DEPARTMENT OF MEDICINE & DIVISION OF DERMATOLOGY
PRESENT

ALVIN S. ZELICKSON, M.D.

CLINICAL ASSOCIATE PROFESSOR
DEPARTMENT OF MEDICINE, DIVISION OF DERMATOLOGY
UNIVERSITY OF MINNESOTA MEDICAL SCHOOL

"MELANOGENESIS & MELANOMAS"

FRIDAY, SEPTEMBER 16, 1966 4:00-5:00 P.M. 1364 MED. SCI. BLDG.

DEA
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UNIVERSITY OF CALIFORNIA SCHOOL OF MEDICINE

Department of Dermatology

GRADUATE TRAINING PROGRAM

The Department of Dermatology at the University of California, San Francisco Medical Center, is accredited for a three year training program by the American Board of Dermatology.

The program encompasses all phases of clinical dermatology and syphilology and the basic sciences related to these subjects. There are daily seminars and lectures. In addition, there are several special seminars and clinics throughout the week. These include the Visible Tumor Conference, Histopathology Conference, Hemangioma Clinic, Hair and Nail Clinic, Psoriasis Clinic, Collagen Disease Clinic, Atopic Clinic, Special Surgery Clinic, and Virus Clinic. There is a weekly Staff Conference, at which time a special guest lecture is given, followed by presentations and discussions of problem cases. Active research and investigative work is being conducted by the Department and resident staff participation in this field is encouraged.

Our residents have a very flexible rotation schedule which allows them to pursue their individual interests. When the resident works at affiliated hospitals and clinics this is for no more than 4 hours daily.

The resident staff has the responsibility for the care of the ward patients and their treatment in the hospital under the supervision of several members of the attending staff. The program utilizes the facilities of the Herbert C. Moffitt-University of California Hospitals, San Francisco General Hospital, Laguna Honda Hospital, U. S. Public Health Service Hospital, Veterans Administration Hospital, and Kaiser Foundation Hospital.

The salary range for assistant residents and residents at the Medical Center is $_____ to $_____ annually. Living quarters are available for single men and single women in the Parnassus Residence and the Millberry Union facilities. Further information is available from the Housing Officer, University of California, San Francisco Medical Center, San Francisco, California 94122. Group health insurance is also available.

Vacation and educational leaves consist of 2 weeks each.

Training fellowships are available for qualified individuals who wish to follow an academic career. These emphasize research approaches in dermatology. Stipends are based on the years of relevant postdoctoral experience plus a dependency allowance of $500 per dependent.

It is necessary for anyone taking a clinical residency at the University of California, San Francisco Medical Center to obtain a California license to practice medicine.

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TO: Internal Revenue Service

FROM: William L. Epstein, M.D.
Acting Chairman
Department of Dermatology
University of California, San Francisco

DATE:

SUBJECT: Graduate Training Program in Dermatology

The Department of Dermatology, UCSF, has a large physician graduate program. A trainee stipend is paid each physician. The primary purpose of the program is to further the education and training of the recipient in his individual capacity and the amount provided by the grantor for such purpose does not represent compensation for services to patients nor does it serve the interest of the grantor. In other words, services are of only incidental benefit to the hospital.

The trainee stipend is defined as an amount paid or allowed to, or for the benefit of, an individual trainee to aid him in the pursuit of study and research in medicine.

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UNIVERSITY OF CALIFORNIA
SAN FRANCISCO MEDICAL CENTER

BERKELEY · DAVIS · IRVINE · LOS ANGELES · RIVERSIDE · SAN DIEGO · SAN FRANCISCO

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SCHOOL OF MEDICINE

SAN FRANCISCO, CALIFORNIA 94122

[redacted]

DEPARTMENT OF DERMATOLOGY

Dear

The purpose of this letter is to bring to your attention the work of an investigative team at the University of California at San Francisco, whose chief aim is solution of an ancient and far-reaching human health problem, namely the diseases spread by the bite of the mosquito. President Kennedy remarked in 1962: "For centuries, malaria has outranked warfare for human suffering." Malaria is but one of the diseases transmitted by mosquitoes. Until recent years, malaria and other significant examples of such mosquito-borne diseases such as typhus, yellow fever, and plague raged almost completely unchecked. The toll in human suffering and lives taken by these diseases is astonomical. The advent of DDT brought with it the possibility of control, but problems with this approach soon occurred, first with the development of insect resistance to pesticides and, more recently, with the problem of pollution in our environment by such insecticides, suggesting that the cure could be as dangerous to man as the diseases controlled by them.

The research this team has carried on in the past 6 years (see appended Synopsis) suggests an alternate possibility for controlling mosquito-borne diseases, based not on developing more acceptable insecticides but rather on rendering humans less appealing to the mosquito. This necessitates basic research to understand and delineate the total complex of host-vector relationships, and the nature of the factors affecting mosquito response to man. This group has recently made significant strides in this direction through support by the Office of the Surgeon General, Department of the Army. However, recently adopted regulations require that Defense Department support go only to mission-oriented projects with clear military applications.

We are therefore turning to you in the hope that the basic phase of this research can be continued. The required support will be in the area of $100,000 annually for a period of 5 years.

Your consideration is appreciated, and we look forward to hearing from you regarding this proposal, which we are sending to several agencies for an expression of interest.

Sincerely yours,

Howard I. Maibach, M.D.
Associate Professor and
Vice Chairman

HIM:ims
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BACKGROUND

Insect vectors of disease went virtually unchecked before the advent of DDT, with the result that millions of people perished from malaria, typhus, yellow fever, plague and other mosquito-carried diseases. The chlorinated hydrocarbons and later cyclodene compounds, carbamates and organophosphates controlled most of such disease vectors but could not eradicate them. Moreover, constantly expanding applications of these insecticides brought about the problem of resistance to them. This in turn necessitated the synthesis of more and more insecticides. Recently, another complication entered the picture. An insecticide like DDT, which not long ago was hailed as among the greatest boons to mankind, suddenly and for good reasons has become a villain, and all chemical control methods have become greatly suspect. With the present national concern regarding our ecology and the poisoning of our environment, it is evident that the development of still more insecticides is not the right answer to the problem of containing insect-borne diseases. One possible alternative to the use of insecticides lies in controlling insects through the production and release of sterile males. This approach has some merits but some serious limitations. The latter include the following:

a) Methods must be developed by which the insect can be easily and massively produced in the laboratory.

b) The sterilization must be such as not to reduce the mating competitiveness with the normal males and

c) The fact that such a method seems to be more suited to small islands or isolated areas than to large land masses.

In general, it can be noted that chemosterilization is hazardous and does not seem to be very practical in the present state of our knowledge.

HYPOTHESIS

A better long-term solution to the problems caused by mosquito-borne diseases would appear to lie in methods to render man immune to mosquito bites. We believe that an understanding of why mosquitoes bite human skin will lead to the development of an effective method for the prevention of biting. Such research might well result either in the development of a systemic drug or in changing the skin's chemical composition by altering man's diet.

ACCOMPLISHMENTS TO DATE

In a series of biological experiments, we have attempted to discover why mosquitoes are attracted to humans, what prompts the biting reaction, and why certain individuals are more attractive to mosquitoes than others. We have demonstrated that mosquitoes are consistently more attracted to human skin than to any combination of heat, moisture, and carbon dioxide produced by the skin. This strongly suggests the presence of a chemical olfactory substance secreted by the skin.

In search of this attractant substance, we isolated chemicals from human eccrine sweat which, in a bioassay system (dual-port olfactometer), proved very attractive to mosquitoes. We also isolated from human skin, certain substances which repel mosquitoes. One of the repellent groups has been tentatively identified as unsaturated fatty acids. It has been noted that heavily sweating skin is more attractive to mosquitoes; apparently the attractant is released through the sweat glands and is secreted in direct proportion to the degree of sweating.

Further experiments could lead to identification of the specific chemical substances which repel or attract mosquitoes, syntehesis of these compounds, and development of a safe method of introducing them into the human body so as to provide a simple, continuous immunity to mosquito bites.

ORGANIZATION

The research effort has been a multidisciplinary program involving: chemists (Dr. W. A. Skinner, Director of Life Sciences, Stanford Research Institute, and Home Hong), a biochemist (Dr. Howard Johnson), and entomologist (Dr. Abdul Khan), an internist interested in tropical medicine (Dr. Walter Strauss), and a dermatologist (Dr. Howard Maibach). It is housed in the following three separate, fully equipped functioning laboratories, each specifically adapted for its portion of the study: (1) for the collection of human specimens and testing of humans, the California Medical Faciility (a state prison); (2) for mosquito testing and physiology, the University of California Medical Center; and (3) for complex chemical fractionation and identification with the most modern techniques, the Stanford Research Institute.

REASON FOR GRANT REQUEST

This study has been adequately funded in the past by the U.S. Army Surgeon General. The initial support allowed us to develop considerable insight into the problem and to develop knowledge and skills needed to complete this important project. Under recently adopted regulations, the Army Surgeon General is now forbidden to support such basic research. It seems to us vital, however, that the present team, representing a unique complex of talents and facilities, be kept together, for we are now in the best possible scientific position to take advantage of our previous efforts and produce a practical solution to the problem.

Funding required: Approximately $100,000 per year for five years.

W. A. SKINNER, Executive Director, Life Sciences Division, Stanford Research Institute

EDUCATION:

University of California at Los Angeles: B.S., Chemistry, 1948
University of Oklahoma: M.S., Organic Chemistry, 1950
University of Texas: Ph.D., Organic Chemistry, 1952

POSITIONS HELD:

Teaching Assistant, University of Oklahoma, 1948-50
Research Chemist, Basic Cotton Research Laboratories, University of Texas, 1950-52
Research Chemist, Aerojet-General Corp., 1952-53
Research Chemist, Celanese Corporation, 1953-55
Senior Organic Chemist, 1955-60; Chairman, Department of Pharmaceutical Chemistry, 1960-present; Executive Director Life Sciences Division, Stanford Research Institute, 1965-present

RESEARCH EXPERIENCE:

Graduate thesis, Ullman synthesis of biphenyls, oxidation products of vitamin E.
Aerojet-General: Synthesis of boron alkyls, polymerization reactions, propellent development.
Celanese Corp.: Synthesis and polymerization of hydrocarbon and chlorinated monomer, process development research.
Stanford Research Institute: Synthesis of a variety of organic compounds for biological evaluation. Structure-activity problems in drug research; free radical reactions; enzyme-inhibition studies. Synthesis of indoles, imidazoles, benzimidazoles, uracils, nitrogen mustards and amino acids, thiourethans, carbamates, phenoxyacetic acid analogs, organometallic compounds, guanidine and nitroguanidines, chemosterilants. Isolation and identification of natural products.

CURRENT FIELDS OF ACTIVITY:

Supervising research on synthesis of compounds having biological activity; investigation into the chemistry of the tocopherols and their oxidation products; vector control studies; direction and management of research in the life sciences research group of over 200 people.

MEMBERSHIPS:

American Chemical Society
Research Society of America
American Association for the Advancement of Science
New York Academy of Sciences

SKINNER

PUBLICATIONS:

1. V. L. Frampton, W. A. Skinner, and P. S. Bailey. Some oxidation products of DL-α-tocopherol obtained with ferric chloride. Science 116, 34 (1952).

2. J. C. Colbert, D. Fox, and W. A. Skinner. Characterization of 2-hydroxy-2'-nitrobiphenyl. J. Am. Chem. Soc. 75, 2249 (1953).

3. V. L. Frampton, W. A. Skinner, and P. S. Bailey. Production of α-tocored from tocopherol with ferric chloride. J. Am. Chem. Soc. 76, 282 (1954).

4. W. A. Skinner, J. D. Johnston, and M. Fisher. Telomerization of ethylene with methyl bromoacetate. J. Am. Chem. Soc. 79, 5790 (1957).

5. W. A. Skinner, E. Bishop, D. Tieszen, and J. D. Johnston. Uncatalyzed addition of bromotrichloromethane to ethylene and substituted ethylenes. I. Nature and scope of the reaction. J. Org. Chem. 23, 1710 (1958).

6. W. A. Skinner, E. Bishop, D. Tieszen, and J. D. Johnston. A new route to flame-resistant polymers, synthesis and polymerization of 3,3,3-trichloro-1-propene. Ind. Eng. Chem. 51, 1359 (1959).

7. W. A. Skinner, H. F. Gram, Carol W. Mosher, and B. R. Baker. Potential anticancer agents. XX. Diazoacetyl analogs of chlorambucil. J. Am. Chem. Soc. 81, 4639 (1959).

8. W. A. Skinner, M. G. M. Schelstraete, and B. R. Baker. Potential anticancer agents. XXV. Monofunctional alkylating agents derived from 2-methylbenzimidazole. J. Org. Chem. 24, 1827 (1959).

9. W. A. Skinner, M. G. M. Schelstraete, and B. R. Baker. Potential anticancer agents. XXVIII. Synthesis of 5-(chloromethyl)uracil. J. Org. Chem. 25, 149 (1960).

10. V. L. Frampton, W. A. Skinner, P. Cambour, and P. S. Bailey. α-Tocopurple, an oxidation product of α-tocopherol. J. Am. Chem. Soc. 82, 4632 (1960).

11. W. A. Skinner, Helen F. Gram, Mary O. Greene, J. Greenberg, and B. R. Baker. Potential anticancer agents. XXXI. The relationship of chemical structure to antileukemic activity with analogs of 1-methyl-3-nitro-1-nitrosoguanidine (NSC-9369). J. Med. Pharm. Chem. 2, 299 (1960).

12. W. A. Skinner, H. F. Gram, and B. R. Baker. Potential anticancer agents. XXXII. Analogs of chlorambucil. II. Monofunctional alkylating agents derived from 3-(p-aminophenyl) propionic acid. J. Org. Chem. 25, 777 (1960).

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13. W. A. Skinner, Helen F. Gram, and B. R. Baker. Potential anticancer agents. XXXIII. Analogs of chlorambucil. III. Monofunctional alkylating agents derived from 3-(acetylphenyl)propionic acid. J. Org. Chem. 25, 953 (1960).

14. W. A. Skinner, K. A. Hyde, Helen F. Gram, and B. R. Baker. Potential anticancer agents. XXXVIII. Alkylating agents related to phenylalanine mustard. II. J. Org. Chem. 25, 1756 (1960).

15. A. P. Martinez, W. A. Skinner, W. W. Lee, L. Goodman, and B. R. Baker. Potential anticancer agents. XLV. Alkylating agents related to phenylalanine mustard. III. Synthesis of phenylpyruvate mustard. J. Am. Chem. Soc. 82, 6050 (1960).

16. B. R. Baker, W. W. Lee, W. A. Skinner, A. P. Martinez, and E. Tong. Potential anticancer agents. L. Non-classical antimetabolites. II. Some factors in the design of exo-alkylating enzyme inhibitors, particularly of lactic dehydrogenase. J. Med. Pharm. Chem. 2, 6 (1960).

17. W. A. Skinner, E. Bishop, P. Cambour, S. Fuqua, and P. Lim. Studies of the reaction of ethylene with aluminum trialkyls. Ind. Eng. Chem. 52, 695 (1960).

18. W. A. Skinner and D. Tieszen. Production of maleic acid by oxidizing butenes. Ind. Eng. Chem. 53, 557 (1961).

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21. A. P. Martinez, W. A. Skinner, W. W. Lee, L. Goodman, and B. R. Baker. Potential anticancer agents. XLVII. Alkylating agents related to phenylalanine mustard. IV. Transformation products of ethyl o-amino-α-benzamidocinnamate. J. Org. Chem. 26, 860 (1961).

22. W. A. Skinner, M. G. M. Schelstraete, and B. R. Baker. Potential anticancer agents. XLVIII. Analogs of chlorambucil. VI. Ring isomers. J. Org. Chem. 26, 1554 (1961).

23. W. A. Skinner, M. G. M. Schelstraete, and B. R. Baker. Potential anticancer agents. XLIX. Analogs of chlorambucil. VII. Nitrogen mustards derived from cinnamic acid. J. Org. Chem. 26, 1674 (1961).

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24. L. O. Ross, E. M. Acton, W. A. Skinner, L. Goodman, and B. R. Baker. Potential anticancer agents. LX. Synthesis of 5-diazouracil and related compounds. J. Org. Chem. 26, 3395 (1961).

25. K. A. Hyde, E. M. Acton, W. A. Skinner. L. Goodman, and B. R. Baker. Potential anticancer agents. LXIII. Analogs of chlorambucil. VII. Monofunctional alkylating agents derived from ω-(aminophenyl)-alkanoic acids. J. Org. Chem. 26, 3351 (1961).

26. K. A. Hyde, E. M. Acton, W. A. Skinner, L. Goodman, J. Greenberg, and B. R. Baker. Potential anticancer agents. LXII. The relationship of chemical structures to antileukemic activity with analogs of 1-methyl-3-nitro-1-nitrosoguanidine (NSC-9369). II. J. Med. Pharm. Chem. 5, 1 (1962).

27. W. A. Skinner, R. D. Mathews, and R. M. Parkhurst. Alarm reaction of the top smelt, Atherinops affinis (Ayres). Science 138, 681 (1962).

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29. W. A. Skinner and P. Alaupovic. Vitamin E oxidation with alkaline ferricyanide. Science 140, 803 (1963).

30. W. A. Skinner and P. Alaupovic. Oxidation products of vitamin E and its model, 6-hydroxy-2,2,5,7,8-pentamethylchroman. V. Studies of the products of alkaline ferricyanide oxidation. J. Org. Chem. 28, 2854 (1963).

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45. J. K. Horner, J. I. DeGraw, and W. A. Skinner. The preparation of 5-alkylthio, branched tryptamines. Can. J. Chem. 44, 307 (1966).

46. V. H. Brown, J. I. DeGraw, S. A. Ferguson, and W. A. Skinner. The role of analgesic drug metabolites in the formation of lens opacities. J. Med. Chem. 9, 261 (1966).

47. H. I. Maibach, W. A. Skinner, W. G. Strauss, and A. A. Khan. Factors that attract and repel mosquitoes in human skin. J. Am. Med. Assoc. 196, 3, 363-6 (1966).

48. J. I. DeGraw, J. G. Kennedy and W. A. Skinner. The preparation and reduction of 5-cyano-3-indolylketones. Synthesis of 5-cyanotryptamines. J. Heterocyclic Chem. 3, 9 (1966).

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50. J. I. DeGraw, V. H. Brown, S. A. Ferguson, N. E. Kontaxis, and W. A. Skinner. Histamine releasers. I. Structure of the dimer formed from p-methoxy-N-methylphenethylamine and formaldehyde. J. Med. Chem. 9, 292 (1966).

51. W. A. Skinner, J. Hayford, T. E. Shellenberger, and W. T. Colwell. Effect of organic compounds on reproductive processes. II. Alkylating agents derived from various α,ω-alkylenediols. J. Med. Chem. 9, 605 (1966).

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53. J. E. DeGraw, V. H. Brown, A. S. Ferguson, and W. A. Skinner. Histamine releasers. II. Synthesis of a trimer in the formaldehyde-p-methoxyphenethylamine series of histamine releasers. J. Med. Chem. 9, 838 (1966).

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59. H. L. Johnson, W. A. Skinner, H. I. Maibach, and T. R. Pearson. Repellent activity and physical properties of ring-substituted N,N-diethylbenzamides. J. Econ. Entomol. 60, 173 (1967).

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60. T. E. Shellenberger, W. A. Skinner, and J. M. Lee. Effect of organic compounds on reproductive processes. IV. Response of Japanese quail to alkylative agents. Toxicol. Appl. Pharmacol. 10, 69 (1967).

61. W. A. Skinner, M. Cory, T. E. Shellenberger, and J. I. DeGraw. Effect of organic compounds on reproductive processes. V. Alkylating agents derived from aryl, aralkyl, and cyclohexylmethylene diamines. J. Med. Chem. 10, 120 (1967).

62. J. I. DeGraw, V. H. Brown, N. E. Kontaxis, S. A. Ferguson, G. R. Gordon, J. H. Peters, and W. A. Skinner. Histamine releasers. III. Dibasic acid amides of 4-phenyl-4-aminomethylpiperidines. J. Med. Chem. 10, 174 (1967).

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65. M. A. Leaffer, W. A. Skinner, J. J. Menn, J. B. McBain, and L. W. Fancher. Synthesis of N-(mercaptomethyl)-phthalimide-carbonyl-C^{14}-S-(O,O-dimethylphosphorodithionate). J. Labelled Compounds, 3, 334 (1967).

66. W. A. Skinner and J. Scholler. Anticancer activities of alkylating agents derived from various diamines and diols. Effects on Ehrlich Ascites carcinoma. Cancer Chemotherapy Rpts. 51, No. 4, (1967).

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80. W. A. Skinner. Chemosterilants in rodent control. In Proceedings: Rodents as Factors in Disease and Economic Loss, Asia-Pacific Interchange meeting, June 17-27, 1968, Honolulu, Hawaii.

81. W. A. Skinner, M. Leaffer, J. Johansson, and C. Mitoma. In vitro studies of the metabolism of 6-hydroxy-2,2,5,7,8-pentamethylchroman, an α-tocopherol model, in rat and rabbit liver homogenates. Submitted to Archives of Biochem. Biophys.

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82. W. A. Skinner, J. Kennedy, J. DeGraw and H. Johnson. Structure-activity studies of 3,4,5-trimethoxybenzamides. I. Variation of the amine function. Submitted to J. Med. Chem.

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SCHOOL OF MEDICINE

SAN FRANCISCO, CALIFORNIA 94122

[redacted]

DEPARTMENT OF DERMATOLOGY

Dear

The purpose of this letter is to bring to your attention the work of an investigative team at the University of California at San Francisco, whose chief aim is solution of an ancient and far-reaching human health problem, namely the diseases spread by the bite of the mosquito. President Kennedy remarked in 1962: "For centuries, malaria has outranked warfare for human suffering." Malaria is but one of the diseases transmitted by mosquitoes. Until recent years, malaria and other significant examples of such mosquito-borne diseases such as typhus, yellow fever, and plague raged almost completely unchecked. The toll in human suffering and lives taken by these diseases is astonomical. The advent of DDT brought with it the possibility of control, but problems with this approach soon occurred, first with the development of insect resistance to pesticides and, more recently, with the problem of pollution in our environment by such insecticides, suggesting that the cure could be as dangerous to man as the diseases controlled by them.

The research this team has carried on in the past 6 years (see appended Synopsis) suggests an alternate possibility for controlling mosquito-borne diseases, based not on developing more acceptable insecticides but rather on rendering humans less appealing to the mosquito. This necessitates basic research to understand and delineate the total complex of host-vector relationships, and the nature of the factors affecting mosquito response to man. This group has recently made significant strides in this direction through support by the Office of the Surgeon General, Department of the Army. However, recently adopted regulations require that Defense Department support go only to mission-oriented projects with clear military applications.

We are therefore turning to you in the hope that the basic phase of this research can be continued. The required support will be in the area of $100,000 annually for a period of 5 years.

Your consideration is appreciated, and we look forward to hearing from you regarding this proposal, which we are sending to several agencies for an expression of interest.

Sincerely yours,

Howard I. Maibach, M.D.
Associate Professor and
Vice Chairman

HIM:ims
Enc 1

BACKGROUND

Insect vectors of disease went virtually unchecked before the advent of DDT, with the result that millions of people perished from malaria, typhus, yellow fever, plague and other mosquito-carried diseases. The chlorinated hydrocarbons and later cyclodene compounds, carbamates and organophosphates controlled most of such disease vectors but could not eradicate them. Moreover, constantly expanding applications of these insecticides brought about the problem of resistance to them. This in turn necessitated the synthesis of more and more insecticides. Recently, another complication entered the picture. An insecticide like DDT, which not long ago was hailed as among the greatest boons to mankind, suddenly and for good reasons has become a villain, and all chemical control methods have become greatly suspect. With the present national concern regarding our ecology and the poisoning of our environment, it is evident that the development of still more insecticides is not the right answer to the problem of containing insect-borne diseases. One possible alternative to the use of insecticides lies in controlling insects through the production and release of sterile males. This approach has some merits but some serious limitations. The latter include the following:

a) Methods must be developed by which the insect can be easily and massively produced in the laboratory.

b) The sterilization must be such as not to reduce the mating competitiveness with the normal males and

c) The fact that such a method seems to be more suited to small islands or isolated areas than to large land masses.

In general, it can be noted that chemosterilization is hazardous and does not seem to be very practical in the present state of our knowledge.

HYPOTHESIS

A better long-term solution to the problems caused by mosquito-borne diseases would appear to lie in methods to render man immune to mosquito bites. We believe that an understanding of why mosquitoes bite human skin will lead to the development of an effective method for the prevention of biting. Such research might well result either in the development of a systemic drug or in changing the skin's chemical composition by altering man's diet.

ACCOMPLISHMENTS TO DATE

In a series of biological experiments, we have attempted to discover why mosquitoes are attracted to humans, what prompts the biting reaction, and why certain individuals are more attractive to mosquitoes than others. We have demonstrated that mosquitoes are consistently more attracted to human skin than to any combination of heat, moisture, and carbon dioxide produced by the skin. This strongly suggests the presence of a chemical olfactory substance secreted by the skin.

In search of this attractant substance, we isolated chemicals from human eccrine sweat which, in a bioassay system (dual-port olfactometer), proved very attractive to mosquitoes. We also isolated from human skin, certain substances which repel mosquitoes. One of the repellent groups has been tentatively identified as unsaturated fatty acids. It has been noted that heavily sweating skin is more attractive to mosquitoes; apparently the attractant is released through the sweat glands and is secreted in direct proportion to the degree of sweating.

Further experiments could lead to identification of the specific chemical substances which repel or attract mosquitoes, syntehesis of these compounds, and development of a safe method of introducing them into the human body so as to provide a simple, continuous immunity to mosquito bites.

ORGANIZATION

The research effort has been a multidisciplinary program involving: chemists (Dr. W. A. Skinner, Director of Life Sciences, Stanford Research Institute, and Home Hong), a biochemist (Dr. Howard Johnson), and entomologist (Dr. Abdul Khan), an internist interested in tropical medicine (Dr. Walter Strauss), and a dermatologist (Dr. Howard Maibach). It is housed in the following three separate, fully equipped functioning laboratories, each specifically adapted for its portion of the study: (1) for the collection of human specimens and testing of humans, the California Medical Faciility (a state prison); (2) for mosquito testing and physiology, the University of California Medical Center; and (3) for complex chemical fractionation and identification with the most modern techniques, the Stanford Research Institute.

REASON FOR GRANT REQUEST

This study has been adequately funded in the past by the U.S. Army Surgeon General. The initial support allowed us to develop considerable insight into the problem and to develop knowledge and skills needed to complete this important project. Under recently adopted regulations, the Army Surgeon General is now forbidden to support such basic research. It seems to us vital, however, that the present team, representing a unique complex of talents and facilities, be kept together, for we are now in the best possible scientific position to take advantage of our previous efforts and produce a practical solution to the problem.

Funding required: Approximately $100,000 per year for five years.

W. A. SKINNER, Executive Director, Life Sciences Division, Stanford Research Institute

EDUCATION:

University of California at Los Angeles: B.S., Chemistry, 1948
University of Oklahoma: M.S., Organic Chemistry, 1950
University of Texas: Ph.D., Organic Chemistry, 1952

POSITIONS HELD:

Teaching Assistant, University of Oklahoma, 1948-50
Research Chemist, Basic Cotton Research Laboratories, University of Texas, 1950-52
Research Chemist, Aerojet-General Corp., 1952-53
Research Chemist, Celanese Corporation, 1953-55
Senior Organic Chemist, 1955-60; Chairman, Department of Pharmaceutical Chemistry, 1960-present; Executive Director Life Sciences Division, Stanford Research Institute, 1965-present

RESEARCH EXPERIENCE:

Graduate thesis, Ullman synthesis of biphenyls, oxidation products of vitamin E.
Aerojet-General: Synthesis of boron alkyls, polymerization reactions, propellent development.
Celanese Corp.: Synthesis and polymerization of hydrocarbon and chlorinated monomer, process development research.
Stanford Research Institute: Synthesis of a variety of organic compounds for biological evaluation. Structure-activity problems in drug research; free radical reactions; enzyme-inhibition studies. Synthesis of indoles, imidazoles, benzimidazoles, uracils, nitrogen mustards and amino acids, thiourethans, carbamates, phenoxyacetic acid analogs, organometallic compounds, guanidine and nitroguanidines, chemosterilants. Isolation and identification of natural products.

CURRENT FIELDS OF ACTIVITY:

Supervising research on synthesis of compounds having biological activity; investigation into the chemistry of the tocopherols and their oxidation products; vector control studies; direction and management of research in the life sciences research group of over 200 people.

MEMBERSHIPS:

American Chemical Society
Research Society of America
American Association for the Advancement of Science
New York Academy of Sciences

SKINNER

PUBLICATIONS:

1. V. L. Frampton, W. A. Skinner, and P. S. Bailey. Some oxidation products of DL-α-tocopherol obtained with ferric chloride. Science 116, 34 (1952).

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15. A. P. Martinez, W. A. Skinner, W. W. Lee, L. Goodman, and B. R. Baker. Potential anticancer agents. XLV. Alkylating agents related to phenylalanine mustard. III. Synthesis of phenylpyruvate mustard. J. Am. Chem. Soc. 82, 6050 (1960).

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80. W. A. Skinner. Chemosterilants in rodent control. In Proceedings: Rodents as Factors in Disease and Economic Loss, Asia-Pacific Interchange meeting, June 17-27, 1968, Honolulu, Hawaii.

81. W. A. Skinner, M. Leaffer, J. Johansson, and C. Mitoma. In vitro studies of the metabolism of 6-hydroxy-2,2,5,7,8-pentamethylchroman, an α-tocopherol model, in rat and rabbit liver homogenates. Submitted to Archives of Biochem. Biophys.

SKINNER

82. W. A. Skinner, J. Kennedy, J. DeGraw and H. Johnson. Structure-activity studies of 3,4,5-trimethoxybenzamides. I. Variation of the amine function. Submitted to J. Med. Chem.

DIVISION OF DERMATOLOGY TEACHING PROGRAM

SPECIALTY LECTURES

1966 - 1967

E N T I R E T H I R D Y E A R C L A S S

DATE & TIME	LECTURER(S)	SUBJECT
Saturday January 7 9:00-10:00 a.m.	Richard S. Goodman S. William Levy	The Whys and Wherefores of the Skin Biopsy
Saturday January 14 9:00-10:00 a.m.	John H. Epstein Denny L. Tuffanelli	Dermatologic Manifestations of Internal Disease
Saturday January 21 9:00-10:00 a.m.	William L. Epstein	Sherlock Holmes in Dermatology
Saturday January 28 9:00-10:00 a.m.	Theodore A. Tromovitch James P. McGinley	The Most Curable Cancer
Saturday February 4 9:00-10:00 a.m.	Denny L. Tuffanelli Roy W. Leeper	The Dermatologic Significance of Collagen Diseases
Monday May 22 12:00-1:00 p.m.	Paul Fasal	Leprosy - With Case Presentations
Monday May 29 12:00-1:00 p.m.	Rees B. Rees	Drug Reactions
Monday June 5 12:00-1:00 p.m.	Max E. Krause Gilbert H. Barnes Kirk D. Wuepper	The Return of Syphilis

NOTICE TO LECTURER: Please read attached NEWSLETTER FOR SEPTEMBER dated September 1, 1966 from Irving R. Merrill, Ph.D., Acting Coordinator, Educational Television Division - Locations may be selected to suit the convenience of the lecturer.

PRINCIPLES OF TREATMENT AND FORMULARY

One should develop familiarity with a few reliable prescriptions and treatment methods.

I. TOPICAL THERAPY

Consider these points:

A. General character of the skin. If dry, use lubricating agents. If moist or oily, use wet dressings, greaseless bases or drying lotions. For dry skin, stop soap entirely and apply lubricant to the wet skin. This traps moisture in the skin, which one cannot do by applying grease to the dry skin.

B. Start with mild simple remedies. For acutely inflamed skin, use soothing non-irritating wet dressings or hydrocortisone cream. An example of a wet dressing would be Burow's (Domeboro^{R} Powder packets or tablets dissolved in a pint of cool water) or cool water alone. Wring out an old soft torn up sheet and lay it on inflamed areas, dipping the cloth into the solution frequently. The wet dressing benefits by its evaporation and therefore cooling effect, shrinking capillaries and promoting decongestion. If topical corticosteroids are used, use a greaseless base to avoid the occlusive and heating effect of petrolatum, as is often used in commercial ointments. 1/2% hydrocortisone in hydrophilic ointment, U.S.P., is an excellent and relatively inexpensive preparation. For chronic and thickened skin eruptions, use keratolytic agents such as tar ointments, pastes or lotions, or salicylic acid, 1-3% in hydrophilic ointment.

C. Test strong medications on one small site first, to rule out sensitivity to the topical medication. Sensitivity may develop at any time, however.

D. Remedies should not be changed too frequently. Stop treatment at once if irritation appears.

E. Careful instructions should be given to the patient. Over abundant application of a tar preparation, for example, may discourage the patient because of its color. Similarly, if hydrocortisone is used lavishly, the time and expense may be too great.

F. Undertreat rather than overtreat. Overtreatment of dermatitis is probably the single most common error in dermatology. Do not use strong medications when weak ones will accomplish the same purpose.

G. Avoid sting, stink or stain wherever possible.

H. Avoid the application of toxic substances to extensive inflamed or denuded skin. Examples of this would be phenol, salicylic acid, mercury, etc.

I. Avoid known sensitizers, such as topical penicillin, sulfonamides, antihistamines, local anesthetics, nitrofuran preparations, etc.

J. Have one good emulsion base in mind. This will serve as a vehicle for almost any topical medication. Hydrophilic ointment, U.S.P., is readily available. Another base well known in this San Francisco area is Haldane's Emulsifying Base (HEB).

K. For pseudomonas infections a polymyxin-neomycin ointment is the treatment of choice.

L. 10% DDT in powder is excellent for pediculosis pubis, capitis and corporis. This is available as Stay-Dee Powder (Stayner Company, Berkeley). For scabies, "Kwell," which is the gamma isomer of benzine hexachloride, is effective. It may be used as a generalized application for 3 nights.

M. Topical antibiotics are reasonably safe to use. Penicillin should not be used topically because of its high sensitizing index. Neomycin may sensitize.

N. For localized cutaneous moniliasis 1% aqueous gentian violet is still effective. Various other preparations are available, including nystatin (Mycostatin^{R}) cream, ointment, and topical powder, amphotericin B lotion (Fungizone^{R}) and Sporostacin^{R} cream, lotion, and solution.

O. A good antifungal preparation for ringworm is 1% salicylic acid and 3% sulphur in an emulsion base, twice a day.

P. Tolnaftate (Tinactin^{R}) appears to be an effective fungicide even for Trichophyton rubrum infections. It should be available soon as a 1% cream.

Q. Acrisorcin (Akrinol^{R} cream) is a new promising therapeutic agent for tinea versicolor.

R. A bleach for freckles and hyperpigmentation is 2% hydroquinone (Eldoquin^{R} cream); it is reported to be less sensitizing and irritating than older preparations.

S. Podophyllin, 25% in acetone, has one unequivocal indication: treatment of acuminate warts of the genitalia or perianal area. Surrounding skin should be protected with Lassar's paste and the podophyllin painted on once, then washed off within a couple of hours. This may be repeated at weekly intervals if necessary. Occasionally a violent reaction will occur, requiring analgesics.

T. Vioform, or iodochlorhydroxyquinolone, is commercially available as a 3% ointment or a 3% cream. It tends to yellow the skin or hair and is irritating to eyes, but otherwise replaces tar. Vioform is effective against bacteria and fungi generally. It may be used for eczemas, seborrheic dermatitis, psoriasis, and various bacterial and fungal infections.

U. Pruritus and pruritus vulvae may be treated with 1/2% hydrocortisone and 1% Vioform in an emulsion base.

V. Corns and calluses may be pared and 40% salicylic acid plasters (Duke Laboratories) cut to fit the lesion, then held in place with adhesive tape for five days. For severe calluses ripple sole shoes may be excellent.

W. Gelfoam powder helps in the treatment of varicose and stasis ulcers, as well as healing wounds. It may be combined with a topical antibiotic powder.

X. Steroid preparations under an occlusive dressing are useful in the treatment of chronic localized dermatoses such as psoriasis, lichen simplex chronicus, etc. The local steroid preparation is applied to the lesion and light pliable moisture-retaining film (Saran^{R} Wrap) or plastic bag or plastic glove is applied and kept in place with tape. It may be repeated each night. The lesion should be kept airtight.

II. SYSTEMIC TREATMENT

A. Sulfonamides: For widespread pyoderma or cases resistant to topical applications, triple sulfa or Gantrisin may help. They also may help pustular acne.

1. Sulfapyridine or the sulfones (Diasone, Promacetin) are used in the treatment of dermatitis herpetiformis. Two to four tablets may be required initially but the dose should be decreased as the symptoms subside. Check blood count and urinalysis frequently.

B. Antibiotics:

1. Penicillin: still the treatment of choice for syphilis (see section on specific dosages). For various pyodermas, particularly when accompanied by fever, one or more injections of penicillin 600,000 units intragluteally constitute excellent treatment. However, because of the high rate of anaphylactic reactions and other manifestations of sensitivity, many physicians prefer not to use penicillin, but employ either sulfa drugs or broad spectrum antibiotics. Newer oral penicillins may be preferable to the injectable forms.

2. Broad spectrum antibiotics: such as tetracycline, are required frequently in cases of pyoderma with fever, or widespread involvement. In severe cases cultures and sensitivity tests are an aid in the selection of the appropriate antibiotic.

C. Antihistaminics: Many antihistaminics are available. If one is familiar with two or three, this should be adequate for treating dermatologic conditions. The primary indication for these drugs is urticaria. The therapeutic dose is that which will keep the patient free of hives without toxic effects.

D. Chloroquine: is effective treatment for chronic discoid lupus erythematosus and sun sensitivity eruptions. One to two of the 0.25 gm. tablets may be given daily. One should look for drug eruptions and possible effect on the hematopoietic system. The most important side effect is that of corneal opacities and retinal damage. For this reason, patients who will be on therapy for more than a few weeks at a time should have routine ophthalmologic care consisting of a base-line observation and examination every three months thereafter.

E. Isonicotinic acid, para-aminosalicylic acid, streptomycin, and dihydrostreptomycin: now the treatment of choice for skin tuberculosis.

F. Amphotericin B: the treatment of choice in systemic blastomycosis and other deep fungal infections including coccidioidomycosis. It must be given intravenously, which necessitates long-term hospitalization, and is nephrotoxic.

G. Psoralens (Oxsoralen^{R}): two 10 mg. capsules each morning after breakfast, 1-3 hours before sun exposure have been recommended in the treatment of vitiligo. Treatment rarely produces complete or even satisfactory involution. Trisoralen^{R}, a synthetic preparation, may be used in place of Oxsoralen.

H. Corticosteroids: the treatment of choice of pemphigus and systemic lupus erythematosus. One may use corticotropin, hydrocortisone, triamcinolone, prednisone or prednisolone, etc., either singly or in combination. Also, such drugs may be used in the treatment of acute inflammatory processes, severe pruritus and exfoliative dermatitis, but one must pay due heed to such contra-inducations as hypertension, peptic ulcer, diabetes, etc.

I. Griseofulvin: is an effective oral fungistatic agent against dermatophyte or "ringworm" fungal infections. The drug is deposited in keratinous structures and apparently acts by interfering with reproduction of the fungus elements. It is most effective for "ringworm" infections of the scalp and is quite effective for involvement of the face, neck, and trunk; reasonably effective for involvement of the groins, and less effective for involvement of the hands and feet. Nail infections are least responsive to griseofulvin therapy. The drug is now available in micronized forms in capsules of 125 mg. to tablets of 500 mg. Absorption is enhanced when taken after a "high fat meal." The average daily dose to 0.5 - 1 gm. orally for adults and comparably less for children. A total of 3 gm. in one oral dose will cure most cases of ringworm of the scalp in children. Prolonged treatment may be required for onychomycosis.

III. PHYSICAL THERAPY

X-ray, Grenz or ultraviolet therapy may be used in selected situations by the expert.

IV. MINOR SURGERY

A. Gelfoam powder allows better hemostasis and forms substrate for healing of ulcers and indolent wounds.

B. The dermal curet is a useful instrument in dermatological surgery. In combination with high frequency current it is a useful tool for the removal of small epitheliomas, warts, keratoses, etc.

C. High frequency current, when used in combination with the curet, is useful for the removal of selected epitheliomas. It can also be used in removal of benign growths.

D. Electric cautery may be used for superficial seborrheic warts and keratosis, tiny skin tags on the neck, eyelids, and elsewhere. A blade cutting cautery can be employed to excise malignant neoplasms. An endothermy knife can be used in the same manner.

E. Carbon dioxide snow and liquid nitrogen may be used in the refrigeration treatment of warts and other benign growths.

V. CHEMICAL DESTRUCTION

Liquified phenol on the tip of a tightly wound cotton applicator is helpful in the removal of senile freckles. One painting, without neutralizing the phenol usually suffices. Trichloracetic acid used in a similar fashion following curettage of warts serves as an excellent hemostatic agent. It may be painted on the warts under

and about the fingernails, then covered with an occlusive dressing, such as Tensoplast or Elastoplast which is left in place for five days. The wart is then so macerated that it may be easily curetted or the procedure can be repeated until the process of removal is complete. Silver nitrate stick is helpful in the treatment of granulation tissue and pyogenic granulomas. 10% silver nitrate on a small tipped cotton applicator is useful in the treatment of fissures and painful aphthous ulcerations in the mouth.

VI. INTRALESIONAL STEROID INJECTIONS: are effective in patches of psoriasis, lichen simplex chronicus, discoid lupus erythematosus, alopecia areata, keloids, synovial cyst, acneiform cysts, etc. Triamcinolone acetonide aqueous suspension (10 mg./cc.) is used and is injected directly into the localized lesion with a fine bore needle. The suspension may be diluted up to 1:4 with normal saline solution. Temporary local atrophy sometimes occurs but usually disappears within weeks to months.

FORMULARY

NAME	ACTION	PRESCRIPTION	TECHNIC
Starch and soda baths.	Cleansing and soothing.	1/2 cup each of cornstarch and soda to a tepid bath.	No soap. The patient is bathed for 15 to 60 minutes then dabbed (not rubbed) dry.
Aluminum acetate, U.S.P.	Cleansing, mildly atringent.	Domeboro® powder - 1 tsp. to 1 qt. or 1 liter of cool water.	Wring out a white cloth and lay on the affected areas 15 minutes twice a day or continuously. Use no water-proof covering, as benefit is from the cooling effect of evaporation.
Starch lotion (shake lotion)	Soothing and drying; for subacute and chronic processes.	Rx. Starch 36 Zinc oxide 36 Glycerin 18 Lime water q.s. ad 180	Apply with cotton b.i.d. One may add 5% coal tar solution, U.S.P.
Hydrophilic ointment, U.S.P.	Vehicle for water-soluble medications	One may add:	Apply sparingly with fingertips b.i.d.
	For psoriasis or seborrhea	5% ammoniated mercury	
	Fungicide	1% salicylic acid 3% sulfur	
	For eczemas & psoriasis	5% detergent solution of coal tar	
Gamma benzene hexchloride, U.S.P.	For scabies or pediculosis.	Dispense 30 Gm. "Kwell" cream.	Locally h.s., for 1 to 3 days to entire body below neck.
Tetracycline 3% ointment	For pyodermas.	Dispense 15 Gm.	Apply b.i.d. to q.i.d.
Benzophenone 10% lotion	Protects from actinic rays	Dispense 75 Gm. Uval lotion (Pharmafac, Inc. Austin, Texas).	Apply to exposed surfaces each morning.

NAME	ACTION	PRESCRIPTION	TECHNIC
Absorbent gelatin sponge, U.S.P. (non-sterile)	For leg ulcers and other indolent ulcers.	Gelfoam^{R} powder 10.0 Gm.	It is absorbent hemostatic gelatin. Use antibiotic (oxytetracycline) powder also, if desired. Apply b.i.d.
Chlorophenothane, U.S.P. (DDT) 10% powder	Effective against all pediculoses.	Rx. Stay-Dee powder 30 Gm.	Apply to affected areas b.i.d. for 2-4 days
Acne lotion	For acne. Drying peeling and regulatory for pilosebaceous apparatus.	Rx. Sulfur, ppt Zinc sulfate aa 3.6 Sodium borate Zinc oxide aa 6.0 Acetone 30.0 Camphor water Rose water aa q.s. ad 120.0	Apply locally at night.
Underarm lotion (antiperspirant)	Useful antiperspirant.	Rx. Aluminum chloride 60.0 Glycerin 30.0 Distilled water q.s. ad 240.0	Apply small quantity to underarms each morning.
Mystatin U.S.P. (Mycostatin^{R})	Treatment for moniliasis	Vaginal tablets Oral suspension Oral tablets Topical powder Cream Ointment	Dusting powder is the simplest for all around cutaneous use. Dispense 15 Gram insufflator squeeze bottle. Apply b.i.d.
Amphotericin B (Fungizone^{R})	Treatment for moniliasis	Lotion	
Chlordantoin (Sporostacin^{R})	Treatment for monilasis	Cream Lotion	Solution works well for nail and paronychial involvement.
Anthralin, N.F.	For psoriasis.	0.1-0.25% ointment Dispense 30/0	Start with 0.1% strength. Apply b.i.d. with fingertip (excellent for body folds). Avoid eyes.

NAME	ACTION	PRESCRIPTION	TECHNIC
Iodochlorhydroxyquin, U.S.P. (Vioform^{R})	Tar-like and antimicrobial.	3% vioform cream or ointment 30/0	Locally b.i.d. Stains clothing. Good for psoriasis, seborrheic dermatitis, infected eczemas. Caution: may be sensitizing.
Coal tar, U.S.P. (prepared Coal tar, B.P.); Pine tar, N.F. (Tar, B.P.); Juniper tar, U.S.P. (Oil of Cade, B.P.)	Stimulating to epithelial healing; antieczematous.	0.5-4% in Lassar's paste or petrolatum. Dispense 30/0	May be bandaged on to chronic eczemas daily, or applied sparingly b.i.d. with the fingertip. Caution: may be sensitizing or cause folliculitis.
Ammoniated mercury, U.S.P., B.P.	Anti-seborrheic and psoriatic.	5 or 10% ointment. Dispense 30/0 (available without prescription).	May be applied once or twice daily to seborrheic dermatitis or psoriasis of the scalp or elsewhere
Neomycin, bacitracin and polymyxin	BACTERICIDAL-avoid use of penicillin and sulfonamides in ointments (sensitizers)	Neosporin^{R} ointment, cream or lotion 15/0. Available without prescription.	Apply twice to four times a day for impetigo and other pyodermas. Neomycin may sensitize
Hydrocortisone, U.S.P.	ANTIPRURITIC-for nonspecific relief of itching. Always determine cause of pruritis first.	Cortril^{R} powder 0/08 Emulsion base q.s. 15/ or Hydrocortisone /3 Acid mantle cream 30/ (1%)	Locally b.i.d. Contraindication is dendritic keratitis. Add 1% vioform to make an effective remedy for pruritus ani or eczema
Menthol, U.S.P., B.P.	Antipruritic	0.25-1% in starch lotion	Locally b.i.d.
Phenol, U.S.P., B.P.	Antipruritic	0.5% in starch lotion	Locally b.i.d.
Podophylum resin, U.S.P.	Inhibitor of mitosis.	25% in compound tincture of benzoin or alcohol	To be applied by physician once weekly for anogenital warts.
Salicylic acid plaster, U.S.P.	Keratolytic	40% plaster (Duke Labs.) 2 1/2 x 4 inch.	Cut out to fit and apply to plantar corns or warts nightly.

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UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
Department of Dermatology
invites you to
A Memorial Service in memory of

Frances Ansley Torrey, M.D.

Wednesday, September 24, 1986
8:00 - 10:00 a.m.

Room 301
Health Sciences West
University of California, San Francisco
Medical Center