."

—ROBERT GILLETTE

Briefing

the upper atmosphere. The senator is particularly concerned about the destructive effects of chlorine on ozone, the gas that protects the earth from the sun's ultraviolet radiation.

Proxmire, chairman of the appropriations subcommittee that deals with the National Aeronautics and Space Administration, has never felt much affinity for the space shuttle, which he considers a waste of money. But in this case few would disagree with him that not enough is known about the environmental effects of the propellants. The NAS study would complement work being done by NASA, which has sunk $2 million in the past year into studying shuttle effects on the environment. The agency is spending a total of $5 million a year on stratospheric pollution research.

The study of stratospheric pollution is a very young undertaking. Indeed, 2 years ago when NASA filed its environmental impact statement on the shuttle, the effects of chlorine on ozone were not deemed important, says a NASA spokesman. Now scientists are finding that the composition of the stratosphere is less homogeneous and more complex and variable than had been believed a few years ago. All that really is known is that when exhaust chemicals are unleashed into the stratosphere they are trapped there indefinitely.

The climatic impact assessment program committee of the NAS-NAE is currently completing a study for the Department of Transportation, which is an assessment of the state of knowledge on the potential effects of supersonic transports, high-altitude aircraft, and high-flying subsonic craft on the stratosphere. This committee presumably could move on to questions of shuttle pollution after it hands in its report in December. A Proxmire staffer says the Academy officials have informally indicated the study will be performed. NAS President Philip Handler has said that the request is under consideration.—C.H.