

SUMMARIES OF CTR SPECIAL PROJECTS

John R. Carter, M.D.

Richard J. Hickey, Ph.D.

Thomas F. Mancuso, M.D.

Massachusetts Institute  
of Technology

L. G. S. Rao, Ph.D.

Carl C. Seltzer, Ph.D.

Hans Selye, M.D., Ph.D., D.Sc.

Theodor D. Sterling, Ph.D.

RC-6033497

LIG 0064996

LG2000495

INVESTIGATOR: JOHN R. CARTER, M.D.

POSITION:

Director, Institute of Pathology  
Case Western Reserve University, School of Medicine

RELEVANCE:

Dr. Carter's Special Project may indicate a bias related to a patient's smoking history and the subsequent clinical diagnosis of lung disease.

CURRENT SPECIAL PROJECT:

Autopsy study designed to examine the accuracy of, and bias factors operative in, lung cancer diagnoses.

Funded in 1974 for a total of \$86,305 over 2 years.

Participating companies: American, B&W, Lorillard, PM, and RJR.

REVIEW:

CTR / Ad Hoc

RC-6033498

LG2000496

INVESTIGATOR: RICHARD J. HICKEY, Ph.D.

POSITION:

Researcher  
Management and Behavioral Science Center  
Wharton School of Finance and Commerce  
University of Pennsylvania

RELEVANCE:

Dr. Hickey's theories support the constitutional hypothesis, and he has great interest in environmental hazards.

CURRENT SPECIAL PROJECT:

"Ecological Statistical and Theoretical Biological Studies on Relationships between Demographic and Atmospheric Chemical Environmental Variables and Smoking and Chronic Disease Variables with Special Consideration of the Biology of Behavior." (SP#56-AR2)

Funded in 1973 for a total of \$110,132 over a 2 year period.

Participating companies: American, B&W, L&M, Lorillard, PM, and RJR.

REVIEW:

CTR / Ad Hoc

RC-6033499

LG2000497

RECENT PUBLICATIONS AND MANUSCRIPTS OF SPECIAL INTEREST\*:

"Smoking Hazards to the Fetus." British Medical Journal, 3:501 (September 1, 1973).

"Carbon Monoxide: Smoking, Air Pollution, Cardiovascular Disease, and Physiological Homeostasis." The Lancet, 2: 571-572 (September 8, 1973).

"Coffee and Myocardial Infarction." New England Journal of Medicine, 289(18):978-979 (November 1, 1973).

"Smoking and Pregnancy." Nature, 246:177-178 (November 16, 1973).

"Air Pollution, Smoking and Chronic Disease: Influence of Constitutional Factors." Journal of Occupational Medicine, 16(1):4-5 (January, 1974).

"Aryl Hydrocarbons, Smoking and Lung Cancer." New England Journal of Medicine, 290(10):576-577 (March 7, 1974).

On March 9, 1974, Dr. Hickey presented a paper entitled "Atmospheric Sulfur Dioxide, Nitrogen Dioxide, and Lead as Potential Mutagenic Hazards to Human Health," at a meeting of the Environmental Mutagen Society in Washington, D.C.

"Carbon Monoxide and Smoking." The Lancet, 409-410 (March 9, 1974).

"Coffee, Tobacco, and Cardiovascular Disease: The Self-Selection Problem." JAMA, 228(2):160 (April 8, 1974).

"Smoking, Health, and Scientific Method." Ms. submitted to Nature, May, 1974.

"Smoking, Chronic Disease, Constitution and Statistics." Ms. submitted to New England Journal of Medicine, May, 1974.

\* Hickey's articles are normally written with Clelland, Boyce, and Harner/Bowers.

RC-6033500

LG2000498

"Environmental Pollution and Chronic Disease." In Urban Environmental Management: Planning for Pollution Control, ed. B.J.L. Berry and F.E. Horton. Englewood Cliffs, N.J.: Prentice Hall, Inc., (in press).

RC-6033501

LG2000499

INVESTIGATOR: THOMAS F. MANCUSO, M.D.

POSITION:

Research Professor  
Department of Occupational Health  
Graduate School of Public Health  
University of Pittsburgh

RELEVANCE:

Dr. Mancuso's epidemiological studies emphasize environmental and occupational effects on disease, including cancer and heart disease.

CURRENT SPECIAL PROJECT:

"Relation of Place of Birth and Migration to Mortality due to Heart Disease." (SP#72)

Funded September, 1973, for a total of \$24,400 over 1 year.

Participating companies: American, B&W, L&M, Lorillard, PM, and RJR.

A supplemental amount (\$17,250) has been approved to obtain certain additional data for Dr. Mancuso's 1972 Special Project.

REVIEW:

CTR / Ad Hoc

RC-6033502

LG2000500

RECENT MANUSCRIPTS AND PAPERS OF SPECIAL INTEREST:

"Migration and Cancer Mortality Experience - A Study of Native and Southern Born Non-White Ohio Residents." by Mancuso, et al. In Trace Substances in Environmental Health - VI. 1973. A Symposium, ed. D. D. Hemphill. University of Missouri, Columbia, 1973.

In November, 1973, Dr. Mancuso presented his and Dr. Sterling's paper "Lung Cancer Among Black and White Migrants in the U.S.: Etiological Considerations" at a meeting of the American Association for Cancer Research.

"Lung Cancer Among Black and White Migrants in the United States - Etiological Considerations." by Mancuso and Sterling. Ms. accepted by J. Chron. Dis.

"Relation of Place of Birth and Migration in Cancer Mortality in the U.S.: A Study of Ohio Residents (1959-1967)." by Mancuso and Sterling. Ms. accepted by J. Chron. Dis.

"Heart Disease Mortality Among Black Migrants: A Study of Ohio Residents (1960-1967)." Ms. submitted to Amer. Heart Journal.

The American Public Health Association Journal has accepted two manuscripts by Dr. Mancuso; one on black migrants, lung cancer, and heart disease - and the other on lung cancer and leukemia in rubber workers.

Dr. Mancuso hopes to publish a monograph on an intensive study of demographic factors in the distribution of different types of cancer in Ohio. He feels that such a monograph would serve as a clear demonstration of the multiple factors operative in the etiology of cancer.

COMMENT:

Dr. Mancuso has been heavily involved in the recent vinyl chloride controversy. He submitted statements to OSHA and a House subcommittee, presented a paper at the

RC-6033503

LG2000501

New York Academy of Sciences meeting, and will be attending an international conference on industrial chemicals and vinyl chloride.

In July, Dr. Mancuso will present his and Dr. Sterling's "Lung Cancer Among Black and White Migrants in the U.S. - Etiological Considerations" at the First World Congress of Environmental Medicine and Biology.

RC-6033504

LG2000502

INSTITUTION: MASSACHUSETTS INSTITUTE OF TECHNOLOGY

RELEVANCE:

The fellowship will involve studying, with Dr. George Wolf, nutrition's effect on lung cancer.

CURRENT SPECIAL PROJECT:

Graduate fellowship for research into the mechanism by which vitamin A may interfere with carcinogenesis.  
(SP#74)

Funded in 1974 for one year, \$10,000.

Participating companies: American, B&W, L&M, Lorillard, PM, and RJR.

REVIEW:

CTR / Ad Hoc

RC-6033505

LG2000503

INVESTIGATOR: L. G. S. RAO, Ph.D.

POSITION:

Senior Biochemist, Department of Steroid Biochemistry  
Royal Infirmary, Glasgow

RELEVANCE:

Dr. Rao's findings of steroid abnormalities in lung cancer patients (both before and after resection) indicate that lung cancer may be an endocrine disease. He has stated that "The correlation between smoking and lung cancer is much less important than the correlation between low androsterone level and the disease."

CURRENT SPECIAL PROJECT:

Examination of blood steroid levels in lung cancer patients; duplication with blood levels of his original findings on urinary endocrine levels. (SP#73)

Funded in 1974 for a total of \$30,000 over 3 years.

Participating companies: American, B&W, L&M, Lorillard, PM, and RJR.

REVIEW:

CTR / Ad Hoc

RC-6033506

LG2000504

INVESTIGATOR: CARL C. SELTZER, Ph.D.

POSITION:

Senior Research Associate in Biological Anthropology  
Department of Nutrition  
Harvard University School of Public Health

RELEVANCE:

Dr. Seltzer's work emphasizes constitutional differences between smokers and nonsmokers. He is particularly interested in heart disease.

CURRENT SPECIAL PROJECT:

General support of Dr. Seltzer's work. (SP#52R5)

The current renewal of Dr. Seltzer's CTR Special Project grant in the amount of \$50,000 will provide support through June 30, 1975.

Participating companies: American, B&W, L&M, Lorillard, PM, and RJR.

REVIEW:

CTR / Ad Hoc

RC-6033507

LG2000505

RECENT MANUSCRIPTS AND PAPERS OF SPECIAL INTEREST:

"Cigarette Smoking and Exposure to Occupational Hazards." by Friedman, et al., and Seltzer. Amer. J. of Epidem., 98(3):175-183 (1973).

"Smoking and Coronary Heart Disease." NEJM, 288:1186 (May 31, 1973).

"More on Smoking and Heart Disease." NEJM, 289(22): 1200-1201 (November 29, 1973).

Miami Beach paper on smoking and coronary heart disease delivered December, 1973, which concluded that cigarette smoking after age 65 does not seem to increase risk of coronary heart disease.

"Cigarette Smoking and Longevity in the Elderly." Medical Counterpoint, 6(2):29-33 (February, 1974).

"Cigarettes, Alcohol, Coffee and Peptic Ulcer." by Friedman, et al., and Seltzer. NEJM, 290(9):469-473 (February 28, 1974).

"Racial Differences in Serum and Urine Glucose After Glucose Challenge." by L.G. Dales, et al., and Seltzer. Diabetes, 23(4):327-332 (April, 1974).

"Smoking and Cancer." New Scientist, 62:195-196 (April 25, 1974).

"Effect of Smoking on Blood Pressure." American Heart Journal, 87(5):558-564 (May, 1974).

"Smoking and Drug Consumption in White, Black, and Oriental Men and Women." by Seltzer, et al. AJPH, 64(5): 466-473 (May, 1974).

"Smoking, Weight Change, and Age." by A.J. Garvey, et al., and Seltzer. Arch. Environ. Health, 28:327-329 (June, 1974).

RC-6033508

LG2000506

COMMENT:

Dr. Seltzer's article "Critical Appraisal of the Royal College of Physicians' Report on Smoking and Health" in the January 29, 1972, issue of The Lancet sparked over 75 Lancet letters and other comments.

Dr. Seltzer has access to the Kaiser-Permanente, Framingham, and Boston Normative Aging Study data.

Dr. Seltzer's contributions were acknowledged in the 1964 Surgeon General's Report.

RC-6033509

LG2000507

T PUBLICATIONS AND MANUSCRIPTS OF SPECIAL INTEREST\*:

"Smoking Hazards to the Fetus." British Medical Journal, 3:501 (September 1, 1973).

"Carbon Monoxide: Smoking, Air Pollution, Cardiovascular Disease, and Physiological Homeostasis." The Lancet, 2: 571-572 (September 8, 1973).

"Coffee and Myocardial Infarction." New England Journal of Medicine, 289(18):978-979 (November 1, 1973).

"Smoking and Pregnancy." Nature, 246:177-178 (November 16, 1973).

"Air Pollution, Smoking and Chronic Disease: Influence of Constitutional Factors." Journal of Occupational Medicine, 16(1):4-5 (January, 1974).

"Aryl Hydrocarbons, Smoking and Lung Cancer." New England Journal of Medicine, 290(10):576-577 (March 7, 1974).

On March 9, 1974, Dr. Hickey presented a paper entitled "Atmospheric Sulfur Dioxide, Nitrogen Dioxide, and Lead as Potential Mutagenic Hazards to Human Health," at a meeting of the Environmental Mutagen Society in Washington, D.C.

"Carbon Monoxide and Smoking." The Lancet, 409-410 (March 9, 1974).

"Coffee, Tobacco, and Cardiovascular Disease: The Self-Selection Problem." JAMA, 228(2):160 (April 8, 1974).

"Smoking, Health, and Scientific Method." Ms. submitted to Nature, May, 1974.

"Smoking, Chronic Disease, Constitution and Statistics." Ms. submitted to New England Journal of Medicine, May, 1974.

Hickey's articles are normally written with Clelland, Boyce, and Harner/Bowers.

c.

edicine and

ion of stress in  
s used to relieve

25)

ed in 1972 for a

W, L&M, Lorillard,  
lustry is also

RC-6033510

RC-6033500

LG2000498

LG2000508

PUBLICATIONS OF SPECIAL INTEREST:

The Stress of Life. New York: McGraw-Hill Book Company, 1956.

"Some Introductory Remarks." In Smoking Behavior: Motives and Incentives, ed. William L. Dunn, Jr. Washington, D.C.: V. H. Winston & Sons, 1973.

"Stress and the Nation's Health." Modern Medicine of Canada, 28(5):395-400 (May, 1973).

"The Evolution of the Stress Concept." American Scientist, 61:692-699 (Nov./Dec., 1973).

Stress Without Distress. J. B. Lippincott Company, 1974.

COMMENT:

In 1969 Dr. Selye testified before the Canadian Parliament that the relief of stress is an "intensely beneficial effect" of smoking.

RC-6033511

LG2000509

INVESTIGATOR: THEODOR D. STERLING, Ph.D.

POSITION:

Professor and Director of Computing Science Programme  
Simon Fraser University

RELEVANCE:

Dr. Sterling is interested in many subjects, including lung cancer statistics, air pollution, and nonsmokers.

CURRENT SPECIAL PROJECT:

"A Continuing Critical Review of the Major Factors in the Etiology of Lung Cancer and Other Lung Diseases Emerging from Statistical Studies" (SP#71)

Funded in 1973 for 2 years; first year: \$61,420; second year: \$69,700.

Participating companies: American, B&W, Lorillard, PM, and RJR.

REVIEW:

CTR / Ad Hoc

RC-6033512

LG2000510

RECENT MANUSCRIPTS AND PAPERS OF SPECIAL INTEREST:

"A Critical Assessment of the Evidence on the Cigarette Smoking - Lung Cancer Relationship." Presented by Dr. Sterling at the December, 1971, meeting of the AAAS.

"The Incidence of Lung Cancer in the U.S. Since 1955 in Relation to the Etiology of the Disease." by Sterling and S.V. Pollack. AJPH: 152-158 (February, 1972).

"Air Pollution and Smoking." Environment, 15(6):3-5, 25-26 (July/August, 1973).

"The Statistician vis-a-vis Issues of Public Health." The American Statistician, 27(5):212-217 (December, 1973).

"Lung Cancer Among Black and White Migrants in the U.S.: Etiological Considerations." by Dr. Thomas Mancuso and Sterling. Presented by Mancuso at a November, 1973, meeting of the American Association for Cancer Research.

"Relation of Place of Birth and Migration in Cancer Mortality in the U.S.: A Study of Ohio Residents (1959-1967)." by Mancuso and Sterling. Ms. accepted by J. of Chron. Dis.

"Lung Cancer Among Black and White Migrants in the U.S.: Etiological Considerations." by Mancuso and Sterling. Ms. accepted by J. of Chron. Dis.

Dr. Sterling is completing a revision of his 1971 AAAS paper which he will submit to the American Journal of Public Health.

COMMENT:

Dr. Sterling recently participated in an international workshop on the effects of tobacco smoke on the nonsmoker.

Dr. Sterling is currently involved in reviewing Chemicals and Health, the Dorn data, and Dr. Sherman's auto workers' data.

RC-6033513

LG2000511

INSTITUTION: TOBACCO AND HEALTH RESEARCH INSTITUTE  
UNIVERSITY OF KENTUCKY

DIRECTOR:

John P. Wyatt, M.D.

RELEVANCE:

The program is designed to determine whether the relationship between tobacco and health is, or is not, one of cause-and-effect; and, if it is, to develop ways to identify and eliminate detrimental compounds.

PROJECT:

The program receives \$1,500,000 annually from the federal government and approximately \$3,400,000 annually from a 0.5 cent per pack state tax on cigarettes sold in Kentucky.

REVIEW:

The federally-funded portion of the program is administered by the Agricultural Research Service of the USDA; the state-funded portion is administered by the Kentucky Tobacco Research Board.

RC-6033514

LG2000512

COMMENT:

Major areas of study include:

- (1) characterization of smoking behavior.
- (2) in vivo animal inhalation experiments.
- (3) isolation of tobacco smoke components.
- (4) responses of in vitro animal and plant systems to tobacco smoke.
- (5) product modification.

An important part of the program to date has been the development and distribution of the Kentucky reference cigarette.

RC-6033515

LG2000513

INSTITUTION: WASHINGTON UNIVERSITY

PRINCIPAL INVESTIGATORS:

Lauren V. Ackerman, M.D.  
Paul E. Lacy, M.D.

RELEVANCE:

The project involves an intensive study of cancer immunology designed to improve the chances of early detection, treatment and possible prevention of human cancer.

PROJECT:

Funded in 1971 for a total of \$2,000,000 over 5 years. Recently received an extension for \$800,000 over a 2 year period.

Participating companies: B&W, Larus & Brother\*, L&M, Lorillard, PM, RJR, Tobacco Associates, and U.S. Tobacco. (\*not participating in funding renewal)

REVIEW:

Annual reports to the industry.

RC-6033516

LG2000514

COMMENT:

Major areas of investigation include:

- (1) attempts to isolate human tumor-specific and/or tumor-associated antigens on tumor-cell membranes and to identify their presence (or that of their antibodies) in blood serum. Heavy focus on CEA.
- (2) main diseases under study: breast cancer, colon cancer, melanoma.
- (3) animal studies focusing on function of T-lymphocytes (thymus) and B-lymphocytes (bone marrow) by studying thymectomized mice.
- (4) experiments with chemotherapy on leukemic mice which will soon result in specific therapy for human patients.

Drs. Ackerman and Lacy hope to devise (a) specific immunological, serologic tests to detect early cancer, and (b) means of augmenting the patient's immune response.

RC-6033517

LG2000515

INSTITUTION: HARVARD UNIVERSITY

PRINCIPAL INVESTIGATOR:

Gary L. Huber, M.D.

RELEVANCE:

The Harvard project is examining biologic responses to environmental influences (especially tobacco smoke), as manifested in non-neoplastic pulmonary disease and heart disease.

---

PROJECT:

Funded in 1972 for a total of \$2,792,750 over 5 years.

Participating companies: American, B&W, Larus & Brother\*, L&M, Lorillard, PM, RJR, Tobacco Associates, and U.S. Tobacco.

(\*Larus & Brother has paid its share in full.)

REVIEW:

Annual reports to the industry.

RC-6033518

LG2000516

COMMENT:

Major areas of study include:

- (1) host response to environmental influences (especially in vivo and in vitro animal work). Dr. Huber is particularly interested in studying macrophage activity and comparing responses to acute and chronic exposures.
- (2) isolation of tobacco smoke components.
- (3) effects of smoke on heart muscle, in vitro.
- (4) some examination of "passive smoking."

RC-6033519

LG2000517

INSTITUTION: UCLA

PRINCIPAL INVESTIGATOR:

Martin J. Cline, M.D.

RELEVANCE:

50% of the UCLA program (tobacco oriented) will involve the investigation of lung defense mechanisms and pulmonary diseases (especially lung cancer). The other 50% of the program will be directed toward cancer detection and treatment methods.

PROJECT:

Funded in 1974 for a total of \$1,700,000 over 5 years.

Participating companies: B&W, PM, RJR, and U.S. Tobacco.  
Also, Tobacco Associates.

REVIEW:

Annual reports to the industry, and consultation with CTR.

RC-6033520

LG2000518

COMMENTS:

Major areas of study include:

- (1) proliferative capacity of smokers' and nonsmokers' pulmonary cells.
- (2) functional response (e.g., phagocytosis) of pulmonary cells to various factors.
- (3) cell culture systems and specific antigens.
- (4) immunotherapy and chemotherapy.

RC-6033521

LIG 0065020

LG2000519