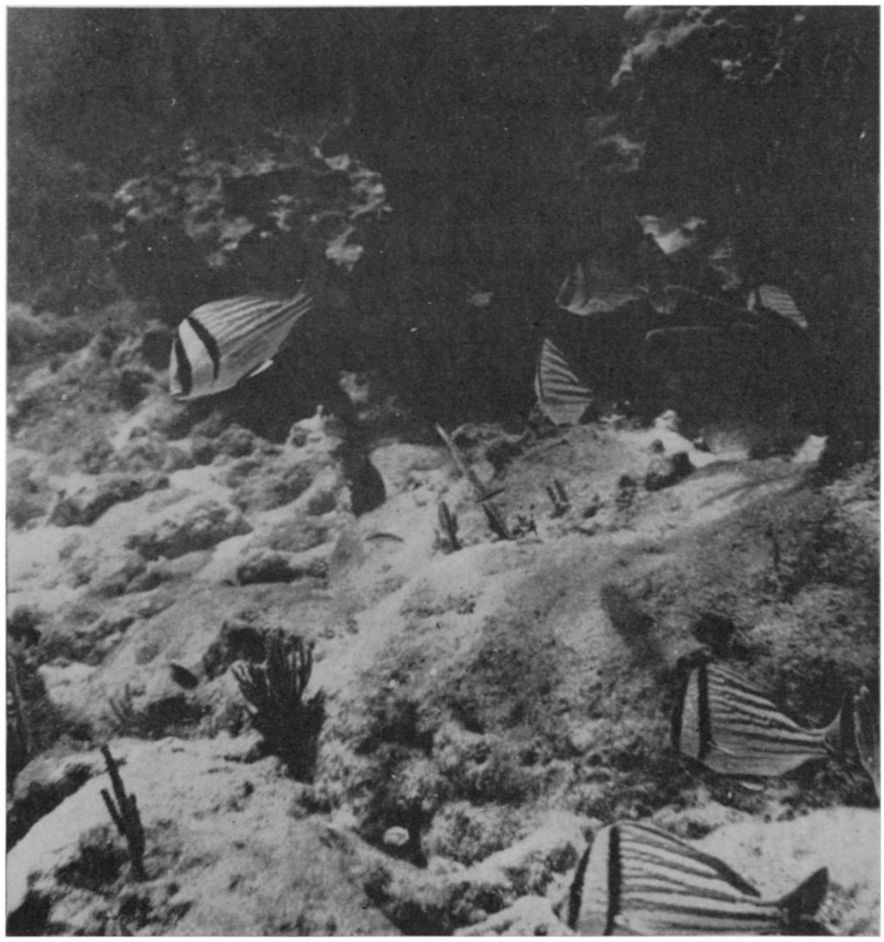
Drugs from the Oceans

A new medicine chest lures researchers, but exploitation is slow.



COAST AND GEODETIC SURVEY

Locked in the teeming myriads of sea creatures: new drugs for men.

Of the vast array of drugs on which mankind depends for cure or comfort, most come directly or indirectly from natural sources such as plants or molds.

Aspirin, quinine, digitalis and the antibiotics barely begin the long list, yet it has been estimated that only some three percent of the plants on earth have been scientifically evaluated for their medicinal potential.

And what may prove to be an even richer source of raw material for new drugs—the 71 percent of the world under water—has been almost entirely overlooked. Those relatively few scientists who have taken an interest in the possibilities of drugs from the sea note that fully four-fifths of earth's animal life—more than 500,000 species—lives in or on the sea.

A sign of the awakening interest in the potential of this enormous resource was a meeting of more than 200 oceanographers, pharmacologists and chemists last week at the University of Rhode Island for the first Conference on Drugs from the Sea. The conference was sponsored by the Marine Technology Society, the University's College of Pharmacy and the American Institute of Biological Sciences.

Marine fauna and flora, scientists noted, have been found to produce a wide variety of toxins (poisons), antibiotics and other potentially medically useful compounds. No more than a handful of these, however, have yet made the transition from laboratory curiosity to the druggist's shelf. (These include an antibiotic, cephalothin, found in a Mediterranean fungus, and an agent against roundworms taken from an algae.)

Besides the general lack of money for such research—whether basic or applied—the work has been hampered tremendously by the difficulty of collecting large enough samples to work with.

Desirable agents may be found only in tiny quantities in a species of sea life—and huge amounts of the source may be needed to produce enough for experimentation. Even if sufficient is found for the laboratory, the problem of assembling enough of a given drug for commercial use is enormous. Without the promise of supplies, drug companies are unlikely to show much interest.

The slow pace of work on drugs from the sea, according to Dr. Heber Youngken Jr., the University's dean of pharmacy, is "due also to our lack of sufficient knowledge of the marine ecology of the oceans and the dearth of enough trained personnel."

While marine biologists have detected many biologically active chemical compounds in fish, shellfish, seaweed and marine microorganisms, the work of identifying them chemically lags behind. Only a handful of the compounds have been reproduced in the laboratory.

A typical project, a search for antibiotic and antitumor compounds in clams, is being carried out at the William F. Clapp laboratories of Battelle Memorial Institute in Duxbury, Mass. There, Drs. Robert E. Hillman and Paul F. Nace have been systematically pickling and mashing up various parts of clams taken from the bay in front of their laboratory and sending them to Battelle in Columbus, Ohio, for further study.

Clam extracts, they and their Columbus colleagues have found, do occasionally inhibit the growth of bacteria and tumors. A key to this property in clams however, is the environment in which they are raised. Clams collected in winter or from polluted water show no antitumor activity, Dr. Hillman told the conference. "We are trying to learn

how to raise clams with a known amount of antitumor activity," he said.

Somewhat similar work concentrating on sponges is in progress at the Lamont Geological Observatory of Columbia University in Palisades, N.Y. There, Dr. Paul Burkholder and his wife, both biologists, are working with Dr. G. M. Sharma, a chemist, who has been able to determine the structure of two antibacterial compounds from the sponges and confirm the analysis by synthesizing them in his laboratory.

The Burkholders, who spent much of their careers searching for new drugs from land plants before they turned to the sea, report a large number of potential antibiotics from sponges but as yet the pharmaceutical industry has shown no interest.

Even with generous financial support and industry encouragement, "it's certainly not going to be easy," Dr. Youngken observes. "The ocean environment is a hostile one" that does not give up its secrets easily.

"But if we get just one drug that will cure a disease—for example heart disease or cancer—it will be worth all the effort in the world to get that." ◈

GOVERNMENT AND INDUSTRY

The Lions and the Lambs

The Food and Drug Administration and the drug industry it regulates have never been the best of friends. The 1962 Kefauver-Harris Drug Amendments and the highly publicized hearings that preceded them turned passive tolerance to active feuding. And since January 1965, when Dr. James L. Goddard took control of FDA, tensions between the two have grown steadily in spite of public protestations of friendly cooperation.

Meanwhile, the academic community has remained as aloof as it reasonably could.

Last week, however, the three factions drew in their daggers and met informally at a closed FDA-sponsored conference on evaluation of anticonvulsant drugs. FDA hopes it will be the beginning of a series of meetings of scientists from the agency, the drug industry and universities looking at the various sides of drug studies.

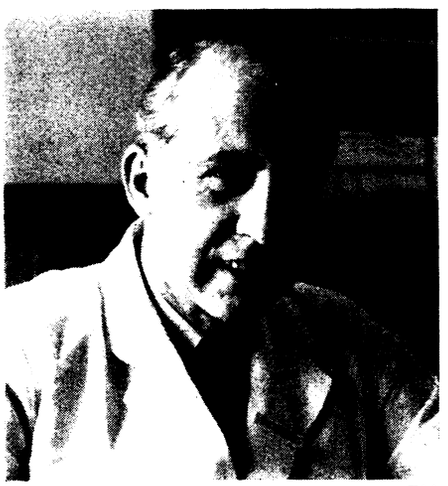
"This was the first such conference of its kind," says Dr. Arthur Wentz, extramural research adviser to the FDA. "The lions and the lambs got together in the same room very peacefully, and, so far, the response we've gotten from the participants has been very favorable."

The purpose of the conference, Dr. Wentz emphasizes, was to evaluate on-going drug studies, to see where more should be done and to spot areas where certain types of research may be unnecessary. Contrary to what everyone thinks, he said, the drug companies haven't got all the money in the world, adding that FDA should not force them into wasteful research spending.

On the other hand, Dr. Wentz says, some research isn't carried far enough. Anticonvulsant drugs, used primarily for epileptics, are a case in point. "Anticonvulsants may be good for other things," he says, "but research seems to have stopped short of exploring these possibilities."

Although the conference summary and recommendations will not be published for several months, Dr. Wentz points to four specific areas of friutful discussion.

He thinks the conference committee will recommend that researchers submit and FDA take note of the identity of subjects in human drug evaluations. Testing anticonvulsants for six months on patients who have seizures on the average of once a year doesn't prove much. If, on the other hand, a product is tested in patients who have 45 or 50 seizures a year and keeps them healthy, then there is evidence of efficacy.



FAA

Wentz: Scientists, not policemen.

The scientists also evaluated the use of electroencephalograms as a measure of drug activity. The concensus was that even though brain wave tracings have been used traditionally as an indication of anticonvulsant drug action, they are not an ideal test.

The kind of animals used in preclinical studies, the scientists agreed, is another area worthy of re-evaluation. Anticonvulsants are often tested in rabbits and cats, though neither species gets epilepsy naturally; it has to be artificially induced. Within the last year, Dr. Wentz says, scientists discovered that East African baboons often develop epilepsy naturally, making better animal models.

The fourth point of discussion concerned the controversial issue of risk versus benefits. Industry scientists, fearful that evidence of toxic effects will mean rejection of new drugs by FDA, sometimes abandon research projects at the first signs of danger. However, Dr. Wentz points out, just because a drug shows some toxicity in a few rats doesn't necessarily mean it will be toxic in humans. Furthermore, there are times when the advantages of a new drug are so great it should be approved in spite of potential side effects in a small percentage of persons.

Although these four probable recommendations will be made with specific reference to anticonvulsants, their greater importance lies in the pattern of scientific exchange they may set for further conferences which have been suggested covering a variety of drug classes including cardiorenal drugs, tranquilizers, and anti-inflammatory agents.

FDA, Dr. Wentz stresses, does not intend to prescribe minute details for drug studies. "We want to meet industry and university scientists as scientists, not as policemen."

Meanwhile, FDA-industry relations took on a more familiar coloration with the issuance by the Pharmaceutical Manufacturers Association of a 46-page legal brief attacking FDA's proposed regulations on advertising of prescription drugs. These are almost completely unworkable and of questionable legality, PMA said. Its members make some 90 percent of U.S. drugs. ◈

EPIDEMIOLOGY

Sick Worms: Well Child

The barefoot child with cheek of tan can get hookworm in the moist sands of the Northwest and Southeast U.S.

Future techniques of deliberately giving the child hookworms—weakened almost to death's door by exposure to radiation—appear to point to the elimination of this disease and many similar parasitical ailments.

Dr. F. G. Tromba of the Beltsville (Md.) Parasitological Laboratory of the U.S. Department of Agriculture is optimistic about the future of several vaccines against such parasites. He has recently returned from a meeting of scientists from 12 countries and two international organizations in Vienna.

The International Atomic Energy Agency, and the Food and Agriculture Organization of the United Nations are