

OCCUPATIONAL SAFETY AND HEALTH

RESEARCH &  
DEMONSTRATION  
GRANTS

1973



U.S. Department of Health, Education, and Welfare  
Public Health Service

National Institute for Occupational Safety and Health

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Title VI of the Civil Rights Act of 1964 states:

"No person in the United States shall, on the ground of race, color, or national origin, be excluded from participation in, be denied the benefits of, or be subjected to discrimination under any program or activity receiving Federal financial assistance."

Therefore, the National Institute for Occupational Safety and Health grant supported programs must be operated in compliance with this law.

This publication is available on request from the Office of Extramural Activities, National Institute for Occupational Safety and Health, Room 501, Post Office Building, Fifth and Walnut Streets, Cincinnati, Ohio 45202.

OCCUPATIONAL SAFETY AND HEALTH  
RESEARCH AND DEMONSTRATION  
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U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE  
Public Health Service  
National Institute for Occupational Safety and Health  
Office of Extramural Activities  
Cincinnati, Ohio 45202



## FOREWORD

The National Institute for Occupational Safety and Health (NIOSH) plans, directs, and coordinates the national program effort to develop and establish recommended occupational safety and health standards and to conduct research, training, and related activities to assure safe and healthful working conditions for every working man and woman. Under the provisions of the Federal Coal Mine Health & Safety Act of 1969 and the Occupational Safety & Health Act of 1970, research investigations, particularly those in which dose-effect relationships may be identified and quantified thereby leading to the development of effective standards, represent one of the principal areas of responsibility of NIOSH.

In fulfilling its mission, the NIOSH employs many mechanisms including the making of grants to eligible institutions and organizations for the purpose of supporting research projects relating to innovative approaches to understanding the underlying characteristics of occupational safety and health problems and for effective solutions in dealing with them. Grant support is also available for demonstration projects which are designed to demonstrate, either on a pilot or full-scale basis, the technical and economic feasibility of new or improved methodologies in dealing with occupational safety and health problems amenable to technological solutions.

This booklet which has been prepared to describe the research and demonstration projects supported through grants, should be of interest and assistance to appropriate institutions, organizations, agencies, and individuals such as scientists, engineers, physicians, and others currently engaged in or contemplating activities germane to the responsibilities and functions of NIOSH.



Marcus M. Key, M.D.  
Assistant Surgeon General  
Director  
National Institute for Occupational  
Safety and Health



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## INTRODUCTION

Project grants for research and demonstrations are available to universities, colleges, research institutions, and other public and private non-profitmaking organizations for the support of scientific and technical activities in all the areas of occupational safety and health which sustain and undergird the mission and functions of the National Institute for Occupational Safety and Health. Examples of appropriate research fields and activities include: 1. Laboratory, clinical, and epidemiologic investigations of diseases, pathologic changes, physiologic and psychologic alterations which arise, or are presumed to arise, from an occupational causation; aspects of prevention, diagnoses, therapy, disease processes and mechanisms, and interpretations of abnormalities are apropos. Specific subjects of interest include: effects (acute, subacute, chronic) of toxic chemicals, metals, dusts, fumes, gases and other fluids, mists and aerosols, acting upon any organ or body system; effects of physical agents, including heat, cold, electromagnetic energy of certain wavelengths, noise, vibration, and pressure changes; effects of living disease agents under conditions of major emphasis on the occupational involvement in the transmission or modification of human physiologic or behavioral response. 2. Investigations of psychologic and motivational factors in occupational situations and their impact on mental health and job performance. Included in this category are studies of effects of impaired physical, mental, and emotional states on safe and effective work performance and the appropriate placement and observation of workers with physical mental, or emotional impairments. 3. Research studies of safety factors in work flow, plant design, work operations, man-machine interrelationships, and occupational environmental situations. 4. Research on methods development, evaluation, and application for the sampling, analysis, measurement or other objective appraisals of chemical, physical, biological, motivational and behavioral, and other components of the occupational environment and of the extent of exposure to these components. 5. Epidemiologic, biometric, and demographic studies of morbidity and/or mortality of human beings exposed to occupational and industrial hazards and the development, evaluation, and application of methods for diagnosing and measuring the effects of such hazards. 6. Investigations of capacities of workers to withstand and deal with occupational stresses in their work environments, and the development and evaluation of methods for protection of workers from such harmful environmental factors. 7. Investigations of interrelationships between employment conditions and the onset, development, and course of chronic diseases. 8. Studies on the nature of fatigue and its role in worker susceptibility to accidents and occupational illness. 9. Investigations of socio-economic factors related to, or arising from, occupational disease. 10. Studies on absenteeism and its causes.

11. Studies of the factors involved in the development, function, and utilization of occupational health programs.

Grants are made under the authority of applicable legislation and in accordance with the prescribed rules and regulations of the Department of Health, Education and Welfare and the National Institute for Occupational Safety and Health. All applications for research and/or demonstration grant support are initially reviewed according to established schedules by a consultative committee of distinguished scientific and technical experts, constituted as a study section using the peer review system, who provide objective appraisals of scientific merit of each proposal. These recommendations are then reviewed by (an advisory Council in some cases as appropriate) the Institute for a funding determination within available budgets, taking into account program relevance and consonance with public policy.

All inquiries about research and demonstration grant applications, eligibility, guidelines, regulations, review schedules, program and procedural matters, and the like should be addressed to:

Director, Office of Extramural Activities  
National Institute for Occupational Safety and Health  
5th and Walnut Streets, P. O. Building, Rm. 501  
Cincinnati, Ohio 45202

Grateful acknowledgement is made to all who contributed to the preparation of this booklet.



Alan D. Stevens, D.V.M.  
Assistant Director, NIOSH  
for Extramural Activities

## BEHAVIORAL AND MOTIVATIONAL FACTORS



STANFORD UNIVERSITY  
Stanford, California

Grant Number: 5 R01 OH 00327-05

Principal Investigator:

Rodney R. Beard, M.D., M.P.H.  
Stanford University  
School of Medicine  
Stanford, California 94305

Title:

Carbon Monoxide and Human Information Processing

Objectives:

By means of behavioral effects studies, this research seeks to investigate in men and in lower animals, effects of exposures to carbon monoxide. What is sought, particularly, is resultant impairments of behavior which are not heralded by symptoms. Developed information may be useful in setting standards for air quality.

Description:

This is an investigation of behavioral effects resulting from exposure to carbon monoxide. In man, small concentrations and brief exposures are investigated as affecting vision (including absolute and relative thresholds), acuity, and critical fusion frequency. In monkeys, chronic exposures are used to study the same behavioral effects. Research is also performed with rats on free operant schedules of reinforcement, principally those that require temporal discrimination.

Publications:

1. Laties, V.G., R.R. Beard, B.D. Dinman, and J.H. Schulte: Behavioral Aspects of Carbon Monoxide Poisoning. Nat'l. Acad. of Sciences, Nat'l. Acad. of Engineering, Washington, D.C. (1969).
2. Beard, R.R. and N. Grandstaff: Carbon Monoxide Exposure and Cerebral Function. Ann. of N.Y. Acad. of Sci. 174: 385-395 (October 5, 1970).
3. Goldsmith, J.R., R.R. Beard, and B.D. Dinman: Epidemiologic Appraisal of Carbon Monoxide Effects. Paper.

STANFORD UNIVERSITY

4. Beard, R.R., and G.A. Wertheim: Behavioral Manifestations of Carbon Monoxide Absorption. XVI Int'l. Congr. Occup. Hlth. 224-226, Tokyo (1969).
5. Beard, R.R.: Toxicological Appraisal of Carbon Monoxide. APCA J. 19: (9) 772-729 (September 1969).
6. Beard, R.R. and N. Grandstaff: Behavioral Responses to Carbon Monoxide in Low Dosage. Interim Report to National Research Council, Committee on Motor Vehicle Emissions (February 10, 1972).
7. Beard, R.R., et al.: Decrements in Visual Vigilance and Perceptual Tracking Associated With Small Doses of Carbon Monoxide. Presented at the May 1972 meeting of the American Industrial Hygiene Conference (San Francisco, California).

UNIVERSITY OF MIAMI  
Coral Gables, Florida

Grant Number: 5 R01 OH 00346-03

Principal Investigator:

Earl L. Wiener, Ph.D.  
University of Miami  
Coral Gables, Florida 33124

Title:

Computer-Based Training for Watchkeeping Tasks

Objectives:

This project is directed toward demonstrating the feasibility of automated training for monitoring or vigil-keeping tasks.

Description:

Watchkeeping or monitoring tasks are those for which an operator must maintain a vigil over a system which may display signals or signs of abnormalities or dangerous conditions. Training sessions are automated by use of a computer-based system which schedules and delivers critical signals and non-critical stimuli, allows the trainee to elect certain options regarding his own trainings, and permits him to test himself. The system allows for adaptive training in which the difficulty of the training task can be linked automatically to the performance of the operator, thereby permitting him to progress rapidly toward a desired performance level when his responses merit it. Simpler problems and tutorial instruction may be administered when warranted; that is when performance level does not indicate satisfactory progress.

Publications: none

UNIVERSITY OF SOUTH DAKOTA  
Vermillion, South Dakota

Grant Number: 5 R01 OH 00365-02

Principal Investigator:

Norman W. Heimstra, Ph.D.  
Dept. of Psychology  
University of South Dakota  
Vermillion, South Dakota 57069

Title:

Noise and Human Performance

Objectives:

This research has, as its end purpose, the experimental evaluation on human performance of novel sounds and "meaningful" noise as contrasted with meaningless noise. A goal of these investigations is the determination, if possible, of a set of personality characteristics which can predict whether or not an individual is susceptible to noise effects.

Description:

This psychologic investigation of noise effects on human performance uses graduate students as experimental subjects. Conditions are identified which seek to explain the effects of noise complicated by meaningfulness (significance to the subject) to the 40 subjects under consideration. Guidelines are being developed for relating meaningful noise to "on-the-job" situations and conditions which may produce unpleasant and distracting meanings for sounds heard on the job. Experimental procedures include measurements of sound pressure levels.

Publications: none

UNIVERSITY OF MISSOURI-ROLLA  
Columbia, Missouri

Grant Number: 5 R01 OH 00366-02

Principal Investigator:

Harold D. Warner, Ph.D.  
Dept. of Psychology  
University of Missouri - Rolla  
Rolla, Missouri 65401

Title:

Effects of Three Sound Environments on Human Behavior

Objectives:

The purpose of these investigations is to evaluate the effects on extended human performance, in simulated "real-life" situations, of noise conditions or sound environments selected on the basis of their actual occurrence and feasibility of implementation.

Description:

The acoustic stimuli (noise, music, silence) effects on extended human performance are calculated to provide predictive patterns relatable to actual work situations. Using human subjects (40 male college-age volunteers) in selected and controlled experimental groups, for various stimuli, the simulated assembly-line inspection tasks and duration of periods of observation are designed to overcome deficiencies of similar studies in that the tasks are not abstract and that the duration of performance is not transitory. The results of these studies are expected to have significance in their application to the specification of noise conditions of work that affect performance.

Publications: none

UNIVERSITY OF WASHINGTON  
Seattle, Washington

Grant Number: 1 R01 OH 00427-01

Principal Investigator:

David B. Chang, Ph.D.  
Department of Physiology & Biophysics  
University of Washington  
Seattle, Washington 98195

Title:

Laser Studies of Effects of Heavy Metals on Synapses

Objectives:

Since mercury and its compounds are widely used in industry, and since alkyl mercury compounds have a tendency to accumulate in nervous tissue and have an especially long half-life in man, it is important to investigate the mode of action of these compounds in neural tissue. The aim of this investigation, in general, is to determine the effects of heavy metals on the central nervous system.

Description:

By means of the very sensitive laser-induced temperature jumps related to effective energy barriers present at different stages of a synaptic process, measurements are made of the effects of methyl mercury (as a representative example of alkyl mercury compounds) on the neuromuscular junction function of frog sartorius muscle. Using an in vitro preparation of dissected frog sartorius muscle in a bathing solution, at both normal and low calcium concentrations, the influence on synapses of methyl mercury in the solution is investigated by measuring rapid temperature jumps (between 5° and 20° C.) induced by exposing this preparation to the radiations of a high-power ruby (or neodymium) laser probe. The magnitude of the jump is determined by the extent to which the laser beam is focused on the region of the synapse. The nerve-evoked synaptic end-plate potential is recorded intracellularly using KCl-filled glass microelectrodes (Katz and Miledi, 1965).

Since the rates in the synaptic processes (of the order of milliseconds) are determined by the free energies of the associated barriers which the laser temperature jump technique measures, the technique provides a direct measurement of functional consequences of heavy metals. It is suggested by the investigators that the technique has general applicability to the investigation of the influence of a wide variety of metals, drugs, and poisons on synaptic stages and that the results obtained have significance in the determination of dangerous levels of toxic materials.

CORNELL UNIVERSITY MEDICAL COLLEGE  
White Plains, New York

Grant Number: 1 R13 OH 00429-01

Principal Investigator:

Alan A. McLean, M.D.  
New York Hospital  
Cornell Medical Center  
21 Bloomingdale Road  
White Plains, New York 10605

Title:

Cornell Conference on Job Stress

Objectives:

The purpose of the Cornell Conference on Job Stress is to bring together a wide diversity of disciplines (i.e., psychologists, psychiatrists, sociologists, occupational physicians, labor and management leaders) to present their multiple points of view on the way in which job stress is conceived by people from varying backgrounds, and to arrive at definitions of occupational stress.

Areas to be considered by the conference include: Physiological methods of Measuring Occupational Stress; Role Theory (job performance under stressful circumstances); Job Stress and Heart Disease; Occupational Differences (and types and quantities of stress); Psychodynamic Concepts of Stress; and Selye's Concepts (disease functions as a single unit even though it is made up of many reaction responses).

UNIVERSITY OF ROCHESTER  
Rochester, New York

Grant Number: 1 R13 OH-00430-01

Principal Investigator:

Victor G. Laties, Ph.D.  
Dept. of Radiation & Biophysics  
University of Rochester School  
of Medicine and Dentistry  
Rochester, New York 14642

Title:

Conference on Behavioral Toxicology

Objectives:

This is an international conference to consider, in some depth, the subtle and long-term deleterious effects of pharmaceuticals, alone or in combination, applied therapeutically or present as environmental contaminants. Subjects covered in special specific detail include: toxicity of inhaled substances and behavioral toxicology considered from the standpoint of cholinergic mechanisms.

This conference represents a continuation of an ongoing successful program at the University of Rochester.

NEW YORK UNIVERSITY MEDICAL CENTER  
New York, New York

Grant Number: 1 R01 OH 00432-01

Principal Investigator:

Erwin R. Tichauer, Sc.D., PE (Q1d)  
Division of Biomechanics  
New York University Medical Center  
Institute of Rehabilitation Medicine  
400 East 34 Street  
New York, New York 10016

Title:

Antihistamine Effects of Motor Skills and Vigilance

Objectives:

The goal of this research is to determine the extent to which subjects in "realistically-simulated industrial work situations," after the ingestion of antihistamines (chlorpheniramine maleate), (a) show changes in sensory-motor function (which may lead to hazardous equipment operation) and (b) show changes in reaction time and decision-making processes during tasks requiring vigilance. The widespread use of these drugs (antihistamines) and their potential to induce drowsiness are recognized as a basis of need to evaluate their effects.

Description:

This is essentially a pilot investigation involving 12 normal female subjects, between the ages of 21 and 50, who are subjected to a series of tests of task performance after administrations, at different times, of two-levels of antihistamine and one placebo. Eye-hand responses to light activations in an array are measured and analyzed in relation to antihistamine dosage. The equipment used was developed in the laboratories of the principal investigator.

Activity levels of the biomechanical parameters of motion, i.e., reaction time and errors (primarily), displacement, velocity, and acceleration are recorded simultaneously with surface integrated myograms of muscles of the neck rotating the head, the muscles involved in eye movement, and selected muscle groups involved in fine manipulation. Losses of "normal" function may be correlated with potential industrial accidents.

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 1 R13 OH 00510-01

Principal Investigator:

Ido deGroot, M.P.H.  
Department of Community Health  
College of Community Services  
University of Cincinnati  
Cincinnati, Ohio 45221

Title:

Behavioral Toxicology Workshop

Objectives:

The goal of this workshop is to provide the participants a "hands-on" experience and a better understanding and appreciation of behavioral toxicological methods, techniques, and procedures used by laboratories for assessing the adequacy of existing recommended worker exposure levels for industrial toxicants, and for quantifying and evaluating functional impairments based on behavioral-performance measures and neurophysiological changes.

It is expected that the proceedings and recommendations resulting from this symposium will serve as a useful guide to researchers and workers in this area. Useful inputs to criteria document development should also accrue.

## BIO-ENVIRONMENTAL SAMPLING AND ANALYSIS



UNIVERSITY OF CALIFORNIA  
Berkeley, California

Grant Number: 5 R01 OH 00368-02

Principal Investigator:

Thomas H. Milby, M.D.  
University of California  
108 Earl Warren Hall  
Berkeley, California 94720

Title:

Occupational Exposure to Organophosphorous Compounds

Objectives:

This research is designed to identify and assess the biochemical and other parameters of organophosphorus pesticide toxicity in agricultural field workers and to develop effective methodologies and procedures to modify or prevent poisoning among field workers who enter pesticide-treated workplaces (fields, vineyards, and orchards).

Description:

This is a systematic, triphasic investigation of agricultural workers and their pesticide-treated workplaces: 1. to develop analytic, toxicologic, air sampling, skin sampling, bioassay, recording systems, and resuspension of weathered residue methods, 2. to apply the developed methods to the study of organophosphorus exposed workers, and 3. to establish controlled conditions for the study of workers and to develop procedures for amelioration of the hazards.

Publications: none

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 1 R01 OH 00371-01A1

Principal Investigator:

James R. Rockwell, Jr.  
Department of Dermatology  
Cincinnati General Hospital  
Cincinnati, Ohio 45229

Title:

Occupational Hazards of Laser Material Processing

Objectives:

This project aims at determining the characteristics and defining the scope of the occupational hazards associated with the processing of a wide variety of materials by means of laser radiation.

Description:

There are four phases of this project which, to some degree, overlap in time:

1. The first phase is a survey of existing commercial laser systems used for materials processing comprising a literature search, project review, and exchanges of correspondence with laser manufacturers and users.
2. The second phase involves laboratory testing of equipment for reflected light hazards and the measurement of particulate and gaseous by-products produced as a consequence of laser irradiation of various materials such as metals, plastics, and possibly other materials such as synthetic fabrics.
3. The third phase is a field survey of exposures of laser operators to dusts produced by laser uses under actual plant conditions.
4. The final phase is the preparation of a laser safety and control program for laser operators. This includes sections on medical surveillance, area control, eye and skin hazards, respiratory hazards, and education and training.

DERMATOLOGY



UNIVERSITY OF PENNSYLVANIA  
Philadelphia, Pennsylvania

Grant Number: 2 R01 OH 00303-15

Principal Investigator:

M. H. Samitz, M.D.  
University of Pennsylvania Hospital  
Duhring Laboratory Building  
Philadelphia, Pennsylvania 19104

Title:

Clinical and Laboratory Studies of Metal Sensitivity

Objectives:

This research project is designed to investigate the biochemical reactions of chromium, nickel, cobalt, and mercury ions with skin proteins, mucopolysaccharides, and synthetic polypeptides. Included are studies of the diffusion of metallic ions through the skin and investigations, in guinea pigs, of the immunologic properties of antigens prepared in vitro.

Description:

Both in vitro and in vivo (animal) studies are performed to elucidate the role of heavy metal ions in metallic sensitivity. Emphasis has been on investigations involving chromium although nickel, cobalt, and mercury are included. Some insights on protective chemical agents have been developed against industrial chromate hazards. These have been pursued with the aim of correlating information with the mechanism of allergic eczematous chromium dermatitis.

Studies in the diffusion of metal ions through human skin (obtained at autopsy) are made with radioactive metals. Radioactive tracers are also used to determine metal binding to proteins. Assays of trace metal content of skin, hair, and nails (obtained from industrial workers) are performed by means of neutron activation analytical techniques. Investigations are also made of the efficacy of barrier creams and metal inactivating agents in the protection against mercury, nickel, and chromium metal dermatitis. Clinical tests are made under field conditions. The investigators claim that data obtained from this research can provide guidelines for future efforts to study delayed allergy in man.

Publications:

1. Samitz, M.H.: Ascorbic Acid in the Prevention and Treatment of Toxic Effects from Chromates. *Acta. Derm.* (Stockholm) 50: 59-64 (1970).
2. Schmunnes, E., et al.: Techniques of Sensitization of Guinea Pigs with Chromium Salts - A Comparative Study. *Env. Res.* 5: 127-134 (1972).

UNIVERSITY OF WASHINGTON  
Seattle, Washington

Grant Number: 5 R01 OH 00321-05

Principal Investigator:

John E. Milner, M.D.  
Dept. of Environmental Health and  
Community Medicine  
University of Washington  
Seattle, Washington 98105

Title:

In Vitro Studies of Occupational Dermatitis

Objectives:

This research is directed toward the development of in vitro tests describing cellular responses characterizing the delayed hypersensitivity skin reaction to 2,4-dinitrochlorobenzene. The aim is to devise a practical method of diagnosing clinical contact hypersensitivity in vitro, thereby avoiding many of the inherent limitations and dangers of the standard patch test of applying suspected contact allergens to the skin of the patient.

Description:

The basic protocol of this project includes the lymphocyte transformation system of guinea pigs sensitized to 2,4-dinitrochlorobenzene and dinitrochlorobenzene - skin protein conjugates. The endpoint being measured consists of counting the proportion of blast cells after appropriate incubation, in vitro, as well as incorporation of tritiated thymidine. Applications to human beings will be sought after guinea pig data are satisfactorily definitive.

Publications:

1. Milner, J.E.: In Vitro Lymphocyte Responses to Contact Hypersensitivity. J. Investi. Derm. 55: (1) 34-38 (1970).
2. Milner, J.E.: In Vitro Lymphocyte Responses to Contact Hypersensitivity II. J. of Investi. Derm. 56: (5) 349-352 (1971).
3. Milner, J.E.: In Vitro Lymphocyte Responses in Contact Hypersensitivity III. J. Inves. Derm. 58: (6) 388-391 (1972).
4. Milner, J.E.: Prevention of Environmental Dermatitis. Post grad. Med. 51: (1) 135-137 (1972).

WAYNE STATE UNIVERSITY  
Detroit, Michigan

Grant Number: 9 R01 OH 00410-04

Principal Investigator:

Hermann Pinkus, M.D.  
Department of Dermatology  
Gordon H. Scott Memorial Hall  
540 E. Canfield Street  
Detroit, Michigan 48201

Title:

Environmental Injury and Repair of Epidermis

Objectives:

To produce controlled injuries of the skin in humans with acids, bases, detergents, or other environmental chemicals. Attempts will be made to identify the injury and to follow the reactions to the injury (principally healing) by morphological methods which will include light and electron microscopy, radioautography, administration of  $^3\text{H}$  thymidine and enzyme histochemistry.

Description:

Its substance concerns a light and electron microscopic analysis of the effects of a variety of common chemicals upon human skin. The chemicals which have been tested have been "pure alkali and acid," soaps, and "lipid solvents." The method in general involves exposure of human skin to the test substances for a series of time intervals. Biopsies are then made in order to describe what the investigators consider to be the progression of experimental alterations.

The long-range proposal presumes to study the effects of other environmental agents known to evoke contact dermatitis, and ultimately they propose to analyze and compare the effectiveness of various protective agents.

Publications: None



## EPIDEMIOLOGY

MOUNT SINAI SCHOOL OF MEDICINE  
New York, New York

Grant Number: 5 R01 OH 00305-08

Principal Investigator:

Irving J. Selikoff, M.D.  
Mount Sinai School of Medicine  
of the SUNY  
Fifth Avenue and 100 Street  
New York, New York 10029

Title:

Asbestos Exposure and Cancer in the General Population

Objectives:

The principal research aim is to answer the broad question, "Is there a relationship between asbestos exposure and cancer in the general population?" Subsidiary and specific objectives are to determine: 1) the quantity of chrysotile asbestos in the lungs of New York City residents who come to post mortem; 2) the direct and indirect occupational, familial, and residency contributions to exposure in the study population and their relationships to chrysotile content of the lung; 3) the association between asbestos lung content and presence of various diseases, as found at autopsy, in the 3,000 study cases; 4) whether or not there has been any change in chrysotile lung content between the years 1910 and 1970; 5) what are some of the likely sources of asbestos exposure in urban dwellers, at the present time; and 6) whether there is a multiple factor effect associated with a combination of asbestos inhalation and cigarette smoking.

Description:

This investigation combines the study of collected data from approximately 3,000 autopsies with statistical and epidemiological data. Light and electron microscopy are applied in identifying and characterizing chrysotile asbestos bodies in lung tissue. Appropriate analytical methodology has been developed. Results to date have been found in small lung samples of post mortem cases in 24 of 28 consecutive New York City autopsies.

## MOUNT SINAI SCHOOL OF MEDICINE

### Publications:

1. Selikoff, I.J. and E.C. Hammond: Community Effects of Non-Occupational Environmental Asbestos Exposure. Am. J. Public Hlth. 58: 1658 (1968).
2. Selikoff, I.J.: Asbestos. Environment 11: (2) 3 (1969).
3. Langer, A.M.: Electron Microprobe Analysis: Study of Asbestos Fibers and Bodies from Lung Tissue in: Laboratory Diagnosis of Diseases Caused by Toxic Agents. E.F.W. Sunderman and F.W. Sunderman, Jr. (1970).
4. Kannerstein, M., et al.: Pathology of Carcinoma of the Lung Associated with Asbestos Exposure. Cancer 30: (1) July 1972.
5. Bader, M.T., et al.: Pulmonary Function and Radiographic Changes in 598 Workers with Varying Duration of Exposure to Asbestos. Mt. Sinai JOM 37:(4) 492-500 (July-August 1970).
6. Langer, A.M., et al.: Chemical Characterization of Asbestos Body Cores by Electron Microprobe Analysis. J. Histochem. & Cytochem. 20: (9) 723-734 (1972).
7. Langer, A.M., et al.: Chemical Characterization of Uncoated Asbestos Fibers from the Lungs of Asbestos Workers by Electron Microprobe Analysis. J. Histochem. & Cytochem. 20:(9) 735-740 (1972).
8. Reitze, W.B., et al.: Application of Sprayed Inorganic Fiber Containing Asbestos: Occupational Health Hazards. AIHA J. 178-191 (March 1972).
9. Langer, A.M., et al.: Inorganic Particles in Cigars and Cigar Smoke. Science 174: 585-587 (November 1971).
10. Selikoff, I.J., et al.: Risque Neoplasique Lie a l'Environnement Industriel. Med. Prat 26: 399 (July 1970).
11. Selikoff, I.J.: Environmental Cancer. The Sciences 12: (2) 4-31 (March 1972).
12. Berson, S.A., et al.: Antibodies to "Alcalase" After Industrial Exposure. New. Eng. J. Med. 284: 688-690 (April 1971).

MOUNT SINAI SCHOOL OF MEDICINE

Publications:

13. Selikoff, I.J., et al.: Asbestos Air Pollution. Arch. of Env. Hlth. 25: 1-13 (July 1972).
14. Miller, A., et al.: Significance of Sublight Microscopic Mineral Particles. Talc Pneumo. 50: 395-402 (March 1971).
15. Selikoff, I. J., et al.: Carcinogenicity of Amosite Asbestos. Arch. Env. Hlth. 25: 183-186 (September 1972).
16. Hammond, E.C., et al.: Relation of Cigarette Smoking to Risk of Death of Asbestos-Associated Disease Among Insulation Workers in the United States. Env. Can. Res. Proj. (October 1972).
17. Selikoff, I.J., et al.: Cancer Risk of Insulation Workers in the United States. Env. Canc. Res. Proj. (October 1972).
18. Nicholson, W.J., et al.: Asbestos Contamination of Parenteral Drugs Science 177: 171-173 (July 1972).

HARVARD UNIVERSITY  
Boston, Massachusetts

Grant Number: 5 R01 OH 00310-13

Principal Investigator:

Benjamin G. Ferris, Jr., M.D.  
Harvard University  
665 Huntington Avenue  
Boston, Massachusetts 02115

Title:

Respiratory Disease and Environmental Exposures

Objectives:

The investigation is directed toward developing dose-response curves, for human beings, for various air-borne pollutant substances.

Description:

This is a prospective study of population groups, their exposures to various air-borne pollutants, and their concomitant impaired pulmonary function and respiratory disease. Random populations and occupationally-exposed groups in Berlin, New Hampshire are surveyed and compared with comparable populations in Canada and England. In addition to data obtained from questionnaires, respirometry and other tests of forced vital capacity are performed. A major observation, to date, is that smoking habits appear much more important than ambient air pollutants, in causing respiratory disease.

Publications:

1. Ferris, B.G.: Use of Pulmonary Function Tests in Epidemiologic Surveys, Ext. du Bull. de Physio-Path. Resp. 6: 579-594 (1970).
2. Ferris, B.G.: Tests to Assess Effects of Low Levels of Air Pollutants on Human Health. Arch. Env. Hlth. 21: 553-558 (October 1970).
3. Ferris, B.G.: Effects of Air Pollution on School Absences and Differences in Lung Function in First and Second Graders in Berlin, New Hampshire. January 1966 - June 1967. Am. Rev. Resp. Dis. 102: 591-606 (1970).
4. Ferris, B.G.: Correlation of Anthropometry and Simple Tests of Pulmonary Function. Arch. of Env. Hlth. 22: 672-676 (1971).

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5. Ferris, B.G., J.M. Peters, and W.A. Burgess: Prevalence of Chronic Respiratory Disease. Arch. Env. Hlth. 23: 220-225 (September 1971).
6. Ferris, B.G., I.T.T. Higgins, M.W. Higgin, J.M. Peters, W.F. Van Ganse, and M.D. Goldman: Chronic Non-Specific Respiratory Disease in Berlin, New Hampshire, 1961-1967: A Cross-Sectional Study. Am. Rev. Resp. Dis. 104: 232-244 (1971).
7. Ferris, B.G., F.E. Speizer, J. Worcester, and W.Y. Chen: Adult Mortality in Berlin, New Hampshire, from 1961-1967. Arch. Env. Hlth. 23: 434-439 (December 1971).
8. Van Ganse, W.F., B.J. Ferris, and J.E. Cotes: Cigarette Smoking and Pulmonary Diffusing Capacity (Transfer Factor) Am. Rev. Resp. Dis. 105: 30-41 (1972).
9. Murphy, R.L.H., et al.: Effects of Low Concentrations of Asbestos Clinical, Environmental, Radiologic and Epidemiologic Observations in Shipyard Pipe Coverers and Controls. New Eng. J. Med. 285: 1271-1278 (December 1971).

UNIVERSITY OF MINNESOTA  
Minneapolis, Minnesota

Grant Number: 2 R01 OH 00353-02

Principal Investigator:

James H. Stebbings, Jr.  
Division of Epidemiology  
School of Public Health  
University of Minnesota  
1158 Mayo Memorial Building  
Minneapolis, Minnesota

Title:

Cardiorespiratory Changes in an Employed Population

Objectives:

The goal of this effort is the analysis and assessment of epidemiologic information acquired in a study of chronic respiratory disease in 2,300 New York City Transit workers.

Description:

This is the termination of a study which involves the examination of medical records and case histories of a specialized employed population, that is New York City Transit workers. The following points are considered:

1. the patterns of change in the electrocardiographic abnormalities related to chronic pulmonary disease and the relationship to changes in respiratory symptoms and pulmonary function values, and
2. the usefulness of industrial absenteeism records in predicting early chronic respiratory disease and, conversely, the degree to which industrial absenteeism may be predicted on the basis of pulmonary function tests and standard respiratory questionnaire responses.

Publications:

None

CENTRO MALATTIE CARDIOVASCOLARI  
Rome, Italy

Grant Number: 5 R01 OH 00362-08

Principal Investigator:

Vittorio Puddu, M.D.  
Via Savoia 80  
Rome, Italy

Title:

Death Rates Among Italian Railroad Employees

Objectives:

The principal aim of this continuing collection of epidemiologic and demographic data of Italian railroad workers is to study the relationship of physical activity to coronary heart disease in the workers.

Description:

Since 1963, these investigators have followed mortality among a cohort of over 172,000 Italian railroad workers, in order to see whether those with jobs requiring greater physical activity develop coronary heart disease (CHD). A five-year follow-up suggests that this may be the case but the differences are not large and those doing heavier work have a greater overall mortality. CHD is generally low in Italy. This investigation continues and increases the number and kinds of observations so as to: 1) establish an age-specific cohort mortality table, by cause of death, of the entire employee population of the Italian railroad system; 2) establish an age-specific cohort mortality table by level of physical activity, job responsibility, and socio-economic class; and 3) to compare the collected and analyzed data with comparable U.S. data. (Consultation and collaboration has been provided on a continuing basis by Dr. Ancel M. Keys and Dr. H. K. Taylor of the University of Minnesota).

Publications: none

HARVARD UNIVERSITY  
Boston, Massachusetts

Grant Number: 1 R01 OH 00369-01

Principal Investigator:

John M. Peters, M.D.  
Harvard University  
665 Huntington Avenue  
Boston, Massachusetts 02115

Title:

Epidemiology of Respiratory Disease in Firefighters

Objectives:

This project seeks to determine both the acute and chronic pulmonary effects of inhalation of gaseous combustion products and smoke in fire fighters. The significance of this work resides in the fact that, in the United States, the number of full-time and volunteer fire fighters approaches one million and that they are subjected to unknown quantities and severities of pulmonary irritants at varying frequencies. The health consequences of these exposure, especially the chronic effects of acute inhalation or the chronic effects of chronic intermittent, and low-level exposures have hitherto not been systematically explored.

Description:

The entire Boston Fire Department (approximately 1900 firemen) is the experimental group under survey in this essentially epidemiologic investigation with The Boston Police Department serving as the control group, under separate investigation and other support (Dr. Speizer). The screening techniques include pulmonary function tests, by means of a Stead-Wells spirometer using a fast paper speed (3.2 cm/sec.), for forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), and determined expiratory flow rates. In addition a questionnaire is employed to elicit demographic, occupational, and appropriate medical history information. The population is to be resurveyed annually. Also, all firemen who are treated in the Boston City Hospital emergency room for smoke inhalation are evaluated and the information compared with the baseline data.

A personal air sampling unit is being devised to be worn by firemen. This is to provide information on personal exposures to CO, O<sub>2</sub>, particulates, phosgene, hydrogen chloride, isocyanates, acrolein, sulfur dioxide, and other materials. The successful accomplishment of this research can be expected to result in significant and highly useful information on respiratory hazards to firemen.



ERGONOMICS

MONTEFIORE HOSPITAL AND MEDICAL CENTER  
Bronx, New York

Grant Number: 3 R01 OH 00331-04S1

Principal Investigator:

Weitzman, Elliott D., M.D.  
Montefiore Hospital and Medical Center  
Division of Neurology  
Bronx, New York 10467

Title:

The Sleep-Waking Cycle and Its Neuro-Endocrine Correlates

Objectives:

This project seeks to determine the pattern and time course changes in the sleep-wake cycle subject to a number of measured variables such as changes in sleep intervals and patterns in a controlled laboratory environment. The rationale of this research is based on the similarities in responses to manipulations of circadian parameters and to certain work stresses.

Description:

Investigations are conducted with human beings in controlled laboratory situations.

Analyses are made of sleep-wake cycles and sleep-stage patterns by means of electrical recordings, measurements of corticoids and growth hormone in plasma and urine, as well as measurements of body temperature, urine volume, electrolytes, and creatinine. Psychological variables are also examined during the manipulations of sleep-wake patterns.

Publications:

1. Hellman, L., E.D. Weitzman, H. Roffwarg, D.K. Fukushima, K. Yoshida, and T.G. Gallagher: Cortisol is Secreted Episodically in Cushing's Syndrome. J. Clin. Endoc. and Metab. 30: (5) 686-689 (May 1970).
2. Hellman, L., E.D. Weitzman, H. Roffwarg, D.K. Fukushima, K. Yoshida, B. Zumoff and T.G. Gallagher: Effect of o,p'-DDD on Cortisol Secretory Pattern in Cushing's Syndrome. J. Clin. Endoc. and Metab. 31: (2) 227-230 (August 1970).

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3. Sassin, J.F., et al.: Human Prolactin: 24-Hour Pattern with Increased Release During Sleep. *Science* 177: 1205-1207 (September 1972).
4. Sachar, E.J., et al.: Growth Hormone Responses to L-Dopa in Depressed Patients. *Science* 178: 1304-1305 (December 1973).
5. Weitzman, E. D., et al.: Acute Reversal of the Sleep-Waking Cycle in Man; Effect on Sleep Stage Patterns. *Arch. of Neuro.* 22: 483-439 (June 1970).
6. Weitzman, E.D., et al.: Persistence of the Twenty-Four Hour Pattern of Episodic Cortisol Secretion and Growth Hormone Release in Blind Subjects. *Trans. of Amer. Neuro. Assoc.* 97: (1972).
7. Tauber, E.S., et al.: Vestibular Stimulation During Sleep in Young Adults. *Arch. of Neuro.* 27: 221-228 (September 1972).
8. Gallagher, T. F., et al.: Hyperthyroidism and Cortisol Secretion in Man. *J. of Clin. Endoc. & Metab.* 34: (6) 919-927 (June 1972).
9. Pawel, M.A., et al.: The Temporal Relation Between High Release and Sleep Stage Changes at Nocturnal Sleep Onset in Man. *Life Sciences* 11: pt. I - 587-593 (1972).
10. Boyar, R., et al.: Synchronization of Augmented Luteinizing Hormone Secretion with Sleep During Puberty. *New Eng. J. O. M.* 287: 582-586 (September 1972).
11. Boyar, R., et al.: Twenty-Four Hour Pattern of Luteinizing Hormone Secretion in Normal Men with Sleep Stage Recording. *J. of Clin. Endoc. & Metab.* 35: (1) 73-81 (July 1972).
12. Boyar, R. M., et al.: Studies of Endocrine Function in Isolated Gonadotropin Deficiency. *J. of Clin. Endoc. & Metab.* 36: (1) 64-72 (January 1973).
13. Perlow, M. J., et al.: Release of Human Growth Hormone, Follicle Stimulating Hormone, and Luteinizing Hormone in Response to L-Dihydroxyphenylalanine (L-Dopa) in Normal Man. *Dis. of Nerv. System* 33: 804-810 (December 1972).



## HEAD AND BODY PROTECTION

VILLANOVA UNIVERSITY  
Villanova, Pennsylvania

Grant Number: 2 R01 OH 00300-03

Principal Investigator:

George N. Quam, Ph.D.  
Department of Chemistry  
Villanova University  
Villanova, Pennsylvania 19085

Title:

Protection of Eyes, Face and Body Against High Impacts

Objectives:

The original aim of this research was the investigation of materials and their fabrication into shields for the protection of chemical laboratory and plant workers against impact injuries. Currently, the terminal phase of this research aims at developing and fabricating appropriate personal protective shields primarily for the protection of policemen, firemen, and other security officers against missile impacts.

Description:

Earlier work by this investigator established the merits of laminated layers of clear polycarbonate sheeting over that of single thicknesses of other recommended materials when fabricated into personal body shields.

This project is now concerned primarily with the investigation and testing of personally worn body and face armor and similar protective "devices" for effectiveness, comfort, and applicability to the functional need. Laminated materials such as, "polycarbonate-ballistic nylon-polycarbonate" are explored along with other plastics to determine the optimum combination for an all purpose police armor garment. Original testing equipment is used in this research.

Publications:

1. Quam, G.N.: Waste Disposal from Academic Laboratories. 17th Campus Safety Conference. University of California Santa Barbara, June 25, 1970. Published in N.S.C. Monograph No. 27 (1970) pp. 1-7.

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2. Quam, G.N. and J. Shea: An Investigation of High Impact Shields for Eyes and Face. Env. Con. & Sfty. Mgmt. (February 1971).
3. Quam, G.N.: Safety Shielding in the Chemical Laboratory. Sixth Middle Atlantic ACS Regional Meeting, Baltimore, Maryland (February 1971).
4. Quam, G.N. and J. Shea: Protection of Eyes and Face Against High Impact. Env. Con. & Sfty. Mgmt. 141: 24-25 (February 1971).
5. Quam, G.N. and J. Shea: XCI. An Investigation of High Impact Body Shields, Safety 49: (5) A295-6 (May 1972).
6. Quam, G.N., et al.: High Impact Shields for Face and Body. National Safety News, September 1972.

SNELL MEMORIAL FOUNDATION INCORPORATED  
North Tarrytown, New York

Grant Number: 5 R01 OH 00301-03

Principal Investigator:

George G. Snively, M.D.  
2315 Stockton Boulevard  
Sacramento, California 95817

Title:

Head Protection of Industrial Workers

Objectives:

There is a threefold objective in this research: 1) to study the head protection afforded by present day helmets (hard hats); 2) to develop methods for realistically testing the afforded protection under dynamic conditions; and 3) to develop appropriate principles for head protection in industrial conditions which will afford superior protection especially from side or glancing blows.

Description:

Current protective headgear is designed on the premise that falling objects constitute the major industrial head hazards. There is evidence to the contrary. Consequently, determinations are made of the characteristics of industrial helmets with respect to accelerated impacts; attenuation properties; and impacts other than direct crown blows. Investigations are also made of head injuries in industrial situations so as to evaluate relationships inherent in injury site, magnitude of energy applied, and other factors involved.

Prototype helmets of various materials such as honeycombed aluminum, stainless steel, or formed polystyrene and other foams are investigated under dynamic conditions.

Publications:

1. Snively, G.G.: Racing Helmet Design, Testing & Standardization: The Snell Standards for Protective Headgear. Soc. of Automotive Engineers #700 600, Los Angeles, California (August 27, 1970) p. 7-9.
2. Snively, G.G.: Linear Acceleration of Impact Type. AGARD Conf. Proc. No. 88, (1971).
3. Snively, G.G.: Evaluation & Testing of Protective Head Gear. AGARD Conf. Proc. No. 88 on Linear Acceleration of Impact Type. AGARD-CP-88-71 (pp. D41-7), NATO Meeting, Porto, Portugal (June 1971).

STANFORD RESEARCH INSTITUTE  
Menlo Park, California

Grant Number: 2 R01 OH-00343-02

Principal Investigator:

George N. Bycroft, Ph.D.  
Stanford Research Institute  
333 Ravenwood Ave.  
Menlo Park, California 94025

Title:

Mathematical Models of Head Injuries

Objectives:

This project is aimed at understanding the relationship between skull and brain damage and mechanical stress waves resulting from a blow to the head.

Description:

A mathematical model, utilizing a computer code, of the skull and brain represented as an elastic spherical shell filled with a visco-elastic medium which is not attached to the shell, is developed to permit calculations of stress waves generated by an impulsive load normal to the shell surface. This work is useful in testing the "cavitation theory" for cerebral concussions as well as the validity of related explanations for other manifestations of brain injury resulting from head blows. The use of the computer code, which was developed at Stanford Research Institute, permits numerical calculations of the size of impact necessary to imitate rupture of the "brain" as well as of the "skull."

Publications: none

UNIVERSITY OF CALIFORNIA  
LaJolla, California

Grant Number: 1 R01 OH-00404-01

Principal Investigator:

Alan M. Nahum, M.D.  
225 West Dickinson  
San Diego, California 92103

Title:

Prevention of Accidental Head Injury

Objectives:

The goal of this project is to reduce and/or prevent head injury resulting in pathophysiologic changes, either permanent or reversible.

Description:

The investigators are trying to correlate post-concussive states (ranging from minimal to severe) in primates with associated impact forces and physiologic parameters of brain function. By means of examinations of cadavers, the researchers are attempting to relate their findings to man. A principal function is the attempt to develop a reproducible experimental and mathematical model relating head injury with the various force parameters. An innovative technique that is employed is the implementation of a floating electrode within the primate brain. This is used to determine unit discharges from central locations so as to provide electroencephalographic information which is more informative than comparable information obtained from surface electrodes.

High speed motion picture photography is used to record kinematics of impact and permit calculations of rotational acceleration. After impact, physiologic and clinical measurements of depth and duration of concussion are made continuously. Recordings of impedance, EEG, intracranial pressure, and multiple unit activity continue. Skull x-rays are also obtained.

Publications: none

## INSTRUMENTATION



LOUISIANA STATE UNIVERSITY  
New Orleans, Louisiana

Grant Number: 5 R01 OH-00345-03

Principal Investigator:

George G. Guilbault, Ph.D.  
Louisiana State University  
Chemistry Department  
New Orleans, Louisiana 70122

Title:

Use of Solid State Detectors in Air Pollution Research

Objectives:

The aim of this research is to adapt and use the solid state devices such as the piezoelectric crystal and the contact potential detectors for the detection and determination of inorganic and organic substances of significance in air pollution.

Description:

This research involves the adaptation of solid state gas chromatographic detectors for applications in air pollution investigations. Various adsorbents are coated onto piezoelectric crystals and contact potential detectors. These devices are then exposed to specific pollutants, the adsorption of which causes a change in the contact potential. Specific detectors are sought for such materials as HF, O<sub>3</sub>, SO<sub>2</sub>, NO, NO<sub>2</sub>, CO, various metals, and hydrocarbons. Measurements which are made of detector response, include sensitivity, linearity of response, accuracy, speed of response, limits of detection, stability, simplicity of design, and selectivity of response.

Publication:

1. Guilbault, G.G. and A. Lopez-Roman: Use of Sodium Tetrachloromercuriate As A Substrate for the Determination of SO<sub>2</sub> on the Piezocrystal Detector. *Envir. Letters* 2: (1) 35-45 (1971).
2. Scheide, E.P., et al.: Piezoelectric Detectors for Organophosphorus Compounds and Pesticides. *Analyt. Chem.* 44: 1764 (September 1972).



OCCUPATIONAL RESPIRATORY DISEASE

*Byssinosis*

*Coal Workers' Pneumoconiosis*

*Farmer's Lung*

*Respiratory Tract Carcinoma*

*Silicosis*

*Unspecified*

DUKE UNIVERSITY  
Durham, North Carolina

Grant Number: 5 R01 OH 00302-03

Principal Investigator:

Kaye H. Kilburn, M.D.  
Duke University Medical Center  
Durham, North Carolina 27710

Title:

Prevalence Pathogenesis and Control of Byssinosis

Objectives:

This project seeks: 1) to determine the prevalence of reactor subjects to cotton textile dust and the correlation with symptoms and decreases in pulmonary function; 2) to establish the relationship between reactors to cotton dust and chronic bronchitis, asthma, emphysema, and allergic disease by epidemiologic and pathologic methods; 3) to isolate and characterize the biologic agent responsible for byssinosis; 4) to determine the mechanism of action of the causative agent, with emphasis on immunopathogenesis; and 5) to select and assess methods for reducing or eliminating reactions to the agent.

Description:

The approach to the problem is essentially epidemiologic. Field studies include investigations of prevalence of reactors in textile plants with high, moderate, and low airborne dust levels. There are comparisons with control populations comprised of workers in plants in which there is no exposure to cotton dust. Chemical and immunologic methods are applied to studies comparing acute decrement in ventilatory function with decrements occurring over a three year period in selected cohorts. These chemical and immunologic methods are also applied to studies of adults, in a small mill town, to determine the prevalence of reactions to cotton dust among those currently employed in the mill, those previously employed, and those who have never been so employed. Included in the project is an historical prospective study utilizing Social Security information and death certificates. This involves development of control methods. The project represents a cooperative endeavor which includes Duke University, the State Department of Health, members of the USPHS, and a large segment of the textile industry.

### Publications:

1. Ayer, H.E., M. Battigelli, D.A. Fraser, J.D. Hamilton, K.H. Kilburn, J. Lumsden, J.R. Lynch, J.A. Merchant, and A.D. Stevens: The Status of Byssinosis in the United States. Arch. Env. Hlth. 23: 230-234 (1971).
2. Hamilton, J.D., et al.: Byssinosis in a Nontextile Workers. Amer. Rev. Resp. Dis. 107: 464-466 (1973).
3. Kilburn, K.H., et al.: Leukocyte Recruitment Through Airway Walls by Condensed Vegetable Tannins and Quercetin. Lab. Inves. 28: (1) 55-59 (1973).
4. Merchant, J.A., et al.: An Industrial Study of the Biological Effects of Cotton Dust and Cigarette Smoke Exposure. J.O.M.15: (3) 212-221 (March 1973).
5. Merchant, J.A., et al.: Dose Response Studies in Cotton Textile Workers. J.O.M. 15: (3) 222-230 (March 1973).
6. Harris, T.R., et al.: Byssinosis and Respiratory Diseases of Cotton Mill Workers. J.O.M. 14: (3) 199-206 (March 1972).
7. Merchant, J.A., et al.: Byssinosis and Chronic Bronchitis Among Cotton Textile Workers. Ann. of Intern. Med. 76: 423-433 (1972).

JOHN B. PIERCE FOUNDATION  
New Haven, Connecticut

Grant Number: 2 R01 OH 00304-09

Principal Investigator:

Arend Bouhuys, M.D., Ph.D.  
John B. Pierce Foundation Laboratory  
290 Congress Avenue  
New Haven, Connecticut 06519

Title:

Physiological Studies on Byssinosis

Objectives:

The investigation aims at: 1) elucidating the mechanism of bronchoconstriction in byssinosis; 2) identifying the pharmacologic agent responsible for the bronchoconstriction; 3) studying objectively medical preventive methods and treatment of byssinotic workers; 4) contributing to the technical prevention of the disease by the removal of dust from the mill atmosphere; and 5) performing a follow-up survey of hemp workers in Spain.

Description:

The approach to the problems is biochemical, physiologic and epidemiologic. Emphasis is put on studying long-term effects of byssinosis in cotton mill workers and attempting to correlate dust density with physiologic effects so that better control mechanisms may be affected. Although the precise chemical entity in cotton bracts responsible for bronchoconstriction has not been characterized, the pharmacologically active fraction has been isolated and associated with impaired pulmonary function. Biochemical characterization is being carried out. Carefully controlled studies have contributed to a better understanding of the problems involved and lead logically to the recognition of the need for additional pharmacologic work.

Publications:

1. Clement, J. and K.P. van de Woestijne: Pressure Correction in Volume and Flow Displacement Body Plethysmography. J. Applied Phys. 27: 845-847 (1969).
2. Bouhuys, A., V.R. Hunt, B.M. Kim, and Z. Zopletal: Maximum Expiratory Flow Rates in Induced Bronchoconstriction in Man. J. Clin. Inves. 48: 1159-1168 (1969).

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3. Dennis, M.W., J.S. Douglas, J.U. Cosby, J.A.J. Stolwijk, and A. Bouhuys: On-Line Analog Computer for Dynamic Lung Compliance and Pulmonary Resistance. *J. Appld. Phys.* 26: 248-252 (1969).
4. Bouhuys, A., R.L. Wolfson, J.D. Brain, D.W. Horner, and E. Zuskin: Byssinosis in Cotton Textile Workers. *Ann. Int. Med.* 71: 257-269 (1969).
5. Bouhuys, A., A. Barbero, R.S.F. Schilling, and K.P. van de Woestijne: Chronic Respiratory Disease in Hemp Workers. *Am. J. Med.* 46: 526-537 (1969).
6. Zuskin, E., I. Zolle, D.V. Proctor, S. Permutt, and A. Bouhuys: Exposure to <sup>131</sup>I-labeled Viscose Rayon Fibers. *Arch. Env. Hlth.* 19: 648-653 (1969).
7. Jaeger, M. and A. Bouhuys: Loop Formation in Pressure vs. Flow Diagrams Obtained by Body Plethysmographic Techniques. *Prog. Resp. Res.* 4: 116-130 (1969).
8. Bouhuys, A.: Byssinosis in Textile Workers. Int'l. Conf. on Pneumo., in Johannesburg, South Africa (April 1969).
9. van de Woestijne, K.P. and A. Bouhuys: Spirometer Response and Pressure Correction in Body Plethysmography. *Prog. Resp. Res.* 4: 64-74 (1969).
10. Bouhuys, A., R.S.F. Schilling, and K.P. van de Woestijne: Cigarette Smoking Occupational Dust Exposure and Ventilatory Capacity. *Arch. Env. Hlth.* 19: 793-797 (1969).
11. Zuskin, E., R.L. Wolfson, G. Harpel, J.W. Welborn, and A. Bouhuys: Byssinosis in Carding and Spinning Workers. Prevalence in the Cotton Textile Industry. *Arch. Env. Hlth.* 19: 666-673 (1969).
12. Douglas, J.S. and A. Bouhuys: Bronchoconstrictor Responses and Anesthesia in Guinea Pigs. *Clin. Res.* 17: 617 (1969).
13. Douglas, J.S., M.W. Dennis, Zuskin, E. and A. Bouhuys: Quantitative Determination of Effects of Bronchoactive Agents in Spontaneously Breathing Guinea Pigs. 4th Int'l. Congr. on Pharm., Basel, Switzerland (July 14-18, 1969).
14. Bouhuys, A. and J.M. Peters: Control of Environmental Lung Disease. *New Eng. J. of Med.* 283: 573-582 (September 10, 1970).
15. Bouhuys, A. and K.P. van de Woestijne: Respiratory Mechanics and Dust Exposure in Byssinosis. *J. Clin. Investi.* 49: 106-118 (1970).

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16. Bouhuys, A.: Airway Dynamics and Bronchoactive Agents in Man. *Airway Dynamics: Physiology and Pharmacology*. Charles C. Thomas, Springfield, Illinois, pp. 263-282 (1970).
17. Dennis, M.W. and J.S. Douglas: Control of Bronchomotor Tone in Spontaneously Breathing, Unanesthetized Guinea Pigs. Charles C. Thomas, Springfield, Illinois, pp. 253-262 (1970).
18. Bouhuys, A.: Byssinosis in the Textile Industry. *Arch. Env. Hlth.* 21: 475-478 (October 1970).
19. Bouhuys, A.: Byssinosis in the United States. *Trans. of Nat'l. Conf. of Cotton Dust and Health*. (May 2, 1970).
20. Bouhuys, A.: Control of Environmental Lung Disease. *New Eng. J. of Med.* 283: 573-582 (September 10, 1970).
21. Bouhuys, A. and K.P. van de Woestijne: Mechanical Consequences of Airway Smooth Muscle Relaxation. *J. of Appld. Phys.* 30: (5) 670-676 (May 1971).
22. Bouhuys, A., J.S. Douglas, and A.R. Guyatt: Pharmacological Modification of Histamine-Mediated Airway Responses. *J. Clin. Investi.* 50: (6) ABST. (June 1971).
23. Piscitelli, D.M. and A. Bouhuys: Histamine Release from Human Lung by A Component of Cotton Bracts. *Fed. Procs.* 30: (2) ABST. (March-April 1971).
24. Popa, V., J.S. Douglas, and A. Bouhuys: Anaphylaxis and Response to Histamine, Acetylcholine, and Propranolol in Guinea Pigs. *Fed. Procs.* 30: (2) ABST. (March-April 1971).
25. Popa, V., J.S. Douglas, and A. Bouhuys: Airway Responses to Antigen, Histamine, Acetylcholine, and Propranolol in Actively Sensitized Guinea Pigs. *Chest* 60: (3) 301 (September 1971).
26. Bouhuys, A.: Byssinosis - Airway Responses Caused by Inhalation of Textile Dusts. *Arch. Env. Hlth.* 23: 405-407 (December 1971).
27. Hitchcock, M., D.M. Piscitelli, and A. Bouhuys: Histamine Release from Human Lung by 48/80 and Methyl Piperonylate. *Procs. Int'l. Union of Phys. Sci's. IX: XXV Int'l. Congress of Physiological Sciences*.
28. Bouhuys, A.: Industrial Workers Needs in Environmental Health. *AIH Conference May 24-28, 1971. ABSTRACT*.

UNIVERSITY OF MISSOURI  
Columbia, Missouri

Grant Number: 7 R01 OH 00511-01

Principal Investigator:

Kaye H. Kilburn, M.D.  
N424 Medical Center  
University of Missouri  
Columbia, Missouri 65201

Title:

Prevalence, Pathogenesis and Control of Byssinosis

Objectives:

This project seeks: 1) to determine the prevalence of reactor subjects to cotton textile dust and the correlation with symptoms and decreases in pulmonary function; 2) to establish the relationship between reactors to cotton dust and chronic bronchitis, asthma, emphysema, and allergic disease by epidemiologic and pathologic methods; 3) to isolate and characterize the biologic agent responsible for byssinosis; 4) to determine the mechanism of action of the causative agent, with emphasis on immunopathogenesis; and 5) to select and assess methods for reducing or eliminating reactions to the agent.

Description:

This project was started by Dr. Kilburn at Duke University (see page 50) but transferred in the terminal year to the University of Missouri. Three of the 5 original aims of the project have been completed (epidemiology, prevalence studies, and control studies); and studies on chemical identification and mechanism of action of the causative agent partially completed. It is these latter aims relating to the pathogenesis of cotton dust disease which will be pursued during this grant period.

UNIVERSITY OF NOTRE DAME  
Notre Dame, Indiana

Grant Number: 5 R01 OH 00342-03

Principal Investigator:

Morris Pollard, Ph.D.  
Lobund Laboratory  
University of Notre Dame  
Notre Dame, Indiana 46556

Title:

Effects of Environmental Pollutants in Germfree Rodents

Objectives:

This project seeks to examine, in lungs of germ-free rats, effects of silica dust, coal dust, and combinations of these dusts and to compare the results with those observed in commercially-bred animals and in germ-free animals in non-sterile environments.

Description:

This is a collaborative effort with Lobund and the Division of Laboratories and Criteria Development (NIOSH) in Cincinnati, Ohio. Comparative studies are performed using germ-free rats maintained in a sterile environment, commercially-bred rats which have endemic infectious diseases, and germ-free rats maintained in a non-sterile environment. Animals are subjected to silica and coal dusts separately and in combination. Lung reactions are investigated. This work has specific relevance to "black lung" problems as well as the tentatively-held view that infection is suspect as an important factor in the pathogenesis of pneumoconiotic fibrosis.

Publications:

1. Reddy, B.S. and M. Pollard: Effect of Germfree Status on Hepatic Xanthrene Oxidase Activity and on Bone Mineral Composition During Development and Senescence in Rats. J. Nutrition 102: 299-305 (1972).
2. Pollard, M. and N. Sharon: Irradiation Induced Lesions in Germfree Rats. J. Nat. Cancer Inst. 47: 229-234 (1971).

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 5 R01 OH 00355-02

Principal Investigator:

Harold G. Petering, Ph.D.  
Kettering Laboratory  
College of Medicine  
Eden and Bethesda  
Cincinnati, Ohio 45219

Title:

Interaction of Coal Dust with Essential Metals

Objectives:

These investigations seek to explore the biological effects of metal-binding ligands in coal dust and coal tar on essential and trace metals such as copper, zinc, and iron. The rationale of this study is the concept that metal-binding ligands in coal dust and coal tar might, in situ, alter essential and trace metal metabolism thereby contributing to some of the observed epidemiological evidence of altered disease patterns in coal miner populations. Examples of such altered disease patterns include cardiovascular disease, obesity, and hypercholesterolemia. It is also known that copper and zinc are essential for the development and maintenance of a healthy cardiovascular system.

Description:

Both in vitro and in vivo experiments are conducted. Extractions are performed to isolate metal-binding ligands from coal, analogously as from tobacco tar. Rats with specific nutritional deficiencies in zinc and copper are used so that slight aberrations in the metabolism of these metals can be magnified and more easily detected. In addition, the action of isolated ligands and their complexes on intact biological systems such as lung macrophages and tissue preparations are studied. The methods used include liquid extraction and liquid chromatography.

Publication:

1. Sorenson, J., H. Petering, P. Eller, and V. Finelli: Studies on Coal as a Source of Trace Metals and Metal Binding Ligands. Paper
2. Sorenson, J.R., et al.: The Concentration of Cd, Cu, Fe, Ni, Pb and Zn in Bituminous Coals from Mines with Differing Incidences of Coal Workers' Pneumoconiosis. A.I.H.A.J. pp. 1-22 (1973).

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 3 R01 OH 00356-02S1

Principal Investigator:

Robert T. Christian, Ph.D.  
Kettering Laboratory  
College of Medicine  
University of Cincinnati  
Cincinnati, Ohio 45219

Title:

Cellular Response to Coal Dust in Vitro CWP

Objectives:

The purpose of this research is the determination of: 1) the fractions of coal mine dust which are cytotoxic; 2) the mechanism of cellular injury by the cytotoxic fractions; and 3) the relationship between the toxic processes and coal workers' pneumoconioses (CWP).

Description:

This is an investigation in vitro at the cellular level using growing cell cultures and coal mine dust obtained from NIOSH. Part of the purpose of these studies is to develop a screening test to determine which fractions of coal mine dust are cytotoxic and then to investigate how the cytotoxicity is responsible for cellular injury.

Coal mine dust fractions are inoculated on primary and continuous-line human and other mammalian cell lines. Observations are then made of cell morphology, growth, and synthesis of collagen. Alveolar macrophages and primary lung cells are used to determine effects of the test materials on host defense mechanisms. Techniques of cytochemistry, phagocytosis, and bactericidal potential are employed as is time-lapse cinematography. Stimulation and inhibition of interferon are studied.

The effects on collagen production of the test materials on cultures of fibroblasts are determined. Tissue cultures are exposed to certain toxic fractions and then tested for syntheses of DNA and RNA using standard techniques.

Publications:

1. Christian, R. T., et al.: Cellular Response to Coal Mine Dust in Vitro - ABSTRACT In Vitro 7: (4) (1972).

OHIO STATE UNIVERSITY  
Columbus, Ohio

Grant Number: 5 R01 OH 00358-02

Principal Investigator:

Gary Warren Davis, D.V.M., Ph.D.  
Dept. of Veterinary Pathology  
The Ohio State University  
1925 Coffey Road  
Columbus, Ohio 43210

Title:

Pathophysiology of Coal Dust Pneumoconiosis in Equidae

Objectives:

This study is designed to establish whether or not the mine pony is a suitable model for the study of coal workers' pneumoconiosis (CWP). The technical objectives are: 1) to characterize the physiological parameters, primarily pulmonary and cardiovascular, in spontaneous coal pneumoconiosis and emphysema and in experimentally-induced pneumoconiosis in equidae exposed to coal dust; 2) to characterize the pathological changes in spontaneous coal pneumoconiosis and emphysema and in experimentally induced pneumoconiosis in the equidae; 3) to correlate the physiological parameters and the pathological findings in equidae exposed to coal dust; 4) to compare spontaneous coal pneumoconiosis and emphysema and the experimentally induced diseases in mine ponies with the naturally-occurring diseases in man and other animals; and 5) to establish the feasibility of using the mine pony as a model for future investigations in preventive, diagnostic, and therapeutic measures in the management of pneumoconiosis in man.

Description:

Using mine ponies which had been worked in coal mines and had thus been exposed to coal dust for periods of up to 15 to 20 years, a variety of cardiopulmonary and pathological investigations are carried out. It is known from other work that British mine ponies do develop lesions similar to CWP. Control animals and other experimental animals given intratracheal injections of coal dust slurry are also used in the investigations. Post mortem examinations are also performed. Measurements are made of cardiovascular, blood, and pulmonary functional parameters. Dynamic pulmonary compliance and morphometric analyses, to determine total alveolar surface and volume and pulmonary capillary surface and volume, are made. Quantitation of silica and histopathologic studies are performed. It is anticipated that the CWP in ponies will be found to be an ideal model for the condition in human beings.

Publications: none

MARSHFIELD CLINIC FOUNDATION  
Marshfield, Wisconsin

Grant Number: 5 R01 QH 00306-13

Principal Investigator:

Dean A. Emanuel, M.D.  
Marshfield Clinic Foundation for  
Medical Research and Education  
510 North St. Joseph's Ave.  
Marshfield, Wisconsin 54449

Title:

Farmer's Lung - An Experimental Investigation

Objectives:

Research aims are directed principally toward: 1) the isolation and characterization of the etiologic agents (thermophilic actinomycetes) of farmer's lung disease; 2) the investigation of the cellular response in this hypersensitivity disease; 3) the determination of the disease incidence in the U.S. and Canada; 4) the description of an immune process in animals; and 5) the characterization of farmer's lung either as a true delayed hypersensitivity or perhaps a modified Arthus reaction. Secondary objectives include, 1) attempts to correlate the amount of rainfall during the haying season and the incidence of disease in the following Spring, and 2) the attempted characterization of the antigens in farmer's lung.

Description:

This is largely an experimental investigation to identify and characterize the causative organisms of farmer's lung disease and to describe the associated immunology. A fluorescent antibody technique which has been developed for the identification of Thermopolyspora polyspora, one of the agents involved in the disease, is being adapted for studying other similar organisms in the lung tissue of patients with farmer's lung disease. The incidence of sensitivity has been found to be 13 per cent, from a study of more than 1000 patients. Elucidation of environmental factors involved in farmer's lung disease should be very helpful in the development of effective preventive methods.

Publications:

1. Wenzel, F.J., D.A. Emanuel, and P.M. Zygowicz: Simplified Serologic Test for Farmer's Lung. Am. J. of Clin. Path. 49: (2) 183-185 (1968).

## MARSHFIELD CLINIC FOUNDATION

2. Emanuel, D.A.: Farmer's Lung - Historical Review and Current Concepts. (May 8, 1968).
3. Hursma, J.R., D.A. Emanuel, F.J. Wenzel and R.L. Gray: Farmer's Lung in a 10 Year Old Girl. J. of Peditc. 75: (4) 704-706 (October 1969).
4. Gray, R.L., F.J. Wenzel, and D.A. Emanuel: Immunofluorescence Identification of Thermopolyspora polyspora, The Causation Agent of Farmer's Lung. Appld. Micro. 17: (3) 454-456 (March 1969).
5. Wenzel, F.J., D.A. Emanuel, and R.L. Gray: Farmer's Lung, Its Geographic Distribution. J. Occ. Med. 12: (12) 493-496 (December 1970).
6. Wenzel, F.J., D.A. Emanuel and R.L. Gray: Immunofluorescent Studies in Patients with Farmer's Lung. J. Allergy & Clin. Immuno. 48: (4) 224-229 (October 1971).
7. Emanuel, D.A., et al.: Farmer's Lung Disease. Hoard's Dairyman 117: 649 (1972).
8. Wenzel, F.J., et al.: A Simplified Hemagglutination Test for Farmer's Lung. Amer. J. Clin. Path. 57: (2) (February 1972).
9. Emanuel, D.A., et al.: Farmer's Lung. Conn's Current Diagnosis 3: Saunders, Philadelphia (1971).

MOUNT SINAI SCHOOL OF MEDICINE  
New York, New York

Grant Number: 5 R01 OH 00320-06

Principal Investigator:

Irving J. Selikoff, M.D.  
Mt. Sinai School of Medicine  
City University of New York  
5th Ave. and 100 St.  
New York, New York 10029

Title:

Relation of Smoking to Neoplasia in Asbestos Workers

Objectives:

This prospective study of some 18,000 asbestos insulation workers is designed to test earlier observations that cigarette smoking is highly related to the very great excess of asbestos lung cancers in asbestos workers, as compared with non-cigarette-smoking asbestos workers who may also have a somewhat elevated risk of neoplasia.

Description:

The investigations include detailed case history studies of some 450 men whose occupational exposure to asbestos had begun some 20 years prior to the onset of this study. Medical and physical examinations as well as case histories and questionnaires are used in the epidemiological investigation. There are strong suggestions in the findings that there is a real and important association between cigarette smoking and the development of lung cancer in asbestos workers.

Publications:

1. Selikoff, I.J. and E.C. Hammond: III Community Effects of Non-Occupational Environmental Asbestos Exposure. Am. J. Pub. Hlth. 58: (9) 1658-1666 (September 1968).
2. Selikoff, I.J.: Asbestos. Environment 11: (2) 1-7 (March 1969).
3. Langer, A.M., I. Rubin, and I.J. Selikoff: Electron Microprobe analysis of Asbestos Bodies. Pneumo., Proc. Int'l. Conf., Johannesburg, p. 57-69 (1969).

MOUNT SINAI SCHOOL OF MEDICINE

4. Selikoff, I.J. and E.C. Hammond: Asbestos Bodies in the New York City Population in Two Periods of Time. *Pneumo., Proc. Int'l. Conf., Johannesburg*, p. 99-105 (1969).
5. Hammond, E.D. and I.J. Selikoff: The Effects of Air Pollution - Epidemiological Evidence. *Pneumo., Proc. Int'l. Conf., Johannesburg*, p. 368-373 (1969).
6. Selikoff, I.J., E.C. Hammond, and J. Churg: Mortality Experiences of Asbestos Insulation Workers - 1943/1968. *Pneumo., Proc. Int'l. Conf., Johannesburg*, p. 180-186 (1969).
7. Langer, A.M. and I.J. Selikoff: Chrysotile Asbestos in Lungs of Residents of New York City. *Procs. of 2nd Int'l. Clean Air Congress*, p. 161-164 (1971).
8. Langer, A.M., V. Baden, E.C. Hammond, and I.J. Selikoff: Inorganic Fibers, Including Chrysotile, in Lungs at Autopsy: Preliminary Report. *Inhaled Particles III, Proc. Int. Symp. 2: London* 683-694 (1971).
9. Selikoff, I.J., E.C. Hammond, and H. Heimann: Critical Evaluation of Disease Hazards Associated with Community Asbestos Air Pollution. *Proc. 2nd Int'l. Clean Air Congress*, p. 165-171 (1971).
10. Langer, A.M., I.J. Selikoff, and A. Saster: Chrysotile Asbestos in the Lungs of Persons in New York City. *Arch. Env. Hlth.* 22: 348-361 (March 1971).
11. Selikoff, I.J., et al.: Asbestos Exposure to Coke Oven Operators. *J. of Occ. Med.* 13: (10) 496-497 (October 1971).
12. Selikoff, I.J.: Asbestos. *Our World in Peril: An Environment Review* pp. 362-373 (1971).

WAYNE STATE UNIVERSITY  
Detroit, Michigan

Grant Number: 5 R01 OH 00323-07

Principal Investigator:

Andrew L. Reeves, Ph.D.  
1400 Chrysler Freeway  
Detroit, Michigan 48207

Title:

Experimental Asbestos Carcinogenesis

Objectives:

The aims of this research project, in the investigation of experimental asbestos exposures, are: to characterize physically, chemically, and biologically the dusts before, and after, dissemination and to compare them with the UICC (International Union Against Cancer) referenced standards; to identify specific types of asbestos *in situ*; to examine biological changes in lung tissue; and to study detectable changes in pulmonary function in exposed animals.

Description:

This is a chemical, biological, physical, and pathological investigation of asbestos and its forms, (i.e. amosite, chrysotile, and crocidolite) and a study of possible associated induction of pulmonary cancer and malignant pleural mesothelioma. Dose-response relationships are studied. Electron microscope examinations of asbestos bodies are performed for analysis and characterization.

Publications:

1. Davis, H.V., et al.: Collagen Biosynthesis in Rats Lungs During Exposure to Asbestos. *AIHA J.* 32: (9) 599-602 (September 1971).
2. Reeves, A.L., et al.: Experimental Asbestos Carcinogenesis. *Environ. Res.* 4: 496-511 (1971).

INDUSTRIAL HYGIENE FOUNDATION  
Pittsburgh, Pennsylvania

Grant Number: 8 R01 OH 00326-04

Principal Investigator:

Paul Gross, M.D.  
Industrial Health Foundation, Inc.  
5231 Centre Ave.  
Pittsburgh, Pennsylvania 15232

Title:

Asbestos Dusts: Their Pathogenic Components

Objectives:

This investigation is directed toward defining the possible factors responsible for the biologic activity of dusts of the three most commonly used forms of asbestos, chrysotile, amosite, and crocidolite. The rationale of this study is based on the belief that the biologic activity of asbestos is not inherent in the hydrated silicate molecule nor in its fibrous morphology. Instead, it is believed that much of the biologic activity resides in some factors that become added to the mineral after it has been mined. During the crushing process of separating the mineral from extraneous rock and during the further crushing for "opening" the fibers, extensive, intimate, and forceful contact is made with steel alloys which may transfer to the asbestos fibers metallic additives such as iron, nickel, cobalt, chromium, and manganese. These may be somehow implicated in carcinogenesis since the prevalence of lung cancer among nickel and chromium workers is generally recognized.

Description:

This is an investigation in experimental animals (rats and hamsters) of the carcinogenic effects of asbestos fibers contaminated with several heavy metals and with hydrocarbons. Results indicate that asbestos fibers of the three most commonly employed minerals, chrysotile, amosite, and crocidolite, when contaminated with nickel, chromium, and cobalt, produced a "high prevalence of lung cancers" in rats while fibers not so contaminated did not produce malignancies.

Publications: none

INDUSTRIAL HEALTH FOUNDATION  
Pittsburgh, Pennsylvania

Grant Number: 1 R01 OH-00354-01

Principal Investigator:

Paul Gross, M.D.  
5231 Centre Avenue  
Pittsburgh, Pennsylvania 15232

Title:

Dose Effect Relationship of Asbestos Dust

Objectives:

The aim of this investigation is to determine the differences which may exist in the lungs of two series of rats which had been dosed with asbestos some years earlier, in a previous study and:

1) developed primary lung cancer following inhalation or intratracheal injection of chrysotile asbestos, and 2) did not develop lung cancer following the administration of chrysotile asbestos under identical conditions.

Description:

The previously dosed animal lungs, which have been preserved in formalin for several years, are examined for asbestos content. A total of 132 rats are involved. All animals were dosed by inhalation or intratracheal injection, with chrysotile asbestos. Of these, 71 also received intratracheal applications of five percent sodium hydroxide solution which damaged the clearance mechanism of the lungs. These animals showed a 48 percent cancer rate as contrasted with a 24 percent rate in the rats which did not receive the sodium hydroxide treatment.

The preserved rat lungs are examined for concentrations of asbestos dust in those organs of animals that inhaled the dust and in those which received the dust by intratracheal injection. Comparisons are made of asbestos content in the cancerous and non-cancerous lungs and in the lungs of sodium hydroxide-treated and non-treated animals. Dose-effect relationships are sought.

Publications: none

LOS ANGELES COUNTY HEALTH DEPARTMENT  
Los Angeles, California

Grant Number: 1 R13 OH 00447-01

Principal Investigator:

Harold V. Brown, Dr. P.H.  
c/O University of California  
Environmental Health & Safety Office  
Center for Health Sciences  
Los Angeles, California 90024

Title:

Symposium - Asbestos and Asbestos-Related Diseases

Objectives:

The objectives of this conference are to attract about 200 industrial hygienists, nurses, physicians, safety engineers, and a limited number of employees and employers for the purpose of reviewing the epidemiology, minerology, geology, industrial uses, and pathologic effects associated with handling asbestos. To be discussed also are threshold limit values, air sampling, and evaluation, and control measures.

TULANE UNIVERSITY SCHOOL OF MEDICINE  
New Orleans, Louisiana

Grant Number: 5 R01 OH 00387-02

Principal Investigator:

Morton M. Ziskind, M.D.  
Department of Medicine  
Tulane University School of Medicine  
1430 Tulane Avenue  
New Orleans, Louisiana 70112

Title:

Accelerated Silicosis in Sandblasters

Objectives:

The aim of this investigation is to characterize the accelerated form of the disease (as contrasted with the classical chronic form) in terms of its clinical course, roentgenographic, pulmonary functional, pathologic and immunologic features and their relationship to intensity and duration of exposure.

Description:

This is essentially a clinical investigation of "accelerated" or rapidly progressive occupational silicosis. Populations of silicosis sufferers which are investigated are screened by means of a standard interview, chest x-ray, and basic pulmonary function studies. Epidemiologic data are collected and correlated with occupational exposures and diagnoses. An extensive follow up of subjects is contemplated.

Publications: none

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 8 R01 OH-00335-03

Principal Investigator:

E. Bingham Mattheis, Ph.D.  
Kettering Laboratory  
Eden & Bethesda Avenues  
Cincinnati, Ohio 45219

Title:

Response of Alveolar Macrophages to Metals

Objectives:

The aim of this investigation is to explore the relationship that may exist between disturbances of the pulmonary macrophage system and resultant impairment of the natural human resistance to typical industrial exposures to metals, specifically, lead, nickel, and zinc.

Description:

This investigation which is conducted in rats, is designed to investigate the influence of lead, nickel, and zinc particulates on the number and biological activity of alveolar macrophages as well as the dose-response relationships, and reversibility and specificity of response. Soluble and insoluble metal or metal salt particulates are administered to laboratory animals via the respiratory exposure route. Viability, phagocytic index, and production of interferon of alveolar macrophages are measured. Studies on the stimulation of interferon involve inoculation of alveolar macrophage cultures with parainfluenza virus or synthetic interferon inducer, harvesting the interferon at various time intervals, and titrating against vaccinia virus.

Publications: none

WEST VIRGINIA UNIVERSITY  
Morgantown, West Virginia

Grant Number: 5 R01 OH 00360-02

Principal Investigator:

Robert Burrell, Ph.D.  
Dept. of Microbiology  
West Virginia University Medical Center  
Morgantown, West Virginia 26506

Title:

Immune Injury in Occupational Respiratory Diseases

Objectives:

The twofold aims of this work are: 1) to assess the role of lung connective tissue antibody in the pathogenesis of selected infectious diseases and its role on normal lung, as measured by histological and pulmonary function techniques, and 2) to attempt to establish an experimental model of extrinsic allergic alveolitis using fungal spores and ovalbumin as antigens. An assessment of the possible role of an Arthus mechanism in such diseases is emphasized by quantitative precipitation analysis, immunofluorescence, and pulmonary function studies.

Description:

This is a bipartite but interrelated study in the attempt to develop an animal model system of the role of lung antibody in chronic pulmonary disease characterized by fibrosis and irreversible parenchymal changes. The information obtained from the model system is used to attempt interpretations of the same type of changes caused by inhalation of materials such as coal dust, silica, etc. (pneumoconioses). The effects of anti-lung sera on the pulmonary function of normal animals is also studied. Earlier work has indicated that anti-lung antibodies are produced in chronic lung disease and may be involved in the continuation of the fibrotic process.

The second aspect of this study is the attempt to define the immune reaction in the so-called extrinsic allergic alveolitis, a term proposed for those chronic lung diseases caused by the inhalation of organic dusts. *Penicillium* is used as the sensitizing agent in the animal model, in the attempt to determine whether or not an Arthus mechanism is involved. Precipitating antibody levels and lung histologic changes are determined.

## WEST VIRGINIA UNIVERSITY

In addition, two sub-projects are described. In an animal system, the determination is made whether or not delayed hypersensitivity is involved in berylliosis. Secondly, the determination is attempted to characterize the type of immune process in byssinosis.

### Publications:

1. Burrell, R. and C.C. Cate: The Effect of Lung Reactive Antibodies on the Pathogenesis of Tuberculosis. Clin. & Exper. Immuno. 9: (6) 809-819 (1971).

UNIVERSITY OF SOUTH FLORIDA  
Tampa, Florida

Grant Number: 1 R01 OH 00435-01

Principal Investigator:

Hollis G. Boren, M.D.  
Veterans Administration Center  
Tampa, Florida

Title:

Autoradiographic Response of Lung to Inhaled Agents

Objectives:

This research aims to develop information on effects of exposures to atmospheres of nitrogen dioxide (NO<sub>2</sub>), iron oxide (Fe<sub>2</sub>O<sub>3</sub>), titanium dioxide (TiO<sub>2</sub>), and cigarette smoke with the objective of relating the information to considerations of air quality standards, to human diseases related to inhaled agents, and to fundamental factors controlling DNA synthesis.

Description:

This is an animal experimental study in golden hamsters with the specific technical objectives of: 1) the determination of which cell populations respond to different types of inhaled agents; 2) the assessment of the relationship of the duration of increased labeling found during recovery from exposure to the parameters of the exposure; and 3) the determination of the relationships of the labeling response to the functional capacities of the lung. Animals are exposed to the pollutant atmospheres containing the substances specified. The exposures are individual, repetitive, and sequential. Cellular response is measured autoradiographically using tritiated thymidine which is injected intraperitoneally prior to killing the animals for assay. The labeled compound is incorporated into the DNA of dividing cells. Cell replacement or turnover in the lungs or other organs following exposures is thus measured and evaluated.

Publications:

1. Boren, H.G.: Deposition and Removal of Carbon Particles by Fluorocarbon Breathing. Fed. Procs. 29: (5) 1737-1739 (September October 1970).

## PHYSICAL AGENTS

*Noise*



PENNSYLVANIA STATE UNIVERSITY  
University Park, Pennsylvania

Grant Number: 5 R01 OH-00341-02

Principal Investigator:

Paul L. Michael, Ph.D.  
Pennsylvania State University  
Box 30  
State College, Pennsylvania 16801

Title:

An Objective Method for Evaluating Ear Protectors

Objectives:

This endeavor is aimed at the "development of a device" (artificial model head) and techniques for use in the measurement of effectiveness of ear protectors, "objectively."

Description:

The investigator is testing ear-muff and ear-insert devices for effectiveness in ear protection against excessive noise. Factors such as adequate fit and design are examined. Comparasins are made with the current American Standard Method.

Publication:

Michael, P.L. and D.F. Bolka: Personal Ear Protection Evaluation - Present and Future. Am. Indus. Hyg. Assoc. J. 32: (11) 753-756 (November 1971).

UNIVERSITY OF MINNESOTA  
Minneapolis, Minnesota

Grant Number: 5 R01 OH 00350-03

Principal Investigator:

W. Dixon Ward, Ph.D.  
University of Minnesota  
Box 461 Mayo  
Minneapolis, Minnesota 55455

Title:

Damage-Risk Criteria for Intermittent Noise Exposures

Objectives:

This research seeks to validate the proposed hypothesis that any pattern of noise exposure over an eight hour period of time is safe if the resultant auditory fatigue (temporary threshold shift or TTS) has disappeared after 16 hours of rest.

Description:

Normal-hearing young adult human beings (10 students) are exposed for eight hours to simulated industrial noise patterns with duty cycles of 2, 10, and 50 minutes and on-fractions of 0.5, 0.25, and 0.125. The intensity level for each pattern is gradually increased in successive sessions until that TTS is produced which is just barely recoverable in 16 hours. The resultant data are meant to improve the definition of noise which leads to permanent threshold shift (PTS).

Publications: none

STATE OF NEW YORK UPSTATE MEDICAL CENTER  
Syracuse, New York

Grant Number: 5 R01 OH 00364-02

Principal Investigator:

Donald Henderson, Ph.D.  
Upstate Medical Center  
Department of Otolaryngology  
750 E. Adams Street  
Syracuse, New York 13210

Title:

The Effects of Impulse Noise on Auditory System

Objectives:

This investigation seeks to determine the relationship between the physical parameters of an impulse noise (i.e. amplitude, duration, spectral content, etc.) and the concomitant psychophysiological effects on the inner ear and on hearing. The goal is the establishment of safe damage-risk criteria for impulse noise.

Description:

This is an animal experimental investigation using the chinchilla. Changes in the anatomy and physiology of the inner ear, of exposed animals, are monitored by means of phase contrast microscopy and surface preparation of the cochlea. Sonic booms are also used as stimuli. In addition to anatomic and physiologic changes, observations are made of temporary threshold shifts (TTS) resulting from exposures to the stimuli.

Publications: none

1. Eames, B.L., et al.: The Role of the Middle Ear in Acoustic Trauma from Impulses. State University of New York ABSTRACT 1973.
2. Salvi, R.J., et al.: Cochlear Nucleus Neurons Response to TTS Producing Noise. State University of New York. ABSTRACT 1973.
3. Henderson, D., et al.: Evoked Response Audibility Curve of the Chinchilla. State University of New York. ABSTRACT 1973.

STATE OF NEW YORK UPSTATE MEDICAL CENTER

4. Henderson, D., et al.: Audiometric and Anatomical Correlates of Impulse Noise Exposure. State University of New York ABSTRACT 1973.
5. Hamernik, R.P., et al.: Impulse Noise Trauma: A Study of Histological Susceptibility. State University of New York. ABSTRACT 1973.
6. Henderson, D., et al.: Audiometric and Histological Effects of Exposure to 40 U-Sec High Level Impulses. State University of New York. ABSTRACT 1973.
7. Sitler, R., et al.: The Temporary and Permanent Threshold Shifts Produced by Three Levels of Impulse Noise. State University of New York. ABSTRACT 1973.
8. Henderson, D., et al.: A Comparison Between Hair Cell Losses and Permanent Threshold Shifts Produced by Three Levels of Impulse Noise. State University of New York. ABSTRACT 1973.
9. Hamernik, R.P., et al.: Cochlear Degeneration Following Impulse Noise Exposure. State University of New York. ABSTRACT 1973.
10. Hamernik, R.P., et al.: Impulse Noise: Some Electrophysiological and Anatomical Effects. Seventh International Congress on Acoustics, Budapest 1971 (pp. 381-384).

## PHYSICAL AND CHEMICAL ANALYSIS



MASSACHUSETTS DEPARTMENT OF LABOR AND INDUSTRIES  
Boston, Massachusetts

Grant Number: 5 R01 OH 00309-15

Principal Investigator:

Leonard D. Pagnotto, M.S.  
39 Boylston Street  
Boston, Massachusetts 02116

Title:

Factors Affecting the Excretion of Industrial Poisons

Objectives:

This very practically oriented investigation seeks to correlate industrial exposures to noxious materials with analytical determinations of corresponding metabolic products which may be found in the urine. This is directed toward the industrial health hazards for which data are either lacking or are unreliable.

Description:

In this applied laboratory and field program, urine is studied as the indicator fluid in industrial toxin exposures. Foundry workers' urine is examined for excretion of lead, zinc, and copper as compared with the urine of appropriate control populations not exposed to the metals. Similarly, metabolic products of such industrial chemicals as trichloroethylene, methy ethyl ketone, acetone, and other organic solvents are investigated in urine and correlated with temporal occupational exposures. Stainless steel welders' urine is examined for excretion of nickel and other metals. The developed results can serve useful purposes in control and elimination of recognized industrial poison hazards.

Publications:

1. Elkins, H.B.: Exposure Tests in Industrial Toxicology. J. Int'l. Union of Pure and Appld. Chem. 18: 143-150 (1969).
2. Pagnotto, L.D. and C.B. Killian: Measurement of Tritiated Organic Compounds in the Presence of Tritiated Water in Urine. Am. Indus. H. Assn. J. 30: 407-412 (August 1969).
3. Elkins, H.B. and L.D. pagnotto: The Specific Gravity Adjustment in Urinalysis. Arch. Env. Hlth. 18: 996-1001 (June 1969).

MASSACHUSETTS DEPARTMENT OF LABOR AND INDUSTRIES

4. Holland, H.D.: Benzene Exposure of Furniture Strippers. Report: Commonwealth of Mass., Dept. of Labor & Industries, Div. of Occup. Hyg., Boston (July 1971).
5. Cuzacq, G., M. Comproni and H.L. Smith: Mercury Contamination in the Dental OH Office. J. of Mass. Dental Soc. (Fall 1971).

WOFFORD COLLEGE  
Spartanburg, South Carolina

Grant Number: 5 R01 OH 00324-05

Principal Investigator:

B.G. Stephens, Ph.D.  
Department of Chemistry  
Wofford College  
Spartanburg, South Carolina 29301

Title:

Extraction of Metal Complexes by Propylene Carbonate

Objectives:

The aim of this project is to establish propylene carbonate as a metal extractant of general utility, thereby replacing several more toxic solvents such as chloroform, carbon tetrachloride, diethylether, and nitrobenzene.

Description:

In straightforward chemical extraction procedures, the investigator uses propylene carbonate, under a wide variety of conditions, to extract metal and non-metal chelate complexes. Recognized analytical methods, techniques, and instruments are employed to collect data which have applicability not only for toxicology but also for analytical chemistry.

Publication:

Stephens, B.G.: Propylene Carbonate Extraction of Tris (pentan-2,4-dione)-ion (III) from Aqueous Solution: Application to the Spectrophotometric Determination of Iron. Analyst 96: 230-234 (March 1971).

UNIVERSITY OF NEVADA  
Reno, Nevada

Grant Number: 5 R01 OH 00332-03

Principal Investigator:

Ross W. Smith, Ph.D.  
University of Nevada  
Reno, Nevada 89507

Title:

Aqueous Surface Chemistry of Asbestos Minerals

Objectives:

These investigations have as their goal the elucidation of the origin of charges of silicates in aqueous media so as to provide insights to their physiological behavior.

Description:

The researchers are conducting measurements of the various properties of silicate minerals, particularly as these properties relate to the surface chemical behavior of the minerals in aqueous solution and suspension. Composition, morphology, physical chemistry, including electrophoretic characteristics, and colloidal properties of charged particulates are being investigated. Turbidimetry (light scattering) as well as dispersion characteristics are being studied. It is anticipated that the information developed will have relevance to the behavior of asbestos particles in vivo.

Publications:

1. Choi, I., et al.: Kinetic Study of Dissolution of Asbestos Fibers in Water. J. Colloid & Interface Science 4: (2) 253-262 (August 1972).

PHYSIOLOGY

*Respiratory*

*Heat Stress*



UNIVERSITY OF ROCHESTER  
Rochester, New York

Grant Number: 2 R01 OH 00334-04

Principal Investigator:

Juraj Ferin, Ph.D.  
University of Rochester  
Department of Radiation Biology & Biophysics  
Rochester, New York 14620

Title:

Influence of Airborne Factors on Lung Clearance

Objectives:

This project is designed to investigate the normal mechanisms of clearance of particles from the respiratory tract and the influence of various airborne factors and some drugs on clearance. The information developed is anticipated to be useful in determining the biological effects of air pollutants.

Description:

Investigation in animals, under controlled conditions, are conducted with test aerosols of specific particulate sizes and other characteristics. Measurements are made, immediately on exposure and at later times, of amounts deposited and their location in the respiratory tract.

The amount of the test aerosol deposited is determined chemically in the case of  $\text{TiO}_2$  and  $\text{SiO}_2$  and by radioisotopic methods in the case of  $\text{Fe}_2^{59}\text{O}_3$ .

By means of the  $\text{TiO}_2$  test system in which animals (rats) are exposed and then serially sacrificed, variations in alveolar clearance are investigated. This system which has been developed by the investigator, has been used to determine the effect (suppressive) of a number of air pollutants such as sulfur dioxide, amosite, and chrysotile on lung clearance. The use of papain to induce emphysema has also demonstrated a suppressive effect. The investigator's thesis that impairment of the alveolar clearance mechanism could result in retention of harmful substances in the lung is an interesting but not unique idea. It remains to be established.

## UNIVERSITY OF ROCHESTER

Histologic examinations are performed using both light and electron microscopy and the electron microprobe. The materials under investigation include asbestos, coal and cement dusts, cigarette smoke and various irritant vapors. Drugs of interest are those which affect the reticuloendothelial system.

### Publications:

1. Ferin, J.: Papain-Induced Emphysema and the Elimination of  $\text{TiO}_2$  Particulates from the Lungs. AIHA J. 32: 157-162 (March 1971).
2. Ferin, J.: Emphysema in Rats and Clearance of Dust Particles. University of Rochester, New York (1971).
3. Ferin, J.: Observations Concerning Alveolar Dust Clearance. Ann. of N.Y. Acad. of Sciences 200: 66-72 (December 29, 1972).

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 5 R01 OH 00357-02

Principal Investigator:

Eula B. Mattheis  
Dept. of Environmental Health  
University of Cincinnati  
Kettering Laboratory  
Cincinnati, Ohio 45219

Title:

Fate of Inhaled Coal Dust

Objectives:

The aim is to evaluate the fate of inhaled coal dust in relation to lung storage, translocation to the G.I. tract, body tissues and fluids, and extraction of coal components by body fluids.

Description:

This is an experimental animal investigation using normal rabbits and rats and animals with papain-impaired lungs (emphysema). The rabbits and rats are exposed to high and extremely high concentrations of coal dust in test chambers which simulate concentrations of coal dust to be encountered by miners in coal mines. Coal samples are characterized as to size, shape, surface area, and content of silica, beryllium, vanadium, cobalt, titanium, total volatiles, polynuclear aromatic hydrocarbons, and ash. After exposures, observations are made in the normal and lung-impaired animals. Quantitative differences are measured of the relative fates of the dust in the normal and abnormal animals. Determinations are made after a three-month's exposure period and after an additional three month's clearance period. Solubilities of coal fractions are determined in lung fluid, serum, and urine and extractibles are measured and identified.

Publications: none

UNIVERSITY OF PITTSBURGH  
Pittsburgh, Pennsylvania

Grant Number: 5 R01 OH 00367-02

Principal Investigator:

Yves C. Alarie, Ph.D.  
University of Pittsburgh  
Dept. of Occupational Health  
Graduate School of Public Health  
130 DeSoto Street  
Pittsburgh, Pennsylvania 15213

Title:

Respiratory Tract Irritants: Mechanisms & Tolerance

Objectives:

This work is aimed at delineating the mechanisms of sensory irritation and stimulation and the development of tolerance with frequent and repeated exposures to airborne chemicals. The work also seeks to demonstrate the importance of the "nasal trigeminal chemoreception phenomenon" in initiating protective mechanisms (relevant to man) to airborne chemical irritants.

Description:

This is an experimental animal investigation (rabbits and mice) of: 1) the correlation between chemical structures and their abilities to stimulate nerve endings in the upper respiratory tract; 2) the characteristics of the sensory stimulation of the trigeminal nerve by the various chemicals; 3) the persistence of the respiratory and cardiovascular reflexes induced by o-chlorobenzylidene malononitrile, beta-nitrostyrene, and diphenylaminochloroarsine during prolonged exposures to these chemicals; 4) the possible synergistic actions of various chemicals in stimulating the endings of the nasociliary nerve; 5) the possible induced tolerance by repeated exposures of aerosols of capsaicin on the nasociliary nerve; and 6) the specificity of this tolerance to the inducing chemical.

This work has considerable public health significance in that it may make possible the identification of those gases that produce a tolerance to irritation.

Publications: none

NEW YORK UNIVERSITY MEDICAL CENTER  
New York, New York

Grant Number: 1 R01 OH 00396-01

Principal Investigator:

Edward D. Palmes, Ph.D.  
New York University Medical Center  
Institute of Environmental Medicine  
550 First Avenue  
New York, New York 10016

Title:

Aerosol Deposition in Human Subjects

Objectives:

This endeavor is directed toward providing a rational understanding of the underlying dynamics of inhaled aerosols as relatable to industrial dust exposures. More specifically, the effort is aimed at determining the fate of aerosols inhaled by human beings.

Description:

This project has essentially a biphasic character:

1. an investigation of the influence of physiologic and anatomic factors on deposition of aerosols in the human respiratory tract, and
2. the development of a simple, rapid screening procedure for measuring aerosol deposition in human populations, under conditions applicable to those in working environments. The rationale of the principal direction of this project resides in the reasonable concept that any given particle of known size and shape is deposited in a shorter time if it is confined in a smaller rather than larger space.

The investigation is carried out by using breath-holding and single breath techniques in human subjects. A new type of apparatus is also used with newly developed procedures to study steady-state breathing of aerosols. Presumably these techniques and procedures are useful in screening procedures such as may be employed for emphysema and other respiratory diseases and conditions.

Publications: None

UNIVERSITY OF PITTSBURGH  
Pittsburgh, Pennsylvania

Grant Number: 2 R01 OH 00308-17

Principal Investigator:

Harwood S. Belding, Ph.D.  
Graduate School of Public Health  
University of Pittsburgh  
130 DeSoto Street  
Pittsburgh, Pennsylvania 15213

Title:

Evolution of Stresses of Exposure to Heat

Objectives:

The long-range objectives are threefold: 1) to acquire better quantitative understanding of the factors determining the physiologic stresses resulting from exposure to hot environments and physical activity; 2) to relate the physical stresses so determined for man to the physiologic strains and overstrains resulting from exposure; and 3) to apply the generated information to the solution of health problems of populations at risk because they work or reside in hot climates.

Description:

This project deals essentially in generating information in the broad area of thermal physiology. There is both a practical as well as theoretical component to the effort. Practically, the role and influence of clothing in modifying thermal exchanges is investigated, whereas, on a theoretical level, consideration is devoted to studying the interrelationships which obtain between local and general stimuli and associated responses to thermal loads.

During the current phase of this project, industrial exposures to intermittent high heat levels are simulated in controlled environmental chamber laboratory settings. Physiologic responses such as body temperatures, heat rate, sweating, and sensations of fatigue are measured.

Heat tolerance of individuals is also tested by means of a new approach which involves exposure of persons, engaged in moderate work, to increasing graduated levels of ambient humidity. Responses are recorded as affected by age, sex, state of health, and acclimatization.

UNIVERSITY OF PITTSBURGH

Publications:

1. Kamon, E. and H.S. Belding: Heat Uptake and Dermal Conductance in Forearm and Hand when Heated. J. Appld. Physiol. 24: 277-281 (1968).
2. Belding, H.S.: Work in Hot Environments. In Industrial Hygiene Highlights, Pittsburgh - Industrial Hygiene Foundation of America, pp. 214-228 (1968).
3. Kamon, E. and H.S. Belding: Dermal Blood Flow in the Resting Arm During Prolonged Leg Exercise. J. Appld. Phys. 26: 317-320 (1969).
4. Belding, H.S. (et al.): Health Factors involved in Working Under Conditions of Heat Stress. WHO Tech. Rept. Series #412 (32 pages) (1969).
5. Belding, H.S., E. Kamon, and G. Larson: Physiologic Cost of Load Carrying (Under Comfortable and Hot Conditions). Am. Indus. Hyg. Assoc. J. 30: 104 (1969).
6. Belding, H.S.: The Search for a Universal Heat Stress Index in Physiological and Behavioral Temperature Regulation, J.D. Hardy and A.P. Gagge, editors. Thomas; Springfield, Illinois, Ch. 13, pp. 193-212 (1970).
7. Kamon, E.: Negative and Positive Work in Climbing a Laddermill. J. Appld. Physiol. 29: 1-5 (1970).
8. Kamon, E. and H.S. Belding: The Physiological Cost of Carrying Loads in Temperate and Hot Environments. Human Factors 13: 153-161 (1971).

UNIVERSITY OF PITTSBURGH  
Pittsburgh, Pennsylvania

Grant Number: 5 R01 OH-00325-04

Principal Investigator:

David Minard, M.D., Ph.D.  
University of Pittsburgh  
130 DeSoto Street  
Pittsburgh, Pennsylvania 15213

Title:

Physiologic Responses to Work Stress in Steelworkers

Objectives:

The aim of this study is to provide information on physiological criteria for assessing job demands and for matching these with the physiological capacities of steelworkers, with particular reference to hot occupational environments.

Description:

Experimental and control groups of steelworkers are studied from the standpoint of physiological stress of muscular work, heat exposure, and resultant physiological effects. Such quantities as heart rate, aerobic capacity, cardiac rhythm, body temperature, and fatigue are studied before and after stress. Heat acclimatization and "job-conditioning" are investigated for their significance to the stress-effect relationship.

Publications:

1. Minard, D. and R. Goldsmith: Heart Rate Responses to Industrial Heat Stress. Symposium Int'l., p. 342-345 (1970).
2. Minard, D., R. Goldsmith, P.H. Farrier, and B.H. Lambiotte: Physiological Evaluation of Industrial Heat Stress. AIHA J. 32: 17-28 (January 1, 1971).
3. Minard, David: Physiological Responses to Industrial Heat Stress. ASHRAE Symposium on Air Conditioning, Climatology and Health, Washington, D.C. (August 22, 1971).

INDUSTRIAL HEALTH FOUNDATION  
Pittsburgh, Pennsylvania

Grant Number: 1 R13 OH-00382-01

Principal Investigator:

Robert T.P. deTreville, M.D., Sc.D.  
Industrial Health Foundation  
5231 Centre Avenue  
Pittsburgh, Pennsylvania 15232

Title:

Industrial Contributions to Standards for Hot Jobs

Objectives:

This is a symposium convened as a follow-up of an earlier short workshop session in June 1971 which produced a Summary of Proceedings and a Guide for Assessing Heat Stress and Strains. The aim is to collect and assess human experience data both within and outside of American industry and to try to develop useful criteria and recommendations for useful safety and health standards for hot jobs.



## TOXICOLOGY AND PATHOLOGY

UNIVERSITY OF OKLAHOMA MEDICAL CENTER  
Oklahoma City, Oklahoma

Grant Number: 5 R01 OH 00312-08

Principal Investigator:

Carl A. Nau, M.D.  
Department of Environmental Health  
University of Oklahoma Medical Center  
800 Northeast 13th Street  
Oklahoma City, Oklahoma 73104

Title:

Occupational Health Hazards of Rubber Dust

Objectives:

This investigation, principally in laboratory experimental animals is designed to: 1) evaluate the biological effects of ingested rubber dust; 2) determine the long-term exposure effects of inhaled rubber dust; 3) elucidate the biochemical mechanisms involved in rubber dust exposures and consequent effects; and 4) improve the quantification of analytical methods and the associated interpretation of results.

Description:

Appropriately dispersed rubber dust has been successfully prepared and administered to monkeys, mice, and hamsters, in inhalation studies. Ingestion studies were performed in mice which were fed 10 per cent rubber dust mixed with their Rockland Chow. Paired feeding studies in rats is projected. Results of feeding studies indicated a shortening of life-span as well as a depression in growth, despite an increase in food consumption. This work, which has possible applicability to general environmental exposure as well as to occupational exposure of workers in garages and vehicular tunnels, is amenable to further quantitative and specific analyses and interpretations.

Publications:

1. Smith, C.G., C.A. Nau, and C.H. Lawrence: Separation of Identification of Polycyclic Hydrocarbons in Rubber Dust. Am. Indus. Hyg. Assoc. J. (29: pages 242-247 (May-June 1968).
2. Smith, C.W., S.H. Wender, and C.A. Nau: Growth and Free Proline Content of Tobacco Callus and HeLa Cells Exposed in Vitro to Rubber Dust and Carbon Black. Am. Indus. Hyg. Assoc. J. 30: 402-406 (July-August 1969).

PAN AMERICAN HEALTH ORGANIZATION  
Washington, D.C.

Grant Number: 5 R01 OH 00313-10

Principal Investigator:

Humberto Torloni, M.D.  
Pan American Health Organization  
525 23rd Street, N.W.  
Washington, D.C. 20037

Title:

Manganese Poisoning - A Metabolic Disorder

Objectives:

These investigations of the metabolic role of manganese are directed toward: 1) developing an understanding of the factors involved in manganese poisoning in miners; 2) delineating common characteristics of manganism and Parkinson's Disease; 3) promoting a rationale for effective biochemical therapy for both manganism and Parkinson's Disease.

Description:

This project effectively combines basic experimental sciences with clinical investigations. The effective utilization of the pharmaceutical, L-DOPA (3,4 - dihydroxy-L-phenylalanine), and 5-hydroxytryptophan in the experimental treatment of Parkinsonism offers promise in the treatment of manganese poisoning in human beings. Experiments are performed in laboratory animals to evaluate the effect of manganese on drug response as well as to study the dynamics of absorption of manganese oxide and manganese salts in healthy and in anemic animals. Chemical balance studies are performed in hospitalized miners on various therapeutic regimens including apomorphine, which has been demonstrated to be effective in the temporary improvement of miners. Alpha-methyl-DOPA-hydrazine is being investigated as a potentiator of the therapeutic effects of L-DOPA.

Publications:

1. Cotzias, G.C., P.S. Papavasiliou, and R. Gellene: Modification of Parkinsonism in Chronic Treatment with L-DOPA. New Eng. J. of Med. 280: 337-345 (February 13, 1969).

PAN AMERICAN HEALTH ORGANIZATION

2. Cotzias, G.C., K. Horiuchi, S. Fuenzalida, and I. Mena: Chronic Manganese Poisoning Clearance of Tissue Manganese Concentrations with Persistence of the Neurological Factor. *Neurology* 18: (4) 336-382 (April 1968).
3. Papavasiliou, P.S., S.T. Miller, and G.C. Cotzias: Role of Liver in Regulating Distribution and Excretion of Manganese, *Am. J. Phys.* 211: (1) 211-216 (July 1968).
4. Papavasiliou, P.S., S.T. Miller, and G.C. Cotzias: Functional Interactions Between Biogenic Amines, 3,5-Cyclic AMP and Manganese. *Nature* 220: (5172) 74-75 (October 5, 1968).
5. Cotzias, G.C.: Metabolic Modification of Some Neurologic Disorders, *JAMA* 210: (7) 1255-1262 (November 17, 1969).
6. Mena, I., K. Horiuchi, K. Burke, and G.C. Cotzias: Chronic Manganese Poisoning Individual Susceptibility and Absorption of Iron. *Neurology* 19: (10) 1000-1006 (October 1969).
7. Mena, I.: Perspectivas de la L. Dopa en la Enfermedad de Parkinson. ACTAS I<sup>o</sup> SIMPOSIO SUDAMERICANO SOBRE EL ESTADO ACTUAL DEL TRATAMIENTO EN LA ENFERMEDAD DE PARKINSON Y PARKINSONISMO, pp. 54-59 (1970).
8. Court, J., J.C. Kase, E. Palacios, and I. Mena: Tratamiento del Parkinsonismo Con L-Dopa. *Rev. Med. Chil* 99: 399-401 (1971).
9. Mena, I.: Levodopa, Involuntary Movements and Fusaric Acid. *JAMA* 218 (12) 1829 (December 20, 1971).
10. Mena, I.: La Barrera Hematoencefalica y Los Oligo-elementos: Manganeso. *Rev. Med. Chil* 100: 171 (1972).
11. Fernandez, O.: Modificaciones en la Absorcion de Citrato Ferroso Fe En La Rata Por El Uso De Atropina. *Rev. Med. Chile* 99: 808-811 (1971).
12. Orrego, H.: Effects of Anticholinergic Agents on the Intestinal Absorption of Fe Ferrous Citrate. *Amer. J. Dig. Diseases* 16: (9) 789-795 (September 1971).
13. Mena, I.: Susceptibility to Cold in Newborns of Levodopa-treated Rats. *Nature* 239:285-287 (September 1972).
14. Mena, I.: Low Survival of Offsprings of Levodopa Treated Rats. *ABST. Intersociety* 77-82; *Fed. Proc.* 31: 224 (Abst. 77), (1972).

HARVARD UNIVERSITY  
Boston, Massachusetts

Grant Number: 5 R01 OH 00315-10

Principal Investigator:

Sheldon D. Murphy, Ph.D.  
665 Huntington Ave.  
Boston, Massachusetts 02115

Title:

Biochemical and Physiologic Response to Toxic Stress

Objectives:

The overall objective of this project is to increase understanding of effects of, and physiological responses to, the toxic action of a variety of chemicals such as some hepatotoxic organic solvents, irritants, neurotoxins, and cholinesterase inhibitors. More specifically, the aim is to determine, in experimental animals, the nature of the stresses imposed by exposure to toxic chemicals and the animal's capacity to adapt to its environment as a consequence.

Description:

This is a four-phase experimental investigation of toxic stress and its consequent biochemical and physiologic responses. Phase 1 is a characterization of the properties of liver alkaline phosphatase after the administration of various toxic agents. Phase 2 is the comparison of effects of adrenocortical hormones (and of the adrenal gland itself) on acute toxicity, hepatotoxicity, and metabolism of aliphatic halogenated hydrocarbons. Phase 3 is the exploration of the relationship between anticholinesterase action of organophosphate insecticides and increased adrenocortical activity. Phase 4 is an investigation of drug effects and associated stress upon acrylamide neurotoxicity and an attempt to obtain biochemical "markers" to peripheral neuropathy.

Publications:

1. Murphy, S.D., and S. Malley: Stress-Inducible Liver Enzymes in Rats Given Hepatotoxic Chemicals. *Tox. Appld. Pharm.* 12: 317-318 (1968).
2. Szor, R.J. and S.D. Murphy: Effects of Phenobarbital and Dexamethasone on the Adrenocortical Response of Rats to Toxic Chemicals and Other Stress. *Tox. Appld. Pharm.* 14: 515-616 (1969).

HARVARD UNIVERSITY

3. Murphy, S.D.: Some Relationships Between Effects of Insecticides and Other Stress Conditions. Ann. of N.Y. Acad. of Sci. 160: (1) 366-377 (June 1969).
4. Murphy, S.D. and S. Malley: Effect of Carbon Tetrachloride on Induction of Liver Enzymes of Acute Stress or Corticosterone. Tox. & Appld. Pharm. 15: 117-130 (1969).
5. Szot, R.J.: Phenobarbital and Dexamethasone Inhibition of the Adrenocortical Response of Rats to Toxic Chemicals and Other Stresses. Tox. and Appld. Pharm. 17: 761-773 (1970).
6. Szor, R.J. and S.D. Murphy: Relationships Between Toxic Chemical Stress and Circadian Changes in Adrenocortical Activity. Fed. Procs. 29: (1970).

UNIVERSITY OF FLORIDA  
Gainesville, Florida

Grant Number: 5 R01 OH 00316-08

Principal Investigator:

Kenneth C. Leibman, Ph.D.  
University of Florida College of Medicine  
Dept. of Pharmacology & Therapeutics  
Gainesville, Florida 32601

Title:

Metabolism of Hydrocarbons and Related Toxicants

Objectives:

The investigator has, as his goal, the systematic study of the metabolic reactions of the carbon-carbon double bond and the effects of substituents on vicinal carbon atoms. The aim is to permit the prediction of the qualitative and quantitative aspects of metabolic reactions of double bonds in compounds more structurally complex than the ones studied.

Description:

This is a rather straightforward investigation in vitro of the ability of various biological systems (e.g. rat microsomal NADPH-requiring systems) to oxidize the test substances enzymically to primary oxidation products, such as epoxides and glycols. Investigations in vitro of other biological systems are similarly carried out. Compounds of interest, initially, are styrene, indene, dihydronaphthalene, heptachlor, and aldrin. Structure - function correlations are sought in the developed data.

Publications:

1. Leibman, K.C. and E. Ortiz: A Colorimetric Method for Determination of Glycols. *Analyt. Chem.* 40: (1) 251-252 (January 1968).
2. Leibman, K.C.: Actions of Insecticides on Drug Activity. *Int. Anes. Clin.* 6: (1) 251-260 (Spring 1968).
3. Leibman, K.C. and E. Ortiz: Oxidation of Indene in Liver Microsomes. *Molec. Pharm.* 4: (3) 201-207 (May 1968).

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4. Sunderman, F. and K. Leibman: Nickel Carbonyl Inhibition of Induction of Aminopyrine Demethylase Activity in Liver and Lung. *Can. Res.* 30: 1645-1650 (June 1970).
5. Leibman, K.C. and E. Ortiz: Oxidation of Cycloalkenes in Liver Microsomes. *Biochem. Pharm.* 20: 232-236 (1971).
6. Leibman, K.C. and E. Ortiz: Epoxide Intermediates in Microsomal Oxidation of Olefins to Glycols. *J. Pharm. & Exper. Therap.* 172: (3) 242-246 (February 1971).
7. Leibman, K.C. and R.W. Estabrook: Effects of Extraction with Isooctane Upon Properties of Liver Microsomes. *Molec. Pharm.* 7: (1) 26-32 (January 1971).
8. Chapman, S.K. and K.C. Leibman: The Effects of Chlordane, DDT, and 3- Methylcholanthrene Upon the Metabolism and Toxicity of Diethyl-4-Nitrophenyl Phosphorothionate (Parathion). *Tox. & Appl. Pharm.* 18: 977-987 (1971).
9. Leibman, K.C.: Reduction of Ketones in Liver Cytosol. *Xenobiotica* 1: (1) 97-107 (1971).
10. Leibman, K.C.: Studies on Modifiers of Microsomal Drug Oxidation. *Chem. Biol. Interac.* 3: 289-290 (1971).
11. Leibman, K.C. and E. Ortiz: Reduction and Hydroxylation of Terpene Ketones in Liver. *Fed. Proc.* 30: 226 (1971). ABST.
12. Leibman, K.C. and E. Ortiz: New Potent Inhibitors of Microsomal Drug Oxidations: The 1-Arylimidazoles. *Pharmacol.* 13: 223 (1971). ABST.
13. Naeger, L.L., et al.: Mechanisms of Decaborane Toxicity. *Tox. & Appl. Pharm.* 22: 517-527 (1972).
14. Deyrup, C.L., et al.: Metabolism of Cyclohexanone in Mammalian Liver. *Volunteer Abstracts.* 5 Int'l. Congr. Pharm. 57 (1972).
15. Herschleb, W.P., et al.: Microsomal Metabolism of Butadiene. *Fed. Procs.* 31: 559 (1972).

HARVARD UNIVERSITY  
Boston, Massachusetts

Grant Number: 5 R01 OH 00322-05

Principal Investigator:

John M. Peters, M.D.  
665 Huntington Ave.  
Boston, Massachusetts 02115

Title:

Health Hazards of the Di-Isocyanates

Objectives:

The general goals of this project are: to investigate the relationship between exposure to diisocyanates (toluene diisocyanate) and the development of acute and chronic respiratory disease; to define the patho-physiological lesion involved and to determine the toxic mechanism related to the exposure; to identify hypersensitive workers; and to define "safe" exposure levels.

Description:

This is a prospective monitoring study of workers exposed to diisocyanates and the attempt to correlate findings with past work history and future work experience. The investigations are interested, in addition to developing the information indicated in the objectives, in the possible effects of chronic diisocyanate exposure, the inter-relationships, if any, with smoking, and in carrying out various immunological studies to see whether or not sensitized workers demonstrate the presence of antibodies. Non-occupational exposures are also of interest. The permanence or reversibility of chemical changes and changes in ventilatory capacity are also studied.

Publications:

1. Peters, J.M., R.L.H. Murphy, L.D. Pagnotto, and W.F. Van Ganse: Acute Respiratory Effects in Workers Exposed to Low Levels of Toluene Diisocyanate (TDI). Arch. Env. Hlth. 16: 242-247 (May 1968).
2. Peters, J.M., R.L.H. Murphy, and B.G. Ferris: Ventilatory Function in Workers Exposed to Low Levels of Toluene Diisocyanate (TDI): A Six Month Follow-Up. Brit. J. Indus. Med. 26: 115 (1969).

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3. Peters, J.M., J. Mead, and W.F. Van Ganse: A Single Flow Volume Device for Measuring Ventilatory Function in the Field. Am. Rev. Resp. Dis. 99: 617-622 (1969).
4. Peters, J.M., R.L.H. Murphy, L. Pagnotto, and J.L. Whittenburger: Respiratory Impairment in Workers Exposed to "Safe" Levels of Toluene Diisocyanate (TDI) Arch. Env. Hlth. 20: 364-368 (March 1970).

UNIVERSITY OF OKLAHOMA  
Oklahoma City, Oklahoma

Grant Number: 5 R01 OH 00330-03

Principal Investigator:

Ronald L. Coleman, Ph.D.  
Department of Environmental Health  
University of Oklahoma Medical Center  
800 N.E. 13th Street  
Oklahoma City, Oklahoma 73104

Title:

Measuring Carbon Monoxide Effect with Trace Metals

Objectives:

This research project aims at assessing and evaluating the translocations of trace metals by carbon monoxide exposure, through the modification of enzyme metabolism.

Description:

Based on the hypothesis that exposure to carbon monoxide alters enzyme metabolism, resulting in trace metal translocations, investigations are conducted to measure the degree and effect of chronic exposure to carbon monoxide by means of evaluating the translocations of copper, cobalt, zinc, iron and magnesium in brain, heart, liver, lungs, kidney, spleen, blood serum, erythrocytes, and urine. Rats are the experimental organisms subjected to prolonged exposures for protracted periods of time.

Publications: none

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 2 R01 OH 00337-04

Principal Investigator:

Harold G. Petering, Ph.D.  
Kettering Laboratory  
Eden and Bethesda Aves.  
Cincinnati, Ohio 45219

Title:

A Study of Mechanisms of Occupational Cadmium Toxicity

Objectives:

This investigation, which originally was directed toward understanding the toxicity of cadmium and its interrelationships with copper and zinc metabolism, has been expanded to include iron metabolism. In addition, effects of concurrent administration of lead compounds and/or metal-binding ligands in air, tobacco smoke, or in certain drug preparations are also studied. The rationale behind this research is the belief that excessive occupational and environmental exposure to cadmium may lead to chronic diseases of the respiratory, cardiovascular, and hematopoietic systems and to other pathologies in man. The disease states of particular interest are: cadmium-induced hypertension, skin alterations, lung pathology, aberrations in lipid metabolism and cell respiration, and the chelation of zinc, copper, and cadmium with certain drugs or other ligands.

Description:

Using rats as the experimental animals, investigations of cadmium toxicity are performed in which the intakes of copper and zinc are carefully controlled at suboptimal and excessive levels. The effect of both quality and quantity of protein on cadmium toxicity, are also examined, including especially the significance of sulfur-containing amino acids in protein metabolism. Biochemical and pathologic studies which include complete tissue and blood analyses, some representative metalloenzyme determinations, respiratory activity and oxidative phosphorylation, and potassium transport in liver tissues, are carried out. The project includes study of gross pathology, organ histology, and electron microscopy of selected tissues.

Continuing experimental procedures in rats have shown that cadmium administration elevates systolic blood pressure and affects some of the metabolic relationships as well as the utilization of zinc and copper. Some of these effects were found to be mitigated by increasing the dietary intake of zinc or copper. The most obvious pathologic

## UNIVERSITY OF CINCINNATI

lesions due to cadmium intake, were found in focal emphysema of the lung, loss of capillaries of skin and testes, and focal atrophy of testes.

### Publications:

1. Petering, H.G., M.A. Johnson, K.L. Stemmer: Studies of Zinc Metabolism in the Rat. Arch. of Env. Hlth. 23: 93-101 (1971).
2. Petering, H.G.: Studies in Zinc Metabolism IV Interactions of Zinc and Cadmium. Preliminary Reports in the Dept. of Env. Hlth., Univ. of Cinti., Annual Report (1971).
3. Petering, H.G.: Cadmium in Tobacco and Its Fate During Smoking. Preliminary Reports in the Dept. of Env. Hlth., Univ. of Cinti., Annual Report (1971).
4. Petering, H.G.: Direct Determination of Cadmium and Lead in Diluted Plasma. Preliminary Reports in the Dept. of Env. Hlth., Univ. of Cinti., Annual Report (1971).
5. Petering, H.G.: In Vitro Distribution of Cadmium and Lead in Rat's Blood. Preliminary Reports in the Dept. of Env. Hlth., Univ. of Cinti., Annual Report (1971).
6. Sell, J.E. and H.G. Petering: Effect of Buffer System on Carbonic Anhydrase Activity in the Presence of EDTA or Peptone. Proc. of 2nd Central Regional Meeting of Amer. Chem. Soc., Columbus, Ohio, ABST. NO. 16, p. 27 (June 3-5, 1970).
7. Menden, E.E., et al.: Distribution of Cadmium and Nickel of Tobacco During Cigarette Smoking. Env. Sci. & Tech. 6: 830-832 (September 1972).

UNIVERSITA DEGLI STUDI DI MILANO  
Milan, Italy

Grant Number: 2 R01 OH 00339-03

Principal Investigator:

Enrico C. Vigliani, M.D.  
Via S Barnaba, 8  
20122 Milan, Italy

Title:

Chromosome Studies in Human Lead Poisoning

Objectives:

The investigators are seeking, in human populations occupationally exposed to abnormal lead absorption, correlative cytogenetic results as compared with those in matched normal control subjects. This work was originally prompted by a report in mice of chromosomal damage in experimental lead poisoning. (Muro, L.A. and Goyer, R.A., "Chromosome Damage in Experimental Lead Poisoning," Arch. Path. 87, 660, 1969).

Description:

This is a cytogenetic investigation of cultured human lymphocytes derived from populations with plumbism (industrial lead exposure only) as compared with control subjects with no known lead exposure. A retrospective cancer study in storage battery workers and a lead-tissue culture study, in vitro, are included.

The current phase of this research is directed primarily at expanding the number of subjects studied, especially for workers with "preclinical" intoxications and for workers no longer occupationally exposed to lead. The biological significance of chromosomal damage from lead is indeterminate, especially since abnormalities in cultured lymphocytes are present not only in workers with clinical lead poisoning but also in subjects with no clinical symptoms or signs of disease. Moreover, preliminary data indicate that these chromosomal abnormalities tend to disappear in a number of months or years, when the workers leave the offending work environment.

Publications:

1. Forni, A., et al.: Chromosome Changes in Preclinical and Clinical Lead Poisoning and Correlation with Biochemical Findings. Int. Symp. Env. Hlth. Aspects of Lead. October 2-6, 1972.
2. Forni, A., et al.: Incidence of Chromosome Changes and Correlation with Clinical and Biochemical Findings in Lead Poisoning. Proc. 1st Int'l. Symposium of Physicians of Chem. Industry (April 1972).

UNIVERSITY OF WASHINGTON  
Seattle, Washington

Grant Number: 5 R01 OH 00340-04

Principal Investigator:

Nedd R. Frank, M.D.  
University of Washington  
Dept. of Preventive Medicine  
Seattle, Washington 98105

Title:

Respiratory Effects of Inhaled Gases and Aerosols

Objectives:

This effort is directed toward investigating effects in vivo of low levels of ozone, nitrogen dioxide, and aerosols.

Description:

In animals (rabbits), which have been experimentally altered so as to have produced unilateral emphysematous-like lung disease by means of papain administration, procedures are performed to measure comparative factors of pulmonary mechanics and ozone uptake.  $Xe^{133}$  is used to measure distribution of ventilation and perfusion in control and diseased lung.

Measurements are also made of effects and changes in inspired oxygen and carbon dioxide administered in vivo to rabbits, on the number, lysosomal enzyme content, phagocytic activity (measured in vitro), and ultrastructure appearance of alveolar macrophages.

Publications:

1. Yokoyama, E., R. Yoder, and N.R. Frank: Distribution of  $^{35}S$  in the Blood and Its Excretion in Urine of Dogs Exposed to  $^{35}SO_2$ . Arch. Env. Hlth. 22: 389-395 (March 1971).
2. Frank, N.R., J.P. Flesch, and J.D. Brain: Effect of Ozone on Elastic Behavior of Excised Lungs of Dogs. Environ. Res. 4: (4) 343-354 (October 1971).
3. Frank, N.R., et al.: Comparative Sensitivity of Four Methods for Measuring Changes in Respiratory Flow Resistance in Man. J. of Applied Physiology 31: (6) 934-938 (December 1971).

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4. Frank, N.R.: Clean and Dirty Lungs. Air and Water Pollution, Colorado Assoc. Univ. Press, Boulder, Colorado (1972).
5. McJilton, C., et al.: Ozone Uptake Model for the Respiratory System. ABST. American Industrial Hygiene Conference, San Francisco, May 14-19, 1972.
6. Watanabe, S.: Functional and Structural Effects of Low Concentrations of Ozone in Cats. American Indust. Hyg. Conf., San Francisco, May 14-19, 1972.
7. Yokoyama, E., et al.: Respiratory Uptake of Ozone in Dogs. Arch. Env. Hlth. 25: 132-138 (August 1972).

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 5 R01 OH 00347-03

Principal Investigator:

Phyllis D. Kaplan, Ph.D.  
University of Cincinnati  
Eden and Bethesda Avenues  
Cincinnati, Ohio 45219

Title:

Biological Interactions of Environmental Metals

Objectives:

This research effort seeks an understanding of the underlying mechanisms of the toxicologic effects (roles) of cadmium and chromium.

Description:

Investigations are made of subcellular distributions, locations, and state(s) of cadmium and chromium in the lung tissue of dogs following inhalation exposures. Emphasis is on the molecular structure surrounding the metal. This is investigated by means of nuclear magnetic resonance (NMR) and electron paramagnetic resonance (EPR) techniques. Modern physical and chemical procedures are used to determine: 1) number of metal atoms per unit molecular weight of interacting material (probably protein); 2) the number of binding sites available to the metal; 3) the ease of exchange of the metal with other atoms; 4) the percentage of total metal concentration present in a paramagnetic state; and 5) the available sites on the metal for ligand exchange. This information is correlated with other toxicologic studies on these metals.

Publications:

1. Blackstone, M., et al.: An Improved Method for the Direct Determination of Cadmium in Biological Materials by Atomic Absorption Spectrophotometry. Report from Univ. of Cincinnati, College of Medicine (1972).
2. Blackstone, M., et al.: Subcellular Distribution of Cadmium within the Lung and Kidney After Cadmium Oxide Inhalation Exposure. Report from Univ. of Cincinnati, College of Medicine (1972).

UNIVERSITY OF MICHIGAN  
Ann Arbor, Michigan

Grant Number: 5 R01 OH-00348-02

Principal Investigator:

Herbert H. Cornish, Ph.D.  
The University of Michigan  
3550 School of Public Health  
Ann Arbor, Michigan 48104

Title:

Enzyme Induction and Environmental Toxicants

Objectives:

The research has as its end purpose the elucidation of the role of induced liver microsomal enzyme activity on the effects of low-level, sub-acute and chronic exposures to various organic chemical solvent vapors such as carbon tetrachloride, chloroform, benzene, and others.

Description:

It has been demonstrated on an acute basis that induced enzyme activity markedly potentiates the toxicity of carbon tetrachloride and chloroform. Experiments are performed in which known inducers of liver microsomal enzyme activity such as phenobarbital, DDT, and tolbutamide are used in low concentration: 1) to study the effect of acute toxicity of these solvents, and 2) to study the chronic effect of simultaneous intake of low concentrations of the inducers and chronic exposures to these solvents over periods of time of from one week to three or more months.

The hepatotoxic reaction to carbon tetrachloride and chloroform is determined by serum enzyme activity (serum glutamic oxaloacetic acid-SGOT) and by histopathology. Blood and bone marrow are studied for benzene toxicity. Microsomal enzyme activity is measured by means of in vitro studies of liver homogenates and microsomal fractions.

Publications: none

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 5 R01 OH 00349-02

Principal Investigator:

Leslie M. Klevay, M.D.  
Kettering Laboratory  
Eden & Bethesda Avenues  
Cincinnati, Ohio 45219

Title:

Vanadium Toxicity: A Study of Mechanisms

Objectives:

This project seeks primarily to test the hypothesis that toxic amounts of vanadium, an emerging potential industrial hazard, produce ill effects by interfering with normal biological utilization of chromium. Secondary objectives are the elucidation of underlying mechanisms of vanadium toxicity resulting from occupational exposure and the understanding of environmental influences on the etiology of atherosclerotic heart disease.

Description:

In closely controlled feeding studies, rats on chromium - deficient diets are provided with vanadium.

Biochemical factors measured include: growth rate, serum cholesterol, serum phospholipids, mineral balance, and glucose tolerance. Radioiodine uptake tests are performed to test thyroid function and rat tissues are examined microscopically after killing the animals.

Publications:

1. Klevay, L.M., H.G. Petering, and K.L. Stemmer: A Controlled Environment for Trace Metal Experiments on Animals. Environ. Sci. & Tech. p. 1196-1199 (December 1971).
2. Klevay, L.M.: Vanadium Toxicity: A Study of Mechanisms. Progress Report, February 13, 1973.

STANFORD UNIVERSITY  
Palo Alto, California

Grant Number: 5 R01 OH 00352-04

Principal Investigator:

Eugene D. Robin, M.D.  
Department of Medicine  
Stanford University, Sch. of Med.  
Palo Alto, California 94305

Title:

Lung Cell Function in Health and Disease

Objectives:

This is a biochemical and physiological project which seeks development of methods to study aspects of biological transport and biochemistry of lung cells and to apply the methods to an investigation of alveolar macrophages under normal and abnormal conditions.

Description:

The approach and methodology in this project include: measurement of key substrates in the glycolytic and oxidative phosphorylation pathways, measurement of enzyme activity of key enzymes (cytochrome oxidase, pyruvate kinase, and lactate dehydrogenase), measurements of sodium and potassium flux and transmembrane potential, measurements of intracellular pH and intramitochondrial pH, and measurements of macromolecular influx and efflux.

Publications:

1. Mintz, S. and E.D. Robin: Redox State of Free Nicotinamide-Adenine Nucleotides in the Cytoplasm and Mitochondria of Alveolar Macrophages. J. Clin. Inves. 50: 1181-1186 (June 1971).
2. Robin, E.D., J.D. Smith, A.R. Tanser, J.S. Adamson, J.E. Millen, and B. Packer: Ion and Macromolecular Transport in the Alveolar Macrophage. Biochem. Biophys. Acta. 241: 117-128 (1971).
3. Simon, L.M., S. Axline, B.R. Horn and E.D. Robin: Macrophage Bioenergetic Adaptations. ABST.
4. Simon, L.M., J. Theodore, and E.D. Robin: Enzymatic Difference in Macrophage Energy Metabolism. ABST.

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5. Theodore, J., J. Acevedo and E.D. Robin: Enzyme Implantation: Acquisition of "de novo" Uricase Activity by Alveolar Macrophages (AM). Draft
6. Simon, J.R., S. Mintz, G. Freeman, J. Theodore, and E.D. Robin: Effects of NO<sub>2</sub> on Redox State of Alveolar Macrophages. ABST.
7. Theodore, J., et al.: Cation Transport and Energy Metabolism in the Nucleated Erythrocyte of the Dogfish Shark, *Squalus Acanthias*. Comp. Biochem. Physiol. 42A: 639-654 (1972).
8. Theodore, J., et al.: Implantation of Exogenous Enzymatic Activity in Isolated Alveolar Macrophages. Science 178: 1302-1304 (December 22, 1972).
9. Acevedo, J.C., et al.: Effect of Intrapulmonary Water Instillation on Pulmonary Lymph Flow and Composition. Amer. J. of Physiol. 223: (6) 1433-1437 (December 1972).
10. Robin, E.D., et al.: Capillary Leak Syndrome with Pulmonary Edema. Arch. Internal Med. 130: 66-71 (July 1972).

UNIVERSITY OF CINCINNATI  
Cincinnati, Ohio

Grant Number: 5 R01 OH 00359-02

Principal Investigator:

Stanley B. Gross, Ph.D.  
University of Cincinnati  
Dept. of Environmental Health  
Kettering Laboratory  
Cincinnati, Ohio 45219

Title:

Variables Affecting Estimation of Human Body Burden

Objectives:

This study seeks to develop "standard" rational sampling methods to determine the human body burden for a variety of "toxic" metals such as lead and mercury, mainly, and subsidiarily, zinc, chromium, copper, and cadmium. The ultimate aim is the establishment of a valid relationship between environmental exposure and the content of heavy metals in human tissues.

Description:

By means of analytic examinations of about 30 tissues from about 20 cadavers supplied through the Coroner's Office, measures of metal body burdens are made and calculated. The bodies are divided into categories of three age groups, the two sexes, and three "body conditions," normal, ischemic, and congested. Variations of metal content in the different tissues are correlated with the cause of death, body condition at autopsy, and any observed abnormalities in terms of age, sex, race, and organ pathology.

Publications: none

NORTHWEST INDUSTRIAL MEDICAL CLINIC, INC., P.S.  
INSTITUTE OF ENVIRONMENTAL MEDICINE AND PHYSIOLOGY  
Seattle, Washington

Grant Number: 1 R01 OH 00448-01

Principal Investigator:

J. Leon Sealey, M.D.  
President and Medical Director  
Northwest Industrial Medical Clinic, Inc., P.S.  
Institute of Environmental Medicine & Physiology  
1500 1st Avenue, South  
Seattle, Washington 98134

Title:

Aseptic Bone Necrosis Survey in Compressed Air Workers

Objectives:

This brief study is directed toward the determination, by roentgenographic examinations, of the incidence of bone injury or joint disruption in compressed air workers.

Description:

This epidemiologic investigation of more than 100 men who had had pre-employment x-ray examinations before exposure to hyperbaric work in the Seattle area and periodic x-rays taken semi-annually while employed, is expected to yield highly useful data on the incidence of subsequent, work-related aseptic bone necrosis. The current investigation of the cohort of previously exposed men, five to six years after exposure, includes follow-up x-ray examinations for the purpose of: 1) determining the incidence of later occurrence of aseptic bone necrosis and 2) evaluating the effectiveness of the Washington State Decompression Regulations. X-rays of shoulders, hips, and knees are taken, studied, and classified according to the criteria of the British Medical Research Council Panel on Decompression. Although no control subjects are involved this deficiency is obviated by the dose categorization of the exposure data, the gradation of which appears to be such that a dose-effect relationship can be anticipated if a sizable number of late sequelae are identified. The absence of significant detectable late effects in this survey would be interpretable only if few or no persons are lost to follow-up.

Publications: none



## DEMONSTRATIONS

BROOKDALE HOSPITAL CENTER  
Brooklyn, New York

Grant Number: 3 R01 OH 00319-05S1

Principal Investigator:

A. Walter Hoover, M.D.  
The Brookdale Hospital Center  
Linden Blvd. at Brookdale Plaza  
Brooklyn, New York 11212

Title:

Occupational Health Services in Small Industries

Objectives:

This is essentially a demonstration project which seeks a workable approach to bridging a gap in provision of comprehensive health care, with particular emphasis on occupational health services. The project is directed toward defining the need, scope, and nature of occupational health services required for small industries, (i.e. those too small to have in-house programs) and to determine whether or not these services can be provided through a plan based on an existing hospital. The estimation of anticipated benefits in relationship to costs is an important aim.

Description:

The program has two overlapping phases. The first phase which includes defining the need, also involves surveying the problems, attitudes, interest, and knowledge of employers with respect to occupational health. The second phase is essentially the provision, by means of an experimental facility, of services encompassed by a complete occupational health program.

Publications: none

# RESEARCH GRANTS IN FISCAL YEAR 1973

<u>GRANT NUMBER</u>	<u>INSTITUTION AND PRINCIPAL INVESTIGATOR</u>	<u>PROJECT PERIOD</u>	<u>FY 1973 AWARD</u>
2 R01 OH 00300-03	Villanova University Quam, G. N.	08/01/72-07/31/74	16,743
5 R01 OH 00301-03	Snell Memorial Fdn., Inc. Snively, G. C.	02/01/70-01/31/74	---
5 R01 OH 00302-03	Duke University Kilburn, K. H.	02/01/71-05/31/73	28,893
2 R01 OH 00303-15	Univ. of Pennsylvania Samitz, M. H.	12/01/72-11/30/75	32,481
3 R01 OH 00304-08S1	John B. Pierce Foundation Bouhuys, A.	09/01/69-10/31/72	12,098
2 R01 OH 00304-09	John B. Pierce Foundation Bouhuys, A.	11/1/72-10/31/75	69,185
5 R01 OH 00305-08	Mt. Sinai Sch. of Med. Selikoff, I. J.	12/01/71-11/30/73	62,537
5 R01 OH 00306-13	Marshfield Clinic Fdn. Emanuel, D.A.	12/01/71-11/30/74	22,944
2 R01 OH 00308-17	Univ. of Pittsburgh Belding, H. S.	11/01/72-10/31/75	51,253
5 R01 OH 00309-15	Mass. Dept. of Labor and Industries Pagnotto, L.	09/01/71-08/31/74	20,465
5 R01 OH 00310-13	Harvard University Ferris, B. G.	10/01/68-09/30/73	43,681
5 R01 OH 00312-08	Univ. of Okla. Med. Ctr. Nau, C. A.	01/01/68-08/31/72	---
5 R01 OH 00313-10	Pan Amer. Hlth. Orgn. Torloni, H.	11/01/70-10/31/74	71,371
5 R01 OH 00315-10	Harvard University Murphy, S. D.	01/01/72-12/31/75	54,550
5 R01 OH 00316-08	Univ. of Florida Leibman, K. C.	01/01/71-12/31/75	40,582

# RESEARCH GRANTS IN FISCAL YEAR 1973

<u>GRANT NUMBER</u>	<u>INSTITUTION AND PRINCIPAL INVESTIGATOR</u>	<u>PROJECT PERIOD</u>	<u>FY 1973 AWARD</u>
3 R01 OH 00319-05S1	Brookdale Hospital Center Wainfeld, B.	05/01/66-04/30/74	---
5 R01 OH 00320-06	Mt. Sinai Sch. of Med. Selikoff, I. J.	05/01/71-06/30/74	---
5 R01 OH 00321-05	University of Washington Milner, J. E.	05/01/71-06/30/74	---
5 R01 OH 00322-05	Harvard University Peters, J. M.	10/01/71-09/30/76	34,234
5 R01 OH 00323-07	Wayne State University Reeves, A. L.	08/01/71-07/31/73	80,658
5 R01 OH 00324-05	Wofford College Stephens, B. G.	03/01/68-08/31/73	---
5 R01 OH 00325-04	Univ. of Pittsburgh Minard, D.	04/01/71-04/30/73	---
8 R01 OH 00326-04	Industrial Hygiene Fdn. Gross, P.	06/01/68-10/31/72	---
5 R01 OH 00327-05	Stanford University Beard, R. R.	06/01/71-06/30/74	---
5 R01 OH 00330-03	Univ. of Oklahoma Coleman, R. L.	06/01/69-12/31/73	---
3 R01 OH 00331-04S1	Montefiore Hospital and Medical Center Weitzman, E. D.	06/01/70-06/30/74	16,224
5 R01 OH 00332-03	University of Nevada Smith, R. W.	09/01/69-04/28/73	---
2 R01 OH 00334-04	University of Rochester Ferin, J.	12/01/72-11/30/74	74,240
8 R01 OH 00335-03	University of Cincinnati Mattheis, E. B.	09/01/69-08/31/72	---
2 R01 OH 00337-04	University of Cincinnati Petering, H. G.	09/01/72-08/31/75	68,293

# RESEARCH GRANTS IN FISCAL YEAR 1973

<u>GRANT NUMBER</u>	<u>INSTITUTION AND PRINCIPAL INVESTIGATOR</u>	<u>PROJECT PERIOD</u>	<u>FY 1973 AWARD</u>
2 R01 OH 00339-03	Universita Degli Studi Di Milano Vigilani, E. C.	11/01/72-10/31/73	13,000
5 R01 OH 00340-04	University of Washington Frank, N. R.	10/01/70-09/30/73	74,270
5 R01 OH 00341-02	Pennsylvania State Univ. Michael, P. L.	06/01/70-09/30/73	---
5 R01 OH 00342-03	Univ. of Notre Dame Pollard, M.	06/01/71-06/30/74	---
2 R01 OH 00343-02	Stanford Research Institute Bycroft, G. N.	12/01/71-06/30/73	---
5 R01 OH 00345-03	Louisiana State University Guilbault, G. G.	04/01/70-12/31/73	---
5 R01 OH 00346-03	University of Miami Wiener, E. L.	02/01/71-01/31/74	50,578
5 R01 OH 00347-03	University of Cincinnati Kaplan, P. D.	04/01/71-03/31/74	32,478
5 R01 OH 00348-02	University of Michigan Cornish, H. H.	04/01/71-03/31/73	---
5 R01 OH 00349-02	University of Cincinnati Klevay, L. M.	04/01/71-03/31/73	---
5 R01 OH 00350-03	University of Minnesota Ward, W. D.	04/01/71-03/31/74	30,577
5 R01 OH 00352-04	Stanford University Robin, E. D.	05/01/71-04/30/74	36,850
2 R01 OH 00353-02	University of Minnesota Stebbins, J.	10/01/72-12/31/73	30,429
1 R01 OH 00354-01	Industrial Health Fdn. Gross, P.	05/01/71-10/31/72	---
5 R01 OH 00355-02	University of Cincinnati Petering, H.G.	06/01/71-06/30/74	---
3 R01 OH 00356-02S1	University of Cincinnati Christian, R.	06/01/72-06/30/75	29,176

# RESEARCH GRANTS IN FISCAL YEAR 1973

<u>GRANT NUMBER</u>	<u>INSTITUTION AND PRINCIPAL INVESTIGATOR</u>	<u>PROJECT PERIOD</u>	<u>FY 1973 AWARD</u>
5 R01 OH 00357-02	University of Cincinnati Mattheis, E. B.	06/01/71-07/31/73	---
5 R01 OH 00358-02	Ohio State University Davis, G. W.	06/01/71-09/30/73	---
5 R01 OH 00359-02	University of Cincinnati Gross, S. B.	06/01/71-08/31/73	---
5 R01 OH 00360-02	West Virginia University Burrell, R.	06/01/71-06/30/74	---
5 R01 OH 00362-08	Centro Malattie Cardio- vascolari Puddu, V.	08/01/71-07/31/76	2,300
5 R01 OH 00364-02	Upstate Medical Center Henderson, D.	05/01/72-04/30/74	43,938
5 R01 OH 00365-02	University of South Dakota Heimstra, N. W.	10/01/71-09/30/73	20,136
5 R01 OH 00366-02	Univ. of Missouri-Rolla Warner, H. D.	11/01/71-10/31/73	7,685
5 R01 OH 00367-02	University of Pittsburgh Alarie, Y. C.	10/01/71-09/30/74	17,571
5 R01 OH 00368-02	University of California Milby, T. H.	02/01/72-01/31/75	115,853
1 R01 OH 00369-01	Harvard University Peters, J. M.	10/01/72-09/30/77	60,887
1 R01 OH 00371-01A1	University of Cincinnati Rockwell, J. R.	10/01/72-09/30/74	55,268
1 R13 OH 00382-01	Industrial Health Fdn. Braun, D.	01/01/72-06/30/73	---
5 R01 OH 00387-02	Tulane Univ. Sch. of Med. Ziskind, M.	06/01/71-07/31/74	---
1 R01 OH 00396-01	New York Univ. Med. Ctr. Palmer, E. D.	08/01/72-07/31/74	55,753

# RESEARCH GRANTS IN FISCAL YEAR 1973

<u>GRANT NUMBER</u>	<u>INSTITUTION AND PRINCIPAL INVESTIGATOR</u>	<u>PROJECT PERIOD</u>	<u>FY 1973 AWARD</u>
1 R01 OH 00404-01	University of California Nahum, A. M.	01/01/72-12/31/74	---
9 R01 OH 00410-04	Wayne State University Pinkus, H.	09/01/72-08/31/74	75,043
1 R01 OH 00427-01	University of Washington Chang, D. B.	11/01/72-10/31/75	35,301
1 R13 OH 00429-01	Cornell Medical Center McLean, A. A.	09/01/72-08/31/73	10,000
1 R13 OH 00430-01	University of Rochester Laties, V. G.	05/01/72-11/30/73	---
1 R01 OH 00432-01	New York Univ. Med. Ctr. Tichauer, E. R.	06/01/73-05/31/74	5,555
1 R01 OH 00435-01	Univ. of Sn. Florida Boren, H.	06/01/72-01/31/73	---
3 R09 OH 00445-01S1	Wayne State University	06/30/72-06/30/74	20,000
3 R09 OH 00445-01S2	Birmingham, D.		10,000
1 R13 OH 00447-01	Los Angeles County Health Department Brown, H. V.	10/01/72-09/30/73	2,760
1 R01 OH 00448-01	Northwest Industrial Medical Clinic, Inc., P.S. Sealey, J. L.	06/01/73-05/31/74	13,430
1 R13 OH 00510-01	University of Cincinnati deGroot, I.	06/01/73-12/01/73	21,805
7 R01 OH 00511-01	University of Missouri Kilburn, K. H.	06/01/73-01/31/74	30,925

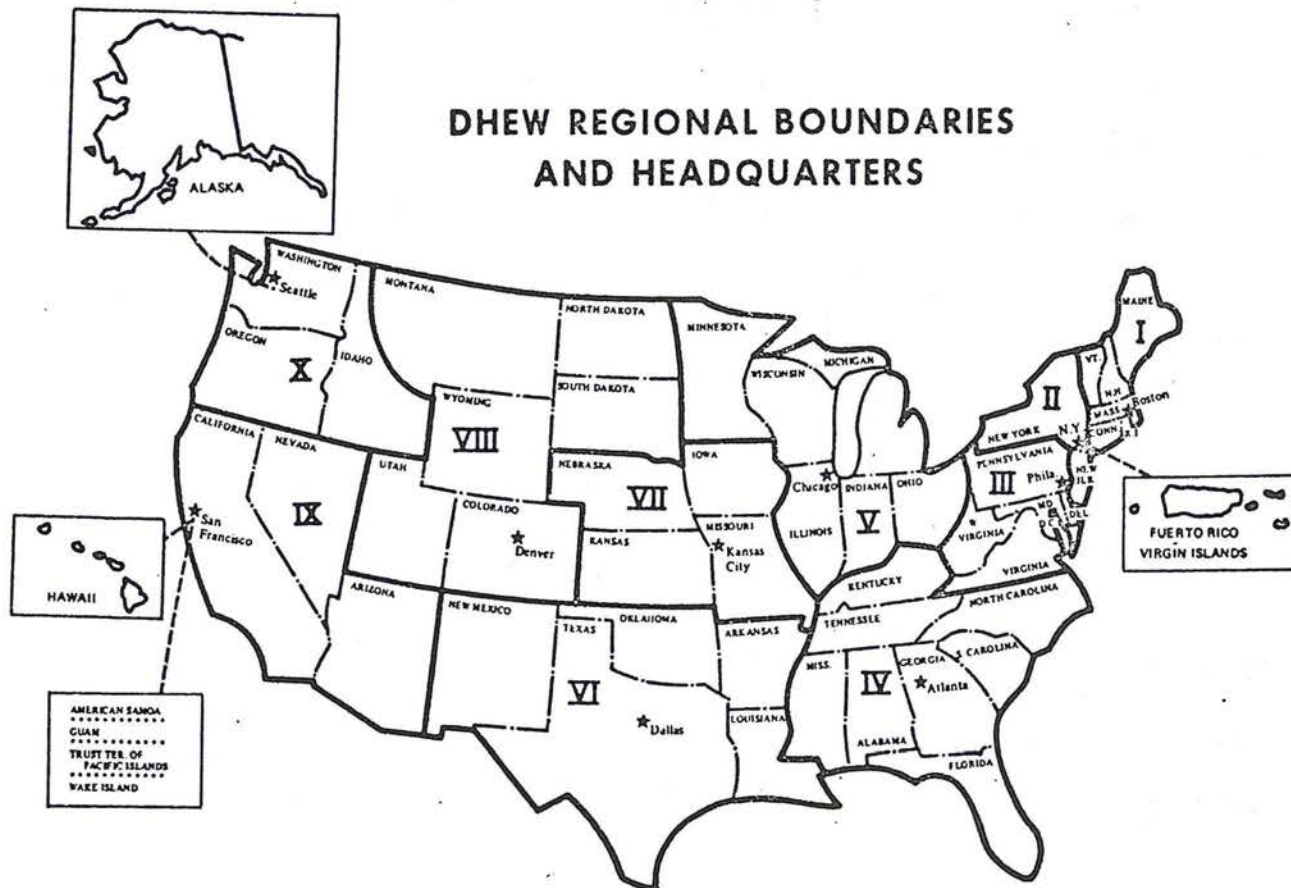
FY '73 Budget \$1,702,000

RESEARCH GRANTS SUMMARY BY PROGRAM AREA

<u>PROGRAM</u>	<u>ACTIVE IN FY '73</u>	<u>SUPPORTED IN FY '73</u>	<u>AMOUNT OF AWARD</u>
BEHAVIORAL & MOTIVATIONAL FACTORS	9	7	\$ 151,060
BIO-ENVIRONMENTAL SAMPLING & ANALYSIS	2	2	171,121
DERMATOLOGY	3	2	107,524
EPIDEMIOLOGY	5	5	199,834
ERGONOMICS	1	1	16,224
HEAD AND BODY PROTECTION	4	1	16,743
INSTRUMENTATION	1	0	---
OCCUPATIONAL RESPIRATORY DISEASE			
Byssinosis	3	3	141,101
Coal Worker's Pneumoconiosis	4	1	29,176
Farmer's Lung	1	1	22,944
Respiratory Tract Carcinoma	5	2	83,418
Silicosis	1	0	---
Unspecified	3	0	---
PHYSICAL AGENTS			
Noise	3	2	74,515
PHYSICAL AND CHEMICAL ANALYSIS	4	1	20,465
PHYSIOLOGY			
Respiratory	4	3	147,564
Heat Stress	3	1	51,253
TOXICOLOGY AND PATHOLOGY	15	10	439,058
DEMONSTRATIONS	1	0	---
(Chairman's Grant)	1	1	30,000
TOTALS.	72	43	\$ 1,702,000

# RESEARCH GRANTS DISTRIBUTION BY REGION

## DHEW REGIONAL BOUNDARIES AND HEADQUARTERS



REGION	NUMBER OF GRANTS	TOTAL AMOUNT
I	6	\$ 295,100
II	11	268,247
III	11	189,419
IV	5	120,053
V	19	476,671
VI	4	---
VII	2	38,610
VIII	1	20,136
IX	7	155,463
X	4	123,001
(Foreign)	(2)	(15,300)
	<hr/> 72	<hr/> \$1,702,000

# RESEARCH GRANTS DISTRIBUTION BY STATES

<u>STATE</u>	<u>NUMBER OF INSTITUTIONS</u>	<u>NUMBER OF PROJECTS</u>	<u>FY '73 AMOUNT</u>
California	3	6	\$ 155,463
Connecticut	1	1	81,283
District of Columbia	1	1	71,371
Florida	3	3	91,160
Indiana	1	1	-0-
Louisiana	2	2	-0-
Massachusetts	3	5	213,817
Michigan	2	4	185,701
Minnesota	1	2	61,006
Missouri	1	2	38,610
Nevada	1	1	-0-
New York	8	11	268,247
North Carolina	1	1	28,893
Ohio	2	11	207,020
Oklahoma	1	2	-0-
Pennsylvania	6	9	118,048
South Carolina	1	1	-0-
South Dakota	1	1	20,136
Washington	2	4	123,001
West Virginia	1	1	-0-
Wisconsin	1	1	22,944
FOREIGN(Italy)	2	2	15,300
			<hr/> \$1,702,000

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