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สถาบันวิจัยวิทยาศาสตร์และเทคโนโลยีแห่งประเทศไทย

สถาบันวิจัยวิทยาศาสตร์และเทคโนโลยีแห่งประเทศไทย

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# Insect Repellents
## 1942-55

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Statistical data--I. G. Farbenindustrie--Hochst. (Gordon.) 1945. 3 p. Deals in part with insecticides. Order from LC. Microfilm $1.25, photocopy $1.25. PB 14

Interview with Dr. Klebert, Jr., Dr. Redies and Dr. Konradi: synthetic rubber, chemical warfare. (Moir and others.) 1945. 4p. Brief description of the plant and methods used at the I.G. Farbenindustrie plant at Leverkusen. Work here dealt with synthetic rubber, chemical warfare agents (such as hydrazine), insecticides (such as Lauseto and Lausetoneu), and drugs (such as Sontochin). Order from LC. Microfilm $1.25, photocopy $1.25. PB 15

Laboratories of Bataafsche Petroleum Maatschappij (B.P.M.). (Vincent.) 1945. 5p. Brief description of the research carried on by the Laboratory during the war, and the methods taken to maintain staff and carry on this research. Report lists chief research problems handled. Order from LC. Microfilm $1.25, photocopy $1.25. PB 42

Pfaffenrode Hailenstalt Fur Geistes Frankheiten (Pfaffenrode insane asylum). (McCarthy.) 1945. 4p. Deals in part with insecticides. Order from LC. Microfilm $1.25, photocopy $1.25. PB 57

Schimmel & Co., Miltitz near Leipzig--Pharmaceutical production. (Leaper.) 1945. 3p. Deals in part with insecticides. Order from LC. Microfilm $1.25, photocopy $1.25. PB 63

Interrogation of Dr. Klebert, Dr. Redies and Dr. Konrad of the I.G. Farbenindustrie (Bayer & Co.) at Leverkusen, target Nos. 8/12, 22/2, 24/1 (production of chlorine, miscellaneous chemicals and insecticides.) (Moir and others.) 1945. 3p. Deals in part with insecticides. Order from LC. Microfilm $1.25, photocopy $1.25. PB 91

Anorgana G.m.b.H. Werk Gendorf. Chemical warfare. (Bidlack, Curtis and Harris.) 1945. 37p. Deals in part with Blattan an insecticide. Order from LC. Microfilm $2.25, photocopy $5. PB 163

I. G. Farbenindustrie Wolfen Farbenfabrik Wolfen Near Halle--Miscellaneous chemicals. (Leaper.) Jun 1945. 8p. Rather superficial examination of a small section of a heavily bombed chemical plant. Plant was completely shut down at times. Principal products were inorganic and organic chemical compounds, dyes, and nitrogen products. Some chemical warfare materials were produced; also detergents and insecticides. Order from LC. Microfilm $1.25, photocopy $1.25. PB 207

Dr. Alexander Wacker--Gesellschaft Fur Elektrochemische Industrie Burghausen, Germany. (Bidlack & others.) 1945. 30p. Deals in part with insecticides. Order from LC. Microfilm $2, photocopy $3.75. PB 208

I. G. Farbenindustrie A. G., Hochst am Main. (Richardson and others.) 1945. 84p. Deals in part with insecticides. Order from L.C. Microfilm $3.75, photocopy $11.75. PB 218

The N.V. Organon pharmaceutical factory, Oss, Holland. (Phelps.) 1945. 27p. The report discusses in part new developments in anti-louse powders. Order from L.C. Microfilm $2, photocopy $3.75. PB 228

Manufacture of insecticides, insect repellents, rodenticides--I.G. Farbenindustrie A.G., Leverkusen and Elberfeld. (Smadel and Curtis.) 1945. 12p. A report on the manufacture of insecticides and related products. It deals with Lausets-old, an analog of DDT and other DDT types, giving preparation and methods of use. Order from LC. Microfilm $1.75, photocopy $2.50. PB 240

Insecticides, insect repellents, rodenticides and fungicides of I.G., Farbenindustrie, A.G., Elberfeld and Leverkusen, Germany. (Hall.) 1945. 48p. The results of investigations in these two places have been combined in this report and should be read in conjuntion with PB 240. Order from LC. Microfilm $2.50, photocopy $6.25. PB 252

Impregnation of Herringbone twill and dimethyl phthalate and various fixatives; a memorandum report. (Glickman.) 1945. 19p. Description of test methods, impregnation methods, laundering fixatives used, etc., are given. Order from LC. Microfilm 50 cents, photocopy $2. PB 2374

Preparation of candidate insect repellents. (Smith, Irvin and others.) 1945. 5p. (OSRD Rept. 5285.) Deals in part with insect repellents. Order from LC. Microfilm 50 cents, photocopy $1. PB 4247

Insect and rodent control: CWS monthly progress reports 1-6, Mar.-Aug. 1945. U. S. Chemical Warfare Service. Mar.-Aug. 1945. 356p. Among other things the synthesis of new compounds in a systematic attempt to eliminate deficiencies in existing insecticides, miticides and rodenticides. Graphs, diagrams, tables and bibliography are included. Order from LC. Microfilm $4, photocopy $24. PB 19258

Investigation of insecticide and insectifuge research and manufacture in western Germany. (Kilgore.) (FIAT Final Rept. 38.) Sept. 1945. 25p. Non-phenol disinfectants, and thallium rodenticides are considered. Order from LC. Microfilm 50 cents, photocopy $2. PB 22413

Insect repellents, attempts to increase duration of effectiveness. (Mathieson and Wilson.) (Bureau of Medicine and Surgery Res. Project X-168, Rept. 1.) Aug. 1944. 4p. Attempts were made to increase the duration of effectiveness of the currently adopted insect repellents by: (1) absorbing them to inert fillers, binders, or adhesives with large absorbing surfaces and (2) incorporating them in film-forming gels. Order from LC. Microfilm 50 cents, photocopy $1. PB 22975

The preparation of some organic compounds for testing as insect repellents. Final report, Oct. 31, 1945. (Bartlett and others.) (OSRD Rept. 6367.) Dec. 1945. 110p. Order from LC. Microfilm $3, photocopy $8. PB 27406

The synthesis of some compounds for testing as insect repellents. Progress report to Sep. 30, 1945. (Heaton and others.) (OSRD Rept. 6368.) Dec. 1945. 21p. Ninety-five compounds were submitted for testing, 5 of which afforded about the same protection. Order from LC. Microfilm $1, photocopy $2. PB 27407

The preparation of some compounds for testing as insect repellents. Final report, Oct. 31, 1945. (Newman and others.) (OSRD Rept. 6369.) Dec. 1945. 90p. Records the preparation of 743 organic compounds for testing as insect repellents. Directions for their preparation are given. Order from LC. Microfilm $2, photocopy $6. PB 27408

The preparation of some compounds for testing as insect repellents. Final report, Oct. 31, 1945. (Drake and others.) (OSRD Rept. 6370.) Dec. 1945. 99p. 631 organic compounds, mixtures and creams were submitted for testing as insect repellents. Order from LC. Microfilm $2, photocopy $7. PB 27409

Some compounds submitted for testing as insect repellents. Progress report to Sept. 30, 1945. (Adkins and others.) (OSRD Rept. 6371.) Feb. 1945. 56p. In the report are recorded insect repellency data for 695 organic compounds. Order from LC. Microfilm $2, photocopy $4. PB 27410

Toxicity of insect repellents. Summary report of the Division of Pharmacology, Food & Drug Administration. Progress report, Nos. 1-17. (Calvery and others.) Apr. 1943-Sept. 1945. 361p. The tests on each compound usually covered composition, acute toxicity, subacute toxicity, primary irritation, sensitization, blood changes and pathology. Numerous tables, structural formulas and a few diagrams and graphs illustrate the text. Order from LC. Microfilm $8, photocopy $25. PB 40929

Screening for irritation of compounds submitted as possible candidates for insect repellents. Summarized report of the Division of Pharmacology, Food and Drug Administration. Bimonthly progress report, Nos. 1-4. (Calvery and others.) (OSRD Insect Control Committee Rept. 64, 81.) Mar.-Sept. 1945. 106p. Order from LC. Microfilm $3, photocopy $8. PB 40944

A study of the action of insect repellents in terms of their effects on insect behavior and in relation to their properties; thereby to facilitate selection of new compounds for practical repellent tests. Bimonthly progress report, Nos. 1-12. (DeLong and others.) Dec. 1943-Oct. 1945. 41p. The insecticidal action of various repellents was studied. Order from LC. Microfilm $1, photocopy $3. PB 41040

Screening for irritation of compounds submitted as possible candidates for insect repellents. A summarized report of the Division of Pharmacology, Food and Drug Administration, for the year ending June 30, 1945. (Calvery and others.) June 1945. 1p. This summary briefly describes the manner of scoring the irritation effects of those passed, not passed or those to be used with caution. No individual compounds are discussed. This work was performed under OSRD Contract 5356. Order from LC. Microfilm $1, photocopy $1. PB 41226

Methods for the analysis of insecticides, rodenticides, and repellents: Estimation of 1, 2, 3, 4-tetrahydro-2-naphthol in impregnated clothing. (Goldenson and Sass.) (CWS Tech. Div. Memo Rept. 1265) July 1946. 19p. Several procedures were considered for the estimation of 1, 2, 3, 4-tetrahydro-2-naphthol, such as oxidation, colorometric, and acetylation methods. Most satisfactory was the acetylation procedure, interference of binders being minimized by running suitable blanks. Much of the report is devoted therefore to this method. Tabulated data and bibliography are included in the report. Order from LC. Microfilm $1, photocopy $2. PB 46449

Insect and rodent control. (Loucks and Abercrombie) (CWS Quarterly progress report, No. 10, Apr. 1-June 30, 1946.) July 1946. 62p. Section A of part 2 deals with the following: rejection thresholds of the blowfly for organic compounds; toxicity of electrolytes to roaches; toxicity of pyrethrins to adult blowflies; experimental rearing of chiggers under laboratory conditions. Order from LC. Microfilm $2, photocopy $5. PB 50383

DDT formulations. Informal monthly progress reports 5-15, Jan. 1945-Nov. 1945. DuPont de Nemours, E. I., and Co. Dec. 5, 1944-Nov. 8, 1945. The major portion of these progress reports covers a study of methods for preparing DDT in a concentrated, readily-dispersed form by grinding DDT and maintaining it as a non-caking powder.
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Control of midges. An interim report of a sub-committee. Gt. Brit. Dept. of Health for Scotland. Scientific Advisory Committee. (British Commonwealth Scientific Office Rept. 117-B2-93). 1946. 9p. A formula for a midge repellent was produced and used successfully in the season of 1946. The formula is included in this report. Order from LC. Microfilm $1, photocopy $1. PB 61380

Insect and rodent control. Quarterly progress report No. 12, Oct. 1-Dec. 31, 1946. U. S. Chemical Corps. Jan. 1947. 29p. The report is divided into two parts. Part I. Technical aspects, and Part II. Medical aspects. Part I screening tests, means of dispersal and impregnation. Part II symptoms and determinations of toxicity. Order from LC. Microfilm $1, photocopy $2. PB 67644

Directions for use and a discussion of insecticides and repellents investigated at the Orlando Laboratory for the armed forces. U. S. Bureau of Entomology and Plant Quarantine. Orlando, Fla. (For revision, see PB 75963). (OSRD CMR Tropical Diseases Rept. 7). Mar. 1944. 27p. Part 1 of the report deals with the use of three insect repellents (dimethyl phthalate Indalone and Rutgers 612 which is 2-ethyl, 1, 3-hexanediol). Part 2 describes the use of various preparations of DDT as mosquito larvicides. Part 3 covers the use of DDT aerosols and DDT spray residues. Order from LC. Microfilm $1, photocopy $2. PB 75955

Directions for use and discussion of insecticides and repellents investigated at the Orlando, Florida Laboratory. U. S. Bureau of Entomology and Plant Quarantine. (For revision, see PB 75955). (OSRD CMR Tropical Diseases Rept. 19; Rept. 7, rev. 1.) May 1944. 36p. Part I is the introduction' the properties and the various uses of DDT are discussed in Parts 2 through 5; Part 6 contains a brief summary of the toxicology of DDT. The method of using repellents is discussed in Part 7. Order from LC. Microfilm $1, photocopy $3. PB 75963

Suggested methods for testing mosquito and other flying and biting insect repellent materials. Contract M-723. (Travis and Smith.) Sept. 1942. 3p. In order to obtain a uniform testing procedure for repellents, a description is given of the field and laboratory techniques which have proved satisfactory at the Orlando laboratory. Order from LC. Microfilm $1, photocopy $1. PB 75965

A summary of investigations on the development of insect repellents and lousicides. Contracts M-723, M-920, and M-631. U. S. Office of Scientific Research and Development, Committee on Medical Research. 1943. 8p. A summary is given of repellent tests with 2-ethyl hexandediol-1, 3, dimethyl phthalate, and Indalone against flying and biting insects and fleas. Order from LC. Microfilm $1, photocopy $1. PB 75966

Treatment of clothing for chigger protection. Progress report. Aug. 14, 1942. Contract M-723. (Madden and Lindquist.) Aug. 1942. 2p. Results of tests using various repellents are given. Order from LC. Microfilm $1, photocopy $1. PB 75967

Insect repellents. Progress reports 1-19, Feb. 28, 1942-Aug. 1, 1944. Contract M-723. (Dove and others.) 1942-44. 106p. These progress reports cover the work performed by the Bureau of Entomology and Plant Quarantine under Contract M-723 on the testing of various repellents against the common flying and biting insects and against crawling and biting insects. Several pages will not reproduce well. Order from LC. Microfilm $3, photocopy $8. PB 75975

Substances tested as repellents against Aedes aegypti and Anopheles quadrimaculatus from April 1942 to October 1944 inclusive. Interim report 0-87. Contract OEM CMR-M-4331. (Morton and others.) (OSRD Insect Control Committee Rept. 16) Feb. 1945. 133p. This report consists of tables in which the various insect repellents have been listed according to the protection time against Aedes aegypti. Order from LC. Microfilm $3, photocopy $9. PB 75998

Screening tests conducted in a search for new miticides. Interim report 0-89. Contract OEM CMR-

M-4331. (Snyder and Morton.) (OSRD Insect Control Committee Rept. 18). Feb. 1945. 14p. About 200 materials were investigated in an attempt to find good miticides which were not readily removed by exposure to water. Order from LC. Microfilm $1, photocopy $1. PB 76000

Screening tests of chemicals impregnated in fabrics for the purpose of selecting materials effective as mosquito repellents. Intermin report 0-94. Contract OEM CMR-M-4331. (Linduska and others.) (OSRD Insect Control Committee Rept. 28). May 1945. 51p. Results of mosquito repellency tests of 1,008 solid chemicals and 212 liquids impregnated in cloth and tested in the laboratory. Order from LC. Microfilm $2, photocopy $4. PB 76009

Resistance of fabrics to mosquito bites. Interim report, abstract. Contract OEM CMR-M-4331. (Annand.) (OSRD Insect Control Committee Rept. 72). Feb. 1945. 1p. Abstract reports on the resistance to mosquito bites of zelan treated or sanforized fabrics from Clarence S. Brown, two herringbone twill fabrics from the Sowa Chemical Company treated with a repellent, and a sample of brown and white striped seersucker. Report from Bureau of Entomology and Plant Quarantine, Beltsville, Md. Order from LC. Microfilm $1, photocopy $1. PB 76018

Insecticides and insect repellents developed for the armed forces at the Orlando, Fla., Laboratory. Interim report, 0-100. Contract M-4331. U. S. Bureau of Entomology and Plant Quarantine. (OSRD CMR Tropical Diseases Rept. 100). July 1945. 81p. In this report only those materials and methods that furnish information for use in practical control operations are discussed. Order from LC. Microfilm $2, photocopy $6. PB 76028

Insect repellents. Monthly progress reports 1-14, Sept. 15, 1943-Aug. 11, 1945. Contract OEM CMR-29, Supp. No. 2. (Clark.) Sept. 1943. 75p. The insect repellents included DDT, dimethyl and dibutyl, and bensyl benzoate. Order from LC. Microfilm $2, photocopy $5. PB 77240

Studies on insect repellents: their mode of penetration into the nervous system and their physiological action in relation to their practical usage. Annual rept. abstracted, progress reports 1-14, Mar. 31, 1943-May 1945. (Richards and others.) (OSRD CMR Tropical Diseases Rept. 6) May 1945. 62p. Compounds tested are listed in abstract given in our Bibliography of Scientific and Industrial Reports, vol. 6, page 403. Order from LC. Microfilm $2, photocopy $5. PB 77268

The disappearing rates of mosquito repellents from jungle clothing. Interim report 8. Abstract, May 1, 1944. Contract OEM CMR-351. (Gerking.) (OSRD CMR Tropical Diseases Rept. 15). May 1944. 1p. The rate of disappearance of 4 mosquito repellents (Dimethylphthalate, Indalone, Rutger's 612, and 6:2:2 mixture) from dry Byrd cloth jungle coats was determined by members of the Indiana University. Order from LC. Microfilm $1, photocopy $1. PB 77522

Field tests of uniforms impregnated with mite toxicants, I. Protection studies, II. (Cross and Snyder.) n.d. 17p. Part I Data are presented on the effectiveness of 18 outstanding materials compared with benzyl benzoate. Part II Discusses the relation between stopping time and protection. Order from LC. Microfilm $1, photocopy $2. PB 78639

Insect and rodent control. Quarterly progress report, Jan. 1-Mar. 31, 1947. U. S. Chemical Warfare Service, Medical Division Rept. 13. Apr. 1947. 22p. Part 1 (Technical aspects) deals with dispersal and impregnation. Part 2 (Medical aspects) deals in part with field studies with miticides; and rodenticide candle. Tables and bibliography included. Order from LC. Microfilm $1, photocopy $2. PB 79158

Field test of miticidal clothing, Camp Blanding, Florida. (Greenberg and others.) (CWS Tech. Div. Memo Rept. 1296). Apr. 1947. 115p. The object of the work described in this report was to test various types of benzyl benzoate-treated clothing worn on combat maneuvers in warm humid areas to determine: a) the life span of the garment with respect to BB content and miticidal efficiency; b) the degree of irritation caused by the clothing; c) the general characteristics of such clothing; and d) the use of dibutyl phthalate as a partial substitute for benzyl benzoate (BB). The tests are described in detail and conclusions and recommendations given. Five appendices and a bibliography are included. Order from LC. Microfilm $3, photocopy $8. PB 79159

Estimation of diphenyl carbonate and dimalone in impregnated clothing. (Goldenson and Sass.) (CWS Tech. Div. Memo Rept. 1313). May 1947. 37p. A variety of methods are discussed for the estimation of insecticides. Diphenyl carbonate has been found to be a good miticide and dimalone a good insect repellent. Order from LC. Microfilm $1.75, photocopy $4. PB 81997

Insect repellents. Bimonthly progress report No. 13. (Clark.) (OSRD Insect Control Committee Rept. 88). June 1945. 9p. This progress report consists of the following six individual reports dealing with insect repellents: (1) Studies on chiggers or red bugs (Acarina: Trombiculinae), by Michener; (2) Acaricides as tick repellents, by Michener; (3) Field tests of repellents against sandflies (Culicoides), by Trapido; (4) Control of sandflies (Culicoides) with DDT residual spray, by Trapido; (5) Experiments on the effectiveness of DDT residual sprays on painted and unpainted wood surfaces, by Trapido; (6) Residual house-spraying with DDT in kerosene, author not given. Contract OEM CMR-29. Order from LC. Microfilm $1, photocopy $1. PB 86446

Field tests of acceptability of insect repellents for application to the skin. (Sulzberger and others.) Nov. 1945. 8p. Order from LC. Microfilm $1.25. photocopy $1.25. PB 91891

Progress on studies of insecticides, miticides and mosquito repellents for clothing impregnation during 1946-47. (Greenberg.) Feb. 1948. 27p. tables. Order from LC. Microfilm $2. photocopy $3.75. PB 94485

Production of oils, anti-caterpillar glues, and paraffin wax emulsions for the paper industry. Investigations into the corrosion of lead drying towers. Properties of lead. (Hoffmann.) Rhenania-Ossag Mineralolwerke A. G., Hamburg, Ger. 1942-45 62f drawings, diagrs, graphs, tables. (In German.) Order from LC. Microfilm $3, enlargement print $10. PB 105447

Fission products for insect control. (Hassett and Jenkins.) U. S. Chemical Corps. Medical Laboratories, Army Chemical Center, Md. Dec. 1952. 19p. photos, graphs, tables. Order from LC. Microfilm $1.75, photocopy $2.50. PB 108883

Field evaluation of termite repellents. U. S. Naval Research Laboratory. (Bultman, Little and Leonard.) Oct. 1955. 10p diagrs, tables. Order from OTS. 50 cents. PB 111737

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# Insect repellents

## Applying one of these can keep the bugs off your back.

If a lot of scientific inquiry has been directed toward learning what attracts insects, at least as much study has been devoted to finding out what repels them. The latter proposition is the more difficult, in a couple of respects.

First, insects are such hardily adaptive creatures that it's hard to find anything on earth that particularly displeases them. Second, when something is found that displeases or threatens them, it's quite likely to be as obnoxious or noxious to humans as well.

Nevertheless, in the 1930's, a chemist synthesized one substance—ethyl hexanediol—that repels many species of biting insects without harming humans. Continuing research in the 40's produced several other compounds suitably abhorrent to certain insect pests. But none were so generally effective and economical as a chemical introduced in the following decade: N,N-diethyl-meta-toluamide, hereafter referred to by its mercifully short nickname of "deet." Deet gives strong offense to a broad range of mosquitoes, chiggers, ticks, fleas, and various biting flies. Note that these are all biting insects. None of the repellents are effective against *stinging* insects, such as bees, wasps, and hornets.

Deet is the major active ingredient in 12 of the 15 leading insect repellents reviewed by CU chemists. The other three repellents—liquid, aerosol, and stick versions of *6-12 Plus*—contain ethyl hexanediol as their major active ingredient and deet as a minor ingredient. The *6-12 Plus* liquid version is out of production, but may still be available in some stores.

The 15 insect repellents we bought are actually the products of only five companies; four of the companies put out multiple versions of their repellents in different formulations and package types. The *Cutter*, *Repel*, *Off!*, and *6-12 Plus* brands are all marketed in both spray containers and small plastic squeeze bottles. *Off!* is available in a pressurized spray version called *Deep Woods Off!* and in foil-wrapped towelettes. *Cutter* also comes in a version called *Evergreen Scent Cutter*. Both *Cutter* and *6-12 Plus* have a stick version. *Muskol* is available in the U.S. only as a liquid in a squeeze bottle.

### Deciphering the labels

As may be inferred from their history as the focus of considerable chemical research, insect repellents fall within a class of products that CU doesn't have to test. Over the years, they've been tested exhaustively by the U.S. Department of Agriculture, by the U.S. Army, and by the manufacturers at the behest of the U.S. Environmental Protection Agency. In fact, every legitimate repellent on the market carries on its label two EPA numbers. One, the "EPA Est. No.," indicates the plant where the product was manufactured. But the other the "EPA Reg. No.," amounts to a kind of Government guarantee of a product's safety and effectiveness when used as labeled.

Just how effective are the products? Considering the vicissitudes of insect behavior, that's a question regrettably beyond the scope of any guarantee. You may start with the assumption that no chemical barrier that's safe for humans will be proof for long against the blood lust of ravenous insects, such as you might find in thickly infested swamps. Given more civilized circumstances, however, you can draw fairly reliable assurance from the labels about the sort of protection you can expect.

Ounce for ounce, deet is more effective than ethyl hexanediol (or any of seven other active ingredients comprising small percentages of some repellents) in two ways. Deet is effective against a

**The products and their percentage of 'deet'**[1]


[1] The main active ingredient in 6-12 Plus products is ethyl hexanediol: 25% in spray, 80% in squeeze bottle, 66% in stick.

broader spectrum of insects and a given amount of it retains its effectiveness quite a bit longer. (Actually, deet's reputation for repelling more kinds of bugs doesn't reflect much of a practical advantage, since ethyl hexanediol, too, has proved effective against the most common biting insects found in the U.S.)

Perhaps a more meaningful measure of a repellent's effectiveness is how *long* it continues to ward off bugs. And here the concentration of active ingredients should also be considered. The most concentrated ethyl-hexanediol product that we reviewed (*6-12 Plus* liquid, with 90 percent active ingredients) may prevent mosquito bites for a few hours. The strongest deet product (*Muskol*, with 100 percent actives) may live up to its labeled claim of "up to 10 hours protection from mosquitoes," if not washed away by rain, sweating, or swimming. On the low end of the protection scale, the weakest ethyl-hexanediol and deet products (*6/12 Plus* and *Off!* aerosols, with 30 and 15 percent actives, respectively) would probably lose their effectiveness much more quickly.

It's no trick at all to detect when a repellent is wearing thin. Hovering insects begin to shoot tentative landings on skin and clothing. Then they build up the confidence to walk around. Finally, in case you've misread their ultimate intentions, they bite. But, well before that stage, if you're alert to the signs of increasing boldness, you can make the bugs back off again by reapplying repellent.

## Recommendations

Deet is a somewhat oily liquid that leaves the fingers feeling a bit icky as it dries. This effect would be more noticeable in products with the highest deet concentration. Two of the squeeze-bottle products have been formulated into creamy lotions that simplify the job of applying thinly and evenly; *Evergreen Scent Cutter* and *Deep Woods Off!* are white creams that disappear like hand lotion when rubbed in well enough.

The sprays will feel chilly momentarily on hot skin because of their high volatile content (which also makes them a fire hazard until they dry). Except for *Repel*, the sprays come in pressurized cans; *Repel* spray has a finger-pump plastic bottle.

The sticks take a bit of persistence to apply over large areas, but their slightly waxy feel shouldn't prove objectionable. The *Off!* towelettes make application a cinch, but each towelette is recommended for covering an area that's only the size of an adult's face and arms. With only 10 towelettes to a package, you could run out pretty quickly.

You may wish to base your selection on the type of dispenser. Spray containers are quick and easy to use, especially if you have to coat clothing to protect against biters that can penetrate through fabric to your skin. However, the containers are bulky, and youngsters might spray into eyes or on sensitive skin.

Small plastic squeeze bottles and sticks are convenient to carry, with the bottled lotion much easier to apply than the waxy stick. Towelettes are well suited for application to wriggling children.

A next consideration would be the concentration of active ingredients. You want strong protection if you venture into the territory of voracious swarms or sit out in the evening when the nighttime biters arise. Where the threat of bites is not severe, any of the products we sampled would do fine.

With the type and strength selected, a final consideration would be price. Here it's hard to give guidance because we have found that the prices vary enormously depending on the store. Also, the differing concentrations of active ingredients throw an added skew into the price. In our shopping experience, the *6-12 Plus* products were the cheapest per ounce of active ingredient in all the product types. However, the main active ingredient in all the *6-12 Plus* products is ethyl hexanediol, bolstered by only small amounts of the more potent bugaboo, deet. Unless your exposure to biting insects will be relatively slight and brief, we think it makes sense to go for the deet-based products.

Since the more concentrated products provide more lasting protection and require less frequent reapplication, you could save a bit of money and bother by choosing one of them, although swimming or sweating can nullify the advantage by washing away the repellent. Among the deet-based squeeze-bottle products, *Repel* and *Muskol* were the cheapest per ounce of active ingredient at the prices we found. The least expensive deet-based sprays on the same basis were the *Cutter* products. The *Cutter* stick repellent was the most expensive repellent we found.

## A caution

Many millions of people have used deet-containing products without a hint of toxic reaction. Indeed, much testing was done by many laboratories before the Federal government declared deet effective and safe for general use. High-strength deet is issued to military personnel in insect-infested areas. However, in 1980, the Children's Hospital of Eastern Ontario, in Ottawa, reported the death of a six-year-old who apparently had a metabolic disease and who had sprayed herself with an insect repellent containing 15 percent deet. The British medical journal The Lancet said, in commenting on the case: "Perhaps . . . the container labels should carry a warning against use by people who are known or suspected to have metabolic defects." The millions who have used deet have nothing to worry about, though they should mind the prudent warnings to avoid getting the product into the eyes or mouth, or on skin with a cut or rash.

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provement however, because about 250 additional establishments were protected during the current year.

The benefits to our control program from adequate entomological services have been numerous and varied. Projects of little or no merit have been decreased in size or terminated; new projects are undertaken only where sufficient justification can be established; doubtful areas are kept under entomological surveillance until a decision can be made. The savings resulting from this procedure have been considerable and in individual cases have ranged from $10,000 where small projects were concerned, to $100,000 or more where large operations were involved. However, the greatest benefit to the program from entomological services has not been the saving in money, but rather the increased efficiency brought about in the control work. Project supervisors point with pride to their excellent work records and construction jobs, but realize that the real test of this work is the maintenance of low densities of malaria vectors. —12-7-43.



# Recent Investigations of Insecticides and Repellents for the Armed Forces[1,2]

E. F. Knipling and W. E. Dove, *U.S.D.A., Agr. Res. Adm., Bureau of Entomology and Plant Quarantine*

Our entry into the present war found our Armed Forces without adequate methods of control for some of the most important arthropods affecting the health of man. During peacetime the necessity of controlling insects and other arthropods of medical importance is generally recognized, but with the beginning of the war the vast movements and large concentrations of troops and civilians have greatly intensified these problems within the United States. Recognition of this domestic situation alone stresses the need for research to develop new or improved control measures for certain disease vectors and noxious species. The worldwide distribution of our troops and civilian war workers, however, has magnified the problems many times. The new combat tactics have outmoded certain methods of control adopted in previous wars, and the problems have been made more difficult by the inadequate supply of pyrethrum and rotenone, which had been counted on to provide means of controlling certain species. In short, means of control were urgently needed for a great majority of the medically important insects and other arthropods throughout the world.

The needs for protecting troops and civilians in occupied territories against body lice, transmitters of typhus and trench fever, and from mosquitoes, vectors of malaria, yellow fever, and other diseases, are especially acute. In addition, there is an urgent need for more effective means of controlling other disease carriers, such as houseflies, sandflies, mites, ticks, and fleas.

Three separate projects were organized for the purpose of making investigations on (1) body louse control; (2) repellents for mosquitoes and other flying and biting insects, and for such parasites as mites, ticks, and fleas; and (3) larvicides for the treatment of breeding places of *Anopheles* and other mosquitoes. In conjunction with these projects investigations have been conducted also on insecticides for the control of adult mosquitoes, houseflies, and adults of other disease-bearing insects, as well as certain noxious species, such as bedbugs and cockroaches. This paper presents a summary of some of the more important developments to date.

Control of Lice Affecting Man.—Army officials considered a powder that could be carried in the soldier's pack to be most desirable for body louse control. Efforts were therefore concentrated on the development of a powder for individual treatment, although studies also were

[1] Presented as a part of the Columbus Symposium, 1943.

[2] The data recorded in this paper were obtained in connection with investigations conducted at Orlando, Fla., under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Bureau of Entomology and Plant Quarantine.

made with clothing impregnated with lousicides by using suitable solvents.

Since a louse powder was needed as quickly as possible, lousicidal properties of commonly used insecticides were determined in early investigations. These included studies with pyrethrum and rotenone products as well as certain synthetic organic compounds.

Since natural infestations of body lice, *Pediculus humanus corporis* Degeer, are difficult to find in suitable numbers, it was necessary to devise means of testing materials under laboratory and simulated natural conditions. Excellent methods were developed which contributed materially to the rapid progress of the work. The methods used in evaluating these materials have been briefly described by Bushland *et al.*[1] Since large numbers of lice were needed, it was necessary to establish and maintain a large colony of body lice. The methods used in maintaining the colony are described by Culpepper.[2]

The work on the louse project has been aided materially by Dr. W. A. Davis and associates of the Rockefeller Foundation, who evaluated the more effective treatments on large numbers of natural infestations.

Several hundred synthetic organic compounds were tested under laboratory conditions during the first few months after investigations were initiated. Coincident with these studies, tests with pyrethrum and rotenone products were in progress. Rotenone and pyrethrum in the early tests showed most promise for the development of suitable louse treatments at concentrations that were thought to be safe for applications to the body.[3]

A number of comparative tests indicated that, when impregnated on pyrophyllite, pyrethrins and rotenone (from derris or cube resinates) were about equal in their lousicidal value. Pyrethrum seemed most suitable because of its more rapid insecticidal action and because no physiological reactions were noted on research subjects. The rotenone powders, on the other hand, caused scrotal dermatitis in a high percentage of subjects when 1 ounce of the powder was applied inside the undergarments.

To improve the effectiveness of pyrethrins, investigations were made with several pyrethrum synergists. Because their value had been proved in fly sprays, sesame oil, *D.H.S. Activator*, and N-isobutylundecyleneamide were among the first of approximately 300 synergists tested. The first two materials showed only slight synergistic properties at concentrations of 2 per cent in dusts containing pyrethrins. On the other hand, the N-isobutylundecyleneamide showed remarkable synergism for pyrethrins against the body louse. The synergistic action of this material allowed the use of pyrethrins in a 0.2 per cent concentration, and the resulting formula proved more effective than 1 per cent of pyrethrins without an activator.

Since pyrethrum and rotenone are not ovicidal, various synthetic organic compounds were tested as ovicides. Among the effective materials, 2, 4-dinitroanisole seemed most promising.

On the basis of these studies a formula (MYL formula) was recommended to the Office of Scientific Research and Development in August 1942. The powder is composed of 0.2 per cent of pyrethrins (using a 20 per cent pyrethrum concentrate), 2 per cent of N-isobutylundecyleneamide, 2 per cent of 2, 4-dinitroanisole, and 0.25 per cent of *Phenol S* (anti-oxidant) in pyrophyllite. Details of the tests leading to the formulation of this powder and results of tests are discussed in the paper by Bushland *et al.*[1] The MYL formula in comparative tests proved more effective against the body louse than other louse powders known to the investigators. It also proved effective in controlling the crab louse, *Phthirus pubis* (L.), and the head louse, *Pediculus humanus humanus* L.

REPELLENTS FOR MOSQUITOES AND OTHER FLYING AND BITING INSECTS.—The project on insect repellents is designed to evaluate repellents for a variety of bloodsucking insects and arthopods, other than lice, of importance to the

[1] Bushland, R. C., L. C. McAlister, Jr., G. W. Eddy, Howard A. Jones, and E. F. Knipling. 1943. A powder treatment for the control of lice attacking man. (Unpublished.)

[2] Culpepper, G. H. 1943. The rearing and maintenance of a laboratory colony of the body louse. (Unpublished.)

[3] Some observations on physiological effects on man of the various insecticides tested were made in connection with the investigations at Orlando, Fla. However, all promising materials that were considered for practical applications have been submitted to H. O. Calvery and associates, of the Food and Drug Administration, for toxicological tests. Toxicological tests were also made by M. I. Smith, Division of Chemotherapy, and P. A. Neal and W. F. von Oettinger, Division of Industrial Hygiene, National Institute of Health, U. S. Public Health Service. The work of these toxicologists has been an essential and highly important phase of the investigations.

Armed Forces, such as mosquitoes, biting flies, sandflies, and other flying and biting insects, as well as mites, ticks, and fleas. The primary objective is to develop materials that can be applied by the individual soldier for protection against the insects and arthopods mentioned. In many cases the control of mosquitoes or other insects by the chemical treatment or destruction of the breeding areas is not feasible. The use of repellents or insect nets is the only feasible means of protection.

Of the various disease vectors considered in connection with this project, most emphasis has been placed on the development of repellents for *Anopheles* and other mosquitoes.

Citronella was the only well-known and widely used insect repellent at the time of our entry into the war, although many other repellents were being sold to the general public. The first objective was to evaluate as many materials as possible for the purpose of recommending a satisfactory repellent that could be supplied for military use at the earliest possible date. A repellent was developed which after careful research proved to be among the best in use. However, this material was tested by H. O. Calvery and associates of the Food and Drug Administration and was found to be too toxic for use under military conditions.

Tests of mosquito repellents were made under laboratory conditions, using *Aëdes aegypti* (L.), *Anopheles quadrimaculatus* Say, and *Stomoxys calcitrans* (L.), The technique employed was a slight modification of that devised by Granett (1940). The more promising repellents were evaluated in the field against *Aëdes taeniorhynchus* Wied.) and *A. sollicitans* (Walk.) In addition to tests by B. V. Travis and associates of the Orlando station, various individuals and agencies have cooperated in testing repellents against other species in different parts of the world.

On the basis of early tests, three safe repellents were found to give good protection against *Aëdes* mosquitoes, and these were recommended for use by the Armed Forces. Details of the results are given in a manuscript by Travis and Smith,[1] which has been prepared for publication.

Dimethyl phthalate had been found by the Orlando workers to be a good flea repellent. Later it was learned that the chemical had been sold as a repellent by the Standard Oil Company as a 25 per cent solution in alcohol. *Rutgers 612* was found by P. Granett to be effective against *Aëdes aegypti* in laboratory tests, and *Indalone*, supplied by Kilgore Development Co., was one of the more effective repellents against flies.

These repellents under experimental laboratory and field conditions will protect against *Aëdes aegypti* and *A. taeniorhynchus* for from 3 to 5 hours, on the basis of complete protection to the first bite. Rutgers 612 has proved most effective against *Aëdes*, whereas dimethyl phthalate is most effective against *Anopheles quadrimaculatus*. *Indalone* is of little value as a repellent for *A. quadrimaculatus*, whereas it is the most effective of the three against *Stomoxys calcitrans*.

It has been found that the repellents mentioned remain effective for a much longer period on clothing than when applied to the skin. When sprayed on a suit of clothing at the rate of from 50 to 100 cc., protection from *Aëdes taeniorhynchus* was obtained for a period of about 1 week. Similar results were obtained with *Aëdes aegypti* and *Anopheles quadrimaculatus* in laboratory tests. Since mosquitoes readily bite through clothing, the treatment of clothing is important and will provide much more complete protection than skin treatment alone.

Results of tests with the three repellents mentioned, as well as with many other materials, emphasize the importance of testing materials against a variety of species. Individual variation in the protection afforded by different repellents on different subjects is also an important factor. Other considerations are important in evaluating a repellent, such as conditions under which the user is living. The repellents in general prove much less effective when users are under exertion and are perspiring freely. The relative effectiveness of different repellents on the basis of partial protection after some mosquitoes begin biting is also important.

Chigger-Repellent Investigations.

from the importance of chiggers, *Eutrombicula* and *Acariscus* spp., in causing extreme irritation which frequently leads to secondary infections, they also are important in the transmission of a typhus-like disease in certain foreign countries where our troops are located.

Various insecticides and repellents were tested as a chigger prophylaxis. These included sulphur, derris, rotenone, and pyrethrum. These materials in powder form did not provide adequate protection when the test subjects sat or crawled about in infested areas. The results were generally erratic, and treatments did not last as long as desired. The application of liquid repellents such as dimethyl phthalate, *Indalone*, and *Rutgers 612* to the legs and arms provided good protection for periods of short duration.

The most effective means of protection from chiggers was found to be the application of liquid repellents to clothing. Clothing can be sprayed with repellents or dipped into repellent solutions with effective results. The simplest method of treatment, however, consists in the application of a repellent barrier on the socks, cuffs of trousers, leggings, sleeves, and other openings in the clothing where chiggers may crawl through. This can be done without special equipment by using the bottles of repellents issued for military personnel. A thorough treatment as described, which requires about 1.5 to 2 ounces, will protect the individual from chigger attack for a week or more, or until the clothing is removed for laundering. Of the three repellents mentioned above, dimethyl phthalate is considered most effective and desirable.

Tests of repellents were also made against ticks by using the same materials and methods that proved effective against chiggers. The powders in general proved unsatisfactory. The liquid repellents applied to clothing proved effective against larval and nymphal ticks of *Amblyomma americanum* (L.), but results against adult ticks were in general unsatisfactory.

FLEA REPELLENTS.—Tests of flea repellents were conducted in a manner similar to that used in testing mosquito repellents. A reared mixed culture of the dog flea, *Ctenocephalides canis* (Curtis), and the cat flea, *C. felis* (Bouché), was used, and these species proved satisfactory for the purpose. The oriental rat flea, *Xenopsylla cheopis* (Rothsch.), proved unsatisfactory as a test species, since it did not readily bite in captivity.

Although a number of repellents were tested, the three materials dimethyl phthalate, *Indalone*, and *Rutgers 612* provided several hours' protection when applied to the skin. Preliminary tests indicate that the application of the repellent to clothing will provide protection for several days.—1-28-44.

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# Population Studies of Florida Mosquitoes

V. G. DETHIER[1] and F. H. WHITLEY[2]

In the course of a mosquito-survey conducted by the United States Army near Tampa, Florida, considerable data was gathered on the frequency and seasonal distribution of the more common and economically important species. The nature and extent of the collections from which these data were derived permit of a more complete study of population densities and fluctuations than was heretofore possible in this section of Florida. Daily light-trap, biting, and resting collections as well as collections of larvae were made over a period of 20 months. Meteorological data were also obtained for the same period.

The area under consideration is a peninsula near the city of Tampa comprising approximately 10 square miles. A fringe of mangrove characterizes the coastline. Inland from this are grassy salt marshes. The greater part of the area supports a flora represented predominantly by palmetto and scattered stands of pine. Ap-

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# REPELLENTS[1]

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*Introduction.*—The bulk of research on repellents was stimulated by the military requirements of World War II and has been continued since then principally with these requirements in mind. Few investigations had been undertaken prior to the war. The results of these investigations together with a history of repellents were reviewed by Dethier (22). Work done by British units just prior to and during the early war years was reviewed by Christophers (19). Work done in the United States by and for the Armed Forces during the same period is tabulated chiefly in the papers of Haller (64), King (73, 74, 75), Morton *et al.* (91), Finkelstein & Schmitt (40), Travis *et al.* (127), and Travis & Smith (128). Additional reviews which also contain information on commercially developed repellents are those of Gil (51), Utzinger (131), and Lesser (79). All of the aforementioned papers treat almost exclusively of repellents for use against blood-sucking arthropods. Accounts of the status of mothproofing since 1946 are given by Lindgren (80), Luttringhaus (84), Stoves (120), Bloomfield (9), Borghetty (10), Borghetty *et al.* (11), Utzinger (131), Zinkernagel (144), and Matsui (89). Wood preservatives are discussed in the papers of Schulze (106), Becker (6), Sedziak (107), Wolcott (138, 143), and in an article in the *Caribbean Forester* (2).

Before the wartime period of intensive investigation there were four standard repellents for use against biting arthropods: oil of citronella, dimethyl phthalate, Indalone, and Rutgers 612. Oil of citronella was the most widely used repellent from about 1901 and was the repellent against which new compounds were tested. Dimethyl phthalate (dimethyl benzene orthodicarboxylate) was originally reported as a fly repellent in 1929 (U. S. Patent 1,727,305). Indalone ($n$-butyl mesityl oxide oxalate or $\alpha$-$\alpha$-dimethyl-$\alpha$-carbobutoxy-$\gamma$-dihydropyrone) was reported in 1937 (U. S. Patent 2,070,603). Rutgers 612 (2-ethyl hexanediol-1,3) was the eventual development of a long testing and screening program begun in 1935 by Granett [Granett & Haynes (59)]. At the start of the war the last three compounds were combined in a mixture designated as 6-2-2 and used as a standard all-purpose military repellent. The proportions of the components were: six parts of dimethyl phthalate, two parts of Indalone, and two parts of Rutgers 612. It was partly the failure of this formulation to provide the protection demanded by military requirements which was the stimulus to increased and accelerated research on repellents.

The major share in the accelerated program fell to the Orlando Labora-

[1] The survey of the literature pertaining to this review was completed in June, 1955.

tories of the United States States Department of Agriculture. Between 1942 and 1947 from 5000 to 6000 candidate repellents were screened by these laboratories [Haller (64); Morton *et al.* (91)]. To 1952 approximately 11,000 candidate repellents, insecticides, and rodenticides were screened [King (75)]. The total is currently in excess of 20,000. Less than 10 per cent showed repellency equal to or greater than existing standards, and only three per cent of the promising materials were considered by the United States Food and Drug Administration to be safe for use on man [Travis & Smith (128, 130)]. Of 1339 solid repellents tested at one stage, approximately 9 per cent were outstanding [Linduska & Morton (82)]. Two of the outstanding repellents developed by this program were M-2020 [Smith *et al.* (113)] and M-1960 [Smith & Cole (110)]. At the present time the standard all-purpose skin repellent mixture used by the Armed Forces is M-2020, which consists of dimethyl phthalate 40 per cent, Rutgers 612 30 per cent, and dimethyl carbate (bicyclo [2.2.1]-5-heptene-2, 3-dicarboxylic acid, *cis*-, dimethyl ester) 30 per cent. This mixture as applied is effective for about two hours against anopheline mosquitoes and for about four hours against *Aedes*, ticks, and chiggers. The standard clothing repellent, M-1960, consisting of benzyl benzoate 30 per cent, *n*-butylacetanilide 30 per cent, 2-butyl-2-ethyl-1,3 propanediol 30 per cent, and "Tween 80" 10 per cent is effective when applied at the rate of 2 gm./sq. ft. of cloth for about 7 days against *Aedes*, chiggers, ixodid ticks, and fleas. Recent tests by Smith & Gilbert (114) of modifications of the standard M-1960 have shown that mixtures with undecylenic acid are superior against *Aedes* but inferior against *Anopheles quadrimaculatus*. Species differences of this sort are well known [Travis (125)]. Replacement of *n*-butylacetanilide with *n*-propyl- or *i*-propylacetanilide caused no change in effectiveness. None of these formulations are available for civilian use. Nor have the following highly effective tick repellents been cleared for civilian use: *n*-butylacetanilide, *n*-propylacetanilide, undecylenic acid, and hexyl mandelate [McDuffie & Smith (86); cf. also Granett & French (58)]. Indalone, dimethyl phthalate, and Rutgers 612 are still the repellents of choice [cf. also Cole & Smith (20)].

The avowed purpose of most of the aforementioned work was to develop as speedily as possible a nontoxic [cf. Goldman (53)], nonplasticizing, nonirritating repellent of long lasting efficiency which would repel mosquitoes, biting flies, ticks, fleas, and chiggers. Consequently, most of the tests were screening tests run on a field and laboratory scale, and little thought was given initially to refinement of testing methods and standardization. Few serious attempts were made to investigate the mechanism of repellency or the relation between chemical constitution and repellency. Almost nothing was known of the behavioral and physiological aspects of the problem.

*Variables encountered in testing repellents.*—In designing tests of repellency it is imperative that one first ask himself what information is being sought. If one wishes to determine how well a compound or formulation operates under actual field conditions, obviously a field test is indicated. If, on the other hand, one wishes to screen candidate repellents, compare relative effectiveness, or relate repellency to chemical properties, a laboratory test is indicated. Clearly, tests should be carried out with full realization that the results can have significance only if all variables are rigidly controlled. Although Travis (124) stated, "A review of the literature shows that the wide ranges in repellent times seem to be characteristic of tests with repellents against biting insects," Pijoan *et al.* (99) had very narrow ranges in their tests. The presence of wide ranges in repellent times shows only that tests are not precise, not that there is an inherent variability which cannot be controlled. There is no a priori reason why a greater basic variability should exist in repellent tests than in toxicity tests or any other type of biological experiment. The need for precision, caution, and control of variables was pointed out very early and very forcefully by Christophers (19) but has been largely ignored.

The variables include not only the obvious ones such as temperature, relative humidity, and light intensity, but more intangible ones such as biting rate, nutritional state, amount of activity and disturbance, behavioral peculiarities, age, and state of development (e.g., nymphal ticks are more sensitive than adults [Brennan (12); Smith *et al.* (111)], sex, brood differences, sample differences, and a whole group of variables associated with differences in host attractiveness.

The importance of biting rate was first described in detail by Granett (55) who showed that the period of protection offered by a repellent decreased as the biting rate increased [cf. also Travis & Smith (128)]. The decrease is not directly proportional since there is a sharp break at 10 bites per min. Over the range studied, from 0 to 25 bites per min., the ratio of repellent times for any two repellents appeared to be approximately constant. It would be of value to extend the observations to the higher biting rates commonly experienced in the arctic.

All of the factors which affect biting rate are by no means well known. Travis *et al.* (126) and many others have observed that insects do not bite uniformly all day. Christophers (19) noted that the fierceness of attack varied with species and "other conditions" (*sic!*) but could detect no difference in settling which could be correlated with season, strain of mosquito, or the identity of the human host. On the other hand, Terzian & Stahler (122) found that the biting rate was related to the population density at which *Anopheles quadrimaculatus* was reared and also to the sex ratio. It was felt that the latter effect was tied in with the copulation rate. Christophers (19) found that both the number of settlings and of wheals increased from the fifth to the seventh day of emergence. Since practically all mosquitoes which settle do eventually bite, the settling rate may with sufficient accuracy be called the biting rate. As might be expected, the biting rate in a cage falls off with time as mosquitoes become engorged and retire to the sides of the cage. McCulloch & Waterhouse (85) observed a similar phenomenon in the field and suggested that the subjects in a field test should move about periodically from one spot to another.

The biting rate and the repellency of a given compound vary with different host factors. It has been known for some time that different subjects are susceptible to different degrees [McCulloch & Waterhouse (85); Travis & Smith (128)]. Attempts have usually been made in screening tests to control for this by such measures as paired tests on both arms or legs of a subject [Granett (56); Granett & French (57)], replications on different subjects, etc. The factor of host susceptibility has been evaluated most carefully in studies of dairy cattle repellents [Fryer *et al.* (47)]. Similar careful analyses are required with human hosts. Furthermore, since the repellent must work against host attractants, it is desirable that much more be learned of host attraction than now is known [cf. Laarman (77) for a complete discussion of host attraction].

McCulloch & Waterhouse (85) observed that there seemed to be a difference between the attractiveness of arms and legs not correlated with hairiness. On the other hand, Travis *et al.* (126) and some later workers felt that there were no such differences. Pijoan *et al.* (99) and Pijoan (98) stressed the very great importance of the condition of the host and the ambient environment in affecting repellent time. They showed that the greatest change was produced by dry heat. Thus, a change from 80°F. dry bulb and 70°F. wet bulb to 90°F. dry bulb and 70°F. wet bulb caused the protection time afforded by dimethyl phthalate to drop from 267 to 99 min. With increasing relative humidity, i.e., from 90°F. dry bulb and 70°F. wet bulb to 90°F. dry bulb and 80°F. wet bulb, there was little additional decrease (from 99 to 84 min.). The temperature of the host itself is certainly important because biting rate decreases on a cold arm [Christophers (19)]. Furthermore, Kasman *et al.* (71) found by correlating repellency with temperature that the shorter protection times on guinea pigs as compared to man could be explained in terms of the higher body temperature of the guinea pig.

Effective protection by a repellent varies not only with the behavior, etc. of the mosquito and the environmental conditions but also with loss and changes in the repellent itself as a result of host factors as well as environmental factors. The amount of repellent applied is very important [Christophers (19)]. Protection time and amount are not, however, directly proportional [Granett & Haynes (59)]. Sweating has an effect on repellent time attributable in part to its diluting action [Pijoan *et al.* (99); Jachowski & Pijoan (68); Starnes & Granett (119)]. Decrease in repellent time under simulated tropical conditions is partly attributable to sweat [Pijoan (98)]. However, Starnes & Granett (119) in some experiments which show that the effect of sweat may not be a dilution one only, found that a synthetic sweat diminished the repellency of Indalone but enhanced that of Crag Fly Repellent. According to Kasman *et al.* (71) the chief loss of repellency, at least of some repellents, is through skin absorption [cf. also Wiesmann & Lotmar (136)]. Tests of the rate of evaporation of dimethyl phthalate showed that the rate of loss by this route is much lower than the loss of protective action on the back of a guinea pig or on the human hand. It is argued that the loss of protection must therefore be a result of hydrolysis or absorption through the skin. To test rates of skin absorption 0.25 ml. of 1-phenyl-2-hydroxy-propanone-1 was placed on the shaved back of a guinea pig and the urine analyzed for excess benzoic acid, the presumed metabolic product. The yield represented 4.5 per cent of that theoretically available from oxidation of the original compound and indicates a significant loss by absorption.

Certainly in some cases breakdown of the repellent from chemical causes results in changes in protection time. Pijoan *et al.* (99) and Jachowski & Pijoan (68) were able to show, for example, that beta tetralol first became more effective as it oxidized and then later decreased in effectiveness.

Finally, the long effectiveness of repellents on cloth (days or weeks) as compared with that of the same repellents on skin points clearly toward the importance of absorption or breakdown as a limiting factor in the duration of effectiveness of skin repellents. It is probably as a result of many of the limiting factors which have been discussed and others compounded that protection time in the laboratory is almost always longer than in the field [Christophers (19); Travis & Smith (128); Starnes & Granett (119)].

Variability in techniques and poor choice of criteria of repellency have also contributed to the wide range in results observed by all. Laboratory and field tests as they have been conducted to date possess one virtue, a rapidity of screening. There has been very little uniformity and standardization from one experimenter to the next. Dosages per unit area are measured in drops [Pijoan *et al.* (99)], teaspoons [Travis (124); Travis & Smith (128)], cc. (most workers), or grams [Roadhouse (101)]. They may be applied at the rate of 1 cc. on the arm and 2 cc. on the leg [Granett (55)], 1 cc. per 100 sq. in. of skin [Granett & Haynes (59)], 1 cc. on the arm and 1.5 cc. on the leg [Travis *et al.* (126, 129); DeFoliart (21)], varied dosage [Christophers (19)], 0.5 to 0.8 cc. on hand and arm and 3 cc. on leg [McCulloch & Waterhouse (85)]. They may be applied full strength or as 25 per cent ethanol solutions [Travis (123); Applewhite & Smith (4); Applewhite & Cross (3); Altman & Smith (1)]. The criterion of skin repellency when mosquitoes are employed has usually been time to first, second, third, or fifth bite; for clothing repellents the criterion has been time to first bite, rate of biting, number of bites. With biting flies the criterion is sometimes time to first, second, third or fifth bite or the number of bites in a given time. With ticks and fleas the criterion is usually the number of animals in the treated area. For any given laboratory there has been extreme variability in results. This has been remarked upon by Granett (56), Pijoan (98), Linduska & Morton (82), and Travis (124).

*Control and evaluation of variables.*—The prototype of all tests and the first major attempt to standardize was the technique developed by Granett (55). His original test, a field test, consisted of exposing first an untreated arm or leg for 2 min. to determine the biting rate. Then an arm rubbed from wrist to elbow with 1 ml. of repellent or a leg rubbed from ankle to knee with 2 ml. was exposed continuously. The untreated control was exposed for 2 min. at 15 or 30 min. intervals to determine the biting rate based on the average of all counts. The criterion of repellency was the time to the first bite. Christophers (19) pointed out quite clearly the objection to this criterion. He noted that one is actually testing for two things (*a*) the essential effectiveness (intrinsic repellency) of the compound and (*b*) the duration of repellency. He advocated mapping and counting of wheals and pointed out that if this procedure were not feasible, even the simple contrast of biting rate on check and control arm is a better criterion than time to first bite. This point will be discussed further on in greater detail.

Variability could be reduced or at least statistical reliability of results could be ascertained. In place of human arm tests, tests with mice [Eddy & McGregar (36); Wiesmann & Lotmar (136)], with canaries [Wasicky *et al.* (133)], with guinea pigs [Wasicky *et al.* (133); Kasman *et al.* (71)], and with rabbits [Starnes & Granett (119)] have been tried, From the results obtained there is no reason to judge that these animals are inferior to man as test animals; and with respect to ease of manipulation, etc. they are superior. Toxicological screening tests are run on animals; there is no more reason why repellent tests should not be. Yet, like tests on man, these can serve only the purpose of quick gross screening. The many variables still exist.

Nowhere has this been better realized than in tests of repellents of cattle flies. The earliest methods are reviewed by Dethier (22). In 1947 Waterhouse adapted the indol plug method of Mackerras & Mackerras (87) for studying blowfly repellents. This consisted of soaking cotton plugs in 0.04 per cent indol, 2 per cent $NH_4CO_3$, and 2.5 per cent ethanol and tying them on the fleece of living sheep. Of two plugs so tied, one (the control) was surrounded by a ring of paraffin oil and the other (the test) by a ring of the candidate repellent. An area of untreated fleece was left between the plug and the ring. The criterion of repellency was the number of egg batches laid on the plug. Two kinds of repellency were observed. Flies attracted to the plug either alighted at some distance from it and walked to it or landed inside the ring. In the first instance walking flies were repelled when they came to the ring (contact repellency). In the second case they were repelled only if the ring consisted of a volatile material (vapor repellency). Loeffler & Hoskins (83) tested the toxicity and repellency of certain organic compounds to the larvae of *Lucilia sericata* by allowing the larvae to form sinuses in an agar medium covered by raw wool. After treatment with test compounds this simulated wound was placed adjacent to an unsprayed sinus so that larvae could migrate if repelled. Repellency was determined by the number which emigrated.

Fryer *et al.* (47) made a thorough study of variability and experimental design. Two methods had previously been used, the whole-cow and the half-cow methods. There are basic disadvantages to both. In the former there is marked variation in the susceptibility (attractiveness) of each cow. Granett *et al.* (61) allowed for varying susceptibility of cows to *Stomoxys calcitrans*, *Siphona irritans*, and *Tabanus* spp. by first obtaining a corrected normal count

$$\frac{\text{average number on checks during test}}{\text{average susceptibility count of checks (three or more counts before or after tests)}} \times \text{susceptibility of treated animals.}$$

The per cent repellency was derived from the expression

$$\frac{\text{corrected normal count} \times \text{treatment count}}{\text{corrected normal count}} \times 100.$$

In the half-cow method the fly's choice of which side on which to alight depends upon what is on the opposite side. Also, if the test material on one side kills flies, there will be fewer flies on the other side even if it is untreated. This could lead to the anomalous conclusion of no repellent being superior to a toxic repellent [cf. also Granett *et al.* (60)]. In order to evaluate the two methods Fryer *et al.* made comparable experiments with each. First, balanced groups were made on the basis of each cow's attractiveness. A latin square design was employed in the whole-cow method and a symmetrical pair design for the half-cow method. The raw data obtained showed a serious nonhomogeneity of variance among group counts, days, weather, etc. Because of their anormality the data must be transformed mathematically to a normal frequency distribution in order to be analyzed for significance. The most successful transformation was the reciprocal square root although a log transformation also seems to be satisfactory. Analyses of this sort demonstrate the superiority of the whole-cow method. For this method to be successful, however, one must first carefully obtain a measure of individual cow susceptibility (attractiveness), set up a balanced group, employ a latin square design, and make periodic counts. The analyses of Fryer *et al.* prove beyond all doubt that statistical methods must be employed in repellent research. This conclusion is most certainly applicable to tests with man, and much more reliable results could be obtained if more careful attention were given to the design of experiments.

*Design of experiments.*—As has already been pointed out, in designing a test for repellency one should first ask what information is being sought. If one hopes to relate repellency to chemical constitution, the problem must be broken down into its component parts before any useful analyses can be made. Tests with man and animals present an extremely complicated situation. Assuming for the moment that such variables as transient differences in insect behavior and biting rate, diurnal and individual differences in host attractiveness, etc. can be rigidly controlled, one is then confronted with (*a*) the intrinsic repellency of the compound to the insect, i.e., the chemical/physiological activity which affects the insect nervous system via the sensory system or otherwise and causes the insect to depart, (*b*) the change of effectiveness with concentration, i.e., whether or not the dosage-stimulation curve has the same slope for all compounds (one should know the slope in order to ascertain which concentration of compound $x$ is comparable to a given concentration of compound $y$), (*c*) differences in vapor pressure which cause changes in concentration as the test progresses and as the ambient temperature and the temperature of the host changes [Kasman *et al.* (71)], (*d*) changes in repellent concentration as a result of absorption by the skin [Wiesmann & Lotmar (136); Kasman *et al.* (71)], and (*e*) changes in concentration and constitution on the host as a result of sweat [Jachowski & Pijoan (68); Pijoan *et al.* (99); Starnes & Granett (119)].

Christophers (19) recognized some of these difficulties when he pointed out objections to the time to first bite as a criterion of repellency. He showed that in reality one was measuring two different factors, repellency and duration. The same objection holds with reference to time to first confirmed bite, or second, third, or fifth. Curiously enough, in tests with ticks, fleas, and cattle flies, numbers of arthropods are counted [e.g., Smith *et al.* (112); Smith & King (116)]. Actually there is no reason now why repellency should not be studied with tests analogous to dosage-mortality tests of insecticides.

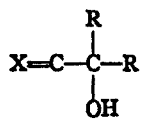
Let us assume for the sake of simplicity that the repellent concentration remains constant in a test where a population of insects is exposed. There is every reason to believe that there is a normal distribution of thresholds in the population [Dethier & Chadwick (30); Dethier & Yost (33)]. The time to first bite or alightment would be a measure of a rise in threshold of the least sensitive individual attributable to adaptation or other changes. If the concentration did change (as in reality it does), the time to first bite would be a measure of a drop in effective concentration to a level of threshold of the least sensitive individual. Comparisons based on time to first or even fifth bite are based on the ends of a normal distribution curve, statistically the least significant portion and hence subject to great variability. To study intrinsic repellency with a view to comparing effective chemical structures, it would be better to compare the concentrations of different compounds that would repel 50 per cent of the population.

The first step toward answering this question demands a different type of test. In practically all present tests repellency is determined as the ability of a compound to overcome the natural attractiveness of a host. Whether the host is man, canaries [Wasicky *et al.* (133)], mice [Eddy & McGregar (36)], rabbits [Starnes & Granett (119)], guinea pigs [Kasman *et al.* (71)], or cattle (many), the variations in attractiveness and all additional phenomena introduced by the host mean that a repellent is being tested against a varying background which is very difficult to control and in many instances totally unknown. One can only agree with Hocking (65) that "no scientific approach to the problems of personal protection from biting flies (and all biting arthropods) is possible without an understanding both of the factors which attract these insects to their hosts, and those which stimulate them to feed." In the present absence of adequate information of this kind the test could be balanced against some controllable attractive force, e.g., temperature, light, humidity, or gravity. The selection of the force should bear some relation to the attraction to hosts [cf. Laarman (77)].

This has been done with some success in certain cases. Although Smith & Gouck (115) found that tests in which ticks were allowed to cross treated bands were inconsistent and unsatisfactory, Granett & Sacktor (62) reported good results with comparable tests using the tick *Amblyomma americanum*. Linduska *et al.* (81) and Smith & Burnett (109) used treated and untreated cloth patches waved over jumping fleas in successful tests. Loeffler & Hoskins (83) in testing repellency for blowfly larvae used standard simulated wounds. Mackerras & Mackerras (87) and Waterhouse (134) used artificial attractants in the form of indol plugs. Most of the studies of repellency of DDT made use of inanimate surfaces [Kennedy (72); King & Gahan (76); Baranyovits (5); Brett & Rhoades (13); Dicke *et al.* (34); Rogoff (103); Hadaway & Barlow (63); Granett *et al.* (60)]. With the exception of the results reported by Christophers (19) and by Sarkaria & Brown (105), testing against a controlled attractant has not been done with mosquitoes.

Not only must this be done, but a distinction must be made between contact repellents and olfactory or vapor repellents. The difference has been noted by Christophers (19), Dethier (22), Waterhouse (134), and Sarkaria & Brown (105). There seems little reason why contact repellents for mosquitoes cannot be tested against some inanimate substrate as has been done with other insect repellents. Compare, for example, the methods used with cockroaches by Block (8) and Goodhue & Linnard (54) and the use of ants by Geigy & Utzinger (50). Vapor repellency can be tested against some standard controllable attractant as heat, moisture, or light. Christophers (19) and Sarkaria & Brown (105) have done this with *Aedes aegypti*, Dethier & Yost (33) and Dethier (26) with *Phormia regina*. Hughes (67) has tested the action of aliphatic compounds against species of *Glossina* without resorting to the use of any attractant. Kasman *et al.* (71) stated that an olfactometer does not satisfy the requirements of a test that would enable a correlation to be made between the results of the test and chemical groupings. They offer the following as objections: (*a*) it is not a rapid analytical method; (*b*) it does not take into account the essential function of a repellent as a barrier between the insect and the subject to be protected, and it defines only the effect of the repellent vapor without the surface from which that vapor must arise; (*c*) it does not define tactile repellency. Admittedly, present methods are slow and laborious. This is all the more reason for a concerted effort in alleviating the handicaps. The second objection fails to take cognizance of the importance of studying intrinsic repellency. The third objection requires no answer.

*The chemical basis of repellency.*—Considering the amount of effort which has been expended to date in the empirical testing of thousands of compounds, there has been disappointingly little advance in our understanding of the relation between chemical properties or structure and repellency. In 1925 Bunker & Hirschfelder (14) conducted a few poorly controlled field tests with *Anopheles*, *Aedes*, *Psorophora*, and *Culex* mosquitoes in an attempt to relate repellency and chemical structure. Their tentative conclusions were that repellency is correlated with the presence of the oxygen atom, hydrocarbons being poorer repellents than alcohols, ketones, aldehydes, and esters. Not until 1953 was a further attempt in this direction made. Roadhouse (101) undertook an analysis of some of the data of Morton *et al.* (91) as a prelude to further critical testing. He selected for study the groups which Morton *et al.* had found especially effective in mass screening tests. His results confirmed the earlier conclusions of Bunker & Hirschfelder in showing that oxygen is an important constituent of the molecule. But, inasmuch as many compounds containing oxygen are not repellent, we must seek more subtle relationships than the mere presence or absence of a given element. Some of these subtleties are suggested by the findings of Roadhouse (101), Okazaki *et al.* (96), and Geigy & Utzinger (50). Roadhouse found that repellency is greatest when OH is once removed from unsaturation, e.g.,



and the 1,2 or 1,3 glycols or their dehydration products. Geigy & Utzinger (50) on the basis of biting tests with *Aedes aegypti* and orientation tests with the ant, *Formica rufa*, found that the most effective of the chemical groups tested were diethylamide, adjacent dimethyl with C—C, and adjacent diethylamide plus dimethyl groups.

Surveys of the lists of compounds which have been tested in the field or against animals in laboratories show that certain chemical categories are more often repellent than others under these conditions of testing. For example, Travis *et al.* (127) in summing up the work at Orlando for the period 1942 to 1947 found that the most effective compounds were esters, amides, imides, ethers, and alcohols. Roadhouse (101) found that aldehydes and ketones were poor, α-hydroxy esters with a boiling point range of 230° to 260°C. were effective, and cyclic mono-alcohols with a boiling point near 260°C. were also effective. He could demonstrate no difference between primary, secondary, and tertiary alcohols. It is difficult, however, to assess the significance of these conclusions because, of those compounds which are effective, we can only say that they possess the proper balance of properties which make for inherent repellency, long duration, and nontoxicity. For this reason, attempts to relate field performance to some molecular characteristic are bound to be less fruitful than a laboratory study. For example, an examination of repellent times for homologous series of phthalic acid esters, based on routine screening tests with *Aedes aegypti* and *Anopheles quadrimaculatus* revealed no uniform progression of effectiveness except for a rapid decrease above the three carbon compound [Haller (64)]. On the other hand, Dethier & Yost (33) and Dethier (26) in laboratory studies of the repellent effect of aliphatic alcohols and aldehydes to blowflies found that within homologous series the molar concentrations necessary to cause rejection by 50 per cent of the population decreased progressively as chain length increased and that there was no rejection beyond the 12 carbon homologue. In terms of thermodynamic activities all intermediate members of each series are effective at the same concentration. Measured in molar concentrations the alcohols are more repellent than the aldehydes.

Similarly, in studies of the relation between vapor pressure and repellency, field and screening tests reveal the vapor pressure limits for effective field performance but shed little light on the relation between repellency and vapor pressure. Christophers (19) pointed out, for example, that an effective repellent must have a boiling point of approximately 280°C. to protect for 6 hr. but that effectiveness declines with boiling point above 350°C. With few exceptions substances with melting points above 37°C. are nonrepellent. Roadhouse (101) found that the best mono-alcohols were cyclic compounds with boiling points near 260°C.

Sarkaria & Brown (105) examined the question of boiling point (vapor pressure) by testing in an olfactometer the reaction of starved mosquitoes to 42 selected repellents. The vapor pressures at 25°C. of all compounds tested ranged from $0.1\times10^{-3}$ mm. Hg to $660\times10^{-3}$. Dimethyl phthalate was $1.2\times10^{-3}$. The more volatile compounds tended to have the greatest repellency, but repellency is not just a measure of vapor pressure. Vapor repellency can vary independently of vapor pressure. Dimethyl phthalate, Indalone, and cyclohexanol have high vapor repellency and low volatility. This combination makes for long lasting repellents. The most repellent compounds were citronellal, *n*-hexyl mandelate, and 6-2-2. Dethier & Yost (33) also determined that there is no causal relationship between vapor pressure or boiling point and repellency [cf. also Ferguson & Pirie (37)].

As far as contact repellents are concerned, the most careful analytical work has been the laboratory studies of Frings (43) and Frings & O'Neal (46) of the stimulating efficiency of inorganic materials and similar studies by Dethier & Chadwick (29) of organic materials. This work has been reviewed in Roeder's *Insect Physiology* (102). However, stimulating effect alone is not sufficient to insure that a compound which is effective in the laboratory is equally effective in the field. Such is seldom the case. For example, Travis & Smith (128) found that repellents against *Stomoxys calcitrans* protected for a longer time in the laboratory than in the field. And Frings & Hamrum (45) found that substances which were irritating to *Culex* did not necessarily force the insects to move away [cf. also Wiesmann & Lotmar (136)]. Dethier (25) working with *Glossina* came to similar conclusions. Block (8) showed that some compounds which were rejected by cockroaches in taste tests were not necessarily effective against free cockroaches. But there are also some compounds (e.g., potassium thiocyanate) which repelled free cockroaches and yet were not unacceptable in taste tests.

*The nature of repellency.*—The relationship between repellency, stimulating effect, and irritating effects brings up the question of the repellent action of certain insecticides. When DDT first appeared it was believed that it had no repellent properties [Cameron (16); Buxton (15); Dethier (22)]. However, Gahan *et al.* (49) observed, probably for the first time, that DDT activated mosquitoes and caused them to leave buildings which had been sprayed. About the same time Wolcott (137) observed that wood which had been soaked for 10 min. in benzene solutions of DDT was immune to attacks by nymphs of the termite, *Cryptotermes brevis*, for as long as one year. Since mortality was negligible, Wolcott concluded that DDT was acting as a repellent. McCulloch & Waterhouse (85) observed that mosquitoes preferred not to rest on DDT-treated surfaces when others were available to them and that after feeding through treated surfaces the mosquitoes did not suffer high mortality. Gabaldon (48) showed that the disappearance of anophelines from sprayed huts was attributable to DDT and not to the solvent kerosene. King & Gahan (76) reported that DDT reduced the number of flies which would rest on grids. Muirhead-Thomson (92, 93) observed that DDT causes an increase in the activity of *Anopheles gambiae*, a change in the light response, and departure from treated huts without ensuing death, whereas benzene hexachloride was without noticeable repellent effect and killed mosquitoes in the huts. Bertram (7) had similar results with *A. minimus;* Wharton & Reid (135) with *A. maculatus;* Nair (95) with *A. maculatus* and *A. letifer;* and Baranyovits (5) with flies. Musgrave (94) reported a slight and temporary repellency to honey bees.

The first careful study of the nature of the reaction was that of Kennedy (72) with *Aedes aegypti* and *Anopheles maculipennis atroparvus.* He found that the presence of DDT on a surface (*a*) reduced the duration of resting periods, (*b*) increased the number of alightments, and (*c*) reduced the number of insects (*Anopheles*) settled at any one time. Quite clearly the DDT excited the insects to greater activity. Where they had a choice of treated and untreated papers, they rested nearly equally long if they had previously been exposed to DDT. They also moved preferentially toward light. In short, DDT produces an undirected excitation after a delay of some seconds or minutes and before a lethal dose is picked up. Firtos & DeJong (41) have called the DDT effect an "alarm reaction" and considered it, on no evidence, a respiratory excitation. It gives rise to events in the following sequence: (*a*) restlessness, (*b*) readjustment of sitting position, (*c*) change in normal light reaction, (*d*) flight followed by death. Hadaway & Barlow (63), studying the behavior of *Anopheles stephensi* on insecticidal deposits, found that the insects flew from all deposits in 2 to 4 min. but that death ensued only when the deposit consisted of particles less than 10 $\mu$ in diameter. DDT activation appears to be attributable to penetration of sense organs on tarsi during the contact period, and lethal effects are a result of dosages retained after pick-up. Smyth & Roys (117) have recently shown that DDT-sensitive houseflies spend more time on DDT-treated surfaces than on control surfaces but that a resistant strain does not. In neither strain was this result obtained with DDE. It was suggested on the basis of convincing electrophysiological evidence that increased sensory input from tarsal chemoreceptors attributable to DDT gives an illusionary attractiveness.

This raises the question of just what a repellent is. Dethier (22) defined a repellent as "any stimulus which elicits an avoiding reaction." He pointed out that theoretically there may exist as many categories of repellents as there are classes of external stimuli. He recognized two primary divisions, physical and chemical, the latter consisting of olfactory (vapor) and gustatory (contact) repellents. Kennedy (72) recognized the same categories of stimuli which give rise to a repellent effect and then went on to make the important point that the reactions may take the form of merely random activity or of activity directed away from the source of stimulation. Reactions may be quick or slow to appear and weak or strong in character. He added, ". . . there is a widespread implicit assumption that repellency necessarily involves an immediate withdrawal from a treated surface." He suggested that "repellency" be confined to observed effects on distribution, that it not be used to describe the reactions of insects, that it involves reactions but is not a reaction, and that it is not necessarily of a normal sensory nature. "For practical purposes most workers would agree that a surface is repellent if insects are found to spend less time and so occur in smaller numbers on it than on other available and comparable surfaces." Rogoff (103) defined repellency as anything which reduces the numbers of insects on a treated surface. Utzinger (131) understood as repellents those substances which reduce insect bites by 10 per cent over an untreated control. Van Thiel (132) in speaking of the repellent effect of insecticides thought of it in terms of the total effect and behavioral aspects in the field. He recognized three main categories. (*a*) Insects are prevented from entering a hut. The effect may be "initial," i.e., attributable to the solvent; or "definite," i.e., attributable to the insecticide itself. (*b*) Insects do not remain in a hut. This repellency may be "complete," i.e., insects enter the hut, may bite, do not come into contact with the insecticide, leave. It may be "incomplete," i.e., the insects alight but are irritated and leave without biting ("primary") or after having bitten ("secondary"). Or they may bite first, then alight on a treated surface, become irritated, and leave ("tertiary"). (*c*) Insects never settle in a hut. Van Thiel concluded that in category (*a*) "initial" does occur, that in (*b*) "complete" could not be demonstrated, that (*b*) "incomplete" occurs, and that there are no grounds for assuming category (*c*) exists. He offered no explanation for categories (*a*) "definite" and (*b*) "complete," but agreed that (*b*) "incomplete" results from the alarming effect after DDT contact. He agreed with Firtos & DeJong (41) that this last should not be considered a repellent effect unless there is a clear understanding that it is a contact repellent effect.

From what we know of the action of chemicals on insects it is evident that some act as stimuli on the olfactory or gustatory sense and cause directed avoiding reactions which are more or less immediate. Such stimuli would be true warning stimuli. Other compounds, like DDT, have some sort of an irritating effect upon an insect which may not necessarily be immediate but which causes undirected increased activity. Usually this would result in a decreased number of insects in the area causing the excitation. This would be positive orthokinesis of Fraenkel & Gunn (42). Obviously it need not work through the sensory system nor need its effect be immediate. It would be incorrect to confine "repellency" to observed effects on distribution, for the simple reason that such an application of the term is not informative and may actually be misleading. The absence of insects on a given surface could equally well be attributable to the attraction of some other surface as to the repellency of the first for any cause whatsoever. It seems best to realize that effects on distribution may be attributable to the insect actually avoiding an area, actually being attracted to some other area, or being excited to greater or lesser activity so that there is a biased distribution. In other words, a surface cannot be said to be repellent merely because it has fewer insects on it than on some other surface available at the time or a different time (e.g., paired and unpaired tests or half-cow method). It is more informative to recognize a compound as having produced a known effect. Thus, it would be best to recognize as chemical repellents those compounds which produce an immediate avoiding reaction. These repellents may be olfactory, i.e., vapor or distance repellents, and act either through olfactory or common chemical sense and cause a directional avoiding reaction (taxis).

They may be contact (gustatory) and cause under certain special conditions an immediate directional avoiding reaction (taxis). Then there are compounds which stir an insect to greater undirected activity either immediately or after some delay (DDT alarming reaction) and so cause the insect to leave a treated surface. It would seem best to reserve a special term for this type of phenomenon. It is very much like a kinesis. The question of whether these compounds react via sense organs or otherwise is not important as far as terminology is concerned.

Failure to eat a material has also been taken as a sign of repellency, but is not in itself proof of repellency. In plant feeding insects, for example, failure to feed may be a result of an absence of attractants to trigger the reaction; to olfactory repellents which prevent even the initiation of biting; to contact repellents which prevent feeding after sampling, or reduce it; and to toxic materials which, while they might not necessarily kill the insect, cause it to cease feeding or to move elsewhere. Thus the failure of termites to eat wood samples impregnated with DDT, even though mortality is negligible is not a sure sign of the repellency of DDT *sensu strictu* [Wolcott (137, 139 to 142)]. Protection against mites was at one time thought to be a repellent phenomenon [Madden *et al.* (88); Snyder & Morton (118)] but is now known usually to be attributable to paralysis of the mites; and the compounds now used for protection are termed miticides [King (74)]. In the case of mothproofing agents where protection is measured in terms of reduced frass production, loss of weight of cloth patches, etc. [Sweetman *et al.* (121)] effective compounds need not be repellents. The proprietary substance Mitin FF (a substituted urea containing dichlorodiphenyl ether) is a stomach poison for clothes moths but is said to be a repellent to carpet beetles. Eulan BL (dichloro-benzene-sulfon-methylamide) inhibits the action of digestive enzymes and renders wool indigestible. Eulan CN is not eaten by clothes moths and is said to be repellent but is a poison for carpet beetles. Eulan NK (dichloro-benzyl-triphenyl-phosphonium chloride) prevents digestion in clothes moths but is said to be a repellent for carpet beetles because it reduces the amount of feeding [Luttringhaus (84); cf. also Stoves (120); Bloomfield (9)].

Whether or not an insecticide is a repellent depends a great deal on the definition of repellency and the circumstances of the experiment [cf. Kennedy (72)]. Thus DDT was said to be repellent to termites [Wolcott (137)] and to clothes moths and carpet beetles [Luttringhaus (84)] on the basis of its prevention of feeding. Chamberlain & Hoskins (18) found that DDT was repellent to termites when a choice between a treated and an untreated surface was possible. In other situations repellency could not be demonstrated. On the basis of flies and mosquitoes leaving various DDT-treated surfaces, DDT was said to be repellent by some [Kennedy (72); Gabaldon (48); King & Gahan (76); Bertram (7); Field (38); Rogoff (103)] and an irritant by others [Gahan *et al.* (49); Muirhead-Thomson (92, 93); Firtos & DeJong (41); Wharton & Reid (135); Baranyovits (5); Nair (95); van Thiel (132)]. In terms of the reduction of the number of horseflies on a treated surface Howell (66) found that DDT was not especially repellent. Waterhouse (134) found that it did not discourage the landing of gravid females of *Lucilia cuprina* on sheep but did prevent oviposition. Under some conditions comparative counts of insects on treated and untreated surfaces have shown DDT to be an attractant [Kennedy (72); Smyth & Roys (117)]. In a Y-tube olfactometer Dicke *et al.* (34) found DDT to be definitely attractive.

Similar confusion arises as far as other insecticides are concerned. Brett & Rhoades (13) found that a barrier of dust and 5 per cent gamma isomer of benzene hexachloride was effective for as long as 72 hr. in causing the harvester ant to turn aside. Gammexane was found to be repellent to larvae of *Lucilia sericata* [Loeffler & Hoskins (83)] and to the housefly [DuChanois (35)]. On the basis of the comparative numbers of houseflies settled on grids King & Gahan (76) found that technical grade benzene hexachloride was more repellent that DDT, refined benzene hexachloride less repellent than DDT, and both wettable chlordane and methoxychlor nonrepellent or even slightly attractive. On the basis of fly counts on treated and untreated cattle Howell (66) found that benzene hexachloride, chlordane, and toxaphene were not repellent to horseflies. On surfaces treated with benzene hexachloride houseflies are generally quiescent and acquire a lethal dose before departing [Baranyovits (5)]. Rogoff (103), studying the reduction in numbers of greenhouse thrips on leaf disc preparations, found that DDT, chlordane, parathion, heptachlor, and dimethyl phthalate were repellent and that gammexane was not repellent. In tests of the behavior of houseflies in a Y-tube olfactometer Dicke *et al.* (34) found that benzene hexachloride, chlordane, heptachlor, toxaphene, aldrin, lindane, DFDT, wettable powder of DDD, regular kerosene, and odorless kerosene were repellent while DDT and methoxychlor were attractive and dieldrin and technical grade DDD were neutral. Menke (90) found that toxaphene and parathion were only slightly repellent to alkali bees (*Nomia melanderi*). Hadaway & Barlow (63) found that *Anopheles stephensi* flew from surfaces treated with any DDT formulation in 2 to 4 min., and from chlordane, dieldrin, aldrin, and toxaphene after more than 30 min. Fresh deposits of benzene hexachloride activated and killed; but vapor from benzene hexachloride deposits did not disturb the mosquitoes if contact was impossible until after an advanced stage of intoxication was reached. With reference to pyrethrum, Findlay *et al.* (39) found that its presence on the skin reduced the number of tsetse flies alighting and biting. Johnson (69, 70) found that pyrethrum reduced the number of mosquitoes biting after they had momentarily landed and that lethane impregnated into clothing reduced biting by *Aedes* spp. Ribbands (100) found on the basis of night and day catches within huts that pyrethrum vapors and, to a lesser extent, lindane vapors deterred *Anopheles minimus* from entering sprayed huts. Paulini & Ricciardi (97) demonstrated what they interpreted as a repellent effect of pyrethrum on *Culex fatigans*. Laudani & Swank (78) demonstrated repellency of pyrethrum to several species of grain beetles.

It is certainly clear from the evidence at hand that repellency by whatever criterion it be judged is different from toxicity. There is no good reason a priori why toxicants should be repellent, e.g., CO is not repellent to man, nor Antu to some rats, boric acid to *Blattella*, formaldehyde to flies. Loeffler & Hoskins (83) found that there was no correlation between the ability of a compound to force larvae of *Lucilia sericata* to emigrate from treated wounds and its ability to kill. Chamberlain & Hoskins (18) found no correlation between repellent properties and toxic effects of series of compounds which were tested on the termites *Zootermopsis angusticollis* and *Z. nevadensis*. Sarkaria & Brown (105) studying the responses of female *Aedes aegypti* to vapors found that there was no correlation between repellency and knockdown (narcosis). Similar results were obtained with houseflies [Dicke *et al.* (34)]. In the case of the behavior of greenhouse thrips toward chlordane, DDT, parathion, heptachlor, and dimethyl phthalate there was an inverse relationship between toxicity and repellency [Rogoff (103)]. With isomers of benzene hexachloride there was no relation between the amount of time *A. stephensi* remained undisturbed on the surface and the per cent killed [Hadaway & Barlow (63)]. The insects rested more than 30 min. on the alpha and beta isomers and 1.3 min. on the delta isomer without being killed, but there was 100 per cent mortality from the gamma isomer where the resting time was 4.7 min.

*Mode of action.*—At the present time the most critical evidence suggests that repellents act directly on chemosensory systems. Wiesmann & Lotmar (136) showed that *Musca* and *Stomoxys* deprived of their antennae, the principal loci of olfactory receptors, were unable to direct themselves away from vapor repellents. A similar result was obtained with species of *Glossina* by Dethier (25). Dethier (24) and Dethier & Yost (23) demonstrated with the blowfly, *Phormia regina*, that extirpation of all organs bearing olfactory receptors (antennae, palpi, and labellum) renders the flies insensitive to vapors which normally repel them. Furthermore, it was proved that failure to respond resulted from absence of the necessary receptors and not from interference with locomotion or induction of shock. Gradual reduction by surgery in the number of receptors leads to gradual increase in the concentration of vapor required to repel. Moreover, in the case of those compounds which are attractants at low concentrations and repellents at high, as for example *iso*-valeraldehyde [Dethier (26, 27); Dethier *et al.* (32)], removal of sensory areas mediating acceptance results in an inability to be repelled.

It is abundantly clear from the work of Frings (43), Frings & Frings (44), Frings & O'Neal (46), Chadwick & Dethier (17), Dethier & Chadwick (31), and Dethier (23) that contact repellents act upon specialized chemoreceptors which are not normally sensitive to vapors. Even DDT, when it acts as a repellent, affects chemoreceptors [Hadaway & Barlow (63); Smyth & Roys (117)].

Such receptors, located on the mouthparts and tarsi, are concerned with monitoring some aspect of feeding. One would expect that repellent compounds acting on these receptors would prevent feeding. Experiments with tethered insects bear out this expectation. And with free insects, contact repellents applied to mouthparts act similarly. However, as far as tarsal chemoreceptors are concerned, contact repellents may or may not prevent feeding depending upon other conditions, some of which are mentioned below. At the moment there is no good evidence that contact repellents on the legs invariabily affect locomotor behavior. Insects do not always walk out of or avoid contact repellents although tethered insects frequently attempt to withdraw their feet from such solutions. Wiesmann & Lotmar (136) observed that some species of insects would be repelled by a chemical barrier while others would not. In special cases differences in response between free and fixed insects may be attributable to the experimental conditions under which the solutions are presented [cf., Block (8)].

On the other hand, there is some evidence that certain compounds in high concentrations act upon a common chemical sense [cf., Dethier & Chadwick (28)]. Roys (104) has shown by behavioral and electrophysiological methods that repellent vapors of such compounds as benzene act upon the leg (not known to bear olfactory receptors) and even on the isolated nerve cord of cockroaches. Slifer (108) has demonstrated that certain odorous materials held near the feet of grasshoppers provoke withdrawal of the appendages. Thus, while it is undoubtedly true that some vapor repellents can act upon senses other than the olfactory and gustatory, such repellents would act at lower concentrations and therefore, first, on the olfactory sense.

Some data illustrating this point have been collected from experiments with honey bees [Glynne Jones (52)]. Phenol and acetic acid act on the olfactory sense at low concentrations, but at higher concentrations the olfactory sense appears to cease operating while the common chemical sense takes over.

The practical problem of repellency is essentially a behavioral one, namely, to alter or interrupt a normal response operating through chemosensory pathways. One desires either to force an insect to depart from a given surface or to refrain from feeding through it. To be effective a compound must first possess inherent repellency, i.e., it must be capable of stimulating some sensory system other than that which mediates attraction or it must inhibit the system which mediates attraction. Second, since the response of the insect depends upon which sensory system has been stimulated and which reflex arcs are placed in operation, the repellent must act upon a system which has some influence on locomotion or feeding. As Frings & Hamrum (45) have shown, a mosquito may be intensely irritated by a compound touching the tarsi and still not step out of it. Furthermore, common field experience has shown that mosquitoes will stand in a spot of repellent and bite through a small unprotected area. In the case of *Phormia*, HCl vapor directed on the antennae will cause the fly to move away whereas HCl solution on the tarsi will not affect locomotor behavior but does under certain circumstances prevent feeding. If a fly is stimulated simultaneously by HCl on the tarsi and an attractive odor on the antennae, or HCl on the tarsi and sucrose on the mouthparts, feeding will not be prevented [see also Glynne Jones (52)].

It is clear that the nature of the response elicited by repellent compounds depends not only upon a variety of intrinsic biological factors such as age, state of nutrition, etc., but upon the concentration of the repellent, which sensory system it is stimulating, and whether and to what extent other sensory systems are being acted upon simultaneously by other stimuli.

In view of these considerations it would seem that a proper understanding of the mechanism of repellency depends upon knowledge of (*a*) the intrinsic repellency of a compound (stimulating efficiency), (*b*) the neural pathways through which the excitation is directed, and (*c*) the interaction of the various sensory and motor systems which determine the final response. Many compounds are eminently satisfactory from all of these points of view. The principal desideratum as far as repellents are concerned is to increase the duration of repellency. This is no longer primarily a problem of insect/repellent interaction. It is a question of absorption, dilution, alteration, etc. in the case of repellents applied to the skin and of ability to withstand wear and laundering in the case of repellents impregnated into clothing.

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# SOIL INSECTS AND THEIR CONTROL[1]

By J. H. Lilly

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"Some may feel that our soil insect problems are solved and that little remains to be done, but in my book we have only written the introduction to what should be one of the largest and best chapters in the history of economic entomology." This quotation from a recent address by Dr. G. C. Decker of Illinois is a concise appraisal of both the present status and the future possibilities of research on soil insects and their control.

Soil insects probably do at least some damage in every cultivated field throughout the world. Many times they mean the difference between a satisfactory crop and little or no return for the farmer's efforts. Any insect which, during its growing or feeding stages, lives either on or beneath the soil surface may be considered a soil insect. Many of them are not harmful to crops, but some rank among our most important pests.

Soil insects vary in both taxonomic relationships and habits (5, 33, 44, 66, 69, 83). Some of them like white grubs (*Phyllophaga* spp.) and wireworms (Elateridae) live persistently below the soil surface for long periods of time and feed on a wide variety of plants. Others like some of the cutworms (Phaleanidae) are nonpersistent forms and may not be present in great numbers in the same field for more than one or two years. Insects of these two groups, as a result of their ability to feed on numerous plants, usually occur in the fields before the crops are planted.

There is still another group of soil insects, including rootworms and root and seed maggots, which tend to be restricted in their choice of host plants and which usually invade a field only after a particular crop has been planted. A few species in this group, though commonly referred to as soil insects, do at least part of their damage by feeding above the ground. Corn rootworm (*Diabrotica longicornis* Say), flea beetles (*Epitrix* spp.), and sweetclover weevil (*Sitona cylindricollis* Fabr.) are examples.

Agricultural soils provide all the life requirements of a wide variety of insects. Both food and shelter are there for those adapted to take advantage of them. In addition soil provides refuge from natural enemies and buffers critical changes in temperature and moisture which might otherwise destroy them.

## Damage Symptoms

All underground plant parts are attacked by soil insects, including the planted seed. Thus seeds, sprouts, stems, roots, bulbs, and tubers are at-

[1] The survey of the literature pertaining to this review was completed in June, 1955.

# AËDES AEGYPTI (L.)

# THE YELLOW FEVER MOSQUITO

## ITS LIFE HISTORY, BIONOMICS AND STRUCTURE

BY

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(*b*) the intensity of selection (that is the size of the population exposed to the insecticide and the proportion killed);

(*c*) The number of generations per year.

The method by which resistance is produced in the case of DDT is thought to be through possession by the resistant insect of an enzyme (dehydrochlorinase) which converts DDT into a harmless compound DDE ((2,2-bis-(*p*-chlorophenyl)-1,dichlorethylene), the process being known as dehydrochlorination. The enzyme is present in all tissues of the fly and especially the integument. DDT does not induce mutation, but those with resistance become the form of the insect left by elimination of non-resistant forms (Brown and Perry, 1956).*

## (*f*) REPELLENTS

Repellents are substances that can be smeared on the skin without being irritant or poisonous and which prevent mosquitoes biting. They are usually oily fluids and may be used 'neat', or in some form of cream. They are also used to impregnate clothing to afford protection from bites and also wide-mesh netting used as a protection to the face and hands. They include a very large number of substances of varied chemical nature and different degrees of effectiveness depending upon their essential repellent properties, the time for which they remain effective when applied and whether they act at a distance or only on contact by the mosquito.

Substances especially effective are (1) certain natural essential oils, notably oil of citronella, or their essential principles, or synthetic substances of this type (for example the very powerfully repellent substance hydroxycitronellal); (2) a number of the dihydric alcohols (diols) among which is Rutger's 612 (ethylhexane diol-1:3); and (3) certain esters, for example dimethyl phthlate or other less well known esters of this type, such as isopropyl cinnamate or diethyl cinnamate or many others.

An important character largely determining their suitability for use is the boiling point. Organic compounds with boiling points below 200° C. are of little practical use as they evaporate from the human skin too rapidly. Substances with boiling point much above 300° C., whilst they give lasting effect usually lose in effective repellency. A high boiling point may, however, be useful for a special purpose, for example dibutyl phthalate (b.p. 325° C.) has been used for impregnating clothing since it stands up to washing.

Probably the two most generally useful repellents are dimethyl phthalate for military or similar purposes where a strong and lasting effect is essential and a good oil of citronella for civilian use where a milder and less permanent effect may serve all that is required. The former can be used 'neat' and applied after anointing the palms over all exposed skin (avoiding the near neighbourhood of the eyes or mucus membrane) or as a cream, a very satisfactory formula being the following:

Dr Hamill's cream (see Christophers, 1947)

| | |
|---|---|
| Dimethyl phthalate | 12·5 c.c. |
| White wax (cera alba) | 9 g. |
| Arachis oil | 27·5 c.c. |

* For further information see reviews by Metcalf (1955 *b*), Hoskins and Gordon (1956), and papers by Busvine (1957) and later. See also Brown (1956), Hadaway and Barlow (1956). On genetics of insect resistance see Crow (1956). For instances of resistance developed during operations against yellow fever see Jenkins and West (1954), Severo (1956).

Melt the wax in the arachis oil on a water bath and stir in the dimethyl phthalate. It can be modified by slightly changing the proportions of wax and arachis oil to suit a hotter or colder climate. It spreads very readily and is pleasant to use.

Oil of citronella if of good quality (a good Java oil) has the advantage of acting very strongly at a distance so that smearing of all exposed skin is unnecessary and a little on the clothing, socks, etc., may be sufficient to afford all that is required for comfort where danger of infection is not present.

Little is known as to the reason why particular substances have repellent properties or what determines the degree of effectiveness. For an account of repellents and their testing see Christophers (1947). See also references there given and some recent papers on mosquito repellents given here under references.

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# MOSQUITO REPELLENTS

## BEING A REPORT OF THE WORK OF THE MOSQUITO REPELLENT INQUIRY, CAMBRIDGE 1943–5

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(With 6 Figures in the Text)

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