

DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
Medical Research and Development Board
Washington 25, D.C.

APPLICATION FOR CONSIDERATION OF RESEARCH PROJECT

1. INSTITUTION AND LOCATION WHERE WORK IS TO BE DONE:

Medical College of Virginia
School of Dentistry
Richmond, Virginia

2. NAME AND ADDRESS OF RESPONSIBLE INVESTIGATOR:

Seymour J. Kreshover, Medical College of Virginia, Richmond, Va.

OFFICIAL POSITION AND TITLE OR RANK:

Professor of Oral Pathology & Diagnosis, & Director of Dental Research

SPECIFY OTHER CURRENT RESEARCH ACTIVITY:

Prenatal influences on development of teeth & their supporting tissues.
The placental barrier with particular reference to vaccinia virus.

3. PRINCIPAL ASSISTANTS, IF ANY:

None

4. SUBJECT OF INVESTIGATION: The Effect of Whole Tobacco Smoke on Oral
Tissues.

a. BACKGROUND AND PURPOSE OF STUDY:

Interest in tobacco smoke as a tissue irritant has been manifested for many years. Past experimental studies have utilized tobacco in various forms, such as extracts of the unburned leaf, whole smoke or tar. Also varied have been such factors as animal species and site, mode and number of applications. In most instances tar has been used, usually by painting on skin surfaces. In general, the reported findings have been lacking in agreement, ranging from no effect to inflammatory response to occasional production of "benign and malignant tumors". Rarely has any attention been given in experimental studies to the mouth or to the use of whole smoke. In the reviewed literature, only Roffo (Rev. Sudamer. de med. et de chir. 1:321;1930) undertook to demonstrate the effect of tobacco on oral tissues. His findings in 10 rabbits receiving daily whole smoke applications to the gingivae showed "leukokeratotic" lesions after 25 days. A similar study carried out recently by the applicant (J.A.D.A. 45:528;1952) showed no gross or microscopic changes in the lips of Swiss albino and C57 mice receiving multiple, alternate day,

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applications of whole smoke for 3 months. In contrast to these negative lip findings, the treated ears of the same animals showed epidermal hyperplasia, inflammation and fibrosis. Other groups of mice, previously rendered deficient in vitamin A and B complex, likewise, showed no lip lesions but did show appreciably more severe ear changes; particularly in the B complex group. Of some interest was the effect of gonadectomy on tissue response; there being a striking absence of pathology even in the vitamin B deficient animals.

The demonstrated absence of lip lesions in the above cited preliminary study might be attributable to a "protective" action of the tongue and saliva in removing deposited tars. In this regard it is of interest that although considerable difference of opinion prevails on the subject of the possible relationship of increased use of tobacco to a real or apparent increased incidence of lung cancer, there is little or no indication of a like relationship to oral tissues (Krantz, J. & Carr, C.: Pharmacologic Principles of Medical Practice, 1951).

It is the purpose of the proposed study to further investigate the question of susceptibility of oral tissues to whole tobacco smoke, with particular reference to the gingivae, buccal mucosa and lips.

b. NATURE OF CONTROL WORK, IF ANY:

It would be necessary in the proposed investigation to carry out control procedures in order to demonstrate the effect on tissues, if any, of suction and pressure alone incident to the use of the smoking apparatus. It is suggested that each experimental animal may serve as its own control by utilizing different but corresponding tissue sites for such "non-smoke" applications.

c. METHOD OF PROCEDURE, INCLUDING OBSERVATIONS TO BE MADE IN EACH CASE:

By means of an apparatus designed for previous studies on mice, whole tobacco smoke applications of controllable volume and exposure time may be made to selected tissue sites. Several groups of hamsters will be used to study the effects of such repeated applications on gingival tissue, buccal mucosa and lips. Tissue response will then be studied by means of daily clinical observations and periodic biopsy preparations. Although it is planned to similarly treat and study additional numbers of desalivated animals (extirpation or duct ligation), such a procedure might be of questionable value due to the difficulty of accomplishing comparable degrees of desalivation and the possibility of introducing other uncontrollable factors such as altered states of nutrition, etc. It is, therefore, proposed to also study other treated epithelial tissues that do not receive the possible "protective benefits" of the tongue and saliva. This will be accomplished by smoke applications to selected tissue sites such as the ear and trachea. The latter procedure, suggested as a future phase of this study, may be carried out via tracheotomy preparations.

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As in the case of studies to date, it is planned to sub-group the animals in the initial stages of the proposed investigation in order to evaluate the possible significance of such influencing factors on oral tissue response as avitaminosis A, B complex deficiency and gonadal hormone imbalance (gonadectomy).

The possible significance of the proposed study is to further clarify the effect of whole tobacco smoke on oral tissues and the influence of certain local and systemic factors on tissue response.

5. REQUIREMENTS FOR STUDY:

a. FACILITIES:

(1) AVAILABLE: Well equipped laboratory and animal quarters.

(2) NEEDED: None

b. PERSONNEL REQUIRED (BRIEFLY INDICATE DUTIES AND ANNUAL SALARIES):

Laboratory technician. (For preparation of histologic material and assisting with the daily experimental procedures) \$2,732.00

Laboratory assistant. (For care and maintenance of experimental animals, etc. Owing to the time consuming nature of the experimental procedures incident to oral applications of tobacco smoke, it is requested that this be a full time position.) \$1,946.00

c. MATERIALS NEEDED (EQUIPMENT AND SUPPLIES):

Experimental animals, special diets, histologic materials and other items in the nature of consumable supplies. \$800.00

6. FUNDS REQUESTED:

a. Responsible investigator	\$ None
b. Professional assistants	\$ None
c. Technician services	\$4,678.00
d. Equipment	\$ None
e. Supplies	\$ 800.00
f. Travel	\$ 200.00
g. Overhead	\$ 567.00
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TOTAL	\$6,245.00

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7. HAVE FUNDS BEEN RECEIVED OR REQUESTED FROM OTHER SOURCES FOR THIS PROJECT? SPECIFY.

No.

8. ASSISTANCE DESIRED OTHER THAN FINANCIAL. SPECIFY.

None

9. EXPECTED TIME OF BEGINNING WORK AND PROBABLE DURATION OF PROJECT:

1/1/53
November 1, 1953 -- One year

10. OTHER INFORMATION WHICH IT IS DESIRED TO OFFER MAY BE GIVEN IN THIS SPACE OR ON ADDITIONAL SHEETS:

Signature /s/ Seymour Kreshover

Application approved by authorized administrative official of institution or federal agency

/s/ William T. Sanger
(Signature)

William T. Sanger
(Name: printed or typed)

President
(Official title)

Medical College of Virginia
(Institution or agency)

Application approved by chief medical officer of hospital, or head of department where work is to be performed

/s/ Harry Lyons
(Signature)

Harry Lyons, Dean
(Name: printed or typed)

Dean
(Official title)

Medical College of Virginia
School of Dentistry
(Hospital or department)

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BIOGRAPHY

Date: 8 June 1953

1. NAME: Seymour J. Kreshover AGE: 40 SEX: M CITIZENSHIP: U.S.A.

2. MAILING ADDRESS: Medical College of Virginia, School of Dentistry,
Richmond, Virginia.

3. EDUCATIONAL BACKGROUND

	<u>Institution</u>	<u>Dates Attended</u>	<u>Degree and Date Rec'd</u>
College	Syracuse University	1930-'32	
	New York University	1932-'34	B.A. 1934
Professional School	Univ. of Penn.	1934-'38	D.D.S. 1938
	Yale University	1939-'42	Ph.D. 1942
	New York University	1947-'49	M.D. 1949

4. RESEARCH TRAINING

<u>Institution</u>	<u>Director of Research</u>	<u>Subject</u>	<u>Dates</u>
Univ. Penn.	Dr. L. W. Burket	Periodontal disease	1937-'38
Univ. Ill.	Dr. S. S. Arnim &	Histology	1938-'39
	Dr. O. Kampmeier		
Yale Univ.	Dr. M. C. Winternitz	Pathology	1939-'42

5. MILITARY SERVICE

<u>Branch</u>	<u>Arm or Service</u>	<u>Date Entered Active Duty</u>	<u>Date Separated</u>	<u>Overseas Service Theater: Approx. Dates</u>
Army	Dental	April 1942	Feb. 1946	Pacific Nov. '42 - Sept. '45

<u>Organization</u>	<u>Duties</u>	<u>Highest Rank</u>
39th General Hosp.	Chief of Dental Service	Major

NATURE OF ANY RESEARCH DONE DURING MILITARY SERVICE:

None stated

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6. OTHER INFORMATION BEARING ON QUALIFICATIONS:

Assistant in Operative Dentistry, Univ. Illinois. 1938-'39
University Fellow (Univ. Illinois) in pathology. 1938-'39
Carnegie Fellow (Yale Univ.) in pathology & clinical medicine. 1939-'41
Calhoun Scholar (Yale Univ.) in pathology. 1941-'42.
Clinical Assistant in Oral Surgery, Yale Univ. 1942
Teaching Fellow in Histo-anatomy, New York Univ. 1946-'47
Chief of Periodontia Clinic, The Roosevelt Hosp. N. Y. 1946-'47
Professor of Oral Pathology, Med. College of Va. 1949 - present
Member - American Dental Association
- American Medical Association
- Intern. Ass'n. Dental Research
- American Acad. Oral Pathology
- A.A.A.S.

7. BIBLIOGRAPHY:

Histopathologic Studies of Abnormal Enamel Formation in Human Teeth, Am. J. Orthodontics & Oral Surgery, 26:1083, 1940.

The Histopathology of the Incisor Teeth of Mice with Experimentally Produced Tuberculosis, J. D. Res. 21:27, 1942.

A Critical Microscopic Technic Applied to Study of Human Dentin. (with L. W. Burket and W. Hammond), J. D. Res. 23:111, 1944.

The Pathogenesis of Enamel Hypoplasia: An Experimental Study, J. D. Res. 23:231, 1944.

Histopathology of the Dental Pulp of Dogs Following Exposure. (with G. Bevelander), J. D. Res. 27:467, 1948.

Auto-polymerizing Resin Fillings. (with H. Coy and D. Bear), J. A. D. A. 44:251, 1952.

The Effect of Tobacco on Epithelial Tissues of Mice, J. A. D. A. 45:528, 1952.

Prenatal Influences on Tooth Development. Artificially Induced Fever in Rats. (with O. Clough), J. D. Res. In press.

Prenatal Influences on Tooth Development. Alloxan Diabetes in Rats. (with O. Clough and D. Bear), J. D. Res. 32:246, 1953.

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