

## Pesticide causes nerve damage in humans

A pesticide manufactured in Bayport, Texas, has caused neurological symptoms in workers there and death and illness among people in Egypt. The chemical, leptophos, was produced between 1971 and 1975, but never approved for use in the United States. It was exported to Egypt, and also to Indonesia and Vietnam through sales supported by the Agency for International Development, according to Rep. David R. Obey (D-Wis.).

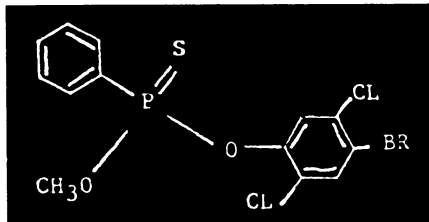
A variety of evidence of leptophos's harmful effects on the nervous system has been available for a number of years. According to Obey, in 1969 Velsicol Chemical Corp., the company that later manufactured leptophos, asked a biological testing laboratory to examine the effect of the chemical on chickens. The results indicated that leptophos causes nervous disorders and the highest dosage causes deaths.

When leptophos was introduced in Egypt in 1971 to protect the cotton crop, about 1,200 water buffalo died. Mohammed B. Abou-Donia, currently at Duke University, did experiments that implicated leptophos in that poisoning. In more recent experiments Abou-Donia and other researchers have found nerve degeneration and destruction of the nerve sheath in chickens, cats and rabbits. Other laboratory animals—mice, rats and dogs—are resistant to this effect.

The action of leptophos (O-(4-bromo-2,5-dichlorophenyl) O-methyl phenylphosphonothioate) on the nerve cells and sheaths is a second, delayed effect on the nervous system. The immediate effect of leptophos, and its mode of action as a pesticide, is to inhibit the action of cholinesterase, an enzyme important in nerve signaling. Cholinesterase breaks down acetylcholine, the chemical carrying signals between nerve cells and between nerves and muscle.

About 14 workers in the Bayport plant and one in another plant that occasionally processed and packaged leptophos have reported symptoms of neurological disorder. The effects range from dizziness to partial paralysis. Some persons have recovered, while others have not. The National Institute of Occupational Safety and Health has contracted with a clinic in Houston to give complete medical examinations beginning Jan. 6 to present and past employees of the Velsicol plant in order to determine the extent of the problems. Those examinations, which will cost a total of \$77,000, will be the most extensive ever arranged by the institute.

There is also concern for leptophos's effect on the environment, because the pesticide is a very stable chemical. A recent Environmental Protection Agency report, which recommended a ban on imported tomatoes and lettuce containing leptophos residues, stated, "Leptophos is



*Leptophos molecule: Nerve damager.*

the most accumulative and persistent organophosphorus insecticide ever examined in the terrestrial-aquatic model ecosystem." In experiments by James Sanborn and Robert L. Metcalf at the University of Illinois, the amount of leptophos measured in snails was 48,000 times that in the surrounding water. Preliminary results, however, suggest that environmental leptophos will not be a problem in Texas. "The samples show very insignificant amounts in the environmental situation," says Betty Williamson of the EPA office in Dallas. Grass and soil alongside the chemical plant had less than 1 part per million leptophos and oysters in Galveston Bay showed less than 2 parts per billion. The agency is to submit its final report next month.

The effects of leptophos in Egypt appear to be through the food supply, rather

than through contact with pesticide in the fields. Entire families there, rather than just field workers, are reported to suffer the neurological symptoms.

At present no leptophos is being manufactured in the United States and no residue is permitted on imported vegetables. Manufacture has also stopped in Japan, although no health problems there have yet been reported. The Japanese government is currently examining health records of workers in the pesticide plants. Leptophos was used on rice and sugar beet crops in Japan, but at only a fifth the maximum strength permitted in Egypt. In Egypt the pesticide is still being used, but no more will be purchased, according to a government decision. Other countries, including Syria and the Dominican Republic, are still receiving shipments of leptophos.

The pesticide problem will probably not end with the banning of leptophos. The chemical that the Bayport Velsicol plant is now manufacturing in its place is even more toxic, says Abou-Donia. EPN (O-ethyl O-4-nitrophenyl phenyl phosphonothiolate) closely resembles leptophos and, according to experiments in Abou-Donia's laboratory, is almost twice as potent a neurotoxin in tests on chickens. Abou-Donia says that systematic study of all the related organophosphorus pesticides is necessary. "There is no room in the environment for neurotoxic pesticides," he insists. □

## Contraceptive methods of the future

In spite of a wide range of contraceptives on the market, the ideal method of birth control remains to be found. Tubal ligation and vasectomies are 100 percent effective, but largely irreversible. Oral contraceptives and intrauterine devices are almost 100 percent effective, but are being linked with an increasing number of health hazards. Condoms, diaphragms, foams, rhythm and coitus interruptus have few health drawbacks, but are not always effective. They also are either aesthetically unsatisfactory, a bother to apply or require the utmost in physical restraint at certain times of the month or during intercourse.

Consequently biomedical scientists are attempting to devise more effective, safe, convenient and aesthetic kinds of birth control. Some of those that should become available in the next five, 10 or more years were discussed at a Dec. 14 conference on new developments in contraception, held by the Ford Foundation in New York City. Some of the methods on the horizon for women are longer-acting hormone contraceptives, an oral antipregnancy vaccine and a chemical that binds with sex-hormone receptors in the uterus. Some of the methods looming large for men are oral contraceptives and a chemical that interferes with proteins in the testes that are required for sperm formation.

Probably the first of these new kinds of contraceptives to be marketed will be longer-acting hormone contraceptives for women. This is the prediction of Daniel R. Mishell Jr., chairman of obstetrics and gynecology at the University of Southern California School of Medicine. These contraceptives would consist of synthetic versions of female sex hormones just as oral contraceptives do. They would likewise switch off gonadotropin hormones released by the pituitary gland in a negative feedback reaction and thus prevent the normal release of sex hormones and ovulation. However, unlike oral contraceptives, they would be given by injection every month, three months or six months.

Such contraceptives, in fact, are already marketed in Europe and some developing countries. Mishell believes that they are more acceptable to many women than are oral contraceptives that have to be taken daily, and especially to those women in developing countries who are used to lining up for shots. He also believes that the injectables would have fewer side effects than the orals since it would take less of them to achieve comparable effects and also because they are made of synthetic progesterone, not synthetic estrogens. Estrogens rather than progesterone have been linked with most of the health haz-

*Continued on page 398*

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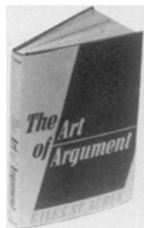
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## ... Contraceptive

ards of oral contraceptives.

Sex hormone contraceptives that exert these effects from six months to six years are also being tested on some 2,000 patients at seven clinical centers, including his own, Mishell reports. A tiny capsule containing contraceptive hormones is implanted under the skin of the forearm. The capsule then releases the hormones at a constant rate, preventing ovulation.

Another method of birth control that may reach the market before long is an antipregnancy vaccine, according to Sheldon J. Segal, vice president of the Population Council of Rockefeller University. The vaccine would immunize women against human chorionic gonadotropin (HCG), a hormone synthesized early in pregnancy and essential for it. Ordinarily a woman would not make antibodies against a hormone or other chemical that is natural to her body. But some months ago G.P. Talwar and his colleagues at the All India Institute of Medical Sciences got what Segal calls "a brilliant idea." They purified a chemical subunit of HCG, linked it to the tetanus toxoid and injected the chemical packet into female mice and human subjects to see whether it would provoke formation of antibodies not only to the toxin but to HCG. As they reported last February, it does (SN: 2/21/76, p. 117).

Since then, the technique's ability to raise antibodies against HCG has been confirmed in women by Segal and his colleagues and by some investigators in other countries. However, all these subjects had previously had tubal ligations, and hence the antibodies' ability to prevent pregnancy could not be demonstrated. So the next step was to show that antibodies raised by the vaccine could prevent pregnancy in animal subjects. As Segal and his team reported at the Ford Foundation conference and also in the December *JOURNAL OF CONTRACEPTION*, the antibodies indeed prevented pregnancy in 13 primate subjects. After the antibody levels fell to about 10 percent in one of the monkeys, it was mated and gave birth to a normal offspring. The vaccine thus appears effective, safe and reversible and does not interfere with pregnancies.

However, the antibody levels lasted 18 months in the studies of Talwar and his colleagues, but only six months in those of Segal and his team. So the challenge now, Segal says, is to obtain standard batches of vaccine that can provide contraception over a predictable period.

Many people are unaware that male reproduction is similar to women's in that the same pituitary gonadotropins control the release of sex hormones and in turn the release or maturation of germ cells. Thus an obvious question is, why hasn't a chemical been found that men can take just as women do in order to switch off gonadotropins, sex hormones and germ cell production? The problem until re-

cently, explains C. Alvin Paulsen, professor of medicine at the University of Washington, is that interrupting sex hormone production in men also destroys their libido. However, he and his colleagues have now gotten around this problem by giving male volunteers not just a compound that will switch off gonadotropins, sex hormones and sperm production, but also a small amount of testosterone, not enough to initiate sperm production but enough to keep sex drive intact.

Preliminary results with 12 subjects, Paulsen reports, show that the drug combination can switch off sperm production one to two months after drug exposure without serious adverse reactions and that sperm production returns to normal some six months after drug use is discontinued. Fifty-three men have now entered the same trial, and some 242 others are enrolled in similar studies in several other countries.

One form of contraception that holds promise for the future, is a chemical that would bind to progesterone receptors in the uterus and thus keep a fertilized egg from implanting there. Such a contraceptive has only become possible over the past several years as more has been learned about the molecular action of hormones and as the protein receptor for progesterone has been purified. Such a contraceptive, Bert O'Malley, chairman of cell biology at Baylor College of Medicine, envisions, should be safe, easily given, inexpensive, efficient and reversible and might well totally replace current oral agents.

A similar form of male contraception also lies in the future, reports Emil Steinberger, chairman of reproductive medicine at the University of Texas Medical School at Houston. If specific proteins can be found in the testes that are required for the action of testosterone on germ cells, then some chemical might be found that will interfere with this protein but not with other proteins in the body.

Whether these or other new forms of birth control become available to Americans and people in other countries, depends on how much money is allotted for such research. As Oscar Harkavy, officer in charge of population at the Ford Foundation, points out, "Not only have worldwide expenditures for the reproductive sciences and contraceptive development decreased in terms of constant dollars (1970 dollars), but these expenditures, measured in current dollars, reached a peak in 1974 and have decreased in 1975 and 1976. When inflation is taken into account, it is clear that the amount of relevant research being supported throughout the world has declined at a time when the promise of major new developments is extremely high and when bringing new products to market requires large expenditures of funds to assure their safety and efficacy." □