hydrogen-oxygen. The two oxygens are located about 2.3 angstroms apart with the hydrogen centered between them at about 1.15 angstroms from each. The unit is held together by so-called hydrogen bonds that are much stronger than those in ordinary water, and this accounts for the high stability of the substance. The hydrogen-bond energy of polywater is between 60 and 100 kilocalories per water formula unit, compared with only 4 kilocalories for ordinary water. The three-atom elements, say the Maryland-NBS chemists, can be arranged either into hexagons or into complicated branched chains to form the polymer.

The possibility of forming such structures leads to the suggestion that other substances containing oxygen-hydrogen groups may form similar polymers. Condensation of anomalous acetone, methanol and acetic acid has been reported from Russia. At Maryland, says Dr. Lippincott, "we have prepared and characterized some other materials." But this part of the work is still in a preliminary stage.

"It seems unbelievable," says Dr. Lippincott, "that water like this hasn't been found before. For two or three hundred years it was never picked up." But he points out that the chemical literature of the past shows indications that some researchers may have come upon polywater without realizing what it was.

"Prof. [Walter A.] Patrick of Johns Hopkins," says Dr. Lippincott, "said that the vapor pressure of water in capillaries was not right. Prof. [J. Leon] Shereshefsky at Howard came out with the flat statement that water in capillaries didn't obey the laws."

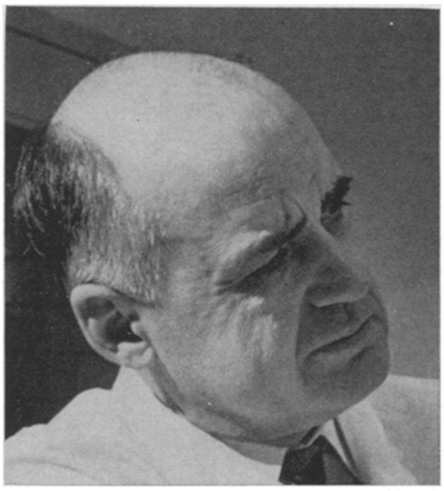
But now that polywater has definitely been identified, says Dr. Lippincott, "the whole concept is going to shake things up." He believes that it probably does exist in nature. If it does, it may play a role in many biological and geophysical processes. It may have to do with the nucleation of water droplets in rain, snow and fog. It may be important in accumulation and adhesion of ice, and it may play a role in the formation and structure of clays.

"Biologists," says Dr. Lippincott, "will want to see whether it has a function in life systems." Phenomena involving membranes and the biology and chemistry that take place at interfaces between different substances are especially interesting, he says.

Quantities of polywater so far made in laboratories are measured in millionths of a liter, but sizeable quantities can be made, thinks Dr. Lippincott. "It's a question of doing the right tricks," he says, "and there would be a lot of it." ◇

INTERFERON

Hard times for a panacea



Merck

Hilleman: Inducers are the answer.

Interferon, once hailed as a panacea for virus diseases from hepatitis to the common cold and possibly even cancer, has fallen from grace in some scientists' eyes. And it is a focus of controversy among those who continue to believe in its future.

When, in 1957, British researchers Alick Isaacs and Jean Lindenmann identified interferon as the body's natural defense against viruses, scientists throughout the world predicted that by giving or inducing natural production of this protein they could immunize persons against invading viruses.

The interferon antiviral system seems to be ubiquitous in animals, as it has also been demonstrated in birds, reptiles and fish. Perhaps it even operates in plants. A malarial parasite of rats was found to produce interferon last year (SN: 10/19, p. 391).

A number of research programs were launched. European researchers generally aimed at finding ways of using interferon itself, while scientists in the United States, contending that the costs and difficulties in obtaining natural interferon were prohibitive, tended to concentrate on a search for materials that would stimulate the protein's natural manufacture in the body. Two years ago, Dr. Maurice Hilleman of the Merck Institute for Therapeutic Research in West Point, Pa., announced that a synthetic chemical called poly I:C, a double-stranded material that mimics the RNA core of many infectious viruses, effectively induces interferon production (SN: 8/17/67, p. 173). "Our hopes are especially high for preventing common colds," he said then, and still maintains his optimism in spite of evidence that poly I:C is toxic. "Toxicity is minimal," he says.

Another interferon devotee, Dr. Samuel Baron of the National Institutes of Health in Bethesda, Md., declared, "Dr. Hilleman's work could be the breakthrough we've been waiting for," and went on this year to show that interferon, induced by poly I:C, cures rabbits of a potentially fatal eye disease caused by herpes simplex viruses (SN: 1/18, p. 60). In still other studies with poly I:C, Dr. Hilton Levy and co-workers, also of NIH, report that the chemical causes tumors to regress, though the mechanism of action, he suggests, is not related to its ability to induce interferon. Within months he plans to initiate clinical trials of poly I:C on terminal cancer patients at NIH.

At Stanford University, Drs. Thomas C. Merigan and Erik DeClercq have taken an architectural approach to inducers, suggesting that by modifying the molecular structure of poly I:C or other double-stranded inducers including Pyran copolymer, they can derive a less toxic material. By substituting sulfur atoms for oxygen atoms, they produce a compound that they believe is less toxic, less susceptible to degradation by enzymes in the body and more potent in inducing a prolonged interferon response. Trials in patients with serious infections, including hepatitis and encephalitis, are under consideration.

But for every hopeful view, there is another that is either entirely negative or somewhere in the middle. At an international meeting of the New York Academy of Sciences the arguments surfaced as authorities debated interferon's future.

From the beginning, interferon studies have yielded conflicting results, partly due to unpurified preparations.

Dr. Ernest C. Herrmann Jr. of the Mayo Clinic says, "I don't think interferon can be made practical," and calls Dr. Hilleman's decision to invest close to a million dollars of Merck money in poly I:C and other inducers a "ridiculous mistake." And Dr. Herbert Kaufman of the University of Florida College of Medicine in Gainesville points out that the interferon system suffers from fatique if it is stimulated continually. "The study of interferon has been disappointing. It is relatively unpromising in therapy. Evidence that the interferon system fatigues suggests it is unlikely we will be able to stimulate it continually."

Dr. Warren Stinebring of the University of Vermont in Burlington is among those who hold that poly I:C's effectiveness is, in fact, dependent on its toxicity. Interferon, he believes, is preformed and stored in cells, ready to be released if the cells are broken by some agent or event.

"Poly I:C," he says, "sequesters in the phagocytic cells of the reticuloendothelial system and, by damaging those cells, causes them to release interferon along with other cellular components."

Dr. Hilleman, on the other hand, believes interferon is produced when the system is stimulated and that storage accounts for only small quantities of the protein. He argues that the idea that effectiveness and toxicity of inducers is a single mechanism is "nonsense."

The focus of European work is England, where scientists on the 10-year-old Scientific Committee on Interferon are planning new trials of exogenous interferon—that produced elsewhere and injected—in man. "Past studies in man," says Dr. Norman B. Finter of Imperial Chemical Industries, Ltd., "have been equivocal. Animal studies have been much clearer. We will go ahead in three promising areas: eye infections, respiratory infections and acute viral and tumor diseases."

"Dr. Finter's human trials using exogenous interferon should give us a clear understanding of the true interferon mechanism," Dr. Stinebring predicts. Artificial stimulation of the system in man, he explains, can lead to dubious results because it is difficult to tell whether the interferon, the inducer or some other system is at work. He also postulates that producing human interferon in a culture system employing human diploid cells (cells that contain two sets of chromosomes and replicate indefinitely) is a promising route toward mass production.

Some work is going on along these lines, he says, but results will probably come from foreign work.

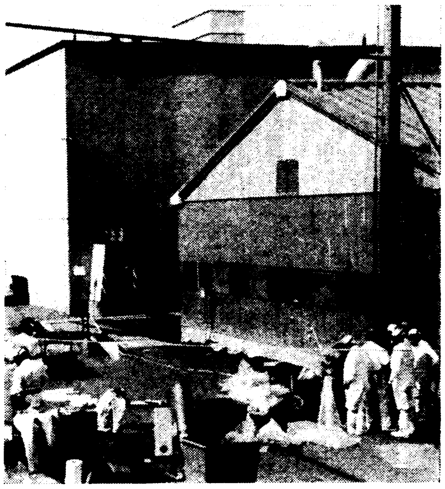
The NIH Division of Biologic Standards opposes use of this cell system on grounds that it may contain unidentifiable human viruses or that as the cells replicate in culture, harmful mutations may occur. Dr. Stinebring, on the other hand, argues that with available techniques, purification of the interferon, which would be induced in culture by introduction of an inactivated virus, presents no problem and no threat.

The British get their human interferon from a Finnish scientist, Dr. Kari Cantell of the State Serum Institute in Helsinki. Dr. Cantell produces it from white blood cells by a method that yields sufficient quantities for research but is unlikely to ever become a production line operation, because it would require millions of pints of human blood.

The pure interferon tests should, however, reveal much about the action of the substance itself, and whether the results are due to it or to an inducer.

NUCLEAR SAFETY

Plutonium fire raises questions



Dow

After the fire: Detoxification needed.

On May 11, fire broke out in the Atomic Energy Commission's nuclear weapons plant at Rocky Flats, Colo., about 12 miles from Boulder. The blaze, which went largely unnoticed until a Senate hearing focused attention on it, is estimated to have cost about $50 million, the worst fire in the history of the AEC.

An AEC investigating team was sent in to check for radioactive contamination and found that plutonium contamination was confined to the damaged building.

But a group of scientists—representing the year-old Colorado Committee for Environmental Information, and headed by Dr. H. Peter Metzger of Ball Brothers Research Corp., Boulder—is still not satisfied that the area is safe. They call for new measurements.

For one thing, the committee is worried that plutonium could have been carried a good distance downwind by a smoke plume. Although the AEC contends that there was no radioactive smoke, the committee wonders how a $50 million fire—not including $20 million in burned plutonium—could fail to produce contaminated smoke. A second reason for the new measurements is that plutonium is difficult to measure. Some contamination, it feels, could have escaped detection.

To allay fears, the scientists drew up and last week submitted a list of written questions that the AEC has agreed to answer in writing. The answers are expected within a month.

The questions reflect two main areas of concern. The scientists are uneasy about whether the radioactivity was confined to the one building and would like that matter finally cleared up. Their concern stems from the fact that plutonium has a half life of 24,400 years, which means that if there was any radiation leakage outside the plant, it would in effect constitute a permanent contamination.

The group is also worried about day-to-day operations. The plant will be back in operation in a year, and they would like to be sure that no radioactivity does leak out. Such leakage could threaten residents of Boulder and Denver.

The Colorado scientists will make their own evaluation of the AEC answers and deliver it to the AEC and the Dow Chemical Company, which operated the plant.

Because the plant had a unique function, the fire has dealt a temporary blow to U.S. capacity to produce nuclear warheads. In the production of nuclear weapons, each plant in a chain performs a specific function and then sends the weapon to another facility for additional processing. Although the fire knocked out a vital link in nuclear warhead production, the plant will be restored in time to meet its commitments.

Beyond the military implications, the fire raises another question: how safe is the nuclear industry in general and plutonium processing in particular?

As far as the Rocky Flats incident is concerned, Dr. Manson Benedict, professor of nuclear engineering at Massachusetts Institute of Technology, says that "there is no relationship between that unfortunate fire and power plants." He points out that the material used at Rocky Flats is not the same material used as fuel in nuclear reactors. Pure plutonium metal, which is highly flammable, is used for nuclear weapons while today's reactors employ nonflammable plutonium oxide.

Dr. Ralph E. Lapp, a nuclear consultant, thinks, however, that the Rocky Flats fire "calls for a re-evaluation of safety procedures, plant construction and plant operation."

Questions Dr. Lapp, "What happened to their firebreaks? I would think they would want to sectionalize production facilities so you don't get this destruction."

Dr. Metzger is more outspoken on the safety issue. He says that as a result of the incident the AEC, which owns an excellent safety record, has been forced to admit that it had more than one fire a month at the installation, although they have been quickly extinguished. "It's not the impressive safety record they've talked about," he contends, adding, "plutonium is far more difficult to manage than anyone thought."

Dr. Metzger is worried that small fires over a period of years could build up deadly accumulations of radioactivity. As far as he's concerned, the whole subject of nuclear safety is finally being revealed.