Meetings

Pesticide Research

The rapidly expanding field of pesticide research and regulation was reviewed at the 5th International Pesticide Congress, held in London from 17 to 23 July. Selective toxicity, the mode of entry and translocation of pesticides in arthropods and plants, chemical factors of phytopathogenicity, the metabolism of pesticides, correlation between biological activity and chemical structure, and analysis of pesticide residues were the six main topics. Basic chemical aspects were given special emphasis.

Pesticides fall into three principal categories—insecticides, fungicides, and herbicides—and the sessions of the congress were planned to reflect this grouping.

Insecticides

A. J. Lehman (Food and Drug Administration, Washington, D.C.) discussed the possibility of harmful effects of insecticides on nontarget organisms. This paper was of great interest to the entire congress, in part because of its bearing on a recent report of the President's Science Advisory Committee, "The Use of Pesticides." Lehman stated that three levels of toxicity must be known in assessing the tolerance of an organism to an insecticide. These are the LD_{50} when the insecticide is ingested orally over a short period or only once; the level at which toxicity is subacute; and the level at which the insecticide is toxic when ingested orally over a long period. Determination of these toxicities requires consideration of the following factors: mortality, body weight, organ weight, clinical laboratory findings, storage, metabolism, reproduction, the occurrence of neoplasms, and histopathology. Of greater importance than data on the LD_{50} for short periods of ingestion are data on dosage levels at which there are no harmful effects and levels at which the effects are significant. From data such as these it is possible to determine the intake acceptable to man. From Lehman's presentation and the discussion that followed, it is apparent that increased attention will be directed to reproduction studies (in line with recommendations of the President's committee) and that in these studies increasing use will be made of the electron microscope.

N. N. Melnikov, a leading phosphate chemist in the U.S.S.R., spoke on the action of organophosphorous insecticides and stated that, in general, the safety criteria in Russia and the United States are the same. He said that in Russia there is more emphasis on polarographic methods of analysis, and he expressed a desire for greater exchange of information. He added that in Russia tumor formation is intensively studied and that methods have been developed for studying the effect of pesticides on conditioned reflexes in higher animals.

A number of papers were concerned with advances in the determination of pesticide residues, through infrared spectroscopy, bioassay, chromatography, electroanalysis, and other methods. The relatively new, highly specific methods, involving complex instrumentation, are providing increasingly accurate results.

H. Hurtig (Canada) stated that the current concern to determine safe levels of pesticide residues in food is providing stimulus for intensive investigation of the behavior and metabolism of parent molecules and metabolites. This research could result in the development of new techniques of pesticide use. "Let us hope," he said, "that the current concern for establishing safeguards in use of pesticides does not end with legislative action. A more desirable approach would be administrative and financial support for the new emerging field of residue chemistry and analysis."

R. L. Metcalf (United States), in discussing selective toxicity of pesticides, presented strong evidence that all insecticides are probably selective to some degree, even though many—for example, DDT and parathion—are commonly considered broad-spectrum chemicals. He pointed out why there is special interest in chemicals that are not particularly toxic to mammals and that are toxic to only certain insect groups. A selective insecticide of this kind may be used in solving a specific pest problem without destroying population-regulating species; the undesirable side effects of a chemical with a broader spectrum of insect toxicity is thus avoided. This is the "integrated" approach to pest control, in which the use of a chemical is not antagonistic to agents of biological control in the environment but, rather, acts as a supplement.

M. J. Canney (United Kingdom) reviewed the movement of systemic pesticides in the three major kinds of transport mechanisms in the plant: movement within and between cells by diffusion and protoplasmic streaming; movement in the xylem system (most important in applications to soil and stem); and movement in phloem (most important in applications to foliage).

The metabolism in plants and animals of a wide range of pesticides was discussed by J. R. Busvine (United Kingdom), and the breakdown of pesticides in the soil by microorganisms, by W. C. Evans (United Kingdom). Many papers dealt with the correlation of biological activity and chemical structure. Y. Nishizawa (Japan) presented data on the increased selectivity obtained by introducing compounds of the *meta*-methyl group to 0,0-dimethyl phosphorothioates. Apparently this increase in selectivity occurs with compounds of the *p*-nitro and *p*-sulfamoyl groups but not with those of the *p*-cyano group.

Fungicides

P. W. Brian (Glasgow) discussed biochemical aspects of plant pathology and the role of substances produced by parasitic microorganisms in the etiology of plant disease. Examples of such substances are the toxins in wildfire (a disease of tobacco) and in *Helminthosporium* blight of cereals and growthstimulating substances that may lead to gall formation in corn smut and crown gall and to stimulation of plant growth through production of gibberellin in the "bakanae" disease of rice. Spencer and his associates (London, Ontario) described the chemical nature of the toxin helminthosporal, a mono-unsaturated, bicyclic sesquiterpenoid containing two aldehyde functions that is associated with damage to cereals by *Helminthosporium sativum*. Kern (Zurich) presented evidence for the presence of wilt toxins in plants affected by wilt diseases and outlined the function of slimy polysaccharides and of toxins of low molecular weight, such as fusaric acid and lycomarasmin. The latter compounds have in common the ability to form metal complexes, to inhibit the action of enzymes, and to act as antimetabolites. They affect the permeability of host cells and destroy the water balance of the plant.

The fungitoxic compounds produced in both normal and infected plants may provide useful leads in the development of fungicides. This theme was presented by Wain (Wye College) and documented more fully by Fawcett (Wye College), who has isolated fungitoxic polyenes, polyenynes, phenolics, lactones, quinones, tropolones, and isothiocyanates from plants.

Plant pathologists are exploring the chemotherapy of plant diseases—the introduction into plants of compounds that control disease, either directly through their toxicity to the pathogen or indirectly through their effects upon the host. In the usage of van der Kerk (Utrecht), compounds of the first type are called "systemic fungicides," those of the second, "systemic compounds." This approach was discussed by Dimond (New Haven) and by van der Kerk (Utrecht). Dekker (Wageningen) reported on a systemic compound, 6-azauracil, in the control of powdery mildew in cucumber. This compound is nontoxic to the mycelium of the powdery mildew fungus, yet in plants that have absorbed it the fungus does not develop beyond the formation of the first haustorium.

We need to know more about the metabolism of toxicants by fungi and higher plants in order to understand the mode of action of fungicides, to assess the possibility that new fungitoxic compounds will form in the plant from nontoxic compounds, to estimate the period of effectiveness of the treatment, and to assess the health hazard when treated plants are consumed. Faulkner and Woodcock (Long Ashton, Bristol University) reported on the fate of chlorophenoxyacetic acids introduced into *Aspergillus niger*. 4-Chlorophenoxyacetic acid is converted to 4-chloro-2-hydroxyphenoxyacetic acid and to the expected 2-hydroxy compound. 2-Chlorophenoxyacetic acid is converted to 4- and to 5-hydroxyphenoxyacetic acid predominantly, but 3- and 6-hydroxyphenoxyacetic acid are also formed. 2,4-D is converted primarily to 5-hydroxy-2,4-dichlorophenoxyacetic acid. Somers and Richmond (Long Ashton, Bristol University) reported on the reaction between Captan (N-trichloromethylthio-4-cyclohexene-1,2-dicarboxyimide) and conidia of *Neurospora crassa*. Captan is rapidly decomposed, and a number of enzymes and coenzymes with functional sulfhydryl groups are inactivated by Captan in the process. But when functional sulfhydryl groups are blocked by alkylation, the susceptibility of spores to Captan remains unchanged, although the uptake of Captan is greatly reduced. Uptake of Captan was shown to be related to the content of sulfhydryl groups in spores, but toxicity is not related to the sulfhydryl content of spores.

Kaars Sijpesteijn (Utrecht) discussed the fate of fungicides (in particular, sodium dimethyl dithiocarbamate) in plant and fungal cells. Potato tuber tissue converts about 10 percent of the dithiocarbamate to a β-glycoside, and about 1 percent to α-alanine dimethyl dithiocarbamate. Yeast cells convert dimethyl dithiocarbamate to the same β-glycoside and to dimethyl dithiocarbamyl-α-amino butyric acid and to the corresponding α-keto butyric acid.

Sexton (England) discussed the principles underlying the relation of chemical structure to biological activity. These principles were illustrated in a series of papers dealing with newly described fungicidal groupings. Among these groupings are the aryl-ethyl-ketones (described by Pellegrini and his associates, Montecatini, Milan); the aryl and alkyl esters of vinyl sulfonic acid (Kistler and Pommer, Ludwigshafen am Rhein); the pentaerythrityl analogs of chlorophenesin (Moreau and his associates, Paris), and the N-trichloromethylthiobenzoxazolones (Desmoras and his associates, France).

The papers dealing with disease control in plants reflected growing interest in studying natural products for clues on ways to form new structures for disease control, and interest in modifying the host plant by chemical means so that it resembles the plant that is naturally resistant to disease.

Herbicides

In surveying selective toxicity, J. H. Gaddum (United Kingdom) stated that certain biological agents which affect organisms or control pests are "living pesticides." The action of thalidomide on the human fetus represents a type of selective toxicity, as does the action of drugs which have differential effects on various organs and tissues. The lethal effects of pesticides depend largely on the factors which concentrate chemicals at their site of action.

Selective toxicity in herbicides was discussed by W. B. Ennis, Jr. (Beltsville, Maryland). Utilization of the principles of selective toxicity was described as involving (i) various techniques of physical placement, (ii) exploitation of differences in the morphology of plants, and (iii) consideration of differences in biochemical processes among plants. Among the biochemical processes which determine the relative toxicity of herbicides to vital tissues are metabolic activation and detoxication of compounds and alteration in growth-limiting substances. Selective toxicity in herbicides is complex; the data largely resemble parts of a jig-saw puzzle, and their relationship is not well understood.

The mode of entry and the translocation of pesticides in plants and arthropods were discussed in relation to selective toxicity. A great deal about the processes involved has been learned from research on herbicides and growth-regulating chemicals. G. E. Blackman (United Kingdom) stated that the rate of accumulation of herbicides and the threshold of toxicity differ widely in various species. Some herbicides, such as 2,2-dichloropropionic acid (dalapon), are steadily accumulated until individual cells are injured. Differential susceptibility of plants to dalapon appears attributable to differences in the rate of its accumulation rather than to differences in susceptibility at the cell level. Wolfgang Franka (West Germany) discussed the entry of pesticides into leaves. He gave evidence that ectodesmata—special structures representing continuations of the protoplasts in the outer walls of epidermal cells—provide pathways for the excretion of substances from the epidermal cells to the surface of the leaves and for the absorption and transport of pesticides from the surface to the interior of leaves.

Other facets of entry and translocation that were dealt with were root uptake, polar transport, and plant and environmental characteristics which influence the behavior of herbicides in and on plants.

Conclusion

The remarks of Sir Robert Robinson, president of the congress, were of interest to everyone. He stressed the role of pesticides in increasing the world's food supply and in fighting human disease. Annual crop losses are estimated at from 15 to 30 percent, or £20 to £30 billion. The world's population now stands at some 3 billion, and it is expected to double by A.D. 2000. Food production must be doubled by 1980. In the area of disease, as recently as 1953 some 200 million people suffered from malaria and 2 million people died of it; these statistics, a matter of medical record, underline the importance of the continued use of DDT in bringing malarial mosquitoes under control. Sir Robert gave statistics on the safe use of pesticides in Great Britain. On farms in England there were 140 accidental deaths per year from 1956 to 1960, and none was caused by pesticides. During this period there were 20,000 nonfatal accidents on farms per year; only five of these were from toxins and none was from toxic residues on food. In the United States the Public Health Service has stated that the use of pesticides is compatible with public health. Sir Robert made it clear that the consequences of abandoning the use of pesticides, or the consequences of injudicious legislation against their use and development, might be disastrous.

The congress, attended by over 500 participants from 38 countries, was sponsored by the International Union of Pure and Applied Chemistry.

A. E. DIMOND
Connecticut Agricultural Experiment Station, P.O. Box 1106, New Haven
H. T. REYNOLDS
Department of Entomology, University of California, Riverside
W. B. ENNIS, JR.
Crops Protection Research Branch, U.S. Department of Agriculture, Beltsville, Maryland