

overstrain and damage of the heart and of blood vessels in various parts of the body.

In successive collaboration with Restall (5) and Alstad (7) the effects of test doses were studied in 170 patients, and treatment of 1-16 months' duration has been in progress in 68 patients, including hypertension of the malignant, essential, renal, and postpregnancy toxemic types. It is clear that blood pressure reduction can be obtained in hypertension cases, irrespective of the etiology, and also in normal controls. Clinical details of improvement in papilledema, retinal edema, retinal hemorrhages, headache, encephalopathic and dizzy attacks, general congestive heart failure, left ventricular failure, and exercise capacity are given elsewhere (5, 7-9).

The observations on normal subjects give direct evidence that the factors responsible for maintaining normal blood pressure levels are influenced by the drugs. In severe hypertensives the effect of a methonium injection may be sufficiently great to reduce the blood pressure by as much as 140 mm Hg systolic and 80 diastolic, which reduction is of the same order as the entire normal blood pressure (120 systolic, 75 diastolic). Hence it seems that the pathological fraction of the high blood pressure in essential hypertension is also reduced by methonium halides.

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A Test of the Infrared Absorption Theory of Olfaction

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Beck and Miles (1) have proposed an ingenious explanation for the sense of smell, based on differential radiation losses by the receptors responsible for the function. According to their theory, these receptors radiate and absorb selectively as a result of their size and shape, and when a substance with an absorption band in the appropriate region (8μ - 14μ) enters the nasal passages a transient loss of heat will occur, resulting in the perception of smell. Beck and Miles substantiated this theory by experiments performed on certain insects ideally suited for the purpose because of their external olfactory receptors. The difficulty of performing their experiment—i.e., the illumination of the olfactory receptors with radiation passing through an odorous vapor—on humans or

mammals in general led us to seek an indirect confirmation of the theory.

A gas in an opaque chamber will approach temperature equilibrium with the walls, a state in which the radiation absorbed and that emitted by the gas are of identical nature. If an odorous gas were enclosed in an opaque chamber at body temperature for a sufficient length of time to come to equilibrium with the chamber walls, and then inhaled through an opaque tube, also at body temperature, the radiation to the walls of the nasal passages would be unchanged. If the theory of Beck and Miles, as interpreted above, is correct, no sensation of smell would be produced, whereas according to the old explanation based on a chemical reaction induced in the nasal passages, the smell would be relatively unaffected by the temperature of the gas.

In an experiment involving this principle, the sensation of smell showed no evident dependence on the temperature of the gas inhaled. The procedure was to submerge a collapsible rubber bag, the connecting rubber tube, and the observer's head, with a small attached diving mask, in a reservoir of temperature-controlled water. Air mixed with vapor of cloves in the rubber bag was inhaled by the observer after he had remained submerged for several minutes, during which time breathing took place through a separate tube. It was calculated that temperature equilibrium for the gas and equipment should have required about 20 sec. A range of temperatures from 36.7° to 42.4° C in approximately 0.5° steps was used. Calculations showed that any cooling of the gas because of expansion while inhaling had a negligible effect.

A second related experiment required no special equipment. In this test the vapor of cloves was inhaled through the mouth, held in the lungs for 15 sec or more, and exhaled slowly through the nose. The odor of cloves was easily discernible in the exhaled vapor despite the fact that the vapor was very close to body temperature.

The failure of these experiments to yield any pronounced disappearance in sensation of smell when the vapor was at body temperature does not necessarily exclude infrared absorption as the basis of olfaction in humans. It becomes necessary, however, to assume that inside the nasal passages there are temperature differences resulting in a sensation roughly independent of the temperature of the gas as it enters the nose. Should this prove untenable, it may be necessary to return to the chemical theory of olfaction for mammals.

An experiment similar to that Beck and Miles performed on insects might be performed on humans. If a sealed tube of material transparent to the 8μ - 14μ region, and containing an odorous gas, could be inserted into the nasal passages, the ability or failure to smell this gas would be conclusive evidence for or against the infrared theory.

Addendum. Since the submission of this manuscript for publication, Lloyd H. Beck suggested in a private communication that phenyl ethyl alcohol would have

been a much better substance to use than cloves, which is detected through its pungency. Accordingly, Milton F. Metfessel, of the Psychology Department, and the senior author repeated the experiment on olfactory identification during exhalation, using β -phenyl ethyl alcohol, a substance that smells very much like roses.

Although a mere trace of the substance in a room produces a strong fragrance, under the conditions of the experiment most subjects (5 of 7) reported only a faint or transitory smell, and the others (with which Forrester's sensations agreed) were conscious of a strange sensation which, as one of the observers said, was "not a smell exactly." These results may, perhaps, be explained by the rapid adaptation that occurs for strong doses of the substance.

A positive check on the theory may have to await a test of the type suggested above, and Metfessel and Forrester are investigating its practicability.

Reference

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The Potentiation of DDT against Resistant Houseflies by Several Structurally Related Compounds

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The discovery of a potent synergist for DDT against DDT-resistant insects would provide a means of controlling such insects in the field (especially the housefly) and might be helpful in elucidating the mechanism of resistance.

Claims have been made that at least three quinones (1), two fluorinated DDT-analogs (2), octachloro-4,7-endomethylene-tetrahydrodrindine (2), several halogenated phenols (2), some 2,4-dinitrophenols (3), three diaryl sulfides (4), and sabadilla (5) promote and extend the toxicity of DDT toward certain insects. More recently, Perry and Hoskins (6) reported a marked increase in effectiveness of DDT-piperonyl cyclonene (the latter in considerable excess) against DDT-resistant houseflies, but not against susceptible strains.

Most of the synergists listed above were tested in this laboratory at a 1:10 ratio with DDT against DDT-resistant houseflies and were found to be weakly or only moderately active. This appears to confirm the observation of Perry and Hoskins (6) that the DDT-resistance of houseflies depends on one or more biological factors not encountered in the normal fly.

It is possible that the mechanism of DDT-resistance developed by the insect could be interrupted by a compound structurally related to DDT, and more especially by an analog which shared a good measure of its physical properties. In fact, this is borne out by the fair degree of synergistic activity provided for

DDT by its *p,p'*-difluorine analog, 2,2-bis(*p*-fluorophenyl)-1,1,1-trichloroethane (2). It therefore appeared worth while to test a series of DDT analogs, both with and without insecticidal activity, for their synergistic effect toward DDT, with especial reference to field strains of resistant flies. This is the first report of an investigation of this series of compounds for their synergistic activity.

The selected compounds, listed in Table 1, were

TABLE 1
TWENTY-FOUR HOUR MORTALITY OF WILD FEMALE DDT-RESISTANT HOUSEFLIES FOLLOWING A 2-HR EXPOSURE TO A DEPOSIT COMPOSED OF DDT (200 MG/SQ FT) AND A CANDIDATE SYNERGIST (20 MG/SQ FT) ON A POSTER BOARD SURFACE

No.	Synergist	Ratio of percentage mortality*
1	2,2-bis-(<i>p</i> -Chlorophenyl)-1,1,1-tribromoethane	10/1, 16/17
2	2,2-bis-(<i>p</i> -Chlorophenyl)-1,1-dichloroethane	14/7
3	1,1-bis-(<i>p</i> -Chlorophenyl)-ethanol	89/0, 63/7, 80/11
4	1,1-bis-(<i>p</i> -Chlorophenyl)-2,2,3-trichlorobutane	4/7
5	2,2-bis-(<i>p</i> -Fluorophenyl)-1,1,1-trichloroethane	11/7, 10/0
6	2,2-bis-(<i>p</i> -Bromophenyl)-1,1,1-trichloroethane	3/7
7	2,2-bis-(Phenyl)-1,1,1-trichloroethane	18/7
8	2,2-bis-(<i>p</i> -Ethylphenyl)-1,1,1-trichloroethane	10/7
9	2,2-bis-(<i>p</i> -Hydroxyphenyl)-1,1,1-trichloroethane	6/17, 3/1
10	2,2-bis-(<i>p</i> -Ethoxyphenyl)-1,1,1-trichloroethane	3/1, 34/17
11	1-(<i>p</i> -Chlorophenyl)-2,2,2-trichloroethanol	9/7, 8/0

* The numerators in these ratios are the average percentage kills produced by replications of the DDT-synergist combination on a single day. The denominators are the average percentage kills produced by DDT alone in a comparable number of replications. The multiple ratios were obtained by repeating the tests on more than one day.

tested as synergists for DDT by dissolving 125 mg of each separately in 25 ml of a 5% solution of DDT in methyl ethyl ketone. This solution was pipetted on a poster board surface at the rate of 200 mg DDT and 20 mg of candidate synergist per sq ft. (Conventional glass panels could not be used in these tests because of the failure of the DDT-synergist combinations to crystallize adequately even with waiting and stroking.) The solvent was allowed to evaporate, and test lots of approximately 40 wild DDT-resistant flies were held in contact with the deposits in Petri-dish wall cages (7) for a period of 2 hr. The flies then were removed and held under optimum conditions for recovery for a period of 24 hr. Mortality counts were made, and the percentage kills of female flies are given in Table 1.

1,1-bis-(*p*-Chlorophenyl)-ethanol is the outstanding compound among those under test, as judged on the basis of its consistent performance in the individual