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Cross Resistance in Sevin-selected House Flies and a Summary of Resistance Among the Carbamate Insecticides*. W. M. Hoskins and Sumio NAGASAWA** (Laboratory of Insect Physiology and Toxicology, Department of Entomology and Parasitology, University of California, Berkeley, California). Received Oct. 5, 1961. *Botyu-Kagaku*, 26, 115, 1961 (in English).

19. Sevin で淘汰されたイエバエにみられる交叉抵抗性と carbamate 系殺虫剤にたいする抵抗性研究の現状

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近年における carbamate 系殺虫剤の使用の増大は，これらにたいする抵抗性の発達をもたらしつつあり，これと系列を異にする殺虫剤間における交叉抵抗性の究明は，carbamate 系殺虫剤のいずれのものがこれら抵抗性昆虫個体群にたいして有効であるかの推定にあたつて，きわめて重要である．今日まで抵抗性の究明にもちいられたこの種殺虫剤の数は，まだすくなく，また昆虫の種類もおもにイエバエにおいてなされているにすぎない．先学者の幾人かによつてもちいられた昆虫は，不幸にして既にある種の殺虫剤にたいしてたかい抵抗性をもつていて，これらの報告の結果は carbamate 系殺虫剤にたいする抵抗性の解析に役立てることは不可能である．ここに報告する実験結果は，淘汰の歴史のあきらかな Sevin 抵抗性イエバエについてえられたもので，これは DDT, parathion および他の4種の carbamate 系殺虫剤にたいしては，抵抗性をもたない系統である．

The increasing use of carbamate insecticides in recent times makes the development of resistance to them and cross resistance between this group and other types of insecticides matters of prime importance for estimation of the probable usefulness of any member of the carbamate family. The available data concern only a few compounds and insects, primarily the house fly. Unfortunately the insects used by some experimenters were already highly resistant to certain other insecticides and hence the results obtained cannot be attributed solely to the carbamate concerned. The experiments to be reported concern the susceptibility to DDT, parathion and four carbamates of a Sevin-resistant strain of house flies of known history.

Procedures

The so-called SCR strain of *Musca domestica* was obtained from the Stauffer Agricultural Research Laboratory, Mtn. View, California, in 1956 and reared since that time without intentional exposure to insecticides. In 1959, when selection with Sevin was begun, the flies were normally sensitive to Sevin, the LD 50 for topical application of acetone solution to the notum being 1.2μg/♀. After selection for ten generations by exposure of adults to boards treated with Sevin the resistance was not measurable by topical application since about 10 per cent mortality resulted from application of 100 μg. (Eldefrawi, 1960). This colony, hereafter called SR to denote resistance to Sevin was then kept under larval exposure to Sevin to maintain the resistance until completion of the present work in the spring of 1960. Each generation used in tests was, of course, reared in uncontaminated medium. The SCR strain maintained in the laboratory was used for comparison.

All tests were made with females 3 to 5 days old. They were sexed under light anesthesia with carbon dioxide and kept for 24 to 30 hours with sugar and water until used. Then under

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light anesthesia 1 μl acetone solution of the chosen insecticide was applied to the notum in groups of 30 flies and the treated flies were kept at 25°C in 150 ml beakers with sugar and water until mortality was read 24 hours later. Four to eight amounts were applied in each run and all runs were repeated three times. The dosages were chosen to give a range from low to high mortality in each case. The insecticides used were: *p, p'*-DDT, parathion, Sevin (1-naphthyl, N-methyl carbamate), Dimetilan (2-dimethylcarbonyl, 3-methyl, pyrazolyl, 5-dimethyl carbamate), Isolan (1-*iso*propyl, 3-methyl, 5-pyrazolyl, N, N-dimethyl carbamate), and Pyrolan (1-phenyl, 3-methyl, 5-pyrazolyl, N, N-dimethyl carbamate). The DDT sample was recrystallized from a research grade lot and the others were of research grade as furnished by the manufacturers.

Results

Table 1 gives the LD 50's and slopes of the ld-p lines for the six insecticides used as described on the susceptible laboratory colony and on the Sevin-selected strain. All lines were consistent with the data by the χ^2-test, provided one widely divergent point for Isolan at low dosage is ignored. It will be noted that Sevin is the least toxic to the laboratory flies and that its ld-p line has a low slope, indicating a wide spread in sensitivity among the members of any sample. In a few tests the ld-p line showed a break as if a portion of the population was relatively immune to the toxicant. Selection with Sevin for the relatively short period of ten generations transformed the laboratory colony into an almost totally resistant population as shown by the data for the Sevin-selected strain. It was not possible to obtain points at sufficiently high mortalities to define the ld-p line for the SR strain, because of limitation in solubility of the toxicant and, perhaps, from ineffective absorption of large dosages. The increases in LD 50 for the other three carbamates were much less (3.1 to 4.3 fold) which fall within the range often found for non-specific vigor tolerance (Hoskins and Gordon, 1956). The slope of the ld-p line was unchanged in the case of Dimetilan, which commonly occurs in vigor tolerance. The comparatively slight flattening of the lines for Isolan and Pyrolan was not accompanied by any inflection and hence it may be concluded that selection with Sevin to a highly resistant level did not lead to specific resistance of the flies against the other three carbamates. The same situation obviously holds for parathion.

In the case of DDT the ld-p lines for both strains are unusually flat and there is evidence that each strain contained susceptible and resistant individuals. Fig. 1 shows the experimental points and the best straight lines (A, B) from which the quantities in Table 1 were calculated, and the inflected lines (C, D) which represent more accurately the relation of dosage to mortality. In accordance with the principle that the proportion of susceptible individuals in a population is given by the mortality level at which an inflection occurs in the ld-p line (Hoskins, 1960), line C indicates that about 53 per cent of the

Table 1. Dosage-mortality relations for six insecticides applied topically in acetone to females of the susceptible laboratory strain of *Musca domestica* and to females of the Sevin-selected strain.

Insecticide	Susceptible strain		Sevin-selected strain	
	LD 50 in μg/♀	Slope of ld-p line	LD 50 in μg/♀	Slope of ld-p line
Sevin	1.53	1.7	>100	indeterminate
Dimetilan	0.10	3.5	0.31	3.5
Isolan	0.27	3.6	1.16	2.9
Pyrolan	1.24	3.2	4.65	2.3
p, p'-DDT	0.18	0.7	2.0	0.9
Parathion	0.014	5.9	0.027	5.9

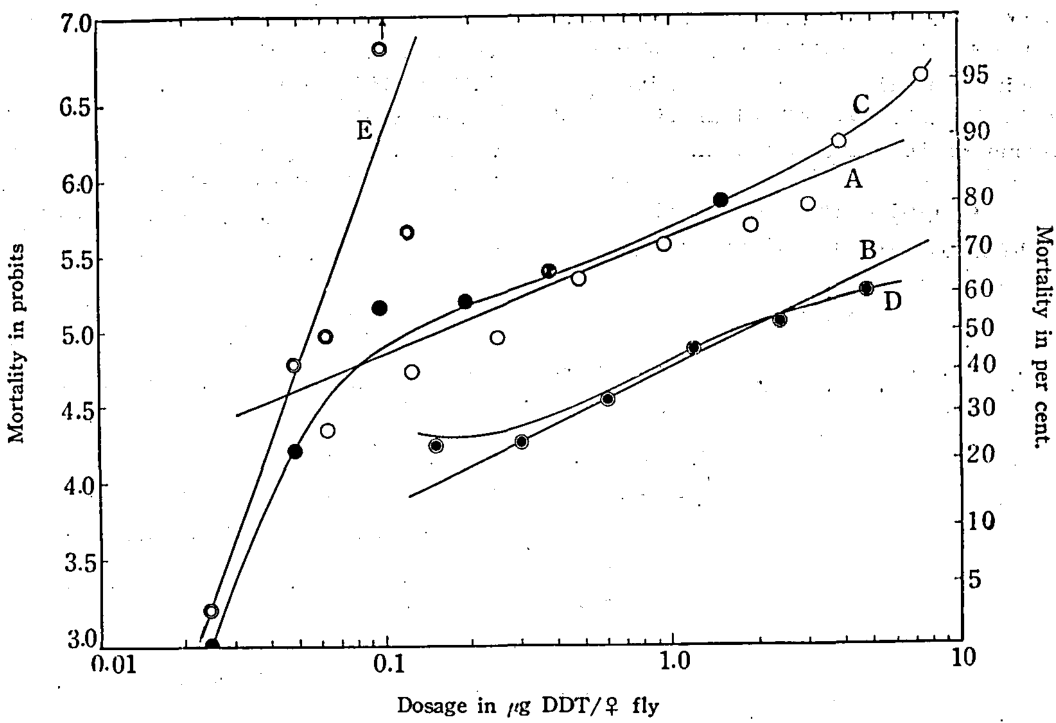

Fig. 1. Log dosage-probit lines for susceptible and Sevin resistant strains of *Musca domestica* treated topically with *p, p′*-DDT. For further explanation see text.

laboratory strain were susceptible. That these individuals actually were the susceptible genotype rr, lacking the gene for DDT resistance, is established by dividing the experimental mortalities by 0.53 to give the points x, which define E, the ld-p line for the susceptible component of the population. This has an LD 50=0.06 μg/♀ and slope 5 which are characteristic of the purest colonies of fully susceptible *Musca domestica* females. It is not known why nearly half of this laboratory colony was more resistant, presumably mostly hybrids with a few homozygous resistant individuals, except that what was thought to be minor accidental exposure to DDT and other insecticides is known to have occurred since the colony was brought into the laboratory.

With the understanding that the proportions indicated by the Hardy-Weinberg law for a panmictic population may not hold strictly for the present case (Hoskins, 1961), it is interesting to calculate that if rr individuals comprise 53 per cent of the population, the frequency of the r gene is $(0.53)^{1/2}=0.73$, and hence that of the R gene is 0.27. The hybrids, rR then make up $2\times0.73\times0.27\times100=39$ per cent, and fully resistant individuals $(0.27)^2\times100=8$ per cent, giving the make up of the population 0.53 : 0.39 : 0.08. Unfortunately, the experimental points at high mortality are not numerous enough to reveal the presence of such a small percentage of homozygous resistant insects.

The experimental points for the Sevin-selected strain do not show an inflection in the ld-p line so clearly but they do demonstrate that at a dosage which is fatal to all susceptible individuals, e.g., 0.3 μg/♀, the mortality is only about 23 per cent, which accordingly measures the fraction of rr individuals. With the same reservation as before and calculating in the same manner, the composition of the population appears to be 0.23 : 0.50 : 0.27. The significant point is that the selection with Sevin which resulted in a high resistance to that material, also shifted the sensitivity toward DDT in a manner that can be expressed as a decrease in the proportion of the homozygous susceptible individuals. The effect is not marked, but this case illustrates the value of knowing the composition of a population before it is put under pressure from an insecticide if the change in susceptibility is to be interpreted in terms of the genetic components.

Comparison With Other Results

The instances of resistance within the carbamate group or among other types of insecticides resulting from use of carbamates are included in Table 2 which summarizes the results for which quantitative data are given. It is arranged in the order: A and B) use of carbamates as selecting agents giving rise to resistance among that class of compounds or among other kinds of insecticides, and C and D) use of other types

Table 2. Insecticide resistance associated with the carbamates

Selecting agent and level of resistance or number of generations selected		Effect on susceptibility: Chemical	Degree[1]	Change in slope	Reference
		A. Carbamates to other carbamates			
Sevin	(F_{10})	Sevin*	> ×18	No data	Moorefield, 1960
			> ×36	–, and 10% mortality at 100 μg/♀	Eldefrawi, 1960
	(> ×18)	Isolan	×1.3	No data	Moorefield, 1960
		Pyrolan	×1.1		
		Compound III	×1.1		
		Compound VI*	> ×13		
Pyrolan[2] (from diazinon-r strain)	(×41)	Sevin	> ×18		
		Isolan	×3.1		
		Pyrolan	×4.1		
		Compound III	×2		
		Compound VI*	> ×13		
Pyrolan	(F_9)	Pyrolan	×1	No data	Wiesmann and Kocher, 1951
Pyrolan (DDT-r)	(F_{18})	Pyrolan	×1		
Pyrolan	(2 yrs.)	Pyrolan*	×300	No data	Wiesmann, 1956
Isolan	(F_{20})	Isolan	×7	+	Georghiou *et al*, 1961
	(×7)	Compound III*	> ×50	–, and maximum mortality 18% at 10 μg/♀	
		Pyrolan*	×30	–	
		Compound I	×4	0	
		Compound II*	> ×47	0 mort. at 100 μg/♀	
		Compound IV*	×41	maximum mortality 50% at 20 μg/♀	
		Compound V*	×9.2	–	
Compound I[5]	(F_{13})	Compound I	×1.2[3]	No data	Meltzer, 1956
Compound III	(F_{22})	Compound III*	> ×50	3% mortality at 100μg/♀	Georghiou *et al*, 1961
	(> ×50)	Isolan	×5.5	+	
		Pyrolan*	×15	–	
		Compound I	×2.8	0	
		Compound II*	> ×47	0 mortality	

Selecting agent and level of resistance or number of generations selected		Effect on susceptibility: Chemical	Degree[1]	Change in slope	Reference
		Compound IV*	> ×213	maximum mortality 15%	
		Compound V*	×10	–	
Compound III	(F_{59})	Compound III	×5	No data	Moorefield, 1960
	(×5)	Isolan	×1.5		
		Pyrolan	×1.6		
		Sevin*	> ×18		
		Compound VI*	> ×13		
Compound VI	(F_{16})	Compound VI*	> ×13		
	(> ×13)	Sevin*	> ×18		
		Isolan	×1.6		
		Pyrolan	×4		
		Compound III	×1.7		
		B. Carbamates to other types			
Sevin	(> ×18)	DDT	×1.5	No data	Moorefield, 1960
		Diazinon	×1		
Pyrolan[2] (from diazinon-r strain)	(×41)	DDT	> ×250		
		Diazinon	×42		
Pyrolan	(F_9 from a susceptible strain)	DDT	no change	No data	Wiesmann & Kocher, 1951
	(F_{18} from DDT-rstrain)		< ×1		
Pyrolan	(×300)	Diazinon*	resistant	No data	Wiesmann, 1956
Compound I[5]	(×1.2)	Lindane*	×13[3]	No data	Meltzer, 1956
Compound I[5]	(F_{39})	Lindane*	×27[3]	–	Meltzer, 1958
	(F_{15})	Toxaphene*	> ×1250[3]	?	
	(F_{14})	Chlordane*	×28[3]	–	
	(F_{20})	Aldrin*	×600[3]	–	
	(F_{40})	Aldrin*	×900[3]	–	
	(F_{19})	Dieldrin*	> ×23,000[3]	?	
	(F_{16})	DDT*	×0.6[3]	–, very flat above 50% mortality	
	(F_{22})	Diazinon	×6[3]	0	
Compound III	(> ×50)	DDT	×1	slightly –	Georghiou *et al*, 1961
		Methoxychlor	×7	–	
		Lindane*	> ×1100	?, probably –	
		Prolan	×2	slightly +	
		Parathion	×4	0	
		Malathion	×4.3	–	
		Chlorthion	×1	0	
		Diazinon	×5.5	0	

Selecting agent and level of resistance or number of generations selected		Effect on susceptibility: Chemical	Degree[1]	Change in slope	Reference
		Dicapthon	×1.6	0	
		Ronnel	×5	0	
Compound III	(> ×50)	Allethrin	×1.5	slightly −	Georghiou *et al*, 1961
Isolan	(×7)	Practically identical results for chemicals used on Compound III-selected flies			
		C. Chlorinated hydrocarbons			
DDT	(×24)	Sevin	×7	0	Eldefrawi *et al*, 1959
			×10	+	Eldefrawi *et al*, 1960
		Isolan	×3	+	
		Pyrolan	×2	+	
		Dimetilan	×1	+	
DDT	(> ×250)	Sevin*	> ×18	No data	Moorefield, 1960
		Pyrolan	×1.8	No data	
DDT	(> ×250)	Isolan	×1.5	No data	Moorefield, 1960
		Compound III	×1	0, probably	
DDT	(> ×400)[5]	Compound I	×1[3]	No data	Meltzer, 1956
DDT	very resistant	methyl carbamate	×6.5	0	LaBrecque *et al*, 1959
		Pyrolan*	×9.7	−	
DDT+ Lindane	very resistant to both	Pyrolan*	> ×27	−	Georghiou *et al*, 1961
		Isolan	×5.7	+	
DDT+ Lindane[4]	very resistant to both	Compound III*	×10	−, and maximum mortality 50%	
		Compound II*	> ×47	3% mortality at 100 μg/♀	
		Compound IV*	> ×200	5% mortality at 1μg/♀; 50% mortality at 100 μg/♀	
DDT+ Lindane[4]	very resistant to both	Compund V*	×13	−	Georghiou *et al*, 1961
		Compound I	×2	+	
Lindane	(×400)[5]	Compound I	×1.5[3]	No data	Meltzer, 1956
		D. Organic phosphates			
Parathion	(×10)	Sevin*	×20	10% mortality at 5-30 μg/♀	Eldefrawi *et al*, 1959
		Isolan	×5		Eldefrawi *et al*, 1960
		Dimetilan	×3.4		
		Pyrolan	×8.6		
Malathion	(×400)	methyl carbamate	×7.5	0	LaBrecque *et al*, 1959
		Pyrolan*	×7	inflection at 15% mortality LD 50=1.6 for rR	
Diazinon	(×38)[5]	Sevin*	> ×37[7]	Susceptibility had inflection at 70% mortality from 2.20 μg/fly	Forgash and Hansens, 1959

Selecting agent and level of resistance or number of generations selected	Effect on susceptibility		Change in slope	Reference
	Chemical	Degree[1]		
	Isolan	×14[7]	+	
	Pyrolan	×10[7]	0	
	Dimetilan	×6[7]	−	
Diazinon	Compound I	×1	No data	Meltzer, 1958
Chlorthion (> ×140)[6]	Isolan	×6.4	+	Georghiou *et al*, 1961
	Pyrolan*	> ×27	0 mortality at 100 μg/♀	
	Compound II*	> ×47	−, 10% mortality at 20 μg/♀; 30% mortality at 100 μg/♀	
	Compound III*	×4.1	−, and maximum mortality, 72%	
	Compound V*	×7.5	−	
	Compound I	×3.5	+	
	Compounp IV*	×6	−, and maximum mortality, 70%	

1. All comparisons are based on topical application except as noted.
2. This strain was resistant to Diazinon at start of selection with Pyrolan. Part of the resistance reached may be due to selection with Diazinon. Data on initial LD 50's refer to CSMA strain not to Diazinon-r strain actually used.
3. Exposure to residual deposits.
4. This laboratory strain was also highly resistant to cyclodienes and Sevin.
5. Mixed ♂'s and ♀'s used.
6. Calculated from LD 50 of laboratory strain=0.72 (Georghiou, 1961) and LD 50 of Chlorthion-r strain=>100 (March, 1960).
7. Dosage in μg/gms. wt. of flies.

* All instances considered to be true resistance are marked with an asterisk.

resulting in resistance to one or more carbamates. Unless noted otherwise, resistance levels are given in terms of the ratio of LD 50's. For the sake of consistency, those compounds not already described will be referred to by the same terms used by Meltzer (1956), Georghiou *et al* (1961) and others, namely: Compound I (phenyl N, N-dimethyl carbamate, also called S 17), Compound II (2-isopropyl, N-methyl carbamte), Compound III (3-isopropyl, N-methyl carbamate, also called AC 5727), Compound IV (2-isopropoxy, N-methyl carbamate), Compound V (3, 5-dimethoxy, N-methyl carbamate), Compound VI 3-*tert*butyl, N-methyl carbamate, and methyl carbamate (2-propyl, 4-methylpyrimidyl, N,N-dimethyl carbamate). The non-carbamate insecticides concerned are all referred to by the names approved by the ESA Committee on Insecticide Nomenclature.

Sometimes it is very difficult to decide if a measureable decrease in the effectiveness of an insecticide is due to the selecting out of individuals having a specific resistance to the compound, such as would result from the possession of an inherited detoxifying system, or to general higher tolerance to all adverse factors (Hoskins and Gordon, 1956; Hoskins, 1960). It has been pointed out often that when selection increases the number of individuals having a specific resistance factor and hence belonging to the hybrid and the homozygous resistant genotypes, the slope of the best line through experimental log dosage-mortality points will be decreased because of the greater spread in susceptibility of the mixed population. Hence, as criteria for deciding if resistance has resulted from the various uses or selection programs the following are suggested: a) the LD 50 has increased at least several fold compared to that of the susceptible strain, and b) the slope of the ld-p line is much less than that of the susceptible strain or there is an inflection indicating more than one component in the selected population. It is to be noted that very severe selection may result in a population consisting entirely of individuals of maximum resistance, in which case the ld-p line may be steep. In such instances the change in LD 50 also must be large. Unfortunately all writers have not given sufficient data for estimation of the change in slope or shape of the line. In these cases a large change in LD 50 is the only possible criterion.

The results of Moorefield (1960), of Eldefrawi (1960), and those of the present study show that resistance to Sevin is readily brought about by selection of adult flies. The resistance was high in all cases but could not be measured quantitatively because of limitation on the solubility of Sevin in the applied solutions. Among other carbamates resistance extended to Compound VI. No data appear to be available for Compounds I, II, IV, V and methyl carbamate. The results of Moorefield for Pyrolan-selected flies are difficult to interpret for the strain was already highly resistant to diazinon which is known to confer cross resistance to Sevin and possibly to other carbamates (Forgash and Hansens, 1959). Among those used upon the diazinon-Pyrolan-resitstant flies by Moorefield, however, only Compound VI showed a large change in LD 50. Wiesmann's (1956) results indicate that continued use of Pyrolan brings on real resistance (×300), though at an earlier time Wiesmann and Kocher (1951) had failed to find such an effect with a shorter selection period. Selection with Pyrolan did not lead to DDT resistance according to Wiesmann and Kocher (1951), and that found to DDT and diazinon by Moorefeld in his Pyrolan-selected strain was due undoubtedly to its previous exposure to diazinon. Wiesmann (1956) reported resistance to diazinon from Pyrolan selection but did not supply data on its level.

While Georghiou *et al* (1960) found a clear case of vigor toleranoe from twenty generations of selection with Isolan, these flies were resistant to all the other carbamates tested, i.e., Pyrolan and Compounds I to V. Components of the population differng in sensitivity were shown with Compounds III and IV, but the data are too fragmentary to permit calculation of the separate ld-p lines and LD 50's. No data are available on possible resistance to non-carbamates resulting from selection with Isolan.

Selection with Compound I for fourteen to twenty generations led to resistance to a series of chlorinated hydrocarbons (Meltzer, 1956, 1958), which was increased at least in the cases of lindane and aldrin by several more generations of selection. Meltzer's results with DDT are not clear since the the LD 50 was apparently *decreased* slightly but the LD 95 was raised some fifteen fold, probably corresponding to a break or inflection in the ld-p line above the 50 per cent mortality level. If this is the case, a change in ratio of susceptible to resistant individuals would be indicated and the situation would be similar to that found for resistance to DDT in Sevin-selected flies in the present investigation.

No data on effects of selecting with Compound II seem to be available, but selection with Compound III gave the same spectrum of resistance as with Isolan (Georghiou *et al*, 1961). Sevin and Compound VI were added to the list by Moorefield (1960). Among chlorinated hydrocarbons, resistance was found only to lindane. The only other carbamate with which selection has been made is Compound VI, and resistance to only itself and to Sevin are recorded (Georghiou *et al*, 1961).

In addition to the resistance arising from use of a carbamate insecticide, there is the converse effect of resistance to one or more of that group caused by selection of an insect population with another type of insecticide. Table 2, C and D, contains the available data. Considering first selection with chlorinated hydrocarbons, a strain highly resistant to DDT was also resistant to Sevin according to Moorefield (1960), though Eldefrawi *et al* (1959, 1960) found six-fold DDT resistance to be accompanied by what appeared to be vigor tolerance of a rather high order to Sevin. Moorefield's same strain of flies was not resistant to Pyrolan, but LaBrecque *et al* (1959) found a very resistant DDT strain to have a flattened ld-p line and nearly ten-fold increase in LD 50 for Pyrolan. Data were not given for calculating a change in ratio of components of the population but true resistance doubtless was concerned. Simultaneous selection with DDT and lindane resulted in high resistance to both, accompanied by resistance to Pyrolan and Compounds I to V (Georghiou *et al*, 1961). This resembles their results with the fly strain selected with Isolan.

Relatively few data have been recorded on the effect of selection with organic phosphates in causing resistance to carbamates. Table 2 D gives a case of Sevin resistance of a higher order than that to the selecting agent, parathion (Eldefrawi *et al*, 1959). A rather small change in LD 50 of Pyrolan (seven-fold) but an inflected ld-p line which permits calculation of the LD 50 for the hybrids=1.6μg Pyrolan/♀ resulted from selection with malathion (LaBrecque *et al*, 1959). Diazinon selection was accompanied by Sevin resistance (Forgash and Hansens, 1959). Lastly, the work of Georghiou *et al* (1961) with a chlorothion-selected strain showed resistance to Compounds II, III and IV, but not to I and an uncertain situation with V.

In contrast to the cases of resistance listed in Table 2, there are numerous instances in which severe selection did not lead to resistance to carbamates. Thus a strain more than eighteen-fold resistant to Sevin had normal susceptibility to Isolan, Pyrolan and Compound III (Moorefield, 1960). Continued selection with Isolan led to only a moderate increase in LD 50 (seven-fold) with a steeper ld-p line and the susceptibility to Compound I was but slightly decreased (Georghiou *et al*, 1961). The same workers found that selection with Compound III, resulting in high resistance to that material (> 50 fold) was not effective in bringing about resistance to Isolan or to Compound I. Moorefield (1960) selecting with Compound III found no appreciable change in susceptibility to Isolan or Pyrolan. His results on resistance to Compound III itself are doubtful since the change in LD 50 was only five-fold, and the effect on slope was not given. With Compound VI (>thirteen-fold change for it) he obtained only moderate change with Isolan, Pyrolan and Compound II. Finally, Meltzer (1956) after thirteen generations of selection with Compound I found sensitivity to that material unchanged.

Selection with Sevin resulting in over eighteen-fold increase in LD 50 gave no appreciable change in susceptibility to diazinon or DDT (Moorefield, 1960), contrasting with results of the present work for that compound. Wiesmann and Kocher (1951) were unable to change the susceptibility to Pyrolan by selection for eighteen generations, and the resistance to DDT (originally high) appeared to decrease slightly. Likewise, Meltzer (1958) changed the susceptibility to Compound I inappreciably by selection for some forty generations while the susceptibility to DDT increased somewhat. The comprehensive study of Georghiou *et al* (1961) showed that selection with Compound III (to fifty-fold increase in LD 50) had slight effect upon susceptibility to DDT, Pyrolan, parathion, chlorothion, diazinon, dicaphthon, Ronnel and allethrin, with uncertain increase in the cases of methoxychlor and malathion, but development of great resistance to lindane as mentioned before. Almost precisely the same situation was found for selection with Isolan except that toward the selecting agent only vigor tolerance (seven-fold increase in LD 50 and steepening of the ld-p line) was shown.

A number of cases are on record in which selection with a non-carbamate insecticide did not lead to resistance to members of that group, despite the considerable number of examples to the contrary in Table 2. Thus, a strain moderately resistant to DDT (twenty-four-fold) was still susceptible to Isolan, Pyrolan and Dimetilan, and the change with Sevin (seven to ten-fold, with steeper ld-p line) appeared to be a case of vigor tolerance (Eldefrawi *et al*, 1959, 1960). Moorefield's (1960) DDT-selected strain of flies was still susceptible to Pyrolan. To the contrary, a "very resistant" strain appeared to be resistant to Pyrolan since the ld-p line was flatter and the LD 50 greater by ten-fold (LaBrecque *et al*, 1959). Moorefield's (1960) highly DDT-resistant flies were still susceptible to Isolan and Compound III, and Meltzer (1956) using the technique of exposure to residual deposits detected no resistance to Compound I in his highly DDT-resistant strain.

Organic phosphate resistance appears to have no general relation to carbamate resistance. Thus selection with parathion (Eldefrawi *et al*, 1959) which led to genuine Sevin resistance had a lesser effect with Isolan, Dimetilan and Pyrolan (Eldefrawi, 1960). And a strain of flies highly resistant to malathion was doubtfully resistant to methyl carbamate as shown by an ld-p line of unchanged slope and seven-fold increase in LD 50. Diazinon selection was ineffective in bringing about resistance to Compound I (Meltzer, 1958), and the situation is not clear with three other carbamates (Forgash and Hansens, 1959). Finally, chlorothion resistance was not accompanied by resistance to Isolan or Compound I (Georghiou *et al*, 1961).

Very limited information on the resistance relations of certain carbamates is available for other insects. *Anopheles quadrimaculatus* mosquitoes (♂ and ♀) at least one hundred-fold resistant to dieldrin by the World Health Organization's adult test method were exposed to residual deposits of carbamates on plywood panels (LaBrecque *et al*, 1960). Compound III (called Hercules AC-5727 by the authors) was the most effective among thirteen materials tried, giving complete kill for at least twenty weeks from one minute's contact with an initial deposit of 1 mg/ft^2. Sevin also was effective, ranking among the best half dozen materials. With dieldrin-resistant strains of *A. albimanus*, *Aedes taeniorhyncus*, and *A. aegypti* adults, Compound III was also effective (Gahan *et al*, 1961). There seems to be no cross resistance from dieldrin to carbamates in these few species of mosquitoes.

With *Culex quinquefasciatus* mosquitoes which were fifty-fold resistant to DDT as larvae and six-fold resistant as adult ♀'s, Hassan (1960) found both stages as susceptible as a normal colony to Sevin, Isolan, Pyrolan, Compound III and Pyramat (2-*n*-propyl, 4-methyl, 6-pyrimidyl, N, N-dimethyl carbamate). The pattern of cross resistance between DDT and carbamates appears to differ from that for adult house flies as found by Moorefield (1960) and LaBrecque *et al* (1959), cf. Table 2 C.

A final instance of lack of cross resistance between chlorinated hydrocarbons and carbamates is given by the success obtained with Sevin in control of DDT-resistant codling moth in several districts of North America. Thus Marshall and Williams (1960) compared the effectiveness of practical control programs in an apple orchard in British Columbia with the results (each the average from three plots) DDT at twelve pounds per acre, 36.5 per cent injured fruit; Sevin at six pounds per acre, Test A, 2.4 per cent, Test B, 2.4 per cent, Test C, 1.9 per cent injured fruit. The contrast was actually greater than these figures indicate for over half the total fruit in the DDT plot were injured in early development and fell from the trees and hence were not counted. The control secured with Sevin was equal to that in localities where DDT resistance does not occur and hence it may be concluded that no cross resistance existed in the codling moth.

Discussion

It will be obvious from the foregoing account that in the present state of fragmentary information, any conclusions regarding the status of resistance to the carbamate insecticides must be only tentative. However, it is clear that these materials differ from one another greatly in the readiness with which resistance may be developed, both to the selecting compound and to other carbamates or to entirely different types of insecticides. Some discrepancies between experimenters are due to differences in the severity of selection as in the case of Pyrolan selection for two years leading to resistance to that compound (Wiesmann, 1956), whereas in earlier work this did not occur in a shorter selection time (Wiesmann and Kocher, 1951). Selection with DDT to a twenty four-fold increase in LD 50 caused what appeared to be vigor tolerance toward Sevin (Eldefrawi *et al*, 1959), but severe selection raised the LD 50 for Sevin to over eighteen-fold (Moorefield, 1960). Similarly Moorefield's strain of flies was not resistant to Pyrolan, but those of LaBrecque *et al* (1959) very clearly were truly resistant.

The carbamates inhibit the normal activity of cholinesterase and other esterase(s) and are themselves hydrolyzed in the insect body, probably at the R-$\overset{\|}{C}$- bond (Eldefrawi, 1960; Eldefrawi and Hoskins, 1961). The relative susceptibility or resistance of a given insect species or strain to a chosen carbamate depends largely upon the dynamic balance attained between the processes of inhibition of vital esterase(s) and of decomposition of the carbamate. That the balance is subject to very subtle factors is indicated by the observation of Moorefield (1960) that whereas Sevin, Compound III and Compound IV have almost identical I_{50} values for inhibition of fly-head cholinesterase, there are decided differences in their toxicities and cross resistance patterns. These three substances differ in structure chiefly in the presence of an H atom, an *iso*propyl group and a *tert*-butyl group on the carbon *meta* in position to the carbamate linkage. Only further work to reveal the details of the metabolic processes involved will permit explanation of the numerous puzzling behaviors of the carbamates and their cross resistance relations with other kinds of insecticides.

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On the Synergistic Effect of Natural and Synthetic Synergists on Barthrin. Studies on Synergist for Insecticides XXI. Hiromichi MATSUBARA (Department of Agricultural Chemistry, Faculty of Agriculture, Gifu University) Received Oct. 28, 1961. *Botyu-Kagaku*, 26, 125, 1961 (with English résumé, 132)

20. Barthrin に対する天然および合成共力剤の共力効果について（農薬の共力剤に関する研究 第21報）

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アカイエカ幼虫に対するノックダウンおよび致死効果ならびにイエバエに対するノックダウン効果を検する生物試験によつて，barthrin に対する天然および合成共力剤の共力効果を研究した．Barthrin のアカイエカ幼虫に対するノックダウン効力への各種共力剤の共力効果とその致死効力へのそれらの共力効果との間には平行関係が認められない．また一般に barthrin に対する天然および合成共力剤の共力効果はピレトリンおよびアレスリンに対する共力効果よりはるかに劣つている．

先に著者[1)]は barthrin の有効度および安定性をアカイエカの幼虫を用いる生物試験によつて研究し，アカイエカの幼虫に対する barthrin の致死効力は極めて強大で，アレスリンおよび *p,p'*-DDT よりはるかに勝り，ピレトリンの1.46倍に相当し，熱および紫外線に対しても他のピレスロイドより安定であるが，ピレトリンよりはるかに遅効性である事を報告した．本化合物はピレスロイドに対して共力効果を有するため