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The Chief of the Malaria Section has the honour to communicate hereunder a note on

H-24, A NEW PROCESS FOR THE REACTIVATION OF INSECTICIDES PRELIMINARY TRIALS. ACTION ON RESISTANT DOMESTIC FLIES

by

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The problem of the resistance of insects to insecticides is one of the most serious which has confronted the health services in recent years, since, although it is true that in the case of certain vector species such resistance has not arisen or has appeared only after there has been time to eradicate the disease, nevertheless in many cases of great importance the insecticides have generally failed.

On analysing the circumstances leading to this state of affairs, many features can readily be explained. Actually, it is possible to deduce a priori a relationship between the resistance and the type of insecticide. It has now been clearly demonstrated that such resistance is stronger and develops more rapidly in the case of stable compounds. Chemical stability, although on the one hand it helps to ensure a longer residual effect, has, on the other hand, the disadvantage of acting solely by dermal contact, thus depriving us of any other way of overcoming the new situation which has arisen.

As early as 1944, when we commenced our studies of the BHC series, we were able to prove that it could act at a distance, through sublimation, and already in 1945 we noted this action on the larvae and adults of A. maculipennis in the

laboratory. Subsequently, and before the failure of the stable insecticides, we continually stressed the stronger effect of BHC, advocating a repetition of the tests in this connexion. Such tests were carried out by Brazilian colleagues, who suggested that in disinfecting houses the latter should be kept closed for as long as possible so as to favour the fumigating action. Furthermore, the International Symposium on the control of insect disease vectors held in Rome under the auspices of WHO in 1953, has already dealt with the longer time necessary for the development of resistance to the volatile insecticides.

The most unsatisfactory feature in this connexion is fly control. Stable insecticides rapidly lose their activity, as do also the volatile ones eventually, if their action is confined solely to contact.

SOME ASPECTS OF H-24

H-24 does not represent in itself a new series, but is rather an industrial process applicable to already known insecticides. Its history is a very brief one. In 1947, the Spanish chemist, NEBRERA, started to look for an insecticide based on chlorination of the terpenes since the derivatives of spirits of turpentine would in fact be good insecticides if they did not have the drawback of being caustic. NEBRERA observed that when such derivatives were combined with the molecule of other insecticides such as DDT, BHC, phosphoric esters, and pyrethrum, the activity of these insecticides increased considerably. In the following years, in collaboration with MARRON, tests were carried out in the field of agriculture and it was not until 1953 that PASCALIN and VARGAS in Mexico and ourselves in Spain, applied this process to the public health field, when its great possibilities commenced to appear.

One of the most important aspects of the H-24 process is its general applicability to organic insecticides. PASCALIN, the chief engineer of the entomological laboratory of "Petroleos Mejicanos" states in this connexion, in a report published in 1953, that in all cases the toxicity of such insecticides towards insects appreciably increases, due to new properties conferred on the basic product. Thus,

DDT acquires fumigating properties. These results are achieved by incorporating one or more terpene groups into the insecticide molecule, when its contact properties are also strengthened, with no change in the toxophoric group, due to increased solubility of the cuticular lipoids arising from the terpene radical.

Nevertheless, a whole series of new properties observed in the laboratory still remain without explanation, although the increase in sublimating power partly accounts for those features relating to reactivation by inhalation.

In 1953, VARGAS, without specifying the basic insecticides used, stated that it was an effective larvicide and satisfactory imagocide, while being non-toxic towards man and animals. Tests we have carried out on flies, Tribolium, Ornithodorus and Anopheles fully support this, while toxicity tests carried out in Spain by the Pharmaco-biological Technical Centre also indicate favourable results with mice.

FIELD EXPERIMENTS

We had occasion to use a small amount of a product in the experimental stage, termed TC-1 by the manufacturers, for practical tests in July 1953 in part of the town of Talayuela. The said insecticide, made by the H-24 process, contained 0.4 per cent. of Lindane. The results were sufficiently encouraging for the trials to be continued with a higher dose.

Experiments in this connexion were carried out in 1954 to measure the activity with regard to flies in areas of resistance. For this purpose a series of hamlets ("caseríos") were selected in the El Guadalperal and Berzenuno pastureland area, situated in the valley of the river Tajo in the province of Cáceres, where disinsecting operations had been carried on for six years with various products and all hope of eradication had been given up.

Some preliminary tests were performed in two houses surrounded by stables. In the first, which contained two dwellings, the northern half was treated with H-24 containing 2 per cent. of Lindane and the southern half with H-24 containing 6 per cent. of the same insecticide. The second dwelling was treated with a usual type of BHC emulsion containing 6 per cent. Lindane. Our aim was to test the

killing effect on flies which were coming in huge numbers from the neighbouring stables. While the usual emulsion lost its fly killing effect after little more than a week, with definite slowness of action from the outset, the H-24 containing 2 per cent. Lindane retained it for a fortnight and the H-24 containing 6 per cent. Lindane for more than a month. In both cases, activity was greater when the flies were confined in the rooms treated.

Subsequently, in October 1954, 11,565 square metres in this area were treated with five types of H-24, all in the form of emulsions with a characteristic and very pleasant smell, as well as having completely satisfactory properties as regards stability and uniform dispersability in water. The attached table gives the most outstanding data from this experiment, the results being shown schematically so that they can be more readily grasped. Nevertheless, some explanation is unavoidable and certain aspects call for special consideration.

The date for the experiments was selected so as to be at a time when the breeding of the flies was at its height. In fact, after a summer when the relative humidity was extremely low, an acceptable density of insects did not build up until early in October. Normally the experimental period should have been very short, but in view of the mild autumn it was prolonged to some extent until adverse climatic conditions appeared. The fact that the experimental period was exceeded for some of the H-24 types does not impair the value of the tests, but it would be advisable to continue them so as to establish the maximum limit for the residual action.

A mere glance at the results shows the activity of the five types tried out and the notable effect of numbers 2, 4 and 5. In reality, we had considered for years that fly control in resistant zones was impossible. In this connexion it may be mentioned that in the experimental area the population showed a certain scepticism, consequent on the failure of many previous attempts. Thus a rough indication of the success achieved was the attitude of the inhabitants of the area treated. For example, in the hamlet of La Vega, (experiment No. 5) the house of the muleteer, which is completely surrounded by stables, was literally

besieged by flies, having to be kept completely closed during the day and fitted with curtains in the outer openings to be at all habitable. In the course of the trials it was found unnecessary to keep the house closed and the occupants were very surprised by this.

On analysing in detail the results which we have summarized in the table, it is evident that types 4 and 5 of H-24 are clearly more effective than the others. Naturally, both contain the maximum percentage of active ingredients and in the case of No. 5 there is a possibility of synergic action owing to the addition of DDT, although only in a small proportion. It is possible that this factor plays some part but we cannot exclude other reasons, since various features of the industrial process connected with the insecticidal action are unknown to us.

The increase in sublimating power is certainly the fundamental, if not the sole cause of reactivation. Thus, whatever may be the dose and types tried, in the first five days the results were equally conclusive. It may be supposed that at the outset inhalation takes place directly when the insect settles on the wall and that gradually this direct action becomes inadequate as the insecticides sublimate, but is strengthened by accumulation and acts indirectly in closed spaces. The insecticidal effect is restored when flies are shut in rooms where activity is absent when the door is left open.

Furthermore a large part of the reactivating effect may be due to the high dissolving power for lipoids conferred by the terpenes. However this would be valid above all for non-resistant populations or for those with a moderate degree of resistance, and more debatable in zones where the flies have remained unaffected by all doses and types of insecticide. In addition, certain accepted ideas on the genesis and maintenance of resistance would not fit in very well with this theory.

Neither the animals in the stables nor the inhabitants of the hamlets, nor the technicians and workmen handling H-24 and coming into close contact with it during spraying, showed the least sign of poisoning or repulsion. In many cases the stables were sprayed when the animals were already in them and the personnel did not use gloves or masks.

We intend to continue the work in the same zone in the coming campaign, with the aim of determining the conditions under which resistance, if any, can develop.

SUMMARY

The effects of various insecticidal compounds, manufactured by a special reactivating technique are studied. This new industrial process, known as H-24, has shown itself very effective in these experiments, certain types of the compounds tried out having a residual effect lasting more than 30 days on populations of resistant flies.

Because of an activated sublimation, there is a selective, air-borne action. This seems to be the fundamental reason for the success of these insecticides, although some part may be played by the greater solubility of the cuticular lipoids resulting from the presence of terpenes, as well as by other as yet insufficiently studied causes.

The authors propose to continue this work in the laboratory and in the field so as to determine the exact duration of the residual effect, the possibility of resistance developing in previously untreated fly populations and other details of public-health interest.

REFERENCES

There are no publications on H-24 apart from the reports mentioned.

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Date	Hamlet ("Caserío")	Area treated	Type of H-24	Dose per m^2	Results after 5 days	10 days	20 days	30 days
9.10.1954	Palacio y Dep.	4,421 m^2	No. 1. 3% Lindane	0.05	+ + +	+ +	+	+
7.10.1954	Bercenuño	1,100 "	No. 2. 6% Lindane	0.187	+ + +	+ + +	+ + +	+ + +
8.10.1954	Gallineros	1,006 "	No. 3. 3% Lindane	0.06	+ + +	+ +	+	—
8.10.1954	El Vegano	3,250 "	No. 4. 6% Lindane	0.187	+ + +	+ + +	+ + +	+ + +
8.10.1954	La Vega	1,788 "	No. 5. 5.5% Lindane + 3.5% DDT	0.10 Lindane + 0.063 DDT	+ + +	+ + +	+ + +	+ + +

(+ + +) All flies entering the houses die

(+ +) Only a few flies die in open rooms, it being necessary to close them for total extermination

(+) Lethal action only in closed rooms