and other agricultural crops, as well as to millions of livestock. The vast majority of these insecticides are being applied by airplane or ground power equipment, with the result that spray and dust drifts are undoubtedly floating across a high percentage of rural premises, subjecting the fly population found there to sublethal dosages of the insecticides being used. Many of these insecticides are volatile and their fumes, drifting with the breezes, are also subjecting the flies to sublethal exposures. The frequency with which the odor of benzene hexachloride is encountered during a few hours' drive through the cotton belt on a summer afternoon is striking evidence of the extent of this condition, since for each instance where benzene hexachloride makes its presence known, there are undoubtedly several others of more subtle odor whose presence goes undetected.

The use of insecticides in agriculture is a factor in the fly resistance problem over which the health worker has little or no control and is one which will no doubt eventually bring about the development of insecticide-resistant strains of house flies in rural areas. In urban areas, however, where the principal fly breeding sources generally could be eliminated by improved sanitation, every effort should be devoted to approaching the fly control problem on a permanent basis through improving basic sanitation, with a resort to insecticides only as a supplementary or emergency tool. Such a procedure should delay indefinitely the development of fly resistance and prolong the effective use of presently available insecticides. It would also provide research agencies with more time to develop new materials or procedures with which to meet what presently appears to be the inevitable problem of insecticide-resistant flies in all areas.

THE NEWER ECONOMIC POISONS OF USE IN DISEASE CONTROL

WILLIAM M. UPHOLT, Sr. Scientist*

Insecticides have been used for disease control for a good many years. As early as 1892, L. O. Howard** suggested the use of oil to kill mosquitoes. By 1914 oiling for mosquito control was a recognized part of the malaria vector control program in Malaya. Insecticides of one form or another, particularly pyrethrum space sprays, have supplemented sanitation and screening for control of adult mosquitoes and house flies since early in this century. Paris green was used for the control of mosquito breeding in the early 1920's. With the advent of DDT a new technique was added, in that it became possible to apply to a wall an insecticidal residue capable of killing mosquitoes and flies which rested on that wall weeks and even months after treatment. The idea of a residual insecticide was not entirely new since agriculture had used residual stomach poisons for many years. It is very likely that some of the residual stomach poisons, particularly sodium fluoride as used against cockroaches, actually may have acted, at least in part, as a residual contact insecticide as well. However, the general application of an insecticide designed to kill by contact weeks after application was a revolutionary phenomen.

Insecticides immediately spring into the public

*Technical Development Services, Savannah, Ga.
**Howard, L. O. (1892) Insect Life, 5: 12.

limelight largely because of their importance in war time. The control of the typhus epidemic in Italy by the use of DDT was dramatic and captured the attention of people whose previous contact with insecticides was limited to "Quick, Henry, the Flit" advertisements. DDT was rapidly applied to other military uses and then, as soon as supplies permitted it, to world-wide efforts at malaria control. Examples of malaria control and even of eradication of anopheline mosquitoes by the use of DDT can now be found in areas covering essentially every continent of the world. The importance of this can hardly be overestimated. Areas which had become nearly uninhabitable due to the ravages of malaria have been restored to normal economic production. One of the most dramatic illustrations of this has been the experience on the antimalaria campaign in Sardinia, an island where the population had been reduced to about one-third the density of the mainland because of malaria, and which is now again being made an attractive spot for immigrants from Italy. Few would question the wisdom of awarding the Nobel Prize in Medicine to Paul Müller, the chemist who discovered the insecticidal effectiveness of DDT.

Early enthusiasm over the potentialities of DDT were, however, sometimes misguided. There were those who suggested that DDT would replace all other insecticides and that DDT would eradicate house flies from large areas – even entire States. Such optimism was short lived. Within 3 years of the general use of DDT, house flies in many areas began to develop a resistance to this insecticide. At first it was claimed that the newer production of DDT was of a poorer quality than that obtained originally. Others thought that perhaps the spray crews were careless in their applications. But eventually the fact had to be faced that the flies themselves had adapted to this new hazard in their environment. The recognition of the development of resistance to DDT by these flies emphasized the fact that new insecticides are ever-essential to our economy.

The insecticidal chemist had not been fooled and already there were other new insecticides on the market which were claimed to be superior to DDT. Rapidly the number of new insecticides and a variety of names for each new insecticide developed a maze of names which would confuse anyone. Each manufacturer claimed that his particular material or his particular formulation was far superior to any that preceded it. The fact that there are so many widely different uses for economic poisons meant that most manufacturers could substantiate their claims by proper selection of their test insects and of their methods of use.

When, however, all of the recently established economic poisons are analyzed and classified, it becomes apparent that we have even fewer classes of insecticides which are of major importance to communicable disease control today than was true before the advent of DDT. Previous to the second World War, the student of economic entomology had to familiarize himself with a large number of inorganic materials including such widely different elements as sulphur, copper, arsenic, thallium, mercury, lead, and fluorine. The organic insecticides included not only the relatively simple cyanides and the more complicated synthetic materials such as the thiocyanates, but also the often undetermined active ingredients of plant derivatives such as pyrethrum, derris, and nicotine. Although it is true that most, if not all, of these many different materials are still useful and still in actual use as economic poisons, nevertheless the newer economic poisons are so much more efficacious that for many purposes, including most public health applications, a large proportion of the older materials can be ignored. For practical purposes, therefore, in the control of most demonstrated or potential vectors and reservoirs of communicable diseases, attention can be centered on the chlorinated hydrocarbons (which include all of those newer insecticides which have demonstrated long residual effectiveness as contact poisons), a few synergists and synthetic insecticides which are used in connection with pyrethrum as space sprays, and a handful of rodenticides.

The amount of information which a sanitarian concerned with communicable disease control needs to know about these various materials is again not too voluminous. If he knows enough about their chemical relationship to be able to recognize and classify the information which is required by law to appear on the labels, if he has a few basic facts in regard to the operational uses and limitations of these various classes of materials, if he has an approximate idea of the hazards associated with their use, and if he knows where to look for more detailed information on any one which may be of major importance in his own experience, then he will be in a position to make proper use of the available insecticides. He must, of course, have some basic information on the different types of formulations in which the economic poisons may be used. Very often confusion is associated with the fact that there are available many different formulations of each material and that many commercial preparations involve two or more basic insecticides. Another paper in this issue is designed to provide some basic information on the types of formulations in use in public health activities. The following summary is designed to furnish some of the basic information on the active ingredients.

It must be realized that many economic poisons which are still in widespread use have been excluded from this list, not because they are no longer of any importance, but because the public health sanitarian is less likely to contact them or because, like the arsenicals, they are already well known.

CHLORINATED HYDROCARBONS

The chlorinated hydrocarbons are a group of chemicals which, though not new, have become of major importance only since the advent of DDT. Paradichlorobenzene (PDB) and orthodichlorobenzene have long been used as insecticides and are still used for specialized purposes. Orthodichlorobenzene especially may be encountered by the sanitarian in connection with the control of fly breeding since it has been and still is successfully used as a fly larvicide. It is not, however, as effective as some of the newer chlorinated hydrocarbons. With the exception of orthodichlorobenzene and a few of the other chlorinated hydrocarbons which have high vapor pressures, this class of insecticides is noted particularly for its long-lasting residual deposits which kill insects by contact. They have been included in space sprays to some extent, and DDT particularly is of value in insuring the death of insects that are knocked down by other ingredients of space sprays.

They are the insecticides which are currently of greatest concern to the sanitarian.

DDT AND ITS ANALOGS

It is well known that DDT was the first residual contact spray that obtained world-wide importance. Even before DDT was released, the chemists who had developed DDT had also tested many closely related compounds and, as might be expected, several of them have insecticidal activity. It is not necessary to be thoroughly familiar with all of these analogs. For instance, the fluorine analog has been shown to have considerable activity and is of considerable academic interest, but is not available commercially in this country. The analogs that are available commercially in this country are methoxychlor (which is, as the name implies, the methoxy analog) and a compound with one less chlorine atom on the ethane linkage, namely, DDD. These two and DDT are therefore the ones to be considered.

DDT — DDT is known commercially by a variety of names. When it was first produced in Switzerland by the Geigy Corporation, it was known under the generic name of dichlorodiphenyl trichloroethane. It was this name which provided the now general designation DDT. Since there are, however, a number of specific chemicals, all of which could be known by this general name, and since one of them is much more effective insecticidally than any of the others, the name is now limited in use to this active isomer which is chemically 2,2,bis-(p-chlorophenyl)-1,1,1-trichloroethane. It is sometimes referred to as the para,para isomer of DDT, or p,p'-DDT to distinguish it from the ortho, para, and other isomers. The material has been known under a variety of trade and common names. Many manufacturers have trademarked names by which they refer to DDT. The original manufacturer used the trademark names Gesarol and Neocid. Since these two names are trademark names applied primarily to finished formulations, the manufacturer referred to the basic chemical as GNB for Gesarol-Neocid Base. The first produced in the United States was referred to as GNB-A, indicating the American production of Gesarol-Neocid Base. All of these names will be found without further identification in some of the early literature on DDT.

DDT is a white crystalline solid that is soluble in most organic solvents and insoluble in water. It has been so widely used and publicized that it seems redundant to point out that it is effective against most adult household pests and other medically important arthropods, as well as many agricultural insects. It is effective against mosquito larvae, but is relatively ineffective against fly larvae. It is being used throughout the world for the control of many disease vectors.

It is available commercially in the technical grade as well as in a diversity of formulations — solutions, emulsifiable concentrates, dusts, wettable powders, aerosol preparations, and emulsion concentrates.

There have been a few cases of poisoning due to DDT reported in literature; however, it has been claimed that most, if not all, reported fatalities were caused by some other ingredient such as the solvent rather than by the DDT itself. The fact

915375 O - 50 - 2

that it has been used on such a large scale throughout the world over a period of several years without apparent ill effects to users suggests that it is relatively safe, at least from the standpoint of acute toxicity. However, DDT is known to be toxic to fish, and has killed various species of mammals exposed to large doses. Reasonable precautions, therefore, should be taken to avoid breathing DDT dusts, mists, or powders, and to avoid direct skin contact. Contaminated skin should be washed with soap and water and excessively contaminated clothing should not be worn.

If DDT is to be used as a mosquito larvicide where fish and related organisms are important, the dosage should not exceed approximately 0.10 pound DDT per acre for a single application, or 0.05 pound DDT per acre where repeated applications are necessary. The Food and Drug Administration has ruled that DDT in milk is considered as a contaminant. DDT, therefore, should never be used on dairy animals, in dairy barns, nor on food products of man or animals.

With these restrictions, DDT can be used very effectively against most household pests, including mosquitoes, flies, bedbugs, and, if the application is sufficiently thorough, cockroaches. It has been used successfully for the control of rat fleas. Perhaps the most serious restriction on DDT is the fact that in many areas house flies have developed a greater or lesser resistance to DDT, and in some such areas, DDT will be found of little value in house fly control. There is some evidence that where house fly populations are kept within reasonable bounds by good sanitation, there is less danger of resistance developing. Where resistance has already developed, the only solution is to immediately promote sanitation to the point where chemical control becomes an auxiliary method rather than the primary instrument of control. Having done this, it may be possible to find a substitute material to which the flies are not resistant. Chlordan, lindane, methoxychlor, and dieldrin should be given consideration in this connection.

DDD — DDD is exactly what the name would imply in relationship to DDT. As the generic name for DDT is dichlorodiphenyl trichloroethane, the generic name for DDD is dichlorodiphenyl dichloroethane. Thus, it is exactly the same as DDT except that it has one less chlorine atom on the ethane linkage.

Another common name which has been suggested and is widely used for this compound is TDE. The reason TDE was suggested is because it was felt that "DDD" is so similar to "DDT" that it was hard to distinguish one name from the other. "TDE" is based upon another generic chemical name, namely, tetrachloro diphenylethane. The argument in favor of "DDD" rather than "TDE" is simply that the former name clearly shows the relationship to DDT. As was explained under DDT, neither of these generic names is sufficiently specific to satisfy the chemists, but again, the active isomer is the para,para isomer, and this is properly designated as 1,1-bis(p-chlorophenyl)-2,2-dichloroethane.

DDD has not had so many trade names as has DDT because it is not manufactured by such a great number of concerns, and is not as widely used. Probably the most common trade name is Rothane D-3.

Like DDT, DDD is a white crystalline solid that is soluble in most organic solvents and insoluble in water. It is effective against flies, mosquitoes, and other household pests, as well as a variety of agricultural insects, but in most cases it is less effective than DDT. It is somewhat less effective than DDT in its residual effect on most arthropods of public health significance. From the public health standpoint, DDD is most useful as a mosquito larvicide due to the fact that it is fully as effective as DDT, but less toxic to fish. Where fish are to be protected 0.05 pound DDD per acre should be sufficient. It has not proved of any value as a substitute for DDT against resistant flies.

It is commercially available as a technical grade material, as a dust, as a wettable powder, or as a solution. It may be formulated in essentially the same manner as DDT.

While it is somewhat less toxic than DDT, reasonable precautions should be taken to avoid unnecessary contact and breathing of DDD-laden air.

Methoxychlor — Methoxychlor is the common name given to the p,p'-dimethoxy analog of DDT, and is also known as the methoxy analog or dianisyl analog of DDT. Its proper chemical name is 2,2-bis(p-methoxyphenyl)-1,1,1-trichloroethane.

Methoxychlor also is a white crystalline solid, soluble in most common organic solvents and insoluble in water. Technical methoxychlor contains about 88 percent of the pure p,p'-isomer, and 12 percent of related materials.

Apparently due to some production complications, the technical material is most commonly sold as a 90 percent concentrate. This 90 percent concentrate has the appearance of a technical material even though it contains 10 percent oil. In general it can be formulated as though it were a technical material, making proper allowance for the oil present. It is also available as a 50 percent water-wettable powder which apparently does not contain the oil. For most uses the wettable powder is recommended by the manufacturer.

Methoxychlor is not as toxic as DDT or most of the other newer insecticides. However, reasonable care should be used in handling it, as in handling other insecticides, to avoid unnecessary breathing of dusts or sprays, or direct skin contact.

Though results obtained with methoxychlor as an insecticide have been somewhat erratic, it is one of the residual insecticides which is approved for use on dairy animals and in dairy barns for fly control. Because of the erratic results, it cannot be given blanket endorsement against DDT-resistant house flies, but in some areas it has given good results and therefore should be considered in any place where DDT is no longer giving satisfactory results in the control of house flies.

BENZENE HEXACHLORIDE AND LINDANE

During the second World War, the British discovered that a well-known chemical now commonly known as benzene hexachloride had considerable insecticidal activity. The common name arises from the fact that one of the classical methods of producing the material is by chlorinating benzene. Since each of the six carbon atoms of the benzene take up one atom of chlorine, the end product became known as benzene hexachloride. Strictly speaking, it should be called 1,2,3,4,5,6-hexachlorocyclohexane, since each of the carbon atoms retains one hydrogen atom, and therefore the compound is no longer related to benzene.

There are actually 16 possible geometrical isomers of this compound. Five of these occur in technical benzene hexachloride. Of these, the gamma isomer is the most active insecticidally. Since the common technical compound contains a relatively small amount of the gamma isomer, the purified gamma isomer which is commercially available has been given the separate common name of lindane. Therefore, even though both materials contain the same active ingredient, it is desirable to discuss them separately.

Benzene Hexachloride – Benzene hexachloride is commonly abbreviated BHC, though it has also been referred to as HCH, as an abbreviation for the more proper chemical name, hexachlorocyclohexane. Since the molecular formula for benzene hexachloride is $C_6H_6Cl_6$, it was given the common name of "666" at the time of its introduction to this country. Since there is a proprietary chill and fever tonic known under the trade name of "666," this name has not found favor here for the insecticide. Again, in view of the fact that the gamma isomer is the active isomer, a British manufacturer coined the trade name Gammexane. The name "Gammexane" is not restricted to lindane, but is used in connection with the technical product. Apparently it refers only to the gamma isomer, regardless of whether the gamma isomer is found in association with other isomers as is true in technical BHC, or whether the isomer is in a pure state, as in lindane. In the use of this name, therefore, care should be taken that the actual amount of gamma isomer and the presence or absence of other isomers is specified. In general, with the technical material, it is considered preferable to use the common name, benzene hexachloride, and to specify the gamma isomer content. Technical grades of benzene hexachloride which are available commercially range from 12 percent to 36 percent of gamma isomer, so that it is obvious that the designation of the common name by itself is inadequate.

The technical material is a somewhat dirty-appearing crystalline solid which is soluble in varying degrees in a wide variety of common solvents, but practically insoluble in water. It possesses fumigant properties and has a strong, highly persistent musty odor which is disagreeable to many persons. The odor appears to be associated with some of the impurities rather than with the gamma isomer, and therefore the purer compounds such as lindane have somewhat less odor.

Benzene hexachloride is available commercially as technical material, wettable powders, dusts, solutions, and emulsifiable concentrates. Every type of preparation should be clearly labelled to indicate the percentage of gamma isomer that it contains.

The various isomers are not equally toxic to man nor are they eliminated from the body with equal ease. Therefore the danger of use varies with the composition of the technical material. In general, the use of benzene hexachloride requires somewhat greater precautions than DDT and its analogs. It should not be applied to dairy animals or to the food of man or animals.

The odor of benzene hexachloride is one of the greatest limitations to its use. It may impart an off-taste to certain foods. It has, therefore, only limited use in the control of household pests, though there are certain parts of the world where it is not found objectionable, and it has been rather widely used, particularly in Africa, as a residual spray for malaria control. It is quite effective as a mosquito larvicide. The technical grade containing 12 percent gamma isomer has been applied to small, landlocked ponds at the rate of 1 pound per acre, and as often as five times per season with no detectable injury to fish. Such an application was found to give satisfactory mosquito control for as long as 1 month per application, so that under many conditions, five applications per season should be as many as are required.

Lindane – The common name, lindane, is restricted to the essentially pure gamma isomer of benzene hexachloride. The name cannot be used if the material is less than 99 percent pure. The name may be used to indicate the composition of formulations prepared from lindane, but it cannot be used to refer to the gamma isomer content of formulations prepared from technical benzene hexachloride. The reason for this very strict definition is that various isomers of benzene hexachloride vary in their behavior within the mammalian body. From the standpoint of acute toxicity, the gamma isomer is the most toxic of the various isomers of benzene hexachloride, but it is excreted relatively rapidly, and therefore shows the lowest chronic toxicity. This distinction is obviously of considerable importance from the standpoint of the health hazard associsted with the use of these materials, and therefore, for the safeguarding of anyone who may be exposed to them, it is important that the distinction in names be rigidly adhered to.

Chemically, as explained above, it is known as gamma-1,2,3,4,5,6-hexachlorocyclohexane. Like BHC, it is a crystalline solid which is soluble in most organic solvents, but insoluble in water. It has a slightly musty odor but less so than benzene hexachloride, is more volatile than DDT, and possesses some fumigant properties.

Because of its acute toxicity, care should be taken to avoid breathing fumes, dusts, or sprays, and to avoid skin contact with lindane in any form. Contaminated skin areas should be washed promptly with soap and water, and contaminated clothing should not be worn. Lindane should not be applied directly to dairy animals, to animal foods and water, or to equipment used in feeding and watering animals.

On the other hand, because of its low chronic toxicity, lindane has been approved for use in dairy barns for the control of flies. The recommended dosage is 25 milligrams per square foot, or a relatively small fraction of the recommended dosage of DDT. It should be quite clear that though lindane is satisfactory for use in dairy barns, technical benzene hexachloride is not. Like methoxychlor, lindane has given somewhat erratic results in the control of flies which are resistant to DDT. However, it should be considered as a possible insecticide for fly control in places where DDT is no longer satisfactory.

CHLORDAN AND ITS ANALOGS

As indicated heretofore, soon after DDT made its debut as a residual insecticide, the world was swamped with a number of other materials which were supposed to be even more effective than DDT. Benzene hexachloride was a contribution from Europe. In this country, one of the first and still one of the most effective substitutes for DDT was chlordan. The same chemists who developed chlordan continued investigations of related compounds and have since released a series with slightly different characteristics, but all highly effective insecticides.

Chlordan – Chlordan is perhaps more widely known in this country under the common name of "chlordane." The latter spelling has been accepted by the Interdepartmental Committee for Pest Control, by the American Association of Economic Entomologists and by various other organizations. The editor of Chemical Abstracts, however, maintains that the use of the "e" on the end of the name is misleading as regards the chemical structure of the compound, and that therefore the spelling without the "e" is preferable. The argument revolves around the question of whether or not a common name of this type should be in keeping with accepted chemical nomenclature. It is true that it is not designed as a chemical name. However, as a common name, it is used to refer to the chemical itself rather than to the insecticide, as is evidenced by the fact that it is frequently used in connection with the designation of a particular isomer. Thus it is not uncommon to speak of alpha-chlordan. On the other hand, there seems to be little danger of confusion, regardless of which name is chosen. Even though "chlordane" is more commonly used in this country, "chlordan" is still the preference of Chemical Abstracts and is used by such other world-wide abstracting journals as "The Review of Applied Entomology," and since there seems to be no logical objection to it, it has been chosen for use in this article.

When the material was still in the experimental stage, it was referred to as "1068," for much the same reason that benzene hexachloride got the common name "666," – namely, the molecular formula, which is $C_{10}H_6Cl_8$. This common name is still used in connection with the trade name "Velsicol 1068." It has also been referred to in the past under the trademarked name "Octa-Klor." As is true with the other insecticides, formulations containing this material may be known under a wide variety of trade names, but under present registration laws the lable must indicate the active ingredient as chlordan. The proper chemical name for the material is 1,2,4,5,6,7,8,8-octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindane.

Chlodan is a dark, viscous, oily liquid which is soluble in most organic solvents and is insoluble in water. Though it does not consist entirely of the material indicated by the chemical name, the related compounds present to the extent of 25 to 40 percent in the technical material are also toxic to certain insects and therefore all of the ingredients are considered insecticidally active. In view of the variation in activity of various isomers and impurities it is not possible to insure uniform insecticidal activity by chemical requirements. Therefore, in purchasing chlordan from the manufacturer, the purchaser should be assured that the material has been tested biologically and that it measures up to a reasonable standard in bio-assay.

Chlordan is commercially available as wettable powders, emulsifiable or solubilized concentrates, oil solutions, low percentage dusts, and technical chlordan. Technical chlordan is available in two grades – refined and agricultural. Both grades appear essentially equal in their insecticidal properties. The agricultural grade may be used where-ever the staining of treated surfaces is not a problem. The refined grade is generally used around premises for the control of household insect pests.

Upon standing for long periods of time, chlordan tends to solidify to a somewhat gummy mass, which nevertheless will readily dissolve in organic solvents. Of more importance is the fact that it is rather readily decomposed with the liberation of hydrocloric acid, which, in turn, may attack metal containers and encourage further deterioration of finished formulations. It is therefore unwise to store chlordan or formulations containing it in containers other than glass, aluminum, aluminum-clad steel, or high-bake phenolic lacquer-lined metal. In general, chlordan concentrates should be used while as fresh as possible, and the sprayers in which such emulsions are used should be washed thoroughly at the end of each day's work.

Chlordan is more toxic to man and animals than DDT, and considerable care should be exercised in using it to avoid breathing chlordan fumes, dusts, powders, or mists, and to avoid skin contact in any form. Waterproof xylene-resistant gloves should be worn by operators of mixing stations. Skin areas contaminated with chlordan sprays, concentrates, or the technical material should be washed immediately with soap and water, and contaminated clothing should not be worn. Though a great deal of chlordan has been used with no apparent ill effects to users, there have been several cases reported where animals have been injured or killed when held in cages treated with chlordan, and there has been at least one human death in which chlordan apparently was a contributing factor.

Chlordan and its related compounds are even more dangerous than some of the other chlorinated hydrocarbons in that most experimental animals which have shown any symptoms of poisoning from these materials have died even though removed from further exposure. Warning symptoms of chlordan poisoning therefore are not reliable. Since it is known that young animals are more susceptible to poisoning by chlordan than adults, it has been recommended that the interior walls and ceilings of homes should not be sprayed with chlordan in such a way that the occupants, including infants, might be exposed for 24 hours a day to the fumes of this relatively volatile material. When proper precautions are taken, chlordan is very effective against a variety of insects and is particularly useful against DDT-resistant flies. It has been widely used around baseboards and other selected portions of kitchens, porches, and other parts of homes for the control of roaches and ants. Since it is somewhat more effective than DDT, a lower concentration is satisfactory.

Heptachlor – Heptachlor is the name given to an insecticide which is closely related to chlordan. Chemically, it is known as 1,4,5,6,7,8,8-heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene. The origin of the common name is apparent from the chemical name, when it is compared with the chemical name of chlordan, a material which was isolated and found to be insecticidally active previous to heptachlor.

Heptachlor is a white crystalline solid which is readily soluble in a wide variety of organic solvents, but insoluble in water. It is more volatile than DDT and some of the other chlorinated hydrocarbons, and therefore not as long lasting in its residual effectiveness.

Heptachlor is not yet commercially available and appears to be somewhat more toxic than DDT, although less work has been done on its toxicity. Since it seems to have little advantage over the other chlorinated hydrocarbons as regards control of insects of public health significance, it is not anticipated that it will be commonly encountered in public health work.

Aldrin – Aldrin, which was known originally as Compound 118, is another chlorinated hydrocarbon rather closely related to chlordan. It has been given the trade name "Octalene," and it is chemically known as 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4,5,8-dimethanonaphthalene.

It is a white crystalline solid which, like the other chlorinated hydrocarbons, is soluble in most organic solvents and is insoluble in water. It is even more volatile than chlordan and therefore possesses considerable fumigant properties.

It is available in essentially the same types of formulations as the other chlorinated hydrocarbons, and because of its toxicity must be handled with extreme caution. Considerably more must be learned about its toxicity if it is to be generally used. So far, its use has been restricted to a few agricultural crops. In view of its volatility, which cuts down the length of its residual effect and adds to the hazard of its use, it is not anticipated that it will find wide use in control of insects of public health importance.

Dieldrin – Dieldrin is a chlorinated hydrocarbon which is very closely related to aldrin, differing from it only in the presence of an additional oxygen atom. Experimentally it was known as Compound 497, and the manufacturer gave it the trade name "Octalox" at the same time that aldrin was known as "Octalene." The origin of the common names aldrin and dieldrin lies in the fact that both compounds are manufactured by a process developed by the chemists, Diels and Alder. This origin of the name provides a clue to the pronunciation of it, which should be with two syllables instead of three.

The chemical name is 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4,5,8-dimethanonaphthalene.

Dieldrin, which like many of the other chlorinated hydrocarbons is a crystalline solid soluble in some organic solvents but insoluble in water, is one of the most interesting of the newer chlorinated hydrocarbons. It is only very slightly volatile, but because of its very high toxicity to insects, it does have some fumigant properties in tightly enclosed areas. It is perhaps even more stable than DDT and therefore is effective as a residual for prolonged periods.

Up to the present, its sale has been restricted to experimental uses, but for such purposes it has been available in the usual forms. It is very much more toxic to man and animals than is DDT. Users should exercise extreme care in handling it, since it is readily absorbed through the skin, even in the dry state.

Because of its very great effectiveness it can be used in much lower concentrations than DDT, and therefore it is quite possible that it may become useful in control of various insects of public health significance. For the present, however, in view of its high toxicity, even if it is licensed for sale, its use should be closely supervised until such a time as the necessary precautions can be more firmly established.

Unfortunately, house flies which are resistant to DDT have in certain cases been able to develop a resistance to dieldrin very rapidly. Therefore it is too early to predict how satisfactory it may prove to be for the control of DDT-resistant house flies.

TOXAPHENE

Even before the end of World War II, several new insecticides were suggested as supplements to DDT. One of these was given the experimental name of Compound 3956. It is now known under the accepted common name of toxaphene. It is a mixture of compounds containing principally polychlorinated bicyclic terpenes of the camphene type, and therefore has also been known as chlorinated camphene.

Toxaphene is an amber, waxy solid having a mild odor suggestive of chlorine and camphor. It is readily soluble in most organic solvents but is insoluble in water.

It is available in the usual forms, including technical grade. It is somewhat more toxic to mammals than is DDT, and though it is effective against most household pests, it is inferior to DDT for the control of most of these insects. For this reason it has had little place in medical entomology. Toxaphene is quite effective against fly and mosquito larvae. It has been so toxic to fish that it has been suggested as a substitute for other fish poisons for use in studying fish populations; therefore it should never be used in water where wildlife must be conserved. Its greatest use has been in the control of agricultural insects.

POLYPHOSPHATES

The polyphosphates are a group of insecticides which are closely related to various war gases. Most of them were developed in Germany during World War II as insecticides. Their relationship to war gases is the most critical thing for the sanitarian to know, since it indicates their extreme toxicity. None of them are currently considered useful in the control of household insects, because of their high toxicity and the fact that they rapidly decompose and therefore have no residual effectiveness. Experimentally, some of them have been tested as mosquito larvicides but have never been so recommended. In view of the extreme hazard connected with their use, it is not considered necessary to discuss each of them separately; but the most common ones are listed below, together with their synonyms and common names. Most commercial formulations which are using polyphosphates as their active ingredient will contain a mixture of two or more of those listed, or related compounds.

Parathion – The polyphosphate most commonly used in agriculture in this country at present has been known under the experimental designations E-605 and Compound 3422. It has been given the common name, "parathion," and has been referred to under a variety of trade names, including "Thiophos" and "Niran."

Chemically it is designated as o,o-diethyl-o-p-nitrophenyl thiophosphate.

Tetraethyl Pyrophosphate – Tetraethyl pyrophosphate is often abbreviated as TEPP, and the chemical name is the same as the common name.

Hexaethyl Tetraphosphate – Hexaethyl tetraphosphate has been abbreviated HETP, and has been known under the trade name "Bladan." Again, its chemical name is the same as its common name.

PYRETHRUM AND ITS SYNERGISTS

This group of insecticides is of importance primarily in space sprays, including aerosols. They are in general very effective in knocking down insects, though sometimes somewhat less effective in producing final kill. In other words, it is not uncommon for insects to recover from the effects of some of the members of this group of insecticides. The compounds, particularly those found in pyrethrum, are somewhat unstable, being readily decomposed even by light and air. For this reason, they ordinarily have very little residual action.

Pyrethrum is of course a plant extract, though there have been synthesized some organic chemicals which are very similar to the active ingredients of pyrethrum. Several synthetic materials have been useful as synergists with pyrethrum, and they therefore are also considered under this general heading.

Pyrethrum – Pyrethrum is probably the oldest of the insecticides which are included in this discussion. The flower of *Chrysanthemum cinerariaefolium* is the source of this powerful insecticide which has been known, particularly early in this century, as insect powder, or as Kenya flowers, or Trieste flowers. The extract of the flower heads was used in fly sprays for many years before the chemists had determined the chemical nature of the active ingredients. Four of the most active ingredients have now been isolated and are known as Pyrethrins I and II and Cinerins I and II. The separate ingredients are never used in a pure state, but the strength of a pyrethrum solution is usually expressed in terms of the concentration of pyrethrins and the concentration of other active extractives. It is interesting that pyrethrum can be used to control flies which are resistant to all of the chlorinated hydrocarbons. However, pyrethrum not only is expensive, but because of its lack of residual action must be applied so frequently that under ordinary circumstances it is not considered practical for use on an operational program.

Of all of the insecticides currently in use, pyrethrum is perhaps the least toxic to mammals. It is often used in combination with other insecticides for space sprays or aerosols directed at a variety of livestock pests, as well as insects occurring in the household.

Allethrin – There recently has been placed on the market a synthetic material which has been widely publicized as a synthetic pyrethrum. Actually this is a misnomer, for chemically the material is more closely related to cinerin than it is to pyrethrin, and, more properly known as the allyl analog of cinerin. The development of this material is very important because of the fact that pyrethrum continues to be an insecticide of major importance in the control of a variety of insects and yet it is an insecticide which is very susceptible to war shortages, since it has never been produced economically in this country. It was actually the wartime shortage of pyrethrum in this country that stimulated a search which uncovered the merits of DDT. The possibility of synthetically manufacturing an insecticide with characteristics similar to pyrethrum therefore is of considerable importance to national security.

The currently available allyl analog of cinerin has not proven as generally useful as natural pyrethrum, but its development is certainly a very important step in the right direction.

Synthetic Synergists – In view of the above described critical shortages or anticipated shortages of pyrethrum, a great deal of effort has been devoted to searching for methods of extending the usefulness of short supplies of pyrethrum. Sesame oil was first found to serve as a synergist for pyrethrum. That is to say that by the addition of a small amount of sesame oil, which in itself is essentially valueless as an insecticide, a small dosage of pyrethrum may be made as effective as a large dose of pyrethrum would be by itself. In trying to improve aerosol formulations, it was found that the addition of simple lubricating oil served in much the same manner. The search was continued, and there are now several synthetic chemicals which have been proven to be quite effective as synergists for pyrethrum. It should not be necessary to describe these synergists in detail, but the current list includes the piperonal derivatives, piperonyl butoxide and piperonyl cyclonene. Piperonyl cyclonene has also been known under the name piperonyl cyclohexenone. Both of these piperonal derivatives have been claimed as stabilizing agents for pyrethrum and thus permit some residual action. However, this has not been particularly successful and they must still be considered primarily as extenders for pyrethrum when used as a space spray. N-isome and Synergist 264, formerly known as VanDyk 264, are other synergists which also have been shown to have considerable value when used with pyrethrum in space sprays. The use of these and other synergists with so-called synthetic pyrethrum is under investigation at present.

THIOCYANATES

A number of years before the beginning of World War II, the group of insecticides known as thiocyanates was developed for use in combination with pyrethrum in space sprays in order to insure that insects knocked down by the pyrethrum would be killed and not recover. The thiocyanates, of which there are a number, have been sold under the trade names of "Lethane" and "Thanite." They have been useful in a variety of other applications and are not dependent upon the presence of pyrethrum, and therefore they cannot be considered as synergists. However, their usefulness as regards the control of insects of public health importance is largely restricted to space sprays. Since they are appreciably more toxic than pyrethrum, and presumably more toxic than the above-named synergists, they must be used with caution and their concentration in a space spray should not exceed recommended dosages.

RODENTICIDES

There has been a large number of new rodenticides introduced in this country since the beginning of World War II. Most of these have been found to be of little value. Several of the older rodenticides such as sodium arsenite and red squill are still in use but are not included because they are well known to anyone who has been working with rodenticides.

Of the newer ones, ANTU, 1080, and warfarin are the only ones which need be considered.

ANTU – Alpha naphthyl thiourea is commonly abbreviated to form the common name, ANTU, for this rodenticide which found considerable use during World War II. Because of the physical nature of ANTU, it was possible to use it as a dust and rats could be killed simply by tracking through the dust and subsequently cleaning their paws with their mouths. ANTU has proven reasonably effective against adult Norway rats, but much less effective against immature Norway and roof rats. Since the roof rat predominates in many areas, this selective action has greatly limited its usefulness. Even against Norway rats it was not 100 percent effective, though it was somewhat of an improvement over the old rodenticides. It has now been largely supplanted by better materials.

Sodium Fluoroacetate – Sodium fluoroacetate is commonly known as "1080," a name which has no significance except that it was an arbitrary number assigned to an experimental chemical. It is one of the most toxic rodenticides that has been used, being comparable in toxicity to sodium cyanide. It is a white crystalline material slightly resembling flour or sugar. It is odorless and very soluble in water. When exposed to the air it absorbs water, becoming quite gummy. It is extremely fast acting, producing symptoms in rats within 30 minutes and resulting in death in 1 to 8 hours. Because of its high toxicity to man and domestic animals, its use has been restricted to trained personnel, and even under these restrictions, some accidents have occurred. It should never be allowed to fall into the hands of untrained individuals and should always be handled with utmost respect.

Warfarin — Warfarin is the common name which was given to the experimental rodenticide known as Compound 42 to honor the Wisconsin Alumni Research Foundation which owns the patent on this material. It has recently been licensed for general sale as a rodenticide. It is one of the most interesting of the newer economic poisons since it successfully employs a new principle as a rodenticide. It is primarily an anticoagulant, and in single doses, even massive doses, produces no noticeable harm to the animal. However, repeated doses, even though they be extremely small, eventually produce spontaneous hemorrhage which results in death.

It is sold under the trade names of "Dethmor" and "Rax Powder," and the accepted chemical name is 3-(α-acetonylbenzyl)-4-hydroxycoumarin, though it has also been known chemically as 3-(α-phenyl-β-acetylethyl)-4-hydroxycoumarin.

Warfarin is a stable, colorless, crystalline solid at ordinary temperatures and pressures. It is odorless and tasteless not only to man, but also to rats which accept baits containing the compound as readily as they do the same bait containing no poison. It is available in the form of a 0.5 percent powder. The diluent is corn starch, making it suitable for mixing with such additional baits as corn meal, bread crumbs, and meat.

It has been tested in solution, but ordinarily is not recommended for use in this form since one of its attractive features is the fact that it can be left in permanent bait stations with only infrequent checking. Dry baits are obviously desirable from this standpoint.

Warfarin is toxic to other mammals and to birds the same as it is to rats. The key to its safety is the fact that single large quantities are not likely to be fatal. If the bait is properly selected so that it will be attractive to as few animals other than rats as possible, and if it is placed in protected situations where it is not readily available to other animals to which it may be attractive, it can be rendered very safe. The greatest danger when the material is properly used is that cats — and presumably dogs — might be killed if, over a period of several days, they ate a number of rats sick or dead from ingesting the poisoned bait. It is suggested that under some circumstances the use of a suitable warning coloring agent may be advantageous.

INSECTICIDAL FORMULATIONS

DR. GEORGE W. PEARCE, Chemist,

MARY B. GOETTE, Sr. Asst. San. (R), JANET T. SPILLANE, Jr. Asst. San. (R)*

During the last decade a singularly large increase in the number of chemicals useful in controlling insect and other pests of plants, animals, and man has occurred. Practically all of these new pesticidal chemicals are organic in nature and generally have proved superior to the older inorganic poisons such as lead arsenate, calcium arsenate, and paris green. The initial inspiration for this large increase in the number of new insecticides was the discovery of the insecticidal properties of DDT, one of the most useful of the new materials. This compound was prepared originally about 75 years ago, but it was only during the second World War that the remarkable insecticidal

*Technical Development Services, Savannah, Ga.