day-to-day routine for chemists, physicists, engineers and architectural members of the staff to meet together to discuss the practical implications of information obtained. The effective teamwork thus made possible is commonly the subject of comment by visitors, particularly visitors from abroad. It now seems likely that other similar organisations will be established in the Dominions and other countries—an uninvited testimonial to the form of organisation which has been developed for the application of science to an industry so practical and traditional as building, and an acknowledgment of the value of the twenty-five years research work of the Building Research Station.

Finally, it is of interest to note how the basis of building research has been broadened as the work has proceeded. Starting in the relatively restricted field of materials and structures, the Station at once found it necessary to join hands with sister establishments of the Department of Scientific and Industrial Research having special facilities for certain classes of work. Then it became desirable to establish a link with the physiologist, through the Medical Research Council; and more recently the help of the War-time Social Survey of the Ministry of Information was enlisted for certain inquiries. Again, the Station is extending its work on materials to cover their assembly on the site, and the properties of the finished building. The main question now is one of scale, and this is under consideration by the Department of Scientific and Industrial Research.

SOME USES OF D.D.T. IN AGRICULTURE

THE discovery in recent years of a new class of insecticides has given man an advantage over his insect enemies such as he has never before enjoyed. Although these materials kill insects by contact, they possess a stability and persistence which confer a protective effect far exceeding that of any previously known contact insecticide. Best known among them is D.D.T., a substance the properties of which are so remarkable that it has been accorded the doubtful honour of becoming 'news'. Very little of the vast amount of experimental work done has yet been published, and the door has thus been opened wide to the wildest speculation and exaggeration. A meeting of the Association of Applied Biologists on October 5 sought to adjust the outlook at least upon some of the agricultural uses of D.D.T. by bringing together workers qualified to speak on original investigations.

Mr. C. T. Gimingham, of the Ministry of Agriculture and Fisheries Plant Pathology Laboratory, introduced the proceedings with a plea for a restrained and balanced approach. The peculiar circumstances in which D.D.T. was introduced had led to intensive investigations on an unprecedented scale. The substance had proved to be of inestimable value and, by controlling disease-carrying insects, had probably been a major factor in the success of several Allied campaigns. Unfortunately, much of the resulting publicity had not been in the highest tradition of scientific accuracy. Contrary to the popular view of D.D.T. as a cure-all, it had recently been reported in the United States[1] that while it excelled the commonly used insecticide against some thirty insect species, it was only about equal against nineteen and was inferior against fourteen. Most of the work so far had been exploratory, and increased knowledge of dosage, timing and compounding would doubtless lead to improved performance in many cases. At present little was known as to which of the variety of possible forms of application was most effective and safest for particular purposes. A special problem in agriculture was the risk of harmful effects upon beneficial insects. Injury to birds and fishes also might follow widespread use over large areas. There appeared to be little danger to warm-blooded animals, but more information was required about cumulative effects. D.D.T., said Mr. Gimingham, was of such outstanding interest and promise that it would be peculiarly unfortunate if its future were prejudiced by misuse in the early days.

Dr. G. H. L. Dicker described experiments at East Malling Research Station on the control of apple blossom weevil. Emergence from hibernation begins in late February or early March and may extend over five weeks. Egg-laying starts at bud burst and continues for about three weeks, so effective treatment demands continuous protection over this period, with the first application timed for bud burst. In laboratory tests a 5 per cent D.D.T. dust consistently gave more than 90 per cent kill in five days, and this concentration was chosen for field trial. In comparison a 5 per cent benzene hexachloride dust killed about 60 per cent, reaching the maximum in sixteen hours. In 1944, 60–70 lb. of 5 per cent D.D.T. dust per acre, applied as soon as practicable after egg-laying began and twice following at weekly intervals, reduced an infestation of 5–6 per cent to 0·02 per cent, whereas a 1 per cent rotenone dust gave only about 50 per cent reduction. In 1945 two applications of 5 per cent D.D.T. at 40–45 lb. per acre gave more than 90 per cent control, but at 3 per cent only about 60 per cent control resulted. In another trial, however, 3 per cent D.D.T. apparently gave no kill, whereas 3 per cent benzene hexachloride gave 50 per cent. It remained to be seen whether a single dusting with 5 per cent D.D.T. at bud burst would suffice, whether 5 per cent benzene hexachloride was as good, and whether control could be attained by wet spraying. A spray containing 0·05 per cent D.D.T. gave complete kill in laboratory tests. As the optimum time of application was a month before flowering, there seemed to be little risk to beneficial insects. Dr. Dicker thought that D.D.T. would be compatible with lime-sulphur or a winter petroleum wash, but he preferred the dust because of the speed of application and because the best time for the weevil treatment was after petroleum oil and before the first lime-sulphur. Dr. W. Heeley said that other trials[2] showed a wet spray to be far superior to a dust, but Dr. Dicker pointed out the surprisingly poor results given by the dust in these trials.

Dr. M. Cohen reported exploratory work on the production of D.D.T. 'smokes' by burning impregnated filter papers. The heavy smoke produced settled quickly and gave a firmly adhering deposit. By drawing this smoke through benzene, unchanged D.D.T. could be recovered. Houseflies, stable flies (*Stomoxys calcitrans*), Drosophilid flies, mosquitoes (*Culex* spp.), thrips, clothes moths, and pollen beetles were knocked down within five seconds of being exposed to the smoke. Aphides, though less obviously affected, appeared not to recover. The deposit produced when the smoke settled consisted of minute droplets that remained liquid until mechanically disturbed, as by brushing lightly or by the movement of insects. This induced crystallization along the track of the disturbance, the resulting crystals closely resembling those of D.D.T. The deposit was assumed to contain D.D.T. as it gave a reaction for chloride after treatment with alcoholic potash. It was still toxic to house- and stable-flies after sixteen days, and the effect on the insects closely resembled that of D.D.T. Dr. Cohen reported that Mr. W. Steer had heated D.D.T. just above its melting point for several hours in a glasshouse. Paralysed white flies, aphides and caterpillars were afterwards found on the soil, and centipedes and a devil's coach horse beetle were affected. Foliage from the greenhouse plants was toxic to houseflies. These results suggested that the possible application of D.D.T. as a fumigant merited further investigation. Dr. R. L. Wain said the direct heat treatment described would certainly result in quantitative decomposition of the D.D.T.; the crystals formed from the smoke deposit might well be the ethylene derivative. A minute amount of unchanged D.D.T. could account for the effects described. He suggested that inorganic chloride should be estimated as a measure of decomposition. Dr. Kennedy said experiments at Porton showed that it was possible to make smokes in which a considerable proportion of the D.D.T. persisted unchanged.

Mr. K. J. Coghill and Mr. W. Steer discussed the effect of D.D.T. on flies in farm buildings. All the interior surfaces in one of two almost identical shippons were sprayed with 0·1 per cent D.D.T., and a fall in the fly population was evident within a few hours. Dead and moribund flies counted daily in the feeding passages were fully ten times as many in the treated shippon as in the untreated. In the following year the two shippons were transposed as untreated and treated. The number of dead flies in the untreated, though still less than in the treated, was much higher than the corresponding figure in the previous year, despite a much lower infestation. This suggests the persistence of a lethal effect for fourteen months in the shippon sprayed in the first year. *Stomoxys calcitrans* was the most abundant species involved in these trials, with *Fannia canicularis* next. *Lyperosia irritans* comprised less than 10 per cent of the fly population; but this species was unaffected since it did not leave the cattle and so never came into contact with treated surfaces. While the 'resident' population was substantially reduced by the D.D.T. treatment, there was a fresh influx of flies each time the cattle came in. Nevertheless, although affected flies continue to annoy the animals for at least fifteen minutes, the cattle in the treated shippon were usually quieter than those in the untreated. Flies were almost eliminated from a bull-box in which the animal was penned continuously. To test the efficacy of D.D.T. in lime-wash two calf pens were treated, one with lime-wash alone and the other with D.D.T. added. The latter pen had the higher fly population at the start, but the position was reversed after treatment. In the following discussion, Mr. Steer said no attempt had been made to spray the cows or to treat nearby gateposts, trees, etc. There had been no hint of harmful effects upon those applying the spray.

Mr. J. B. Cragg described field trials on the control of sheep blowflies, chiefly *Lucilia sericata*. Following promising laboratory tests, Welsh mountain sheep were dipped in a bath containing 0·5 per cent D.D.T. in a finely dispersed emulsion, a commercial arsenic-sulphur dip being used as control treatment. There were far fewer strikes on the sheep treated with D.D.T. and the protection remained effective for six weeks[3]. This result was confirmed in a second season, but in parallel trials in other areas results were not so uniformly satisfactory, for example, with black-face sheep in Aberdeen, where D.D.T. was less effective than the proprietary dip. When a range of concentrations of D.D.T. was tried, 0·5 per cent was the minimum suitable for field use. Whereas the arsenic-sulphur dip is larvicidal, D.D.T. acts on the adult fly rather than on the egg or larva. Flies die after contact with the treated fleece and the action is sufficiently rapid to prevent normal oviposition. On the other hand, normal egg batches were laid within two days of treatment with an arsenic-sulphur dip. The odour of D.D.T. is not repellent to blowflies and, indeed, by applying an attractant also, the sheep can be made a live blowfly trap. By rubbing together in the flock, dipped sheep can pass on the toxicity to untreated animals as is revealed by the fact that wool from the flanks, but not from the back, of untreated sheep is toxic to the flies. Although D.D.T. has not given complete control of sheep blowfly it has substantially reduced the number of strikes and increased the period of protection in comparison with an arsenic-sulphur dip. Of the strikes that occurred, more than 90 per cent were in the region of the tail, a fact which indicates that a combination of D.D.T. treatment with crutching might be very effective. It is suggested, too, that since attack on the adult fly requires cover of the outside of the fleece rather than penetration to the base as with the current treatment, dipping might well give place to application by sprays or jets.

Mr. G. B. S. Heath and Dr. J. G. Mitchell reported similar field trials of D.D.T. against sheep ticks (*Ixodes ricinus*) on hill farms in Cumberland. In this area there is a major peak of infestation in April–May and a minor one in August–September. More than half the ticks on the animals were found on the ears and face; few were present in the fleece proper. In laboratory tests by Dr. E. T. Burtt, D.D.T. had given promising results, and field trials of several experimental emulsions of D.D.T. were started, using as control a commercial arsenical dip which reduced infestation significantly only for about fourteen days. Good control of ticks for seven weeks followed dipping in 0·5 per cent D.D.T., while 0·3 per cent gave protection for four weeks. The concentration of D.D.T. in the fleece exceeded 1 per cent, and rapid exhaustion of the bath occurred. But on repetition with a similar, though not identical, emulsion, protection was no better than with the control dip, the concentration of D.D.T. in the fleece did not exceed that in the bath, and this did not fall appreciably during dipping. The latter emulsion was much more finely dispersed than the former, and further work showed this to be the principal factor determining high or low deposition on the fleece and consequent tick control. In ordinary anionic emulsions the oil globules show no affinity for the fibre, but in cationic emulsions they are strongly attracted. Pre-treatment of the fleece with dilute acetic acid reverses these affinities. In field trials heavy deposits and good protection generally resulted from dipping in coarse anionic emulsions, in fine anionic emulsions after swabbing heads and axillæ with acetic acid, or in a cationic emulsion. A cationic dip containing only 0·2 per cent D.D.T. was effective.

Dr. Mitchell demonstrated the affinity relationships discussed. He said that although the emulsions used by Mr. Cragg and Mr. Heath were all experimental, the success achieved had stimulated a vigorous demand among farmers for preparations for field use.

Answering questions, Mr. Heath said that spraying did not wet the fleece, but jetting at 150 lb. pressure did. The main growth of new fleece occurred after the tick season. The effect of D.D.T. on keds was even more spectacular than on ticks. Mr. Bracey wondered what retention of D.D.T. there was in the short hair of the face. If large crystals were deposited from a spray they might easily be rubbed off, so the problem might resolve itself into getting a deposit of the smallest possible crystals. [See also p. 311 of this issue.]

H. SHAW.

[1] *Soap*, 21, No. 4, 139 (1945).
[2] *The Grower*, 23, 430 (1945).
[3] *Nature*, 155, 394 (1945).

ALKYL FLUOROPHOSPHONATES: PREPARATION AND PHYSIOLOGICAL PROPERTIES

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THIS article gives a very brief preliminary account of some of the work initiated and carried out on toxic fluorophosphonates during the War at Cambridge by an extra-mural Ministry of Supply research team working under our direction. For security reasons during the War, this work has not hitherto been published, though secret reports (which were also made available to American workers almost from the inception of the investigations) have from time to time been submitted to the Ministry of Supply. More detailed accounts of these investigations and a fuller bibliography will be published in due course in the appropriate journals.

Until this work began in Cambridge in 1941, the alkyl fluorophosphonates had received practically no attention. Lange[1] gave a tedious and laborious method for preparing dimethyl and diethyl fluorophosphonates in very poor yield as follows. Phosphorus pentoxide was fused with ammonium fluoride, a mixture of ammonium monofluorophosphonate and ammonium difluorophosphonate being produced. The monofluorophosphonate was converted into the silver salt which was then heated with the alkyl iodide, the overall yield being less than 4 per cent. Passing reference was made to an effect on the vision, but no record was made of the toxicity of these two compounds. No other fluorophosphonates were recorded. During 1941, we prepared several alkyl fluorophosphonates R_2PO_3F (R = Me, Et, *n*-Pr, *iso*-Pr, and *n*-Bu) and one of us made a preliminary report[2] to the effect that:

(1) These substances have high toxicity as lethal inhalants. Death takes place rapidly (for example, a concentration of 1 : 10,000 of the di-*iso*-propyl ester killed 6/6 rats, 10/10 mice and 2/3 rabbits within 25 minutes from the beginning of exposure of 10 minutes). Such rapid effect and quick knock-out action is shown by few other gases or vapours.

(2) At lower and non-fatal concentrations, a peculiar effect is produced on the eyes, quite distinct from lachrymation. The material causes the pupils to become acutely constricted, and the effect may last for several days. In addition there is interference with visual accommodation. There is no tear formation and little or no irritation produced in the eyes. Reading is rendered difficult and vision at night is seriously affected.

Synthetic Methods. It then became obvious that practicable methods of synthesizing fluorophosphonates must be devised, and in Report No. 2 on Fluorophosphonates[3] we proposed the following methods:

(1) $POCl_3 \rightarrow POCl_2F$
$POCl_2F + 2ROH = (RO)_2POF + 2HCl$
(2) $2(RO)_3PO + POCl_3 = 3(RO)_2POCl$
$(RO)_2POCl + NaF = (RO)_2POF + NaCl$
(3) $3ROH + PCl_3 + 3C_5H_5N = (RO)_3P + 3C_5H_5N,HCl$
$(RO)_3P + Cl_2 = (RO)_2POCl + RCl$
$(RO)_2POCl + NaF = (RO)_2POF + NaCl$

Method 1 and a modification of method 3 were destined to play a very important part in subsequent researches. In our next report[4] we showed that method 1 could be employed in the case of ethyl alcohol and phosphorus oxydichlorofluoride giving a 93 per cent yield of diethyl fluorophosphonate. (See also British Secret Patent[5].) In preparing the trialkyl phosphite (method 3), the use of pyridine imposed a severe restriction for large-scale preparation, and it was soon found that the cheaper and more readily available dimethylaniline could be used in its place[4,6].

Although substitution of dimethylaniline for pyridine provided an important modification in the preparation of alkyl phosphites, the method was still not sufficiently cheap for large-scale work. It was decided then to try the effect of eliminating the tertiary base altogether. The result of the action of phosphorus trichloride on ethyl alcohol was *diethyl-hydrogen phosphite* in high yield. It seemed at first that this modification was useless, as the required triethyl phosphite was not produced. We decided nevertheless to try the effect of chlorine on the hydrogen phosphite and found that the essential *chlorophosphonate* was produced in 80 per cent yield[6,7].

As subsequent reports will show, it may be said that this discovery altered the whole course of fluorophosphonate chemistry. It now became possible to prepare the fluorophosphonates in excellent yield[8] and from cheap and readily accessible materials, in particular no tertiary base being required.

The synthesis may then be represented as follows:

	Yield
$PCl_3 + 3ROH = (RO)_2POH + RCl + 2HCl$	89 per cent
$(RO)_2POH + Cl_2 = (RO)_2POCl + HCl$	80 ,,
$(RO)_2POCl + NaF = (RO)_2POF + NaCl$	84 ,,

Semi-Technical Scale. Further modifications were then made in this 'hydrogen-phosphite' method of preparing diisopropyl fluorophosphonate (the most toxic of the series) in order to put it on a semi-technical scale.

After a large number of experiments, we found that the preparation could be run virtually as a *one-stage process*[9]. Other simplifications were introduced, and the whole process now consists simply in adding phosphorus trichloride to isopropyl alcohol, dissolved in carbon tetrachloride, without external cooling. The crude product (still in carbon tetrachloride) is chlorinated and then heated with sodium fluoride. After filtration, the carbon tetrachloride is distilled off and the pure diisopropyl fluorophosphonate distilled[10,11].

This process formed the basis of the method employed both in Great Britain and afterwards in America for the production of this and similar compounds.