CDC

CENTERS FOR DISEASE CONTROL AND PREVENTION

NIOSH

Research and Demonstration Grants

Annual Report
Fiscal Year 1994

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

NIOSH

RESEARCH AND DEMONSTRATION GRANTS

FISCAL YEAR 1994

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
Atlanta, Georgia 30333

May 1995

DISCLAIMER

Mention of company names or products does not constitute endorsement by the National Institute for Occupational Safety and Health.

The grant summaries in this report were prepared by the principal investigators, so any questions regarding the contents should be directed to them.

DHHS(NIOSH) Publication No. 95-112

FOREWORD

The National Institute for Occupational Safety and Health (NIOSH) is mandated by the provisions of the Occupational Safety and Health Act of 1970 and the Federal Mine Safety and Health Amendments Act of 1977 to conduct research and demonstrations relating to occupational safety and health. Our overall goal is the prevention of illnesses, injuries, and deaths. Recognizing the valuable contributions of extramural scientists to this endeavor, NIOSH sponsors innovative research through a grants program, which complements the Institute's intramural research program. The creativity and special resources available in the scientific community make the grants program a key component in achieving the Nation's goal to have safe jobs and healthy workers. In fiscal year 1995, we are increasing our commitment to extramural research through Requests for Applications in areas of high priority. Our goal is to continue expanding the extramural research program in the coming years.

To maximize the grants program's usefulness in protecting workers, NIOSH funds projects that are scientifically sound and related to program priorities. We are interested in funding grants that will ultimately be of practical value in solving workplace problems. Thus, support is focused on projects that make contributions to applied technical knowledge in the identification, evaluation and/or control of hazards.

This report provides a readily available source of information on the status and scope of the research grants program of NIOSH (all active grants during fiscal year 1994: October 1, 1993, to September 30, 1994). It is also intended to stimulate the submission of more proposals for high quality research on significant occupational safety and health concerns. We invite investigators in the biomedical sciences, engineering, and related disciplines to become partners in preventing United States workers from suffering adverse effects caused by occupational hazards.

Linda Rosenstock, M.D., M.P.H.
Director, National Institute for
Occupational Safety and Health
Centers for Disease Control and Prevention

TABLE OF CONTENTS

Development of Environmental Exposure Measurement Tools

Investigation of Adverse Effects

Animal Experiments

Cellular Experiments

Epidemiological and Related Studies

Human Laboratory Studies

Other Laboratory Studies

Discovery of Biological Exposure and Response Markers

Development of Control Approaches/Interventions

Assessment of Effectiveness of Controls/Interventions

INTRODUCTION

The organization of this annual report on the NIOSH research grants program is designed to facilitate the reader's understanding of the types of extramural research projects supported by NIOSH.

- Summaries of the supported projects are grouped by research objective, as indicated in the *Table of Contents*.

Each grant summary contains administrative information about the grant, followed by a synopsis of the project and any publications that have resulted to date.

- Principal investigators prepare the summaries for inclusion in this report. The synopsis is an explanation of the nature of the project and a discussion of results, with sections on *Importance to Occupational Safety and Health, Objectives, Methodology, and Significant Findings*.

- Publications are listed so that the reader may gain more information about the projects than is given in the brief summaries. Although some citations are not yet published or may not be retrieved easily, they have been included for the sake of providing maximum information.

> **Note:** *Should there be an interest in more information, principal investigators should be contacted directly.*

Statistics on the number and amount of funds awarded by grant type (activity), research objective, and region/state are given in tabular form. Indices are included for ease in locating particular grants if the reader knows the grant number, the principal investigator, or the grantee institution.

> **Note:** *See glossary on page 3 for an explanation of the components of a grant number.*

Suggestions on content or format of this report to make it more useful to the reader would be welcomed. The process of assembling the report begins in the fall of each year, so comments should be received at least by the end of September.

- Inquiries or ideas should be addressed to:

NIOSH Grants Office
1600 Clifton Road
Building 1, Room 3053, MS - D30
Atlanta, Georgia 30333
404/639-3343

ACCESS TO LITERATURE

In addition to the publications listed after each grant summary, readers may wish to refer to NIOSH's Document Information Directory System (DIDS).

What is DIDS?

DIDS is a computerized data base of documents that are produced from NIOSH-sponsored research (intramural and extramural). This data file is maintained by the NIOSH Division of Standards Development and Technology Transfer to track the following types of NIOSH documents: Alerts, Current Intelligence Bulletins, criteria documents, control technology reports, hazard evaluation and technical assistance reports, industrywide study reports, contract reports, health and safety guides, Fatal Accident Circumstances and Epidemiology (FACE) reports, research grant publications and reports, training documents, testimony, and books, book chapters, and journal articles authored by NIOSH employees.

What Specific Data does DIDS include?

Each entry includes the document title, publication number, subject index terms, availability information, NIOSHTIC accession number, name of principal investigator for research grants, and complete citations for books, book chapters, and journal articles. Approximately 11,000 entries are currently maintained in the system.

Who may use DIDS and What is the Cost?

DIDS is used primarily by NIOSH personnel, but searches are often requested by persons from industries, unions, academic institutions, and the general public. Searches are free of charge.

How can a Search be Requested?

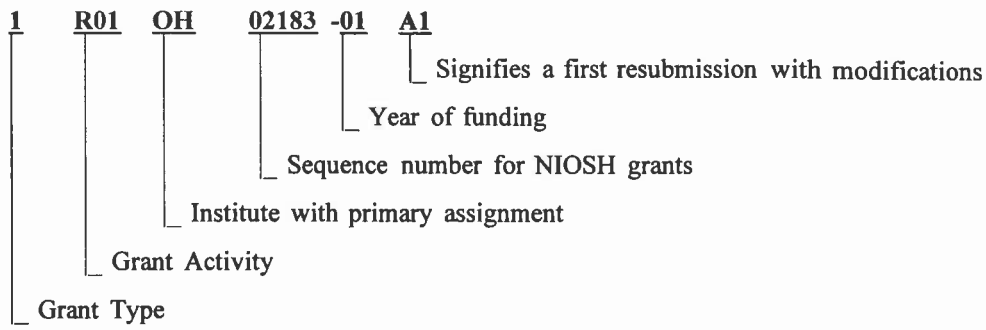
Contact NIOSH at the following address and telephone number:

Technical Information Branch
Division of Standards Development and Technology Transfer
National Institute for Occupational Safety and Health
4676 Columbia Parkway
Cincinnati, Ohio 45226-1998
Telephone: 513/533-8350

GLOSSARY

Grant Number - The identification number assigned to a grant application

EXAMPLE: 1 R01 OH02183-01A1



Typical Codes:

Grant Type

The first component of an application number which identifies the type of application that has been submitted.

1 - New Competing application
2 - Competing renewal application
5 - Noncompeting continuation application
7 - Change of grantee institution

Grant Activity

This three-digit code indicates the activity to which application is being made.

R01 - Research Project Grant
K01 - Special Emphasis Research Career Award (SERCA) Grant
R03 - Small Grant
R13 - Conference Grant
R18 - Demonstration Grant
R43 - Small Business Innovation Research (SBIR) Grant

Institute

This two letter code identifies the primary funding institution.

OH - NIOSH

Sequence Number

Five-digit serial numbers are assigned in sequence.

Year of Funding

This 2-digit number identifies the budget period of a project. An 01 indicates the first year of the grant award and the series of years continues through succeeding renewals.

Department of Health and Human Services
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

Research and Demonstration Grants
Occupational Safety and Health

A. Introduction

The National Institute for Occupational Safety and Health (NIOSH) of the Centers for Disease Control and Prevention (CDC), is soliciting grant applications for research and demonstration projects related to occupational safety and health (see Section E, "Availability of Funds").

B. Authority

This program is authorized under the Public Health Service Act, as amended, Section 301 (42 U.S.C. 241); the Occupational Safety and Health Act of 1970, Section 20 (a) (29 U.S.C. 669[a]); and the Federal Mine Safety and Health Amendments Act of 1977, as amended, Section 501 (30 U.S.C. 951). The applicable program regulations are in 42 CFR Part 52.

C. Eligible Applicants

Eligible applicants include domestic and foreign non-profit and for-profit organizations, universities, colleges, research institutions, and other public and private organizations, including State and local governments and small, minority and/or woman-owned businesses. Exceptions: applicants for the Special Emphasis Research Career Award Grant and Small Grant programs must be citizens or persons lawfully admitted to the U.S. for permanent residence (resident alien) at the time of application and must be employed by a domestic institution.

D. Smoke-Free Workplace

The Public Health Service strongly encourages all grant recipients to provide a smoke-free workplace and to promote the non-use of all tobacco products, and Public law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities that receive Federal funds in which education, library, day care, health care, and early childhood development services are provided to children.

E. Availability of Funds

For fiscal year (FY) 1995, the budget for research grants is $9,373,900. Of that amount, $5,300,000 is to support 44 non-competing continuation awards, and $4,073,900 is available for approximately 35 new and competing renewal awards, which includes $400,000 for Small Business Innovation Research grant awards.

Within the $9,373,900 budget, there is emphasis for health and safety research within the construction industry, totaling $2,500,000. Of this figure, $1,850,000 is to support 10 non-competing continuation awards, and $650,000 is available for approximately 6 new and competing renewal awards.

Grant applications should be focused on the research priorities described in Section I, "Funding Priorities," which includes several new research priorities. Grant proposals in these new areas will compete for the available funds given above, as well as for funds announced through Requests for Applications that are anticipated in FY 1995 and FY 1996.

F. Background

Americans are now working more hours than ever before. The workplace environment profoundly affects health. Each person, simply by going to work each day, may face hazards that threaten one's health and safety. Risking a person's life or health should never be considered part of the job.

In 1970, Congress passed the Occupational Safety and Health Act to ensure Americans the right to "safe and healthful working conditions," yet workplace hazards continue to inflict a tremendous toll in both human and economic costs.

In 1992, employers reported 3.3 million disabling work injuries and 370,000 cases of occupational illness. According to the most current statistics an average of 17 American workers die each day from injuries on the job. Moreover, even the most conservative estimates find that about 137 additional workers die each day from workplace diseases.

Medical payments under workers' compensation rose to almost $17 billion in 1991. Considering that workers' compensation is received by only 60 percent of injured workers and does not cover most cases of chronic occupational illness, medical costs alone for these conditions may total $30 - $40 billion.

Occupational injury and disease creates needless human suffering, a tremendous burden upon health care resources, and an enormous drain on U.S. productivity (estimated to exceed $100 billion annually). Yet, to date, this mainstream public health problem has somehow escaped mainstream public attention. Workplace injury and disease is neither inevitable nor acceptable. The time has come to protect one of the nation's most valuable resources: the American worker.

The philosophy of NIOSH is articulated in the Institute's vision statement: Delivering on the Nation's Promise: Safety and Health at Work for All People...Through Prevention. To identify and reduce hazardous working conditions, the Institute carries out disease, injury, and hazard surveillance and conducts a wide range of field and laboratory research. Additionally, NIOSH sponsors extramural research in priority areas to complement and expand its efforts. These are listed in Section I, "Funding Priorities."

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity to reduce morbidity and mortality and improve the quality of life. This program announcement is related to the priority area "Occupational Safety and Health." Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report, Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325, (telephone 202-783-3238).

G. Purpose

The purpose of this grant program is to develop knowledge that can be used in preventing occupational diseases and injuries. Thus, NIOSH will support the following types of applied research projects: causal research to identify and investigate the relationships between hazardous working conditions and associated occupational diseases and injuries; methods research to develop more sensitive means of evaluating hazards at work sites, as well as methods for measuring early markers of adverse health effects and injuries; control research to develop new protective equipment, engineering control technology, and work practices to reduce the risks of occupational hazards; and demonstrations to evaluate the technical feasibility or application of a new or improved occupational safety and health procedure, method, technique, or system.

H. Mechanisms of Support

The types of grants NIOSH supports are described below. Applications responding to this announcement will be reviewed by staff for their responsiveness to the following program requirements. Grants are funded for 12-month budget periods in project periods up to five years for research project grants and demonstration project grants;

three years for SERCA grants; and up to two years for small grants. Continuation awards within the project period are made on the basis of satisfactory progress and on the availability of funds.

1. Research Project Grants (R01)

   A research project grant application should be designed to establish, discover, develop, elucidate, or confirm information relating to occupational safety and health, including innovative methods, techniques, and approaches for dealing with occupational safety and health problems. These studies may generate information that is readily available to solve problems or contribute to a better understanding of the causes of work-related diseases and injuries.

2. Demonstration Project Grants (R18)

   A demonstration project grant application should address, either on a pilot or full-scale basis, the technical or economic feasibility of implementing a new/improved innovative procedure, method, technique, or system for preventing occupational safety or health problems. The project should be conducted in an actual workplace where a baseline measure of the occupational problem will be defined, the new/improved approach will be implemented, a follow-up measure of the problem will be documented, and an evaluation of the benefits will be conducted.

3. Special Emphasis Research Career Award (SERCA) Grants (K01)

   The SERCA grant is intended to provide opportunities for individuals to acquire experience and skills essential to the study of work-related hazards, and in so doing create a pool of highly qualified investigators who can make future contributions to research in the area of occupational safety and health. SERCA grants are not intended either for individuals without research experience or for productive, independent investigators with a significant number of publications and of senior academic rank. Moreover, the award is not intended to substitute one source of salary support for another for an individual who is already conducting full-time research; nor is it intended to be a mechanism for providing institutional support.

   Candidates must: (1) hold a doctoral degree; (2) have research experience at or above the doctoral level; (3) not be above the rank of associate professor; (4) be employed at a domestic institution; and (5) be citizens or persons lawfully admitted to the U.S. for permanent residence (resident alien) at the time of application.

   This non-renewable award provides support for a three-year period for individuals engaged in full-time research and related activities. Awards will not exceed $50,000 per year in direct costs for salary support (plus fringe benefits), technical assistance, equipment, supplies, consultant costs, domestic travel, publications, and other costs. The indirect cost rate applied is limited to 8 percent of the direct costs, excluding tuition and related fees and equipment expenses, or to the actual indirect cost rate, whichever results in the lesser amount.

   A minimum of 60 percent time must be committed to the proposed research project, although full-time is desirable. Other work in the area of occupational safety and health will enhance the candidate's qualifications but is not a substitute for this requirement. Related activities may include research career development activities as well as involvement in patient care to the extent that it will strengthen research skills. Fundamental/basic research will not be supported unless the project will make an original contribution for applied technical knowledge in the identification, evaluation, and/or control of occupational safety and health hazards (e.g., development of a diagnostic technique for early detection of an occupational disease). Research project proposals must be of the applicants' own design and of such scope that independent investigative capability will be evident within three years. At the completion of this three-year award, it is intended that awardees should be better able to compete for individual research project grants awarded by NIOSH.

   SERCA grant applications should be identified as such on the application form. Section 2 of the application (the Research Plan) should include a statement regarding the applicant's career plans and how the proposed

research will contribute to a career in occupational safety and health research. This section should also include a letter of recommendation from the proposed advisor(s).

4. Small Grants (R03)

The small grant program is intended to stimulate proposals from individuals who are considering a research career in occupational safety and health; as such, the minimum time commitment is 10%. It is expected that a recipient would subsequently compete for a career development grant (K01 - see section H.3.) or for a traditional research project grant (R01 - see section H.1.) related to occupational safety and health. The award is not intended to supplement ongoing or other proposed research; nor is it intended to be a mechanism for providing institutional support. Please note, as in section H.3., that fundamental/basic research is generally not supported.

The small grant investigators must be U.S. citizens or persons lawfully admitted to the U.S. for permanent residence (resident alien) at the time of application who are predoctoral students, post-doctoral researchers (within 3 years following completion of doctoral degree or completion of residency or public health training), or junior faculty members (no higher than assistant professor). If university policy requires that a more senior person be listed as principal investigator, it should be clear in the application which person is the small grant investigator. Except for applicants who are assistant professors, there must be one or more named mentors to assist with the project. A biographical sketch is required for the small grant investigator, as well as for the supervisor and other key consultants, as appropriate.

This non-renewable award provides support for project periods of up to two years to carry out exploratory or pilot studies, to develop or test new techniques or methods, or to analyze data previously collected. Awards will not exceed $25,000 per year in direct costs for salary support (plus fringe benefits), technical assistance, equipment, supplies, consultant costs, domestic travel, publications, and other costs. The indirect costs will be based upon the negotiated indirect cost rate of the applicant organization. An individual may not receive more than two small grant awards, and then, only if the awards are at different stages of development (e.g., doctoral student, post-doctoral researcher, or junior faculty member).

I. Funding Priorities

The NIOSH program priorities, listed below, are applicable to all of the above types of grants listed under Section H, "Mechanisms of Support." These priority areas represent both new areas and traditional diseases and injuries related to risks on the job. NIOSH intends to support projects that facilitate progress in understanding and preventing adverse effects among workers. The conditions or examples listed under each category are selected examples, not comprehensive definitions of the category. Investigators may also apply in other areas related to occupational safety and health, but the rationale for the significance of the research to the field of occupational safety and health must be presented in the grant application.

Potential applicants with questions concerning the acceptability of their proposed work are strongly encouraged to contact the "Technical Information Contact," Dr. Roy M. Fleming, listed in this announcement under Section Q, "Where to Obtain Additional Information."

New Research Priorities are:

- Surveillance: The ability to identify the occurrence and emergence of work-related injury and disease is vital for prevention. While some targeted surveillance efforts address specific conditions, such as adult lead poisoning, occupational lung disease, and carpal tunnel syndrome, a national surveillance system for occupational disease and injury does not exist. To broaden current surveillance systems, it is necessary to: (1) improve hazard surveillance by developing systems that identify hazardous work conditions, rather than cases of disease or injury; (2) evaluate new disease surveillance efforts to better fill the gaps in current reporting systems; (3) explore additional surveillance methods for nonfatal injury, including workplace violence and; (4) assess the economic burden of occupational conditions and potential economic benefits of their prevention.

- Work Organization: Through surveillance and research, NIOSH and others have identified many physical and chemical hazards of work. However, there is growing evidence that the way work is organized, itself, affects the health and well-being of workers, both directly and in combination with other hazards. Investigations are needed on broad aspects of employment, including underemployment, overemployment, unemployment, shift-work, alternate work schedules, and job stress. Also encompassed are special risks that may result from the ongoing evolution to a service economy; to a workforce that is increasingly comprised of women, minorities and older workers; and to conditions of employment and demands for productivity increasingly pressured by global market forces.

- Control Technology and Intervention Research: NIOSH seeks to prevent work-related diseases and injuries by designing, implementing, and evaluating measures to reduce occupational hazards at their source. If prevention measures are not currently available, new technologies need to be developed for controlling hazardous exposures. Such new technologies must be evaluated to determine that the prevention measures are feasible, even for smaller businesses. Intervention research, of which control technology is a part, examines the utility and impact of new and existing preventive measures in the workplace. Assessments are needed of the effectiveness of regulations, educational efforts, government and private outreach programs, employer policies, worker training, and protective technology in preventing disease and injury.

- Health Services Research: This area includes (1) assessing the adequacy of the supply of occupational safety and health professionals, including specialist or generalist physicians and nurses, industrial hygienists, safety specialists, and engineers; (2) evaluating the accessibility, availability, and delivery of occupational health services, the role of workers' compensation, and the integration of occupational health services and primary health care; (3) improving the quality of occupational health care, through clinical and preventive practice guidelines; (4) assessing the effectiveness of screening and treatment of select occupational conditions; and (5) evaluating the economics of treating and preventing occupational injuries and illnesses.

Traditional research priorities are broadly intended for investigator-initiated research of emerging or reemerging issues, particularly those affecting a large number of workers. These areas include: occupational lung diseases, musculoskeletal injuries, occupational cancers (other than lung), severe occupational traumatic injuries and fatalities, cardiovascular disease, disorders of reproduction, neurotoxic disorders, noise-induced hearing loss, dermatologic conditions, and psychological disorders.

J. Inclusion of Minorities and Women in Study Populations

Applicants are required to give added attention (where feasible and appropriate) to the inclusion of minorities and/or women study populations for research into the etiology of diseases, research in behavioral and social sciences, clinical studies of treatment and treatment outcomes, research on the dynamics of health care and its impact on disease, and appropriate interventions for disease prevention and health promotion. Exceptions would be studies of diseases which exclusively affect males or where involvement of pregnant women may expose the fetus to undue risks. If minorities and/or women are not included in a given study, a clear rationale for their exclusion must be provided.

K. Applications Submission Deadlines and Review Dates

The research grant application Form PHS-398 (rev. 9/91; OMB NUMBER 0925-0001) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Office of Grants Information, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/593-7248; and from the contacts listed under Section Q, "Where to Obtain Additional Information."

The original and five copies of the PHS-398 must be submitted to the address below on or before the specified receipt dates also provided below. A mailing label is provided in the Form PHS-398 application package.

Division of Research Grants
National Institutes of Health
6701 Rockledge Drive - MSC7710
Bethesda, MD 20892-7710
Bethesda, MD 20817 (for express mail)

The timetable for receiving applications and awarding grants is given below. This is a continuous announcement, consequently, these receipt dates will be on-going until further notice.

Research and Demonstration Project Grants:

Receipt Date*	Initial Review	Secondary Review	Earliest Possible Start Date
February 1	June/July	September	December 1
June 1	Oct/Nov	January	April 1
October 1	Feb/Mar	May	August 1

*Deadlines for competing continuation applications or revised applications are 1 month later.

SERCA and Small Grants

Receipt Date	Initial Review	Secondary Review	Earliest Possible Start Date
March 1	June/July	August	November 1
July 1	Oct/Nov	December	March 1
November 1	Feb/Mar	April	July 1

Applications must be received by the above receipt dates. To guard against problems caused by carrier delays, retain a legible proof-of-mailing receipt from the carrier, dated no later than one week prior to the receipt date. If the receipt date falls on a weekend, it will be extended to Monday; if the date falls on a holiday, it will be extended to the following work day. The receipt date will be waived only in extenuating circumstances. To request such a waiver, include an explanatory letter with the signed, completed application. No request for a waiver will be considered prior to receipt of the application.

L. Evaluation Criteria

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by study sections of the Division of Research Grants, NIH in accordance with the standard NIH peer review procedures. Following scientific technical review, the applications will receive a second-level programmatic review by NIOSH. Notification of the review recommendations will be sent to the applicants after the initial review. Awards will be made based on results of the initial and secondary reviews, as well as availability of funds.

Applications that are complete and responsive to the program announcement will be evaluated for scientific merit by an appropriate peer review group. As part of the initial merit review, all applications will receive a written critique and undergo a process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed, assigned a priority score, and receive a second level review by the Institute programmatic review committee.

1. The initial (peer) review is based on scientific merit and significance of the project, competence of the proposed staff in relation to the type of research involved, feasibility of the project, likelihood of its producing

meaningful results, appropriateness of the proposed project period, adequacy of the applicant's resources available for the project, and appropriateness of the budget request.

Demonstration grant applications will be reviewed additionally on the basis of the following criteria:

- Degree to which project objectives are clearly established, obtainable, and for which progress toward attainment can and will be measured.
- Availability, adequacy, and competence of personnel, facilities, and other resources needed to carry out the project.
- Degree to which the project can be expected to yield or demonstrate results that will be useful and desirable on a national or regional basis.
- Documentation of cooperation from industry, unions, or other participants in the project, where applicable.

SERCA grant applications will be reviewed additionally on the basis of the following criteria:

- The review process will consider the applicant's scientific achievements, the applicant's research career plan in occupational safety and health, and the degree to which the applicant's institution offers a superior research environment (supportive nature, including letter(s) of reference from advisor(s) which should accompany the application).

Small grant applications will be given consideration to the fact that the applicants do not have extensive experience with the grant process.

2. In the secondary review, the following factors will be considered:

- The results of the initial review.
- The significance of the proposed study to the mission of NIOSH.
    1) Relevance to occupational safety and health, by contributing to achievement of research objectives specified in Section 20(a) of the Occupational Safety and Health Act of 1970 and Section 501 of the Federal Mine Safety and Health Amendments Act of 1977,
    2) Magnitude of the problem in terms of numbers of workers affected,
    3) Severity of the disease or injury in the worker population,
    4) Potential contribution to applied technical knowledge in the identification, evaluation, and/or control of occupational safety and health hazards, and
    5) Program balance, and
    6) Policy and budgetary considerations.

Questions regarding the above criteria should be addressed to the Technical Information Contact listed under Section Q, "Where to Obtain Additional Information."

M. Technical Reporting Requirements

Progress reports are required annually as part of the continuation application (75 days prior to the start of the next budget period). The annual progress reports must contain information on accomplishments during the previous budget period and plans for each remaining year of the project. Financial status reports (FSR) are required no later than 90 days after the end of the budget period. The final performance and financial status reports are required 90 days after the end of the project period. The final performance report should include, at a minimum, a statement of original objectives, a summary of research methodology, a summary of positive and negative findings, and a list of publications resulting from the project. Research papers, project reports, or theses are acceptable items to include in the final report. The final report should stand alone rather than citing the original application. Three copies of reprints of publications prepared under the grant should accompany the report.

N. Executive Order 12372 Review

Applications are not subject to review as governed by Executive Order 12372, Intergovernmental Review of Federal Programs.

O. Catalog of Federal Domestic Assistance Number

The Catalog of Federal Domestic Assistance number is 93.262.

P. Public Health System Reporting Requirements

This program is not subject to the Public Health System Reporting Requirements.

Q. Where to Obtain Additional Information

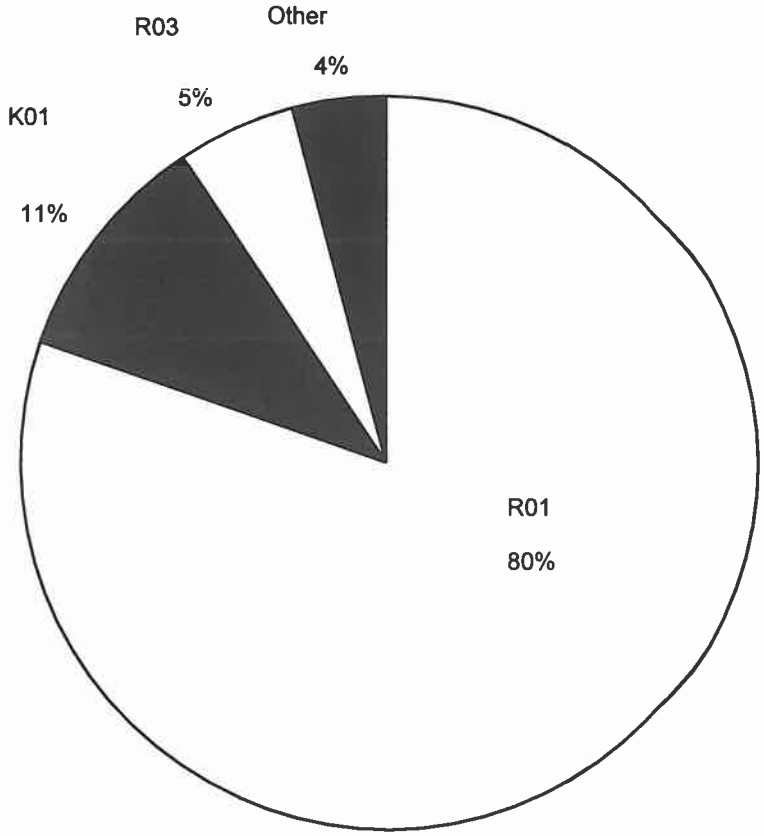
For Technical Information Contact:

Roy M. Fleming, Sc.D.
Associate Director for Grants
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
1600 Clifton Road, NE.
Building 1, Room 3053, Mail Stop D-30
Atlanta, Georgia 30333
Telephone: (404) 639-3343

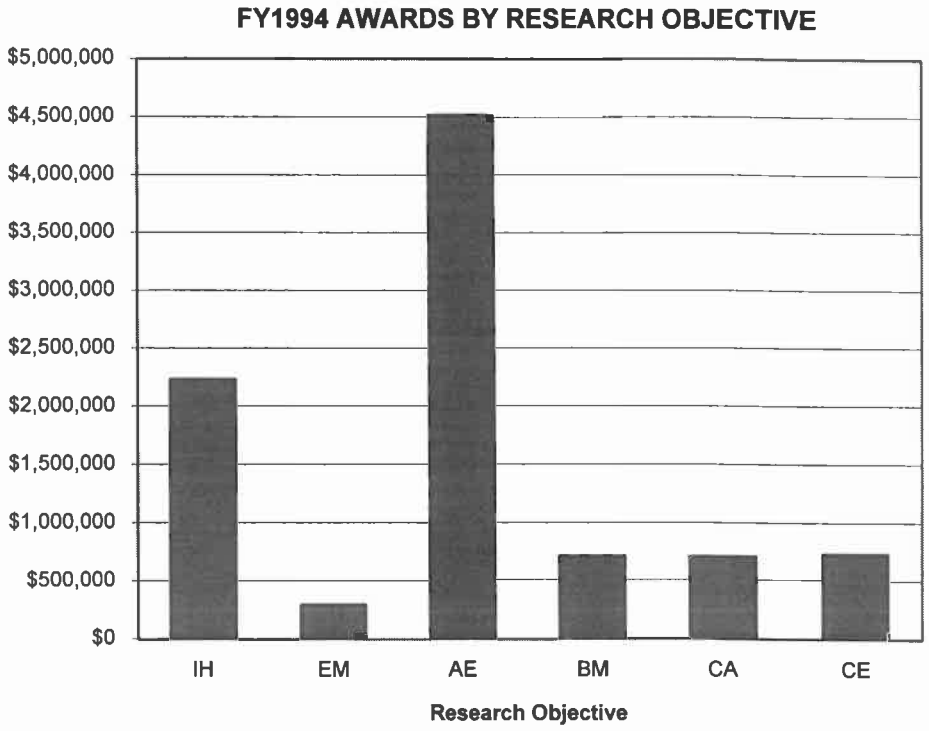
For Business Information Contact:

Ms. Georgia L. Jang
Grants Management Specialist
Grants Management Branch, PGO
Centers for Disease Control and Prevention
255 E. Paces Ferry Road, NE.
Room 321, Mail Stop E-13
Atlanta, Georgia 30305
Telephone: (404) 842-6814

FY94 Grant Awards by Activity
Percentage of Total Budget



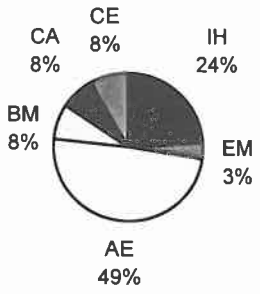
Activity	New Awards No.	New Awards Amount	Continuation Awards No.	Continuation Awards Amount	TOTAL Awards No.	TOTAL Awards Amount
R01	16	$2,754,925	27	$4,619,851	43	$7,374,776
K01	5	$268,243	13	$698,235	18	$966,478
R03	8	$292,215	6	$179,084	14	$471,299
Other	3	$218,352	1	$169,290	4	$387,642
Total	32	$3,533,735	47	$5,666,460	79	$9,200,195



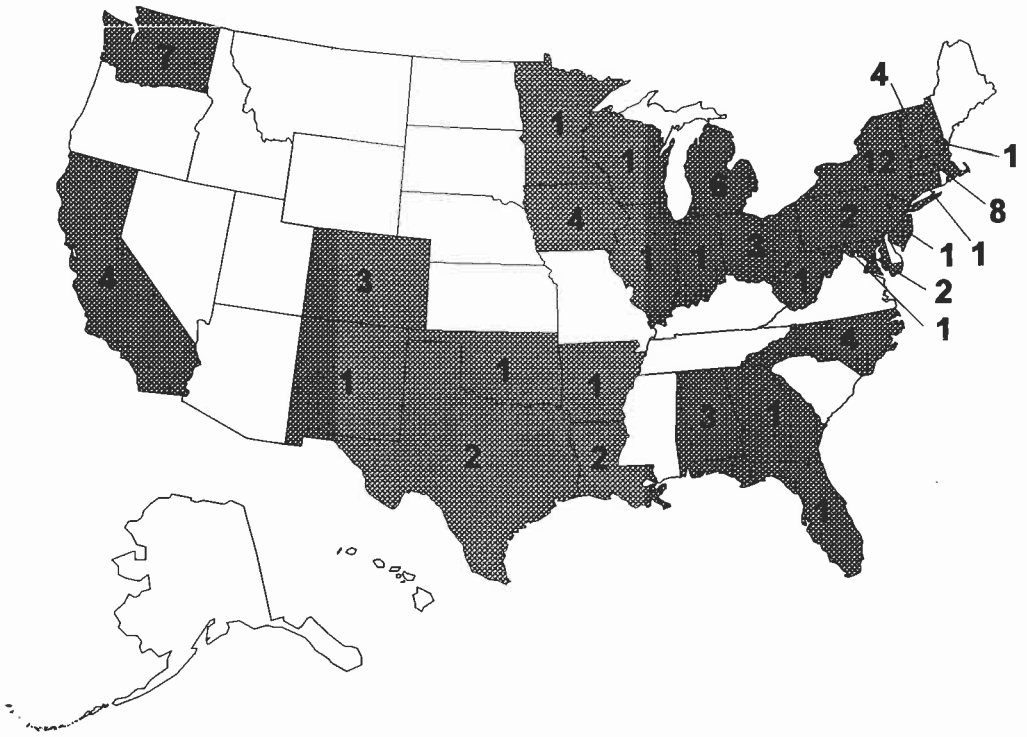
RESEARCH OBJECTIVES

	Amount	Percent
IH = Identification/Characterization of Hazards	$2,233,413	24%
EM = Development of Environmental Exposure Measurement Tools	$289,605	3%
AE = Investigation of Adverse Effects	$4,519,084	49%
BM = Discovery of Biological Exposure and Response Markers	$715,711	8%
CA = Development of Control Approaches/Interventions	$709,529	8%
CE = Assessment of Effectiveness of Controls/Interventions	$732,853	8%

A traditional system for classifying research is to consider identification, evaluation, and control of hazards. By grouping the above six categories into three pairs (IH & EM; AE & BM; CA & CE), the distribution of grant funds is 27% for identification, 57% for evaluation, and 16% for control. A special subset of identification is highlighted because of the importance of development of exposure assessment tools. A special subset of evaluation is highlighted because of the relatively new and potentially powerful technique of biological markers. Control research can be broken into the development of techniques and the assessment of their effectiveness.



FY94 Grant Awards by State
79 Totaling $9,200,195



State	Amount	%
Alabama	$294,813	3.2
Arkansas	$29,988	0.3
California	$312,342	3.4
Colorado	$470,858	5.1
Connecticut	$220,358	2.4
Florida	$54,000	0.6
Georgia	$338,727	3.7
Iowa	$214,685	2.3
Illinois	$38,876	0.4
Indiana	$152,600	1.7
Massachusetts	$946,069	10.3
Maryland	$223,290	2.4
Michigan	$1,089,192	11.8
Minnesota	$119,271	1.3
Missouri	$21,375	0.2

State	Amount	%
New Hampshire	$37,433	0.4
New Jersey	$257,626	2.8
New Mexico	$54,000	0.6
New York	$1,095,002	11.9
North Carolina	$396,399	4.3
Ohio	$461,351	5.0
Oklahoma	$342,514	3.7
Pennsylvania	$143,273	1.6
Texas	$284,435	3.1
Utah	$130,588	1.4
Vermont	$442,623	4.8
Washington	$742,083	8.1
Washington, D.C.	$114,448	1.2
Wisconsin	$35,638	0.4
West Virginia	$136,338	1.5

Development of Models to Predict Optimal Lifting Motion

Mohamed M. Ayoub, Ph.D.
Texas Tech University
Department of Industrial Engineering
Mail Stop 3061
Lubbock, Texas 79409

Grant Number: *5 R01 OH02434-06*
Start & End Dates: *01/01/88 – 08/31/95*
Funding Level: *$43,696 ($398,227 Cum)*

Importance to Occupational Safety and Health

Back injuries due to manual lifting are a serious problem in terms of human suffering and cost. An ergonomic approach to solve the problem is to redesign the lifting tasks to better fit human capabilities. Thus, biomechanical models serve a very useful purpose in analyzing the human motion patterns and estimating the stresses on the musculoskeletal system especially the lumbar spine. With the development of simulation lifting models, it is possible to provide an indirect means of performing the biomechanical analysis without collecting the displacement–time information. The model predicts the motion pattern based on the specified characteristics of anthropometry, of work station, and of lifting task, using optimization techniques.

Objectives

The goal of this study is to develop a biomechanical simulation model which can predict displacement time information for five selected joints during manual lifting. The five selected joints are the elbow, shoulder, hip, knee, and ankle.

Methodology

To accomplish the objective, there are three general tasks to be undertaken. The first task is to generate the possible posture assumed by the joints at each time frame during the course of the lift. The second task is to evaluate the kinematics and kinetics of the lifting generated from the first task. Within the two–dimensional space defined by the ankle–origin coordinate system, the lifting motion from the starting posture to the ending posture is computed and mathematically described. The third task is to improve the lifting motion by minimizing an objective function. By considering that different lifting motion patterns have different objective function values, the smallest objective function value within the feasible operation region indicates the best lifting motion pattern.

Significant Findings

The predictions and the actual displacement–time information were compared by closeness (average of the sum of squares of errors) and trend (average of the disconcordant pairs). The model, considering both kinematic and kinetic capabilities, provides promising results. In general, the envelope formed by the predicted motion patterns overlapped with the envelope formed by the actual motion patterns. In addition to the displacement–time plot comparison, model analyses were also carried out by comparing the box and joint trajectories using stick diagram and animated stick motion. Analyses using data collected on trained subjects showed a significant decreasing trend in the objective function during the training period, which was indicative of the optimization hypothesis of the model. Overall, the analyses showed:

1. The prediction of the box and joint trajectories may violate physical constraints such as object avoidance. Object avoidance constraints were implemented to produce reasonable lift trajectories which avoided collisions between the box–table and box–knee relationships.
2. Phase relationships, evaluated by the disconcordant pairs, can be found in the displacement–time plot comparisons. In most cases, actual displacement arose faster than the prediction in the early stage of the lift. The animated stick motion also showed that the model lagged behind the actual lift at the beginning of the lift.
3. Actual and predicted joint velocities were compared at the beginning of the lift, defined as the lift–off of the box. The predicted motion was based on the assumption that each joint started from an initial zero–value velocity. However, examination of the velocity–time plots of the joints of the actual lifts showed that the joints were in motion and had non–zero velocities prior to lift–off. This has important implications in accounting for the lag of the prediction as described in 2. Non–zero initial velocities will be implemented and evaluated to better predict the motion.
4. Training data showed that the decreasing trend in objective function was primarily due to the decrease in total lifting time.

Publications

Bernard TM, Ayoub MM, Lin CJ, Macedo JA: Simulation of the Optimal Lifting Motions. Proc of the 12th Congress of the International Ergonomics Association, Toronto, August 17–18, 1994

Lin CJ, Bernard TM, Ayoub MM, Macedo JA: Biomechanics of Manual Material Handling Through Simulation. Advances in Industrial Ergonomics and Safety, 6:635–640, 1994

Bernard TM, Lin CJ, Ayoub MM, Hsiang MS: Predicting the Optimal Lifting Motions Through Simulation, Proc of the M.M. Ayoub Occupational Ergonomics Symposium, pp 97–100, April 16–17, 1993

Hsiang MS, Ayoub MM: Development of Methodology in Biomechanical Simulation of Manual Lifting. International Journal of Industrial Ergonomics, accepted 1993

Ayoub MM, Hsiang MS: Biomechanical Simulation of a Lifting Task. 1st Industrial Engineering Research Conference Proceedings, Institute of Industrial Engineers, Norcross, Ga., 1992

Ayoub MM, Hsiang MS: Biomechanical Simulation of a Lifting Task. Advances in Industrial Ergonomics and Safety, IV, 1992

Ayoub MM, Blair EL, Hsiang S, Chinnam B: Biomechanical Simulation of Lifting. Proc of the 11th Congress of the International Ergonomics Association, Paris, pp 63–65, 1991

Ayoub MM, Blair EL: From Biomechanical Modelling to Biomechanical Simulation. Proc of Human–Centered Design Technology for Maintainability Workshop. Air Force Human Resources Laboratory, Wright–Patterson Air Force Base, Ohio, September 13, 1990

Lee YH: Toward Electronic Work Design. Proc of Human Factors Society, 32nd Annual Meeting, Volume 1, pp 622–626, 1988

Stochastic Model of Trunk Musculature During Lifting

Gary A. Mirka, Ph.D.
North Carolina State University
College of Engineering
Department of Industrial Engineering
P.O. Box 7906
Raleigh, North Carolina 27695

Grant Number: *5 K01 OH00135-02*
Start & End Dates: *09/30/93 – 09/29/96*
Funding Level: *$53,124 ($104,608 Cum)*

Importance to Occupational Safety and Health

Traditionally, biomechanical models of the lumbar spine have assumed that the forces exerted by the trunk muscles in response to external loads are deterministic. That is, given a set of lifting conditions (torque, position, velocity, etc.) the activation of the trunk muscles is precisely determined such that equilibrium exists. However, because of the indeterminate nature of the biomechanical system, variability in the individual muscle forces is not only possible, it is likely. Variability in the individual muscle forces alters the loading patterns on the spine because each muscle has its own vector line of action which has a component in compression, anterior shear and lateral shear. Therefore, by omitting the stochastic nature of trunk muscle activation from the analysis, it is believed that deterministic biomechanical models are not capable of modelling the range of potential spine reaction forces and ultimately are underestimating risk of manual materials handling tasks.

Objectives

The objective of this research project is to develop a stochastic model of the lumbar trunk during lifting. This model will use stochastic principles to predict the activation levels of ten trunk muscles under occupational lifting conditions including varied weights, postures, dynamic components, and asymmetric lifting. This stochastic model is being developed in two phases. In the experimental phase, human subjects are asked to perform highly controlled simulated lifting motions repeatedly. The electromyographic (EMG) activity of ten trunk muscles will be sampled and is used to develop a database describing that particular lifting motion. In the modelling phase, this database will be used in a simulation model which will generate potential

muscle activities. Multiple runs of the simulation model will generate possible time dependent EMG traces suitable for input into an EMG assisted biomechanical model which will then generate stochastic spine reaction forces. As the modelling efforts proceeded, it became evident that one aspect which required further investigation was the variability in human performance– specifically the variability in the kinematic and kinetic parameters describing trunk motion during lifting tasks. The following is a description of this study which was conducted over the past year.

Methodology

Seven subjects performed 8 repetitions of a series of simple lifting tasks. The independent variables in this study were the magnitude of the load and the quality of the coupling interface between the subject and the box being lifted. The levels of load magnitude were: 4.5, 9, 13.5 18, 22.5, 27, and 31.5 kg. The coupling levels were good, fair and poor as described by the revised NIOSH lifting guidelines. All lifts were performed in sagittally symmetric postures.

The dependent variables were the kinematic parameters describing the position and motion of the lumbar trunk in the sagittal, coronal and transverse planes. Calculations using a dynamic biomechanical model of the torso allowed for the calculation of torque in the sagittal plane about the L5/S1 joint.

The motion of the lumbar trunk was monitored using an device called the Lumbar Motion Monitor (LMM). This device was secured to the subject's back and measured the angular position of the lumbar spine in the sagittal, coronal and transverse planes. These position signals are then differentiated in software to get angular velocity and angular acceleration in the three cardinal planes.

Subjects were asked to lift a 35cm x 35cm x 30cm wooden box containing the designated weight. In the good coupling condition, the subjects used cut–out handles on the box. In the fair coupling condition, the subjects were instructed to lift the box from underneath. In the poor coupling condition the subjects were instructed to the lift the box with a compression type hold on the sides of the box.

The lift rate was set at 4 lifts per minute and the duration was two minutes for each experimental condition, rendering the eight repetitions. The subjects were asked to lift the box "using the maximum comfortable speed that you would normally lift an object of this weight" while keeping their elbows and knees at a constant degree of flexion throughout the range of lifting motion.

The biomechanical model used the kinematic data to calculate the time dependent, dynamic external torque about the lumbosacral joint. The body was partitioned into a 5–link system consisting of two upper extremity links, two lower extremity links, and a composite head/neck/trunk link beginning at the lumbosacral joint.

Significant Findings

The results of a quantitative analysis of trunk kinematics showed a significant motion in all three planes. Comparing the three levels of kinematic data, these results show that higher derivatives of motion become relatively more variable. The coefficient of variation (CV) for the range of motion in the sagittal plane was 2.5% while the CV for peak velocity was 8.1% and the CV for peak acceleration was 10.4%.

From an ergonomic point of view the greatest impact of this kinematic variability is in its effect on trunk kinetics. In an attempt to understand the effect of workplace factors on the magnitude of this variability, differences in the variance of the peak torques were tested using the Bartlett test for equality of variances. These results showed a significant effect due to the load weight, with greater weight levels showing a higher level of variability. Numerically, consideration of the range of potential torques about L5/S1 shows that the torques at 2 standard deviations above the mean are between 5% and 15% higher than the mean sagittal torques.

Kinematic results from the transverse and coronal planes also revealed a significant amount of dynamic activity in these "off–planes". The results of the present study have illustrated that there is significant motion in these off–planes– a result which indicates that current research may be over–simplifying spinal loading by considering primarily the compression forces in the spine to the exclusion of the more complex, coupled loads which would result from motion in these off–planes.

When the human performance variability demonstrated in this study is combined with the variability in internal forces, it becomes evident that in order to accurately quantify spine loading and risk of low–back injury, a clear representation of the stochastic nature of the system is required. This study has shown that by considering only the mean or average performance profile, the peak torque is underestimated by between 5% and 15%, as compared to values at 2 standard deviations above the mean. If, in fact, it is the peak loads which best describe injury, then it is believed that it is these extreme loads which need to be quantified in order to establish risk. Stochastic models are uniquely qualified to describe this risk because (1) they are capable of describing the magnitude of variable peak loads, (2) they are capable of quantifying the likelihood that these peak loads occur and (3) the may render a better understanding of the long–term cumulative effect of lifting.

Publications

Mirka GA, Baker A: An Investigation of the Variability in Human Performance During Sagittally Symmetric Lifting Tasks. IIE Transactions, accepted for publication, 1994

Mirka GA: An Investigation of the Variability in Human Performance During MMH Activities. Proc of the Human Factors and Ergonomics Society 38th Annual Meeting, Nashville, TN, p 578–582, October 24–28, 1994

Characterization of Posture, Force, and Repetitive Motion

Robert G. Radwin, Ph.D.
University of Wisconsin
College of Engineering
Department of Industrial Engineering
1513 University Avenue
Madison, Wisconsin 53706

Grant Number: *5 K01 OH00107-03*
Start & End Dates: *09/01/91 – 06/30/95*
Funding Level: *$0 ($160,578 Cum)*

Importance to Occupational Safety and Health

Cumulative trauma disorders are caused, aggravated, and precipitated by repetitive exertions and movements that workers are routinely required to perform, as well as awkward postures they must assume. Currently, there are no quantitative standards available for protecting workers from excessive exposure to these hazards. But before dose–response relationships can be established leading to exposure standards for preventing these disorders, practical methods are needed for measuring and characterizing worker exposure to cumulative trauma stress factors. This project is developing efficient analytical techniques for assessing physical stress and strain associated with hand–intensive tasks containing repetitive motion and forceful exertions. Applications of this theory include assessing exposure to physical stress in a manner analogous to the way sound level meters are used for measuring exposure to acoustic noise.

Objectives

It is hypothesized that if the associated power spectrum magnitudes correspond to joint excursion angles and forces at a particular frequency of repetition, then the degree of stress and repetitiveness will be indicated by the spectrum frequency components. Capability for characterizing and reducing stress and strain associated with repetitive motion and exertions are being tested using both industrial tasks simulated in the laboratory and actual tasks performed in the workplace. This investigation further hypothesizes that frequency–weighted filters for continuous biomechancial measurements of joint motion and force can be developed, corresponding to human exposure response characteristics as a function of frequency, in order to reduce the data in a single quantity while retaining the relationship between amplitude and frequency.

Methodology

Spectral analysis was investigated as a method for characterizing repetitive wrist motion and postural stress using a simple peg transfer task. Wrist posture was controlled by adjusting the pegboard location and by having subjects reach over an obstruction. Work pace was externally controlled using an auditory signal. Angular wrist flexion/extension and ulnar/radial deviation was recorded using a Penny and Giles strain gage electrogoniometer and sampling the analog signal at a 60 Hz sample rate. Wrist movement data was transformed into the frequency domain for determining the frequency and magnitude of repetitive motion and forceful exertions performed during manual work. Power spectra were computed by stratifying data segments into individual work elements, divided by break points associated with the task. This frequency domain approach was used for averaging elemental data from repetitive cycles.

To test the feasibility of frequency–weighted filters, a psychophysical experiment was conducted for studying the effects of repetition rate (frequency) and repetitive motion (wrist flexion angle) on subjective discomfort. Low force repetitive wrist flexion was studied. A fixture was constructed for limiting wrist flexion limits. Subjects grasped a handle and repetitively flexed and extended at the wrist. Two mechanical stops were adjustable so wrist flexion can be limited between 0° and ±90°. An electronic timer produced a tone indicating the pace.

The full–factorial experiment consisted of five paces and two wrist flexion angles. The timer produced a brief tone indicating to the subject to perform a wrist flexion every 1 s, 2.5 s, 5 s, 10 s, and 20 s. Wrist flexion was limited to 35° and 65°. Each experimental condition was performed for one hour. Five female subjects were randomly recruited and paid on an hourly basis. Discomfort was measured using the cross–modality matching method. Subjects marked localized discomfort on a 10 cm linear scale, anchored on the left as a no discomfort,"

and on the right as a very high discomfort." Localized forearm discomfort was assessed every fifteen minutes during a one minute break in the hour long experimental session.

An experiment was conducted to study the relative effects of repetition, exertion and postural stress on discomfort. The task involved repetitively flexing the wrist from a neutral posture to given angle against a controlled force. A fixture similar to the above–mentioned apparatus was constructed for controlling force from the resistance of an electric magnetic brake with a clutch so subjects flexed against resistance to a predetermined angle, but felt no resistance when extending the wrist. Three subjects performed the wrist flexion task every 3 s and 15 s. Force was set at 15 N and 25 N, and wrist flexion was limited to 15° and 45°. Each condition of the full–factorial experiment was performed for one hour. Discomfort was reported on a linear analog scale between 0 and 10 anchored between "no discomfort" and "very high discomfort."

Significant Findings

Peak spectral magnitudes and frequency components corresponded closely with joint displacement amplitudes and repetition rates. Power spectra fundamental frequencies corresponded to the cycle repetition frequency, within the frequency resolution of the spectrum. Spectrum fundamental frequency magnitudes were able to resolve differences in postural changes between different peg board rows. Therefore, this method was not only demonstrated useful for measuring the rate of repetition, but for indicating the magnitude of postural stress for movements at each repetition rate. Spectrum DC component magnitudes were directly related to sustained wrist postures. These components independently measured sustained posture while the AC components measured repetitive movements. Although eliminating the obstruction affected the DC component magnitude, due to the absence of sustained wrist flexion, ulnar/radial deviation DC components and the flexion/extension fundamental frequency magnitude were unaffected.

A linear polynomial regression model for log–transformed discomfort was fitted against the log of wrist flexion angle and the log of frequency. Equal discomfort strata for wrist flexion were determined by solving the regression equation for flexion range at given frequencies for different discomfort levels. This equation was used for specifying attenuation levels needed for high pass filters that weigh repetitive wrist flexion in proportion to the discomfort function. This resulted in a high–pass filter having a slope of 10 dB/decade. A validation experiment resulted in good agreement between reported discomfort and frequency–weighted wrist movement.

Equal discomfort strata for frequency, exertion, and angle were similarly determined. This investigation showed that frequency–weighted filters corresponding to discomfort responses associated with exertions and movements at specific frequencies can be developed.

Publications

Radwin RG, Lin ML, Yen TY: Exposure Assessment of Biomechanical Stress in Repetitive Manual Work Using Frequency–Weighted Filters. Ergonomics 37:1945–1959, 1994

Radwin RG: An Analytical Method for Characterizing Repetitive Motion and Postural Stress Using Spectral Analysis. Ergonomics 36(4):379–389, 1993

Radwin RG, Lin ML, Yen TY: Exposure Assessment of Biomechanical Stress in Repetitive Manual Work Using Spectral Analysis. Proceedings of the Human Factors and Ergonomics Society Annual Meeting, 1993

Radwin RG: Development of An Efficient Analytical Method for Quantifying Repetitive Motion. Proceedings of the International Scientific Conference on Prevention of Work–Related Musculoskeletal Disorders, Stockholm, Sweden, May, 1992

Intracarpal Pressure During Hand Maneuvers

David M. Rempel, M.D.
University of California
Center for Occupational and Environmental Health
SFGH, Bldg. 30, 5th Floor
San Francisco, California 94110

Grant Number: *5 K01 OH00121-03*
Start & End Dates: *08/01/92 – 07/31/95*
Funding Level: *$54,000 ($162,000 Cum)*

Importance to Occupational Safety and Health

Carpal tunnel syndrome is the most common entrapment neuropathy in humans and accounts for significant disability, suffering, and cost. There is strong evidence that it is related to occupations

involving hand intensive work activity. The long–term objective of this line of research is to use intracarpal pressure to specify hand maneuvers that can be safely performed in the workplace, which, if followed, will prevent carpal tunnel syndrome and wrist tendinitis.

Objectives

The specific aims are to (1) determine whether the relationships between CTP and elementary hand maneuvers are consistent between subjects and identify what those relationships are, (2) determine whether the CTP varies significantly within subjects performing typical work–related activities and identify the predictors of that variability, and (3) develop a mathematical model that will predict CTP as a function of elementary hand motions.

Methodology

Twenty subjects without, and 4 patients with, carpal tunnel syndrome have been tested to date. An additional 20 normal subjects will be recruited from local newspapers to participate in this laboratory study. A blunt tipped 23– gauge catheter connected to a pressure transducer will be inserted at the wrist into the carpal space (Weiss, 1992).

We are currently developing a new system for measuring joint angles to replace the use of electrogoniometers. This system utilizes video tracking of infrared LEDs to determine three dimensional movements of the body segments. The application of this video technology to our study will increase the accuracy of our angular displacement measurements. It will have no effect on the experimental protocol or subjects.

The angular outputs and the output of an electronic pinch meter will be sampled at 40 Hz and stored on a microcomputer. The hand maneuvers to be evaluated are: wrist extension/flexion angle and wrist ulnar/radial deviation angle, metacarpophalangeal joint angle, and pinch force. During the first phase, subjects will perform elementary hand maneuvers while data is collected. In the second phase, typing tasks will be performed to clarify the relationship between hand maneuvers and CTP.

Significant Findings

Twenty subjects without, and 4 patients with, carpal tunnel syndrome have been tested to date. Twenty subjects were asked to move their wrist and fingers to the one hand position associated with the lowest CTP. The group mean wrist position selected was 3 degrees ulnar deviation (s.d. 8) and 2 degrees of flexion (s.d. 11). This position is similar to the "optimal" "neutral" position suggested by ergonomists and industrial engineers for task design. As observed by others, the normal population had mean baseline CTP of 7.3 mmHg (s.d. 5.1). In the patients with CTS, the mean baseline CTP was 18.2 mmHg (s.d. 1.7). The CTP baseline was measured 8 times over a 4 hour period and did not vary: the estimated within–subject variance was 2.2 and the between–subject variance was 22.7.

Subjects moved their wrists slowly in extension/flexion and ulnar/radial deviation. CTP varied as some parabolic function of wrist position in all subjects. That is, the lowest CTP was near 0 degrees extension/flexion and ulnar/radial deviation and then rose to its highest levels at extremes of extension and flexion, and ulnar and radial deviation. The highest CTPs were recorded at extremes of extension and radial deviation. The highest CTP measured was 220 mmHg. MP angle also modified CTP, but the relationship between MP and CTP remains to be analyzed.

Nineteen of the volunteers who demonstrated no evidence of carpal tunnel syndrome performed a repetitive material handling task involving loading and unloading 1 lb. cans from a box at a rate of 20 cans per minute for a period of 5 minutes (Rempel et al., 1994a). The task was performed with and without a flexible wrist splint. Pressure and position were also recorded at rest with and without the splint. Without the splint, CTP rose from a median baseline level of 13 ± 5 mmHg to 21 ± 12 mmHg during activity. With the splint, CTP rose from a median baseline level of 8 ± 6 mmHg to 18 ± 13 mmHg during activity. Median CTP during activity with the splint was not significantly different from that without the splint.

Fourteen normal subjects also performed a task involving fingertip loading of the index finger (Rempel et al., 1994b). Fingertip load was measured using a pinch meter, in addition to the measurement of CTP and wrist position as described. The subject was instructed to press down on the pinch meter with their index finger with 0, 6, 9, and 12 N force. The other fingers were not loaded. This experiment was repeated with the wrist in 10 different positions. Across all subjects and wrist angles, the CTP increased significantly as a function of static load at the fingertip. CTP rose to a high of 80 mmHg in one subject.

Publications

Rempel D, Manojlovic R, Levinsohn DG, Bloom T, Gordon L: The Effect of Wearing a Flexible Wrist Splint on Carpal Tunnel Pressure During Repetitive Han Activity. The Journal of Hand Surgery, 17(1):106–9, 1994

Unexpected Trunk Loading Following Seated Vibration

David G. Wilder, Ph.D.
University of Vermont
Department of Orthopaedics
and Rehabilitation
430B Stafford Building
Burlington, Vermont 05405-0068

Grant Number: *5 K01 OH00090-03*
Start & End Dates: *07/01/90 – 06/30/94*
Funding Level: *$0 ($204,967 Cum)*

Dr. Wilder is currently located at:
The University of Iowa, Department of Biomedical Engineering, EB 1216, Iowa City, Iowa 52242

Importance to Occupational Safety and Health

This work studied *in vivo*, the effects of common loading environments on the mechanical response of the seated human. The eventual goal of this work is to evaluate and control the occupational health hazard of low back pain, a musculoskeletal injury, by establishing an "envelope" of loading conditions which should not be exceeded if the spine is not to experience mechanical damage. Proceeding from prior *in vitro* findings of short–column buckling in the lumbar spine following vibration exposure, this proposal is evaluating how the supporting trunk musculature responds to an unexpected load application after a 40–minute load intervention [seated vertical vibration, seated lateral vibration, seated lateral and vertical vibration or sitting still (as a control)]. This simulated the sudden and unexpected shift of an object in the hands of the car or truck driver who has driven for 40 minutes. Normal walking (as a break) for five minutes, prior to an unexpected load application, was also tested to determine if it would be a reasonable control. This would allow lumbar discs to return, via creep behavior, to the upright posture orientation where the facets are more firmly engaged.

Objectives

These hypotheses will be tested using a repeated measures analysis of variance:

1. There are significant differences in trunk muscle activity during unexpected load application between:
   a. subjects with chronic back trouble and normal controls and
   b. subjects with different load exposure histories [seated vertical vibration, seated lateral vibration, seated lateral and vertical vibration, or sitting still (as a control)].
2. There are significant differences in main and coupled mechanical driving point impedance characteristics during brief vibration exposures for mechanical response evaluation between:
   a. subjects with chronic back trouble and normal controls and
   b. subjects with different load exposure histories [seated vertical vibration, seated lateral vibration, seated lateral and vertical vibration, or sitting still (as a control)].
3. A walking break for 5 minutes "resets" the system.

Methodology

Trunk muscle activity (from normals and patients via surface electromyography) and main and coupled mechanical driving point impedance (from normals only via brief vertical vibration exposures for mechanical response assessment) of subjects were recorded and used as the outcome measures of the tests. Twenty two subjects were tested: 9 males and 13 females of whom 16 were normal controls and 6 right–handed subjects (3 male and 3 female) had diagnosed chronic back trouble (2 with disc herniation, 2 with spinal stenosis, 1 with disc degeneration and osteophytes, and 1 with facet arthrosis). Outcome measures were obtained before and after sustained exposure to specific loading environments. Low back trouble patients were randomly assigned to quiet sitting or seated vibration for 40 minutes, before and after which sudden load applications were repeated six times. The procedure was then repeated with the patient in the other seated exposure. The vertical vibration input was 5 Hz and 0.315 ms^{-2} rms, at the ISO 8–hour FDP level. Trunk muscle activity was monitored during the sudden, unexpected flexion load applied to the patient.

Significant Findings

Data for the normals are still being analyzed. Results for the chronic low back trouble patients follow: Under all conditions there was a reaction time difference between the erector spinae muscle groups to the right and left sides of the lumbar spine averaging 73–108 msec. There was no significant effect of side in the responses. However, there was a trend ($p<.07$) for the left side to respond faster than the right side after exposure to seated vertical vibration. Walking for 5 minutes, following the initial muscle/flexion–moment calibration significantly

shortened the muscle reaction time on the right side ($p<.025$). But, with the same prior activity, there was only a reaction time decreasing trend ($p<.10$) on the left side. Walking tended to decrease the reaction time after the initial calibration and after vibration exposure. Walking tended to increase the reaction time after static sitting.

Avoiding asymmetrically applied loads is important for the long-term health of the lumbar spine. This study suggests that due to timing differences in the back muscles' response to unexpected loads, there is the potential for asymmetric loading of the lumbar region. The greater the reaction time, the greater the load application asymmetry between right and left sides. The greater the delay in counteracting the unexpected flexion moment, the larger the muscle force necessary to compensate, hence the greater the load on the intervertebral disc. It is not clear whether these subjects' ability to respond to unexpected loads were the cause or the result of their low back trouble.

Publications

Wilder DG, Wasserman DE, Pope MH, Pelmear PL, Taylor W: Occupational Vibration Exposure, Measurement, Standards and Control. In: Physical and Biological Hazards of the Workplace, (eds. P Wald, G Stave), Van Nostrand Reinholdt, New York, NY, in press, August 1994

Pope MH, Wilder DG: Whole Body Vibration. In: Occupational Musculoskeletal Disorders: Assessment, Treatment and Prevention, (eds. M Nordin, MH Pope, GBJ Andersson), In Press: Mosby Year Book, 1993/1994

Brinkmann P, Wilder DG, Pope MH: Effects of Repeated Loads and Vibrations. In: The Lumbar Spine, (eds. JN Weinstein, SW Weisel), 2nd Edition, International Society for the Study of the Lumbar Spine, W.B. Saunders Co, Philadelphia, in Press, 1994

Pope MH, Jayson MIV, Blann AD, Kaigle AM, Weinstein JN, Wilder DG: The Effect of Vibration on Serum Levels of Von Willebrand's Factor. A Preliminary Communication. European Spine Journal 3(3):143-145, 1994

Blann A, Jayson MIV, Pope MH, Kaigle AM, Wilder D, Weinstein JN: Postural Variation In Von Willebrand Factor Antigen [letter]. Annals of the Rheumatic Diseases 52(1):82, 1993

Wilder DG: The Biomechanics of Vibration and Low Back Pain. American Journal of Industrial Medicine 23(4):577-588, 1993

Magnusson M, Wilder DG, Pope MH, Hansson T: Investigation of the Long-term Exposure to Whole Body Vibration: A 2-country Study. Winner of the Vienna Award for Physical Medicine. European Journal of Physical Medicine and Rehabilitation 3(1):28-34, 1993

Magnusson ML, Wilder DG, Pope MH, Hansson T: Back, Shoulder and Neck Pain in Occupational Drivers - A Two-center Screening of Long-term Exposure. In: Advances in Idiopathic Low Back Pain, (eds. E Ernst, MIV Jayson, MH Pope, RW Porter), Blackwell-MZV, Vienna, 1993

Blann AD, Allen J, McKenna K, Wilder DG, Pope MH, Kaigle AM, Weinstein JN, Jayson MIV: Vibration and Induction of Endothelial Injury [letter]. Lancet 340(8819):616-617, 1992

Pope MH, Wilder DG, Magnusson M, Hansson T: Impact and Its Effects on the Lumbar Spine. In Proceedings of the Canadian Society of Mechanical Engineers FORUM 1992 "Transport 1992+", Montreal, June 1-5, 1992

Pope MH, Jayson MIV, Blann AD, Kaigle AM, Weinstein JN, Wilder DG: The Effect of Vibration on Serum Levels of Von Willebrand's Factor, A preliminary communication. Orthopaedic Transactions 16(1):245-246, 1992 (Abstract)

Wilder DG, Magnusson M, Kaigle AM, Beliveau J-G, Pope MH: Seated Subject Vibration Response: Analysis of A Heavily Damped System. Orthopaedic Transactions 15(2):291, 1991 (Abstract)

Effect of Load Asymmetry on Internal Loading of The Trunk

Ali Sheikhzadeh
Hospital For Joint Diseases
Occupational and Industrial
Orthopaedic Center
63 Downing Street
New York, New York 10014

Grant Number: *5 R03 OH03087-02*
Start & End Dates: *08/01/93 - 07/31/95*
Funding Level: *$35,900 ($71,800 Cum)*

Importance to Occupational Safety and Health

In industry, carrying and lifting objects asymmetrically is the rule rather than the exception. This situation is hazardous to the musculoskeletal system due to an increase in coactivation of the musculature and an increase of the forces on the spine.

The present study will provide a better understanding of the effect of asymmetrical lifting on mechanical and neuromuscular performance and on the risk of injury to the back.

Objectives

The aim of this study is to quantify the activities of ten trunk muscles by using the surface electromyography (EMG) during maximal and submaximal isometric exertion under pure and combined loading conditions of the trunk. Combined loading is defined as the vectorial sum of moments in the sagittal and transverse planes. These planes are selected based on their prevalence in industrial tasks and low back injuries.

Methodology

To calculate the effect of internal loading, the muscle parameters are calculated from CT–scan images of each individual participant and individual muscle forces are estimated using an EMG–driven model. The compression and shear forces are calculated under suggested conditions. The effects of planar exertion (pure exertion) and combined exertion on the patterns of trunk muscle recruitment and compression and shear forces will be compared.

The primary hypotheses of this study are:

1. The peak EMG activity of trunk muscles will be higher during the maximal combined exertion than during pure maximal exertion.
2. The mean of RMS–EMG of the ten selected trunk muscles will change significantly with the orientation of the net resultant moments of the trunk.
3. The compression and shear forces will be changed significantly by the orientation of the resultant moment.

Significant Findings

None to date.

Role of Postural Stability in Industrial Falls

Amit Bhattacharya, Ph.D.
University of Cincinnati
College of Medicine
Department of Environmental Health
3223 Eden Avenue
Cincinnati, Ohio 45267-0056

Grant Number: *5 R01 OH02794-02*
Start & End Dates: *09/30/91 – 09/29/94*
Funding Level: *$0 ($373,611 Cum)*

Importance to Occupational Safety and Health

Falls have been found to be a significant contributor in causing lumbar spine injury, fracture of bones, and disability. A review of occupational injury data in U.S. industries and those in other countries indicates that the construction industry has the highest incidence rates of accidents, including fatalities, among major industries. As per literature review, various field studies have identified several risk factors as contributing to falls at the workplace. These are: Environmental (surface contamination and friction, standing surface firmness and lighting); Job–Task (blocking of peripheral vision due to poor work layout and workload); and Personal (age, sex, and physical fitness level) factors.

This study will help identify and quantify the influence of individual and combination effects of Environmental, Job–Task and Personal risk factors on fall potential. The results from the proposed study will help develop a statistical model showing relationship between fall potential and the independent variables characterizing the Environmental, Job–Task and Personal risk factors. In future field studies, use of the statistical model to help evaluate the fall potential can be accomplished by measuring, in a walk–through evaluation, existing risk factors at the work site. The model can then be used to determine which of the risk factors need to be corrected to reduce the fall potential. Availability of such models will have significant impact in identifying risk factors and their reduction will help prevent fall–related injuries, disabilities, lost work days, and higher medical costs as well as increasing national productivity.

Objectives

1. To measure the upright postural balance (stability or sway) under different standing surface

contamination conditions (dry/clean and oily), standing surface firmness (firm and compliant), environmental lighting (good and poor), and peripheral vision conditions (blocked and unblocked) after being exposed to different workloads (40 watts and 100 watts) in workers in the age range of 21 to 55 years.

2. To investigate the age–associated differences in the maintenance of upright postural balance under above mentioned risk factors.
3. To investigate the age–associated differences in postural corrective responses to: (a) sudden perturbation in the body segment movement; (b) forward reach and lifting; and (c) sudden external loading under all combinations of risk factors.
4. To investigate the age–associated differences in the relationship between an objective measure of postural instability and the subjective perception of postural instability, under all combinations of risk factors.

Methodology

In this study, postural instability and fall potential of risk factors are evaluated for industrial workers' performance on 32 test conditions which represent combinations of these risk factors. These tests simulate conditions which occur in industrial/occupational environments. The current pool of industrial subjects represent a wide range of occupations. Subjects are tested immediately after exposure to light and moderate–to–heavy workloads (bicycle ergometer) to quantitate their postural stability. Before and immediately after completion of a workload, the subject is tested for upright postural sway and postural corrective responses to simulated tasks which might occur in an industrial environment. Also, their subjective perception of postural balance is assessed immediately after each test using a subjective Scale of Rating of Perceived Sense of Fall. The postural stability is measured with a six–component force platform located inside our Fall/Stability Assessment Facility. Each subject's "Functional Stability Boundary" is also determined. This information is used to determine which of the test conditions pushed the body's center of pressure to or beyond its stability boundary and, therefore, had the potential to create an accident due to a fall or near fall.

Significant Findings

The data have been collected from all 52 industrial workers and final analyses are in the process of being performed. A quantitative method of characterizing fall potential has been developed and is being used to determine the effectiveness of this technique with the data from this study. A preliminary analysis of the data collected from all subjects (providing data from 11,648 postural tests) has been performed. All conditions (workload,surface firmness, surface slipperiness, lighting and peripheral vision) show a significantly ($p<0.05$) detrimental effect on postural balance as measured by the sway length parameter in a repeated measure analysis of variance. Each of these significant effects are consistent with our proposed hypotheses. Certain interactions among the experimental conditions or between age or gender and the within–subject conditions are also significant. For example, a significant lighting/surface firmness interaction indicated that subjects had even more difficulty while standing on a compliant surface in dim lighting than would be expected from either of these factors alone. A short questionnaire–type loss of balance perception scale was developed and tested in this project also. The reproducibility of this scale was tested and found that there is no learning effect and the effect of different visit on the score was not significant. The subjective measure of loss of balance was significantly correlated with the objective measure of postural sway for the tasks of rapid trunk movement and sudden external loading. The subjective measurement of loss of balance scale was effective in detecting significant effects of task ($p<0.001$), workload ($p<0.001$) and environmental factors including lighting ($p=0.0001$) and surface firmness ($p=0.0001$) and peripheral vision ($p<0.001$). It is interesting to note that except for the slipperiness condition the subjective scale for balance was able to detect the loss of balance effect of all other risk factors as effectively as that determined by the objective measure of postural sway. This data provides new light toward workers' ability to correctly perceive the balance demands so that necessary postural stabilization processes can be deployed. Also, this technique may provide a simple method for evaluating the propensity of loss of balance at the workplace.

Publications

Bagchee A, Bhattacharya A: Method for Estimating Fall Potentials in Clinical, Occupational and Environmental Exposure Cases. Presented at the Second North American Congress on Biomechanics, Chicago, IL, August, 1992; J Biomechanics, 26(3):305, 1993 (Abstract)

Ergonomics of Task Performance On Slippery Surfaces

Amit Bhattacharya, Ph.D.
University of Cincinnati
College of Medicine
Department of Environmental Health
3223 Eden Avenue
Cincinnati, Ohio 45267-0056

Grant Number: *5 R01 OH03079-02*
Start & End Dates: *09/15/93 – 09/14/96*
Funding Level: *$197,945 ($431,016 Cum)*

Importance to Occupational Safety and Health

Previous studies have shown that the event which immediately led to injury was slip in about 50% of the cases. This type of underfoot "first event" has been the main contributor to falls. The proposed study provides an experimental design which has the potential for investigating the interaction between age, sex and other fall risk factors such as psychophysical aspects of slipperiness evaluation, objective measure of surface slipperiness, shoe wear/tear, and lighting, while performing simulated industrial tasks. The proposed study will provide dynamic coefficient of friction (DCOF) and the rate of change in DCOF as criteria for slip prevention for (1) dynamic task performance while standing on a slippery surface and (2) walking with and without a turning motion with a weight in hand. Additional information will be provided regarding the change in the above criteria when wearing a used shoe with a worn–out sole surface in a young and an older age group of workers. The gait pattern characteristics can significantly influence the required DCOF demand which provides the necessary slip protection. This type of information will have significant impact on the development of better portable slip–testing devices which can be used in a more realistic manner at the worksite (such as, the use of worker shoes which were involved in a slip–related accident) and can measure appropriate variables which better predict slips at the workplace.

Objectives

1. To determine the relationship between subjective assessment of slipperiness and the objective measure of coefficient of friction under optimal environmental lighting, job–task, and shoe sole wear/tear conditions. Also, determine the age–associated influence on the above relationship.
2. To determine the effect of risk factors of environmental lighting, job–task, shoe sole wear/tear and the subject's age on her/his ability to correctly assess the slipperiness of a surface.
3. To determine the effect of environmental, job–task, and personal risk factors on the subject's ability to perform tasks requiring demands on her/his static (upright balance) and dynamic (gait) postural balance while her/his shoe sole surfaces are in contact with a slippery surface. To determine the age–associated differences in postural balance and gait characteristics associated with task performance on a slippery surface.
4. To identify and quantitate postural balance variables relevant for assessing the fall potential associated with task performance on slippery surfaces under various combinations of fall risk factors.
5. To determine the characteristics of the required coefficient of friction values and body segment movement dynamics for performing tasks without slipping under various combinations of environmental lighting, job–task, and shoe sole wear/tear conditions.

Methodology

In the proposed study, gait and postural instability and fall potential of all risk factors will be evaluated for industrial workers' (21–29 and 50 to 59 years of age) task performance on a slippery surface. The upright postural sway test (stability) and tests of postural corrective responses to the testing of upright postural balance, rapid movement of body segment, and forward/upward reach during lifting will be administered under all combinations of the following test conditions. After the postural stability test, the subjects will undergo gait evaluation tests with and without a five pound weight in hand under all combinations of the following three test conditions. Condition 1: Three levels of randomized slippery surface (low, medium and highly slippery). Subjects will know that the surface is slippery but will be without the knowledge of its degree of slipperiness. Condition 2: Under acceptable (good) or unacceptable (poor) environmental lighting as per American Illuminating Engineering Society guidelines for rough to moderately precise work. Condition 3: Shoe conditions will be not worn–out sole (new) and worn–out sole. The order of administration of postural stability and gait tests will be randomized. An initial baseline measure (standing on a dry, nonslippery surface) will be performed before the randomized combinations of these conditions. The subject's stability boundary will be calculated from

the outer perimeter of the shoe print for the postural balance test and for the gait test the stability boundary will be estimated by the location of the foot placement on the force platform with the multi–camera video analysis system. Before initiating the postural balance and gait tests each subject will undergo subjective assessment of slipperiness test. During subjective slipperiness assessment test, postural stability test and gait test each subject's insole pressure distribution will be also measured.

Significant Findings

Before initiating the main study as described in the above, a pilot study was carried out to develop a quantitative method of characterizing workers' old shoe wear pattern and its effect on subjective and objective measure of slipperiness. Subjective rating of slipperiness tests were conducted for twelve male worker subjects under three different slippery surfaces, poor or good lighting conditions, and with new or workers' own old shoes. A strain gauge type force platform was used to evaluate DCOF of shoes for the same surface conditions representing objective measurements. The shoe wear, available tread pattern, and hardness of old shoes were determined by instruments including a digital caliper, a digitizer, and a durometer, respectively. The surface effect was found to be highly significant on subjective ratings as well as dynamic COF ($p < 0.0001$). The correlation between dynamic COF values and subjective ratings was only significant for old shoes under medium oily conditions ($r=0.55$, $p < 0.04$). For a slightly oily surface, decreasing the percent of tread available significantly increased dynamic COF values ($p < 0.016$). In addition, the effect of increased shoe hardness significantly increased the available tread pattern when only the data from the most deteriorated old shoes were included in the analyses ($p < 0.004$). This study indicates the need to consider the effect of available shoe tread on COF values and slip potential. Further investigation is needed to determine if guidelines should be developed regarding when work shoes should be replaced to reduce slip and fall injuries. So far, 13 industrial workers have undergone the main study protocol. Preliminary analysis of kinematic data collected with multicamera human body motion analysis system provided information regarding movement of whole–body center of gravity (CG) motion associated during walking along a straight line and a right angled turn path. In comparison to straight walk the walking along a turned path caused the whole body CG to move further out of the base of support (defined by the feet position) causing the potential of loss of balance to increase. The effect of whole body CG displacement was further accentuated when the subject walked on a slippery surface as the slipping foot (during single stance) moved laterally away from the center of the body. This raises an interesting question regarding how well the work shoes protect from slipping in the lateral direction while walking along a curved path. This issue willl be investigated further with new and old shoes.

Fall Potential of Work on Elevated & Inclined Surfaces

Amit Bhattacharya, Ph.D.
University of Cincinnati
College of Medicine
Department of Environmental Health
3223 Eden Avenue
Cincinnati, Ohio 45267-0056

Grant Number: *1 R01 OH03107-01A1*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$209,406 ($209,406 Cum)*

Importance to Occupational Safety and Health

Falls from elevated/inclined surfaces present significant potential for debilitating accidents causing permanent disability or fatality. Nationally, in 1991, the National Safety Council estimates that work–related falls caused the second highest level of fatalities. Among all industries, the construction trade has the highest rate of fall–related fatalities. An analysis of the database from the National Institute for Occupational Safety and Health (NIOSH) National Traumatic Occupational Fatalities (NTOF) for the period of 1980–1985 indicates that 17% of the workers had fatal falls while performing a task on a scaffold. In another study of data from NIOSH's database of Fatal Accident Circumstances and Epidemiology (FACE) for 1987–1989, it was found that fatal falls have occurred from heights as low as three feet. In an analysis of accident profiles among New York industries, it was found that falls were attributable to a combination of surface conditions and poor lighting. They also reported that 66% of these accidents occurred indoors where lighting conditions may be less than optimal, as in the case of new construction.

There are environmental (lighting), job–task (stationary versus dynamic) and personal (age) risk factors which can individually and/or collectively jeopardize one's ability to perform tasks on elevated/inclined surfaces without experiencing postural imbalance and, eventually, a fall. This grant application will find answers to the following

questions: (a) How do work surface inclination and elevation and distraction affect postural balance under conditions of good and poor lighting for young and older age groups? and (b) What type and positioning of visual cues will be beneficial in reducing postural instability while performing simulated industrial tasks on inclined and elevated surfaces? The results from this study will also help develop a statistical model showing the relationship between propensity of loss of balance and the independent variables characterizing the environmental, job–task, and personal risk factors. A determination of which of the risk factors need to be corrected to reduce the propensity of loss of balance and/or fall potential will then be possible.

Objectives

1. To determine the postural balance effects of performing simulated industrial tasks by industrial workers aged 21 to 29 years and 50 to 59 years while standing on three inclined surfaces (0°, 14° and 26°) at three elevations (ground/floor, one foot, and two feet above floor) under good (72 foot–candles) and poor lighting (0.2 foot–candles) conditions (Phase I).
2. To determine the contributions of individual and combined risk factors of standing surface inclination, elevation, environmental lighting, and age on modifying the propensity for postural imbalance (which might contribute to fall potential) during performance of industrial tasks (Phase I).
3. To determine the types (horizontal or vertical or horizontal plus vertical) and number of visual cues (in periphery or in central visual field or both) needed to help in the reduction of propensity for postural imbalance while performing tasks under various combinations of risk factors (Phases II and III).

Methodology

In the proposed study, postural instability and propensity of loss of balance risk factors will be evaluated for industrial workers' performance (21 to 59 years of age) on test conditions which represent combinations of these risk factors. The upright postural sway test (stability) and tests of postural corrective responses to the testing of upright postural balance, rapid movement of a body segment, and lateral sideways (both left and right side of the sagittal plane) reach during lifting will be administered under all combinations of the following test (treatment) conditions (independent variables). Inclined Surface (Condition 1): Three levels of inclination will be used, 0°, 14° and 26°. Elevated Surface (Condition 2): Floor (or ground), 12" and 24" above floor levels will be used. Work Environment Lighting (Condition 3): (1) Acceptable, good lighting: 320 – 800 lux and (2) Unacceptable, poor lighting: < 20 lux. Visual Cues (Condition 4): At least three types of cues will be used: None, Vertical and/or horizontal cues (white lines or, if necessary, fluorescent material may be used for visibility in poor light) in the central visual field, and visual cues in the periphery.

The order of administration of postural stability tests and treatment conditions will be randomized. An initial baseline measure (standing on floor, 0° inclination, and good lighting) will be performed before presentation of the randomized combinations of these treatment conditions. The objective criteria used for propensity of loss of balance will be: (a) proximity of the body's sway to the subject's stability boundary as well as other loss of balance and sway parameters; and (b) number of falls experienced during the performance of simulated industrial tasks. The project will be carried out in three phases. Phase I. Effect of standing surface inclination, elevation, and environmental lighting on postural instability (Specific Aims a to b); Phase II. Determination of location, number and types (vertical *vs* horizontal *vs* both vertical and horizontal) of visual cues needed for minimizing propensity for loss of balance while working on elevated surfaces (Specific Aim c): A Pilot Study and Phase III. Effect of visual cues in minimizing the risk of postural instability while performing industrial tasks under exposure to two types of standing surface conditions, i.e., inclination, and elevation (Specific Aim c).

Significant Findings

None to date.

Vibration Oculomanual Coordination and Traumatic Injuries

Bernard J. Martin, Ph.D.
University of Michigan
School of Engineering
Center for Ergonomics
1205 Beal Avenue, 156 IOE
Ann Arbor, Michigan 48109-2117

Grant Number: *5 R01 OH02967-02*
Start & End Dates: *05/01/92 – 12/31/94*
Funding Level: *$0 ($189,066 Cum)*

Importance to Occupational Safety and Health

The focus on manual control perturbation resulting from vibration exposure as a potential risk factor is of particular importance. Indeed, performance of visually guided motor activities is an important factor of accidents involving falls, dropping objects and improper use of controls. Furthermore, an estimated 1.45 million workers use vibrating tools and disabling injuries numbered 570,000 for mining, construction and manufacturing industries where vibrational hand–tools and vibrating machines are intensively used. Although one cannot blame vibration as a common denominator to those injuries, a significant number is likely to be related to manual control impairment resulting from vibration exposure.

The aim of this project is to contribute to the reduction of risk of acute occupational traumatic injuries associated with vibration–induced alterations of oculo–manual coordination. The proposed work will model eye–hand performance and the withdrawal reflex responses as a function of vibration frequency, displacement amplitude and exposure time of vibration applied to the hand.

The expected results will be used to estimate a vibration limit relevant to manual performance effects. Further disclosure of the importance of visual control of the limbs should lead to the formulation of safety and design recommendations concerning the placement of controls and handles.

Objectives

The overall objective is to emphasize the often ignored or neglected role of movement errors in accidents occurring in vibratory environments. The general hypothesis is that vibration–induced modification of sensory messages, used by the central nervous system to control and regulate sensorimotor activities, contribute to the alteration of both movement accuracy and oculo–manual coordination. The following hypotheses are tested:

1. Involuntary motor activities, such as reflexes, are significantly affected during vibration,
2. Sensory perception is significantly affected by vibration,
3. Oculo–manual coordination is significantly affected during vibration,
4. Vibration–induced alterations persist after exposure and vary with intensity,
5. Permanent visual control of the upper limbs should compensate to some extent vibration–induced affection of other sensory modalities and contribute to performance improvement,
6. Vibration displacement amplitude should exhibit a high correlation with performance decrement over the 80–200 Hz frequency range,
7. Sensorimotor performance should be less affected by high frequency vibration (> 200 Hz)

Methodology

Withdrawal reflex

This protective muscular response, elicited in the forearm flexor muscles by electrical stimulation of the radial nerve at the wrist is studied during low level grip exertion (at rest or 10% MVC). Electrical activity of the fingers and wrist flexor and extensor muscles are monitored using pairs of small cupular electrodes. Hand vibration (90, 150, 200 Hz, 0.2 mm) is applied perpendicularly to a vertical handle held by the subject. Changes in the amplitude of both components of the reflex responses are quantified as a function of vibration parameters.

Manual dexterity

Manual movement precision and performance time are evaluated through a visuo–manual tracking task performed before and after long term hand vibration exposure (90, 150, 300 Hz, 0.2 mm and 0.3 mm, 10 min. duration). The alterations of tracking errors and tracking time are analyzed as a function of the vibration parameters.

Oculo–manual coordination

A pointing task consisting in aiming simultaneously with the hand and the eye at visual targets is performed before, during short term hand vibration exposure (200 sec) and after long term hand vibration exposure (10 min.). The vibration frequencies are 50, 100, 200 Hz, the amplitude is 0.2 mm. Eye and hand position are measured to quantify ocular and manual performance. Eye movement pattern is analyzed to evaluate oculo–manual coordination. The influence of vibration parameters is analyzed.

Significant Findings

Withdrawal reflex

Motor effects – Both components of the reflex response are facilitated by hand vibration and this facilitation increases with initial muscle contraction; however, each component is affected differentially by vibration frequency. For the early component, the facilitation is significantly less pronounced for a 200 Hz vibration, while for the late component vibration frequency had no significant effect.

Effects on perception – When the muscles were initially at rest, a decrease in perceived discomfort elicited by the electrical stimulus was indicated by 7/10 subjects during vibration exposure. When a

moderate level of voluntary contraction was exerted the differentiation between pre and per– vibration sensation evoked by the electrical stimulus was not statistically significant.

Manual dexterity

Vibration induced a significant increase in errors and a significant decrease in tracking time. These impairments decay with time after vibration exposure. The recovery period is greater than 5 min. but less than 10 min. The subjective rating of the performance indicates that the subjects tend to perceive the task as being easier after vibration exposure. Thus, the results show that vibration affects precision and velocity control of visually guided hand movements and that performance decrements are not perceived. Vibration frequency and amplitude do not seem to have a strong influence.

Oculo–manual coordination

Hand pointing error, eye fixation error and error variability increase during 100 Hz short term vibration exposure.

All studies indicate that vibration–induced alterations of involuntary or voluntary motor activities are not consciously perceived.

Validity Assessment of Self-Reported Construction Tasks

Katherine L. Hunting, Ph.D.
George Washington University
Department of Medicine
2300 K Street, NW, Room 201
Washington, D.C. 20037

Grant Number: *1 R01 OH03266-01*
Start & End Dates: *09/30/94 – 09/29/95*
Funding Level: *$114,448 ($114,448 Cum)*

Importance to Occupational Safety and Health

Work–related musculoskeletal disorders (WMDs) are a prevalent and important problem among construction workers, thus ergonomics research in this industry is critical. Most previous work in construction ergonomics has focused on observational or measurement methods for detailed characterization of the ergonomic features of work tasks performed by the different trades. Ergonomic assessment of construction work is difficult because the work is highly variable; the distribution of tasks is likely to differ from day to day and worker to worker.

Epidemiologic studies can identify the tasks that pose the greatest ergonomic risk for work–related musculoskeletal disorders. In order to do this, researchers must be able to characterize the ergonomic exposures of individuals. Because of the variable task–mix of most construction work, it is necessary to know which tasks are done by which workers, and how often. In a large epidemiological study, it would be impractical to rely on observational or measurement methods to make such individual exposure estimates.

This study will develop and evaluate a questionnaire method for assessing the amount or proportion of time individuals spend doing specified tasks. In applying this method, data on time spent at each task could then be combined with expert ergonomic characterization of the hazards inherent in each task to derive semi–quantitative estimates of ergonomic hazards for each worker. If valid, this method would be useful in epidemiologic studies of construction worker WMDs, to identify risky tasks, to explore such issues as exposure thresholds and dose–response effects, and to evaluate the effectiveness of intervention studies.

Objectives

This one–year pilot study will evaluate the validity of self–reported exposures to construction work tasks among sheet metal workers. The variable, multiple–task nature of sheet metal work is typical of many other skilled construction trades. Approximately 110 sheet metal workers will be observed for three days each. These workers will be asked to complete questionnaires detailing the proportion of time spent at various tasks on the days they are observed. Questionnaires will also ascertain factors such as the gauge and dimensions of sheet metal materials handled.

Worker–reported data on time spent on tasks will be compared to observational data, and the extent of agreement will be assessed. Task factors and other factors related to the quality of agreement will be characterized.

The ultimate aim of this pilot study is to develop a valid instrument for the collection of self–reported data on duration of exposure to identified work tasks. Such an instrument would be valuable in future epidemiological studies seeking to identify tasks associated with the prevalence and/or severity of musculoskeletal disorders, and also in the evaluation of intervention studies.

Methodology

- Develop and pretest a self–administered questionnaire which workers will use to report the time spent on sheet metal work tasks, and materials handled.
- Enroll approximately 110 sheet metal workers into this study. These workers will be employees of a few large contractors.
- Observe study participants to determine the time spent performing various sheet metal work tasks, and materials handled. Have participants complete questionnaires on same day.
- Provide each participant with feedback on how his/her responses compare with observer data.
- Observe each participant for two more days. Have each participant complete questionnaire for those days.
- Compare the data from worker–report method with the observational data to determine the validity of worker–reporting method, both pre–feedback and post–feedback. Characterize task factors and other factors related to agreement.

Significant Findings

None to date.

Development of a Construction Injury Predictive Model

Kweku K. Bentil, Ph.D.
University of Washington
College of Architect & Urban Planning
Department of Building Construction
116 Architecture Hall, AL-15
Seattle, Washington 98195

Grant Number: *5 R01 OH02743-02*
Start & End Dates: *09/30/93 – 09/29/95*
Funding Level: *$100,543 ($207,376 Cum)*

Importance to Occupational Safety and Health

Analysis of previous injury data has been used to prevent injuries in other industries (such as manufacturing and transportation) in the past. As asserted by the National Safety Council (1982):

> Job safety analysis has proven time and again to be an accident and occupational illness prevention tool in many industries over the past years. (p. 2)

The ability to analyze accident data and predict the number of injuries that can be expected can make it possible for safety programs to be narrowly tailored to each specific construction project and contractor in order to make existing safety programs more effective in preventing injuries. Therefore the results of this study can greatly expand available knowledge about safety in the construction industry and lead to lower injury rates. Results of this research will be disseminated to the Occupational Safety and Health Administration (OSHA), the major construction contractor organizations (such as the Associated General Contractors, Associated Builders and Contractors, Mechanical Contractors Association and the National Electrical Contractors Association) for distribution to their membership, the Center for Excellence in Construction Safety, and the major insurance companies. The results of this study will be published in the relevant journals. (such as the "Constructor" and "Builder & Contractor").

The results of this research will provide the construction safety research community, contractors, insurance companies, risk managers, and OSHA a tool that can help measure the effectiveness of safety programs. Specifically, it will also enable OSHA to target projects with high risk factors for inspection and more aggressive prevention programs. Finally, the results will also serve as the basis for future research on developing injury predictive models for other categories of construction (residential, industrial, heavy and highway).

Objectives

The purpose of this research is to develop knowledge that can be used in preventing traumatic injuries at commercial construction sites. The main objective of this study is to develop a parsimonious empirical model that will have good capabilities of predicting the incidence of traumatic injuries requiring medical care among construction workers employed by commercial construction contractors. The first aim is to investigate and identify the most significant risk factors that can influence the occurrence of injuries at commercial construction sites. The general categories of risk factors to be addressed are characteristics of commercial construction contractors, projects and workers. The second aim is to analyze these categories of risk factors and understand the relationship between them and the number of traumatic injuries at commercial construction sites requiring medical treatment by a licensed caregiver. The third aim is to utilize these factors and their functions in a model that will have good capabilities of predicting the incidence of

injuries at given construction sites before the commencement of that project.

Methodology

The main outcome of interest will be the rate of traumatic injuries occurring at commercial construction sites that require medical treatment by a licensed caregiver. The injuries studied will be the same as those that are required to be reported by OSHA. Data will be collected for a minimum of 100 commercial construction contractors and 400 projects from commercial construction contractors and the State of Washington Department of Labor and Industries, and a data base created. Risk factors focussing on specific characteristics of construction contractors, projects and workers will be analyzed.

Analysis will involve fitting Poisson regression models, with adjustment for overdispersion, and for shared contractor and project effects. Model fitting will be accomplished using the GLIM Computer Software, developed by the Royal Statistical Society. The characteristics of commercial construction contractors, projects, and workers will be investigated as explanatory variables in order to determine their significance in predicting injuries. Rates of injuries will be calculated as injuries/FTE. Relative risks and corresponding confidence intervals will be estimated for combined injuries, and for individual types of injury. Standard likelihood methods of generalized linear models will be used for testing the effect of each explanatory variable on the injury rate, both alone, and adjusted for the confounding effects of other explanatory variables.

Significant Findings

None to date.

Publications

Bentil KK: Predicting Construction Site Injuries Using Contractor and Project–related Independent Variables. Proc of the Fifth Annual Rinker International Conference Focusing on Construction Safety and Loss Control, Gainesvile, Florida, pp 267–276, October 12–14, 1994

Bentil KK: Prevention of Construction Site Injuries: Significant Contributory Factors. Proc of the Fifth Annual Rinker International Conference Focusing on Construction Safety and Loss Control, Gainesville, Florida, pp 315–324, October 12–14, 1994

Analysis of Construction Tasks For Overexertion Injuries

John G. Everett, Ph.D.
University of Michigan
Department of Civil
and Environmental Engineering
2352 G.G. Brown Lab
Ann Arbor, Michigan 48109-2125

Grant Number: *5 R03 OH03154-02*
Start & End Dates: *09/30/93 – 09/29/95*
Funding Level: *$37,460 ($74,380 Cum)*

Importance to Occupational Safety and Health

Overexertion injuries are the single largest classification of injury in construction, accounting for about 24% of all injuries. Overexertion injuries generally occur as a result of performing a given task as planned. While overexertion injuries are not intentional, the underlying causes of the injuries are built into the prescribed tools and work methods. If the causes can be identified, it should be possible to engineer them out of the work. Once afflicted with an overexertion injury, many construction craft workers can be excessively challenged by the physical demands of their jobs.

Construction injuries have been categorized in many ways, including by trade but no attempt has been made to identify a causal relationship between specific tasks within a trade and the associated overexertion injuries. For example, carpenters account for 17% of all injuries and illnesses, but carpenters perform many fundamentally different tasks such as erecting concrete formwork, installing suspended ceilings, hanging drywall, etc. Carpenters who install formwork for concrete experience high rates of tendinitis in their elbows from banging the forms and connectors with hammers, carpenters who install suspended ceiling systems experience neck and shoulder problems from constantly looking and reaching up, and carpenters who hang drywall often suffer nerve damage in their hands from the vibration of the screwguns used to fasten the drywall to the framing system. All of these injuries fall into the general classification of overexertion injuries to carpenters, but the underlying causes are quite different and they call for fundamentally different types of workplace intervention.

The goal of this project is to identify specific construction tasks which place craft workers at high risk for overexertion injuries and disorders. High risk tasks can then be identified so that ergonomic

and administrative principles can be applied to modify the task or work environment to accommodate human capabilities and limitations.

Objectives

The objective of this project is to analyze construction tasks for the presence of seven generic risk factors for overexertion injuries and to identify high risk tasks for possible ergonomic or administrative intervention. The hypotheses to be tested are that it is possible to identify the underlying risk factors for overexertion injuries for many specific construction tasks and that it is technically and economically feasible on many construction tasks to reduce the level of physical demands placed on craft workers.

Methodology

Overexertion injury data are currently reported by construction trade. No attempt has been made to determine which specific tasks within each trade place workers at high risk. This study will analyze specific construction tasks for the presence of seven generic risk factors for overexertion injuries: repetitive exertions, static exertions, forceful exertions, localized mechanical stresses, posture stresses, low temperature, and vibration. Ratings for each risk factor will be made on a three point scale: Insignificant – The job is free of potentially harmful ergonomic stresses in the risk factor of interest. No corrective actions are necessary; Moderate – The job has stresses in the risk factor of interest that could be problematic (i.e. cause fatigue and/or injury) for some workers. Additional analyses using more precise methods should be used to determine the necessity for intervention; and High – The job has significant stresses in the risk factor of interest that are likely to cause fatigue and/or injury in some workers. Additional analyses and interventions should be taken at a high priority. This study will identify particularly high risk tasks for ergonomic or administrative intervention.

Significant Findings

At slightly past halfway in this project, most of the effort to date has been spent cataloging the work of each trade into tasks, each broken down into individual steps. Each step has been or is being analyzed for the presence of generic risk factors. A library of video tapes of common building construction tasks is being developed.

Two themes are emerging from the dozens of tasks analyzed to date. The first may appear obvious to ergonomists, but seems to be a novel concept to many construction practitioners. In tasks generally considered to be high risk for overexertion, there are usually one or two steps in the overall task that create most of the risk. For example, ironworkers who fabricate rebar mats for concrete slab construction perform a series of steps, but bending over to tie the bars together places the ironworkers at particularly high risk for overexertion injuries. The other steps are relatively free from risk. In considering ergonomic intervention, it may be necessary only to address the bending–over–and–tying step, rather than redesigning the entire sequence of steps, or using different technology. In many cases, there are easy or well known solutions to the problems. The biggest problem seems to be motivating, educating, and training management and labor alike that a problem exists and that there may be cost effective solutions.

The second theme, perhaps related to the first, but more general, is that everyone in the entire construction process, from owners to designers to construction managers to craft workers to insurance and other agencies, frequently have a choice or can influence the choice of the technologies used to perform any given construction process. This choice can range from large scale decisions such as the choice of steel versus concrete structural systems, to very small scale decisions such as selection of hand tools, but very little consideration is given to the occupational health and safety implications of the various alternatives, except possibly at some very small scale decisions. The means and methods of construction have traditionally been the responsibility of the general contractor or construction manager, but regulatory and design decisions limit the range of alternatives. Education of those not normally concerned with the day–to–day details of occupational health and safety about the implications of their decisions may be as important as implementing detailed interventions.

Publications

Everett JG: Ergonomics, Health, and Safety in Construction: Opportunities for Automation and Robotics. Proceedings of Eleventh International Symposium on Automation and Robotics in Construction, Bristol, England, 19–26, May 24–26, 1994

Development of a Work Safety Scale

Bob E. Hayes, Ph.D.
Medical Consultants Northwest, Inc.
Suite 1400
901 Boren Avenue
Seattle, Washington 98104-3512

Grant Number: *1 R43 OH03099-01*
Start & End Dates: *09/30/93 – 07/30/94*
Funding Level: *$0 ($49,225 Cum)*

Importance to Occupational Safety and Health

The National Safety Council (NSC) estimated that the total cost of industrial accidents in 1992, including insurance administration costs, wage losses, and medical costs, was 115.9 billion dollars (NSC, 1993). Millions of dollars annually could be saved if the number of accidents was decreased.

Fewer work related accidents have been linked to employees who perceive their jobs as relatively safe. These same employees report experiencing less anxiety, stress, and exposure to environmental hazards, all of which have been linked to accident rates. Therefore, the perceptions of the work environment and safety are correlated. By assessing the perceptions of employees, companies can alter the workplace and decrease the likelihood of accidents.

There are four existing measures of workplace safety perceptions: The Occupational Hazards Survey (Guastello & Guastello, 1988); Safety Climate Scale (Zohar, 1980); Physical Demands and Dangers scale, a sub–scale of the Job Stress Index (Sandman, 1992); and the Perceptions of Workplace Hazards Scale (Smith et al., 1992), though they are not comprehensive nor psychometrically sound. The reliability and validity of each instrument is not well established, and no measure adequately taps the domain of workplace safety. Thus, there is a need for a comprehensive and psychometrically sound instrument to assess issues of workplace safety.

Objectives

The aim of the present research was to complete Phase I of the development of a questionnaire assessing employees' attitudes toward workplace safety. The proposed instrument: (a) possesses adequate psychometric integrity – reliability and validity information; (b) comprehensively assesses important dimensions of perceptions of workplace safety; and (c) is easy to complete. Scores on this measure can assist decision–makers in industrial settings to: (1) predict the extent of accidents; (2) determine the need for workplace safety programs; (3) help organizational officers design specific workplace safety programs to address specific employee concerns; and (4) determine the effect of such safety programs.

The series of proposed studies was designed to develop and validate a measure of workplace safety, the Work Safety Scale (WSS). The WSS was designed to assess five dimensions of work–related safety: perceptions of job safety; coworker safety; supervisor safety; management safety; and satisfaction with the safety program. This multidimensional approach to safety assessment was necessary because ample evidence exists that work safety is not a unidimensional construct.

Methodology

For each of the five scales of the WSS, descriptive adjectives or phrases were written to tap into relevant content domains. For each item, respondents indicated the extent to which they agree that the item describes their job situation using a five–point Likert scale 1 – Strongly Disagree to 5 – Strongly Agree). Twenty–two to 29 items were written for each of the sub–scales being developed (a total of 124 items), with the expectation that, after item analysis, at least half of the items were to be retained for the final form of the instrument.

Two studies were conducted. The respondents consisted of patients being seen at a medical consulting firm for independent medical evaluations. In addition to a standard questionnaire patients complete for their medical evaluation (not used in the current study), patients were given the initial items of the WSS and other measures used for the current study (e.g., self–reported accident rates, occupational title, educational status attained, shift work status, sleep complaints, physical complaints, psychological complaints, and compliance with safety behaviors). Responses to the WSS were anonymous. In the first sample, out of 5551 patients seen during a six–month period, 787 patients completed the materials used in the current study for a response rate of 14%. For the second study, out of 8464 patients seen during a four–month period, 879 patients completed the materials used in the current study for a response rate of 10%.

Significant Findings

Results of both studies showed that the Work Safety Scale (10 items per subscale) were reliable and valid measures of perceptions of work safety. Initial item analysis (corrected item–total correlations) revealed that all nearly all WSS items possessed

acceptable psychometric properties (high item–total correlations with high internal consistency estimate for each of the five WSS subscales). Consequently, retention of items were based on the content of the items. Items with a behavioral component were retained over items with a global attitudinal component. As a result, 50 items were retained (10 for each WSS subscale).

A factor analysis (with oblique rotation) of the 50 WSS items revealed a clear five–factor solution. Each subscale of the WSS had internal consistency estimates above .90. The correlations among the WSS subscales were lower than each of the subscale's reliability. Additionally, the WSS subscales were related to self–reported accident rates. People who reported having a safer work environment also reported experiencing fewer industrial accidents compared to people who reported having a less safe work environment. The WSS subscales were related to measures of psychological and physical well–being and compliance with safety behaviors. People who reported having a safer work environment also reported experiencing fewer physical and psychological complaints and also reported complying more frequently to safety behaviors at work. Based on a stepwise regression analysis, important WSS predictors of these accident–related outcomes were supervisor safety, co–worker safety and management safety practices.

Emission Factor Development for Intermittent Workplace Sources

Richard A. Wadden, Ph.D.
University of Illinois at Chicago
School of Public Health
Environmental & Occupational Health Sciences
P.O. Box 6998
Chicago, Illinois 60680

Grant Number: *5 R01 OH02804-03*
Start & End Dates: *12/01/90 – 11/30/94*
Funding Level: *$0 ($177,423 Cum)*

Importance to Occupational Safety and Health

The conceptual thrust of this proposal was to develop a method for generalizing the design of engineering control of workplace hazards. In particular, we are developing emission factors, based on field observations, for four types of commonly encountered, hazardous, open–tank processes: vapor degreasing, electroplating (chromium and copper plating), offset printing, and wave soldering.

Objectives

The value of the emission factor approach is that the effect of the particular interior space in which the data are collected is removed. The factors are developed from the area concentration pattern surrounding each device while production is taking place, using mathematical models describing a mass balance for the contaminant in order to transform this pattern for a particular source to an emission rate. To systematically describe the variability of emissions, the release rate is related to measures of source activity, process conditions, and equipment geometry. A total of 11 source tests have been carried out consisting of 12 1–hour sampling periods which also include measurements of general and local exhaust ventilation. The results of this study will provide: (1) A compilation of activity–based emission factors for Cr and Cu electroplating, vapor degreasing, wave soldering, and offset printing; (2) A measure of the variability in emissions which can be expected from such processes; (3) Actual determinations, based on an emission mass balance, of control device performance for each of the processes studied; (4) A generalized basis for estimating workplace concentrations from these types of sources; and (5) A mass–balance basis for evaluating control design alternatives.

Methodology

Field tests under production conditions have been carried out on: (1) Three methyl chloroform degreasers in a microcircuit production facility; (2) A terpene degreaser using limonene; (3) Four Pb wave soldering lines of different designs in two plants making electronic circuit boards; (4) Two decorative chrome–nickel electroplating lines; (5) Cu emissions from an electrolytic copper plating line; (6) A methylene chloride degreaser; and (7) Three different offset printing plants using, respectively, sheetfed offset, offset web, and heatset web offset printing processes.

Significant Findings

Average total emissions from three uncontrolled methylchloroform degreasers were determined to be between 0.39 kg/hr and 0.74 kg/hr depending on the model used. The approximate usage inventory value for the same time period was 0.62 kg/hr. Emissions were related to uncovered tank conditions, dragout, and type of parts, and 80% were identified as coming from a single line. Emission factors were about 0.2 g/part in addition to 0.22–0.4 g/in^2 of part area.

Manual cleaning was also important with a rate of (58–90 g/hr)(% of time on manual operation.)

Total emissions from a terpene degreaser were 0.68 kg limonene/hr with an emission factor of 2.2 g limonene/circuit board cleaned.

Total uncontrolled emissions from three Pb wave soldering lines in the same space averaged 86 mg Pb/hr. Total lead bath scrapings and dedrossings appeared to be the most important source activity variable with an emission factor of 4 mg of Pb/solder cleaning for explained area emissions. Although each line was served by a local exhaust system, the overall control efficiency for lead for the three lines was only 56%. Lead concentrations in the workspace were highly correlated (r^2= 0.7–0.9) with the combined number of scrapings and dedrossings which occurred on the open solder pot nearest to the sampling point. Two of the lines were of a much newer design than the other. One hypothesis which we examined was whether operation and control was less effective on the older line. This proved not to be the case as the combined contribution to area lead concentrations of the two newer lines was 50% which was not different from the 23% from the older line. A chemical mass balance receptor model was used to determine these allocations.

The copper emission factor for releases into the workspace from electroplating was 0.5–2.7 μg/amp·hr. The emission factors for hexavalent chromium from piston plating was 81 μg/amp·hr for controlled (hood) emissions, and 0.3 μg/amp·hr for releases into the workspace. These findings were in good agreement with measurements carried out in California on hood emissions from hard chrome plating operations.

The release rates of volatile organic compounds (VOC) as fugitive emissions from offset printing are difficult to quantitate and the compositions are usually not known. Tests on three offset printing plants during production indicated that fugitive releases into the workplace were strongly related to press cleaning activities. In each case the building shell served as the test "enclosure" and air flow and concentration measurements were made at each air entry and exit point. Air samples and solvents were analyzed by gas chromatography (GC) for total VOC and 13–18 individual organics. Average uncontrolled emissions from a sheet–fed offset print shop were 4.7–6.1 kg VOC/day, and 1.4–2.0 kg BTEX/day (the sum of benzene, toluene, ethyl benzene, and xylenes); with an emission factor of 30–50 g VOC/press cleaning depending on the type of equipment. VOC emissions of 0.4–0.9 kg/day (0.04–0.08 kg BTEX/day) were determined for a medium size industrial in–house print shop. Emission factors varied between 2.5–56 g VOC/cleaning and again depended on the type of press. Daily emissions of 79–82 kg of VOC (12–13 kg BTEX/day) were measured from one print room, within a large commercial concern, which contained 3 web–fed, heat–set lines served by catalytic air pollution control devices. Emission factors included 17 g VOC/minute of "make ready" (which included solvent cleaning), 49 g VOC/manual press cleaning, and possibly 10 times this value for automatic web blanket cleaning. Emission compositions were similar for all the plants. In one case benzene concentrations were at the OSHA action level of 0.5 ppm. Comparison of the emission rates with mass balance estimates based on solvent usage and composition were quite consistent.

Additional wave soldering emission factors are still being developed as well as those for methylene chloride, and chromium electroplating.

Publications

Wadden RA, Scheff PA, Franke JE, Conroy LM, Javor M, Keil CB, Milz SA: VOC Emission Rates and Emission Factors For A Sheetfed Offset Printing Shop. Amer Ind Hyg Assoc J, in press, 1994

Conroy LM, Prodans R, Lachman M, Yu X, Wadden RA, Franke JE, Scheff PA: Hood Efficiencies Of Vapor Degreasers Under Operating Conditions. J Environ Engin, American Society of Civil Engineers, in press, 1994

Wadden RA, Scheff PA, Keil CB, Franke JE, Conroy LM: Determination Of VOC Emission Rates and Compositions For Offset Printing. J Air Waste Manage Assoc, in press, 1994

Evaluation of Controls Protecting Lead-Exposed Workers

Lewis D. Pepper, M.D.
Boston University
School of Public Health
Department of Environmental Health
80 E. Concord Street, T3-C
Boston, Massachusetts 02118

Grant Number: *5 R01 OH03177-02*
Start & End Dates: *09/30/93 – 09/29/96*
Funding Level: *$237,083 ($473,763 Cum)*

Importance to Occupational Safety and Health

The study is a response to the persistent reports of elevated blood and air lead levels in bridge construction and maintenance activities and it represents an attempt to determine why high blood levels continue to occur despite government regulations and industry recommendations. It is designed to evaluate which work processes, controls, and practices contribute most to the lead overexposures and to determine whether and why the recommendations that have been made are or are not being implemented. Air and surface sampling as well as blood lead and changes in blood lead over a 2–week period will be done as measures of the effectiveness of the lead exposure control programs in use at each job site. The lead exposure control programs will be evaluated through examination of background on the company; the controls in place at the work site; the processes and work practices used on the work site; and the knowledge and attitudes of the workers themselves.

The investigators will provide the results of the blood lead tests to each study subject, and upon request, their physician. All blood test results will be reviewed by an occupational physician who will send a letter informing the individual of the health significance of the results and the recommended medical follow–up. Subjects will also be provided with a fact sheet describing the health effects of lead exposure.

Project participants will be provided a project summary at the end of the study. Information to be included will be summary blood lead levels, environmental sampling data, study conclusions, and recommendations. The final report, which will be completed at the end of the study, will be provided to appropriate agencies and institutions, e.g., OSHA and EPA.

This study is one of the first evaluations of structural steel paint abatement activities following the extension of OSHA's Lead Standard to the construction industry. The study will permit an early assessment of the impact of federal regulatory requirements and the barriers to optimal worker protection.

Objectives

The overall objective of this project is to determine why high blood levels continue to occur in bridge construction workers despite government regulations and industry recommendations. The project objective will be met through the following specific aims:

1. Perform a set of structured observations of work practices and the use of personal protective devices and control technologies at times coinciding with the exposure measurements. These observations will be combined into ordinal index variables representing containment, ventilation, personal protection and similar variables.
2. Measure lead particle exposure using a sampler which meets the Inhalable Sampling Criteria approved by ACGIH (the IOM sampler, developed at the Edinburgh Scotland Institute of Medicine, simulates the particle collection behavior of the human nose and mouth) and perform surface wipe measurements for 110 Massachusetts bridge construction workers working in a variety of state Highway Department sites; there will be three to five exposure measurements during a two week study period at each site.
3. Perform a project baseline blood lead on this group, followed by a second measurement 14 days later.
4. Use ethnographic techniques (observation, questionnaires and semi structured interviews) to assess management and worker awareness of lead poisoning issues associated with bridge repair work practices at each site.
5. Develop predictors of blood lead and air concentrations using industrial hygiene controls, work practice, training and company and worker attitude variables.

Methodology

This project is a cross–sectional survey of bridge repair and maintenance workers at work sites in Massachusetts. It is anticipated that project staff will visit ten work sites, and assess five to ten workers at each site each year for two years. This will result in a total sample of 120 bridge workers in the survey. Workers will be interviewed in person using a questionnaire used in a previous study; they will also be asked to keep a work task diary during a two–week period. In addition, blood samples and air samples will be taken to determine individual–level exposures and biological markers of effect. Other information on environmental conditions and work practices will be gathered by project staff and used to construct a personal exposure score which will be used in the analysis. Blood lead levels at the beginning of the two week observation period will be compared with levels at the end. This is primarily to note whether biological measures changed significantly during the time period and, if so, to examine changes in job assignments or work tasks that might be associated with the changes. The mean blood levels for all workers involved in a particular task will be compared at the beginning and at the end of the two week observation period. The analysis of

the data collected over the two year period will be focused on associations between specific work activities and environmental factors and blood lead levels and airborne lead levels for bridge repair and maintenance workers. The basic method of analysis will be analysis of variance (ANOVA) and analysis of covariance (ANCOVA).

Significant Findings

Environmental and blood lead measurements, questionnaire, and semistructured interviews have been completed at six bridge site as of October 4, 1994. Only environmental samples from the first site have been analyzed to date. The daily TWA's measured range from 7 to 1,439 mcg Pb/m3. Task and area samples in containment range from 16 to 13,650 mcg Pb/m3 during blasting. The wide range of exposure levels suggests that the approach of collecting task levels measurements along with individual diary information on how the time spent in tasks varies from day to day will be fruitful in explaining the variance in exposure levels.

Forty–seven construction workers have been evaluated. Two blood lead concentrations were obtained. The first blood lead test values (n=47) ranged from 2.5 to 39 mcg/dL with a mean of 16.3 mcg/dL. The second blood lead test values (n=47) ranged from 7 to 42 mcg/dL with a mean of 19 mcg/dL. There were 44 individuals who had both a first and last blood lead test. The difference between the two tests, as measured by paired t–Test was statistically significant ($p<0.0001$) at alpha = .05. The study subjects mean age was 35 (n=47).

Each study subject was interviewed for approximately 45 minutes using a combination of structured and probing questions. Separate interview protocols were established for workers, working contractors, non–working contractors, and Massachusetts Highway Department (MHD) resident engineers. The project's industrial hygienists have compiled field observations for each site which will be included in our semi–qualitative evaluation. This data will be evaluated during the project's second year.

The Boston University–University of Massachusetts Consortium has established a two–year Memorandum of Understanding with the MHD and the MHD has included the Lead Exposure Study in seven contracts as a required addendum. The project staff are meeting with the other state agencies responsible for bridge maintenance and repair to establish a similar collaboration with them for the project's second year.

An Exposure Matrix For Construction Painters

Philip L. Bigelow, Ph.D.
Colorado State University
Department of Environmental Health
110 Veterinary Science Building
Fort Collins, Colorado 80523

Grant Number: *5 K01 OH00138-02*
Start & End Dates: *09/30/93 – 09/29/96*
Funding Level: *$53,898 ($107,433 Cum)*

Importance to Occupational Safety and Health

Construction painters are exposed to a wide variety of substances that may cause acute and chronic adverse health effects. Relatively little work has focused on this occupational group despite the extent of exposure, the large population of workers, and the potential for severe effects neurotoxicity, increased accident rates, cancer, reproductive disorders, and respiratory disease. The investigation will provide much needed quantitative information on exposures in construction painting. By focusing on specific work tasks, a new methodology will be developed in which exposures can be accurately estimated on the basis of self reports of work activity. This exposure assessment technique will be valuable when dealing with workers who perform tasks at different jobsites or who perform a variety of activities. The new technique will enhance the capabilities of health scientists in the assessment of exposure of individuals that in the past have been difficult to characterize.

Objectives

The major hypothesis of the study is that by studying specific job tasks, a construction painter's overall occupational exposure can be estimated. In order to test this hypothesis, methods are under development to standardize the measurement of organic vapor exposures during specific construction painting tasks. Another important objective of the study is to determine the relationships between occupational exposures and variables that characterize the work environment. Through the analysis of data collected during this investigation a method will be developed that will allow the prediction of overall occupational exposures based on descriptions of work tasks and characteristics of the occupational environment.

Methodology

Measurements of exposures during specific work tasks will be evaluated for 200 construction painters in Colorado. The focus of the exposure assessments will be organic vapors. Collection and analytical techniques will vary depending on the expected contaminants in the work environment and the expected durations of exposure. Gas chromatography and IR spectrophotometry will be extensively used methods of analysis. Video taping of the work tasks will be undertaken to assist in the collection and interpretation of data.

A database of tasks and exposure levels will be developed for later use in the characterization of exposure on the basis of information from self–reported activities. Self–reported work activities will be obtained through the administration of a task history questionnaire. The statistical relationships between variables that characterize the work (tasks and environment) and exposure levels will be determined. Information obtained at the job sites will be used to develop and modify the task history questionnaire, and statistical analyses will be performed to assess its' utility in developing overall exposure profiles. A short questionnaire will be administered before and after each workshift in order to assess the relationship of painting exposures on the incidence of specific symptoms. The statistical associations between peak and time weighted average exposure levels and symptom scores will be determined.

Significant Findings

The first year of the project focused on the development of tools to aid in exposure assessment. Experiments, as well as field validation of instrumentation were completed and field data collection forms were developed to meet the requirements of data collection in the construction industry. Standard methods of data collection, applicable for industrial settings where workers perform a series of similar tasks in controlled environments, cannot be used in construction where work site conditions vary tremendously. Data collection forms were developed that incorporated the common work tasks which are performed by construction painters yet allows for the documentation of many variables that characterize worksite conditions.

Specific findings that have resulted from work on the project include:

- Field and controlled experiments using a portable nondispersive infrared analyzer provided evidence that, due to similarities in wavelengths, such an instrument was not suited to the characterization of components of many paints, lacquers, or solvents used in construction painting.
- Initial field testing of a portable gas chromatograph indicated its utility in characterizing specific vapor exposures during lacquering operations with potential exposures to toluene, xylene, n–butyl acetate, and hexone. However, the initial field evaluation highlighted the difficulties in characterizing all components of complex organic vapor exposures using field portable instrumentation.
- During the field testing, information on constituents of coatings and solvents from material safety data sheets (MSDS), labels, and other sources was used to target specific chemicals. The targeting of compounds that were more likely to be present in the workplace at concentrations of health significance was necessary because it was not feasible to identify and quantify all possible exposures. Further validation of this method of targeting components using available literature and subsequent characterization by portable gas chromatography is underway.
- Approximately 12 hours of video exposure monitoring has been completed for workers engaged in staining and lacquering of cabinets. The data are currently being analyzed to determine the association between exposures to organic vapor, as measured by a portable photoionization detector, and specific work tasks.

Analysis of Industrial Noise For Hearing Conservation

Sheau-Fang Lei, Ph.D.
State University of New York
Auditory Research Laboratory
107 Beaumont Hall
Plattsburgh, New York 12901

Grant Number: *1 K01 OH00139-01*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$53,558 ($53,558 Cum)*

Importance to Occupational Safety and Health

Hearing loss following years of noise exposure in industry or the military constitutes one of the significant occupational health problems affecting the quality of life for large numbers of employees. This

grant focuses on the extraction of physical metrics from the acoustic noise that can be used to estimate the hazards to hearing from prolonged exposure to that noise. The statistically based metrics that will be obtained, when used in conjunction with the L_{eq} may allow the better characterization of noise for the purpose of hearing conservation practice.

Objectives

Current methods for assessing the hazards of a noise exposure rely primarily on a time averaged, integrated approach to quantifying a noise exposure, i,e. an energy metric. Experiments have shown that measurements such as sound pressure level and spectrum based on the above approach are not adequate for estimating the hazards to hearing in a variety of industrial/military noise environments. Recent studies [e.g., Lei *et al.* (1994), J. Acoust. Soc. Am. 96; 1435–1444] suggest that the temporal structure of a noise must be taken into account in order to predict hearing trauma especially when the noises are of a non–Gaussian and nonstationary character. Contemporary signal processing technology will be used in this project to analyze both the temporal and frequency structure of a non–Gaussian and nonstationary noise. The objective of this project is to obtain the following: (1) the distribution of time domain kurtosis, which can provide an estimation of the percentage of time a signal deviates from Gaussian and a quantification of the extent of the deviation; (2) the frequency domain kurtosis, which quantifies the fluctuations of the energy of the signal at each given frequency scale relative to those for Gaussian conditions; (3) the joint peak–interval histogram surface which will identify each impact level, within a predetermined peak bin, with its inter peak interval distribution. Conventional peak and interval histograms will be obtained from this surface.

Methodology

The wavelet transform and bicepstrum analytical techniques will be used to develop signal analysis algorithms on the complex noise waveforms (generated from computer simulations of non–Gaussian and nonstationary noises). The wavelet transform performs a joint time–frequency analysis of the signal and incorporates a nonlinear scaling of frequency. In effect this transform is analogous to the cochlear analysis of a signal wherein a nonstationary stochastic signal is mapped logarithmically into the frequency domain on the basilar membrane as a continuous function of time. Frequency domain kurtosis can be obtained from the wavelet transform. The bicepstrum analysis derived from higher order spectra will yield information on the peak amplitudes and temporal spacing (timing) of transients within the noise and allow us to construct a joint peak and interval histogram surface. The above algorithms will be implemented in computer programs so that they can be integrated into the open architecture of a PC–based data acquisition and analysis system so that cost–effective and flexible noise measurements can be performed and ultimately incorporated into noise exposure standards.

Significant Findings

None to date.

Computational Methods in Industrial Ventilation

Michael R. Flynn, Sc.D.
University of North Carolina
School of Public Health
Environmental Sciences and Engineering
CB 7400 Rosenau Hall, Room 118
Chapel Hill, North Carolina 27599-7400

Grant Number: *5 R01 OH02858-03*
Start & End Dates: *07/01/91 – 06/30/94*
Funding Level: *$0 ($123,846 Cum)*

Importance to Occupational Safety and Health

This project is designed to bring the methods of computational fluid mechanics to bear on the problem of estimating worker exposure. At the present time the inability to estimate exposure remains a serious deficiency in the design process for contaminant control ventilation systems, as well as in retrospective epidemiological studies.

Objectives

The specific objectives are: (1) expand an existing computer code based on discrete vortex methods to predict airflow patterns around a worker and a nearby obstacle; (2) develop predictions of exposure using particle tracking methods; and (3) conduct wind tunnel simulations to validate computer predicted flow patterns and exposure estimates.

Methodology

Significant improvements in numerical algorithms for discrete vortex methods continue to appear in the

fluid mechanics literature. These improvements have been integrated into an existing code to improve speed and flexibility. Sulfur hexafluoride tracer gas studies using infrared spectrophotometry and electron capture detectors are employed to validate exposure estimates. Smoke wire techniques are used to explore flow patterns around mannequins and objects in the wind tunnel.

Significant Findings

A discrete vortex code (DVM) has been developed employing a boundary integral potential flow solver, for prediction of the time dependent flow around a worker and object. In addition a particle tracking algorithm for estimating concentration fields has been incorporated into the code. Several wind tunnel studies to collect data for model validation are complete. Studies have identified appropriate zones for the spatial and temporal averaging of concentration within the algorithm, and measured exposures are in good agreement with computer predictions. Experimental studies confirm predicted air flow patterns around a mannequin and obstacle and the algorithm correctly identifies orientations leading to reduced exposure.

Publications

Kim T, Flynn MR: Numerical Simulation of Air Flow Around Multiple Objects Using the Discrete Vortex Method. Journal of Wind Engineering and Industrial Aerodynamics, in press, 1994

Flynn MP, Chen M, Kim T: Computational Simulation of Worker Exposure Using A Particle Trajectory Method. Annals of Occupational Hygiene, in press, 1994

Transport Modeling of Industrial Ventilation

Kyle D. Squires, Ph.D.
University of Vermont
Mechanical Engineering Department
209B Votey Building
Burlington, Vermont 05405-0156

Grant Number: *5 R01 OH03052-02*
Start & End Dates: *09/30/93 – 09/29/96*
Funding Level: *$148,650 ($300,663 Cum)*

Importance to Occupational Safety and Health

Accurate, robust computational models must play an integral role in any plan directed towards significantly improving the design and development of ventilation systems. An area in which improved predictive methods are especially critical is contaminant transport in unsteady turbulent flow fields in which the contaminant is comprised of dense particulates. Because dense particles cannot follow the fluctuations of gas–phase turbulence, the range of interactions between the turbulent gas flow and suspended particles are very complex and not particularly well understood at the present time. It is not surprising, therefore, that design of ventilation hoods for applications of particulate removal is for the most part empirical. Consequently, there is no well–developed rationale for current design practices and design techniques applicable to large classes of ventilation systems are lacking. Improved predictive capabilities are especially important because the complex interactions between the turbulent gas flow and suspended particles may pose greater risk to industrial workers than is currently accounted for by present day design practices.

Thus, given the complex nature of gas–particle interactions in turbulent flows and their impact on industrial ventilation, new predictive methodologies are needed to improve the design and development of these systems. The long–range goal of this research program is therefore development of a new generation of predictive techniques for contaminant removal in industrial ventilation applications.

Objectives

The principal objectives of the present study are development of transport models for prediction of turbulent flow fields laden with small, dense particles. A major emphasis of the work is model development in the framework of the most promising approach to turbulence modeling developed within at least the last 10 years: dynamic subgrid–scale modeling. Crucial to achievement of these objectives is extension and development of large eddy simulation (LES) as a technique for prediction of the complex turbulent flows encountered in industrial settings.

Because of the complex nature of gas–particle flow fields in industrial ventilation applications, it is unrealistic at the present time to attempt development of a general computational methodology suitable for arbitrary ventilation systems. Thus, efforts are directed towards model development in canonical flows containing the essential physics present in actual ventilation systems, viz. particle–laden turbulent shear flows.

Methodology

Traditionally, predictive techniques for turbulent gas–particle flows have been limited by deficiencies in not only the particle transport models but also the turbulence models employed in the Navier–Stokes equations. This difficulty has been alleviated in the present work by employing large eddy simulation of the Navier–Stokes equations as the solution technique for the gas–phase carrier flow.

Filtering of the Navier–Stokes equations in LES introduces turbulent stresses which cannot be resolved by the computational grid. One of the novel features of this work is parameterization of the turbulent stresses using dynamic subgrid–scale modeling. The main improvement of dynamic modeling over traditional methods is that the subgrid–scale stresses are modeled using information from the resolved scales. This approach has yielded extremely accurate descriptions of several canonical flows. Its application to turbulent two–phase flows represents an important step in furthering the use of LES for engineering applications. The dispersed phase of solid particles is treated using a Lagrangian approach, i.e., the equation of motion is integrated along discrete trajectories for a large ensemble of particles.

Significant Findings

A robust numerical method has been developed for simulation of the incompressible Navier–Stokes equations. The numerical scheme is based on the fractional step method in which the governing equations are solved on a staggered grid. A conservative treatment of spatial derivatives is employed using second–order accurate finite differences; the non–linear terms are advanced using second–order Adams–Bashforth while the viscous terms are treated implicitly using Crank–Nicholson. The pressure field is obtained using computationally efficient fast transform methods.

The dynamic subgrid–scale turbulence model and overall numerical model using large eddy simulations of the turbulent flow between plane channels was implemented and tested. These calculations have served two important purposes: (1) validation of the numerical method for computation of the underlying turbulent gas flow, and (2) providing a framework for measurement of Lagrangian statistics of both fluid elements and heavy particles in a well–defined turbulent shear flow. The simulations used to measure Lagrangian statistics of fluid elements are especially relevant to this work development of transport models for industrial ventilation applications requires an improved understanding of the nature of Lagrangian statistics in complex turbulent shear flows. Of the simulations performed in this area during the past year the most significant findings are that the ratio of Lagrangian to Eulerian timescales is independent of Reynolds number and that the asymptotic condition of particle diffusion is obtained only for extremely long transport times. Each of these findings will directly impact the particle transport models currently under development.

Simulations of heavy particle transport in turbulent channel flow have been used to determine the importance of various forces in the particle equation of motion, resolve numerical issues related to velocity interpolation, and provide insight into the ability of large eddy simulation to capture particle–turbulence interactions in turbulent two–phase flows. In particular, various forms for inertial lift by mean velocity shear have been investigated and found to have little effect for the class of two–phase flows of primary interest in this work, i.e., small heavy particles in gas–phase turbulence. Furthermore, though the numerical method employed in the present work is formally second order accurate in space and time, calculations of particle trajectories in turbulent shear flows require interpolation schemes having at least third order accuracy. Second order accurate linear interpolation excessively filters small scale variation, leading to relatively inaccurate predictions of particle motion and velocity. This finding is especially significant to the present work since it contradicts the conventional view that interpolation schemes need only be as accurate as the underlying numerical method. Finally, results from calculations of aerosol deposition in turbulent channel flow using large eddy simulation are in good agreement with experimental results. This finding significantly improves the viability of LES as a means for computation of complex particle–laden turbulent shear flows for industrial applications since traditional methods based on the Reynolds–averaged Navier–Stokes equations cannot accurately represent particle–turbulence interactions.

Publications

Squires KD, Eaton JK: Effect of Selective Modification of Turbulence on Two–equation Models for Particle–laden Turbulent Flows. Journal of Fluids Engineering, in press, 1994

Wu X, Squires KD, Wang Q: On Extension of the Fractional Step Method to General Curvilinear Coordinate Systems. Num Heat Transfer, in press, 1994

Wang Q, Squires KD: Lagrangian Statistics Obtained from Large Eddy Simulations Flow. Bulletin of the American Physical Society 39(9):1845, 1994

Statistical Issues For Compliance to Exposure Standards

Michael J. Symons, Ph.D.
University of North Carolina
School of Public Health
Department of Biostatistics
CB #7400, 3101 McGavran-Greenberg
Chapel Hill, North Carolina 27599-7400

Grant Number: *5 R18 OH03073-02*
Start & End Dates: *09/15/93 – 09/14/95*
Funding Level: *$70,999 ($139,138 Cum)*

Importance to Occupational Safety and Health

NIOSH's Occupational Exposure Sampling Strategy Manual (Manual) contains industrial hygiene and statistical guidelines for sampling occupational environments and analyzing exposure data. The consequence of selecting high risk employees, namely those with maximum exposures, however, could be better recognized in the analysis of these sample data for compliance to an environmental standard in a workplace. The application of extreme value theory will be explored.

Objectives

Three areas of statistical investigation are proposed: (1) to apply the theory of extreme values in the analysis of exposure measurements obtained by compliance sampling; (2) to examine alternative assumptions about the distribution of exposures by comparing a nonparametric procedure with fitting of a Burr XII distribution to exposure measurements; (3) to address the time series sampling of occupational environments by incorporating serial correlation into the analysis models.

Methodology

Applying the sampling theory of extreme values is the major objective. Specifically, the distribution of a maximum deals with the Manual's sampling of high risk employees and selection of the greatest exposure sites for evaluating ceiling standards. The basics of compliance sampling is to document the maximum exposures. The exact distribution of the maximum in samples from a specific distribution and the limiting Gumbel distribution of extremes are two aspects of the proposed approach. And, knowing the number of workers/sites at lower exposures should be informative.

The concern for the distribution of exposure measurements will be addressed in two ways. First, a Bayesian nonparametric approach to compliance classification is provided and will be compared with parametric procedures. Second, an empirical feel for the relevance of normal, lognormal, Weibull and gamma distributions will be gained by plotting a variety of occupational exposure data on a moment–ratio diagram. Since the relevant portion of the skewness–kurtosis plane is covered by the Burr XII distribution, the fit of this distribution to a variety of exposure data will be explored.

The effect on compliance decisions of correlated exposures will also be examined. Short, partial–shift samples collected on a maximum risk employee during a single shift are likely to exhibit higher serial correlation than a sequence of 8–hour samples. First–order autoregressive models will appropriately increase estimates of variance, for example of mean exposures. Consequently, not incorporating autocorrelation may result in anti–conservative inferences.

Significant Findings

Important progress has been made on the major objective. Specifically an interpretation of the n compliance samples as the largest exposures among N possible workers/sites, with the N–n workers/sites at lower, unobserved exposures, permits likelihood based inference for the distribution of in–plant exposures. A right, Type II censored likelihood is appropriate and effective when the industrial hygienist can select the n largest of the N possible exposures. This survival–type likelihood uses all the observations, while the original proposed examination of the maximum with extreme value theory would use much less of the available data. For the situation where the industrial hygienist is not perfect at selecting the n largest of the N available, treating the n compliance samples as being truncated from below appears promising. The single, unknown truncation point, above which the compliance samples are perceived as a random sample, adds one parameter to the distribution of exposures. A penalized likelihood is being developed to achieve likelihood based inference. Limiting forms of this model may reflect (1) random sampling, as the truncation point goes to zero, and (2) right, Type II censoring, as the truncation point approaches the (N–n)/N percentile of the exposure distribution.

The ability of an industrial hygienist to rank exposures collected in compliance sampling is the topic of Ms. Sonya Cato's Masters research, under the direction of Mike Flynn. Additional data in one plant will bear directly on the industrial hygienist's ability to select the n largest of N possible exposures as the compliance sample. The relevance of the

above likelihoods for censoring or truncation will be clarified by this research.

Progress has been made on assaying the distribution of exposure measurements. Unfortunately, simulations with the movement–ratio diagram suggest that even hundreds of observations are inadequate for accurately characterizing extreme skewness in lognormal samples. Statistical information available for shape parameters of right skewed distributions, in particular, is probably small and will be examined. Fits of the Burr XII distribution to a variety of exposure data probably will not yield very specific information on distributional shape. Additional Bayesian nonparametrics seem attractive if the truncation from below sampling model is shown to be relevant for compliance sampling.

The effect of correlated exposures on the left censoring and truncation from below models for compliance sampling is now thought most relevant.

Knowledge-Based Framework For Automating Hazop Analysis

Venkat Venkatasubramanian, Ph.D.
Purdue University
School of Chemical Engineering
Laboratory for Intelligent Process Systems
West LaFayette, Indiana 47907

Grant Number: *5 R01 OH03056-02*
Start & End Dates: *09/15/93 – 09/14/96*
Funding Level: *$152,600 ($366,508 Cum)*

Importance to Occupational Safety and Health

Occupational safety and health hazards pose threats to an estimated 20 million workers in the manufacturing sector in the United States. Industrial statistics show that even though major catastrophies and disasters of chemical plants may be infrequent, minor accidents are very common, occurring on a day–to–day basis, resulting in many occupational injuries, illnesses, and costing the society billions of dollars every year. The occurrence of several catastrophic accidents in the refining and chemical industries during the 1980s has intensified public concern about process safety. The chemical industry, the federal government, and many state governments have responded to address these concerns in the form of new guidelines and requirements. The recently published final *Occupational Safety and Health Administration (OSHAJ)* standard on process safety management, Rule 29 CFR 1910.119, requires the use of a process hazards analysis (PHA) technique for the identification of hazards for process systems containing toxic substances and/or flammable process materials above specified threshold quantities. OSHA estimates that such a process hazards analysis will be required at approximately 25,000 existing plant sites in the U.S. and for all the new ones that are built or retrofitted in the future. This comprehensive mandatory review of process hazards will directly impact on the safety of about one million workers who are employed in the chemical industry, and many millions of people residing in the neighboring communities surrounding chemical plants. It is estimated that about 50 million person–hours and five billion dollars might have to be spent using the current PHA approaches to meet this new regulation. This project proposes to develop a novel computer–based framework that has a great potential to decrease this massive effort and also increase the productivity by providing for a fast, systematic, thorough, and detailed analysis of routine process hazards.

Objectives

HAZOP analysis is the study of systematically identifying every conceivable deviation, finding all the possible abnormal causes, and the adverse hazardous consequences of that deviation in a chemical plant. This is a very difficult, labor–intensive, and time–consuming process. Such an analysis is often carried out by a group of experts poring over the process P&IDs for weeks or months, applying a set of `guide words' to the process variables associated with each process line and equipment, and finding the causes and consequences for those process variable deviations This is a major labor– and knowledge–intensive problem that can benefit from automation using Artificial Intelligence (AI) techniques. An automated HAZOP system can cut down on the time and effort involved in performing a HAZOP review, make the review more thorough, complete, and detailed, and minimize or eliminate human errors. The main goal of this proposal is to develop a knowledge–based system for automating certain aspects of HAZOP analysis and demonstrate its utility and performance on complex, industrial–scale, HAZOP case studies. Related subgoals involve the solution of various problems such as process knowledge representation, search and inference, HAZOP models development, system modification, validation and maintenance, graphical user interfaces, information overload etc.

Methodology

The automation of HAZOP analysis demands the solution of a number of important problems such as: represent different types of knowledge, dealing with the propagation of causes and effects due to abnormal deviations through out the process plant, both in the forward and the reverse directions of material flow, handling loops and recycles in the plants, developing a convenient graphical user–interface and so on. In our proposed framework, we address all these problems and some other related issues by utilizing several novel techniques. Some key aspects of our methodology are: (1) A generalized object–oriented framework is used to represent and organize all kinds of knowledge including heuristics, causal models, procedures etc. This is a very powerful framework that will facilitate default reasonings, reasoning with composite objects, provide flexibility of control, facilitate inter–object communications etc. (2) Divide the HAZOP knowledge into "process general" and "process specific" knowledge and allow for interactions between these two tiers of knowledge. This way, the general, basic knowledge required for performing HAZOP can be kept in the generic knowledge base, which remains fixed irrespective of the process plant under consideration and the process specific knowledge can be created separately for each process plant. The `process general' knowledge would be stored as a library of causal models that capture all the generic features of the process equipments and their behavior. The `process specific' knowledge would consist of the type of the process materials, properties of process materials and the process P&ID. (3) A sophisticated inference algorithm for reasoning about the causes or abnormal deviations all the way to their root and to propagate the consequences all the way to the end (4) An object–oriented graphical user–interface to attend to the needs of the developer and the user.

Significant Findings

Significant progress was made on several fronts of this project. A generalized object–oriented hierarchical backbone structure for representing process equipments was developed. A similar structure was also developed for representing process materials and process situations. HAZOP models of simple valves, tanks, streams and pumps were developed. A preliminary version of the graphical user–interface was also completed. A refined cause–consequence propagation algorithm was developed. Progress was also made on the development of the initial digraph representation for HAZOP models. Testing and evaluation with case studies 1 and 2 were completed. These are the first two parts of a three–part complex, real–life, industrial case study dealing with a sour water stripper plant. This is an actual case study that had been reviewed using HAZOP analysis by our collaborators from Arthur D. Little and Company. This process contains a refinery stream that is separated in to sour water and slop oil in a surge drum. The sour water is pumped in to a storage tank where any carried slop oil is skimmed out. From the storage tank the sour water is pumped through a heat exchanger in to a steam stripper where the ammonia and hydrogen sulfide are stripped from the sour water.

We compared HAZOP*Expert's* results with those obtained by a team of HAZOP experts for the sour water stripper process. Nineteen process variable deviations have to be considered for each of the fifteen pipelines in the plant. In addition to these deviations in pipelines, HAZOP analysis was performed for all possible process variable deviations in all the major process units in the plant. Thus, approximately 400 process variable deviations were considered for the HAZOP analysis of the sour water stripper plant by HAZOP*Expert*. For all these deviations HAZOP Expert was able to find all the abnormal causes and adverse consequences that were found by the HAZOP team. In general, HAZOP*Expert* generates more HAZOP results than those recorded in a conventional HAZOP analysis performed by experts. This is due to the qualitative nature of the HAZOP analysis procedure. In a conventional HAZOP analysis, experts filter the initial HAZOP results generated using additional quantitative information they have and record only part of the results. This aspect of experts' reasoning has not been incorporated in our system yet and is one our future goals to be accomplished.

Publications

Venkatasubramanian V, Vaidyanathan R: HAZOP*Expert*: An Expert System for HAZOP for HAZOP Analysis. Proc of the Fifth International Conference on Process Systems Engineering (PSE '94), Kyongju, South Korea, June, 1994

Measurement of Alkenyl/Epoxy DNA Adducts by GC-MS

Roger W. Giese, Ph.D.
Northeastern University
Bowe College of Pharmacy
and Health Sciences,
and Barnett Institute
360 Huntington Avenue
Boston, Massachusetts 02115

Grant Number: *3 R01 OH02792-03S1*
Start & End Dates: *01/01/91 – 12/31/94*
Funding Level: *$136,446 ($401,386 Cum)*

Importance to Occupational Safety and Health

DNA is an ultimate target in the body for carcinogenic and mutagenic chemicals. Measurements of DNA adducts therefore can help to sort out some of the uncertainties in exposure and risk assessment arising from exposure of individuals to chemicals. Understanding biological significance of chemical damage to DNA is dependent on the ability to measure it.

Objectives

New analytical methodology is being developed to measure DNA adducts arising from occupational human exposure to ethylene, ethylene oxide, butadiene, styrene and propene. These chemicals were selected since they are widely used and genotoxic. Also, they are anticipated to give similar types of DNA adducts.

Methodology

The proposed methodology comprises four steps: (1) isolate the DNA from a biological sample; (2) separate the DNA adducts from the bulk of the DNA; (3) derivatize the adducts with an electrophoric reagent; and (4) detect the electrophoric products by gas chromatography–electron capture mass spectrometry (GC–EC–MS).

Significant Findings

An analytical procedure for measuring the N7–guanine (N7–G) DNA adduct of ethylene oxide was developed. The procedure has been transferred to the toxicology laboratory directed by Dr. James Swenberg at the University of North Carolina, where it is being used routinely to measure this adduct in tissues from animals exposed to ethylene oxide. The sensitivity of the method allows endogenous levels of this adduct to be detected (about 1–6 N7G ethylene oxide adducts in 106 guanines, depending on the tissue).

The procedure, as intended, is general for adducts of this general type. For example, the procedure has been used to detect standards of related styrene, butadiene, and benzene N7–G adducts. Also N7–methyl–G has been detected.

Both solid phase extraction and HPLC are important sample cleanup techniques for the kind of methodology that we are developing. The performance was compared for the second derivatization reaction (a pentafluorobenzylation) of the N7–G ethylene oxide adduct and it was found that HPLC has a carryover problem. This problem was found to be due to the injector. The use of two injectors overcomes the carryover problem.

Work has begun on the detection of the corresponding O^6–G ethylene oxide adduct. A novel chemical transformation reaction was required for this adduct that would retain the O^6–hydroxyethyl group. This has been achieved by converting the exocyclic amino to fluoro.

Some of the trace contamination in the methodology was found to derive from the Teflon liner and plastic cap employed to seal the reaction vial. This was overcome by introducing an all–glass vial.

This work is significant in two general respects. First, is the general significance of detecting DNA adducts in humans as biomonitors for exposure to chemicals. Second, is the broader methodological significance of the new chemical and physical techniques that have been developed to date for the N7–G and O^6–G ethylene oxide adducts.

Publications

Giese RW, Saha M, Abdel–Baky S, Allam K: Measuring DNA Adducts by GC–EC–MS: An Example of Trace Organic Analysis. Meth Enzymol, in press, 1993

Saha M, Giese RW: HPLC vs Solid Phase Extraction for Post–Derivatization Cleanup Prior to GC–ECNI–MS for N1,N3–Bis–(pentafluorobenzyl)–N7–(2–[pentafluorobenzyloxy}–ethyl)xanthine, A Product Derived from an Ethylene Oxide DNA Adduct. J Chromatogr 629:35–40, 1993

Saha M, Giese RW: Primary Contribution of the Injector to Carryover of a Trace Analyte in HPLC. J Chromatogr 631:161–163, 1993

Saha J, Saha M, Giese RW: 4–(Trifluoromethyl)–2,3,5,6–Tetrafluorobenzyl

Bromide: A New Electrophoric Derivatizing Reagent. J Chromatogr 641:400–404, 1993

Chiu CS, Saha M, Abushamaa A, Giese RW: Chemical Transformation/Derivation of O^6–Methyl– and O^6–(Hydroxyethyl)guanine for Detection by GC–EC–MS. Anal Chem 65:3071–3075, 1993

Abdel–Baky S, Allam K, Giese RW: Derivatization in Trace Organic Analysis: Use of an All–Glass Conical Reaction Vial. Anal Chem, 2882–2884, 1992

Abdel–Baky S, Giese RW: Gas Chromatography/Electron Capture Negative–Ion Mass Spectrometry at the Zeptomole Level. Anal Chem 63(24):2986–2989, 1991

On-Site Enumeration of Fungal Spores and Bacteria in Air

H. Kenneth Dillon, Ph.D.
University of Alabama
School of Public Health
Department of Environmental Health Sciences
UAB Station
Birmingham, Alabama 35294

Grant Number: *5 R01 OH02914-03*
Start & End Dates: *02/01/92 – 01/31/95*
Funding Level: *$142,643 ($376,961 Cum)*

Importance to Occupational Safety and Health

The sampling and analysis methodology is expected to yield a measure of exposure to viable and nonviable bioaerosols that have been implicated in the occurrence of many diseases of the lower airways (e.g., hypersensitivity pneumonitis, mycotoxicosis, asthma, aspergillosis, and bronchitis) and diseases of the upper airways (e.g., allergic rhinitis and sinusitis). The onset of acute HP symptoms have been observed upon repeated exposures to high concentrations of viable and nonviable fungi and actinomycete spores. Repeated exposures over several weeks to relatively low levels of fungal spores and bacteria can cause mucous membrane irritation (MMI) of the eyes, nose, and throat. Continuous MMI at high levels of exposure to bacteria and fungal spores may lead to chronic bronchitis after several years of exposure. Because most all fungal spores are apt to be allergic at least to some atopic individuals, spore count is expected to correlate with fungal allergenic potential. The developed method will yield information that will aid in the identification of fungal spores and bacteria. The method will, also, allow timely on–site analyses which will facilitate the correlation of currently observed symptoms with exposure conditions and the development of timely disease prevention strategies. Sampling sequentially with the sampling manifold will allow the development of time and spatial concentration profiles over extended periods which will aid in locating sources of bioaerosols and in the determination of environmental conditions or work activities that may induce or influence the release of bioaerosols to the indoor air environment.

Objectives

1. The overall objective of the proposed work is to develop an on–site screening method involving air sampling with membrane filter discs and subsequent analysis by brightfield and epifluorescent microscopy.
2. The primary goal of the first phase of study was the development of an analysis protocol that can be used in the field and that will yield results within minutes of the cessation of air sampling. The analysis method has been developed and evaluated.
3. In the second phase, an air sampling device was fabricated that provides sequential sampling with replicates. The evaluation of the sizing characteristics of this device has been completed, using test aerosols generated in a wind tunnel built specifically for this project.
4. The final phase of the proposed work, which is now underway, is the field evaluation of the developed technique.

Methodology

Commercially available track–etched, 0.2 and 0.4–μm polycarbonate filter discs darkened with Irgalan black were found suitable for air sampling and microscopy. Slides of fungal spores and bacteria on filters were prepared with 0.2 to 2 mM acridine orange (AO) in neutral buffered saline (NBS) or with glycerin jelly (a solution of gelatin and glycerin in water) containing 0.2 mM AO. The laboratory evaluation of the sizing characteristics of the developed sampler were conducted in a wind tunnel based on the design of the Air Cleaner Standard Test Duct recommended for rating air cleaners by the American Society of Heating, Refrigerating and Air–Conditioning Engineers (ASHRAE). The wind tunnel was built, evaluated and modified to the final design in order to meet acceptance criteria consistent with those established by the US Environmental Protection Agency for PM_{10} sampler testing. The APS Model 3310 aerodynamic particle sizer (TSI Inc., St. Paul,

Minnesota) was used to compare particle size distributions and concentrations inside the developed sampling device to particle size distributions and concentrations in the wind tunnel over a range of wind velocities from 0.2 to 1.4 m/sec at aerosol concentrations of 0.2 to 1.1 mg/m^3. A preliminary field test of the sampler was conducted in a cotton dust environment, a simulated cotton carding room, as a courtesy of the U.S. Department of Agriculture laboratory at Clemson University.

Significant Findings

Examination of slides at 1250x by bright field and epifluorescence (EPI) microscopy using oil immersion objectives demonstrated the ability to size and count individual as well as aggregates of spores and bacteria over a broad range of sizes and morphologies. Mean bacterial and fungal spore counts >100 consistently yielded CVs ≤13%. No statistically significant bias (α=0.05) was observed when microscopically counting fungal spores at a density of 14 in a 0.042–mm^2 viewing field. At lower levels, biases were inversely related to density; a 30% bias was observed at a density of 2 spores in a field. Desiccation of osmotically fragile *E. coli* on filters exhibited no effects on morphology or the enumeration of the bacteria. Macroscopic and microscopic examination of colonies grown from filter extracts demonstrated the capability to identify viable fungi at least to the genus level. A sampling system was designed with variable aerodynamic particle size cutpoints and optimized to collect the "inhalable" size fraction. One of the primary design features of the sampler was a twelve–filter sampling manifold to allow the collection of replicate samples over sequential sampling periods. A field test of the sampler demonstrated satisfactory performance in a relatively heavy cotton dust environment, a concentration of about 1 mg/m^3. Cotton fibers were excluded from the sampling manifold and, thus, did not interfere with spore counting. Spore concentrations averaged 1.28 x 10^5/m^3 over the 5–h sampling period, and 1–h averages exhibited a concentration–time profile that was similar to that for cotton dust sampled with vertical elutriators. Paired filter samples taken with the manifold sampling system demonstrated good agreement between the duplicates with an average difference of 9%.

A Dichotomous Sampler for TRIG Aerosol and Vapor

Roy Rando, Sc.D.
Tulane University Medical Center
Section of Environmental Medicine/SL15
1430 Tulane Avenue
New Orleans, Louisiana 70112

Grant Number: *5 R01 OH02664-02*
Start & End Dates: *02/01/92 – 01/31/95*
Funding Level: *$0 ($209,735 Cum)*

Importance to Occupational Safety and Health

The isocyanates are an important class of commercial chemicals used in the production of polyurethanes and certain pesticides. Exposure may result in occupational asthma, hypersensitivity pneumonitis, and accelerated decline in lung function. The compounds are highly reactive, and some have a high affinity for surfaces and relatively low vapor pressures at ambient temperatures. These properties result in a tendency for some isocyanates to partition into gaseous and particulate phases in the atmosphere. The physical state of the compound will affect its site of deposition/adsorption in the respiratory tract, as well as dictate the appropriate sampling techniques and engineering control methods. This project entails the development of a dichotomous sampler for total reactive isocyanate group (TRIG) vapor and particulate which will be used to characterize TRIG in representative workplace atmospheres. This work will improve our understanding of the fundamental behavior of TRIG in the atmosphere and will result in a powerful analytical tool for future studies of the toxicity of vapor and condensed phase isocyanate.

Objectives

A critical laboratory comparison of the selectivity, sensitivity, accuracy, and precision of analysis of the methoxy–phenylpiperazine (MOPIP), methyamino–methylanthracene (MAMA), and tryptamine (TRYP) reagents for TRIG will be performed using a series of model aliphatic and aromatic isocyanate monomers and oligomers. The best of these techniques will be adapted for use in an annular denuder for dichotomous sampling of condensed and vapor phase TRIG. After a thorough evaluation of the performance of the dichotomous sampler in the laboratory, it will be used in a survey of TRIG in representative workplace atmospheres,

such as isocyanate manufacture and flexible polyurethane foam production.

Methodology

Analytical derivatives of eleven isocyanate monomers with MAMA, MOPIP, and TRYP were synthesized in the laboratory. The isocyanates included methyl–, butyl–, phenyl–, benzyl–, o–tolyl–, and p–tolyl–isocyanate, and 1,6–hexamethylenediisocyanate, 2,4–toluenediisocyanate, 2,6–toluenediisocyanate, methylene–bis–(4,4'–cyclohexylisocyanate)(HMDI), and methylene–bis–(4,4'–phenylisocyanate) (MDI).

The analytical response of each of the derivatives was compared for consistency within derivatizing agent. Equimolar amounts of each derivative based on isocyanate content were analyzed by reversed–phase HPLC using three detection modes: MAMA derivatives were analyzed using fluorescence, and UV absorbance at two wavelengths; MOPIP derivatives were analyzed with electrochemical detection and with UV absorbance at two wavelengths; TRYP derivatives were analyzed with fluorescence, with electrochemical detection, and with UV absorbance. For each analysis, a response factor was calculated as the ratio of the integrated chromatographic peak area to the sample concentration in terms of isocyanate equivalence.

From the above work, MAMA was chosen as the derivatizing agent and was applied to quantitation of TRIG content in a series of oligomers of MDI and HDI in comparison to a reference titration procedure. It was also adapted to use in a dichotomous sampler.

Tested configurations of the dichotomous sampler consisted of an impactor or cyclone inlet, annular diffusional denuder (University Research Glassware) and either a filter, coated with MAMA, or impinger containing MAMA in DMSO. Sampling of test atmospheres of vapors and aerosols of the model isocyanates was performed with the sampler.

Significant Findings

Statistically significant intra–group differences were found across isocyanates for each of the three derivatizing agents and their three associated detection modes. The variabilities as measured by relative standard deviations of the mean response factors were as follows: MAMA derivatives; fluorescence, 55%; UV at 245 nm, 14%; UV at 370 nm, 8.6%; for MOPIP derivatives – electrochemical, 26%; UV at 242 nm, 50%; UV at 277 nm, 35%; for TRYP derivatives – electrochemical, 55%; fluorescence, 24%; UV at 280 nm, 24%. The MAMA derivatives were clearly the most consistent when detected by UV absorbance. The ratio of absorbance at 254 to that at 370 nm averaged 10.46 with a RSD of only 8.3%. These results led to the choice of MAMA for use in the TRIG technique. Assay of three oligomeric isocyanate materials based on MDI monomer using MAMA reagent resulted in average recovery of 100.6 ± 4.7% of TRIG content in comparison to a reference assay utilizing titration with di–n–butylamine. Several TRIG containing peaks were identified during chromatography, including the parent MDI monomer. Two HDI based oligomeric materials were also assayed resulting in a recovery of 103.2 ± 1.1%. HDI monomer and HDI–biuret were easily identified in these samples along with an unknown TRIG containing compound. One TDI–based polyurethane varnish was assayed by MAMA and was seen to contain 2,4– and 2,6–TDI monomers as well as two other isocyanate containing compounds. Recovery of TRIG by MAMA assay was 103% of the reference titration value.

For 8 of the 11 isocyanate monomers, little penetration past the denuder component of the dichotomous sampler was noted indicating that these materials were in the vapor phase in the test atmospheres. Approximately 50% of MIC was found on the backup device because of poor collection of this very volatile material. For MDI monomer, the dichotomous sampler clearly separated test atmospheres ranging from 24 to 355 $\mu g/m^3$ into vapor and aerosol fractions. Aerosols of MDI began to penetrate the diffusional denuder and collect on the backup filter at an MDI level of 75 $\mu g/m^3$, very near the saturated vapor pressure of MDI at 26°C. Conversely, HDI–biuret produced by nebulization was found only on the impactor and back–up filter, indicating no vapor formation. Interestingly, the small amount of HDI monomer contained in the HDI–biuret was evenly distributed among the components of the dichotomous sampler, an indication of partitioning between aerosol and vapor phases.

Publications

Rando RJ, Poovey HG: Dichotomous Sampling of Vapor and Aerosol of Methylene–Bis–(Phenylisocyanate) [MDI] with an Annular Diffusional Denuder. American Industrial Hygiene Association Journal 55:716–721, 1994

Rando RJ, Poovey HG, Lefante JJ, Esmundo FR: Evaluation of 9–Methylamino–Methylanthracene as a Chemical Label for Total Reactive Isocyanate Group: A Comparison of Mono– and Di–Isocyanate Monomers. Journal of Liquid Chromatography 16:3977–3996, 1993

Physiologic Sampler For Airborne Health Hazards

Michael G. Yost, Ph.D.
University of Washington
School of Public Health
Department of Environmental Health
Mail Stop SC-34
Seattle, Washington 98195

Grant Number: *1 R01 OH03134-01*
Start & End Dates: *09/30/93 – 09/29/96*
Funding Level: *$114,711 ($234,473 Cum)*

Importance to Occupational Safety and Health

Inhalation exposures are typically assessed by personal breathing zone air monitoring using a constant flow sampling device. Although breathing zone sampling accounts for spatial and temporal variability in the air concentrations, it does not take into account spatial and temporal variability in the uptake of contaminants due to changes in pulmonary ventilation rate. This may well represent an important source of variability in exposure to inhalation hazards, since many common work tasks in construction generate exposures coupled with increased physical activity which alters breathing rates.

Furthermore, efforts to measure body burden of volatile organic compounds (VOC) have employed several methods, including breath sampling, to estimate the contaminant concentration in blood. Interpretation of these readings in complicated by the pharmacokinetics of VOC in humans, which can vary widely for different compounds. Single time–point measurements have limited value when attempting to estimate body burden from breath samples; multiple time course (washout) measurements however, can provide the basis for estimating decay rates and, in many cases, body burden. The difficulty with multiple measurements is the additional time they impose on workers, and increased analytical costs to employers. A simple and rapid breath analysis method, particularly one that employs a direct reading instrument and a repeated measures sampling strategy optimized to account for the wide range of VOC excretion rates, could provide a cost effective method for breath monitoring.

Objectives

The hypothesis of this project is that a personal air sample whose volume is proportional to the construction worker's inhaled air volume will yield a measure of inhalation exposure which is better correlated with the body burden, estimated through biological monitoring, than a constant flow air sample taken in the traditional way. If supported, this hypothesis will lead to significant improvement in the estimates of construction worker exposure to VOC using personal air sampling.

The specific aims of this study are:

1. to develop a physiologic sampling device, which samples at a rate proportional to an individual's pulmonary ventilation rate, and which can be worn as a free ranging personal monitor suitable for construction workers. Data on VOC concentration and exposure rate collected with this sampler from active subjects under laboratory conditions will be compared to conventional personal samples and to breath samples.
2. to use a novel instrument, the Rapid Exhaled Breath Analyzer (REBA), for monitoring expired air from solvent exposed construction workers. This direct reading instrument employs a customized Fourier Transform Infrared (FTIR) spectrometer to measure VOC mixtures in breath samples. Existing pharmacokinetic data for several target VOC will be used to develop a repeated measures sampling strategy aimed at providing an estimate of body burden and hence absorbed dose, to be compared with the two measures of inhalation exposure.
3. to conduct a field pilot study using the physiologic sampler and REBA to analyze air and breath samples from solvent–exposed construction workers. The field pilot study will provide data to explore both the analytical sensitivity and sampling strategy that is most appropriate for VOC exposures in the construction industry.

Methodology

The sampling pump will use an input signal, derived from either heart rate or thoracic dimensions, to alter the air flow rate. Thus the amount of contaminant collected during the sampling period will be proportional to the mass inhaled by the worker. This contrasts with the traditional constant flow sampling methods which give a result proportional to the average ambient concentration of contaminant. The sampler will first be validated in laboratory experiments in which volunteers will wear the sampler while exercising on a bicycle at rates chosen to simulate work rates on construction jobs. Once validated in the controlled setting, the device will be placed on selected workers at local construction sites where exposure to paint solvents occurs. Performance

of the sampler will be evaluated by taking breath samples from the workers at the start of the next shift to estimate absorbed dose. A high correlation between absorbed dose from breath samples and the physiologic sampler measurement will demonstrate the effectiveness of the new method.

Significant Findings

Significant progress has been made in developing the sampling apparatus. We have obtained 4 sample pumps (Gillair–5) along with complete circuit documentation from the manufacturer. We have tested the pumps and found a suitable method of controlling the pump motor to produce a flow rate that is linearly proportional to a DC control voltage. Two control points were evaluated, and access point 2 produced the best results with less scatter in the data; a regression line fitted through these data yielded an R^2 of 0.99 with a nearly 0 intercept (equation: $y = .05 + .021x$).

We have conducted tests to evaluate the ability of the pumps to maintain a constant flow rate. The data indicates that the pump can compensate for changes in resistance and maintain a fairly constant flow rate ($<\pm 7\%$) even with relatively large changes in flow resistance.

We have modified the pumps so the control voltage can be applied through a miniature plug–in jack located on the pump housing. (The jack is similar to the headphone jack for a portable tape player.) When the jack is in place, the pump is controlled by our external circuit; when the jack is removed the pump performs like a conventional constant flow sampler. Also, the battery protection and fault protection circuits provided in the pump continue to function at all times.

The external control circuit has been protyped and tested. The circuit produces a time averaged DC control voltage that is proportional to the fluctuating input signal. The prototype controller can accept several physiologic input signals. These signals include two channels to measure rib cage and abdominal cross section, a combined scaled rib cage/abdominal signal representing minute ventilation (L/m), and a signal for heart rate (beats/min). In the present control circuit, all input signals are rectified and time averaged over a 1 minute interval. We are currently evaluating these different input signals to determine the amplitude and frequency spectral characteristics that might be expected from various work conditions.

The data collected to date demonstrate the feasibility of a physiologic sampler. We have devised a modified personal sample pump to accept a proportional voltage control of the flow rate over a wide range (>10:1) of flow conditions. The control method appears to be robust, stable, and repeatable. We have developed a controller circuit that can accept a variety of signal inputs from physiologic monitoring and creates a time–averaged proportional control voltage as the output. At this point the prototype sampler design work is sufficiently completed to allow us to progress to the laboratory phase of the study.

Western Blot Analysis of Organophosphate Exposure

Alan M. Jeffrey, Ph.D.
Columbia University
Division of Environmental Sciences
701 West 168th Street
New York, New York 10032-2704

Grant Number: *1 R03 OH03256-01*
Start & End Dates: *09/30/94 – 09/29/95*
Funding Level: *$41,003 ($41,003 Cum)*

Importance to Occupational Safety and Health

A program to prevent organophosphate toxicity through a comprehensive biological monitoring program of exposed workers would use the IN assay for the following applications.

1. To confirm the presence or absence of exposure in workers lacking baseline AChE measurements.
2. To correctly classify the exposure status of workers. The ability to measure low levels of inhibition would permit the evaluation of the relationship between chronic low level exposures and health effects.
3. To assess industrial hygiene control measures. The ability to monitor small changes in AChE levels would aid in the evaluation of altered work practices and new personal protective gear.

Objectives

The aim of this project is to detect erythrocyte acetylcholinesterase (AChE) inhibition with a Western blotting procedure that separates inhibited and native enzyme (IN assay). This approach will directly measure AChE quantities rather than their activity as is done with current assays. The advantage of this assay lies in the internal control gained by measuring enzyme concentrations. The variability due to differences in normal cholinesterase levels between

individuals is eliminated and it is no longer necessary to compare the results with earlier measurements. IN assay development will be as follows:

1. Separate and measure inhibited and native AChEs by Western blotting .
2. Optimize the IN assay for detection limit, sensitivity and variability.
3. Compare the levels and sources of variability obtained with the IN assay with a standard method currently used for measuring AChE activities; the Ellman's assay.
4. Use the IN assay to measure AChE inhibition in OP–exposed workers and compare the results with the activity obtained with the Ellman's assay.

Methodology

This project will develop a Western blotting assay to detect erythrocyte AChE inhibition. The assay will simultaneously measure inhibited and native enzyme (IN assay), eliminating the problems encountered in those that measure only enzyme activity. AChE levels differ both between people and in successive measurements taken from the same individual. These variabilities necessitate the use of pre–exposure measurements and limits the ability to detect low levels of inhibition. The internal reference incorporated into the IN assay will permit direct measurements of inhibition and eliminate the need for comparison with earlier measurements.

The IN assay will separate native and inhibited AChEs electrophoretically and transfer the enzymes to a membrane where they will be detected with an immunoenzyme procedure using murine anti–human AChE monoclonal antibodies.

The goal of optimization is to produce an assay able to detect inhibition levels of 2% or less. Once optimized, the impact of different organophosphates on the measured inhibition will be evaluated by comparing the results obtained with the IN assay with those from the Ellman's assay, which is the standard method for measuring AChE activities. The effect of the IN assay's internal control will be assessed by measuring the intraindividual, interindividual and analytical variabilities found in the assay and comparing them with the variabilities found in the Ellman's assay. Blood taken from a cohort of five people drawn weekly for five weeks and inhibited *in vitro* with diisopropylfluorophosphate will be used. The effect of different cholinesterase inhibitors upon AChE activity will be measured using blood samples modified *in vitro* with equimolar quantities of mevinphos, oxydemeton methyl, methyl paraoxon, or malaoxon. Finally, the inhibition measured by the two assays will be compared using 12 samples from organophosphate exposed workers obtained from a clinical laboratory in Fresno, CA.

Significant Findings

None to date.

Dosimetry for Workplace EMFs at Power-Line Frequencies

Om P. Gandhi, Sc.D.
University of Utah
College of Engineering
Department of Electrical Engineering
3280 Merrill Engineering Building
Salt Lake City, Utah 84112

Grant Number: *5 R01 OH02945-02*
Start & End Dates: *05/01/92 – 11/30/94*
Funding Level: *$130,588 ($248,776 Cum)*

Importance to Occupational Safety and Health

There is an increasing concern that electromagnetic fields (EMFs) at power frequencies may have health effects. A key research need, therefore, is to establish the mechanisms of bioeffects of these EMFs. An important aspect of this is to understand the coupling of the EMFs to the tissues in the human body. Knowledge in this area is relatively poor, since, in the past, only simple saline–filled and metal–coated idealized models have been used.

Objectives

The focus of our project is to obtain internal electric fields and induced current densities in heterogeneous, anatomically based models of the human body for a variety of worker exposure conditions encountered in occupational situations. Another objective is to develop two new instruments, namely the contact–current meter and the stored–energy meter, which may be used to assess the potential for shock and burns in the EMF workplace. Using an equivalent circuit as the human surrogate, the contact–current meter will measure the current that will flow for different conditions of contact such as finger or grasping contact, with or without rubber–soled shoes, and with or without safety gloves. Likewise, the stored–energy meter will measure the open–circuit voltage and short–circuit current for various locations of possible worker contact, allowing an evaluation of the stored energy

which is related to the possibility of spark discharge for transient contacts.

Methodology

The accomplishments of the 01 year of the project are as follows:

1. We have developed a new high–resolution model of the human body based on the magnetic resonance imaging scans of a male volunteer that were taken with a resolution of 3 mm along the height of the body and 1.875 mm for the cross–sectional planes. For this model we have incorporated the an isotropic conductivities of the various tissues such as the skeletal muscle and heart that are important for power–frequency EMFs. We have started to use this model to calculate induced electric–field and current–density distributions for exposure of the human body to incident vertical electric fields (up to 10 kV/m) and horizontal magnetic fields (up to 50 μT) associated with high–voltage power transmission and distribution lines.
2. We have developed computer graphical methods to obtain color pictures of the spatial variations of the calculated electric–field and current density distributions for the various cross sections of the body. Because of the fairly high electrical conductivity associated with regions of the cerebrospinal fluid (CSF), the highest current densities are calculated for these regions. We are also examining the current densities and E–fields induced for the region of the pineal gland, since alterations in the melanonin levels have been observed in laboratory animals exposed to EMFs at power frequencies.
3. We have started to calculate the induced currents in the human body for exposure to EMFs encountered in the workplace. To date we have calculated currents induced in the human arm and the body by the spatially varying magnetic fields of an electric drill and for linemen exposed to magnetic fields of high–voltage power transmission lines.
4. We have fabricated prototype contact current and stored energy meters to assess the potential for electrical and for hazardous transient spark discharges in the EMF workplace situations. The specifications for the contact–current meter are 0–50 mA and for the stored energy meter are 0–15 kV open circuit voltage and 0–50 mA short circuit current, respectively.

Significant Findings

1. The highest induced electric fields and current densities for a hand drill are for the front half of the right arm and for the sections of the torso that are in proximity to the hand drill. For a power drill with a maximum magnetic field of 500 μT the section–averaged current densities for the hand are as high as 2.5 mA/m2 and the highest local current densities are on the order of 8.5 mA/m2.

2. For linemen working on high–voltage power transmission lines the magnetic fields may be as high as S Gauss (500μT). Since these repairmen are often in a horizontal position parallel to the high–voltage line, they are subjected to these high magnetic fields that are fairly uniform over the extent of the body and are generally in the direction of arm to arm of the body. For such exposures we calculate a maximum induced current density of 1.0 mA/m2 and a maximum induced electric field of 7.3 mV/m.

We have surveyed the magnetic fields at the power generation facilities of a utility company. The highest magnetic fields on the order of 0.5 – 0.7 Gauss were found close to the output leads of the power generators. These magnetic fields were generally vertical and the highest magnetic fields occurred for the region of the floor above these leads or else underneath the leads on the primary side of the voltage step–up transformer. Using the millimeter resolution model of the human body we are presently calculating the induced current densities and electric fields for such occupational environments.

Inhalation and Sampling of Large Particles, 10-150 μm

William C. Hinds, Sc.D.
University of California
School of Public Health
Department of Environmental Health Sciences
405 Hilgard Avenue
Los Angeles, California 90024-1772

Grant Number: *1 R01 OH03196-01*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$105,943 ($105,943 Cum)*

Importance to Occupational Safety and Health

Exposure to large particles, 10–150 μm, occurs in occupational activities such as mining, woodworking, painting, pesticide application,

grinding, and mineral processing. Generally, large particles such as heavy metals, pesticides, radioactive materials, and corrosives are harmful if inhaled, regardless of where they deposit in the respiratory system. Occupational health professionals need to know what fraction of large particles will be inhaled under different conditions, and how well different types of samplers collect these particles. Few data are available on the inhalation of large particles and the performance of samplers for these particles. For particles greater than 30 μm, there are no data on inhalability for liquid particles, for nasal inhalation, and for sampling performance of 37 mm filter cassettes. Data for solid particles greater than 60 μm are presently available from only one laboratory. Experimental measurements of these quantities under simulated industrial conditions are needed to support standards based on recent ACGIH and CEN sampling criteria for inhalable particulate matter (IPM).

Objectives

The overall objective of this research is to improve our knowledge and understanding of the inhalation of large particles, those in the 10 to 150 μm aerodynamic diameter size range, and to evaluate current and modified personal samplers for their ability to sample accurately these particles under simulated industrial conditions.

Specific objectives are:

1. Develop a liquid particle aerosol generator that will produce a uniform concentration of monodisperse, or narrow distribution, liquid particles in the size range of 10 to 150 μm in the wind tunnel.
2. Make measurements of inhalability (mouth and nose) for solid and liquid particles as a function of ambient air velocity, orientation of the mannequin relative to the direction of air motion, aerodynamic particle size (10–150 μm), and mannequin breathing pattern (work rate).
3. Evaluate the sampling performance of available personal samplers for large solid and liquid particles as a function of ambient air velocity, orientation of the mannequin to the air motion, and aerodynamic particle size (10–150 μm).

Methodology

This research is conducted using UCLA's fully operational low–velocity wind tunnel to simulate, under controlled conditions, air motion typical of indoor work environments. Specific test conditions for solid and liquid particles are: eight particles sizes (10–150 μm), three air velocities (0.4–1.8 m/s), three breathing profiles (work rate of 0–102 W), two orientations (0° and orientation average), and three replications for each condition. Personal sampler evaluation will include current "total," IPM, and prototype IPM samplers over the same range of conditions for solid and liquid particles.

The UCLA inhalable particle test facility is a low velocity open–cycle, closed–jet wind tunnel with a cross–section of 1.6 m square and a length of about 8 m. Maximum flow rate is 11,000 cfm (310 m^3/s). Air velocity range in the tunnel is 0.1 to 2 m/s and is uniform to within 10% across the test section. The solid particle test aerosol material is resuspended aluminum oxide optical abrasive powder. The dust is dispersed by a generation system consisting of three NBS type dust feeders mounted on top of the wind tunnel.

Multiple vibrating orifice aerosol generators will be used to generate a uniform concentration of monodisperse liquid particles. The same distribution system as used for the solid particles will be used. The test aerosol will be oleic acid tagged with a fluorescent dye, approximately 1% uranine (sodium fluorescein) dye.

Inhalability and sampler performance are determined gravimetrically for the solid particles and by UV fluorescence for the liquid particles. Three isokinetic samplers are positioned 30 cm on either side and above the head to measure the aerosol concentration in the tunnel. Inhalability is calculated as the ratio of mass concentration determined by the mouth samplers to that determined by the isokinetic samplers. Sampler performance (aspiration efficiency) is calculated as the ratio of mass concentration determined by the personal samplers to that determined by the isokinetic samplers.

Significant Findings

None to date.

Theory and Evaluation of a Workplace OP-FTIR Monitor

Steven P. Levine, Ph.D.
University of Michigan
School of Public Health
Department of Environmental
and Industrial Health
1420 Washington Heights
Ann Arbor, Michigan 48109-2029

Grant Number: *5 R01 OH02666-05*
Start & End Dates: *09/01/92 – 08/31/95*
Funding Level: *$198,775 ($898,074 Cum)*

Importance to Occupational Safety and Health

FTIR, and OP–FTIR in particular, might be chosen as the air monitoring method of choice for the workplace because:

1. FTIR is capable of quantitating most individual gasses or vapors in air, alone or in complex mixtures, down to 10% of the PEL.
2. FTIR shows promise for the identification of unknown gas or vapor species in air.
3. FTIR is fast, with complete spectral scans being completed in from 1–60 seconds.
4. The FTIR instrument has only one moving part, so it is far less mechanically complex than non–Fourier transform instruments that were used in the past.
5. OP–FTIR, which uses an IR beam across open air, eliminates the need for sampling pumps and devices.
6. OP–FTIR is capable of monitoring labile (easily destroyed, transient) and/or polar species that are frequently lost in monitors that require the use of sampling systems.

The work has or will solve significant problems related to:

1. Hardware and software design and use.
2. Theoretical foundation of beam placement strategy for single and multiple (or moving) beam systems.
3. Strategy and software for identification of components of unknown mixtures.
4. Strategy and software for use in situations when a background spectrum cannot be acquired.
5. Theoretical foundation of use with respiratory level decision logic.
6. Theoretical foundation of use with process upset decision logic.

In addition, each of the above has been or will be pilot scale and field tested, and there has been pilot scale testing of the tomographic concept, hardware and software.

Objectives

1. Perform chamber trials to verify the suitability of the fixed beam geometry of the OP–FTIR in establishing upper limits on personal exposure and to detect departures from standard operating conditions.
2. Conduct field trials to evaluate the applicability to workplace monitoring of the fixed beam.
3. Develop the hardware to allow the use of multiple (or steerable) beams.
4. Develop the theoretical framework and the software to allow optimal placement of multiple beams with the object of relating beam data to traditional personal monitoring data with special reference paid to the time–rate–of–change of the concentration field.
5. Conduct field trials to evaluate the applicability of the theoretical framework for multiple and steerable beam hardware and geometries.
6. Evaluate, in field trials, the strategies and software for, and the accuracy of, iterative least squares fitting methods applied to OP–FTIR for the qualitative analysis of mixtures of gasses and organic vapors in air, and differential method software for situations where valid background spectra are unobtainable.
7. Evaluate strategies for time series analysis of data for alarming out–of–control situations.
8. Evaluate PC–based software for the optimization of parameters and calculation of results for computed tomographic representation of moving beam data.
9. Train professionals in the design, strategy and application of open path air monitoring instruments.

Methodology

Mathematical frameworks were developed for the relationship of beam averaged air contaminant concentrations to a critical volume of contaminated air that moves along with the worker as the worker moves through the workplace. The framework and software were also developed for optimizing the placement of a beam system for monitoring of

exposures of workers in a concentration gradient. An OP–FTIR system with the capability of rapidly moving the beam was developed. A new series of pilot experiments were then performed. Field tests are planned to parallel the pilot tests and evaluate the mathematical framework.

Significant Findings

1. During pilot scale evaluations, an OP–FTIR system, including newly designed hardware and software, operated in a manner suitable for use in the workplace.
2. A pilot scale test room was modeled and built for the OP–FTIR, and found to be suitable for evaluation of the instrument & for development of strategies for optimal beam placement in the workplace.
3. The OP–FTIR system was found to yield both quantitative and qualitative information regarding organic vapor and inorganic gas contaminants in workplace air during field testing at Abbott Pharmaceutical Co.
4. Modeling strategies developed have been found in pilot scale testing to be useful for determination of the relationship of OP–FTIR data to real time decisions of required levels of respiratory protection.
5. Software–based strategies have been developed and found to be useful for the analysis of data obtained from the OP–FTIR system when there is no clean air with which to obtain a background spectrum.
6. Time series analysis was found to be a useful method of determining when a statistically significant departure from normal airborne contaminant concentrations occurred during field testing at Monsanto Co.
7. Tomographic reconstruction of air contaminant profiles was demonstrated for full room–sized chambers.
8. Initial work performed in support of the methanol exposure experiment resulted in reconsideration of the ACGIH BEI, and in several publications (listed below).

Publications

Simonds M, Xiao HK, Levine SP: Open Path Spectroscopic Air Monitoring Methods – A Review. Amer Ind Hyg Assoc 55:953–965, 1994

Levine SP, Russwurm G: FTIR Optical Remote Sensing for Monitoring Airborne Gas and Vapor Contaminants. Trends in Anal Chem 13:258–262, 1994

Malachowski MS, et al.: Workplace and Environmental Air Contaminant Concentrations Measured by Open Path FTIR Spectroscopy: A Statistical Process Control Technique to Detect Changes from Normal Operating Conditions. Air Waste Manage Assoc J 44:673–682, 1994

Yost MG, et al.: Imaging Indoor Tracer–Gas Concentrations With Computed Tomography: Experimental Results With a Remote Sensing FTIR System. Amer Ind Hyg Assoc J, 55:395–402, 1994

Nowak JL, Puskar MA, Levine SP, Xiao HK: Real–Time Measurement of Methyl Nitrite in Air by Nitrogen Oxide Indicating Tubes. Appl Occup Environ Hyg 8:645–649, 1993

Xiao HK, Levine SP: Application Of Computerized Differentiation Technique to Remote Sensing Fourier Transform Infrared Spectrometry for Analysis of Toxic Vapors. Anal Chem 65:2262–2269, 1993

Franzblau A, et al.: Absence of Formic Acid Accumulation in Urine Following Five Days of Occupational Methanol Exposure. Appl Occup Environ Hyg 8:883–888, 1993

Xiao H, Levine SP, Nowak J, Puskar M, Spear RC: Analysis of Organic Vapors in the Workplace by Remote Sensing Fourier Transform Infrared Spectroscopy. Am Ind Hyg Assoc J 54(9):545–556, 1993

Yost MG, Spear RC, Xiao HK, Levine SP: Comparative Testing of A Remote Sensing Optical System with Area Samplers in A Controlled Ventilation Chamber. Amer Ind Hyg Assoc J 53:611–616, 1992

Wythoff B, et al.: Computer–Assisted IR Identification of Vapor–Phase Mixture Components. J Chem Info Comp Sci 31:392–399, 1991

Xiao HK, Levine SP, Herget WF, D'Arcy JB, Spear R, Pritchett T: A Transportable Remote Sensing Infrared Air Monitoring System. Amer Ind Hyg Assoc J 52:449–457, 1991

Franzblau A, et al.: The Use of A Transportable FTIR Spectrometer for the Direct Measurement of Solvents in Breath & Ambient Air: Methanol. Amer Ind Hyg Assoc J 53:221–227, 1991

Levine SP, et al.: FTIR Least Squares Method for the Quantitative Analysis of Multi–Component Mixtures of Airborne Vapors. IN: Measurement of Toxic and Related Air Pollutants, Air Waste Manage. Assoc., Pittsburgh, PA, pp 895–900, 1990

Wythoff B, et al.: Spectral Peak Verification and Recognition Using a Multi–Layered Neural Network. Anal Chem 62:2702–2709, 1990

Xiao HK, et al.: Qualitative Aspects of the Use of Iterative Least Squares Fit Procedures for the Identification of Organic Vapor Mixtures by FTIR Spectrophotometry. Anal Chem 61:2708–2714, 1989

Ying LS, Levine SP: FTIR Least–Squares Methods for the Quantitative Analysis of Multi–Component Mixtures of Airborne Vapors of IH Concern. Anal Chem 61:677–683, 1989

Ying LS, et al: FTIR Spectroscopy for Monitoring Airborne Gases and Vapors of IH Concern. Amer Ind Hyg Assoc J 30:354–359, 1989

Ying LS, Levine SP: Evaluation of... FTIR...for Quantitation of the Components of Airborne Solvent Vapors. Amer Ind Hyg Assoc J 50:360–365, 1989

Studies of Aerosol Sampler Performance Characteristics

James H. Vincent, Ph.D., D.Sc.
University of Minnesota
Division of Environmental
and Occupational Health
Box 807 Mayo
420 Delaware Street, SE
Minneapolis, Minnesota 55455

Grant Number: *1 R01 OH02984-01A1*
Start & End Dates: *09/01/94 – 08/31/97*
Funding Level: *$119,271 ($119,271 Cum)*

Importance to Occupational Safety and Health

New criteria for health–related aerosol sampling for occupational exposure assessment have recently been agreed by prominent international standards–setting bodies. In the United States, the American Conference of Governmental Industrial Hygienists (ACGIH) has adopted these new criteria, and plans to base future TLVs on them. This will require new approaches to industrial hygiene sampling methodology. At present, knowledge about the basic factors governing sampler performance is limited by the lack of good experimental data backed up by sound theory. It is important for future industrial hygiene aerosol exposure assessment to extend our knowledge in this area.

Objectives

The overall aim of the project is to conduct physically based research to elucidate the factors influencing particle transport around and into aerosol samplers, and to express the results in forms which can enable their practical application in designing new sampling devices and interpreting the performances of current ones.

Methodology

The general approach taken is to adopt a balanced and complementary program of experimental and theoretical enquiry. Experiments will be carried out in a small wind tunnel using simple, relatively–idealized sampler models to provide new data against which to test some of the theoretical and numerical models which have been developed and to provide the basis of new theoretical models. The approach to developing new models will include extending existing semi–empirical models and exploring new numerical fluid and particle transport simulations.

Significant Findings

None to date.

Optical Remote Sensing and Computed Tomography in Industrial Hygiene

Lori A. Todd, Ph.D.
University of North Carolina
School of Public Health
Department of Environmental Sciences
and Engineering
CB #7400 Rosenau Hall
Chapel Hill, North Carolina 27599-7400

Grant Number: *5 K01 OH00103-03*
Start & End Dates: *07/01/91 – 06/30/94*
Funding Level: *$0 ($160,355 Cum)*

Importance to Occupational Safety and Health

Current methods for sampling and evaluating air concentrations of gases and vapors involve the use of integrated samplers or direct–reading instruments.

The integrated sampling devices result in a time–weighted average result; fluctuations in concentrations are smoothed out resulting in poor temporal resolution of chemical concentrations. Although direct–reading instruments do not suffer from the temporal resolution problem, both methods are essentially point samplers and give poor spatial resolution of concentrations. Currently, there are no methods which can give both good spatial and good temporal resolutions of chemical concentrations in an area.

This research is investigating an air sampling and evaluation system that does not suffer from these problems. This method combines the techniques of optical remote sensing with computed tomography to determine the concentration distribution of a gas or vapor in a workplace. Chemicals would be detected over large areas remotely, non–invasively, and in real–time; the system would produce a topographical map of the distribution with both good spatial and good temporal resolution.

The optical remote sensing/computed tomography system would have wide application in industrial hygiene work. It could be used for routine monitoring of chemical vapors in a workplace, evaluation of ventilation systems by using tracer gases or monitoring airflow of chemicals, and detection of leaks from an operation.

Objectives

This research proposes to combine the techniques of optical remote sensing with computed tomography to determine the concentration distribution of a gas or vapor in a room. The aims of the research are to develop and test theoretical designs for a remote sensing/computed tomography system in a workplace, and to evaluate them by constructing a prototype system. The result of this research will be the development of an operating system for measuring gas and vapor concentration distributions that is non–invasive and operates in real–time.

Methodology

Specific goals of this research involve: (1) designing and testing feasible optical remote sensing geometries for the placement of light sources and detectors in a room; (2) developing image reconstruction algorithms and computer code to produce the maps of concentration distributions; and (3) validating the remote sensing/computed tomography system in a controlled chamber, using a tracer gas to create test concentrations.

Successful completion of this work will demonstrate the feasibility of the proposed technique. The next step in the research program, following completion of the work proposed here, will be field evaluation of the system.

Significant Findings

A systematic method has been developed to compare the effectiveness of different algorithms and different optical remote sensing configurations for tomographically reconstructing chemical concentrations in air from an optical remote sensing system. The underlying assumption is that the performance of an algorithm, and usefulness of a configuration cannot be accurately assessed without thorough testing using a wide variety of possible concentration maps under ideal and non–ideal sampling conditions. Four different algorithms, and ten configurations have been evaluated using 120 different test concentration maps, and six different sampling conditions.

The algebraic reconstruction algorithms, ART and ART3 were found to be superior to other algorithms tested. In terms of resolution, the equal angle configuration is optimal because it floods the room with contiguous parallel rays; however, it is hardware intensive. An alternative configuration, that provides reasonable reconstructions, but introduces more artifacts, is the scan configuration. For the ten different scan configurations, reconstruction quality was found to be related to the number of detectors, the location of detectors in the room, and the complexity of the test maps. Configurations using the same number of detectors, placed in different locations in the room, resulted in reconstructions that differed in quality. The results of this research underscored the need to thoroughly test configurations through numerical studies prior to field implementation; a wide variety of concentration maps, relevant to the application, should be tested under both ideal and non–ideal sampling conditions.

A prototype scanning system was designed and deployed in an exposure chamber that simulated a four source scan configuration. Multiple concentration maps of sulfur hexafluoride were reconstructed using this system. Tomographic maps were compared with maps created from point samples taken within the chamber and analyzed using an ECD detector.

Publications

Todd LA, Ramachandran: Evaluation of an Infrared Open–Path Spectrometer Using an Exposure Chamber and a Calibration Cell. AIHA Journal, in press, 1994

Todd LA, Ramachandran: Evaluation of Optical Source/Detector Configurations for Tomographic

Reconstruction of Chemicals in Indoor Air. AIHA Journal 55(12), 1994

Todd LA, Ramachandran: Evaluation of Algorithms for Tomographic Reconstruction of Chemicals in Indoor Air. AIHA Journal 55(5), 1994

Todd LA: Optical Remote Sensing/Computed Tomography Systems for Workplace Exposure Assessments. Proceedings Optical Remote Sensing: Applications to Environmental and Industrial Safety Problems, SP–81:356–360, 1992

Todd LA: Optical Remote Sensing/Computed Tomography Beam Geometries for Monitoring Workplace Gases and Vapors. Proceedings Optical Remote Sensing: Applications to Environmental and Industrial Safety Problems, SP–81:390–393, 1992

A Volatile Aerosol Sampler and Particle Size Analyzer

Judy Q. Xiong, Ph.D.
New York University
Medical Center
Department of Environmental Medicine
Long Meadow Road
Tuxedo, New York 10987

Grant Number: *5 R03 OH03039-02*
Start & End Dates: *09/30/92 – 09/29/94*
Funding Level: *$0 ($50,595 Cum)*

Importance to Occupational Safety and Health

The airborne particle and vapor phases of a volatile organic chemical (VOC) often coexist in the real workplace environment. Assessment of worker exposure to VOC requires measuring not only the total airborne concentration but also the phase distribution because the deposition efficiency of the material will depend on the form in which it is inhaled. Thus, the lung dose and doses at other critical sites resulting from equal inhaled concentrations can differ substantially. The American Conference of Governmental Industrial Hygienists (ACGIH) Chemical Substances Threshold Limit Values (TLV) Committee has suggested establishing dual TLVs for the two phases of a volatile substance. The particle aerodynamic size distribution is also a basic information needed for the assessment of inhalation risk to workers. However, due to vapor evaporation from and absorption by particle surfaces in the sampling process, air samplers presently in use are not adequate for efficient separation of the VOC vapor and particles, and there are currently no simple field sampling methods to measure the size distribution of particles that contain VOCs. The proposed Vapor/Particle Sampler (VPS) and the Multiple Vapor/Particle Sampler (MVPS) system will be appropriate for monitoring the airborne concentrations of VOCs in the industrial spray work environment, such as the reinforced plastic industry and the paint spray booth. They are relatively simple and inexpensive field sampling devices and will provide essential data for the assessment of worker exposure to the vapor and particle phases of a VOC and important reference data for establishing dual TLVs for both phases. The same principle may be applied for sampling and size classifying the particles that contain volatile, or semi–volatile components that are traditionally sampled with other sorbent collectors (silica gel, porous polymer, etc.).

Objectives

The first goal of this work is to develop a prototype personal VPS sampler for rapid anisokinetic separation of the vapor phase and coexisting particle phase of an airborne VOC substance into gaseous and particulate fractions according to their differential inertia. The second goal is to develop a prototype MVPS particle size analyzing system, which not only can separate vapor and particles, but also can provide the size classification of the particles that contain VOCs. The aerodynamic cut–off sizes of the MVPS system will be designed to be 1, 2.5, 4, 10 and 20 μm aerodynamic diameters, where, 4 and 10 μm are the ACGIH defined particle cut sizes for respirable and thoracic particulate mass fractions, respectively.

Methodology

The VPS sampler was designed for anisokinetic separation of the vapor molecules and particles into two identifiable fractions due to their differential inertia. The MVPS sampler system was designed to measure the particle size distribution of VOC containing particles by using a series of single–stage VPS samplers of designed cut–off size. Experimental studies were carried out to determine the optimum sampler geometric parameters, flow conditions and sampling time for efficient (>90%) separation of vapor and particles with reasonable sensitivity.

Laboratory–generated vapors and aerosols are used for sampler calibration and performance evaluation. A vibrating orifice aerosol generator (VOAG) was employed to produce monodisperse fluorescein–tagged oleic acid particles in the particle

size range greater than 1 μm. Monodisperse submicron fluorescein particles were obtained from a system that includes a Collison nebulizer, an electrostatic classifier (DMA), and a condensation particle counter (CPC). The mass concentrations of fluorescein–tagged oleic acid particles or fluorescein particles were quantitatively analyzed by fluorometry. The sampling efficiencies were measured at various inlet flow rates and various ratios of the dichotomous flow rates. The vapor collection efficiency was measured with toluene, xylene and styrene in a test chamber equipped with a vapor generating device. The performance of the VPS was tested by comparing: (1) the total airborne particle concentration measurements of VPS with those of glassfiber filters; and (2) the airborne gas concentration measurements of VPS with those of charcoal sorbent tubes and 3M diffusion monitors. The intersampler comparison tests between the MVPS system and the other particle size analyzing devices, such as, the Climet Particle Size Analyzer and the multi–stage Mercer Cascade impactor were carried out to determine the data comparability of the particle size distribution measurements.

Significant Findings

The preliminary design of the VPS sampler and MVPS sampler system has been completed. The VPS Sampler has been developed as a personal sampler for sampling and quantifying the phase distribution of volatile components in particles and coexisting vapors. The sampler is designed to operate at a sample inlet flowrate 1.8 LPM, which can be conveniently and reliably provided by a single lightweight, commercial personal sampling pump. The quantities of the volatile components collected by the sampler can be determined by standard chemical analytical procedures. The optimum sample geometrical parameters, such as nozzle diameter and length, distance of nozzle to filter, have been examined. The experimental tests and calibration of the VPS sampler have been carried out. The particle collection efficiency was measured for particle aerodynamic diameters of 0.2 – 10 μm. The particle cut–off diameter (D_{50}) of the VPS sampler is 0.95 μm at a sampling flowrate of 1.8 LPM, which is determined from the particle collection efficiency as a function of particle aerodynamic diameter. It is adequate for use in general industrial spray operations, where the particles are frequently large. Intersampler comparison results showed a good agreement between the mass concentration data of monodisperse particles measured by the VPS sampler and the 37 mm Glassfiber filters (GF) with a correlation of $(C_{VPS}/C_{GF}) = 0.96 \pm 0.06$ (95% confidence interval, n=13). Agreement between the VOC vapor concentration measurements (toluene, xylene, and styrene) of VPS with those of SKC charcoal sorbent tubes and 3M diffusion monitors is within 6%. An average wall loss of the VPS sampler is 2.2%. It was also found that with some simple modifications, the VPS sample could be used as a personal mine diesel exhaust sampler for measuring phase partitioned volatile or semi–volatile organic compounds in diesel–equipped mines. Many of these components of diesel exhaust have the potential to produce adverse health effects.

The MVPS system, a volatile particle size analyzer, has been designed and fabricated. The experimental tests and calibration of the MVPS system are in progress.

Personal Monitor For Toxic Vapors

N. L. Jarvis, Ph.D.
Microsensor Systems, Inc.
62 Corporate Court
Bowling Green, Kentucky 42103

Grant Number: *1 R43 OH03103-01*
Start & End Dates: *09/15/93 – 03/14/94*
Funding Level: *$0 ($49,616 Cum)*

Importance to Occupational Safety and Health

There is a need in the industrial workplace for very small, sensitive, rugged, and easy–to–use personal monitors for hazardous organic vapors. Many existing methods, e.g. electrochemical detectors, are not well suited for most toxic organic compounds while other methods such as dosimeter badges do not offer real–time response. The Surface Acoustic Wave (SAW) microsensor devices being developed at Microsensor Systems are well suited for the real–time monitoring of higher molecular weight, low volatility, toxic organics that are difficult to detect by other techniques.

Objectives

The objective of this program is to develop a miniature SAW vapor detection system with the size, sensitivity, reliability and power requirement appropriate for a pocket size Personal Exposure Meter (PEM) or Personal Monitor for Toxic Vapors. The aim of the Phase I effort was to develop a laboratory or "breadboard" unit that demonstrates sensitivity to glutaraldehyde, a hazardous chemical used as a disinfectant for a number of medical applications, such as endoscope sterilization. It is also widely used as a biocide for aqueous based

lubricants and cutting fluids and is very difficult to monitor by present detection technologies. In Phase II the detection capability of the Personal Monitor for Toxic Vapors will be extended to other hazardous vapors that are also difficult to detect by other means, such as the isocyanates. Also in Phase II small, pocket size demonstration models of the Personal Monitor for Toxic Vapors will be designed, built and evaluated.

Methodology

The work conducted in the Phase I study was intended to show the feasibility of using SAW microsensors as the detectors for a new class of small, sensitive, real–time Personal Monitors for Toxic Vapors. SAW chemical microsensors are surface mass sensitive micro–chip devices that can be made sensitive to organic vapors by the application of suitably specific sorbent coatings. The primary task of the Phase I effort was to identify and characterize a glutaraldehyde sensitive coating for a SAW sensors that has the sensitivity, and other chemical and physical characteristics, required for personal monitoring. Important sub–tasks in this program were the development of a calibrated system to generate glutaraldehyde vapor, fabrication of an electronic sensor test system, application of several candidate coatings to the SAW device surfaces, and evaluation of the coated sensor responses when challenged by know concentrations of glutaraldehyde vapor.

Significant Findings

A glutaraldehyde generator was developed that could accurately deliver glutaraldehyde vapor over a wide range of concentrations. An automatic syringe pump was used to deliver precise quantities of a 25% solution of glutaraldehyde in water into a constant flow of "zero air" at 1000 sccm. A needle valve and electronic mass flowmeter were used to regulate the air flow. A steel Swagelok™ mixing TEE and a 75cc stainless steel cylinder mixing "reservoir" were thermally insulated and heated to 200°C. Glutaraldehyde concentrations from less than the current TLV level (0.2 ppm) to well over 100 mg/m3 could be accurately and reproducibly delivered to the SAW "breadboard" test system.

Five materials were selected for evaluation as glutaraldehyde sensitive SAW coatings: dinitrophenylhydrazine (DNPH), poly(epichlorohydrin) (PECH), Carbowax 20M (C20M), poly(isobutylene) (PIB), and fluoropolyol (FPOL). Dilute solutions of each were prepared in a volatile solvent and applied to the SAW device surfaces using an air brush technique. The coatings were applied as very thin films, equivalent to a total frequency shift of approximately 200 KHz. The SAW devices used were two port resonators with a nominal resonant frequency of 250 MHz.

A "breadboard" instrument was developed for testing the response of the coated SAW devices to the glutaraldehyde vapor. Each of the coated SAW resonators was installed on a small printed circuit board that contained RF amplifiers to excite the resonator, as well as a reference SAW oscillator and a mixer circuit. Each of the four SAW sensor cards was installed in a gold plated manifold that was connected to the glutaraldehyde generator. Four separate frequency counters were used. Vapor response signals were sent to a computer data acquisition systems via a 9600 baud RS232C serial line.

The coating evaluation study found that several of the polymer coated SAW resonators could detect glutaraldehyde vapor at very low concentrations. The best coating was the fluoropolyol (FPOL) which exhibited a sensitivity of almost 80 Hz/mglm3. The sensor response time was on the order of 30 seconds. The detection limit was estimated to be approximately 0.5 mg/m3 (i.e., 0.125 ppmv) for a 2:1 signal–to–noise ratio. This is below the NIOSH recognized TLV for glutaraldehyde which is 0.82 mg/m3 (i.e., 0.2 ppmv). Few commonly occurring chemicals would be likely to offer any significant interference to this measurement. The dinitrophenylhydrazine (DNPH) coated SAW sensor was found to be even more sensitive, but the response was not reproducible. With further study the DNPH could offer enhanced performance.

In conclusion, this Phase I study has demonstrated the feasibility of building a SAW based Personal Exposure Meter (PEM) for glutaraldehyde. A PEM using a SAW microsensor would be a very compact instrument with a simple, valveless vapor sampling system. Existing RF circuitry and signal processing electronics are very compact and consume very small amounts of power (e.g., < 0.25 Watts) suggesting that a pocket size instrument should be readily achievable with modest effort. Such an instrument could serve as a generic platform for a family of PEMs that differ only in the vapor to be monitored, the coating applied to the SAW device, and the signal processing software installed into an onboard microcomputer.

Development of Personal Electrostatic Sampler

Frank A. Leith
Aerosol Associates
120 Muir Lane
Chapel Hill, North Carolina 27514

Grant Number: *1 R43 OH03223-01*
Start & End Dates: *09/30/94 – 03/31/95*
Funding Level: *$74,523 ($74,523 Cum)*

Importance to Occupational Safety and Health

Oil mists from machining operations have long been associated with occupational disease in exposed workers. Concern has increased with recent evidence that exposure to these mists is associated with throat, pancreas, rectum, and prostate cancers as well as breathing problems and respiratory illnesses. As a result, the ACGIH has published a notice of intent to change the TLV for mists of "mildly refined oils" from 5 to 0.2 mg/m^3. Thus, accurate methods to monitor the personal exposure of workers to these mists is important.

Unfortunately, mineral oils used in machining operations contain semi–volatile compounds that, during sampling itself, can evaporate from the filter used to monitor mist concentration using the NIOSH standard method. To the extent that evaporation occurs, such measurements will underestimate workers' true exposures. Similar problems with evaluating the concentration of semi–volatile mists are present wherever semi–volatile compounds must be sampled.

Objectives

The objective of this project is to develop a personal monitor for oil mists that is less susceptible to evaporation of semi–volatile compounds. Recent advances in electronics make possible a personal electrostatic monitor that collects oil mists in a way that minimizes the potential for evaporation, and so allows assessment of workers' true exposures. In the work conducted here, such a monitor is being developed and evaluated through laboratory and field trials.

Methodology

Factors that affect the efficiency of electrostatic precipitators have been studied for many years and are the subject of classic reference books. The most relevant design equations are also presented in aerosol physics references. Although these equations are intended primarily for the design of large–scale industrial precipitators that handle large gas flows, the same principles can be used to design a small–scale precipitator used for personal sampling. Preliminary calculations based on this theory suggest that a personal electrostatic sampler that is 5 cm long and 1.5 cm in diameter, about the size of a human thumb, can have high efficiency on sub–micrometer droplets such as those found in oil mists.

We are determining whether the efficiency of prototypes designed according to these principles is adequate by comparing the mass of oleic acid mist collected by the precipitator with the mass of oleic acid mist collected by a filter when both samplers are operated at the same flow and sampling conditions. Oleic acid is a non–volatile, non–toxic oil that is the prime constituent of edible corn oil. Because oleic acid is non–volatile, it will not evaporate from the filter surface so that results from filter measurements can be used to establish whether the precipitator collects essentially all particles sampled. For each prototype, we will establish whether power consumption is minimized by establishing the voltage for which efficiency for the electrostatic monitor equals that for the filter. In the second part of the experimental work, we will determine the extent, if any, to which collected oil evaporates from the collection surface of the prototype precipitator. In this work we will collect samples of semi–volatile oil using a filter and using an electrostatic precipitator, then pass clean air through each for several hours. Weighing both the filter and the precipitator substrate before and after air stripping will establish whether evaporation of collected sample is a problem in the precipitator.

When a satisfactory prototype precipitator has been designed and tested, we will conduct a field study with the help of industrial hygienists at Ford Motor Company. In this work we will take field samples using both the prototype precipitators and conventional, NIOSH filters, to determine whether and to what extent the sampling method affects the value of mass concentration determined.

Significant Findings

None to date.

Micromachined System For Selective Measurement of VOCs

Stuart W. Wenzel
Berkeley MicroInstruments
1301 South 46th Street, Bldg. 164
Richmond, California 94804

Grant Number: *1 R43 OH03102-01*
Start & End Dates: *09/15/93 – 03/14/94*
Funding Level: *$0 ($49,975 Cum)*

Importance to Occupational Safety and Health

A major problem in the field of occupational health is the lack of adequate data for assessing worker exposure to toxic chemicals. Exposure assessment is critical for correlating chemical exposure with occupational disease, establishing safe exposure limits, and identifying work practices that expose workers to harmful chemicals. Detailed exposure data is needed to reduce the incidence of occupational disease and injury and to lower the associated healthcare expenditures. However, existing chemical–sensing technologies, particularly in the area of portable air–quality instrumentation, are inadequate for collecting exposure data.

Sensors for personal chemical–exposure monitors must be reliable, have sufficient sensitivity to detect a fraction of the OSHA–dictated permissible exposure limit, and have high selectivity to the target chemical in the presence of interferants. They should also be small, inexpensive, fast–responding, and energy–efficient so that they can operate on batteries for extended periods. Existing sensor technologies do not meet these requirements, either because they are too expensive and complicated to use, or too limited in their capabilities. The sensing technology we propose is designed to overcome these limitations, so that it can be widely employed in occupational health and safety and in other applications.

Objectives

The long–term goal of this research is to make a chemical–measurement system for real–time detection of volatile organic compounds (VOCs) using a silicon–micromachined system of components, such as ultrasonic flexural–plate–wave sensors. This system will be designed for use in personal chemical–exposure monitors. It will be small, inexpensive, robust, battery–operated, sensitive enough to detect VOCs at a fraction of the OSHA permissible exposure level, and selective enough to identify toxic chemicals in a realistic environment.

The objectives in Phase I were to establish feasibility of the proposed approach by (1) showing that the individual micromachined components could be fabricated; (2) evaluating the performance of the micromachined components individually; and (3) evaluating the performance of a simplified chemical–measurement system built with the components.

Methodology

Work in this phase focused on three interrelated tasks: (1) designing and fabricating prototype chemical–identification chips incorporating micromachined chemical–sensing components; (2) optimizing computer–based algorithms for controlling and coordinating the function of these components and analyzing output data; (3) testing the ability of the micromachined system to sense specific volatile organic compounds in the presence of interferants, including water vapor. The first–generation chip included an ultrasonic flexural–plate–wave sensor and a preconcentrator with its associated heater.

Significant Findings

A first–generation chemical–identification chip, associated drive circuitry and a data acquisition and control system were built and tested. Initial electrical and chemical testing showed that the individual chip components function as designed. Chemical–vapor tests with the prototype system showed excellent performance in terms of sensitivity and selectivity: Benzene and toluene at 250 ppb and 200 ppb concentrations, respectively were detected (a fraction of their permissible exposure levels). Benzene and toluene could be distinguished in the presence of interfering water vapor, which had almost no effect on the system. This system used an average power of only 11 mW, and permitted "auto–zeroing," which virtually eliminated measurement uncertainty due to baseline drift. Analysis of the chemical testing results point clearly to design changes that can be made to improve performance. Based on this, small, inexpensive, high–performance chemical–sensing systems should be able to be made with this technology.

Detecting Lung Overload by Magnetometry

Juraj J. Ferin, M.D.
University of Rochester
School of Medicine and Dentistry
Department of Environmental Medicine
Box EHSC
575 Elmwood Avenue
Rochester, New York 14642

Grant Number: *5 R01 OH02772-04*
Start & End Dates: *09/01/90 – 08/31/95*
Funding Level: *$0 ($832,522 Cum)*

Importance to Occupational Safety and Health

The concept of lung overload is based on observations made in chronic inhalation exposures of rats to high concentrations of coal dust, iron oxide, titanium dioxide, diesel engine exhaust and polymer particles. The accepted indicator of lung overload is a significant decrease in the alveolar clearance rate of particles. Besides decreased alveolar clearance, lung overload is associated with inflammatory responses in the alveoli (influx of neutrophilic leukocytes, protein leakage), macrophage accumulation, fibrotic changes and even tumors. Extrapolation of data from rats suggests that decreased particle clearance may occur in humans at a mass burden of 1–3 mg/g lung when inhaling particles of density 1 g/cm^3 and clearance could cease at 30 mg/g lung. Under reasonable assumptions for the deposition rate and clearance half–times in humans, the accumulated dust burden would exceed 3 mg/g lung after 1 1/2 years of exposure to "nuisance" dusts at the concentration of 5 mg/m^3, which is the present OSHA standard of exposure limit for respirable dusts. If pulmonary mass load in the range of 1–3 mg/g lung causes a decrement in clearance in humans, as it does in rats, then lung overload related effects might occur in humans inhaling concentrations of dust allowed by governmental regulations.

Magnetometry is the non–invasive measurement of the amount of ferro– and ferri–magnetic materials in a sample. If this technique could be adapted for use in humans to assess particle retention and clearance, it would mean a great advancement to clarify questions regarding overload in humans.

Objectives

The long–term objectives of the proposed line of research are to characterize and clarify lung overload in rodents and to develop magnetometry to a level which makes assessment of overload in humans realistic. The overall aims of this project are to: (1) develop needed aerosol generation and magnetometry systems; (2) demonstrate that dust clearance rates can be measured reliably using magnetic aerosols, and (3) test hypotheses which suggest that magnetometry may have unique capabilities to detect and characterize lung overload.

Methodology

The thorax of animals was placed in a strong DC magnetic field for a short time to align the magnetic moments of individual particles by both rotating particles and rotating magnetic domains within particles. After the magnetizing field was removed, the remanent field was measured by an array of 8 fluxgate magnetometers arranged such that the magnetic moment and subsequent relaxation of as little as 0.1 mg of magnetite in the lungs of rats could be recorded. In addition to the 8 magnetometers, the system consists of shielding, analog signal processing hardware and a computerized digital signal processing system. Rats were exposed nose–only to magnetite or to a mixture of magnetite and TiO_2 particles. When sacrificed the pulmonary tissue was analyzed chemically for iron and titanium in addition to a number of biological parameters (determined from lavage, e.g., cells, proteins).

Significant Findings

As reported previously, magnetometric results clearly show the increase in lung burden during exposure and also clearance of magnetite particles when the exposure was discontinued. However, post–exposure clearance of particles based on magnetometry measurements seemed to be unexpectedly fast (up to T 1/2 = ~20 days) compared to clearance based on chemical analysis of magnetite (T 1/2 = ~150 days). We tested the lung contents using x–ray crystallography and concluded that neither solubility nor changes of magnetite into a different form (e.g. hematite) can explain the discrepancy. Results of other experiments indicate that rearrangement of particle agglomeration affects magnetometric measurements. For example, if the same mass of magnetite particles was dispersed in various volumes of plastic the magnetometric reading was different. Magnetite particles dispersed in fluids (water, saline, saline plus surfactant) behaved differently with a maximum dispersion in the surfactant containing medium. In another experiments, rats were irradiated (thorax only) before particle exposure. The compromised AM may change the pulmonary tissue response at the time of exposure to magnetite which may show in the

magnetometric measurements. It is conceivable that during particle translocation within the lung such rearrangement may occur. A clarification of the discrepancy between the magnetometric and chemical clearance determination may be decisive for the practicality of using magnetometry in human studies.

Publications

Ferin J, Oberdörster G, Soderholm SC: Magnetometric Analysis of Pulmonary Retention of Particles. Ninth Congress of the International Society for Aerosols in Medicine. J Aerosol Medicine 6:50, 1993

Ferin J, Soderholm S, Oberdörster G: Quantitative Analysis of Particle Translocation Within the Lung. Am Rev Respir Dis 145(4):A801, 1992 (International Conference Supplement)

Pulmonary Effects of Machining Fluid Aerosols

Terry Gordon, Ph.D.
New York University
Medical Center
Department of Environmental Medicine
Lanza Lab
Long Meadow Road
New York, New York 10987

Grant Number: *5 R01 OH03044-02*
Start & End Dates: *09/01/93 – 08/31/95*
Funding Level: *$109,466 ($207,419 Cum)*

Importance to Occupational Safety and Health

This research proposal examines the acute and subchronic pulmonary effects of machining fluid aerosols – an occupational hazard for nearly one million workers in this country. Machining fluids/cutting oils are hypoosmolar, alkaline fluids which are frequently contaminated with a variety of microbial agents.

Objectives

The major goals of the proposed studies are to (1) determine the roles of contaminating endotoxin, hypotonicity, and alkalinity in the adverse pulmonary effects associated with occupational exposure to machining fluid aerosols; and (2) compare the potential of different classes of machining fluids to produce inflammatory and functional changes in the lung. The proposed studies will determine in an animal model whether sub clinical inflammatory changes may persist in the lung after repeated exposure to machining fluid aerosols at exposure concentrations near the current TLV. The proposed experiments will help to provide a clearer understanding of the role of microbial contamination in the pulmonary effects of inhaled machining fluid aerosols.

Methodology

Adverse pulmonary effects after single and repeated exposures to machining fluid aerosols were examined using functional, biochemical, and morphological techniques in sensitive animal models. Animals were exposed to aerosols of water (the control atmosphere), used machining fluids, or unused machining fluids. During the single exposures, non–invasive measurements of airway resistance were performed at hourly intervals.

Significant Findings

Previous work in this laboratory has demonstrated that exposure to aerosols of a used soluble machining fluid produced more airway injury and inflammation than did the unused machining fluid aerosol. In extending these studies, current work has provided more evidence of a role for endotoxin in the acute injury produced by machining fluid aerosols. Guinea pigs were exposed for 3 hours to 5 or 50 mg/m^3 of soluble, semi–synthetic, and synthetic machining fluid aerosols. For each of these fluids, used material obtained from storage facilities in the work place had a significantly greater toxicity than the unused material. Moreover, microbial contamination appeared to play a major role in the greater toxicity of the used machining fluids. Samples of machining fluids from manufacturing sites with high titers of gram negative bacteria produced significantly greater pulmonary injury than samples from sites with low titers. Thus, the ability of the machining fluids to produce injury is more directly related to microbial contamination than to the presence of other agents, such as heavy metals, that contaminate machining fluids during milling and cutting operations. Greater attention to minimization of microbial contamination during storage and usage may reduce the adverse respiratory effects associated with exposure to machining fluid aerosols.

Chronic exposure to microbial–contaminated machining fluids is associated with a variety of adverse pulmonary effects including chronic bronchitis and increased sputum production. Because previous work has demonstrated that small amounts of inhaled endotoxin can increase the amount of

stored mucus in the respiratory tract of the rat, we examined the effect of endotoxin–contaminated machining fluid aerosols on mucus production. Exposure to 10 mg/m^3 endotoxin contaminated machining fluid (obtained from the work place) for 3 hours/day for 3 days produced significant increases in stored mucus in both the nasal septum and the intrapulmonary airways. A significant increase in mucus was observed in the nasal septum but not in the intrapulmonary airways of animals exposed to 10 mg/m^3 unused machining fluids (no measurable endotoxin). These results suggest that in addition to endotoxin, non–endotoxin components of machining fluids may contribute to the increase in sputum and chronic bronchitis reported for workers exposed to machining fluid aerosols.

Publications

Gordon T: Air pollution. In: Encyclopedia of Toxicology, (ed. P Wexler), Appleton and Lange, in press, 1995

Gordon T: Respiratory Systems. In: Organspecific Metal Toxicology, (eds. RA Goyer, MP Waalkes, CD Klaassen), Academic Press, in press, 1995

Gordon T, Harkema JR: Effect of Endotoxin on Intraepithelial Mucosubstances in F344 Rat Nasal and Tracheobronchial Airways. Am J Respir Cell Mol Biol 10:177–183, 1994

Gordon T: Respiratory Systems. In: Organspecific Metal Toxicology, (eds. RA Goyer, MP Waalkes, CD Klaassen), Academic Press, in press, 1994

Gordon T, Fine JM: Metal Fume Fever. In: Shusterman DJ, Peterson JE, eds. De Novo Toxicants. Occupational Medicine: State of the Art Reviews, Vol 8(3). Hanley and Belfus, Inc., Philadelphia, PA, 1993

Influence of Particles on Occupational Lung Disease

David Warshawsky, Ph.D.
University of Cincinnati
Department of Environmental Health
P.O. Box 670056
Cincinnati, Ohio 45267-0056

Grant Number: *5 R01 OH02277-03*
Start & End Dates: *09/30/89 – 03/31/94*
Funding Level: *$0 ($479,651 Cum)*

Importance to Occupational Safety and Health

Epidemiological and experimental studies indicate that particles and/or chemical carcinogens are important in the development of respiratory disease. Occupational exposure to silica often includes exposure to polycyclic aromatic hydrocarbons (PAH); silica has an enhancing effect on benzo(a)pyrene induced lung carcinogenesis. This study is designed to investigate the ability of pulmonary alveolar macrophage (AM) to metabolize BaP–coated silica. In the evaluation of occupational hazards that may lead to increased susceptibility to lung cancer, the cocarcinogenic potential of other factors in an exposure is an important consideration. This research will provide information on particulate modified BaP metabolism and will contribute to our understanding of the involvement of pulmonary alveolar macrophage in the mechanism of lung disease.

Objectives

The long–term objective of this research is to investigate the role that AM play in the particulate–dependent response of the lung to BaP via mechanisms involving BaP metabolism. Although the mechanism of cocarcinogenic action is unknown, several investigators have implicated BaP metabolism. An important biological response to inhaled particles is ingestion by AM and clearance from the lung. Since these cells have the capacity to metabolize BaP, it is possible that altered BaP metabolism leading to enhanced carcinogenic potential occurs in the AM following phagocytosis of silica particles and adsorbed BaP.

Methodology

Alveolar macrophages (AM) were isolated by tracheal lavage from male Syrian hamsters (100–150 g, 8–9 wks old) and resuspended in

RPMI–1640 medium containing 0.1% gentamicin, 25 mM L–glutamine, 0.2% sodium bicarbonate and 2 mg/ml bovine serum albumin (pH=7.2) (BSA). Viability and the numbers of cells were determined by trypan blue staining procedure. The purity of AM was determined using cellular differential staining (Diff–Quik stain set Sci. Product Inc.). About $1x10^6$ cells in 2.5 ml RPMI–1640 were plated dish. The unattached cells were removed and the AM were incubated with various chemical treatments. Viability analyses were carried out at 24 and 48 hr time points. The remainder of the medium was extracted with ethyl acetate. The ethyl acetate extract was analyzed by HPLC to quantify metabolites and parent compound. Additional studies were conducted to compare the extent of binding to DNA to the release of metabolites from the cell.

Significant Findings

Determination of the Physical Characteristics of Particles. All of the particles were of respirable size with a particle size distribution of greater than 98% less than 5 microns. The count median diameters for aluminum oxide and amorphous silicas were less than 0.36 microns while for crystalline silica the count median diameter was 0.83 microns and for ferric oxide it was 1.8 microns. The surface areas of the particles were consistent with the median diameters and the size distributions in that the values for the aluminum oxide and the amorphous silicas were large varying from 124.8 to 253.1 m^2/g. For crystalline silica and ferric oxide that had larger count median diameters, the surface areas were 4.3 and 10.8 m^2/g, respectively. Neither precipitated nor gelled silica contained any crystalline silica while fumed contained 1.6% crystalline silica. The results indicated that crystalline silica had a smaller surface area and a larger count median diameter than any of the amorphous silicas.

Determination of AM to Phagocytize Particles and the Cytotoxicity of Particles to AM. Comparative viability studies of the AM in the presence of ferric oxide, aluminum oxide, or silica (crystalline, and gelled, fumed, and precipitated) were undertaken to determine noncytotoxic doses during phagocytosis. Doses of particles ranged from 0.0 to 0.5 mg. The viability of the hamster AM in the presence of aluminum oxide and ferric oxide up to the highest dose was similar to controls. After 24 and 48 hours, the viability of the AM for aluminum oxide and ferric oxide was approximately 80 and 70%, respectively. In the presence of silica, the viability of the hamster AM was similar to controls up to 0.01 mg and at least 80 and 66% at 24 and 48 hours respectively with the exception of precipitated silica at 48 hours where the viability was 57%. At doses of 0.05 mg and 0.1 mg of crystalline, precipitated or fumed silica, at 24 hours the viability dropped to 70 and 45%, respectively, and at 0.5 mg the viability dropped to zero. With gelled silica the viability of the AM decreased to 27% at 0.05 mg and zero at 0.1 mg at 24 hours. These data are consistent with the physical characteristics in that the particle with the largest surface area is the most cytotoxic i.e. gelled silica followed by the other forms of silica. The data indicate that the count median diameter of less than .38 microns is sufficient for AM silica cytotoxicity. It would appear that the dose, surface properties and particle size are all important in the cytotoxicity of AM to silica.

Determination of Metabolic profiles from BaP–coated Particles. The data indicate that the major pathway is through the dihydrodiol formation. The 7,8–diol metabolite which is the precursor of the ultimate metabolite 7,8–diol–9,10–epoxide is higher in all of the particle associated BaP relative to BaP alone. This would suggest that BaP–coated particle is metabolized more readily through the active pathway than by BaP itself which would suggest a change in the metabolic pattern due to particle. Of the particles studied the values for the 7,8–diol were higher for the amorphous silicas than that of Fe_2O_3 or crystalline silica.

The level of DNA–binding from BaP–coated particles. The BaP–coated particles were incubated with AM and after 24 hours the AM were isolated. The DNA was isolated using a phenol extraction method and analyzed by ^{32}P–postlabeling techniques. The data indicate that both qualitatively and quantitatively that the BaP–adduct patterns have been altered by the presence of particles. In all cases, ppt, crystalline or Fe_2O_3 adduct #2 is the predominant adduct as opposed to the presence of all three adducts for BaP alone. These data are consistent with the metabolism data previously reported in that particles appear to alter both the metabolic pattern in the media and adduct pattern in AM. What is evident is that particle with the larger surface areas appears to have an increased alteration of the formation of BaP produced active metabolite intermediates.

In summary, BaP–coated particles in comparison with BaP alone have an impact on the metabolism, DNA binding and the extent of adduction. Additionally, dose as well as surface area and surface characteristics of particles are important determinants in the metabolism, DNA binding and cytotoxicity parameters of particles and BaP–coated particles.

Publications

Warshawsky D, Reilman R, Cheu J, Radike M, Rice C: Influence of Particle Dose on the Cytotoxicity of Hamster and Rat Pulmonary Alveolar Macrophage *In Vitro*. J Toxicol Environ Health 42:407–421, 1994

Griefe A, Warshawsky D: Influence of Dose Levels of the Cocarcinogen Ferric Oxide on the Metabolism of Benzo(a)pyrene by Hamster Pulmonary Alveolar Macrophage. J Toxicol Environ Health 38:399–417, 1993

Cumulative Trauma Disorder: Skeletal Muscle Dysfunction

William T. Stauber, Ph.D.
West Virginia University
School of Medicine
Department of Physiology
P.O. Box 9229
Morgantown, West Virginia 26506-9229

Grant Number: *5 R01 OH02918-03*
Start & End Dates: *01/01/92 – 12/31/94*
Funding Level: *$136,338 ($403,395 Cum)*

Importance to Occupational Safety and Health

Chronic pain originating from the musculoskeletal system is a dominant cause of sick–leave in modern industry and can be very disabling and troublesome for the individual. The cause of this problem as it originates in skeletal muscle is unknown. However, one of the most common situations in which muscle pain is experienced is the cumulative trauma disorder (CTD) which results from repeated movements. One aspect of repeated movements is the necessity for muscles to decelerate the body or moving body part by eccentric muscle actions. During eccentric muscle actions, muscles act as shock absorbers and absorb strain energy. It is during these shock absorption activities that strain injuries occur. We have developed a laboratory model for repeated strain injury in order to study the tissue response and adaptation of muscles subjected to repeated strains. From our initial studies, it was apparent that the overall size of the muscles becomes larger but the individual components are smaller – perhaps in an attempt to distribute the strain over a greater number of functional units. However, this response seems to be dependent on the rate of strain. In addition, the non–muscle tissue of some of these strained muscles proliferates as one might see in scar tissue or dystrophy. This additional non–muscle tissue may: (1) alter the action of muscles as motors decreasing their force or ability to shorten at maximal speeds; (2) decrease their compliance causing connecting structures (e.g., fascia, ligaments, tendons) to be injured. Therefore, the development and characterization of a rodent model of repeated strain injury is necessary for the understanding of the physiology or pathophysiology of cumulative trauma disorder in order to develop preventative strategies.

Objectives

The proposed experiments are designed to develop a reproducible technique for producing chronic overload injury to rat skeletal muscles as a model for cumulative trauma disorder (CTD) and to understand the functional outcome of repeated microtrauma in order to develop strategies and programs for its prevention. The objectives of the study are: (1) to design and build a rodent dynamometer which will control the velocity and range of movement of the rat foot during a strain overload and to test the functional outcome in terms of muscle strength, endurance, and stiffness *in vivo*; (2) to document changes in the extracellular matrix (ECM) and sarcolemma of skeletal muscles which could lead to microfibrosis, restricted movement or impaired nutrient flow through the interstitial space using morphological and immunochemical analysis; (3) to characterize the cellular responses of muscle and non–muscle cells following repeated injury in order to understand if the adaptation seen following repeated microtrauma is functional (regeneration and repair) or dysfunctional (fibrosis with myofiber atrophy); (4) to determine the parameters most critical to injury production such as velocity of strain, nature of loading (duration), magnitude of force, frequency of injury and rest periods; (5) to develop immunohistochemical markers for myofiber injury and repair.

Methodology

Cumulative microtrauma was administered three times a week for four weeks to one leg of female rats at two different speeds. Muscle weights, myofiber counts and sizes were analyzed from control soleus muscles and injured (CTD) soleus muscles using image analysis and a technique using 35 mm slides or Photo CD as the source of the images. Accurate and reproducible fiber size distributions can now be made without missing very small fibers.

Immunohistochemical markers have been developed to test for injury and repair. Myofiber integrity is monitored by using dystrophin for plasma membrane, fibrinogen or albumin for extracellular protein entry, and desmin for cytoskeleton organization. Immunohistochemical localization of both dystrophin and desmin in the small cells indicate regeneration. Vimentin uniquely defines the proliferation and migration of fibroblasts.

The extracellular matrix outside that considered the basal lamina appears to proliferate following some

types of repeated injury (CTD) – similar to that seen in dystrophic muscles. Increased amounts of proteoglycans, collagen I and fibronectin were localized with immunohistochemical techniques in injured muscles. Quantitative ELISAs have been developed to measure the content of collagen I, fibronectin and laminin in muscles homogenates and muscle slices. A few samples have been studied with scanning electron microscopy (SEM) to document the presence of fibrosis. Since only collagen remains following the SEM preparation, marked collagen proliferation, indicating fibrosis, can be seen.

In order to understand the physiological significance of the cellular and matrix changes, a dynamometer was needed for the measurement of rat hind–limb muscles *in vivo*. Dynamic movements were measured by the dynamometer which moves the rat foot through a predetermined range of motion while measuring the force, exerted on the dorsum of the foot, opposing the movement. An isovelocity strength test at 30 deg/sec is performed using concentric muscle actions. Subsequently, a series of sinusoidal movements are performed at different velocities of limb movement (e.g. 150–500 deg/sec) to determine if velocity is important in producing damage. The isovelocity test is repeated to document damage (e.g. a force decrement which does not recover after a rest sufficient to restore isometric force).

Significant Findings

Muscle and non–contractile tissue proliferated following repeated strain injury but the response was dependent on the strain rate. If the strains were performed at fast speeds, the size of the myofibers was smaller and there was an increase in fiber number and extracellular matrix content – a dystrophic response. If the strains were repeated at slower speeds, the muscles were unaffected. This unique observation may provide insight into mechanisms of muscle dysfunction with repeated fast movements. Part of the increase in muscle size in fast–stretched muscles could be accounted for by a 40% increase in extracellular matrix (non–contractile tissue) as assessed by morphometric methods. Increased amounts of proteoglycans, collagens I and II and fibronectin were common features of the injured muscles. Of the matrix proteins, collagen I had increased by 25%. The assays for fibronectin have not been completed but it appears that fibronectin increased even more. Scanning electron microscopy verified that muscles from fast stretched animals were fibrotic with marked thickening between fibers. The dynamic parameters responsible for the dramatic muscle changes can now be tested on our dynamometer. For example, muscles which have been deconditioned were much more easily damaged (e.g. twice the force deficit) at velocities (150 deg/sec) which would produce minimal damage to control animals. Higher speed sinusoidal movements (500 deg/sec) such as experienced while using vibrating tools produce greater damage to rat muscles *in vivo*. Sinusoidal loading has not been investigated in animals with respect to the development of muscle damage and CTD and is ongoing.

Publications

Miller GR, Stauber WT: Use of Computer–Assisted Analysis For Myofiber Size Measurements of Rat Soleus Muscles From Photographed Images. J Histochem Cytochem 42:377–382, 1994

Stauber WT, Miller GR, Grimmett JG, Knack KK: Adaptation of Rat Soleus Muscles to Chronic Intermittent Strain. J App Physiol 77:58–62, 1994

Stauber WT: Delayed Onset Muscle Soreness. In: Athletic Injuries and Rehabilitation, (eds. J Zachazewski, D Magee, W Quillen), Saunders, Philadelphia, in press, 1994

Occupational Risks of Pesticide Exposure for Females

William J. Swartz, Ph.D.
Louisiana State University
School of Medicine
Department of Anatomy
1901 Perdido Street
New Orleans, Louisiana 70112-1393

Grant Number: *5 R01 OH00835-14*
Start & End Dates: *09/29/79 – 08/31/95*
Funding Level: *$0 ($1,347,067 Cum)*

Importance to Occupational Safety and Health

With the increasing advance of women in the workplace, the female reproductive system will be placed at elevated risks where exposure to a noxious chemical agent can potentially occur. There is a need to assess toxicity of hazardous chemicals on both pregnant and non–pregnant females.

Objectives

This study is designed to critically evaluate the toxic effects of the estrogenic pesticide methoxychlor

on specific components of the female reproductive system. An analysis will be made of the effects of methoxychlor on reproductive activity of the exposed adult female. In addition, the future reproductive activity of females exposed to methoxychlor neonatally will be evaluated. This study will examine functional outcomes such as effects on fertility and pregnancy and correlate these with the observed anatomic and metabolic alterations within the reproductive system as measured through the use of biological markers. It is anticipated that critical use of these biomarkers will allow the development of a means of identifying women to be at reproductive risk following exposure to a toxic agent.

Methodology

Female mice of the CD–1 strain were used in this study. Mice were randomly distributed into a vehicle control group, an estradiol–17β group and groups treated with different concentrations of methoxychlor. The methoxychlor was the commercial form known as Marlate provided by Kincaid Industries, Inc. This form consists of 50% methoxychlor. The group treated with estradiol served as a positive control in verifying whether the effects observed in the methoxychlor–treated mice were due to the estrogenicity of the pesticide or to the inherent toxicity of the chemical itself. All chemicals were first suspended in sesame oil and then administered by oral gavage to the adults and intraperitoneally to the newborns.

Significant Findings

Non–Pregnant Adult Females

Evaluations after a four–week exposure revealed alterations in the height of uterine epithelial cells immediately after exposure to methoxychlor. This appears to be an estrogenic response since similar increases in heights in these cells were also observed in mice treated with estradiol. Morphologic alterations in cellular organelles such as mitochondria, rough endoplasmic reticulum and Golgi which are actively involved in protein synthesis indicates a disruption in protein synthetic activity. This suggests that a successful implantation of a fertilized egg is unlikely. These cellular alterations appear reversible once exposure ceases. Two months following the termination of exposure animals are able to mate, become pregnant, and deliver what appear to be normal offspring. Therefore, even though a constant exposure of an adult results in reproductive toxicity, removal of the individual from the exposure restores the reproductive integrity of the individual.

Neonatal Females

By two months of age the ovaries of animals exposed to estradiol and 0.5 and 1.0 mg methoxychlor were smaller than controls. These ovaries were characterized by a domination of pale interstitial tissue and the presence of minimal, if any, corpora lutea. These same features were also observed at four months. Thus, unlike the reversibility of methoxychlor–induced effects seen following exposure of the adult reproductive system, when exposure occurs neonatally, it exhibits an effect lasting a lifetime.

Recent preliminary data has revealed that such female mice when exposed to methoxychlor for fourteen days can, in fact mate as adults. There is, however, a reduced number of pregnancies and a significant reduction in the mean number of live young as the dosage of methoxychlor is increased. Whether these reductions in offspring result from a disruption of the ovulatory process or a failure of the uterus to allow for implantation is currently being investigated.

Publications

Swartz WJ, Wink CS, Johnson WD: Response of Adult Murine Uterine Epithelium to 50% Methoxychlor. Reproductive Toxicology, Vol 8 1:81–87, 1994

Eroschenko VP, Swartz WJ, Ford LC: Ovulatory Responses of Adult Mice Treated Neonatally With Estradiol or Methoxychlor (Technical Grade). FASEB Journal, Vol 8 No 5,1994 (Abstract)

Swartz WJ, Wink CS, Johnson, WD: Response of Adult Murine Uterine Epithelium to Methoxychlor Exposure. Anatomical Record Suppl., 1:109, 1993 (Abstract)

Swartz WJ, Corkern M: Effects of Methoxychlor Treatment of Pregnant Mice on Female Offspring of the Treated and Subsequent Pregnancies. Reproductive Toxicology 6:431–437, 1992

Martinez EM, Swartz WJ: Effects of Methoxychlor on the Reproductive System of the Adult Female Mouse. II. Ultrastructural Observations. Reproductive Toxicology 6:93–98, 1992

Martinez EM, Swartz WJ: Effects of Methoxychlor on the Reproductive System of the Adult Female Mouse. I. Gross and Histological Observations. Reproductive Toxicology 5:139–147, 1991

Swartz WJ, Corkern M: Reproductive Alterations Induced by Exposure of Mice to Methoxychlor

During Pregnancy. Anat Rec, 229:87A, 1991 (Abstract)

Swartz WJ, Mall GM: Chlordecone–Induced Follicular Toxicity in Mouse Ovaries. Reproductive Toxicology 3:203–206, 1989

Martinez EM, Swartz WJ: Response of the Murine Ovary to Methoxychlor Exposure. Anat Rec, 223:75A, 1989 (Abstract)

Swartz WJ, Eroschenko VP, Schutzmann RL: Ovulatory Response of Chlordecone (Kepone)–Exposed Mice to Exogenous Gonadotropins. Toxicology 51:147–153, 1988

Functional Correlates of Cochlear Injury

William W. Clark, Ph.D.
Central Institute for the Deaf
818 South Euclid
St. Louis, Missouri 63110

Grant Number: *5 R01 OH02128-08*
Start & End Dates: *09/01/84 – 05/31/94*
Funding Level: *$0 ($1,063,373 Cum)*

Importance to Occupational Safety and Health

The laboratory studies of noise–induced hearing loss in animal subjects and the relation with cochlear pathology directly address the long–term research goals described by the NIOSH prevention document. They will help to establish damage–risk criteria for human noise exposures, delineate the mechanisms of noise–induced hearing loss, determine the role of degenerative and recuperative processes, and determine the relative hazard of different schedules of noise exposure to help develop noise descriptors for workers exposed on an irregular basis. In addition, they address the interaction between aging and noise induced hearing loss.

Measures of hearing sensitivity obtained by positive–reinforcement operant conditioning techniques provide accurate assessment of hearing sensitivity in appropriately trained subjects. Combined with morphometric evaluation of cochlear damage produced by noise exposure, these laboratory studies provide important information about the precise relation between specific noise exposure parameters, i.e., level, duration, schedules, pattern, and the resultant histopathology that is not attainable in human subjects.

Acoustic measures made from ear canals of unanesthetized chinchillas (acoustic intermodulation distortion products and otacoustic emissions) before and after noise exposure will help elucidate cochlear mechanisms and may lead to an objective test for cochlear function.

Field studies of noise exposure and hearing levels of workers exposed at levels below a time–weighted average of 85dBA provide important baseline data for comparison of groups of exposed individuals to determine the relative contribution of occupational noise exposure to the hearing levels of the groups.

Objectives

The major goal of this project is to determine with behavioral and anatomical studies how the magnitude, pattern, and growth of hearing loss and structural damage are altered as the parameters of noise exposure are varied. Secondary objectives include evaluating hearing loss and cochlear damage as a function of age in a group of chinchillas that have never been exposed to noise and comparing the effects of noise exposure in young and old animals. In addition, acoustic measures of spontaneous otacoustic emissions and acoustic distortion products are being made from the ear canals of all subjects. Finally, an attempt is being made to develop a national "Annex B" comparison database for U.S. industry, for use with the new International Standard R 1999.

Methodology

Hearing thresholds are obtained by behavioral methods in chinchillas before, during, and after noise exposure; the ears of all animals are then prepared for microscopic examination of the cochlea. Behavioral measures of thresholds and discrimination ability are controlled by newly–developed virtual instrumentation software which is programmed on a Macintosh II computer system. Acoustic measures are made with small probe microphones and receivers positioned in the ear canal of the unanesthetized animal. Audiometric data from industry are accumulated in a large database on a Macintosh computer, and statistical software packages are used for data selection and analysis.

Significant Findings

1. With continuous exposures which mimic an occupational lifetime, the amount of hearing loss measured after first days of exposure sets the upper bound of permanent hearing loss that will be produced by that exposure. That is, temporary

hearing loss is associated with permanent hearing loss, and can be used as a predictor thereof.

2. Exposures to noise on an interrupted schedule, with rest periods interspersed produce less hearing loss than equal energy continuous exposures. The findings show that a 3–dB exchange rate is over conservative and overestimates the amount of temporary or permanent hearing loss produced by a given exposure.
3. Furthermore, the ear is "toughened" or made more resistant to subsequent noise when exposed on some interrupted schedules. Measures of behavioral thresholds and distortion product amplitudes from the ear canal of exposed chinchillas both support the conclusion that less hearing loss is observed as the exposure continues. Furthermore, reexposing animals after long exposures to continuous noise and then a rest period show that surviving sensory cells become much more resistant to the development of threshold shift after they have been exposed.
4. Anatomical evaluation of young and old exposed ears show that older ears are equally susceptible to noise–induced hearing loss as younger ears. Furthermore, a study of cochlear damage in ears of older animals with ossicular removal, which attenuates acoustic input to that ear by 60 dB showed that although these ears contained age pigment, cells loss was less than that observed in other, unprotected control ears of the same age. These findings strongly suggest that "sociocusis", or exposure to environmental noise, is a major contributor to presbycusis.

The field studies data from hearing conservation programs also resulted in significant findings. Among the most important are:

5. Hearing levels of U.S industrial workers, either newly employed or those working in low–noise environments, were worse than those reported as representative of an unscreened population of Americans (Annex B of ISO 1999). The difference was larger for males than females, and was as much as 20 dB at 3,000, 4,000, and 6,000 Hz for males over age 40. These differences are probably due to different amounts of nonoccupational noise exposure than that observed in a random sample of the U.S. population.
6. Hearing levels of young individuals differed little by gender or race. However, with increasing age, hearing in white males deteriorated more severely at 3,000, 4,000, and 6,000 Hz with age than that observed in white females and African–American males and females. By age 60 the median hearing threshold level at 4,000 Hz for white males was 16 dB worse than for black males. These data suggest that there are no inherent differences in hearing between Caucasian and African American males, but that hearing sensitivity of white male workers deteriorates more rapidly with age, most likely due to nonoccupational noise exposure factors.
7. Individuals working in occupational noise environments continuously for periods of eight years and who had annual audiometric tests did incur some occupational noise–induced permanent threshold shifts (NIPTS) if they did not wear hearing protection. However, the amount of NIPTS observed was significantly less than that predicted by the NIPTS tables in the ISO standard 1999. These data suggest that the NIPTS tables overestimate the risk of noise–induced hearing loss from occupational noise exposures.
8. Hearing levels of workers who reported that they did wear hearing protection did not differ from controls. This finding suggests that hearing protection devices are effective at eliminating the risk of occupational noise induced hearing loss, even for exposures which exceed a TWA of 105 dBA.

Publications

Clark WW, Bohl CD: Hearing Levels of U.S. Industrial Employees Working in Lownoise Occupational Environments. In: Effects of Noise on Hearing: 5th International Symposium, (eds. R Hamernik, D Henderson, R Salvi), Thieme Medical Publishers, in press, 1995

Bohl CD, Clark WW: The Effect of Hand Held Radio Operation on Audio Dosimeters. Am Ind Hyg Assoc J 54:127–134, 1993

Clark WW: Hearing: Effects of Noise. Otolaryngology Head and Neck Surgery 106:669–676, 1992

Clark WW, Bohl CD: Corrected Values for Annex B of ISO 1999. J Acoust Soc Am 91:3064–3065, 1992

Clark WW: Noise Exposure and Hearing Loss in Children and Youths. ASHA 34:93, 1992 (Abstract)

Cherow E, Clark WW, Berger E: A National Noise Abatement Strategy for the United States. ASHA 34:187, 1992 (Abstract)

Clark WW: The ASA's Role in Preventing Nonoccupational Hearing Loss in the United States. J Acoust Soc Am 92:2357, 1992 (Abstract)

Clark WW: Noise Exposure in Children and Youths. J Acoust Soc Am 91:2375, 1992 (Abstract)

Royster L, Lipscomb D, Clark WW, Dobie R, Jayne T: The Expert Witness in Heating Loss Claims and Other Hearing Related Actions. Proceedings of the 1992 Hearing Conservation Conference, sponsored by the National Institute for Occupational Safety and Health and the National Hearing Conservation Association, Cincinnati, OH, p. 3, 1992 (Abstract)

Clark WW: Role of nonoccupational Exposure in Diagnosing Occupational NIHL. Proceedings of the 1992 Hearing Conservation Conference, sponsored by the National Institute for Occupational Safety and Health and the National Hearing Conservation Association, Cincinnati, OH, p. 167, 1991 (Abstract)

Clark WW, Bohne BA: Hearing Loss and Cochlear Damage from Interrupted Exposure to Noise. In: Noise–Induced Hearing Loss, (eds A Dancer, D Henderson, R Salvi, R Hamernik), Mosby, St. Louis, pp 445–455, 1991

Clark WW: Recent Studies of Temporary Threshold Shift (TTS) and Permanent Threshold Shift (PTS) in Animals. J Acoust Soc Am 90:155–163, 1991

Clark WW: Noise Exposure and Hearing Loss from Leisure–time Activities: A Review. J Acoust Soc Am 90:175–181, 1991

Clark WW: A Head Start on Hearing Loss. Spectrum: The National Hearing Conservation Association Newsletter 8:1–6, 1991

Clark WW: Effect of Amplified Music on Hearing of Children. In: Hearing Before the U.S. House Select Committee on Children, Youth, and Families., "Turn it Down: Effects of Noise on Hearing Loss in Children and Youth. July 22, 1991. US Government Printing Office, Washington pp. 54–67, 1991

Clark WW, Lambert PR: Hearing Loss: Occupational and Nonoccupational. In: Combatting Noise in the 90's: A National Strategy for the United States. American Speech–Language Hearing Association, Washington, pp 29–31, 1991

Clark WW: Amplified Music from Stereo Headsets and Its Effect on Hearing. Hearing Instruments 41(10):29–30, 1990

Bohne BA, Clark WW: Studies of Noise–Induced Hearing Loss Using an Animal Model. Hearing Instruments 41(10):13–16, 1990

Clark WW, Popelka GR: Response to Dr. Kryter's Letter Concerning the Article, "Hearing levels of Railroad Trainmen". Laryngoscope 100:1136–1138, 1990

Clark WW: Noise and Leisure Activities. Proceedings of the NIH National Consensus Conference of Noise. Office of Medical Applications of Research and National Institute on Deafness and Other Communication Disorders, 1990

Clark WW, Popelka GR: Hearing Levels of Railroad Trainmen. Laryngoscope 99:1151–1157, 1989

Clark WW, Bohne BA, Reilly TJ: Effects of Periodic Rest on Hearing Loss and Cochlear Damage Following Interrupted Exposure to High–Frequency Noise. J Acoust Soc Am 84:S75–S76, 1988 (Abstract)

Bohne BA, Clark WW: Hazardous Effects of Noise on Hearing. Proc. International Conference on Noise Control Engineering, Vol II, pp 905–908, 1987

Sinex DG, Clark WW, Bohne BA: Effect of Periodic Rest on Physiological Measures of Auditory Sensitivity Following Exposure to Noise. J Acoust Soc Am 82:1265–1273, 1987

Clark WW, Bohne BA, Boettcher F: Effect of Periodic Rest on Hearing Loss and Cochlear Damage in the Chinchilla. J Acoust Soc Amer 84:1253–1264, 1987

Clark WW, Bohne BA: Attenuation and Protection Provided by Ossicular Removal. J Acoust Soc Amer 81:1093–1099, 1987

Clark WW, Solomonson M: Spontaneous Otacoustic Emission from a Chinchilla Ear Following Exposure to Noise. J Acoust Soc Am 82:S117A, 1987 (Abstract)

Clark WW, Bohl CD, Davidson LS, Melda KA: Evaluation of a Hearing Conservation Program at a Large Industrial Company. J Acoust Soc Am 82:S113, 1987 (Abstract)

Bohne BA, Bozzay DG, Harding GW: Inter Aural Correlations in Normal and Traumatized Cochleas. J Acoust Soc Amer 80:1729–1736, 1986

Sinex DG, Havey DC: Neural Mechanisms of Tone–On–Tone Masking: Patterns of Discharge Rate and Discharge Synchrony Related to Rates of Spontaneous Discharge in the Chinchilla Auditory Nerve. J Neurophysiology 56:1763–1780, 1986

Clark WW, Bohne BA: Temporary Threshold Shifts from Attendance at a Rock Concert. J Acoust Soc Am 79, Supp 1, S48, 1986 (Abstract)

Clark WW, Bohne BA: Cochlear Damage: Audiometric Correlates, In: Sensorineural Hearing Loss, Mechanisms, Diagnosis, Treatment, (eds. E Harford, T Glattke), Univ of Iowa Press, pp 59–82, 1986

Clark WW: Spontaneous Otacoustic Emissions and Acoustic Intermodulation Distortion Products as Indicators of Hearing Loss and Cochlear Pathology. In: Sensorineural Hearing Loss: Mechanisms, Diagnosis, Treatment, (eds. E Harford, T Glattke), Univ of Iowa Press, pp 209–232, 1986

Clark WW, Bohne BA: The Effects of Noise on Hearing and the Ear. Resident and Staff Physician 31:6–19, 1985

Bohne BA, Marks JE, Glasgow GP: The Delayed Effects of Ionizing Radiation on the Ear. Laryngoscope 95:818–828, 1985

Bohne BA, Carr CD: Morphometric Analysis of Hair Cells in the Chinchilla Cochlea. J Acoust Soc Amer 77:153–158, 1985

Clark WW, Bohne BA: The Effects of Noise on Hearing and the Ear. Medical Times 112:17–22fm, 1984

Clark WW, Kim DO, Zurek PM, Bohne BA: Spontaneous Otacoustic Emissions in Chinchilla Ear Canals: Correlation with Histopathology and Suppression by External Tones. Hearing Research 16:299–315, 1984

Hearing Hazard Associated with Industrial Noise Exposure

Roger P. Hamernik, Ph.D.
State University of New York
Department of Physics/Speech & Hearing
107 Beaumont Hall
Plattsburgh, New York 12901

Grant Number: *5 R01 OH02317-10*
Start & End Dates: *08/01/87 – 08/31/98*
Funding Level: *$202,700 ($401,236 Cum)*

Importance to Occupational Safety and Health

Hearing loss in industrial workers accumulates following repeated daily (interrupted) exposures to excessive noise over a long period of employment. Most strategies designed to estimate hearing loss from such exposures rely upon: (1) extrapolations from experimental data acquired from short–term acute exposures; (2) data obtained from noninterrupted long–term noise exposures; (3) epidemiological data with its typically 70 dB or more across–subject variability. Recent discoveries show that the peripheral auditory system can modulate the effects of noise exposure as much as 40 dB. These effects are believed to be partially mediated by the outer hair cell motor system which can be activated by a low–level noise exposure that precedes a hazardous noise exposure, or by interrupting a daily noise exposure regime. This outer hair cell bi–directional transduction system is also responsible for generating cochlear emissions. These emissions are important because of their potential use as a noninvasive and objective diagnostic test for early noise–induced changes in outer hair cell function. Although exposure to high–level impact noise continues to pose a problem to hearing in many industrial environments, there is virtually no experimental data on the accumulation of hearing loss from interrupted high–level impact noise and little data available on the relation between cochlear emissions and noise–induced sensory cell pathology. The current research is designed to develop a data base in these two areas.

Objectives

This noise research program is designed to study the issues that are summarized above in an animal (chinchilla) model. The objectives of this research are: (1) to characterize the hearing loss (threshold shift dynamics) and cochlear pathology resulting from interrupted impact and complex noise (i.e., non–Gaussian, high kurtosis noise) in order to determine the extent to which temporal factors of an exposure affect trauma; and (2) to develop correlations among the cubic distortion product emissions (3DPE), permanent threshold shift and sensory cell pathology in an effort to determine the extent to which the 3DPE can be used as a diagnostic or screening tool for persons at risk of acquiring noise–induced hearing loss.

Methodology

The chinchilla is being used as an animal model. Hearing thresholds (brainstem audiometry) and 3DPE frequency/intensity functions are obtained prior to exposure and at regular intervals following exposure

up to 30–days postexposure. After the effects of the acoustic insult have stabilized, surface preparation histology is used to quantify the sensory cell population. The exposure paradigms include interrupted and noninterrupted noise presentations for either 20 or 5 days respectively. Exposures are balanced for total energy so that comparisons based upon energy can be made. The noise stimuli are computer generated and consist of: (1) narrow band (400 Hz) impacts with center frequencies between 0.5 and 8.0 kHz. These frequencies were chosen to characterize the cochlear protective (toughening) mechanisms and threshold shift dynamics across a broad extent of the basilar membrane; (2) broad band impacts; and (3) various complex high kurtosis noises all having the same L^{eq} and spectrum but differing in their statistical properties.

Significant Findings

1. Industrial noise environments consisting of a combination of impact and continuous noise (i.e. non–Gaussian noise environments) are more hazardous to hearing than are Gaussian noises of the same L^{eq} and spectrum.
2. The kurtosis statistic computed on the time domain signal can order the magnitude of sensory cell loss following exposure to noises having the same L^{eq} and spectrum. Kurtosis computed on the time/frequency domain signal reflected the distribution of outer hair cell loss over the length of the basilar membrane for these same noise environments (Lei et al., 1994).
3. Broad band impact noise exposures presented on an interrupted schedule over many days produced a resistance to threshold shift of up to 40 dB from subsequent exposures. Despite an equivalent exposure energy, interrupted exposures produced less permanent changes than uninterrupted exposures (Hamernik et al., 1994).
4. A number of recent papers have shown consistent toughening effects from priming or interrupted exposure paradigms. Our results (Roberto et al., 1995) indicate that interrupted exposures can show consistent toughening effects, however, the dynamic range of the noise that will elicit these effects is small; on the order of 10 dB. The effects of preexposure priming appear to be less reliable in eliciting a toughening response. Depending on the exposure paradigm either a toughening or an exacerbation effect can be measured.
5. Narrow band transient stimuli presented on an interrupted schedule demonstrate that the magnitude and frequency extent of the toughening effect is dependent upon the center frequency of the narrow band stimulus. This effect is similar to the results shown for stimulation on an interrupted schedule using continuous octave bands of noise. The low frequency transients are more effective in generating the toughening effect and have an effect over a larger dynamic range than do the high frequency stimuli.

Publications

Davis RI, Hamernik RP, Ahroon WA, Underwood KA: Threshold Shift Dynamics Following Interrupted Impact or Continuous Noise Exposure: A Review. In Proceedings 5th International Symposium on Effects of Noise on Hearing (eds. A Axelsson, et al), Thieme Medical Publishers Inc, in press 1995

Lei SF, Ahroon WA, Hamernik RP: The Application of Frequency and Time Domain Kurtosis to the Assessment of Complex, Time Varying Noise Exposures. In Proceedings of 5th International Symposium on Effects of Noise on Hearing (eds. A Axelsson, et al), Thieme Medical Publishers Inc, in press 1995

Roberto M, Hamernik RP, Ahroon WA, Case CJ: Effects of Primed and Interrupted Impact Noise Exposure Paradigms on Hearing Loss. In Proceedings of the Symposium on Auditory Plasticity and Regeneration (eds. RJ Salvi, et al), Thieme Medical Publishers, in press 1995

Lei SF, Ahroon WA, Hamernik RP: The Application of Frequency and Time Domain Kurtosis to the Assessment of Hazardous Noise Exposures. J Acoust Soc Am, in press 1994

Hamernik RP, Ahroon WA, Davis RI, Lei SF: Hearing Threshold Shifts from Repeated Six–hour Exposure to Impact Noise. J Acoust Soc Am 95(1):444–453, 1994

Ahroon WA, Davis RI, Hamernik RP: The Role of Tuning Curve Variables and Threshold Measures in the Estimation of Sensory Cell Loss. Audiology 32:244–259, 1993

Davis RI, Hamernik RP, Ahroon WA: Frequency Selectivity in Noise–Damaged Cochleas. Audiology 32:110–131, 1993

Ahroon WA, Hamernik RP, Davis RI: Complex Noise Exposures: An Energy Analysis. J Acoust Soc Am 93:997–1006, 1993

Hamernik RP, Ahroon WA, Hsueh KD, Lei SF, Davis RI: Audiometric and Histological Differences between the Effects of Continuous and Impulsive

Noise Exposures. J Acoust Soc Am 93:2088–2095, 1993

Ahroon WA, Lei SF, Davis RI, Hamernik RP: The Use of Frequency Domain Kurtosis in the Assessment of Industrial Environments for Hearing Conversation Purposes. J Acoust Soc Am 91(A):2381, 1992

The Effects of Impulse Noise on the Auditory System

Donald Henderson, Ph.D.
State University of New York
School of Social Sciences
Communicative Disorders and Sciences
215 Parker Hall
Buffalo, New York 14214

Grant Number: *5 R01 OH01152-13*
Start & End Dates: *07/01/80 – 03/31/96*
Funding Level: *$273,622 ($2,113,653 Cum)*

Importance to Occupational Safety and Health

Impulse and impact noise found in industry constitutes a special hazard to workers' hearing. For equivalent amounts of acoustic energy, impulse and impact noise may cause significantly more hearing loss than exposure to continuous noise. There is consensus that current noise standards are completely inadequate for protecting workers from exposure to impulse and impact noise. Our research is trying to understand the biological basis of impulse noise–induced hearing loss. From a practical perspective, the research is directed at learning the range of parameters of impulse and impact noise that contribute to making an exposure hazardous. The results of this research will serve as part of the scientific foundation of more comprehensive noise standards.

Objectives

The research program has three complementary objectives: (1) to understand the relation between the parameters of impulse/impact noise (peak pressure, duration, number, repetition rate, exposure duration, spectrum) and the effects on hearing; (2) to understand the anatomical and physiological changes in the inner ear following traumatic exposures; and (3) to explore the possibility that "toughening" exposures to non–traumatic noise can reduce the amount of hearing loss from a dangerous noise exposure.

Methodology

An electrical–mechanical system is used to produce realistic noise impacts. The hearing of the experimental animals tested, is before and after exposure for twenty days. Routine data collection consists of measurements of hearing sensitivity, auditory discrimination, and cochlear histology. More detailed studies of certain experimental groups will include scanning Electron Microscopy, as well as more discriminating psychoacoustic measures of hearing.

Significant Findings

Since the inception of this project, a number of findings have been reported. (1) Certain combinations of impulse and continuous noise constitute an especially hazardous situation. (2) Exposures above a certain "critical" level cause direct mechanical damage. This project has begun to document how the critical level varies with the parameters of the impact/impulse. In addition, microscopic studies have elucidated the complicated series of changes that occur in the inner ear following exposure to traumatic levels of impulse and impact noise. (3) The project has developed a number of psychoacoustic tests that better characterize the hearing impairment caused by dangerous noise. (4) The project has shown that the damaging effects of noise can be exacerbated with other agents, i.e., vibration and certain drugs. (5) In the last few years we have shown that certain low level exposures have been shown to protect the auditory system from future higher level exposures. Of special interest, it was found that these prophylactic exposures are effective in reducing the hearing loss produced by high level impact and impulse noise. (6) Most recently, a large scale experiment has been completed on impact noise that evaluates the relative importance of spectrum, duration of the impact, repetition rate and the Equal Engery Hypothesis. All of these results have direct implications for the management of workers in noisy environments.

Publications

Salvi RJ, Henderson D, Clock AE: Effects of Noise Exposure on the Auditory System. In: Handbook of Neurotoxicology Vol. 2, Effects of Mechanisms, (eds. L Chang, R Dyer), Marcell Decker Inc., New York, pp. 907–962, 1995

Henderson D, Subramaniam M: Advances in Our Understanding of Noise Induced Hearing Loss. Archiv Environ Health, in press, 1994

Henderson D, Subramaniam M, Papazian M, Spongr V: The Role of the Middle Ear Muscles in the Development of Resistance to Noise Induced Hearing Loss. Hearing Research 74:22–8, 1994

Henderson D, Spongr V, Subramaniam M, Campo P: Anatomical Effects of Impact Noise. Hearing Research 76: 101–117, 1994

Henderson D, Salvi RJ, Boettcher F, Clock AE: Neurophysiological Correlates of Sensorineural Hearing Loss. In: Handbook of Audiology, (ed. J Katz), Williams and Wilkins Co., Baltimore, p. 37–55, 1994

Henselman LW, Henderson D, Subramaniam M, Sallustio V: The Effect of "Conditioning" on Hearing Loss From Impulse Noise. Hearing Research 78:1–10, 1994

Subramaniam M, Henderson D, Spongr V: The Relationship Among Distortion Product Otoacoustic Emissions, Evoked Potential Thresholds And Outer Hair Cells with Following Interrupted Noise Exposures. Ear and Hear 15:299–309, 1994

Subramaniam M, Salvi RJ, Spongr V, Henderson D, Powers NL: Changes in Distortion Product Otoacoustic Emissions and Outer Hair Cells Following Interrupted Noise Exposures. Hearing Research 74:204–216, 1994

Subramaniam M, Henderson D, Spongr V: Protection from Noise Induced Hearing Loss: Is Prolonged "Conditioning" Necessary? Hearing Research 65:234–239, 1993

Henderson D, Subramaniam M, Boettcher F: Individual Susceptibility to Noise Induced Hearing Loss: An Old Topic Revisited. Ear and Hearing 14:152–168, 1993

Henderson D, Mills J, Colletti V: Psychophysical Limits of Auditory Performance: Implications for the Diagnosis of Hearing Loss. Otolaryngology (ed. M Paparella), Saunders, pp 255–268, 1992

Henderson D, Campo P, Subramaniam M, Fiorino F: Development of Resistance to Noise. Noise Induced Hearing Loss (eds. Dancer A, Henderson D, Salvi RJ, Hamernik R), Mosby Year Book, pp 476–488, 1992

Salvi RJ, Henderson D, Boettcher FA, Powers NL: Functional Changes in Central Auditory Pathways Resulting From Cochlear Diseases. Mosby Year Book, pp 47–60, 1992

Subramaniam M, Henderson D, Campo P, Spongr V: The Effect of "Conditioning" on Hearing Loss From A High Frequency Traumatic Exposure. Hearing Research 58:57–62, 1992

Danielson R, Henderson D, Gratton MA, Bianchi L, Salvi RJ: The Importance of "Temporal Pattern" in Traumatic Impulse Noise Exposures. J Acoust Soc Am 90:209–218, 1991

Campo P, Subramaniam M, Henderson D: The Effect of "Conditionaling" Exposures on Hearing Loss from Traumatic Exposure. Hearing Research 55:195–200, 1991

Subramaniam M, Campo P, Henderson D: The Effect of Exposure Level on the Development of Progressive Resistance to Noise. Hearing Research 52:181–188, 1991

Subramaniam M, Campo P, Henderson D: Development of Resistance to Hearing Loss from High Frequency Noise. Hearing Research 56:65–68, 1991

Henderson D, Subramaniam M, Gratton MA, Saunders SS: Impact Noise: The Importance of Level, Duration, and Repetition Rate. J Acoust Soc Am 1350–1357, 1991

Henderson D, Farzi F, Danielson R: The Concept of Critical Level and Impulse Noise. Environmental International Vol 16 353–361, 1990

Fiorino F, Gratton MA, Subbanna M, Bianchi L, Henderson D: Physiological Mechanism Underlying the Progressive Resistance to Noise Induced Hearing Loss. Valsalva 54(Suppl 1):36–41, 1989

Boettcher FA, Henderson D, Gratton MA, Byrne C, Bancroft B: Recent Advances in the Understanding of Noise Interactions. Archives of Complex Environmental Studies 1(1):15–21, 1989

Byrne C, Henderson D, Saunders S, Powers N, Farzi F: Interaction of Noise and Whole Body Vibration. Recent Advances in Research on the Combined Effects of Environmental Factors, (ed. O Manninen), Pk–Paino Oy Printing House, Tampere, Finland, pp 239–254, 1988

Henderson D, Hamernik RP: A Parametric Evaluation of the Equal Energy Hypothesis. In:

Basic and Applied Aspects of Noise–Induced Hearing Loss, (eds. R Salvi, D Henderson, RP Hamernik), Plenum Press, New York, 1988

Henderson D, Colletti V, Sittoni V: The Role of the Acoustic Reflex in Noise–Induced Hearing Loss. In: Clinical Measurement of Acoustic Impedance, (ed. V Colletti), Amplaid, Milano, 1987

Henderson D, Hamernik RP, Salvi RJ: A Parameter Evaluation of the Equal Energy Hypothesis. In: Noise Induced Hearing Loss: Basic and Applied Aspects, (eds. RJ Salvi, RP Hamernik, D Henderson, V Colletti), Plenum Press, 1985

Henderson D, Hamernik RP, Salvi RJ: Impulse Noise Repetition Rate: Implication for the Equal Energy Hypothesis. J Acoust Soc Am 78, Supple 1–55, 1985

Henderson D, Hamernik RP: Assessing the Hazards of Impulse Noise Superimposed on Background Noise. J Acoust Soc Am 78:S5, 1985

Salvi RJ, Henderson D, Hamernik RP, Colletti V: Basic and Applied Aspects of Noise–Induced Hearing Loss. Plenum Press, NY, 1985

Henderson D, Salvi RJ, Hamernik RP, Ahroon WA: Neural Correlates of Sensorineural Hearing Loss. Ear and Hearing 4:115–129, 1983

Henderson D, Salvi R, Hamernik R: Is the Equal Energy Rule Applicable to Impact Noise? J of the Acoust Soc of Am Supplement 1, Vol 71, S50, 1982

Hamernik RP, Henderson D, Salvi RJ: New Perspectives on Noise–Induced Hearing Loss. Raven, Press, New York, NY, 1982

Role of Worksite-Associated Vanadium in Immunomodulation

Mitchell D. Cohen, Ph.D.
New York University
School of Medicine
Department of Environmental Medicine
Long Meadow Road
Tuxedo, New York 10987

Grant Number: *5 R03 OH03064-02*
Start & End Dates: *05/01/93 – 04/30/95*
Funding Level: *$41,875 ($78,780 Cum)*

Importance to Occupational Safety and Health

The knowledge gained from the proposed studies, while helping overall to clarify the mechanisms of vanadium–induced immunomodulation, will ultimately contribute to the determination (or revision) of minimal acceptable exposure levels for vanadium in the workplace. As macrophages represent the primary mediators of pulmonary immunocompetence, the mechanisms by which this particular pollutant (in both a soluble and insoluble form) alters macrophage biochemistry with respect to immunoregulating cytokines may also provide a model by which other potential workplace toxicants act in exposed workers. By defining the possible mechanism(s) by which immune responses can be affected by workplace contaminants, such as the vanadium oxides, more accurate assessments of their potential immunotoxicity can be made and proper steps can be taken to minimize the risk from exposure.

Objectives

Several epidemiological studies and our previous *in vivo* laboratory studies have indicated a marked increase in host susceptibility to bacterial/viral diseases after vanadium exposure. Our earlier work determined that following host exposure to vanadium, there is a failure in the ability of resident macrophages to become fully activated for participation in host antibacterial responses. We hypothesized that this reduction in the macrophage capacity to become fully activated is, in part, a result of altered macrophage production, binding, and/or processing of autocrine/lymphokine interferons (IFNα and γ). The specific aims of this project are: (1) to assess the levels of inducible IFNα and IFNγ produced by pulmonary macrophages (PAM) (and other lung accessory cells) found in the intact rat lung after inhalation of occupationally–relevant

concentrations of vanadium (in soluble and insoluble forms), (2) to determine whether inhaled vanadium alters PAM surface IFN receptor expression and/or IFN binding, the intracellular delivery and subsequent dissociation of the receptor–IFN complex, and/or the recycling/*de novo* synthesis of surface IFN receptors, and (3) to relate any changes in these measured parameters to overall changes in PAM responsiveness to exogenous IFN, i.e., IFN–induced expression of Class II MHC surface antigens and enhanced production of reactive oxygen intermediates.

Methodology

Male Fisher 344 rats are exposed (nose–only) to atmospheres containing either soluble ammonium metavanadate (NH_4VO_3) or insoluble vanadium pentoxide (V_2O_5) at concentrations found in work environments where vanadium levels are at OSHA permissible levels (0.05 mg V_2O_5/m^3). Control rats receive either air only or inert latex particles of the same mass median diameter as the vanadium–generated particles. Respirable/penetrable (<1 μm) V_2O_5 atmospheres are generated using a Wright dust feeder, while soluble NH_4VO_3 atmospheres are generated with a Laskin aerosolizer. All rats are exposed for 8 hr/d for 4 d in order to approximate the maximal levels of exposure encountered by workers in an average workweek. One day after the final exposure, the rats are either intratracheally–instilled with polyI:C to induce IFN production, or sacrificed and lung macrophages harvested (by serial lavage) for use in all IFN binding/processing/responsiveness experiments.

IFN analyses: All harvested IFN (IFNα, β, γ mixture) are separated from one another by chemical/physical removal prior to quantitation in an ELISA assay developed in this laboratory.

IFN Receptor Binding and Expression: To assess the levels and strengths of IFN receptor binding, radioiodinated IFN is used in both a saturation and competitive binding study with harvested PAM. Scatchard analyses are used to estimate both the strength of binding (K_d) and the relative numbers of surface receptors present on the target cells. To more accurately assess IFN receptor expression, FACS analyses of PAM tagged with FITC–labeled anti–IFN–receptor monoclonal antibodies is performed.

Receptor Internalization, IFN Release and Degradation: The kinetics of IFN–receptor complex internalization are determined using selective stripping of non–internalized complexes from the PAM surface. To monitor changes in the release of internalized IFN from its receptor complex, PAM are lysed at fixed intervals and the receptor proteins collected by immunoprecipitation. Subsequent separation over PAGE gels and analysis by differential densitometry allows determination of the disappearance of signal from the complex band, a measure of complex dissociation. To assess the status of the intracellular IFN, the lysate proteins are separated without prior modifications over PAGE gels and analyzed by autoradiography. The signal at the region for free IFN is measured (after accounting for the appearance of newly–released IFN by accounting for total free IFN and complex signals) and the kinetics of IFN breakdown determined.

Receptor Recycling/Synthesis: PAM are treated with unlabeled IFN to induce maximal receptor expression and internalization. After stripping the surface of remaining complexes or unused receptors, half of the PAM are treated with cycloheximide to block *de novo* receptor synthesis. All cells are then incubated with radiolabeled IFN and harvested at fixed intervals to monitor IFN binding. The relative increases in binding by cycloheximide–treated cells are indicative of receptor recycling, while in untreated cells, the degree of binding above that accounted for by recycling are indicative of *de novo* synthesis.

IFN–Inducible Responses: PAM are treated with IFN for periods up to 48 hr and then analyzed by FACS for Class II MHC antigen expression using standard protocols with anti–rat Class II antibodies. Reactive oxygen intermediate (i.e., superoxide anion and hydrogen peroxide) formation by IFN–treated macrophages are assessed using spectrophotometric measurements of ferricytochrome c reduction and phenol red oxidation by horseradish peroxidase, respectively.

Significant Findings

Male Fisher 344 rats (10 wk old, 200–250 g) were exposed to atmospheres containing 2 mg vanadium/m^3 (as ammonium metavanadate NH^4VO_3, 0.32 μm diameter particles) for 8 hr/d for 4 d in a nose–only exposure system. In exposed rats, lung burdens of vanadium increased in a time–dependent fashion. Nearly all (88%) metal–exposed rats displayed markedly increased levels of bronchus–associated lymphoid tissue (BALT) after each exposure, though the effect was only transitory. Analysis of lung cells and lavage fluid 24 hr after the final exposure suggested that a strong inflammatory response was elicited; levels of free neutrophils and immature monocytes, as well as of lavage protein and lactate dehydrogenase, were greatly elevated as compared with levels observed in air–exposed controls. Vanadium also affected the capacity of pulmonary macrophages (PAM) to both produce and respond to important immunoregulatory cytokines. PAM production of tumor necrosis factor–α in response to lipopolysaccharide was significantly inhibited, as was the ability of PAM to

synthesize/place MHC Class II/Ia molecules on their cell surfaces in response to IFNγ. The PAM from vanadate–exposed hosts were also inhibited in their ability to be primed by IFNγ to produce superoxide anion and hydrogen peroxide in response to stimulation with opsonized zymosan. These studies indicate that subchronic exposure of rats to atmospheric vanadium, at levels encountered in the workplace, can cause strong immunomodulatory effects in the lungs, with the major effect occurring at the level of cytokine–related functions. The studies to quantify lung IFNγ levels and PAM binding/processing of IFNγ are still in progress at this time.

Difficulties have arisen with the use of the insoluble V_2O_5 compound. In order to get particles of a diameter sufficient for deposition within the rat lung and to also mimic that of the vanadate droplets, the commercially–available V_2O_5 powder has had to undergo repeated milling in a system designed on our premises. After several weeks, the particles are of many different sizes, but the majority are not as yet of the size required for our study. Attempts to arrange for milling from outside sources have been too cost–prohibitive. The samples are still undergoing milling and the studies will hopefully be underway within the next few months.

Publications

McManus TP, Zelikoff JT, Schlesinger RB, Cohen MD: Immunotoxic Effects in the Rat Lung from Vanadium Inhalation. Ninth Annual Symposium of the Foundation for Immunotoxicology, Virginia Beach, Eastern Regional Symposium on the Mechanisms of Immunotoxicology 9:26, 1994

Cohen MD, Schlesinger RB, Zelikoff JT: Vanadium–Induced Alterations in Macrophage Responses to Biological Response Modifiers In Vitro. The Toxicologist 13:422, 1993

Protein Damage Caused By Occupational Toxicants

Randal J. Keller, Ph.D.
University of Arkansas
UAMS Division of & Toxicology
4301 W. Markham, MS 638
Little Rock, Arkansas 72205

Grant Number: *5 R03 OH03061-02*
Start & End Dates: *06/01/93 – 05/31/95*
Funding Level: *$29,988 ($64,628 Cum)*

Importance to Occupational Safety and Health

Occupational toxicants are potentially capable of producing free radicals in biological systems which can lead to oxidative stress. There are numerous oxidants encountered in occupational environments which may lead to this damage. These include metals, pesticides, volatile organic compounds, ozone, and components of environmental tobacco smoke. One technique which is useful in the assessment of oxidative stress is the monitoring of protein oxidation. Oxidative damage to proteins has been shown to result in increased protein turnover, decreased enzymatic function, and has been associated with a number of pathological processes, including emphysema, atherosclerosis, and neurological diseases.

Protein oxidation is being utilized as a biomarker for oxidant exposure. Levels of oxidized proteins are increased during conditions of oxidative stress, as occurs from occupational exposure to toxicants. This project addresses a significant gap in the literature because there are currently no antibody techniques available for the study of protein oxidation. This project will develop a method to selectively analyze oxidized proteins in a complex mixture of oxidized and non–oxidized proteins, and to assess oxidative stress in a reliable and noninvasive manner. The development of a sensitive measure of protein oxidation using polyclonal antibody techniques will be a major addition to the area of oxidative damage. This will be particularly important in the area of occupational exposure, due to the long potential exposure times to oxidants and the susceptibility of lung to oxidant damage. The polyclonal antibody technique will be a powerful tool which will have tremendous applicability in exposure assessment. This project will provide information that may lead to development of a simple, inexpensive immunoassay that can be utilized to monitor the effects of exposure to oxidants in occupational environments.

Objectives

This project examines the hypothesis that certain occupational toxicants are capable of causing tissue damage by oxidatively modifying proteins and that these oxidized proteins can be detected using polyclonal antibody techniques to provide a measure of exposure assessment. The research plan includes the following two objectives:

Objective 1. To develop an immunochemical assay to detect oxidative protein damage using a polyclonal antibody assay and validate the assay by direct comparison with the established spectrophotometric techniques.

Objective 2. To test the utility of the immunoassay to detect oxidized proteins in animals exposed to oxidants found in occupational environments.

Methodology

These experiments to complete objective 1 will directly compare the spectrophotometric 2,4–dinitrophenylhydrazine technique with the polyclonal antibody technique. Purified protein preparations and tissue fractions will be oxidized using three *in vitro* free radical generating systems. These include exposing the proteins to radiation damage, metal–ion–catalyzed free radical damage, and to an enzymatic free radical generating system consisting of xanthine/xanthine oxidase. In addition to validating the assay, we will determine a quantitative assessment of the sensitivity of the technique. Carbonyl content will be determined spectrophotometrically by reaction with 2,4–dinitrophenylhydrazine and subsequent absorbance determination.

An immunochemical assay will be developed to detect proteins oxidized by chemicals found in occupational environments. The general principle of the assay is similar to the spectrophotometric method for the detection of oxidized proteins except the dinitrophenol group will be detected using an specific antibody. Briefly, proteins from tissue homogenates or fractions will be separated using SDS/PAGE then transferred to nitrocellulose paper (Western blot). The separated proteins will be treated with 2,4–dinitrophenylhydrazine. The nitrocellulose is immunochemically stained with polyclonal rabbit anti–dinitrophenol, and the staining intensity detected using an alkaline phosphatase based detection system or a system based on enhanced chemiluminescence.

The experiments in objective 2 will test the utility of the immunoassay to detect oxidized proteins in animals exposed to oxidants found in occupational environments, and we will use the model lung toxicant paraquat will be used. Both dose dependent and time course of carbonyl formation *in vivo* will be determined.

Significant Findings

The immunochemical assay was developed to detect carbonyl groups generated by *in vitro* methods on purified proteins. The technique has been shown to be significantly more sensitive than the spectrophotometric method.

There have been further examinations of protein fractions from homogenates, microsomes and cytosol prepared from rat renal and hepatic tissue that were exposed to hydroxyl radicals generated by a radiolysis mechanism or by metal–ion–catalyzed free radical damage. The resulting protein–derived carbonyls were reacted with 2,4–dinitrophenylhydrazine giving the corresponding hydrazones, which were detected by Western blot using anti–dinitrophenyl antisera. Analysis of the immunoblots using a densitometer indicated linear relationships between carbonyl group formation and increasing treatment from radiolysis in all fractions studied. Further analysis of the immunoblots showed the appearance of distinct bands, particularly in the liver microsomes and cytosol, which demonstrated increased susceptibility of these proteins to oxidative damage. These proteins may prove useful as early indicators of oxidative protein damage.

Publications

Keller RJ, Halmes NC, Hinson JA, Pumford NR: Immunochemical Detection of Oxidized Proteins. Chem Res Toxicol 6:430–433, 1993

Asbestos-Induced Alteration in Endothelial Cell Function

Melinda D. Treadwell
Dartmouth Medical School
Department of Pharmacology & Toxicology
Remsen 7650
Hanover, New Hampshire 03755-3835

Grant Number: *1 R03 OHHL03267-01*
Start & End Dates: *09/30/94 – 09/29/96*
Funding Level: *$37,433 ($37,433 Cum)*

Importance to Occupational Safety and Health

This research will contribute to the understanding of the endothelial cell involvement in the pathophysiology of pulmonary fibrosis following asbestos or non–asbestos fiber exposure. The model to be used relies on the ability to measure discrete, cellular and molecular changes in those cells in close contact to relatively low amounts of fibers. This model represents the changes likely to occur as a fiber penetrates into the interstitium of the lung. Participation of other cell types in inducing endothelial changes, is excluded, but the effects of factors, known to be elaborated by these other cells may be tested, on the progression of asbestos–induced endothelial cell dysfunction. These studies will provide a more complete understanding of the etiology of fiber–related diseases and allow for development of rational means for protecting against fiber–induced disorders. Further, these methods will be useful in evaluating the fibrogenic potential of existing or new man–made fibers.

Objectives

The purpose of the proposed research is to investigate the specific hypothesis that asbestos induces an active endothelial cell phenotype, resulting in increased expression of growth factors and proteases, which are relevant to the development of fibrosis. The aims of the research are to: optimize solution hybridization and *in situ* techniques to investigate altered steady state mRNA levels and protein synthesis following exposure to endothelial cells to fibrogenic substances, demonstrate that asbestos alters synthesis and release of active u–PA, and to compare various man–made fibers for their potential to cause endothelial cell activation.

Methodology

Solution hybridization techniques will be used to quantitatively demonstrate alteration in uPA mRNA. This technique will be a good model for screening fibers of different physical and chemical characteristics. Briefly, total cellular RNA is isolated from cell homogenates, hybridized with 5'[^{32}P]–end–labeled 21–30 base cDNA probes specific for the mRNA of interest. Non–hybridized probe is digested with S1 nuclease and the hybridized duplex is precipitated onto glass filters and counted by liquid scintillation. *In situ* hybridization will also be used to investigate the theory that the morphologically altered endothelial cells in close proximity to the fibers are the cells altering uPA mRNA. The cDNA probes used for solution hybridization will be used for the *in situ* studies, with 5' [^{33}P] end–labeling and development of K.5 gel emulsion from Polysciences (Warrington, PA). *In situ* zymography will be completed to investigate whether the morphologically altered endothelial cells display an increase in uPA activity. This technique involves the clearing of an indicator overlay of plasminogen, agar, and casein by active uPA, visualized with dark field microscopy. A microplate fibrinolysis assay will also be used to evaluate uPA activity which is cell associated or released from the cell. In this quantitative assay, the cleavage of Z–lysine thiobenzyl ester and development of 5,5'–Dithio–bis(2–Nitrobenzoic acid) through the activation by uPA will be measured with a Thermomax m icrotitre plate reader. These techniques will provide a qualitative and quantitative understanding of the time course and non–cytotoxic dose of asbestos required for alteration in uPA mRNA and active protein synthesis and release. Additional studies in the laboratory will be directed at comparison of man–made fibers, such as refractory ceramic fiber 1 (RCF–1) or man–made vitreous fiber 10 for their potential to induce alteration of this protease at similar doses and times.

Significant Findings

To date, a seven fold and two fold increase has been demonstratedin uPA mRNA over control following 8 hours of exposure to crocidolite asbestos (5 $\mu g/cm^2$) or chrysotile asbestos (10 $\mu g/cm^2$), respectively. No increase over control expression of uPA mRNA was observed following exposure to RCF–1 (10 $\mu g/cm^2$) for 8 hours. These changes were maintained following 24 hours of exposure to the fibers. *In situ* zymography has demonstrated an increased clearance of the indicator overlay following a 24 hour exposure to crocidolite asbestos (5 $\mu g/cm^2$) or chrysotile asbestos (10 $\mu g/cm^2$), with no altered clearance observed following exposure to RCF–1 (10 $\mu g/cm^2$).

The Role of FE(II) in Dust-Induced Carcinogenesis

Xi Huang, Ph.D.
New York University
School of Medicine
Department of Environmental Medicine
Lanza Laboratory
Long Meadow Road
Tuxedo, New York 10987

Grant Number: *1 R03 OH03253-01*
Start & End Dates: *09/30/94 – 09/29/96*
Funding Level: *$40,528 ($40,528 Cum)*

Importance to Occupational Safety and Health

Increasing evidence demonstrates that an excess of lung cancer and stomach cancer has been observed in workers of iron ore and steel factories. It has been shown that the incidence of cancer is related to the exposure to airborne mineral dusts. However, the active compound(s) responsible for the observed carcinogenicity of mineral dusts has not yet been identified. Although iron oxide (Fe_2O_3) particles have been tested and found to produce little carcinogenicity, this was likely due to the insolubility of iron oxide in water, even in a slightly low pH medium. Ferrous ion, one of the most abundant elements in polluted industrial environment, is capable of producing reactive oxygen species (ROS), and may play an important role in mineral dust–induced carcinogenesis. Due to the complexity of iron chemistry, previous studies on iron–induced cell transformation did not take into account some important chemical factors. For example, oxidation of Fe(II) to Fe(III) which results in ROS formation is greatly dependent upon the pH of the media. Because of the alkaline pH in cell growth medium, oxidation of Fe(II) to Fe(III) takes place quickly in the extracellular medium. Therefore, the short live ROS resulting from interaction of Fe(II) and O_2 may only damage cell membrane which causes cell toxicity. In contrast, when Fe(II) is deposited on a particle, and phagocytized by cells, the released Fe(II) in cells can induce cell transformation. This is relevant to the mineral dust–induced carcinogenesis. Thus, the role of reactive Fe(II) in airborne dusts is a parameter which is worth considering in order to predict which dusts will lead to a higher incidence of cancer.

Objectives

The objectives of this proposed research are to compare the carcinogenicity of Fe(II) ions in solution and Fe(II)–containing dusts. We hypothesize that phagocytosis of Fe(II)–containing dusts may increase the ambient concentration of ROS in cells which can lead to DNA damage and finally cell transformation. Different iron compounds will be tested in Syrian hamster embryo (SHE) cell transformation assay. To further determine the mechanism of Fe(II) containing dust–induced carcinogenesis, ROS formation, 8–oxo–dG, and DNA–protein crosslinkings (DPCs) will be measured to detect the DNA damage induced by iron compounds. In addition to SHE cells, we will also investigate the effect of iron compounds on human tracheal epithelial (HTE) cells. Moreover, we will compare the responsiveness of oxidative stress responsive transcription factors, such as nuclear factor kB and AP–1 to Fe(II) treatment.

Methodology

Many studies have shown that the iron content of the asbestos fibers has an important role in the generation of ROS, which may induce mesothelioma. However, composition of these fibers is too complex to verify the role of Fe(II) in their carcinogenicity. $FeSO_4$ and pyrite (FeS_2) are ideal compounds for this study. SHE cells will be treated with $FeSO_4$ solution, freshly prepared water insoluble pyrite (FeS_2), aged pyrite containing a coating of $FeSO_4$, and water insoluble goethite (a–FeOOH). The frequency of morphological transformation and the relative cloning efficiency will be calculated after treatment with iron compounds. Oxidants produced in intact cells (SHE and HTE) by iron compounds will be directly measured by dichlorofluorescein. The distribution of oxidants in cytosol and nuclei of treated cells will also be measured by isolating nuclei with Triton X–100. Meanwhile, DNA will be isolated from control and iron treated cells. 8–oxo–dG and DPCs will be quantitated using HPLC–EC detector and a fluorometer respectively. Nuclear proteins will also be extracted from nuclei of intact cells which have been treated with the above cited iron compounds. The nuclear extracts will be incubated with ^{32}P–labeled oligonucleotides encompassing the NF–kB or AP–1 consensus motif to assess their binding affinity.

Significant Findings

None to date.

Silica, Silicosis, and Lung Cancer in Diatomite Workers

Harvey Checkoway, Ph.D.
University of Washington
Department of Environmental Health, SC-34
Seattle, Washington 98195

Grant Number: *1 R01 OH03126-01*
Start & End Dates: *04/01/94 – 03/31/96*
Funding Level: *$244,705 ($244,705 Cum)*

Importance to Occupational Safety and Health

Millions of workers world–wide are or have been exposed to crystalline silica. In 1987, the International Agency for Research on Cancer classified crystalline silica as a probable human lung carcinogen. However, nearly all of the epidemiologic studies on this topic have suffered from a lack of detailed exposure data needed for dose–response estimation, and few have had data on chest radiographic readings which would permit clarification of a potential precursor role of fibrosis in lung carcinogenesis. The present investigation is an extension of a previous cohort mortality study of diatomaceous earth industry workers whose exposures to crystalline silica are primarily in the form of cristobalite. The availability of both quantitative exposure information for crystalline silica, and radiographic data for a defined cohort of diatomaceous earth industry workers offers the opportunity to improve on past work.

This study should, thus, generate significant new information needed for quantification of the dose–response relation between silica and lung cancer, which is essential for scientifically–based risk assessments and environmental standard setting. Moreover, the study findings will add further to an understanding of the pathogenetic role of pulmonary fibrosis in carcinogenesis.

Objectives

The aims of this project are: (1) to estimate disease–specific mortality relative risks among a cohort of workers exposed to crystalline silica in diatomaceous earth manufacturing; (2) to quantify exposure–response relations for lung cancer and non–malignant respiratory diseases, including silicosis; (3) to determine the long–term trends of radiographically–detectable silicosis in the cohort; and (4) to examine the potential intervening role of pulmonary fibrosis in lung cancer by comparing exposure–response relations for silica and lung cancer among workers with and without radiographic evidence of fibrosis. The underlying hypotheses to be investigated are that silica may act independently as a lung carcinogen or that its carcinogenic potential requires pulmonary fibrosis as a necessary intermediate step.

Methodology

The study will add 6 years of follow–up to a previously conducted historical cohort mortality study of 2,961 diatomaceous earth (diatomite) workers. The original study revealed a lung cancer mortality excess overall in the cohort during 1942–87 (SMR=1.43), and a strong risk gradient with increasing cumulative exposure to crystalline silica (Relative Risk=2.74 in the highest compared to the lowest exposure category).

Mortality follow–up will be extended through 1993 by searches conducted on data bases maintained by the National Death Index and State Vital Statistics Offices. Quantitative estimates of crystalline silica doses experienced by the cohort will be made from industrial hygiene data and linkage of this information to work history records. Chest radiographs, which have been maintained for the majority of the cohort since the 1930s, will be read and classified by standard International Labour Office criteria for the pneumoconioses. This will allow stratification of workers into categories of "absent," "possible," and "present" silicosis. Comparisons of lung cancer risks among these groups will be conducted to estimate dose–response relations for lung cancer, and will allow a test of the fibrosis/carcinogenesis hypothesis. Additional analyses will focus on temporal trends and dose–response relations for silicosis, other forms of non–malignant respiratory diseases, and other diseases for which overall mortality excesses are observed.

Significant Findings

None to date.

Lung Disease in Chinese Textile Workers

David C. Christiani, M.D.
Harvard University
School of Public Health
Environmental Health
665 Huntington Avenue
Boston, Massachusetts 02115

Grant Number: *5 R01 OH02421-05*
Start & End Dates: *07/01/91 – 06/30/95*
Funding Level: *$89,020 ($512,951 Cum)*

Importance to Occupational Safety and Health

This study is an longitudinal follow–up of cotton textile workers in Shanghai, China. The relevance of the knowledge gained from this work includes: the relative contributions of cotton dust and gram negative bacterial endotoxins in producing acute and chronic respiratory disease; the rate of annual decline in lung function after exposure to cotton dust; and the importance of acute, cross–shift change in FEV_1 in predicting longitudinal loss of lung function. Determination of exposure–response for gram negative bacterial endotoxins is important not only for textile workers, but also for thousands of workers exposed to other organic dusts and environments rich in endotoxin.

Objectives

Briefly stated, the project objectives have been:

1. To determine the 11–year incidence and remission of byssinosis and non–specific respiratory symptoms among cotton textile workers, using silk workers for comparison, and to relate these findings to exposure to cotton dust and endotoxin.
2. To determine the rate of annual decline in pulmonary function in cotton workers and silk referents and relate these outcomes to various estimates of current and historical work exposures.
3. To explore the relative contributions of cotton dust and airborne gram negative endotoxin exposure in the development and progression of respiratory symptoms and pulmonary function change.
4. To explore the assumption of a cross–shift change in FEV_1 at baseline screening and subsequent development of respiratory symptoms and loss of FEV_1.

Methodology

The study is a 11–year follow–up with surveys done at years 0, 5, and 11. Respiratory questionnaire, pulmonary function, and air sampling were performed at both surveys using identical techniques. Retirees and workers on leave were contacted and tested at years 5 and 11. The cause of death, as well as other reasons for loss from cohort, has been ascertained on all subjects.

Significant Findings

Significant findings of the 5–year follow–up study include: (1) a generally good dust–endotoxin correlation in the mill environments; (2) workers with both non–specific and work–related symptoms at the time of first survey had accelerated 5–year losses in lung function; (3) after appropriate adjustments for smoking, age, etc., cotton textile workers had an accelerated loss of FEV_1 over 5 years; (4) cotton–exposed workers, but not silk workers, with a greater than or equal to across–shift loss in FEV_1 at the time of first survey had significantly greater 5–year loss in FEV_1 after appropriate adjustments.

At 11 years, we achieved a 90% follow–up of the original population. The unadjusted decrements in 11–year FEV_1 drop for cotton workers was similar to silk workers (–26 ml/yr versus –27ml/yr respectively). This reflected a reversal of trend in the second period of follow–up (1986–92) and could not be explained by the healthy–worker selection effect, as we had tested retirees at both follow–up periods and their respiratory health experience pre–retirement was similar for cotton and silk workers. Regression modeling revealed an exposure–period interaction which will require more investigation. Moreover, since our original cohort was restricted to those with at least two years of work, early selection effects could not be assessed on internal analysis of the cotton group. Regression models of 11 years which change in FEV_1 include cumulative dust or endotoxin measurements, reveal significant coefficients for smoking, years worked and cumulative dust, but not endotoxin exposure.

Publications

Xu XP, Ding M, Li BL, Christiani DC: Association of Paternal and Maternal Exposure With Low Birth Weight and Preterm Births Among Women Textile Workers. In: Male–mediated Developmental Toxicity: Father's Exposures and Their Child's

Health, (eds. DR Mattison, AF Olshan), Plenum Publishing, in press, 1994

Beckett WS, Pope CA, Xu XP, Christiani DC: Women's Respiratory Health in the Cotton Textile Industry: An Analysis of Respiratory Symptoms. Br Jour Industr Med 51:14–19, 1994

Christiani DC, Ye TT, Wegman DH, Eisen EA, Dai HL, Lu PL: Variability in Symptom Reporting, Across–Shift Drop in FEV_1 and Longitudinal Change in Pulmonary Function in Cotton Textile Workers. Chest 105:1713–1722, 1994

Hayes G, Ye TT, Lu PL, Dai HL, Christiani DC: Respiratory Disease in Chinese Textile Workers, III. Assessment of Small Airways Function. Environmental Research 66:31–43, 1994

Xu XP, Ding M, Li BL, Christiani DC: Association of Rotating Shiftwork With Preterm Births and Low Birth Weight Among Never–smoking Women Textile Workers in China. Br Jour Indus Med 51:470–474, 1994

Christiani DC, Ye TT, Wegman DH, Eisen EA, Dai HL, Lu PL: Cotton Dust Exposure Across–Shift Drop in FEV_1 and 5–Year Change in Lung Function. Am Rev Respir Dis 150:1250–5, 1994

Christiani DC, Velazquez AV, Wilcox M, Olenchock SA: Airborne Endotoxin Concentrations in Various Work Areas within A Cotton Mill in Central America. Environmental Research 60:187–192, 1993

Christiani DC, Wegman DH, Ye TT, Eisen EA, Olenchock SA: Cotton Dust and Gram Negative Bacterial Endotoxin Correlations in Two Mills. Am Jour Industr Med 23:333–343, 1993

Hayes G, Christiani DC: Tests of Small Airways Function As Predictors of Chronic Obstructive Pulmonary Disease. Occup Medicine 8:375–397, 1993

Xu XP, Christiani DC: Occupational Exposures and Physician–diagnosis of Asthma. Chest 104:1364–1370, 1993

Christiani DC: Occupational Lung Disease in the Industrialized and Industrializing World — Commonalities and Contrasts: Measurement Tools in Research. Tubercle and Lung Dis 73:7–13, 1992

Olenchock SA, Christiani DC, Mull JC, Ye TT, Lu PL: Airborne Endotoxin Concentrations in Various Work Areas Within Two Cotton Textile Mills in the People's Republic of China. Biomedical and Environmental Sciences 3:443–451, 1990

Christiani DC, Wegman DH, Eisen EA, Ye Tt, Lu PL: Cotton Dust Exposure and Longitudinal Change in Lung Function. American Review of Respiratory Diseases 141:589, 1990

Occupational Disease Among Carpenters

John M. Dement, Ph.D.
Duke University Medical Center
Department of Community & Family Medicine
2200 W. Main Street, Suite 700
Durham, North Carolina 27710

Grant Number: *5 R01 OH03168-02*
Start & End Dates: *09/30/93 – 09/29/95*
Funding Level: *$197,753 ($375,043 Cum)*

Importance to Occupational Safety and Health

The National Institute for Occupational Safety and Health (NIOSH) has identified occupational lung diseases as one of the ten leading occupational health problems in the United States. The construction industry has been identified as one of the "Special Population Targets" in the Healthy People 2000 document due to the high rate of work–related deaths and work–related injuries among this population.

The use of data bases for epidemiologic research that were developed for other purposes raises a number of issues. Use of both worker's compensation data and data from health insurance claims sources is necessary to fully characterize occupational morbidity and the interaction of occupational and other risk factors. This project will explore the use of medical claims data for study of occupational lung disease among carpenters in Washington State.

Objectives

The major objective of this proposed research project is to study work–related respiratory disorders among members of the United Brotherhood of Carpenters (UBC) international union. Specific aims are as follows:

1. To integrate several existing databases in order to develop a comprehensive data system useful for

study of work–related respiratory disorders among carpenters.
2. To develop epidemiological methods for analyses of medical claims data.
3. To analyze these integrated data with respect to incidence and prevalence of occupational lung diseases among carpenters in Washington State.
4. To conduct an asthma case–control study of carpenters for purposes of identifying possible etiologic associations with specific occupational exposures.

Methodology

Occupational lung diseases to be studied include malignant neoplasms (ICD–9 158, 162, 163), obstructive pulmonary diseases (IDC–9 406–496) and pneumoconioses (ICD–9 500–508). Case definition criteria based on ICD–9 codes have been used to define cases of each target lung disorder using both worker's compensation data and insurance data. A dynamic cohort of 11,232 carpenters who worked at least 3 months of union time between 1989–1992 has been defined using the UBC medical insurance eligibility file. Person–time at risk for each cohort member has been calculated using the UBC file of hours worked for each month of the follow–up period. Crude, age and sex specific period prevalence rates for each target lung disease have been calculated. For identification of high risk carpenter work, further analyses will include calculation of age–adjusted period prevalence rates for each lung disease for various carpenter trades and industries in Washington using Poisson regression procedures.

The asthma case–control study includes approximately 100 newly diagnosed cases of asthma during 1989–1992 from the medical claims file or the State of Washington Worker's compensation files. In order to approximate incident rather than prevalent cases of asthma, a one year lag period without a medical claim for asthma is required for each case. Three controls for each case, matched on age (within 2 years) and sex have been randomly selected from the population of carpenters from the cohort of 11,232 workers using incidence density matching procedures.

Cases and controls will be contacted by mail and asked to complete a self–administered questionnaire soliciting information concerning respiratory symptoms as well as information concerning specific occupational exposures possibly associated with occupational asthma. Both the respiratory symptom and the occupational/environmental exposure questionnaire have been developed and pilot tested. Questionnaire administration and case–control data analyses will be completed in the second year of this study. Stratified analyses will be used to control for possible confounders such as age, sex, smoking, etc. Multiple logistic regression will be used to analyze the association between asthma diagnosis, respiratory symptom data (and combinations of symptoms) and occupational exposures after adjustment for potential confounders.

Significant Findings

Data analyses thus far completed include calculation cohort descriptive statistics as well as crude as well as age and sex period prevalence for each lung disorder. The following are crude period prevalence rates for carpenters:

RESPIRATORY DISEASE	PERIOD PREVALENCE (cases/100 person-months of work)
Malignant Neoplasms of Trachea, Bronchus & Lung (ICD–9 162)	0.004
Chronic Obstructive Pulmonary Disease and Allied Conditions	
Bronchitis (ICD–9 490)	0.185
Chronic bronchitis (ICD–9 491)	0.017
Emphysema (ICD–9 492)	0.007
Asthma (ICD–9 493)	0.077
Bronchiectasis (ICD–9 494)	—
Chronic airways obstruction, NEC (ICD–9 496)	0.033
Pneumoconioses and other Lung Diseases due to External Agents (ICD–9 500–508)	0.010

Asthma period prevalence rates for the UBC locals in Washington show marked variation with rates ranging from 0.0183 to 0.0563 cases per 100 person–months of follow–up. Differences by local and carpenter job will be further explored in the case–control study.

Automated Staging of Coal Workers' Pneumoconiosis

Kendall Preston
Carnegie-Mellon University
5000 Forbes Avenue
Pittsburgh, Pennsylvania 15213

Grant Number: *1 R01 OH03055-01A1*
Start & End Dates: *06/01/94 – 05/31/95*
Funding Level: *$65,474 ($65,474 Cum)*

Importance to Occupational Safety and Health

Coal workers' pneumoconiosis (CWP), also known as black lung disease, exhibits rounded or irregular small opacities in standard chest x–rays caused by a physiological reaction to the deposition of coal dust in the lung. The disease is staged with two parameters: profusion, a measure of opacity concentration, and opacity size/shape. When diagnosing an x–ray, there is a great deal of variability among radiologists in staging the disease. Consistent diagnoses are vital, however, because of medical and legal issues such as prevention of disease progression by early detection and equitable compensation for afflicted workers.

Objectives

The goal of this research is to develop a method to minimize diagnostic variability by automatically staging CWP utilizing computer analysis of digitized chest x–rays. This work is a cooperative effort with the National Institute for Occupational Safety and Health (NIOSH, Morgantown, WV) which maintains a repository of all coal workers' x–rays and corresponding diagnostic and epidemiological data for the United States.

Methodology

No deterministic methodology exists for solving problems of pattern recognition such as the automated staging of CWP. Statistical pattern recognition techniques will be applied utilizing new features derived from mathematical modeling of the digitized image. Pairwise linear discriminant analysis will be employed in dimensionality reduction and the development of a classifier based on an optimal subset of features. Features currently being investigated are based on the spatial gray level dependence matrix, two–dimensional Fourier spectra, image morphology, and Gauss–Markov random fields. Examination will made of the dependence on context (spatial location) of features in classifier development, which has not been applied to this problem previously.

Training and test set films will be obtained from the standard International Labour Organization set of pneumoconiosis films and from NIOSH films. Diagnostic data on the films will be obtained from previous readers (usually two) and the University of Pittsburgh Department of Radiology. From each x–ray, more than 100 tiles are selected from the inter–rib spaces in the lung fields. Image noise from rib structures is therefore eliminated. Mathematical modeling of opacities will be employed to explore the appropriateness of the features to be used, as well as their robustness to variations in exposure and digitization noise, which is unique to this work.

Significant Findings

Utilization of an opacity model in the prediction of image covariance corresponds to results obtained from actual data. This type of analysis will give much more insight into both the value and meaning of each feature.

Preliminary results are being obtained now that the large x–ray database is complete, and software coding is nearing completion.

Respiratory Carcinogenesis in Uranium Miners

Frank D. Gilliland, Ph.D.
University of New Mexico
New Mexico Tumor Registry
Department of Medicine
900 Camino de Salud, N.E.
Albuquerque, New Mexico 87131-5306

Grant Number: *1 K01 OH00142-01*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$54,000 ($54,000 Cum)*

Importance to Occupational Safety and Health

The need for research in the area of respiratory carcinogenesis is evident. Lung cancer remains a pressing worldwide public health problem and indoor radon is now recognized as the second leading cause of lung cancer in the United States. Techniques of molecular and cellular biology will provide new markers for describing the longitudinal process of carcinogenesis and for screening.

Objectives

This application proposes an integrated program of work on lung cancer based on the research opportunity afforded by the high risk of former uranium miners in New Mexico and Colorado for this malignancy. The program includes investigation of quantitative risks of lung cancer in relation to exposure to radon progeny, of determinants of susceptibility, and of molecular and cellular markers of carcinogenesis.

Uranium miners have a markedly increased excess risk of lung cancer that is determined by exposure to radon progeny and smoking. The states of New Mexico, Colorado, Arizona, and Utah have a large number of former miners who are now at high risk for lung cancer because of these exposures.

1. Using a newly developed cohort of high risk uranium miners,
   a. determine the prevalence on enrollment of cellular and molecular changes in exfoliated respiratory cells and define their relationship to radon exposure and smoking; and
   b. describe the temporal pattern of cellular and molecular events in respiratory carcinogenesis as the cohort is followed longitudinally; and
   c. quantify the lung cancer risk associated with cellular and molecular markers that occur with high prevalence,
2. Using the New Mexico Tumor Registry database on incident cancers in Navajo males, 1969–1993.
   a. determine the magnitude and temporal trends in uranium–mining associated risk of lung cancer;
   b. describe the distribution of histologic types in Navajo males and a cohort of New Mexico uranium miners;
3. Using the cohort of underground miners screened through a statewide screening program operated by the Miners' Colfax Medical Center.
   a. assess pulmonary function as a marker of lung cancer susceptibility; and
   b. determine lung cancer risk associated with the presence of silicosis.

Methodology

The risks of lung cancer in a cohort of 3,500 New Mexico uranium miners and in Navajo uranium miners have already been investigated. The program described in this application extends these studies following a molecular epidemiology model. It draws on resources in epidemiology at the New Mexico Tumor Registry in the Cancer Research and Treatment Center at the University of New Mexico and in molecular and cellular biology at the Lovelace Inhalation Toxicology Research Institute.

Significant Findings

None to date.

Radon, Bronchial Morphometry, and Occupational Health

David J. Brenner, Ph.D.
Columbia University
Center for Radiological Research
630 West 168th Street
New York, New York 10032

Grant Number: *5 R03 OH02931-02*
Start & End Dates: *01/01/92 – 12/31/93*
Funding Level: *$24,083 ($47,769 Cum)*

Importance to Occupational Safety and Health

The hazards of occupational exposure to radon daughters relative to environmental exposure is significant both for occupational and environmental health. Much attention has been paid to relative physical factors (bronchial epithelial dose /WLM) in the two situations, but almost no attention to the relative biological factors (risk/unit bronchial dose in miners vs general public). These biological differences arise because of the (average) thicker mucosal layers in the 70% of miners who smoke, compared to the approximately 70% of the general public who do not smoke.

Objectives

The aim of this small–grant pilot study is to produce evaluations of the relative biological hazards of radon daughters per unit lung dose, for pertinent biological endpoints, for miners vs. environmentally–exposed home residents.

Methodology

1. Analyze previously–collected biological data to quantify how the relative biological hazard varies with LET (Linear Energy Transfer, or stopping power) and its microdosimetric correlate, lineal energy. Only biological measurements pertinent to risk estimation, namely oncogenic transformation, mutation, and chromosomal damage, are considered;

2. Use Monte–Carlo simulation of alpha–particle transport, together with the best available data on mucosal and epithelial thicknesses in smokers and non smokers, to estimate the energy deposition characteristics of the radon–daughter alpha particles, in the cells at risk in the bronchial epithelia of miners and the general public; and
3. Combine the data from (1) and (2) to obtain relative biological risk factors for occupational miners and the general public.

Significant Findings

Domestic radon risk estimates are typically based either on uranium miner data or on data derived from A–bomb survivors; comparison of domestic radon risk estimates derived from these two disparate sources represents an important test of their reliability. There is currently a significant discrepancy of about a factor of three between domestic radon risk estimates generated with these two independent methods. To base such risk estimates on the data for A–bomb survivors, who were exposed mainly to low–LET radiation, requires a quality factor for alpha particles from radon progeny; the final risk estimate is then directly proportional to this quality factor. We have used the most extensive quantitative *in vitro* data set currently available at high LET for an oncogenic endpoint, to make the best estimate we can that could be used as a basis for a quality factor. Our best estimates of values appropriate for the quality factor for radon progeny are significantly lower than those (20–25) currently used in estimating lung–cancer mortality due to radon. Specifically, our best estimate for home dwellers is around 10. In addition, because of the different geometry in the bronchial epithelia of non smokers *vs.* smokers, our best estimate of an appropriate quality factor for home dwellers is about 18% greater than that for miners; thus our best estimate of the "effective *K* factor" to convert to effective dose/WLM in home dwellers, from effective dose/WLM in miners, would be increased by this factor. Based on a quality factor of ~10, the dosimetrically–based estimate of radon–induced mortality would be ~35,000 per year in the U.S., rather than a value of ~70,000 obtained using a quality factor of 20. The 35,000 value, while larger than the values based on miner data (~20,000), is much smaller than previous estimates of ~70,000 based on dosimetric methods; thus, risk estimates based on the two approaches, dosimetric and epidemiological, may be partially reconciled. Finally, a quality factor of 10 would reduce the proportion of the collective effective dose caused by radon progeny from the currently accepted value of 55% down to about 38%.

Publications

Brenner DJ, Miller RC, Huang Y, Hall EJ: The Biological Effectiveness of Radon–progeny Alpha Particles III Quality Factors. Radiat Res, accepted, 1994

Brenner DJ: The Significance of Dose Rate in Assessing the Hazards of Domestic Radon Exposure. Health Physics 67:76–79, 1994

Brenner DJ, Sachs RK: A Characteristic, Stable and Detectable Molecular "Fingerprint" Produced by High LET Radiations. In Molecular Mechanisms in Radiation Mutagenesis and Carcinogenesis, (eds. KH Chadwick, R Cox, HP Leenhouts, J Thacker), Luxembourg, European Commission, 1994

Brenner DJ, Sachs RK: Chromosomal "Fingerprints" of Prior Exposure to Densely–ionizing Radiation. Radiat Res 140:134–142, 1994

Brenner DJ, Hall EF: That Which is Crooked Cannot Be Made Straight (1): Response to JS Puskin. Radiation Research 138:144–145, 1994

Brenner DJ, Hall EJ, Randers–Pehrson G, Miller RC: Model Considerations On The Dose–rate/LET Dependence Of Oncogenic Transformation By Charged Particles. Radiation Research 133:365–369, 1993

Ergonomic Risk Factors and Cumulative Trauma Disorders

Alfred Franzblau, M.D.
University of Michigan
Department of Environmental and Industrial Health
1420 Washington Heights
Ann Arbor, Michigan 48109-2029

Grant Number: *5 R01 OH02941-02*
Start & End Dates: *09/30/92 – 04/30/95*
Funding Level: *$296,713 ($610,264 Cum)*

Importance to Occupational Safety and Health

Cumulative trauma disorders (CTDs) are a large, growing and costly problem in industry. NIOSH has identified CTDs as among the 10 most significant occupational health problems in the United States. Prevention of occupational injury and disease relies,

in part, on promulgation of standards which mandate limits of acceptable exposure to harmful agents in the work place. This approach has been applied successfully with regard to metals, solvents, carcinogens, and other toxins. In the realm of ergonomics, NIOSH has issued guidelines for manual lifting and prevention of low back disorders. Ideally, the foundations of such standards are a quantitative understanding of the relationship of exposure to risk of disease or injury. Generic work standards are needed for prevention of cumulative trauma disorders of the upper extremities, but current scientific knowledge does not permit precise quantification of risk of developing CTDs. The current study is intended to address that need.

Objectives

The overall objective of this cross–sectional investigation is to study jobs and perform medical screening of workers who are at risk of developing upper extremity cumulative trauma disorders (CI'Ds) with the goal of modeling quantitative dose–response relations between generic job exposures and medical outcomes. Specific objectives include:

1. To identify jobs with at least three levels of repetition and with at least 20 workers in each category in the study plants.
2. To quantitatively assess job exposures for repetitiveness and other factors which are known to be potential risk factors for developing CTDs, including force, mechanical stress, posture, vibration, and temperature extremes.
3. To perform medical screening of subjects/workers that would include: questionnaire surveys (demographic information, pertinent medical history, occupational history, discomfort/symptom survey), standardized physical examinations of the upper extremities, nonaversive quantitative sensory tests of the upper extremities, strength testing, and limited electrodiagnostic testing of the upper extremities.
4. To model relationships between indices of job exposure (e.g. quantitative rating of repetitiveness) and indices of medical outcomes (e.g. symptoms, physical examination findings, quantitative sensory test results, electrodiagnostic test results, and prevalence of specific CTDs) with the goal of developing quantitative, dose–response relationships between job exposures and medical outcomes.
5. To compare the efficacy of the various medical screening techniques employed to detect CTDs (e.g. to compare the predictive value of quantitative sensory scores in the distal upper extremities to electrodiagnostic test results with regard to identification of possible carpal tunnel syndrome).
6. To make specific recommendations to participating plants and workers about how to reduce ergonomic risk factors identified during the course of this investigation. (If this cross–sectional investigation is successful, then the plants/jobs/workers studied would form the basis of a possible follow–up, prospective study whereby one could assess the medical impact of ergonomic interventions made at the conclusion of the initial cross–sectional investigation).

Methodology

This study will use a cross–sectional design comparing the health of workers in jobs that are stratified on different levels of repetition. Jobs will be analyzed for repetitiveness, force, mechanical stress, posture, vibration, and temperature extremes. Workers in these jobs will undergo standardized medical evaluations that will include a questionnaire, physical examination of the upper extremities, and limited electrodiagnostic studies at the wrists. Exposure–response relationships will be examined through univariate and multivariate analyses.

Significant Findings

The continuing focus of our activities has centered on identifying plant sites and jobs that meet study requirements of having at least 3 levels of repetition with at least 30 workers in each repetition category. This study has been broadly advertised and many companies have responded. Although many plant walk–throughs have been completed, very few sites have qualified for the study. This past spring and summer, jobs for the three repetition categories were identified at Prince Corporation, an automotive parts manufacturer in Holland, MI. Over 35 jobs were identified, videotaped and documented. A panel of experts met to review the jobs and rate the ergonomic risk factors. After independently rating the risk factors for each job, the experts discussed their ratings and came to a consensus. This system of job analysis appears to be a valid and reliable method for experts to rate jobs. The medical survey of workers in jobs at Prince which qualified for the study was completed during the summer. In addition, potential study jobs have been identified at Allied Signal, a spark plug manufacturing facility in Fostoria, Ohio. The appropriate numbers of workers in low and high repetition jobs have been identified, and we expect to complete the analyses for medium repetition jobs in the next few weeks. Approximately 25 jobs that meet study criteria have been identified, videotaped, and documented. The panel of experts has reviewed the jobs and rated the repetition of these

jobs to determine their suitability for inclusion in the study. The medical survey of workers in jobs which qualify has been scheduled for mid–February, 1995. Additional ergonomic and medical surveys will need to be completed before more complete analyses can be performed and the overall goals and objectives of the study can be achieved.

Publications

Werner RA, Franzblau A, Johnston E: Comparison of Quantitative Vibrometry and Electrophysiological Assessment In Screening For Carpal Tunnel Syndrome Among Industrial Workers. Arch Phys Med Rehab, in press, 1994

Franzblau A, Werner RA, Albers JW, Grant CL, Olinski D, Johnston E: Workplace Surveillance For Carpal Tunnel Syndrome Using Hand Diagrams. J Occup Rehab, in press, 1994

Werner RA, Franzblau A, Johnston E: Comparison of Multiple Frequency Vibrometry Testing And Sensory Nerve Conduction Measures In Screening For Carpal Tunnel Syndrome In An Industrial Setting. Arch Phys Med Rehab, in press, 1994

Franzblau A, Lee EW, Schreck RM, D'Arcy JB, Santrock J, Levine SP: Absence of Formic Acid Accumulation in Urine Following Five Days of Methanol Exposure. Appl Occup Environ Hyg, October 1993

Musculoskeletal Disorders Among VDT Operators

Fredric E. Gerr, M.D.
Emory University
School of Public Health
Division of Environmental
and Occupational Health
Room 4047.1
1599 Clifton Road, N.E.
Atlanta, Georgia 30329

Grant Number: *1 R01 OH03160-01*
Start & End Dates: *09/30/94 – 09/29/99*
Funding Level: *$338,727 ($338,727 Cum)*

Importance to Occupational Safety and Health

An investigation will be made of the relationship between occupational use of video display terminals (VDTs) and (a) upper extremity musculoskeletal symptoms and (b) upper extremity musculoskeletal disorders in a prospective epidemiological study. This study is necessary because of substantial methodological shortcomings and inconsistent findings found in this literature. Specifically, few studies have used objective measures of ergonomic exposure or musculoskeletal health outcome. Virtually all currently available studies are cross–sectional in design, leading to bias by unmeasured selective attrition of affected workers and poor or biased estimates of past exposure. Furthermore, few have included measures of psychosocial stress as a potential risk factor for the outcome. The proposed study will be significant because it will *not* be subject to many of the methodological limitations of previous studies and would make a major contribution to knowledge about the effects of VDT use on musculoskeletal health. No previous study in the published literature has simultaneously incorporated objective measures of ergonomic exposure, objective assessment of musculoskeletal outcome, and ascertainment of occupational psychosocial stress. In addition, this is the first prospective study of musculoskeletal disorders among VDT operators in the United States. Given estimates that over 100 million VDTs will be in use in the United States by the year 2000, the public health importance of this issue is enormous.

Objectives

The specific aims are to determine the incidence of self–reported upper–extremity musculoskeletal symptoms and clinically verified upper–extremity disorders among VDT users and to estimate the effect of specific ergonomic, work practice, and occupational psychosocial stress variables on these outcomes. Secondary aims are to determine whether those with musculoskeletal symptoms or disorders are more likely to leave work requiring use of VDTs and to determine the distribution of time to experience of symptoms and time to experience of disorder among VDT users

Methodology

Approximately 550 subjects who use VDTs will be enrolled over a 3–year period. Direct measurements of workstation physical characteristics and worker posture will be performed at the worksite. Study participants will complete weekly VDT use diaries. Weekly symptoms diaries will be used to identify subjects who have experienced a change in symptoms. These subjects will be offered a standard clinical assessment, including a face–to–face interview, physical examination, and measures of median nerve distal motor latency. Occupational

psychosocial stress will be assessed by a standard questionnaire instrument.

Significant Findings

None to date.

Age & Cumulative Trauma Disorders in Garment Workers

Jacqueline Agnew, Ph.D.
Johns Hopkins University
School of Hygiene & Public Health
Department of Environmental Health Sciences, Rm. 7503
615 North Wolfe Street
Baltimore, Maryland 21205

Grant Number: *5 K01 OH00132-02*
Start & End Dates: *09/01/93 – 08/31/96*
Funding Level: *$54,000 ($108,000 Cum)*

Importance to Occupational Safety and Health

Cumulative trauma disorders (CTD) constitute a significant occupational health problem in the United States and other industrialized nations. It is generally agreed that CTDs are of multifactorial etiology; work–related and individual characteristics have been implicated by various studies. Specific ergonomic components of manual jobs are thought to be major risk factors for CTD. Although age has been included among the individual risk factors also thought to play a role in CTD incidence, the role that age plays in the etiology of CTDs among workers is relatively unexplored. Furthermore, it is unknown whether there is a potential interactive effect of increasing age and occupational ergonomic factors.

The role of age as a risk factor for occupational injuries or illness is of particular concern in view of the steadily increasing age of the U.S. work force. The rise in average age of workers has especially been noted in older U.S. industries of the manufacturing sector, such as the apparel industry. This study will therefore examine the association between age and CTD prevalence in a garment worker population exposed on the job to varying levels of ergonomic stresses. Improved understanding of risk factors for CTD will be useful in defining intervention strategies for the prevention of this major cause of worker impairment in occupational settings.

Objectives

This study will examine the association between age and CTD prevalence in garment workers, an industrial population with documented levels of ergonomic stresses and a high incidence of CTD. Ergonomic factors will be analyzed and the interaction between age and these factors will be assessed, controlling for other important confounding or effect–modifying variables.

The specific aims of this research are:

1. determine the prevalence of symptoms consistent with cumulative trauma disorders in a garment worker population by a cross–sectional survey.
2. perform observational analyses of individual workers' jobs to characterize ergonomic exposures.
3. develop variables that describe ergonomic risk factors associated with each worker's job, including a quantitative cumulative exposure variable.
4. evaluate potential interactive effects between age and ergonomic risk factors on CTD symptom prevalence.
5. establish baseline data for this cohort of garment workers in preparation for a future follow–up study.

Methodology

This study will be a cross–sectional survey of apparel industry workers. Participants in this study will be workers in a rainwear manufacturing industry located in the Maryland–Virginia area. Workers of two plants, totalling 566, will be invited to participate voluntarily. Workers of an additional plant from the same company participated in a recent study at a participation rate of 85%.

CTD symptom status, history of CTD diagnosis, age and other individual factors, as well as current ergonomic exposures will be determined concurrently. An on–site job analysis will be performed for each worker using a method of direct observation. An additional measure of ergonomic risk exposure, however, will incorporate retrospective work performance data to create a variable describing each worker's cumulative ergonomic stress experience. The relationships between CTD symptom prevalence, age, and measures of ergonomic exposure will be assessed. This will be done by stratifying data according to levels of ergonomic stressors and analyzing for interactive effects of age and ergonomic factors.

Significant Findings

None to date.

Occupational Physical Loads and Hip Osteoarthritis

Bradley Evanoff, M.D.
Washington University
School of Medicine
Department of General Internal Medicine
660 S. Euclid Avenue, Box 8005
St. Louis, Missouri 63110

Grant Number: *7 R03 OH03091-02*
Start & End Dates: *09/01/93 – 08/31/95*
Funding Level: *$21,375 ($42,685 Cum)*

Importance to Occupational Safety and Health

Osteoarthritis, a common degenerative joint disease, causes substantial morbidity with large attendant economic costs. Establishing an association between this disease and heavy physical loading may give further impetus to efforts aimed at reducing harmful physical exposures in the workplace.

Objectives

Occupational or recreational physical activities which lead to heavy static or dynamic physical loading of the hips may lead to osteoarthritis as a result of cumulative wear or microtrauma. This project will examine the relationship between lifetime occupational physical exposures and severe osteoarthritis of the hips.

Methodology

In this case–control study, both cases and controls will be recruited from a Health Maintenance Organization (HMO). Cases will be persons aged 50–70 undergoing hip replacement surgery for symptomatic primary (or idiopathic) osteoarthritis. Controls will be HMO members matched by age, sex, geographic catchment area, and length of HMO enrollment. All subjects will complete a self–administered exposure questionnaire which assesses lifetime recreational activities and physical activities at work. Telephone follow–up interviews will be performed with subjects unable to complete the questionnaire. Specific exposures which will be evaluated include lifting, jumping, climbing, whole–body vibration, and work postures. Recreational physical activities and subjects' body weight in different decades of life will be controlled for in analyzing the relationship between occupational physical exposures and hip osteoarthritis.

Significant Findings

Crude Univariate Odds Ratios show that some occupational exposures were more commonly reported by the cases than controls, suggesting that these exposures are associated with elevated risks of hip osteoarthritis. For women (n=222), exposures with significantly elevated OR included lifetime exposures to vibration (OR= 4.93, 95% c.i. 1.02 – 23.7), lifetime lifts of 25 pounds or more (OR = 1.93, 95% c.i. 1.13–3.3), and liftetime occupationally–related standing and walking (OR= 1.79, 95% c.i. 1.05–3.05). For men (n=177), significant exposures included lifetime jumping from one level to another (OR= 2.12, 95% c.i. 1.165–3.87), lifetime lifts of 10 pounds or more (OR= 2.23, 95% c.i. 1.222–4.07), lifts of 50 pounds or more (OR= 2.03, 95% c.i. 1.12–3.70), and total lifetime pounds lifted (OR= 1.85, 95% c.i. 1.02–3.36). Body mass index (BMI) at age 40 was also a significant risk factor for hip osteoarthritis for both sexes. Multivariate statistical analysis is now proceeding, to better assess the effects of occupational exposures while controlling for the effects of BMI and recreational activities.

Environmental Exposures and Risk Digestive Cancers

Ellen A. Eisen, Sc.D.
University of Massachusetts
Department of Work Environment
450 Aiken Street
Lowell, Massachusetts 01854

Grant Number: *5 R01 OH02953-02*
Start & End Dates: *09/01/93 – 08/31/95*
Funding Level: *$86,622 ($209,904 Cum)*

Importance to Occupational Safety and Health

NIOSH has estimated that 1.2 million workers in the U.S. engaged in metal grinding or machining operations are exposed to these fluids, while over 6 million workers are more generally exposed to the various components of the fluids. This research will permit better specification of the causal agents

necessary for an assessment of risk associated with metal working fluids in use today.

The applicants have found excesses of several digestive cancers of *a priori* interest in a large cohort of automobile workers with exposure to metal working fluids. Based on results of Poisson regression models, statistically significant relative risks of up to three fold were found between esophagus cancer and increasing levels of exposure of machining fluids used in the course of grinding operations. Evidence of weaker associations, between 1.5 and 2.0, were observed between grinding and stomach and pancreatic cancer. Strong evidence was also observed for associations between straight machining fluids and rectal and larynx cancer.

Objectives

The objective of this research project is to further examine the elevated risks for cancer of the esophagus, stomach, pancreas, colon and rectum in this cohort of autoworkers with exposure to machining fluids. A series of nested case–control analyses will be conducted. The objective of the study is to identify the specific agent(s) in the machining fluids which are causing the elevated cancers in this cohort.

Methodology

Conditional logistic regression models are being used to provide estimates of adjusted Odds Ratios (OR) for the major fluids types as well as specific components of the fluids such as sulfur, chlorine, selected metals, nitrosamines and biocides. Semi–quantitative estimates of exposure to sulfur and polycyclic aromatic hydrocarbons (PAH) are being developed in the proposed study and will be included in the exposure–response models.

Significant Findings

Results from the case–control study of esophageal cancer were presented at the Tenth International Symposium on Epidemiology in Occupational Health, September 1994, Como Italy. Odds ratios from conditional logistic regression suggest that there is a strong association with exposure to metal working fluid aerosol in grinding operations. The association appears to be strongest for soluble fluids. In the highest category of cumulative exposure, the OR reached 12.7 with a 95% confidence interval that excluded 1.0.

Accounting For Errors in Radiation Dose Estimates

Ethel S. Gilbert, Ph.D.
Battelle Memorial Institute
Pacific Northwest Laboratories
P.O. Box 999, MSIN P7-82
Richland, Washington 99352

Grant Number: *1 R01 OH03270-01*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$64,141 ($64,141 Cum)*

Importance to Occupational Safety and Health

A major objective of epidemiologic studies of nuclear workers is to provide a direct evaluation, based on data at low doses and dose rates, of the health risk estimates that serve as the basis for radiation protection standards. The results of these studies are considered by groups that set radiation protection standards, which are of benefit to workers employed in the nuclear industry. The research conducted under this grant will lead to analyses of data from epidemiologic studies of nuclear workers that account for errors in external radiation dose estimates, and thus increase the appropriateness and validity of this direct evaluation.

Objectives

The main objective of research conducted under this grant is to develop and apply methodology for accounting for errors in external radiation dose estimates in analyses of data from epidemiologic studies of nuclear workers. The analyses will aim to correct for bias in risk estimates resulting from both random and systematic errors in dose estimates, provide confidence limits that reflect additional uncertainty resulting from such errors, and, in the case of combined analyses of data from several studies, account for variation in the quality of dose estimates in different studies. The research will thus increase the appropriateness and validity of risk estimates based on a direct evaluation of data at low doses and dose rates.

Methodology

These objectives are accomplished as follows. First, an approach for quantifying biases and uncertainties in external dose estimates will be described in a journal article that focuses on the kind of information that is needed for adjustment of

epidemiologic dose–response analyses. A major contribution will be providing a feasible method of addressing sources of error that are correlated across workers and across different dosimeter readings for the same worker. This article will make methodology currently described in an extensive technical report accessible to a wider audience.

Second, an approach for accounting for uncertainty in systematic bias in doses will be developed and applied to data on Hanford workers. Under this task, the correction factors developed in the report noted in the first task will be applied, and computer simulations will be conducted to allow the estimated uncertainty in these factors to be reflected in confidence limits on risk estimates.

Third, a model will be developed for describing laboratory measurement errors in cumulative doses of workers. Finally, an approach for accounting for all random uncertainties in estimates of cumulative external dose used in nuclear worker studies will be developed and applied to data on Hanford workers. The proposed approach for handling laboratory uncertainties is generally similar to that recently used to account for random error in analyses of Japanese atomic bomb survivor data. For other types of uncertainties, a Berkson error model may be more appropriate.

Significant Findings

None to date.

Occupational Cancer Surveillance: New Approaches

G. Marie Swanson, Ph.D.
Michigan State University
Cancer Center
A-211 East Fee Hall
East Lansing, Michigan 48824

Grant Number: *5 R01 OH02067-09*
Start & End Dates: *09/28/84 – 09/29/94*
Funding Level: *$0 ($1,233,788 Cum)*

Importance to Occupational Safety and Health

The Occupational Cancer Incidence Surveillance System (OCISS) developed by this study will contribute to reduction of morbidity and mortality due to occupational risk factors for eleven types of cancer. It has developed both methodologic and substantive leads that contribute to prevention programs as well as to future research. Findings to date indicate that important new information is being gained regarding the occupational cancer risks of blacks and women, in particular. The significance of leads regarding occupational cancer risks among blacks and women cannot be overemphasized, as to date, more than 95% of occupational cancer epidemiology has included white males only. OCISS data have contributed to the methodology of occupational epidemiology, having demonstrated that occupational information derived from death certificates provides incomplete information about occupational cancer risk. Our studies also have demonstrated that direct information about cigarette smoking histories is essential to occupational cancer studies. Data from OCISS and related studies will ultimately be utilized to develop cancer prevention programs in the workplace.

Objectives

The specific aims of this study are:

1. To determine risks by occupation and industry for black and white males and females in conjunction with detailed tobacco smoking history, socioeconomic status, and age at diagnosis by cancer type.
2. To determine cancer risk within specific occupations in major local industries, such as automobile manufacturing, construction, machinery manufacturing, and primary ferrous metals manufacturing.
3. To investigate work–related cancer risk by race, gender, socioeconomic status, age at diagnosis, and cancer site among persons who have never smoked tobacco.
4. To develop new methodologic approaches for occupational epidemiology.

Methodology

Detailed work histories, tobacco use histories, health history, and demographics have been obtained by telephone interview. Cancer cases were selected from a population–based registry; population referents were selected by random digit dialing. Eleven cancer sites are included in this study. A total of 16,888 cancer patients were interviewed, including 6,349 with lung cancer, 2,443 with urinary bladder cancer, 3,211 with colon cancer, 1,428 with cancer of the rectum, 1,111 with cancer of the esophagus, 795 with stomach cancer, 540 with liver cancer, 570 with cutaneous melanoma, 178 with cancer of the salivary glands, and 127 with eye cancers. There were 3,913 population referents interviewed.

Significant Findings

Analysis of usual occupation and industry among lung cancer cases revealed excess risks for farmers, excavating and mining workers, driver sales, furnace workers, armed services personnel, truck drivers, mechanics, and painters; excess risks also were seen in the mining, farming, and primary ferrous metals manufacturing industries. Five of these occupations have exposure to diesel exhaust. Assessment of these risks separately for black and white men revealed that the risk among mechanics was restricted to black males and that the risk among armed services personnel was considerably higher in black males than among white males.

Analysis of urinary bladder cancer revealed excess risk among armed services personnel for white males and among automobile mechanics for black males. These data also reveal a higher attributable risk for cigarette smoking among bladder cancer than previously observed – 51 % . Industries with elevated risk among bladder cancer patients included wood manufacturing, drug manufacturing, hardware sales, and other transportation manufacturing.

An important contribution of this project to the discipline of occupational cancer epidemiology is the clear demonstration that men and women and blacks and whites have different workplace cancer risks, even when employed in the same occupations or industries. Our analyses of cancer risks among black and white men show that Odds Ratios are different for these two groups in nearly every occupation and industry. This is an important finding, indicating not only that blacks must be included in occupational cancer epidemiology studies, but also that they must be evaluated separately from white men.

A comprehensive analysis of occupational risks among women for each of the eleven cancer sites was conducted, with summary results presented to the International Conference on Women's Health: Occupation and Cancer in Baltimore on November 1, 1993. This conference was the first ever to focus upon occupational cancer risks among women and it was co–sponsored by the National Institute for Occupational Safety and Health, the National Cancer Institute, the National Institute of Environmental Health Sciences, and the NIH Office of Research on Women's Health. The OCISS results provided extensive information about specific methodologic issues that must be addressed in investigations of cancer risk in the workplace among women and provided new leads about several occupations and industries and their association with specific cancers. Methodologic issues include: (1) a large proportion of women in the age range of highest incidence of the cancers studied had a usual occupation of housewife (ranging from 54% among women diagnosed with cancer of the salivary gland to 76% for women diagnosed with eye tumors and 63% for population controls); (2) the small number of categories of either occupations or industries with even 10 cases or controls (there were 10 or more cases in 1 to 14 occupation groups and 0 to 12 industry groups across the eleven cancer sites); and (3) it is necessary to assess occupational risk among women ever employed in specific occupations or industries, as well as usual occupation and industry, since among those with housewife as usual occupation, 80% held some other job). These limitations are particularly striking, since OCISS includes much larger numbers of women than most occupational cancer studies—there are nearly 6,000 cancer cases and 2,000 controls who are women.

Even with these limitations, new leads regarding the association between specific occupations or industries and specific cancer sites were obtained. These include a four–fold increase among women in the computer manufacturing industry among those diagnosed with bladder cancer, a two–fold excess of women employed in restaurants among those diagnosed with cancer of the esophagus, a three–fold excess of women employed in hairdressing shops among those diagnosed with cancers of the salivary gland, an eight–fold elevation of women in the beverage manufacturing industry among those diagnosed with bladder cancer, a three–fold excess of women employed in food stores who were diagnosed with stomach cancer, and four–fold increases among both women employed in bus and truck services and in military service among those diagnosed with eye cancers. Although not statistically significant, there was a large excess of women ever employed as tool and die workers who were diagnosed with cancers of the salivary gland (OR=8.5).

Publications

Swanson GM, Burns PB: The Association Between Occupation, Industry and Cancer Among Women: A Study of Eleven Cancer Sites. Journal of Occupational Medicine, in press, 1994

Swanson GM, Lin C–S, Burns PB: Diversity in the Association Between Occupation and Lung Cancer Among Black and White Men. Cancer Epidemiology, Biomarkers, and Prevention 2(4):313–320, 1993

Burns PB, Swanson GM: Risk of Urinary Bladder Cancer Among Blacks and Whites: The Role of Cigarette Use and Occupation. Cancer Causes and Control 2:317–379, 1991

Burns PB, Swanson GM: The Occupational Cancer Incidence Surveillance Study (OCISS): Risk of Lung Cancer by Usual Occupation and Industry in the

Detroit Metropolitan Area. Am J Ind Med 19:655–671, 1991

Schade WJ, Swanson GM: A Comparison of Death Certificate Occupation and Industry Data with Lifetime Occupational Histories Obtained by Interview: Variations in the Accuracy of Death Certificate Entries. Am J Ind Med 14:121–136, 1988

Illis WR, Swanson GM, Satariano ER, Schwartz AG: Summary Measures of Occupational History. A Comparison of Latest Occupation and Industry with Usual Occupation and Industry. Am J Public Health 77(12):1532–1534, 1987

Swanson GM, Schwartz AG, Brown KL: Population–Based Occupational Cancer Incidence Surveillance – Utilization of the Telephone Interview. J Occup Med 27(6):439–444, 1985

Swanson GM, Schwartz AG, Burrows RW: An Assessment of Occupation and Industry Data from Death Certificates and Hospital Medical Records for Population–Based Cancer Surveillance. Am J Public Health 74(5):464–467, 1984

Mortality Among Female Nuclear Weapons Workers

Gregg S. Wilkinson, Ph.D.
University of Texas
School of Medicine
Department of Epidemiology
700 Strand, Ewing Hall
Galveston, Texas 77555-1147

Grant Number: *1 R01 OH03274-01*
Start & End Dates: *09/30/94 – 09/29/96*
Funding Level: *$240,739 ($240,739 Cum)*

Importance to Occupational Safety and Health

Elevated cancer mortality and cancer incidence for several sites (breast, ovary, uterus, thyroid, lung and bronchus, melanoma, as well as leukemia for both sexes) have been reported for a number of nuclear worker cohorts, but these results have been inconsistent. Several of these tumor sites are known to be radiation sensitive. Female nuclear workers may be at increased risk for these and other health–related endpoints due to occupational exposures to radioactive hazards. In recent years, significant increases have been observed among U.S. women for breast cancer and in cancers of the lung and bronchus (both of which are radiation sensitive organs). At the same time, a small increase has been observed in ovarian cancer, a disease which is frequently fatal and difficult to diagnose. Thus, an investigation of nuclear workers such as this is likely to provide answers to public concerns regarding the long–term effects of low dose exposures to ionizing radiation and other environmental hazards that can be used to estimate risks experienced by the general population. These findings may then be used to set realistic radiation dose standards for females who are occupationally exposed to ionizing radiation and nonradiation hazards.

Objectives

Although women have been employed in the nuclear weapons industry since its inception, little is known about the potential health risks women may experience as a result of work–related exposures. To address the lack of information regarding the health of female nuclear workers, we will conduct a retrospective cohort mortality study of a combined cohort of women who have been employed at 12 of the facilities comprising the U.S. nuclear weapons complex: Los Alamos National Laboratory (LANL), Zia Company (prime contractor to LANL until about 1985), Rocky Flats Plant (RFP), Mound Facility, Hanford Works, Savannah River Plant (SRP), Oak Ridge Y–12, Oak Ridge X–10, Oak Ridge K–25, Fernald Plant, Linde Plant and the Pantex Plant.

The long–term objectives of this research are to: (1) develop risk estimates of neoplastic and non–neoplastic diseases for low dose rates of external and internal forms of ionizing radiation that are valid, precise and appropriate for women; (2) determine whether separate or combined exposures to internal alpha emitters, external penetrating radiation, or nonradioactive hazards increase the relative risk of mortality; (3) conduct nested case–control or case–cohort studies that assess the impact of multiple exposures and control for confounders that cannot be measured in cohort studies; 4) investigate morbidity for conditions that are unlikely to result in death but that may be associated with workplace exposures.

The specific aims of this project are to: (1) combine data on female employees from the aforementioned 12 cohorts of DOE nuclear weapons workers; (2) calculate individual dose or exposure estimates to radiation and non–radiation hazards encountered in the workplace; (3) estimate the relative risk of mortality for neoplastic and other diseases that may be associated with exposures to radiation and nonradiation hazards; (4) estimate the range of uncertainty associated with these risk estimates; (5) assess the feasibility of conducting

nested case–control studies for health endpoints that are elevated among female nuclear workers.

Methodology

An historical cohort mortality study of all women employed at 12 nuclear weapons facilities will be conducted. Data on demographic characteristics, vital status, exposures to external and internal ionizing radiation, and job histories for workers at these 12 facilities will be obtained from the relevant contractors through NIOSH. Death certificates will also be obtained and coded to the 9th revision of the ICDA for underlying cause of death, contributing cause of death and any mention of cancer.

Data regarding external and internal radiation exposures will be obtained from computerized health physics records. Cumulative doses to external radiation will be calculated for total penetrating radiation for each study subject who has been monitored. Internal exposures to radioisotopes of plutonium, americium, polonium and uranium will be considered separately from external exposures. Uptakes of specific internal emitters will be employed in the analyses whenever possible. Exposures to nonradiation hazards will be estimated by means of constructing a relevant job–exposure matrix. Such a matrix will take into account the type of job, potential exposures and length employed in each job.

Analyses will be conducted comparing mortality among female workers with mortality rates for U.S. females while adjusting for age, race and calendar year. The primary emphasis will, however, be placed on internal comparisons between exposed and unexposed workers, monitored and unmonitored workers, and workers with low or zero doses or exposure levels with workers with higher dose or exposure levels.

Significant Findings

None to date.

General Mortality & Cancer Incidence in Florida Pesticide Applicators

Lora E. Fleming, M.D.
University of Miami
School of Medicine
Department of Epidemiology & Public Health
P.O. Box 016069 (R-669)
Miami, Florida 33101

Grant Number: *5 K01 OH00125-02*
Start & End Dates: *09/30/93 – 09/29/96*
Funding Level: *$54,000 ($107,832 Cum)*

Importance to Occupational Safety and Health

Pesticides are chemicals used since ancient times to destroy or control pests. Although the primary hazard to humans associated with pesticide exposure is acute poisoning, there has been considerable concern surrounding the possibility of pesticide carcinogenicity and other chronic health effects in humans. The pesticides which have generated the greatest concern for possible carcinogenicity include the herbicides (chlorophenoxy acids and chlorophenols), heavy metals (especially arsenicals), petroleum products (polyaromatic hydrocarbons), organochlorines, and fumigation agents (EDB, MethylBromide). This is important given the huge volume of pesticides now used throughout the world in agriculture, industry and in homes; in addition, there is concern with regards to the environmental and food residue contamination from pesticides which could lead to mass chronic low–level exposure.

Under EPA since 1970, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) has required that persons who buy or use restricted–use pesticides must be certified as competent pesticide applicators or must be directly supervised by a certified applicator. The State of Florida has computerized records of over 16,000 certified pest applicators for over 10 years and paper records for up to 25 years. In addition, as a highly agricultural and tropical state, Florida is a major pesticide user.

Objectives

The proposed study will be retrospective cohort analyses of the cancer incidence and general mortality, with a nested (synthetic) case control study of cancer incidence, among a cohort of the Florida certified pesticide applicators with occupational pesticide exposure in Florida for at least 20 years.

Because the greatest exposures to pesticides occur in the occupational setting, this study should add to the body of knowledge concerned with pesticides and their health effects in humans. Results from the study (i.e. specific cancer and other mortality rates, protective equipment use, and other risk factors) can be incorporated into existing mandatory educational programs of the Florida Department of Agriculture Bureau of Pesticides to prevent future illness in this and similar workforces.

Methodology

Cancer incidence since 1980 will be obtained by linking the data from the pest applicator licenses with the Florida Cancer Data System (FCDS). Mortality information will be obtained by linkage with the Death Tapes of the Florida Vital Statistics from 1970. In a nested (synthetic) case control study, exposure and relevant risk behavior data will be sought through the distribution of a questionnaire to selected cases of incident cases of cancer and a random sample of matched applicators as controls. Information concerning specific pesticide use, race/ethnic status, and possible confounding factors (such as tobacco use) will be obtained. Analyses will evaluate total cancer incidence and specific cancer incidences compared to age and sex adjusted state and national rates. In addition, risks for specific cancers associated with pesticide exposure will be evaluated, controlling for confounding variables such as tobacco use and using an internal cohort control group. Finally, cause specific mortality and cancer incidence experience of this cohort with national and internal comparisons will be evaluated.

Significant Findings

There are 37,303 licensed applicators since 1970 in this database with the following presently known gender and race/ethnic distribution.

	Non Hispanic	Hispanic	Total
Unknown Sex	981	5	986
Female	3951	129	4080
Male	30920	1317	32237
	35852	1451	37303

Using only Social Security Number and Name for data linkage, over 800 incident cases of cancer have been ascertained in this cohort. Further analyses are pending.

Workplace Assault-Related Injuries: Incidence and Risk

Jess F. Kraus, Ph.D.
University of California
School of Public Health
Department of Epidemiology
10833 Le Conte Avenue
Los Angeles, California 90024-1772

Grant Number: *5 R01 OH02872-03*
Start & End Dates: *09/30/91 – 09/29/95*
Funding Level: *$0 ($547,337 Cum)*

Importance to Occupational Safety and Health

The Occupational Safety and Homicide Act was created in order to "assure as far as possible every working man and woman....safe and healthful working conditions and to preserve our human resources." Though occupational injury has changed significantly since the enactment of the OSHA Act by Congress, no specific portions of the act deal directly with intentional injury in the workplace. The potential for workplace violence, an increasing public health issue, threatens many employers and employees.

Occupational homicides account for 7,000 to 13,000 deaths per year, based on estimates from various data sources. Occupational injuries affect minority groups in high–risk occupations disproportionately. Differences between men and women at work are also important: except for construction, transportation and manufacturing, homicide has been shown to be the leading external cause of injury deaths for females in all industries. This may be especially true for women in sales, clerking or management of food stores, bars and cafes.

Employees of high–risk industries previously identified (convenience food stores, liquor stores, discount retail stores, gasoline service stations, eating and drinking establishments, and taxicab companies) continue to bear the brunt of assault–related injuries and fatalities. Most of the research in this area has focused on workplace homicides, yet the magnitude of non–fatal assault–related injuries has not been assessed. Thus far, no specific risk factors or standards on preventive strategies for these industries have been developed.

Objectives

The overall objective of the proposed research is to understand the magnitude and identify the determinants of workplace assault–related injuries. To accomplish this objective, two specific aims have been undertaken: (1) to estimate the average incidence rates of fatal and nonfatal work–related assault injuries in selected California communities between January 1993 and June 1994; and (2) to identify individual occupational and environmental predictors of fatal and non–fatal assault–related injuries in selected high–risk occupations in the same seven California counties.

Methodology

The study design consists of two components:

1. Incidence determination and rate estimation based on a number of sociodemographic, occupational, environmental and industrial group parameters; and
2. A case–control study to identify risk factors for fatal and non–fatal assaultive injury.

The study encompasses most of the conurban areas within the counties of Sacramento, Alameda, Santa Clara, Los Angeles, Riverside, San Bernardino and San Diego, California. The scope of our collaborative network includes police, sheriff and coroner's departments, Cal–OSHA, and the State Compensation Insurance Fund. This network of data sources serves an important role in linking health information to allow more precise estimates of work–related assaults and homicides.

A detailed survey instrument has been used to assess factors surrounding assault–related violent incidents resulting in mild to severe injuries or fatalities. The survey has been implemented in all seven counties by field researchers, each of whom has received extensive training in survey administration and case– and control–finding protocols. Field research staff has been equipped with a portfolio that contains letters of support from various members of the state legislature and from Cal–OSHA. Additionally, Cal–OSHA representatives invite field staff to join their official on–site investigations whenever appropriate.

Case ascertainment procedures have involved multiple local, state, and federal agencies. For finding appropriate controls, a computerized database of business names, addresses, phone numbers, and contact persons across an identical spectrum of industries has been utilized. Language barriers have been surmounted by use of specially trained translators. However, problems of participation continue as well as unavoidable situations such as when a business closes permanently following a violent incident.

Significant Findings

None to date.

Case-Control Study of Sawmill Injuries in Maine

Laura Punnett, Sc.D.
University of Massachusetts
Department of Work Environment
One University Avenue
Lowell, Massachusetts 01854

Grant Number: *5 R01 OH02741-03*
Start & End Dates: *06/01/90 – 08/31/94*
Funding Level: *$0 ($167,775 Cum)*

Importance to Occupational Safety and Health

Lumber and wood products processing (SIC 24) is the second largest industry in Maine, with about 13% of the manufacturing work force. In 1987, the incidence of OSHA recordable injuries and illness in sawing and related mills (SIC 242–249) was 29.1 cases per 100 workers, more than twice the average statewide rate, with about one–half of all injuries resulting in lost work time.

A number of specific safety and ergonomic hazards have been identified in Maine sawmills. These include unguarded floor openings; dangerous and improperly guarded equipment; manual materials handling of logs and other heavy items; unshielded hot surfaces; and excessive noise. However, the conditions under which they actually result in injury have not been well defined by epidemiologic analysis. The sparse literature is primarily descriptive, with little insight into causal factors that could be preventable, particularly by means of ergonomic or safety engineering controls.

Objectives

The primary objective of the proposed research project was to identify the wood product processing activities, equipment, and working conditions associated with increased risk of acute traumatic events and musculoskeletal injuries, to identify opportunities for preventive interventions.

Methodology

A population–based case–control study has been conducted of risk factors for occupational injury in the Maine wood products industry (SIC 242–249). Cases were identified prospectively from employers' First Reports of Injury. A potential case was eligible if the injury occurred on the employer's premises and was not a highway motor vehicle accident. Controls were randomly selected from employee lists provided by employers or from membership lists provided by union locals. Managers and office employees (clerical, sales, etc.) were excluded. Most subjects were interviewed by telephone at their homes, although one company made workers available during work hours.

A total of 157 cases and 251 controls were interviewed to obtain information on demographics, work history, usual production tasks, characteristics of the equipment, tools and product, and other features of the work environment. For cases, this information was obtained regarding the specific activities performed on a typical work day and at the time of the injury. Controls were asked about their work activities on the last full day worked and on the day of a "near miss," if any. Exposure items included general working conditions and environment (machine pacing, piece rate wages, overtime, shift work, noise, thermal environment, illumination) and specific ergonomic features (tool weight, work pace, heavy lifting, and volume of production output). Subjects were also asked about workplace health and safety programs such as lockout/tagout, worker training or labor–management committees. Cross–product odds ratios were computed to estimate the crude risks associated with specific factors in the task and work environment. Multivariate logistic regression modeling was used to control for potential confounding.

Some supplementary exposure data was sought to attempt to validate the interview information. Information on workplace characteristics was obtained from three supplementary databases and compared with corresponding interview data. In addition, three participating workplaces were visited in order to evaluate working conditions; these observation data have not yet been analyzed.

Significant Findings

A number of work environment features were associated with injury occurrence. Cases were more likely than controls to be employed in SIC 242 (sawmills) versus 249 (wood products other than structural lumber, buildings or containers); to process hard wood; to work in machine–paced jobs; to be exposed to dangerous work methods and materials, higher noise levels and work pace, higher lifting demands and more frequent postural stress; and to experience lower decision latitude and social support at work. Cases' ratings of conditions on the day of the injury were not markedly different from those for their usual jobs. Cases reported more cluttered or slippery floor conditions, greater likelihood of a staffing problem, and less use of any personal protective equipment than the controls.

Within sub–groups by job title, there were also differences in workload and exposures. Among workers who routinely used tools and equipment, cases rated their tools higher in weight, force required to operate, and vibration transmitted to the hand than controls. Cases also reported that they handled heavier loads when feeding stock to machinery. Among manual material handlers, the cases reported higher weights for "the heaviest load lifted in a typical day" and total pounds lifted per day (load weights times load frequencies). Among inspection and packaging workers, the cases performed these tasks about 2 hours more and handled about five times as many items, on average, per day.

Job training for cases had been less likely to address occupational health and safety (OHS). Cases were also less likely to have received any targeted OHS training, although, among those who had, they had received more total hours of training than controls. Lockout/tagout programs were much less common in the workplaces of cases. Regularly meeting safety committees and posted emergency procedures were also significantly less likely in the workplaces of cases than of controls.

The three strongest risk factors in the logistic regression models were processing hard wood, employment in SIC 242, and high physical demands. Decision latitude and social support appeared to have small protective effects. The other variables that were significantly associated with injury occurrence in multivariate analyses were being male, having one year or less on the current job, inability to take a break when tired, and a lockout/tagout program in effect in the plant. The same set of risk factors did not explain as much of the variance in either sub–set of injury types. For the acute incidents, the best–fit model included hard wood, gender, high physical effort, one year or less on the job, a lockout/tagout program and social support; for overexertions the selected risk factors were hard wood, high physical effort, one year or less on the job, inability to take a break, and social support.

These results may be limited somewhat by the potential for non–representative participation of workplaces and of individuals. In particular, plants that contributed cases only were more likely to be in SIC 242 and to process hard wood exclusively than plants that contributed both cases and controls. However, the associations with physical workload,

work organization features, and administrative control programs are judged unlikely to be artifacts of any selection processes.

Occupational Injuries Among Older Workers

Craig S. Zwerling, Ph.D.
University of Iowa
School of Medicine
Department of Preventive Medicine
100 Oakdale Campus, 124 AMRF
Iowa City, Iowa 52242-5000

Grant Number: *1 K01 OHAG00150-01*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$52,685 ($52,685 Cum)*

Importance to Occupational Safety and Health

In the decades to come, the aging of the baby boomers will lead to the graying of the U.S. workforce: by 2005, the mean age of the workforce will have increased by 5 years. In order to maintain productivity, we will need to ask more from older workers. However, there are already data which suggest that older workers are at increased risks for serious occupational injuries. As the workforce ages in the beginning of the 21st century, the problem of occupational injuries among older workers will loom increasingly large. This project will carry out a secondary analysis of the sample of the U.S. population developed for the Health and Retirement Survey (HRS) by the Institute of Social Research at the University of Michigan. This analysis will estimate the risk for occupational injury among older workers and identify those risk factors associated with occupational injuries among older workers. It is expected that the results of this project will define high risk work activities and subgroups of older workers at special risk for occupational injury. This information will allow the design of targeted interventions to prevent these injuries.

Objectives

This project aims to:

- Evaluate the validity of self–reported occupational injury data from the 1992 HRS and the utility of this variable from multi–variate modelling.
- Model occupational injuries among older workers using the 1992 HRS data with special attention to – distribution and risk factors among older workers – the risk and occupational injuries among older workers with disabilities – the differences in occupational injury experience among whites, african–americans, and hispanics – the risks and consequences of occupational injury by gender.
- Assess the stability of risk factors for occupational injury among older workers by comparing the HRS data from 1994 with the HRS data from 1992.
- Use the occupational injury data of the HRS from 1994 to carry out a perspective validation of the multivariate model developed on the cross sectional data of 1992.

Methodology

The HRS is a survey of US households that include one or more persons born between 1931 and 1941. The intention of the HRS is to follow this cohort of 9,756 representative Americans aged between 51 and 61 years as they get older and retire. Secondary analysis of the HRS data will investigate the 6,829 members of this cohort who were employed at the beginning of this study.

The HRS data set includes a wide variety of information on this population including their demographic status, their occupational injury, a variety of personal characteristics including alcohol consumption and disability, their functional status, evaluations of their own health status, their satisfaction with various aspects of their life, their requirements of their job in terms of physical and mental efforts, and whether or not they have suffered an occupational injury in the last year.

The analytic plan for the project is to first validate the response to the occupational injury question using the data of the most recent injury to estimate the decrease in injury recalls and function of time. Next, the risk factors most associated with occupational injury in this cohort of older workers will be evaluated on the cross sectional data from 1992. Finally, the results of this exploratory modelling will be validated using the results of the data provided in the 1994 follow–up survey of the HRS population.

Significant Findings

None to date.

Ergonomic Study of Fire Service Musculoskeletal Injuries

Karen M. Conrad, Ph.D.
University of Illinois at Chicago
Public Health Nursing (M/C 802)
845 South Damen Avenue
Chicago, Illinois 60612-7350

Grant Number: *1 R03 OH03123-01A1*
Start & End Dates: *09/30/94 – 09/29/96*
Funding Level: *$38,876 ($38,876 Cum)*

Importance to Occupational Safety and Health

Musculoskeletal injuries account for almost half of all injuries among the one million firefighters in this country. These injuries result in excessive absenteeism, costly medical claims, and disability. The present study will respond to two research needs in dealing with this costly problem.

First, there have been only a handful of studies on musculoskeletal injuries in the fire service. The present study will provide much-needed basic information about underlying causes of the problem. Second, the handful of studies conducted on musculoskeletal injuries in the fire service have investigated injury only in relation to fire suppression tasks. However, a growing proportion of fire service personnel are cross-trained for paramedic tasks as well as firefighting. Fire departments are cross-training because, for many of them, over 50% of the calls are for emergency medical services rather than for fire suppression. The present study will investigate both paramedic and fire suppression tasks, but emphasize paramedic tasks.

Objectives

There is a need to examine the firefighter/paramedic job from an ergonomic perspective and describe the biomechanical stressors inherent in the job. These stressors include lifting heavy objects, twisting, stretching, and reaching. The present study will identify the most physically strenuous job tasks of firefighter/paramedics. Then, using task analyses, the present study will quantify the static and dynamic trunk motion parameters and workplace parameters relevant to the identified tasks. Particular attention will be paid to those tasks that contribute to back injuries.

The study will conclude by generating hypotheses to reduce musculoskeletal stressors in the identified tasks. These hypotheses will encompass methods of task accomplishment and equipment design, the validity of which can be determined in subsequent laboratory studies.

This study is the ergonomic component of a program of research leading to the development of a series of integrated preventive interventions to reduce the severity and frequency of musculoskeletal injuries in the fire service.

Methodology

The study population is 712 firefighter/paramedics from 17 suburban fire departments. The content domain of frequently performed, very physically strenuous tasks will be identified in two stages. An initial list of such tasks will be identified through structured interviews with a random sample of 50 firefighter/paramedics. Then, a list of the top 20 tasks identified in the interviews will be validated through a survey mailed to a random sample of 256 firefighter/paramedics. The top 10 most frequently performed, very physically strenuous tasks identified in the survey will then be simulated. Each task will be performed by 10 individual firefighter/paramedics who volunteer to participate. Video data will be used to determine gross postures and movement ranges. More detailed kinematic data will be obtained for the torso using the Lumbar Motion Monitor. Task analyses will be performed in two stages. The first stage will focus on task decomposition. The second stage will describe the tasks from a biomechanical perspective focusing on the postures, their duration, the range of motion, and the forces exerted for each body part.

Significant Findings

None to date.

Petrochemical Exposures and Reproductive Outcomes

David C. Christiani, M.D.
Harvard University
School of Public Health
Department of Environmental Health
665 Huntington Avenue
Boston, Massachusetts 02115

Grant Number: *1 R01 OH03027-01A1*
Start & End Dates: *02/01/94 – 01/31/98*
Funding Level: *$333,068 ($333,068 Cum)*

Importance to Occupational Safety and Health

1. This prospective study using recent, improved, more specific assays, aimed at examining the risk of infertility and sub–clinical miscarriage due to occupational or environmental exposures, will provide sensitive, accurate and unbiased estimates of the effects of exposure.
2. Benzene, toluene, and styrene are the major potential toxic chemicals in the petrochemical industry under study. Thus, it is possible to study a large cohort of reproductive age women workers with different duration and intensity of exposures to a variety of chemicals and air pollutants generated by the oil refinery. An exposure–response association can be examined from this large cohort of women, which will provide additional evidence for causation. In addition, we will collect and analyze information on occupational exposure from both wives and husbands, data which was not frequently collected in previous research. The study will lead to better protection for both female and male workers exposed to these agents.
3. This study will provide the accurate and precise exposure assessment for exposure agents and levels. Exposure information will be obtained through occupational records, questionnaire, measurements of air samples, and individual time–activity data.
4. From this large cohort of women, daily urine samples collected for each cycle from enrollment will allow to the assessment not only the reproductive health effects of exposures to aromatic compounds, but also the association with other environmental and occupational agents such as active and passive smoking, indoor coal combustion, diet, cooking oil fumes, alcohol, lifting, and rotating shiftwork.
5. This study represents a collaboration between Harvard Occupational Health Program and Beijing Medical University. Such a collaboration should produce unique and significant results in the study of environmental exposure and human reproductive health, and can become a paradigm for developing other collaborative research projects in environmental and occupational epidemiology between U.S. and Chinese investigators. We believe that this will be a landmark study of human pregnancy.

Objectives

The study is structured to address the following hypotheses:

1. Occupational exposure of women workers to benzene, toluene, and styrene is associated with adverse reproductive outcomes. The end points include menstrual problems, time to conception, fecundability, spontaneous abortion, prematurity, low birthweight, malformation and still birth.
2. There is an exposure–response relationship between chronic and acute (peak) exposure to benzene, toluene, and styrene and the risk of adverse reproductive outcomes.
3. Exposure to those chemicals before conception and during each trimester of pregnancy is associated with different adverse reproductive outcomes, i.e. earlier exposure is likely to affect fecundability and spontaneous abortion, while later exposure may result in prematurity and low birthweight.
4. There is an interactive effect of benzene and toluene on reproductive outcomes.
5. Adverse reproductive outcomes are also associated with personal factors including active and passive smoking, indoor coal combustion, cooking oil fumes, alcohol consumption, diet, use of herbal medicines, heavy lifting, body position during work, rotating shiftwork, and physical activities outside workplace. To the degree detectable, these personal factors will be accounted for confounders in the testing of hypothesis a, b, c and d.

Methodology

The study takes advantage of the current family planning policy in China. A woman becomes eligible for study upon receipt of permission to have a child. A base line survey of all the enrolled women and their husbands is conducted at a local central office. Those not attending the central office are seen in their homes. A standardized questionnaire is administered by trained interviewers to collect information about reproductive history, a detailed history of occupational exposure of these women and their spouses, demographic characteristics and potential confounding variables such as active and passive smoking, indoor coal combustion, cooking oil fumes, alcohol consumption, diet, use of herbal medicines, heavy lifting, body position during work, rotating shiftwork, and physical activities outside workplace. Weight and height are measured by standard methods.

In addition to providing baseline information on menstrual histories, subjects will provide daily morning urine specimens for 12 months, or until a pregnancy has been confirmed clinically. All samples are collected by the subjects in 20 ml double–seal vials provided by the investigators. Subjects deliver their vials daily to one of several refrigerators provided at the workplace. Samples are then transported to the laboratory, aliquoted and stored at –20 °C. Samples will be assayed for β–hCG to

determine "sub-clinical miscarriage" and fecundability. In addition, each woman is requested to keep a diary for her menstrual period, symptoms, sexual activity, general health status, medication, cigarettes smoking, alcohol consumption, diet and physical activity.

If a woman reports a missed or late period, or early signs/symptoms of pregnancy, she is instructed to go to the designated hospitals for a clinical check-up and a lab assay of hCG in urine. Once a woman is confirmed to be pregnant, she receives regular prenatal care, delivery services and postnatal care, and is followed by staff at the designated hospitals. For normal pregnancies, clinical visits are scheduled according to standard clinical guidelines. For complicated pregnancies, clinical visits are scheduled as needed. At each visit, length of gestation, blood pressure, weight gain, fundal height, pregnancy complications, medications, lab tests and examinations, and pregnancy outcomes are recorded. Detailed information on changes of jobs, working hours, occupational exposures, active and passive smoking status, diet, sources of indoor air pollutants, average time spent for daily transportation and household work is also obtained. If a woman gives a live birth, the newborn's sex, gestational age, birth weight, and crown to heel length is recorded.

Significant Findings

None to date.

Menstrual Function and Physical and Mental Job Stress

Maureen C. Hatch, Ph.D.
Columbia University
School of Public Health
Division of Epidemiology
600 West 168th Street
New York, New York 10032

Grant Number: *5 R01 OH02885-03*
Start & End Dates: *08/01/91 – 07/31/94*
Funding Level: *$0 ($495,099 Cum)*

Importance to Occupational Safety and Health

This project was designed to evaluate the menstrual cycle as a marker of reproductive physiology among nonpregnant workers whose reproductive function and risk of hormone-related chronic disease may be affected by the work environment. The particular focus of the study is on job stress, both physical and mental, and on stress-related behaviors like smoking, which could in theory perturb menstrual function. This would be important since stress is a pervasive occupational exposure and one that potentially can be prevented.

Objectives

The primary objective of the research was to determine whether levels of stress women experience on the job can lead to alterations in ovarian function. The study also provided an opportunity to evaluate the feasibility of using menstrual function to identify work-related reproductive disorders among nonpregnant women.

Methodology

We followed 100 female nurses recruited from a New York City hospital for a total of three consecutive menstrual cycles. Nurses were selected because previous research showed them to have high job stress levels. Each subject was asked to maintain a structured daily diary, to record basal body temperature, and to collect a small aliquot of urine daily. Urine samples are being analyzed for estrogen and progesterone metabolites, luteinizing hormone, follicle-stimulating hormone and creatinine in order to evaluate follicular, ovulatory and luteal function. Also, salivary samples were obtained during the mid-follicular and mid-luteal stages of the cycle for measurement of cortisol, a physiologic indicator of stress. Results of the hormone analyses are currently pending. Findings related to self-reported cycle characteristics are presented below.

Significant Findings

1. The protocol for this menstrual cycle study, involving three cycles of observation with menstrual diaries and daily collection of urine samples, proved to be feasible and acceptable, at least in this population. The participation rate among eligible nurses was quite good, with perceived salience and monetary compensation being the most important incentives. Participants completed all three study cycles and compliance with protocol was excellent (<2% missing data for any component). Requirements of the fieldwork were within normal bounds, although recruitment and assembly of urine collection kits both proved to be time-consuming. The protocol produced a rich data base with information on multiple endpoints. Overall, longitudinal menstrual studies would appear to hold promise as a means of evaluating the reproductive toxicity of exposures to premenopausal women workers.

2. The mean age (and range) of the 100 subjects in this sample was 34.2 years (22–52 years). Participants were predominantly white (75%) and well–educated. Over 41% were currently married or living as married. Mean cycle length among participants was 28.6 days with a range from 19 to 77 days. Based on the study definition, 11% of the 100 participants were classified as having cycles of variable length (>7 day difference across cycles). Of the 300 cycles contributed by study participants, 20% were classified as short (≤25 days) and 10% were classified as long (≥33 days).
3. An interesting finding with relevance for future menstrual research, is that there was virtually no within–woman variability in cycle characteristics over the period of follow–up. In addition, there was scant variability in a woman's exposure pattern. The main source of variability was therefore between women rather than within women, simplifying the statistical analysis and increasing its ability to detect significant differences.
4. Job stress was measured using relevant subscales from the NIOSH job stress questionnaire (role ambiguity, role conflict, workload, variance in workload, job satisfaction), with responses scored from 0 to 5. The mean overall level of job stress in the sample was 2.5 (range 1.2–3.7); workload and variance in workload were the primary sources of stress (mean scores of 3.6 and 3.2 respectively compared with means ≤2 for all other sources). Subjects reported very little stress outside of work.
5. Multivariate logistic regression analysis showed an association between long cycles and high job stress scores (odds ratio (OR) = 3.0, 95% confidence interval (CI) 1.0, 9.0), which did not vary by source of stress. However, results did vary when cycles were stratified by whether or not the woman reported any effort at stress management. The association between job stress and long cycles was found to be stronger when there was no stress reduction activity (OR = 5.3, 95% CI 0.6, 44.3), than when there was (OR = 2.2, 95% CI 0.6, 8.1), a pattern that suggests the relationship between stress and longer cycles is real. Job stress was not found to be associated with cycle variability (1.0 (0.2, 4.1)).
6. Physical as well as mental job stress proved to be associated with long cycles. In this sample of nurses, the adjusted odds ratio for exertion on the job (being "on the move" >40% of the time) was 2.2 (95% CI 1.0, 4.9). However, physical job stress appeared to reduce the risk of cycle variability (OR = 0.4, 95% C 0.1, 1.5). Study participants reported low levels of leisure time exercise, perhaps because the physical demands of the job are reasonably high.
7. Among the nurses, cigarette smoking, particularly in heavy amounts (20+ cigarettes a day), was fairly uncommon. However, smoking >1 cigarette per day did tend to be associated with short cycles (OR = 1.5, 95% CI 0.7, 3.3) and with cycle variability (OR = 2.4, 95% CI = 0.5, 11.0). A stronger association with cycle variability was found for alcohol consumption (>1 drink per day); the adjusted OR was 3.8 (95% CI 1.0, 15.0). In addition, there was a trend to long cycles among regular drinkers (OR = 1.6, 95% CI 0.7, 3.7). Caffeine consumption was not associated with cycle characteristics. Exposure to antineoplastics, while of interest, was too uncommon to study.
8. Although stress in the work place exists and may be a common exposure among women workers, data linking job stress to health endpoints have been lacking. The results of this longitudinal study show a moderate to strong association between physical and mental job stress and menstrual cycle length in a sample of otherwise healthy, well–educated women. Associations were also detected between stress–related behaviors and menstrual cycle characteristics. A pattern of unusually long or short menstrual cycles clearly indicates some hormonal perturbation, with possible ramifications for women's chronic disease risk as well as for fertility. Data collected in the course of this study will ultimately allow us to describe the hormonal profile of long and short cycle intervals – something that has not been done previously. Our experience suggests that menstrual cycle studies are both feasible and informative, and deserve a place in research programs dealing with women's health.

Reproductive Health of Female Migrant Farm Workers

Marc B. Schenker, M.D.
University of California
Institute of Environmental Health Research
Department of Occupational
and Environmental Medicine
Davis, California 95616

Grant Number: *5 R03 OH03000-02*
Start & End Dates: *09/30/92 – 09/29/94*
Funding Level: *$0 ($35,670 Cum)*

Importance to Occupational Safety and Health

Migrant farmworkers, especially female farmworkers, have been one of the most underserved and understudied occupational populations in the United States. Occupational risks and hazards associated with agricultural work are ranked among the highest in the United States. Among adverse health outcomes due to occupational exposures, adverse reproductive health outcomes among women in the migrant farm labor force have been studied very little. Female farmworkers experience potential occupational hazards, such as prolonged standing and bending when working at conveyor belts or harvesting, long shifts, overexertion, and fatigue, as well as potential exposure to pesticides, climatic extremes, and insufficient toilet facilities in the fields (which may lead to infrequent use of the toilet facilities and thus may in turn result in urinary infections that can lead to adverse reproductive outcomes). In addition, the low socio–economic status, poor access to health care, and migratory lifestyle of these workers, as well as their often undocumented stay, contribute to the fact that high quality data about the health of farmworkers, specifically female farmworkers and their offspring, are almost non–existent.

Objectives

The primary objective of this cross–sectional hypothesis–generating pilot study is to investigate the reproductive health of a sample of minority, largely Hispanic, women (aged 18–45), living in a California farmworker community, and to evaluate and improve study tools and methods for future research purposes for studying adverse effects in this population. The specific aims of this study are: (1) to conduct a survey of women living in a California farmlabor community, using a questionnaire covering demographic and health characteristics, the availability and the use of basic health care for and by the target population, and occupational activities and exposures; (2) to determine and compare the prevalence of gynecologic and reproductive health problems between women who work as farmworkers as compared to women who do not perform such work; (3) to determine the prevalence of specific gynecologic and reproductive health problems in female farmworkers engaged in different specific farmwork activities and compare them to women who are not performing farmwork; (4) to determine the prevalence of pregnancy complications at birth, experienced by the study women and their newborns, to compare the prevalences to those women not engaged in farmwork, and to determine any relationship to specific occupational farmwork activities; (5) to review and refine the study design, study instruments, and community approach for future studies in farmworker communities in different agricultural regions of California and other states.

Methodology

A pilot study has been carried out, as a necessary step to characterize the population, to develop acceptable and appropriate approaches for community cooperation, to develop the correct sampling methodology, to determine the community response and learn about the bi–cultural setting, all of which will ultimately aid the researchers in developing the most accurate, acceptable and comprehensible bilingual, bicultural approach.

Parlier, an agricultural community in Fresno county, California, was chosen to serve as the target community for the pilot study. Once chosen, the area, which encompassed the zip code district of Parlier, was divided into enumeration parcels, including both urban and rural areas. After random sampling of several enumeration blocks, the dwelling units on each block were mapped out for each parcel of land for later enumeration of the target population. From each sampled and mapped block, dwellings were randomly chosen and their occupants enumerated for further interviewing purposes. After the enumeration, female occupants were randomly sampled, and an extensive interview using a pretested questionnaire was administered by bicultural, bilingual interviewers in the homes of respondents. After the interviews were administered and reviewed for completeness, the answers were coded and entered into a computerized data base. In addition, limited physical examinations of participants were conducted in the community clinic to determine weight, height, pulmonary function, as well as limited blood tests to assess hematocrit and other hematologic values, and urinalysis. Each study participant who completed both the questionnaire and the limited

physical exam was monetarily compensated ($20/participant).

Statistical data analyses of the interview–based and the lab–based findings are now being performed and are nearing completion. The analysis is focusing on the association of reproductive health outcomes with exposure to farming activities. Women not employed as farmworkers will serve as the comparison group. Specific outcome variables of interest are menstrual cycle irregularities, pregnancy and birth complications, as well as spontaneous abortions. The final results of the pilot study will be used to plan and implement a full–scale study in several agricultural regions of California, which is planned to begin in spring of 1994.

Significant Findings

In the community–based pilot study in Parlier, 60 women, aged 18 to 44 years (a subsample of 150 adults interviewed), were enrolled to participate in a cross–sectional assessment of reproductive and gynecological health outcomes among others. The response rate was fairly high (75%) for this population which works long hours and lives in crowded conditions. Preliminary results show that: more than 90% of the women were of Hispanic origin, 67% were born in Mexico; 83% were married or living as married; 91% had at some point performed agricultural work, and 65% had worked in agriculture the previous year; 31% described themselves migrant farmworkers, and 18% moved for work purposes. In terms of reproductive outcomes: 80% had been pregnant (n=48); the miscarriage rate per pregnancy was 11% and low birth weight rate 7% (both of which are comparable to general population rates); the pregnancy and delivery complication rate, however, was 34% and the premature labor rate was 10%.

Lead, Solvents & Neurobehavior In Construction Workers

Nancy L. Fiedler, Ph.D.
Environmental & Occupational Health Sciences Institute
School of Occupational Health
Department of Environmental & Community Medicine
681 Frelinghuysen Road
Piscataway, New Jersey 08855

Grant Number: *1 R01 OH03144-01A1*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$257,626 ($257,626 Cum)*

Importance to Occupational Safety and Health

The construction industry has one of the highest accident and death rates of any occupational group, yet research on these occupational groups has been lacking compared to factory based cohorts. Exposure to neurotoxicants occurs frequently in construction work and may compromise safety, thus, leading to accidents and injuries as well as chronic nervous system disease. Further, since the construction industry was not covered under OSHA regulations for lead exposure until 1993, these workers have been relatively at risk for lead exposure and the resultant health effects. Also, painters in the construction trades are routinely exposed to lead and solvents. However, it is unclear what neurobehavioral effects may result from exposure to mixtures. This grant will investigate health effects among construction workers at risk for exposures to neurotoxicants. If neurobehavioral performance is shown to be compromised, this could have direct implications for safety on the job.

Objectives

(1) To quantify the relationship between bone lead, as an indicator of cumulative exposure, and neurobehavioral performance; (2) to evaluate quantitative and qualitative differences in neurobehavioral performance of workers with three chronic exposure patterns: lead, lead and organic solvents, and organic solvents; and (3) to assess prospectively the impact of the OSHA lead standard, recently extended to construction, on bone lead and neurobehavioral performance.

Hypothesis

Workers with the highest levels of bone lead accompanied by a history of chronic exposure to organic solvents will have significantly greater decrements in neurobehavioral performance relative to the lead only, solvent only, and minimal exposure groups.

Methodology

Specific Aims

1. To develop the following four cohorts of subjects recruited from the construction trades: (a) lead group – workers with an occupational history of ≥ five years of lead exposure and a current or past blood lead level (from the New Jersey lead registry) ≥ 25 ug/dl and minimal solvent exposure; (b) lead–solvent group – workers meeting the criteria for lead exposure in (a) and an occupational history ≥ five years of organic solvent exposure, validated with Union records, standard questionnaires (Occupational History Questionnaire) and current measurement of solvent exposure on three separate days during representative jobs; (c) solvent group – workers with an occupational history ≥ five years of organic solvent exposure but minimal lead exposure; and (d) control group – workers with minimal exposure to lead or organic solvents during the past five years. Subjects across the four groups will be of comparable age, sex, and baseline ability.
2. To estimate cumulative dose of lead and/or solvents using the following methods: (a) body burden of lead using in vivo k wave X–ray fluorescence of bone lead levels along with history of past and current blood lead values, and (b) lifetime solvent exposure based on occupational history, standardized questionnaire, union records, and current exposure measurement. The relative contribution of cumulative versus recent exposure to neurobehavioral performance will be evaluated using these measurements.
3. To compare the groups' current performance on a standardized battery of neurobehavioral tests reflecting attention, learning, memory and psychomotor performance, mood (e.g., irritability, depression, fatigue) and psychological symptoms.
4. To evaluate the impact of extending the OSHA lead standard to construction workers by conducting a longitudinal study. Bone lead and neurobehavioral performance will be repeated for the subgroup (top tercile based on initial bone lead) of lead exposed workers compared to matched control workers with minimal exposure to lead or organic solvents.

Significant Findings

None to date.

A Computerized Tool to Screen Workers for Neurotoxicity

Richard E. Letz, Ph.D.
Emory University
School of Public Health
1599 Clifton Road, NE
Atlanta, Georgia 30329

Grant Number: *1 R01 OH03078-01*
Start & End Dates: *09/15/93 – 09/14/94*
Funding Level: *$0 ($136,688 Cum)*

Importance to Occupational Safety and Health

Exposure to chemicals that can cause effects on the nervous system is common, and neurotoxic disorders are one of NIOSH's 10 leading diseases and injuries. Many epidemiologic studies of workers have demonstrated neurobehavioral effects of chemical exposures. However, screening of individuals for early signs of neurotoxicity from workplace exposures is currently rarely performed. Screening of individuals is rare due to the cost of full–scale clinical neuropsychological testing (averaging over $700 per patient nationally), the limited availability of qualified personnel, and the absence of efficient screening tools. Currently available computer–based neurobehavioral instruments are optimized for efficient collection of epidemiologic outcome information on groups of workers, not for screening of individuals among exposed workers to determine who may require follow–up examinations.

The present project was the first phase of a two–phase effort, development of the new computer–based testing instrument. Successful completion of this project leads to the second phase of the overall research program, which includes: (1) assembling a network of clinics to use the neurobehavioral screening system, (2) performing a normative data collection project, and (3) performing a validation study. The system is also ready to be adapted for effective use in other countries and in populations potentially most susceptible to effects of neurotoxic exposure such as the elderly and children.

Objectives

The main goal of this effort was to produce a new computer–based neurobehavioral testing system to screen workers for early signs of occupational neurotoxicity. The results of this screening test would provide information to help decide whether individual workers exposed to potential neurotoxicants should be referred for more expensive full–scale clinical neuropsychological assessment. This tool is intended for widespread use in clinics and workplaces. The aims of this project were to create a set of computer–based neurobehavioral tests specifically for screening of individuals exposed to potentially neurotoxic agents, to pilot test the instrument for feasibility of use, to develop training materials to instruct potential users of the computer–based testing system, and to evaluate those training materials.

Methodology

The project employed new hardware and software technology to accomplish these aims. Pen–based computer and peripheral sound production hardware were purchased and assembled. This hardware represents improvements over that used by existing computer–based batteries by allowing both auditory presentation of the tests and recording of responses in a manner equivalent to paper–and–pencil neuropsychological tests. Software for digitally recording the speech instructions for the test, manipulating the graphics images shown on the computer video screen, and programming of the modules was also obtained. Five neuropsychological test modules were developed to cover a range of cognitive functions: a list learning task (short–term verbal learning and memory), a visual span (short–term visual–spatial memory), a trail–making task, a digit–symbol task, and a learning delayed recognition task. Two additional software modules were also created: an orientation module that orients the subject to the voice instructions and the computer stylus ("pen") and a "results" module that summarizes the subjects performance for the test administrator. A 15–page written user's manual was created, which provides background information, details of each of the tasks, and additional information about how the software works. The screening instrument was pilot tested for feasibility of use among outpatients at an occupational medicine clinic and the subjects completed a brief semi–structured interview about the testing system. In addition, training materials were developed to instruct potential users of the computer–based testing system. A brief videotape and a written software user's guide were created for use as training materials. A pilot test of these training materials using students in an occupational and environmental health training program was performed. Physicians, nurses, and research assistants viewed the videotape, ran through the test battery, reviewed the user's manual, and completed a brief semi–structured interview on the testing system and training materials.

Significant Findings

All of the aims of the project were accomplished. The computer software to perform neuropsychological screening was created. Pilot application of the testing system in an academic occupational medicine clinic indicated ready acceptance of the testing by the patients and ready feasibility of use there. The training materials were developed and evaluated by subjects similar to those who will be using the software. Important suggestions of these professionals were incorporated as minor modifications of the computer programs and changes to the user's manual.

Neurological Effects of Organophosphates on Farmworkers

Matthew C. Keifer, M.D.
University of Washington
School of Medicine
Department of Medicine
and Environmental Health
325 Ninth Avenue, ZA-66
Seattle, Washington 98104

Grant Number: *5 K01 OH00133-02*
Start & End Dates: *09/01/93 – 08/31/96*
Funding Level: *$51,365 ($101,835 Cum)*

Importance to Occupational Safety and Health

The World Health Organization (WHO) estimates that 600 million people world wide are exposed to pesticides on a regular basis, much of this exposure is to organophosphate pesticides (OP). Past studies have documented persistent neurological effects in previously OP poisoned workers and some with chronic OP exposure. This study will focus on identifying persistent neurobehavioral deficits which may result from chronic long–term pesticide exposure. The results of this study will have direct bearing on the occupational health of the approximately 5 million people in the U.S. who derive some part of their income from agricultural work. The results will also have bearing on the

pesticide application industry as structural pesticide applicators use many of the same products.

Objectives

The goal of this clinical epidemiological study is to determine whether farmworkers chronically exposed to OP pesticides in field work have quantifiable nervous system abnormalities after an exposure season and whether these changes are persistent after a several month period of non–exposure.

Methodology

This cross–sectional study with a follow–up component will compare 60 orchard farm workers, male and female, with chronic low–level organophosphate pesticide exposure to age, education, and language matched unexposed referents. Exposure estimates will be based on orchard spray logs, work questionnaires of subjects, and biological monitoring (cholinesterase testing). In a subgroup of the larger cohort, urinary metabolite monitoring has been done. A neurological battery including the WHO Neurobehavioral Core Test Battery, vibratory threshold, visual screening, R–R interval testing, sympathetic skin response, nerve conduction and repetitive stimulation studies, has been applied to both groups at the end of an exposure season, The battery will again be applied to the same group following a 5–6 month period of non–exposure. Several biological markers which may serve as markers of susceptibility, physiological effect, or dose will also be evaluated: cholinesterase, paraoxonase, chlorpyrifos oxonase levels, and muscarinic receptor density in lymphocytes.

Significant Findings

None to date.

Psychosocial Risk Factors in Fire Fighters Stress

Randal D. Beaton, Ph.D.
University of Washington
Department of Psychosocial Nursing, SC - 76
Seattle, Washington 98195

Grant Number: *1 R01 OH03198-01*
Start & End Dates: *09/30/94 – 09/29/98*
Funding Level: *$99,000 ($99,000 Cum)*

Importance to Occupational Safety and Health

Firefighter and paramedic exposure to occupational traumata is frequent and repetitive, but very little is known about the cumulative impact of such exposures on the health of these professional emergency workers. Additionally, very little is known about how pre–existing moderator and mediating variables such as cognitive coping strategies and workplace social support might buffer or exacerbate exposures to duty–related traumata over time and how other occupational stressors might interact with trauma exposure. Findings from this longitudinal investigation will help illuminate the "natural history" of post–trauma symptomatology in emergency workers, assist in the development of preventive and remedial interventions for professional firefighters and paramedics and serve as a model for parallel endeavors with other high strain occupations.

Objectives

The objective of this longitudinal, prospective study is to identify job–related psychosocial risk factors associated with the onset and progression of adverse secondary traumatic stress health outcomes in professional firefighters and paramedics.

The specific aims of this proposal are:

1. To document the baseline prevalence and new cases of post–traumatic stress disorder and other adverse health outcomes in urban firefighters and paramedics over a three–year time frame.
2. To describe and document the frequency and intensity of urban firefighters'/paramedics' exposure to duty–related trauma including medical, fire and other incidents (e.g. hazardous materials) by objectively assessing Fire Department emergency medical and fire incident reports.
3. To determine the cumulative effect of duty–related trauma exposures on the incidence

of post–traumatic stress disorder and other adverse health outcomes in urban firefighters and paramedics over a three–year time frame.
4. To determine the interrelationships of appraised sources of non–traumatic job–related and non–work stressors with duty–related trauma exposure across time, in firefighters and paramedics in terms of specified (secondary traumatic stress) adverse health outcomes.
5. To identify pre–existing moderator and mediating variables that affect the relationships between predictor exposure and appraisal variables across time in specified adverse (secondary traumatic stress) health outcomes in firefighters and paramedics.

Methodology

The research to be undertaken is a descriptive, longitudinal, prospective study of traumatic stress, psychosocial risk factors and adverse health outcomes in urban firefighters and paramedics. Survey data will be gathered at 6 month intervals for 3 years from individuals currently employed as full–time professional urban firefighters or paramedics. Their Fire Department incident reports will be independently rated in terms of the frequency, severity and category of their incident exposures. The major emergency incident categories to be assessed will include: suicides, DOA's, criminal assault victim responses, industrial and serious MVA's, medical aid to children and infants including SID's, hazardous materials, explosives/bombs, fire fatalities and serious fire injuries.

The survey battery administered at six month intervals will include demographic and background information as well as measures of their occupational stressors, psychosocial and individual mediating factors (e.g. cognitive coping strategies) and adverse physical, emotional and behavioral health outcomes. Appropriate statistical techniques will be used to empirically identify psychosocial risk factors as well as workplace moderator and mediating variables associated with an increased incidence of post–traumatic stress disorder and other adverse health outcomes in these high strain occupations.

Significant Findings

None to date.

Stress in One Occupational Group: Teachers

Irvin Schonfeld, Ph.D.
City College of CUNY
School of Education
Convent Avenue and 138th Street
New York, New York 10031

Grant Number: *5 R01 OH02571-06*
Start & End Dates: *09/30/91 – 09/29/95*
Funding Level: *$0 ($599,479 Cum)*

Importance to Occupational Safety and Health

Because most research on the relation of working conditions to mental health has been cross–sectional, such research cannot adequately link change in mental health to quality of working conditions. This NIOSH–supported study follows longitudinally newly appointed women teachers through their first three years of work–force experience and examines the relation of working conditions to changes in the teachers' mental health and work–related morale. The study begins just prior to the women's entry into the work force and controls for preemployment baseline measures of the various outcomes. Because the teaching profession contributes powerfully to our nation's social and economic well–being, it is important to identify preventable risk factors that undermine the effectiveness of this segment of the work force.

Objectives

1. To compare the mental health (e.g., depressive symptoms) of recent women college graduates who enter the teaching profession with that of similar graduates who enter other occupations.
2. To identify job conditions that affect the mental health, health behaviors (e.g., psychophysiologic symptoms – headaches, etc.), and morale (e.g., job satisfaction) of newly appointed women teachers.
3. To ascertain the effects of different types of resources, including personal dispositions (e.g., locus of control – an individual's belief about the degree to which people control their circumstances), social support, and coping behaviors, on teacher outcomes.
4. To study the formation of one social resource, social support from colleagues.

Methodology

The project recruited subjects from senior–year college (a) education classes that students typically attend en route to teacher certification and (b) psychology classes that are largely taken by students with little intention of becoming teachers. Education and psychology students tend to be similar on a number of social demographic characteristics. The colleges selected have a record of supplying teachers to New York area school districts.

Participants completed specially constructed survey instruments in the summer following graduation (Time 0), the fall (Time 1), and the following spring (Time 2). They also completed instruments during a second summer (Time 3), a second fall (Time 4), a second spring (Time 5), a third fall (Time 6), and a third spring (Time 7). With the Time–0 survey, the project collected critical preemployment data on the various outcome measures (e.g., depressive symptoms). Outcome data and data on working conditions were collected during Times 1 and 2, and Times 4 to 7.

Significant Findings

The findings are limited to women teachers who mainly taught full–time at the same school from one to three years. In order to control for exposure histories, women who taught part–time and women who changed from one school to another between assessment periods were excluded.

1. In a comparison of the women who went on to obtain positions in the "best" schools, the "worst" schools, and schools of intermediate levels of adversity, there were no differences in preemployment levels of depressive symptoms. These women also did not differ from control women who obtained full–time nonteaching jobs. These findings suggest that selection does not explain later differences.

2. Among the teachers, those exposed to the most adverse working conditions (e.g., student violence and disrespect) tended to have the highest levels of depressive symptoms and lowest levels of job satisfaction in the first, second, and third years on the job. Those with jobs in the best run schools tended to have the lowest levels of depressive symptoms and the most satisfaction. The women who obtained jobs in the schools of intermediate adversity and the women who obtained full–time nonteaching jobs tended to show intermediate levels of symptoms and job satisfaction.

   In a series of lagged regression analyses, future problems were predicted (e.g., fall or spring of the teachers' second and third years) from working conditions measured during the fall of the teachers' first year. Preemployment levels of the outcomes, social demographic characteristics, and nonwork stressors were controlled. Adverse school conditions generally predicted future depressive and psychophysiologic symptoms, low self–esteem, and reduced job satisfaction.

3. The above analyses also examined the relation of preemployment social support from nonwork sources to future outcomes. Early support as related to fewer depressive and psychophysiologic symptoms and better self–esteem during the first year. After year–one, Time–0 support was related to better self–esteem. The effects of Time–1 colleague support were limited to Job Satisfaction. The most important factor predicting colleague support was social support from outside sources.

4. Individual coping behaviors tended not affect the outcomes.

Conclusions. The factors that adversely affect teachers' well–being, like levels of student violence and disrespect, are largely preventable. The results highlight the importance of efforts aimed at "environmental protection." More purely teacher–initiated solutions, such as coping behaviors like advice seeking or use of discipline in response to student misbehavior, are of limited efficacy. This conclusion is reinforced by the finding that teachers working in safe, well–run school environments had the lowest levels of depressive symptoms.

Publications

Schonfeld IS, Rhee J, Xia F: Some Methodologic Issues in Occupational Stress Research: Examples From Research in One Occupational Group. In: Job Stress 2000: Emerging Issues, (eds. GP Keita, S Sauter), Washington, DC, American Psychological Association, in press, 1994

Schonfeld IS, Santiago EA: Working Conditions and Psychological Distress in First–Year Women Teachers: Qualitative Findings. In: What works? Synthesizing Effective Biomedical and Psychosocial Strategies for Healthy Families in the 21st Century, (ed. LC Blackman), Indianapolis: University of Indiana Press, 1994

Schonfeld IS: Burnout in Teachers: Is It Burnout or Is It Depression? Human Stress: Current and Selected Research, in press, 1994

Schonfeld IS: Stress in Teachers: Depressive Symptoms Scales and Neutral Self–reports on the Work Environment. In: Work and Well–being: Assessments and Instruments for Occupational Mental Health, (eds. J Quick, L Murphy, J Hurrell, Jr.), Washington, DC: American Psychological Association, pp 270–285, 1992

Schonfeld IS: A Longitudinal Study of Occupational Stressors and Depressive Symptoms in First–year Teachers. Teaching and Teacher Education 8:151–158, 1992

Schonfeld IS: Dimensions of Functional Social Support and Psychological Symptoms. Psychological Medicine 21:1050–1060, 1991

Schonfeld IS, Ruan D: Occupational Stress and Pre–employment Measures: The Case of Teachers. Journal of Social Behavior and Personality 6:95–114, 1991

Schonfeld IS: Coping with Job–Related Stress: The Case of Teachers. Journal of Occupational Psychology 63:141–149, 1990

Schonfeld IS: Distress in a Sample of Teachers. Journal of Psychology 123:321–338, 1990

Schonfeld IS, Shaffer D, Barmack JE: Neurological Soft Signs and School Achievement: The Mediating Effects of Sustained Attention. Journal of Abnormal Child Psychology 17:575–596, 1989

Schonfeld IS, Shaffer D, O'Connor P, Portnoy S: Conduct Disorder and Cognitive Functioning. Testing Three Causal Hypotheses. Child Development 19:993–1007, 1989

Trautman C, Erickson D, Shaffer D, Correra A, Schonfeld IS: Prediction of Intellectual Deficits in Children with Acute Lymphocytic Leukemia. Journal of Developmental and Behavioral Pediatrics 19:122–128, 1989

Risk Factors For Injury in Denver Airport Construction

Kathleen Kreiss, M.D.
National Jewish Center for Immunology and Respiratory Medicine
Occupational Medicine Division
1400 Jackson Street
Denver, Colorado 80206-1997

Grant Number: *1 R01 OH03254-01*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$327,962 ($327,962 Cum)*

Importance to Occupational Safety and Health

Records from the construction of the new Denver International Airport offer the opportunity to describe the epidemiology of work–related injury and illness in several sectors of a hazardous industry, including road building, subway tunnelling, and construction of commercial buildings, such as terminals and concourses. Risk factors for work–related injury and illness identified in this $2.924 billion construction project (which hired 46,354 workers on 2,928 contracts) will be important in planning preventive interventions in the construction industry.

Objectives

The specific aims are to describe the magnitude and rates of work–related morbidity by trade and project; to assess modifiable risk factors for construction–related health problems; and to evaluate the impacts on morbidity and costs of an owner–controlled insurance program and workers' compensation reform in Colorado.

Methodology

Hypotheses pertinent to prevention of construction–related health problems will be answered with four intertwined study designs: (1) a cohort study of all airport construction workers examining workers' compensation claims as the health outcome; (2) an evaluation of claims rates in relation to contractor characteristics obtained through a cross–sectional interview survey of contractors; (3) a comparison of claims experience from the airport construction with that of Colorado's and the nation's construction industry; and (4) an evaluation of the preventive and economic effects of the legislative reform in Colorado's workers' compensation law that occurred during airport

construction. Workforce and compensation claims data bases for all airport construction contractors are available for these analyses through Denver County's owner–controlled insurance plan for the new airport. Comparative data are available from the National Council on Compensation Insurance, the Colorado Division of Workers' Compensation in the Colorado Department of Labor, and the Bureau of Labor Statistics, U.S. Department of Labor.

Significant Findings

None to date.

Elevated Blood Leads in the Iowa Construction Industry

Stephen J. Reynolds, Ph.D.
University of Iowa
College of Medicine
Department of Preventive Medicine and Environmental Health
100 Oakdale Campus - 106 AMRF
Iowa City, Iowa 52240-5000

Grant Number: *5 K01 OH00137-02*
Start & End Dates: *09/30/93 – 09/29/96*
Funding Level: *$54,000 ($108,000 Cum)*

Importance to Occupational Safety and Health

Sentinel data from case reports and surveillance systems strongly indicate that workers in selected construction trades are significantly exposed to lead, are inadequately monitored, and are sustaining serious illness from exposure. Although OSHA's new lead standard for the construction industry should help provide a framework for evaluation and control of lead exposures, there remains an acute need to determine the true scope of the problem and identify contributing risk factors. The results of this study will be useful for developing intervention strategies, and prioritizing prevention activities.

Objectives

The objectives of this project are to: characterize the prevalence of blood lead concentrations in selected high risk construction trades in the State of Iowa; identify and evaluate risk factors that may contribute to occupational exposure to lead in construction; evaluate the utility of using the Iowa Department of Public Health's (IDPH) Adult Blood Lead Surveillance Project for identification and mitigation of lead poisoning cases in construction; evaluate compliance with the new OSHA construction lead standard; collect, organize, and disseminate information concerning lead hazard and controls via the National Hazard Communication Resource Center (NHCRC) and presentations to construction workers; develop intervention strategies and future projects to quantitatively evaluate lead exposure in construction.

Methodology

This project involves a cooperative effort between the University of Iowa and the local construction unions representing painters, plumbers and pipe fitters, ironworkers, laborers, and electricians in eastern Iowa. A sample of 500 workers will be randomly selected from the total population of all union members, using union records. 100 workers will be selected from each of the following high risk trade groups: painters, plumbers and pipe fitters, ironworkers, laborers, and electricians. Venous blood samples will be collected from each participant and analyzed for lead using atomic absorption spectroscopy. Analysis for free erythrocyte protoporhyrine (FEP) will also be conducted. Information on demographics, symptoms, occupational history, work practices, personal protective equipment, training, other potential risk factors and confounders will be gathered using questionnaires at the same time that blood samples are collected. Awareness of, and compliance with OSHA's construction lead standard will also be ascertained. The primary objectives of data analysis will be to describe the distribution of blood lead concentrations, test the null hypothesis that there are no significant differences between the blood lead concentrations of workers in different trade groups, and evaluate the relationships between risk factors, symptoms, and blood lead concentrations. Results will also be used to evaluate the efficacy of the IDPH's Adult Blood Lead Surveillance Program, and the University of Iowa Hospital and Clinic's data base for identification and control of occupational exposure to lead in the Iowa construction industry. Upon completion of the prevalence study, and using the resources of the NHCRC, focus groups will be conducted with construction workers to present the findings and explore methods for reducing exposure.

Significant Findings

Data collection was begun in August 1994 and will continue through winter 1995. Consistent with the demographics of union membership, only one white female has participated in the study to date, all other participants have been white males. Blood lead

results are available for 70 individuals at the time of this report. All blood lead levels have been less than 15 ug/dL. Five have been between 10 and 15 ug/dL. The mean blood lead level for these subjects is 4.6, and the standard deviation is 6.9 ug/dL. The individuals sampled to date work mostly on commercial or industrial job sites. Few subjects report medical or environmental monitoring, training, or provision of other exposure control methods on jobs during the last 3 months.

Measurement Errors in Occupational Epidemiology

Donna Spiegelman, Sc.D.
Harvard University
School of Public Health
Department of Epidemiology
677 Huntington Ave.
Boston, Massachusetts 02115

Grant Number: *5 K01 OH00106-04*
Start & End Dates: *07/01/91 – 06/30/95*
Funding Level: *$54,000 ($161,872 Cum)*

Importance to Occupational Safety and Health

Nearly all types of occupational studies face problems measuring the exposure variable, due to the necessity of retrospective exposure assessment in most cohort studies and the high cost of detailed personal exposure sampling even in prospective and cross-sectional studies. I propose to contribute to a resolution of these problems through the development of statistical methods to adjust point and interval estimates of relative risk for bias due to measurement error. By illustrating these procedures with examples from important occupational data sets, it is hoped that the use of these methods of design and analysis will become standard practice in occupational epidemiology.

Objectives

1-3. To develop new simple measurement error methods for (1) retrospective cohort studies, (2) case-control studies, and (3) cross-sectional studies of occupational exposure-disease relationships.
4. To illustrate the use of these methods through the analysis of important occupational data sets.
5. To develop user-friendly computer software to implement those methods which appear to be most useful in practical settings.

Methodology

All methods considered in this research require the availability of a small validation substudy in which the usual method of exposure assessment is validated against a more accurate method. Then, a measurement error model is developed empirically from these data. This measurement error model is used explicitly in maximum likelihood methods to obtain an unbiased estimate of effect, which takes into account measurement error as modeled through the validation substudy. Semi-parametric methods are being considered in addition to the fully parametric methods.

Significant Findings

Current work has involved investigating fully parametric maximum likelihood methods for a constant prevalence ratio model with a realistic exposure measurement error model, *g*, such as based on the gamma or log-normal distribution. Attention has focused on Valanis et al.'s[1] ACE study of the health effects of occupational exposure to antineoplastics among hospital pharmacists and pharmacists' aides. The gamma family of distributions for modeling the gold standard method of assessing number of antineoplastic drugs per week using an two week on-site work diary (X), as it depends upon the self-reported number (Z), fit these data well, and leads to a closed form likelihood, *h*, for the distribution of symptom prevalence in the main study conditional on self-reported exposure. The full data likelihood can then be maximized

$$L(\beta,\theta) = \sum_{i=1}^{n_1} \log[h(D_i|Z_i;\beta,\theta)] + \sum_{i=1}^{n_2} \log[f(D_i|X_i;\beta)] + \sum_{i=1}^{n_2} \log[g(X_i|Z_i;\theta)]$$

where f is the relative risk model which is assumed when no measurement error is present in the exposure variable. The variance-covariance of the parameter estimates are obtained as the inverse of the observed information matrix, and inference proceeds using standard likelihood theory. Computational difficulties has often prohibited the use of likelihood-based methods despite their well-known optimality properties, and automatic differentiation methods have been applied and developed to greatly increase their feasibility.

Using a recently proposed semi-parametric approach[2], unbiased estimates of the parameters of the relative risk model are obtained in the validation study by solving the consistent estimating equations

$$0 = \sum_{i=1}^{n_2} \hat{w}_i \frac{\partial f}{\partial \beta} [D_i - E(D_i|X_i)]$$

where $\hat{w}_i$ is the i[th] subject's modeled probability of being selection into the validation study, as it depends on all data available in the main study. The usual sandwich estimator can be used to obtain the asymptotic variance of these estimates, and inference can proceed using Wald-type methods.

Detailed analysis of one symptom, fever over the past three months, has been completed and the results are given.

A comparison of several approaches to estimation and inference for the Valanis et al. data on the relationship between fever in the past three months and the number of antineoplastics mixed per week (n=675)

Approach	β	SE(β)	Δ	Prevalence ratio (PR) in Δ	95% CI for PR in Δ	p-value
logistic regression, uncorrected	0.00229	0.00089	IQR[1] (X) = 52	1.13	1.03-1.23	0.01
RSW correction to logistic regression	0.00580	0.00240	IQR (x) = 34	1.22	1.04-1.43	0.02
constant prevalence ratio model, uncorrected	0.00165	0.00099	IQR (X) = 52	1.06	1.03-1.07	0.003
constant prevalence ratio model, maximum likelihood	0.00464	0.00274	IQR (x) = 34	1.17	1.04-1.26	0.003

[1]IQR = inter-quintile range

Because the odds ratio is an over-estimate of the prevalence ratio when symptom prevalence is not rare as here, where the prevalence of fever over the past three months is 17%, we see that the uncorrected logistic regression estimate and the logistic regression estimate corrected for measurement error using the method of Rosner et al.[3] over--stimate the prevalence ratios compared to those directly estimated fitting the constant prevalence ratio model. In addition, the measurement error correction procedures lead to estimates of the effect of occupational exposure which are greater than those observed when measurement error is ignored. Although the true uncertainty around the estimate is correctly evaluated using the measurement error correction procedures, the 95% confidence intervals remain statistically significant although centered around a point estimate which is larger in magnitude.

1. Valanis BG, Vollmer WM, Labuhn KT, Glass AG. Association of antineoplastic drug handling with acute adverse effects in pharmacy personnel. Am J Hosp Pharm 1993; 50:455-462.

2. Robins J, Rotnitzky A, Zhao LP. Estimation of regression coefficients when some regressors ar not always observed. J Amer Statist Assoc 1994; 89:846-866

3. Rosner B, Spiegelman D, Willett WC. Correction of logisitic regression relative risk estimates and confidence intervals for measurement error: the case of multiple covariates measured with error. Am J Epidemiol 1990; 132:734-745.

Publications

Spiegelman D, Casella M: Explicit Correction For Exposure Measurement Error Increases Log Relative Risk Estimates More Than Threefold: A Case Study of Health Effects of Chemotherapeutics Exposure in Hospital Pharmacists, Research Triangle Park, NC: ISEE/ISEA 1994, September, 1994. Am J Epidemiol 139:S80, 1994

Spiegelman D, Casella M: A General Method for Correcting Relative Risk Estimates from Occupational Studies for Exposure Measurement Error, Illustrated by A Case Study of Health Effects of Chemotherapeutics Exposure in Hospital Pharmacists, Como, Italy: ISEOH '94, September, 1994

Dose-Response Assessment Issues in Occupational Studies

Irva Hertz-Picciotto, Ph.D.
University of North Carolina
School of Public Health
Department of Epidemiology
CB# 7400 McGavran-Greenberg Hall
Chapel Hill, North Carolina 27599-7400

Grant Number: *1 R03 OH02971-01A1*
Start & End Dates: *09/30/92 – 09/29/94*
Funding Level: *$0 ($19,363 Cum)*

Importance to Occupational Safety and Health

Dose–response assessment is used as a criterion in establishing causality on the basis of observational studies, and is used to improve understanding of biologic mechanisms. Additionally, it is used to set exposure standards in occupational and environmental settings. Biases in dose–response assessment can occur due to competing risks from morbidity and mortality that manifest as a healthy worker survivor effect. This project is examining the use of a job instability index as a surrogate for job– and dose–related morbidity. Results from this project may be used to increase the sensitivity of analyses of occupational studies that utilize quantitative exposure measures, and hence to improve the ability to set appropriate regulatory standards.

Objectives

The objective of this project is to determine ways to detect and quantify biases that may alter dose–response relationships in occupational studies.

Methodology

Exposure–related morbidity is being assessed using as a surrogate, gaps in employment. The association between exposure and this index of job instability is characterized using Cox hazard regression with time–dependent exposure variables (cumulative exposure, as well as current exposure), controlling for other variables such as age and date of hire. Relationships between gaps in employment and pre–retirement job leaving are also characterized by means of similar proportional hazards regression models, with gaps in employment representing an additional time–dependent variable. Also, the association between this surrogate for exposure–related morbidity and respiratory cancer mortality is analyzed.

Significant Findings

Empirical findings indicate associations between gaps of 30 days or more and the following variables: age–at–hire; year–of–hire; cumulative exposure up to one year previously; current exposure in the preceding year. Younger age at hire, later year of hire, higher cumulative exposure, and lower current exposure were all associated with the risk of a 30–day gap. Three of these variables, however, show an interaction with time since hire. In particular, as time since hire increases, the positive association with cumulative exposure declines, the negative association with current exposure increases in absolute magnitude, and the positive association with year of hire increases. Thus, a higher cumulative exposure predicts a greater hazard for absenteeism in the early years of employment, while lower current exposure predicts a greater hazard for absenteeism in the later years of employment.

About 60% of workers who experience gaps of 30 days or more in their employment history have their first such episode in the first year of employment. Gaps in employment do not predict subsequent exposure level. A history of a 30 day or longer gap is associated with a 10% lower hazard for early termination (pre–retirement). However, a history of such a gap is not a confounder of the associations between exposure and early termination.

Although an overall negative association between a history of at least one gap and respiratory mortality was observed, the risk was increased during the early years of employment among workers with gaps (for instance, the hazard ratio=2.1 after 5 years of employment, comparing workers with a gap history to those without such a history, but by 20 years, the hazard ratio=0.4). These associations are adjusted for exposure, age, year of hire, and interactions between the covariates and time. A recent gap (within the previous 3 years) was associated with a hazard ratio of 2.2 but this effect was somewhat unstable. Absenteeism was not associated with mortality from circulatory diseases.

The predictiveness of a 30–day or longer gap in employment for respiratory cancer mortality but not for circulatory disease suggests that absenteeism may have some limited utility as an imperfect indicator of respiratory health in this industry. Further work is needed to explore these relationships in other cohorts, where work patterns may be different.

Metal Fume Fever

William S. Beckett, M.D.
Yale University
School of Medicine
Department of Occupational Medicine
135 College Street, Room 366
New Haven, Connecticut 06510-2483

Grant Number: *5 R01 OH02987-03*
Start & End Dates: *09/30/92 – 09/29/95*
Funding Level: *$220,358 ($697,800 Cum)*

Importance to Occupational Safety and Health

Metal fume fever is a common occupational illness caused by inhalation of freshly generated zinc oxide and other metal fumes. This illness is characterized by fever, systemic symptoms, and mild lung inflammation with onset several hours after the acute exposure. Repeated exposure results in adaptation with reduction in symptoms and febrile response. There is little information regarding dose–response relationships in naive and chronically exposed individuals, the nature of adaptation to the acute response, or the mechanism by which zinc oxide exposure causes metal fume fever.

Objectives

Our laboratory has developed a quantitative zinc oxide fume generating, monitoring, and exposure system for animal and human subjects. Using this system, we have previously demonstrated: (1) systemic effects in humans at the current OSHA PEL of 5 mg/m^3; (2) induction of human zinc–binding protein (metallothionein) after exposure; (3) acute lung inflammation in animals exposed below the PEL; and (4) alterations in cytokine release from guinea pig lung inflammatory cells. To further understand acute and adaptive responses to zinc oxide exposure and to determine the mechanism by which it causes metal fume fever, the following hypotheses will be tested: (1) acute, febrile, and pulmonary responses to exposure in human subjects occur at and below the current OSHA PEL; (2) adaptive responses to chronic exposures in humans do not eliminate lung inflammatory changes; (3) adaption involves changes in nasal epithelial metallothionein gene induction; (4) mechanism of metal fume fever and adaption involves release of cytokines and a modulation of their response at a central or peripheral level in zinc oxide–exposed human subjects.

Methodology

Using a carefully controlled quantitative pure zinc oxide fume generating system, naive subjects and workers chronically exposed to zinc oxide fume will be exposed for two hours at concentrations below the current OSHA PEL. Symptoms, fever, peripheral blood indices of inflammation and nasal epithelial induction of metallothionein will be assessed. The ability for these low levels of zinc oxide fume to induce inflammatory changes in the lung will be assessed by lavage of lung lining fluid. These studies will be accomplished using an integrated multi–disciplinary approach and should yield important insights into the genesis and adaption of this debilitating occupational illness.

Significant Findings

Using this exposure system, human subjects have been exposed to zinc oxide fume for two hours at and below the current OSHA TLV in a blinded fashion. Subjects have developed characteristic symptoms of metal fume fever as well as symptoms in proportion to their exposure level. At 5 mg/m^3 zinc oxide fume inhaled for two hours, 12 healthy normal subjects not previously exposed experienced a significant elevation in oral temperature, and a significant elevation in peripheral plasma levels of the cytokine interleukin–6, a substance previously associated with the generation of the febrile response. Nine hours after exposure, subjects reported more muscle aches, fatigue, and cough than after clean air exposure.

In related animal studies, it was found that mice which have previously received repeated daily exposure to zinc oxide fume at 5 mg/m^3 have greater inducibility of lung metallothionein gene expression to a single zinc oxide exposure than naive mice.

To better understand the mechanisms of tolerance to zinc oxide fume with recurrent exposures, evaluation is currently underway on the induction of MRNA (messenger RNA) coding for the metal carrier protein metallothionein in epithelial cells from the nose after inhalation of zinc oxide fume using this system. Baseline metallothionein production and responses to challenge among chronically exposed sheet metal workers is being compared as well as studies of the lung inflammatory response (by broncho–alveolar lavage) to serial challenge with zinc oxide fume.

Publications

Cosma GN, Chen LC, Currie D, Garte SJ, Gordon T: Metallothionein (MT) and Cytokine Gene Expression Following Single and Repeated Inhalation to Metal Fumes. The Toxicologist, in press, 1994 (Abstract)

Gordon T, Fine J: Metal Fume Fever, In: Occupational Medicine, State of the Art Reviews. De novo Toxicants: Combustion Toxicology, Mixing Incompatibilities, and Environment Activation of Toxic Agents, (eds. DJ Shusterman, JE Peterson), Philadelphia, Hanley and Belfus, Vol 8, pp. 505–518, 1993

Airway Hyperresponsiveness Due to Cotton Dust

E. Neil Schachter, M.D.
Mount Sinai
Medical Center
One Gustave L. Levy Place
A24-30, Box 1232
New York, New York 10029-6574

Grant Number: *5 R01 OH02593-05*
Start & End Dates: *09/01/89 – 08/31/95*
Funding Level: *$152,602 ($709,316 Cum)*

Importance to Occupational Safety and Health

Byssinosis remains a significant occupational health priority in the United States. Many textile workers exposed to cotton dust over several decades before the advent of the current environmental standards are at risk of impairment due to chronic airway disease. Younger workers are at a lower risk but the current prevalence is unknown.

A growing body of evidence associates occupational and environmental pollutants with airway inflammation. The inflammation may be clinically reflected by non–specific airway hyperresponsivenss, a condition associated with the development of chronic airflow obstruction. By exploring the effects of cotton bract (a major component of cotton dust) extract (CBE) challenge on the development of airway responsiveness in our model of healthy volunteers, we hope to provide insight into the transition between the well characterized acute response to cotton dust and the often irreversible chronic airflow obstruction found in many older workers with byssinosis. Additionally, this study will help validate our *in vivo* model of byssinosis in healthy volunteers exposed to (CBE) and will extend our previous observations concerning the interaction of cigarette smoking and other risk factors with byssinosis.

Objectives

Our specific aims are:

1. To investigate if cotton bract extract induces greater airway hyperresponsiveness in healthy smokers than in healthy non–smokers. The working hypothesis is that smokers have an asymptomatic, low–level airway inflammation that makes them more susceptible to in CBE–induced airway hyperresponsiveness.
2. Examine the effect of repeated CBE exposures on non–specific bronchial hyperresponsiveness. The working hypothesis is that repeated exposures to CBE result in progressively greater inflammatory changes in the airway that will manifest themselves by airway hyperresponsiveness.
3. To compare the bronchoconstrictor effect of CBE with a similarly prepared extract of cotton dust. The hypothesis is that the bronchoconstrictor agent(s) in cotton bract extract are the same or similar to those found in cotton dust and hence will provoke similar effects.
4. To examine the effect of asymptomatic airway hyperresponsiveness on the airway response to methacholine following CBE. The hypothesis is that non–specific mild airway hyperresponsiveness, which is widely distributed in the healthy population, contributes to airway hyperresponsiveness to CBE.
5. To examine the effect of atopic status on airway responsiveness following CBE. The hypothesis is that atopic status, in otherwise healthy individuals without airway symptoms may enhance CBE–induced airway hyperresponsiveness.

Methodology

Our laboratory has developed a clinical model for studying the effects of cotton dust on human airways. The model consists of measuring lung function changes resulting from aerosol challenge with CBE. Aerosol inhalation of CBE consists of a 10 minute challenge using tidal breathing for a total of 120 inhalations. Lung function is measured following these exposures using maximal and partial expiratory flow volume (MEFV and PEFV) curves. The main parameter of interest is the MEF40%(P) (the flow rate on the PEFV curve measured at 60% of baseline vital capacity below TLC).

In study 1 healthy smokers and non–smokers were compared to study the effect of smoking on responsiveness to CBE. In study 2, non–smokers were examined on 7 separate days to examine the pattern of repeated CBE challenge over a work week. Study 3 compares airway responses to CBE and cotton dust extract (CDE) in 20 healthy subjects. Studies 4 and 5 using a protocol similar to study 2

compares healthy subjects to subjects with atopy and with mild airway hyperresponsiveness.

Significant Findings

Studies 1 and 2 of this proposal have been completed and reported upon in full detail in the final report to NIOSH dated November 1992. The major significant findings of those studies were: CBE challenge caused significant drops (responders) in lung function (MEF40%(P) $\geq$ 20%) in 9/28 non–smokers and 27/50 smokers. Significant decreases in PD20MEF40%(P) were demonstrated for methacholine in smokers ($p \leq 0.01$) but not in non–smokers. When only responders were studied, MC responsiveness increased in non–smokers ($p \leq .001$) as well as smokers ($p \leq 0.005$). Repeated daily challenge with CBE in 27 non–smokers brought about accentuated lung function decline on day 1 and 8 but not on days 2 through 5. We conclude that "naive" non–smoking subjects never exposed to cotton dust show characteristic bronchoconstrictor responses (Monday bronchoconstriction) when challenged daily with CBE. Airway hyperreactivity accompanies this response. Smoking is an independent cause for airway hyperreactivity and enhances the effect of CBE challenge.

Work is now well under way on studies 3, 4 and 5. Data collection has been completed for study objective 3. Twenty–one subjects have been studied with CBE and CDE (obtained from NIOSH). In a preliminary analysis of 11 subjects there were 8 responders (R) to CBE and 9 (R) to CDE. All CBE responders were CDE responders. The average maximal response to CBE was a fall in MEF40%(P) to 68 $\pm$ 9/1% of baseline compared to 68 $\pm$ 6.8% for CDE (NS). All subjects R and non–responders (NR) enhanced their MC response following CBE and CDE. We conclude that both CBE and CDE exert similar physiologic effects in naive healthy adults.

In studies 4 and 5 which investigate the role of pre–existing airway hyper– responsiveness and pre–existing atopy on the response to CBE, data has been collected on 80 subjects. Preliminary studies in 22 healthy non–smoking subjects (15 male, 7 female, age 31+/–1.7 years) examined indices of atopy: skin testing and serum IGE. There were 11 subjects who responded positively to skin testing (+) and 11 subjects did not respond (1). Baseline lung function studies were within normal limits for the group as a whole and no significant differences were noted between (+) and (–). The maximal fall in the maximal flow at 40% of vital capacity measured on the partial flow volume curve (MEF40%(P)) was seen 60 minutes following challenge with CBE. The MEF40%(P) as a percent of baseline at this time point was 56.6+/–9.2% for (+) and 86.2+/–6.6% for (–) ($p<0.02$). We suggest that atopy as measured by skin test reactivity to common allergens predicts responsiveness to CBE.

Publications

Zuskin E, Mustajbegovic J, Doko–Jelinic J, Schachter EN, Kern J, Sonicki Z: Respiratory Symptoms and Ventilatory Capacity in Rubber Workers. Croatian Med J 35:42–48, 1994

Zuskin E, Mustajbegovic J, Schachter EN, Kern J: Respiratory Symptoms and Ventilatory Function in Confectionary Workers. Occup and Env Med 51:435–439, 1994

Zuskin E, Kanceljak J, Schachter EN, Kern J: Respiratory Function and Immunological Reaction in Sisal Workers. Int Arch of Occup and Env Health 66:37–41, 1994

Zuskin E, Kanceljak J, Schachter EN, Kern J: Respiratory Function and Immunological Reactions In Jute Workers. Int Arch of Occup and Env Health 66:43–48, 1994

Zuskin E, Mustajbegovic J, Schachter EN: Follow–up Study of Respiratory Function in Hemp Workers. Am J Ind Med 26:103–115, 1994

Zuskin E, Mustajbegovic J, Schachter EN: Respiratory Symptoms and Lung Function in Bus Drivers and Mechanics. Am J Ind Med, in press, 1994

Zuskin E, Kanceljak B, Mustajbegovic J, Schachter EN: Immunological Findings in Confectionery Workers. Ann Allerg, in press, 1994

Zuskin E, Mustajbegovic J, Schachter EN, Kanceljak B, Godnic–Cvar J: Respiratory Symptoms and Lung Function in Wool Textile Workers. In press, 1994

Schachter EN, ZuskinE, Rienzi N, Godbold J: *In Vitro* Pharmacologic Studies of Poultry Dust Extract. Proceedings of the 18th Cotton Dust Research Conference, San Diego, CA, pp. 362–364, 1994 (Abstract)

Schachter EN, Zuskin E, Buck M, Godbold J, Castranova V, Whitmer, Siegel P: Comparison of the Airway Response to Cotton Bract Extracts. Proceedings of the 18th Cotton Dust Conference, San Diego, CA, pp. 316–318, 1994 (Abstract)

Zuskin E, Mustajbegovic J, Schachter EN: Follow–up Study of Respiratory Function in Hemp Workers. Am J Ind Med 26:103–115, 1994

Schachter EN: Byssinosis in: Textbook of Clinical, Occupational and Environmental Medicine. WB Saunders (Philadelphia PA) in press, 1994

Zuskin E, Schachter EN, Kanceljak B, Witek TJ, Jr., Fein E: Organic Dust Disease of Airways. Int Arch Occup Env Health 65:135–140, 1993

Zuskin E, Smoloj–Naranac N, Schachter EN, Mustajbegovic J: Respiratory Symptoms and Ventilatory Capacity of School Children in Urban and Rural Areas. Collegium Anthropologiccum 17:55–66, 1994

Zuskin E, Mustajbegovic J, Schachter EN, Rienzi N: Respiratory Symptoms and Ventilatory Capacity in Workers in a Vegetable Pickling and Mustard Production Facility. Int Arch of Occupational and Environ Health, 64:457–461, 1993

Schachter EN, Russomanno J, Siegal J, Fine E, Rienzi N, Witek TJ, Jr., Buck MG, Godbold J: Does Cotton Bract Extract Challenge Cause "Monday" Bronchospasm? Proc 17th Cotton Dust Conference, pp. 279–280, 1993

Castranova V, Robinson VA, Borger MW, Siegel PD, Judy JD, Schachter EN, Frazer DG: Pulmonary Response of Guinea Pigs To Inhalation of Purified Cotton Bract Extract. Proc 17th Cotton Dust Conference, pp. 248–251, 1993

Schachter EN, Tai A, Cardozo C, Zuskin E, Godbold J, Rienze N, Kesser M: Characterization of the Potentiation of Bradykinin–Induced Constriction By An Inhibitor of Endopeptidase 24.15. Am Rev Resp Dis 147:A851, 1993

Fein E, Godbold J, Chusid E, Schachter EN: The Effect of High Dose Steroids or Sleep Patterns and Respiratory Function in Symptomatic Steroid Dependent Asthmatics. Amer Rev Resp Dis 147:A291, 1993 (Abstract)

Zuskin E, Mustajbegovic J, Schachter EN: Respiratory Function in Sewage Workers. Am J Indust Med 23:751–763, 1993

Zuskin E, Butkovic D, Schachter EN, Mustajbegovic J: Respiratory Function in Workers Employed in the Glass Blowing Industry. Am J Indust Med 23:835–844, 1993

Zuskin E, Schachter EN, Mustajbegovic J: Respiratory Function in Greenhouse Workers. Int Arch of Occup and Environ Health 64:521–526, 1993

Zuskin E, Kanceljak B, Schachter EN, Witek TJ, Maayani S, Goswami S, Marom Z, Rienzi N: Immunological Findings in Hemp Workers. Env Res 59:350–361, 1992

Zuskin E, Kanceljak B, Mustajbegovic J, Schachter EN: Immunological and Respiratory Status in Swine Workers. Allergy 12:251, 1992

Zuskin E, Kanceljak B, Schachter EN, Witek TJ, Maayani S, Goswami S, Marom Z, Rienzi N: Immunological and Respiratory Changes in Animal Food Processing Workers. Am J Ind Med 21:177–191, 1992

Zuskin E, Zagar Z, Schachter EN, Ivankovic D: Respiratory Symptoms and Ventilatory Capacity in Swine Confinement Workers. Br J Ind Med 49:435–440, 1992

Schachter EN, Zuskin E, Mustajbegovic J, Buck MG, Maayani S, Marom Z, Goswami SK, Rienzi N: Pharmacologic Studies of Wool Dust Extract in Isolated Guinea Pig Trachea. Proc XVI Cotton Dust Research Conference, (Volume 1), pp. 290–291, 1992

Zuskin E, Rancelјak B, Schachter EN, Witek TJ, Mustajbegovic J, Maayani S, Buck M, Rienzi N: Immunological Findings and Respiratory Function in Cotton Textile Workers. Int Arch Occup Env Health 64:31–37, 1992

Schachter EN, Marom Z, Goswami S, Gollub E, Rienzi N, Maayani S: Purified Macrophage Mucus Secretagogue is A Potent Bronchial Smooth Muscle Relaxing Agent *In Vitro*. Am Rev Resp Dis 145:A374, 1992 (Abstract)

Cabrera M, Rienzi N, Schachter EN: Patterns of Asthma Admissions to A Metropolitan Hospital. 1990. Am Rev Resp Dis 145:A506, 1992

Zuskin E, Kanceljak B, Stilinovic L, Schachter EN, Kopjar B: Immunological Status and Respiratory Findings in Furriers. Am J Industr Med 21:433–442, 1991

Zuskin E, Ivankovic D, Schachter EN, Witek TJ: A Ten Year Follow–up Study of Cotton Textiles Workers. Amer Rev Resp Dis 143:301–305, 1991

Russomanno J, Siegel J, Witek TJ, Rienzi N, Zuskin E, Buck M, Schachter EN: Does Smoking Status Influence Responsiveness to Cotton Bract Extract? Proc Beltwide Cotton Conference XV, pp 214, 1991

Zuskin E, Kanceljak B, Witek TJ, Schachter EN: Acute Ventilatory Response to Green Coffee Dust Extract. Ann Allergy 66:219–224, 1991

Zuskin E, Kanceljak B, Schachter EN, Witek TJ, Marom Z, Goswami S, Maayani S: Immunological and Respiratory Changes in Soybean Workers. Int Arch of Occup Env Health 63:15–20, 1991

Zuskin E, Kanceljak B, Schachter EN, Mustajbegovic J, Goswami S, Maayani S, Marom Z, Rienzi N: Immunological and Respiratory Findings in Swine Farmers. Env Res 56:120–130, 1991

Russomanno J, Siegel J, Fine E, Rienzi N, Witek TJ, Buck MG, Godbold J, Schachter EN: Does Cotton Bract Extract Challenge Cause "Monday" Bronchospasm? Amer Rev Resp Dis 143:A428, 1991 (Abstract)

Russomanno J, Siegel J, Fine E, Rienzi N, Witek TJ, Buck MG, Godbold J, Schachter EN: The Interaction of Cotton Bract Extract and Methacholine in Smokers and Non–smokers. Amer Rev Resp Dis 143:A428, 1991 (Abstract)

Schachter EN, Marom Z: Erythromycin Reduces Airway Responsiveness to Methacholine. Amer Rev Resp Dis 143:A428, 1991

Schachter EN, Zuskin E, Cardoza C, Godbold J, Rienzi N, Lesser M: Inhibitor of Endopeptidase 24.15 Potentiates Bradykinin–induced Contraction of Guinea Pig Trachea. Amer Rev Resp Dis 143:A616, 1991 (Abstract)

Goswami S, Gollub E, Slavin S, Schachter EN: Erythromycin Reduces Mucus Glycoprotein Secretion and Symptoms in Stable Chronic Bronchitis. Amer Rev Resp Dis 143:A669, 1991 (Abstract)

Fein E, Zuskin E, Rienzi N, Schachter EN: Prevalence of Chronic Respiratory Symptoms in Workers Exposed to Elevated Ambient Dust Levels. Fourth International Conference on Environmental Lung Disease, Montreal, p. 8, September 28, 1991

Schachter EN: Occupational Airway Disease. Mount Sinai J Med 58(6):483–493, 1991

Zuskin E, Kanceljak B, Porkrajac D, Schachter EN, Witek TJ: Respiratory Symptoms and Lung Function in Hemp Workers. Br J Ind Med 47:627–632, 1990

Witek TJ, Schachter EN: Problems in Respiratory Care Volume 3: 1 and 2: Current Issues in Respiratory Public Health. Volumes I and II, JB Lippincott, Philadelphia, 1990

Witek TJ Jr., Schachter EN: Multidisciplinary Approaches to Environmental Lung Disease. Investigations in Byssinosis and Inner City Asthma. In: Current Issues in Respiratory Public Health, (eds. TJ Witek, Jr., EN Schachter), Philadelphia: JB Lippincott Co. 3:206–219, 1990

Witek TJ, Mazzara CA, Zuskin E, Beck GJ, Buck MG, Schachter EN: Bronchial Responsiveness After Inhalation of Cotton Bract Extract. Am Rev Resp Dis 183:1579–83, 1988

Grain Dust Exposure: Physiologic & Biologic Correlates

Paul Jagielo, M.D.
University of Iowa
College of Medicine
Department of Internal Medicine
200 Hawkins Drive
Iowa City, Iowa 52242-1081

Grant Number: *5 K01 OH00134-02*
Start & End Dates: *08/01/93 – 07/31/96*
Funding Level: *$54,000 ($108,000 Cum)*

Importance to Occupational Safety and Health

Inhalation of grain dust is associated with acute and chronic airflow limitation, as well as inflammation of the lower respiratory tract. There are a large number of workers who are exposed to levels of grain dust that are considered to be harmful. Furthermore, there is evidence that a variety of host factors such as atopy, asthma, ethnic background, age, and smoking, modulate the physiologic (airflow) response to inhalation of grain dust. Little work has been done investigating the inflammatory response.

By characterizing the physiologic as well as the inflammatory responses further, insight will be gained into the extent to which these host factors modulate the response to inhaled grain dust. Furthermore, the effects of a variety of interventions (physical manipulation of the environment to pharmacologic methods) can be explored. In this way, groups of workers at greater or lesser risk for disease, as well as preventive measures can be defined.

Objectives

1. Inhalation of aqueous grain dust extract causes inflammation primarily localized to the airways, and is associated with airflow obstruction.

2. Host factors, such as age, ethnic background, gender, atopic status, asthma, and cigarette smoking modulate the duration, intensity and severity of these effects.
3. Repeated exposure results in physiologic and biologic tolerance occurring within days of onset of exposure. This tolerance is modulated by one or several host factors which will be investigated in objective 2 above.

Methodology

Using aqueous extracts of grain dust, subjects will undergo inhalation challenge followed by pulmonary function testing to assess the physiologic effects of the inhalation of the extract, then bronchoscopy, to collect specimens from the airways and alveoli for examination of the inflammatory response. Specimens will be evaluated at the cellular, biochemical and molecular level, to find sensitive and specific markers of inflammation that can be used to characterize the inflammatory response. Subjects endowed with different host factors will then be tested and compared to control subjects. The presence of tolerance will be assessed using repeated inhalation challenge.

Significant Findings

The presence of airflow obstruction and inflammation of the lower respiratory tract has been shown, and this inflammatory response has been partially characterized in 15 subjects. Cellular, biochemical, and molecular markers of inflammation have been elucidated and will be useful in the next experiments involving the effects of host factors on these inflammatory responses.

Endotoxin Epidemiology and Exposure Assessment

Donald K. Milton, M.D.
Harvard School of Public Health
Department of Environmental Health
and Occupational Health
665 Huntington Avenue
Boston, Massachusetts 02115

Grant Number: *1 K01 OH00149-01*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$54,000 ($54,000 Cum)*

Importance to Occupational Safety and Health

Airborne endotoxin, the focus of the proposed research, is associated with certain occupational asthma syndromes and with chronic airflow obstruction. High level endotoxin exposure occurs in a wide range of workplaces including: cotton mills, grain handling and other agricultural workplaces, machining with water based metal–working fluids, industries with recirculating washwater, and in offices or laboratories with contaminated humidifiers. Exposures to endotoxin in recirculating washwater, as a result of water pollution control, and water based metal–working fluids are increasingly common. Yet, important questions remain regarding the validity of endotoxin exposure measurements, and methods are not standardized. Thus the levels and patterns of endotoxin exposure associated with significant health effects have not been well defined, especially in field studies. As a result, neither NIOSH or ACGIH have recommended PELs or TLVs for endotoxin. In the absence of regulations and uniformly valid guidelines, efforts to control exposure are only episodic and often motivated only by outbreaks of severe illness.

Objectives

This project will: (1) analyze endotoxin exposure–response relationships using previously collected and validated endotoxin exposure data, to determine the levels and patterns of exposure associated with acute respiratory symptoms and lung function changes; and (2) validate standard air sampling and Limulus assay methods for endotoxin in a wide range of industrial and agricultural aerosols using 3–hydroxy fatty acids as markers for lipopolysaccharide content and a mammalian bioassay for relevant endotoxin activity.

Methodology

This project will test the hypothesis that short term exposure level rather than time weighted average endotoxin exposure is responsible for acute change in peak expiratory flow and for respiratory symptoms recorded in diaries by workers. The analysis of PEF responses will use a modified short–term prospective cross–over design. The change in PEF across an interval will be regressed on exposure controlling for the time–varying covariates (cigarettes, asthma medications, shift worked) using Generalized Estimating Equations (GEEs). We will also control for the influence of fixed covariates: asthma reported at initial questionnaire, years since starting work, smoking history and age. Exposure will be stratified, as in the preliminary analyses, and also analyzed as a continuous variable assuming linearity across the entire range of exposures. We

expect that the more biologically relevant exposure index will give clear trends across strata and steeper dose–response slopes. We will also apply model validation techniques in choosing among the representations of exposure.

Significant Findings

None to date.

Vascular Effects of Chelation In Lead Exposed Workers

Michael J. Kosnett, M.D.
University of California
Occupational Health Clinic
SFGH, Building 30, Fifth Floor
San Francisco, California 94110

Grant Number: *5 K01 OH00108-03*
Start & End Dates: *09/30/91 – 03/29/95*
Funding Level: *$54,000 ($162,000 Cum)*

Importance to Occupational Safety and Health

There is growing evidence from epidemiological and animal studies that low–level exposure to lead may result in increased blood pressure, a major risk factor in the development of cardiovascular, cerebrovascular, and renovascular disease. In a recent cross–sectional study of San Francisco busdrivers, a strong relationship between lead and blood pressure was found exclusively in black subjects. Other studies have found black hypertensives to have an elevated pressor response to infused catecholamines, and to have higher intracellular stores of calcium, the same mechanisms experimentally implicated in lead's blood pressure effects. Although black adults constitute a key susceptible group, large epidemiological evaluations, such as NHANES II, have found a positive association between lead and blood pressure in non–black subjects as well.

Most investigations of the effect of lead on blood pressure and other health outcomes have relied on blood lead as a biomarker of exposure. However cumulative lead exposure may be better assessed by measurement of lead in bone, where greater than 95% of the adult body lead burden occurs with a half–life of several years. The availability of K x–ray fluorescence as a noninvasive quantitative measurement of the lead concentration of cortical and trabecular bone may enhance the investigation of dose–response relationships in lead–associated disorders. In addition, the recent availability of the oral chelating agent 2,3 dimercaptosuccinic acid (DMSA) permits implementation of an outpatient chelation challenge test to investigate the relationship between bone lead stores and the "mobilizable" pool of lead that may be most closely associated with toxic effects on target tissues.

Objectives

The research objectives are to assess cumulative lead exposure by K x–ray fluorescence, and to elucidate the mechanism of lead's vascular effects in a subset of lead exposed subjects with borderline to moderate hypertension. The latter aim will be approached by determining whether a reduction in soft tissue lead burden by EDTA chelation will reduce the pressor response to infused norepinephrine. The relationship between chelatable lead and bone lead burden will be explored using an outpatient chelation challenge test, and improved methods of assessing bone lead burden will be developed.

Methodology

Bone lead concentration is measured noninvasively by K x–ray fluorescence. In this technique, the tibia (representative of cortical bone) and the patella (representative of trabecular bone) are sequentially irradiated with low energy photons from a ^{109}Cd source, and a germanium detector quantifies fluorescent x–rays with energy characteristic of lead K–shell electron transitions. The lead fluorescence signal is normalized to the elastic, or coherently scattered x–ray signal, yielding a measurement of bone lead concentration expressed as micrograms of lead per gram of bone mineral (ppm).

To investigate the effect of lead chelation on vascular responsiveness, asymptomatic subjects with blood lead concentrations between 15 and 80 μg/dl, are recruited as subjects from industries, unions, and occupational and environmental health clinics. Black adult men are specifically targeted for recruitment. Subjects with diastolic blood pressure between 85 and 105 mmHg on two consecutive screenings, indicative of borderline to moderate hypertension, are admitted to the UCSF General Clinical Research Center, concurrent with outpatient and inpatient stabilization of dietary sodium. In each of 2 intervention cycles, subjects receive a stepped–dose infusion of norepinephrine (NE), immediately before and after an experimental intervention, and the slope of the dose–response lines is assessed. In one cycle, the intervention consists of a 48–hour lead chelation with i.v. EDTA, in the other matched i.v. placebo. The order of the two cycles is assigned in a double blinded, balanced manner. For each subject, the

change in slope between the pre– and post–intervention NE infusion, a measure of the change in pressor sensitivity, is compared between the chelation and placebo cycles.

To assess the relationship between "chelatable" lead and bone lead, selected subjects with occupational lead exposure will collect urine specimens before and after an out–patient challenge dose of the new oral chelating agent, dimercaptosuccinic acid, (DMSA, succimer). The relationship of urinary lead to bone lead concentration measured by K x–ray fluorescence will be investigated using regression models.

Significant Findings

Normative data on K x–ray fluorescence measurement of bone lead concentration has been collected on 100 subjects, age 11 to 78, with limited occupational lead exposure. Results revealed that log transformed tibia (cortical bone) and patella (trabecular bone) lead concentration were highly correlated with age ($r=.71$, $p<0.0001$; $r=.65$, $p<0.0001$). An age–sex interaction existed, resulting in higher bone lead concentrations in older males. Blood lead concentration (mean 5.72 ± 3.98 μg/dl), was not correlated with age. Log blood lead was weakly correlated with log of tibial lead ($r=.23$, $p=.02$) and patella lead ($r=.33$, $p=0.001$). A piece–wise linear regression model in age and sex yielded $R^2=.60$ for tibia lead, and $R^2=.55$ for patella lead. An expanded model for tibia lead ($R^2=.66$) revealed that smoking history was significantly associated with an increased bone lead concentration, and among females, a history of ever having nursed an infant was associated with lower bone lead. These models may serve as a basis for determining whether a subject with a history of occupational lead exposure has elevated bone lead concentration compared to age and sex adjusted norms.

Preliminary data analyzed on four hypertensive subjects completing the norepinephrine infusion protocol, (initial blood lead range 17.3 μg/dl to 56.6 μg/dl) has found that the mean change in slope relating systolic and diastolic blood pressure to norepinephrine infusion rate to be consistent with a slight chelation induced decline in vascular responsiveness. However, the magnitude of change in slope was not related to the magnitude of change in blood lead.

The relationship between K x–ray fluorescence measurement of bone lead concentration and creatinine corrected urinary lead excretion after a single oral dose of DMSA dose has undergone preliminary investigation in 28 subjects, age 22 to 67, with a range of occupational lead exposures. In 28 workers, urinary lead content was measured in two timed, overnight collections obtained at baseline, and immediately following a single oral dose of 10 mg/kg DMSA. Lifetime hours of high intensity lead exposure, as estimated by a detailed, blinded questionnaire, correlated ($p<.01$) with patella lead ($r=.71$), tibia lead ($r=.53$), and blood lead ($r=.47$), but not with chelated lead. Chelated lead was highly correlated with blood lead ($r=.84$). In a multivariable model, bone lead added little to the variance in chelated lead explained by blood alone. Adjustment of chelated lead by creatinine or baseline urine lead yielded similar results. The data are consistent with other findings suggesting that lead mobilized into the urine by DMSA chelation predominantly reflects lead present in blood (and possibly other soft tissues), and not the major body burden of lead in bone. KXRF measurements appear superior to chelation challenge tests as biomarkers of long–term lead exposure.

Studies have also been undertaken to enhance the precision of our laboratory's *in vivo* K x–ray fluorescence bone lead measurements by employing a markedly smaller spot source of ^{109}Cd in a geometry that enlarges the available detector area, utilizing faster spectroscopy electronics, and applying an alternative peak extraction algorithm. Calibration experiments conducted on lead doped plaster of Paris phantoms have yielded calibration lines with R^2 >0.99. Repeated *in vivo* measurements have been conducted to optimize source to target distance, and to characterize human measurement uncertainty.

Publications

Kosnett MJ, Becker CE, Osterloh JD, Kelly TJ, Pasta DJ: Factors Influencing Bone Lead Concentration in a Suburban Community Assessed By Noninvasive K X–Ray Fluorescence. JAMA 271:197–203, 1994

Kosnett MJ, Regan LS, Kelly TJ, Osterloh JD: Interrelationships of Urinary Lead after DMSA Challenge, Bone Lead Burden, and Blood Lead in Lead Exposed Workers. Vet Hum Toxicol 36:363, 1994 (Abstract)

Kosnett MJ, North W, Herzberg W, Wu P: Bone Lead Concentration After Delayed Intoxication From Retained Buckshot. Vet Hum Toxicol 35:354, 1993 (Abstract)

Kosnett MJ, Becker CE, Osterloh JD, Kelly TJ: Assessment of Body Lead Burden by K X–ray Fluorescence Measurement of Lead in Bone. Vet Hum Toxicol 34:355, 1992 (Abstract)

Kosnett MJ: Unanswered Questions in Metal Chelation. Clin Toxicol 30:529–547, 1992

Central Nervous System Effects of PCE Exposure in Humans

Diana Echeverria, Ph.D.
Battelle Human Affairs Research Center
4000 N.E. 41st Street
Seattle, Washington 98105

Grant Number: *5 R01 OH02719-03*
Start & End Dates: *02/01/90 – 04/30/94*
Funding Level: *$0 ($594,962 Cum)*

Importance to Occupational Safety and Health

This study investigated potential relationships between occupational exposure to the solvents PCE and styrene and central nervous system (CNS) deficits. It was hypothesized that solvent exposure particularly affects executive function, visuospatial skill, short–term memory, and mood, leaving motor, language based skills, and long–term memory in tact. The frontal system has been associated with executive function such as measured by Switching Attention, Trail Making A and B, and the Wisconsin Card Sort. Tests associated with the limbic system include mood, as measured by the Profile of Mood States, short–term memory as measured by Digit Span, Visual Reproductions, and Pattern Memory. Consistent with this prediction, we also included tests that would remain unaffected by solvents. Thus the study was an assessment of frontal\limbic systems as underlying sites of solvent pathology. Our behavioral assessment was supplemented with a sub–study evaluating whether subclinical hepatotoxicity was associated with exposure using serum hepatic transaminase activity (ALT, AST, and GGT) and hepatic parenchymal echogenicity on ultrasonography. These effects were assessed in 104 dry cleaners occupationally exposed to different levels of PCE using 48 never–exposed laundry workers as a reference population. The second study population consisted of 68 reinforced plastic fiberglass laminators occupationally to styrene. As a matter of public health policy, the study distinguished exposure–effect relationships for chronic (cumulative), sub–chronic (within weeks), and acute (within one day) exposure, between 0 and 100 ppm encompassing OSHA regulatory levels, and was able to determine a potential threshold for adverse behavioral effects for styrene.

Objectives

To characterize CNS effects from occupational exposure to PCE and styrene.

Methodology

An extensive test battery evaluated visual and verbal analogues for mood scales, simple attention (NES and WAIS digit span), cognitive flexibility (Trail Making and PASAT), reasoning (Similarities and Wisconsin Card Sort), memory (pattern memory, visual reproductions), perception (Color Hue and pattern recognition) and manual dexterity (One Hole Test). In addition, premorbid skills, which were not anticipated to be affected by exposure, included measures of long–term memory based on the scores from the California Verbal Learning Test, Vocabulary, Millhill Synonym, and an Arithmetic test.

The chronic assessment relied on tests administered between 1 to 3 hours during the morning of each subject's day off and additional tests administered 1 hour pre–exposure on the first day of the work week. The pre–exposure test battery was repeated post–exposure in order to evaluate potential acute within–day effects. These tests were thought to have a stronger reversible and acute component. Alveolar breath samples were measured to control for variation in solvent body burden corrected to 5% CO_2, supplementing 8 hour air monitoring for each exposed and 1:8 non–exposed worker. PCE air levels ranged from 0 to 75 ppm where the average exposure among operators, pressors, and counter personnel was 22 ppm, 4 ppm, and <1 ppm respectively. Average styrene air levels ranged from 5 to 58 ppm across industrial sectors but the mean exposure level among higher exposed laminators was between 34 and 60 ppm. Personal 8–hour TWA measures coupled with work histories were used to construct lifetime indices of cumulative exposure as well as using the simple duration of exposed employment. Paid volunteers were 18 to 65 years old, English speaking, and have had no history of diabetes or CNS disorders. The immediate influence of alcohol and drug use was restricted. Multivariate regression on individual tests and rank sum *a priori* groupings of tests controlled for potential confounding effects of age, race, gender, shop ownership, vocabulary, and ethanol consumption.

Significant Findings

Evidence for the Frontal/Limbic Hypothesis

Chronic exposure to PCE resulted in residual deficits in Pattern Memory, Visual Reproductions, and Pattern Recognition (visuospatial functions) only partially substantiating our hypothesis, since the

limbic system but not the frontal system was implicated. A likely explanation is that exposure levels were too low, averaging just under the Washington State compliance level of 25 ppm. However, the previous study results at higher exposures of 40 ppm also found identical chronic effects. Therefore, performance is not readily compromised at exposure levels below 50 ppm. At this time, only residual deficits in limbic system function can be detected. Also hepatic transaminase levels were minimally increased in PCE exposed workers. Elevated ALT levels, between 1.0 and 1.5 times normal limits, were observed in 5 of 27 (19%) of the dry cleaners as compared to 1 of 26 (4%) laundry workers. In contrast, diffuse parenchymal changes in echogenicity, as determined by hepatic ultrasonography, were increased nearly twofold in dry–cleaners, occurring in 18 of 27 (67%) dry–cleaners as compared with 10 of 26 (39%) laundry workers ($p<.05$).

In sharp contrast, the styrene analysis resulted in pronounced subchronic effects, averaging at 34 ppm, providing far more compelling evidence to support our hypothesis. Acute and chronic effects were not as evident. Deficits were strongest for tests evaluating executive function and reasoning such as the WAIS Similarities, Switching Attention, and Trail Making B, as well as limbic system mediated functions involving short–term memory of visual patterns (Pattern Memory and Visual Reproductions) and to a lesser extent, attention (Digit Span and Trail Making A). Consistent with a focal effect, motor function was spared. However, there were some unexpected omissions. Adverse mood scores and symptoms, thought to be associated with the limbic system remained unaffected which is thought to be attributable to a survivor population potentially adapted to the solvent or that the range of exposures were too low. The analysis of summary scores for all objective tests demonstrated a no–exposure threshold. The results provide evidence that the occupational standard of 50 ppm may protect against acute and chronic effects but may not prevent sub–chronic central nervous system effects.

Publications

Echeverria D, White RF, Sampaio C: A CNS Assessment of PCE: I A Comparison Between Clinical and Preclinical Behavioral Effects. J Occupational Medicine, in press, 1994

White R, Echeverria D: A Neurobehavioral Evaluation of PCE Exposure In Patients and Dry Cleaners II: A Medical Summary. J Occupational Medicine, in press, 1994

Echeverria D, Heyer N, Bittner A, Checkoway H, Toutonghi G: A Behavioral Comparison Between Occupational Exposure to Perchloroethylene and Styrene. British Journal of Occupational and Environmental Medicine, submitted, 1994

Echeverria D, Heyer N, Toutonghi G, Ronhovde N, Bittner A: The Stroop Test: The Effect of Age, Sex, and Color Confusion on Selective Attention Among Unexposed Workers. Advances in Industrial Ergonomics and Safety IV, 1992

Ronhovde N, Heyer N, Toutonghi G, Echeverria D: Color Hue Impairment as An Indicator of CNS function. Advances in Industrial Ergonomics and Safety IV, 1992

Toutonghi G, Echeverria D, Bittner A, Ronhovde N: The Use of Switching Ability to Assess Central Nervous System Function. Advances in Industrial Ergonomic and Safety III, 1991

Ronhovde N, Heyer N, Toutonghi G, Echeverria D: The Effect of Age on Color Vision. Advances in Ergonomics and Safety III, Elsevier, Denver, CO, 1991

Echeverria D, Heyer N, Ronhovde N, Toutonghi G: The Effect of Adverse Color Vision of the Stroop Test. Advances in Ergonomics and Safety III, Elsevier, Denver, CO, 1991

Validity of Computerized Tests in Occupational Settings

Roberta F. White, Ph.D.
Boston University
School of Medicine
Department of Neurology
88 East Newton Street #C314
Boston, Massachusetts 02118-2308

Grant Number: *5 R01 OH02767-03*
Start & End Dates: *05/01/91 – 11/01/94*
Funding Level: *$0 ($560,772 Cum)*

Importance to Occupational Safety and Health

This study represents an attempt to validate a computerized neurobehavioral test battery which can then be used in research studies to investigate CNS dysfunction secondary to neurotoxicant exposure in a valid and theoretically meaningful way. If the battery

proves valid as an indicator of CNS function, it will also have utility in clinical examination of patients with suspected encephalopathy secondary to exposure.

Objectives

To examine the relationship between specific types of brain damage (white matter lesions in multiple sclerosis, basal ganglia dysfunction in Parkinson's disease, focal cortical lesions in stroke) and performance on Neurobehavioral Evaluation System (NES) tests.

Methodology

Subjects from each of four neurological groups have been tested with the NES battery and compared to age– and gender–matched controls. The neurological groups include multiple sclerosis, early Parkinson's disease, and focal stroke. The stroke groups comprises subgroups of patients with lesions localized to each of the four quadrants: left anterior, left posterior, right anterior, right anterior.

Significant Findings

As of 11/01/94, 243 subjects have been tested. Subgroups of patients enlisted were Parkinson's Disease (PD; N=73), multiple sclerosis (MS; N=61), focal lesion (FL; N=42) and normal controls (NC; N=67). Most neurologic patients meeting the exclusion criteria used in the study can complete all of the tests in the battery, and the remainder can complete the majority of tests.

A preliminary analysis of results has been carried out for all groups. Correlations between NES tests were estimated for each of the four groups separately. These correlations were generally small in magnitude, suggesting that the battery taps distinct functions in addition to functions common to the several tests. This held for the neurological patient groups as well as for the controls, indicating sensitivity of these tasks to specific deficits rather than merely to degree of overall impairment.

Linear regression models were fit to the data to estimate associations between disease and test performance, adjusting for differences in age, gender, educational level, and a measure of native cognitive ability. Patients in the four neurological groups differed from controls in distinct ways. For the PD sample there was an association between disease and tests of motor speed, hand–eye coordination, visual memory, and a measure of fatigue, all of which had been predicted. In the MS group, significant associations with disease were more widespread. MS patients were impaired on tasks assessing motor speed, hand–eye coordination, psychomotor speed, attention, concentration, verbal memory, visual discrimination, and visual memory. These patients also reported more fatigue than did controls. As a whole, the FL group was impaired on tasks assessing motor speed, hand–eye coordination, psychomotor speed, attention, concentration, visual discrimination, and visual memory.

Although the subgroups of FL patients corresponding to lesion locus (left anterior; left posterior; right anterior; right posterior) are relatively small, differences among them are already apparent. For example, motor function, concentration, and verbal memory deficits were especially sensitive to left–sided lesions whereas simple attention, pattern discrimination, and pattern memory were especially sensitive to right–sided lesions. These differences are consistent with the neuropsychological literature reporting findings based on traditional (non–computerized) tests.

The contrast between the findings in the MS and PD groups suggests that the present NES battery is more sensitive to the neuropathological consequences of MS (especially white matter lesions) than to those of PD (dysfunction of the basal ganglia, especially the substantia nigra). The battery is highly sensitive to cortical lesions and specific tests appear to be differentially sensitive to cortical damage at different sites.

The results indicate that the NES subtests are most effective in measuring the expected motor deficits in all patient groups. However, they failed to detect deficits in complex attention, visuospatial function, and verbal encoding in PD patients, and deficits in verbal functioning and memory in MS patients, that have been identified in past studies using traditional neuropsychological tests. If the NES is to be effective in detecting CNS dysfunction (especially at the subclinical levels to be expected in working populations exposed to neurotoxicants) the battery requires expansion and further validation. Currently, new computerized tests based on traditional neuropsychological tests are being developed and added to the battery to serve these purposes. The new tests include several measures of complex attention, a verbal learning test that permits examination of subprocesses involved in learning, recall, and recognition memory, several nonverbal tests of attention and memory, and a motor–free visuospatial task.

Generation of Fibrous Aerosols in Narrow Size Ranges

Ching-Ping Fang, Ph.D.
New York University
Medical Center
Department of Environmental Medicine
550 First Avenue
New York, New York 10016

Grant Number: *5 K01 OH00129-02*
Start & End Dates: *08/01/93 – 07/31/96*
Funding Level: *$53,848 ($107,659 Cum)*

Importance to Occupational Safety and Health

It has long been recognized that durable fibrous materials (asbestos and Man–Made Mineral Fibers (MMMF)) can become carcinogenic when aerosolized. It has also been accepted that the physical properties of the fibers can be more important determinants of injury than its chemical ones. Due to the fibers' elongated geometries, the efficiencies of lung deposition and clearance for fibers can be significantly different from those of compact particles. Many studies have reported that shorter fibers are removed more effectively from lung than the longer ones. A review of published literature sources by HEI–AR (1991) demonstrates the critical importance of fiber dimensions and durability in tissues to the biological responses. However, there are still insufficient reliable experimental results to fully support the fiber size criteria and toxicity ranges. The difficulties of interpreting results from prior experimental animal and *in vitro* studies of responses to fiber exposures have been due, in part, to the wide–spread ranges of diameter and length of the administered fibers. The first aim of this study is to develop techniques for generating fibrous aerosols with various fibrous materials (asbestos and MMMF) in narrow size ranges for laboratory use. The generated fibers could be used directly in *in vitro, in vivo* instillation, or *in vivo* implantation studies, or could be resuspended (with some losses) for inhalation studies. With these high quality fibrous particles, the research on quantitative assessment of the inhalation hazard from aerosolized fibrous materials (asbestos and MMMF) can be conducted more definitively.

Objectives

Quantitative assessment of the inhalation hazard from aerosolized fibrous materials (asbestos and MMMF) requires geometrically defined fibers. The primary objective of the current proposal is to develop techniques for generating relatively monodisperse fibrous aerosols for laboratory use.

The specific aims of the project are:

1. To develop a system for generating relatively monodisperse fibrous aerosols for a variety of fiber types, both natural and man–made. It will consist of an inertial impactor, a virtual impactor and Nuclepore filters in cascade. The collected fibrous particles, which will have geometric standard deviations less than 1.50 for both diameter and length, will be used in future work to determine the inhalation hazard from fibers of various lengths, diameters, and fiber types.
2. Experimental and theoretical determination of the extent of influence of factors which affect collection characteristics of fibrous particles within sampling systems and lung airways.

Methodology

Polydisperse fibrous aerosols will first be generated by a fluidized bed fibrous generator (FBG) with number concentrations of 102–103/cc. The polydisperse fibrous aerosols will then be classified by an inertial impactor–virtual impactor system in diameter ranges of interest for subsequent biological effects testing, e.g., <0.15, 0.3–0.5, 2–3 μm. The fibrous aerosol in each diameter range then will be sorted by fiber length using Nuclepore filters under conditions where collection by interception is the dominant collection mechanism. Length cuts could be made at 2.5, 5, 10 and 20 μm. The system could be operated in cascade, collecting fractions with lengths <2.5, 2.5–5, 5–10, 10–20 and >20 μm. Our goal is to select fractions having narrow distributions of both fiber diameter and length, e.g., geometric standard deviation for both parameters will be less than 1.50.

Significant Findings

None to date.

Feedback Control of Particles in Fluid Media

David Hemenway, Ph.D.
University of Vermont
College of Engineering & Mathematics
Department of Civil
and Environmental Engineering
Room 226, Votey Building
Burlington, Vermont 05405

Grant Number: *1 R03 OH03185-01*
Start & End Dates: *04/01/94 – 03/31/96*
Funding Level: *$36,475 ($36,475 Cum)*

Importance to Occupational Safety and Health

Results obtained from this research will have immediate relevance to investigators involved in inhalation toxicology research aimed at understanding work related health problems. In order to more accurately determine dose–response relationships, future inhalation protocols will demand greater precision in the level of the dose administered which may be met with the system currently under investigation. It is also our intention that results from this research will be applicable to the automatic control of ventilation systems. For example, this research may enable the control of ventilation rates in mines and tunnels based on contaminant levels which will optimize the removal of the contaminant while minimizing energy costs.

Objectives

This project includes the completion of two objectives:

1. Characterize the relationship between a process input (aerosol generation rate and/or dilution–air flow rate) and the process output (chamber aerosol concentration) under various initial conditions, and
2. determine the relative effectiveness of several feedback control methodologies designed to both maximize the responsiveness of the system when a correction is needed, and minimize the error associated with a desired output level and the actual level.

Methodology

This research has been divided into two primary procedures as outlined below.

1. Investigate the response of chamber concentration levels to various changes in generator speed and chamber air flow rate.
   a. 45 trials will be performed at various flow rates to determine the response of the system to a change in generator speed.
   b. 9 trials will be performed to increase the generator speed in stages to compare the response of the system when different levels of concentration are called for.
   c. Repeat the trials described above with the addition of control algorithms designed to optimize the response performance of the system when a change in concentration (and, hence, generator speed) is desired.
   d. 10 trials will be performed at various flow rates to determine the relationship between aerosol monitor readings and chamber flow rate.
   e. 6 trials will be performed to investigate the response of the chamber concentration level to changes in chamber air flow rate rather than changes in generator speed as in the previous trials.
   f. Repeat the trials performed in part (e) above with the addition of control algorithms designed to optimize the response performance of the system when a change in concentration (and, hence, chamber flow rate) is called for.

A total of 12 to 15 months had been allotted to this phase of the grant research.

2. Investigate the use of various automatic control algorithms, including algorithms designed for statistical process control, to implement automatic feedback control of the instantaneous concentration levels in the chamber.
   a. Use the results obtained in part (1) and a control algorithm based on SPC theory to determine the validity of this technique for maintaining concentration at predetermined levels. This procedure will involve the use of the generator speed to influence concentration levels while the flow rate remains constant. A change in the operating procedure would also allow for an increase in "noise" associated with the monitor readings. The control algorithm will then be tested under these, less favorable, conditions. A total of 30 trials will be performed.
   b. Repeat part (a) with other control algorithms to compare their relative performance abilities (9 trials).
   c. Repeat parts (a) and (b) except the dilution air will be used to manipulate concentrations rather than generator speed (39 trials).

This second part of the grant research is expected to require 9 to 12 months.

Significant Findings

To date, procedures 1(a), (b), and (c) have been performed. Results from part 1(a) indicate the system is capable of producing an increase in chamber concentration close to a desired amount despite the starting level of the concentration (in this case, 1, 10, and 25 mg/m^3). However, the increase was influenced by chamber flow rate, with the largest increase obtained when operating at 0.2 m^3/min and trailing off at higher flow rates. The results also showed the delay time between the sudden change in generator speed and an initial rise in concentration was independent of the flow rate (avg. = 1.54 min.). This result was opposite of what was expected since a slower flow rate should increase the time needed for the increased amount of dust to reach the aerosol sensor. Some time will be spent reviewing work related to the hydraulic behavior of the chamber to attempt an explanation of these results. An average of 8.8 minutes is needed for the concentration to reach a steady level after a sudden change in generator speed.

Parts 1 (b) and (c) were conducted with a similar procedure and can be compared by computing the mean–squared error (MSE) between the actual and expected concentration levels over time. When attempting to increase the concentration from a base level of 10 mg/m^3 with a proportional increase in generator speed during the trials of part 1(b), an MSE value of 0.73 was obtained. This value was reduced to 0.31 when using an automatic control algorithm in part 1 (c).

Publications

O'Shaughnessy PT, Hemenway DR: Computer Automation of A Dry–dust Generating System. Inhalation Toxicology 6:95–113, 1994

Leukocyte DNA Adducts after Carcinogen Exposure

Gerald N. Levy, Ph.D.
University of Michigan
Department of Pharmacology
1301 Medical Science Research Building III
Ann Arbor, Michigan 48109-0632

Grant Number: *5 K01 OH00081-03*
Start & End Dates: *03/01/90 – 02/28/94*
Funding Level: *$0 ($149,975 Cum)*

Importance to Occupational Safety and Health

Humans are exposed to a wide variety of carcinogenic compounds, many of which are unidentified. Individuals within the same occupational environment receive different levels of exposure to chemicals depending on their specific tasks and personal habits. Even individuals receiving the same dose of carcinogen exposure will differ in their sensitivity to the chemical due to differences in metabolism and excretion based on genetics, sex, age, and nutritional and health status. The work supported by this grant seeks to develop a method for determining the actual dose of carcinogen received by individuals in order to set appropriate limits for such exposures and to evaluate safety measures taken to reduce exposures.

Objectives

The major goal of this research is to determine if the measurement of DNA–carcinogen adducts in circulating white blood cells (WBC) can be used as a monitor of *in vivo* exposure to carcinogens. This determination will be made by developing methods of analyzing DNA adducts in white blood cells, investigating the dose–response relationship, and then comparing the levels of leukocyte DNA adducts with DNA–carcinogen adducts found in target tissues of various classes of carcinogens. A secondary goal of the research is to determine if white blood cells have the ability to activate environmental and occupational carcinogens to metabolites capable of forming DNA adducts.

Methodology

Inbred mice are used as an animal model of human exposure to the arylamine carcinogen 2–aminofluorene (2–AF). The animal model allows for controlled exposure to known doses of a specific carcinogen for selected time periods. In addition, the animal model permits access to internal target tissues of the carcinogen. Thus, dose–response measurements comparing carcinogen exposure to DNA–carcinogen adduct production can be made in the bio–marker and in the target tissue.

Acute exposure to 2–AF is achieved by intraperitoneal injection. Subchronic exposure is by addition of 2–AF to the drinking water. DNA is isolated from WBC, liver, and bladder of control and carcinogen treated mice. DNA–carcinogen adducts are detected and quantitated by ^{32}P–postlabeling of nucleotides obtained by enzymatic hydrolysis of DNA followed by HPLC analysis of adducted nucleotides.

The ability of white blood cells to activate carcinogens is examined by isolating mouse white blood cells and incubating them with carcinogen for 12 to 24 hours under standard cell culture conditions. The cells are harvested, DNA prepared, and adducts analyzed by ^{32}P–postlabeling followed by HPLC and scintillation counting.

Significant Findings

In mice, the formation of 2–aminofluorene–DNA adducts in the target tissues liver and bladder is dependent on a number of factors that can modify the metabolic activation of 2–aminofluorene. Among these are age at time of exposure, sex, and acetylator status. Studies of these variables have indicated that acetylator status is of major significance in hepatic DNA adduction, while age at time of exposure is particularly important in bladder adduct formation in male mice. Sex is a significant determinant of which tissue will be the major target of DNA damage (liver in females and bladder in males). In order to simplify initial comparisons between target tissues and WBC, we have examined C57BL/6J (rapid acetylators) male mice at 7 weeks of age.

The formation and disappearance of WBC DNA adducts for 24 hr after exposure to 2–aminofluorene was measured and compared with liver and urinary bladder DNA adducts. In general, adduction of DNA by 2–AF metabolites appeared similar in the three tissues. The highest level of 2–AF–DNA adducts were observed at 3 hr and decreased with time over the period studied. The decline in WBC adducts during the 24 hr period was parallel to the decline in liver adduct levels; WBC adducts were between 11% and 14% of liver adduct levels for the period. A similar relationship between WBC and bladder adducts was only observed for the first 12 hr, during which WBC adducts were about 5% of bladder adduct levels.

Seven day continuous exposure experiments demonstrated a clear dose response between the amount of 2–AF consumed and DNA adduct formation in both leukocytes and the target tissues.

Increasing the concentration of 2–AF in the drinking water produced an almost linear increase in DNA adducts in all 3 tissues examined.

The findings indicate that WBC are potentially useful as exposure indicators both for acute and chronic exposures to the arylamine carcinogen 2–AF and that WBC are worthy of further investigation as biological monitors of DNA damage in internal target tissues. The parallel decline in adduct levels in WBC and liver after acute exposure and the similar dose–response curves for WBC, liver, and bladder DNA adduct formation during continuous exposure indicate WBC may be very useful in determining individual carcinogen exposure levels.

Cultured mononuclear leukocytes (MNL) demonstrated the ability to activate 2–AF and form DNA adducts. The extent of adduct formation was related to the genetically determined ability of MNL to activate 2–AF. Incubation of isolated MNL with carcinogen followed by DNA–carcinogen adduct measurement may give an indication of individual susceptibility to DNA damage.

Publications

Levy GN, Chung JG, Weber WW: 2–Aminofluorene Metabolism and DNA Adduct Formation by Mononuclear Leukocytes from Rapid and Slow Acetylator Mouse Strains. Carcinogenesis 15:353–357, 1994

Chung JG, Levy GN, Weber WW: The Distribution of 2–Aminofluorene and *p*–Aminobenzoic Acid N–Acetyltransferase Activity in Tissues of C57BL/6J Rapid and B6.A–*NAT*^{s} Slow Acetylator Congenic Mice. Drug Metabolism and Distribution 21:1057–1063, 1993

Levy GN: Circulating Leukocytes as Indicators of Arylamine Carcinogen Exposure. Fundamental and Applied Toxicology 21:23–30 1993

Levy GN, Martell KJ, Weber WW: Polymorphic N–Acetylation of 2–Aminofluorene by Cell–Free Colon Extracts from Inbred Mice. Pharmacogenetics 3:71–76, 1993

Chung JG, DeLeon JH, Levy GN, Weber WW: Tissue Distribution of 2–Aminofluorene and *p*–Aminobenzoic Acid N–Acetyltransferease Activity in C57BL/6J Rapid and B6.A–*NAT*^{s} Slow Acetylator Congenic Mice. FASEB J. 7:A51, 1993 (Abstract)

Chung JG, Levy GN, Weber WW: N–Acetylation of 2–Aminofluorene by Mononuclear Leukocytes from Rapid and Slow Acetylator Mouse Lines. The Pharmacologist 35:205, 1993 (Abstract)

Levy GN, Martell KJ, DeLeon JH, Weber WW: Metabolic, Molecular Genetic, and Toxicologic Aspects of the Acetylation Polymorphism in Inbred Mice. Pharmacogenetics, 2:197–206, 1992

Martell KJ, Levy GN, Weber WW: Cloned Mouse N–Acetyltransferases: Enzymatic Properties of Expressed NAT–1 and NAT–2 Gene Products. Molecular Pharmacology 42:265–272, 1992

Levy GN, Weber WW: 2–Aminofluorene–DNA Adducts in Mouse Urinary Bladder: Effect of Age, Sex, and Acetylator Phenotype. Carcinogenesis 13:159–164, 1992

Levy GN: Circulating Leukocytes as Indicators of Arylamine Carcinogen Exposure. The Toxicologist 12:189, 1992 (Abstract)

Martell KJ, Levy GN, Weber WW: Properties of Monomorphic and Polymorphic Mouse N–Acetyltransferases (NAT) Expressed in COS–1 Cells. The Pharmacologist 33:182, 1991 (Abstract)

Cocarcinogenic Particulates in Coculture System

Changhwa Jacob Cheu
University of Cincinnati
College of Medicine
Department of Environmental Health
3223 Eden Avenue
Cincinnati, Ohio 45267-0056

Grant Number: *5 R03 OH02972-02*
Start & End Dates: *08/01/92 – 07/31/94*
Funding Level: *$0 ($23,930 Cum)*

Importance to Occupational Safety and Health

Pulmonary abnormalities are listed among the ten leading occupational diseases in the work place in the United States. Iron and aluminum compounds are widely encountered particles in the occupational settings. In addition to these particles, workers are frequently coexposed to polycyclic aromatic hydrocarbons (PAH). Benzo(a)pyrene (BaP), a ubiquitous PAH resulted from incomplete combustion and cigarette smoke has been well characterized. The adverse effects of BaP are linked to its active metabolites rather than to BaP itself. *In vivo* hamster studies have shown that iron oxide, but not aluminum oxide, can enhance lung tumor formation in

combination with BaP compared to BaP alone. As the defense and target tissue of the host, alveolar macrophages (AM) and tracheal epithelial cells are involving in the pathogenesis of pulmonary carcinoma. Therefore a coculture system which included AM and tracheal epithelial cells was established to study the effects of particles on the metabolism of BaP and BaP–related DNA adduct formation. Understanding of the particle–dependent metabolic activation of PAHs is important for us to estimate the toxic, mutagenic and carcinogenic effects of these particles in the occupational settings. This research provided information on particle–mediated BaP metabolism as well as DNA adduct formation and contributed to our understanding of the etiology of occupational pulmonary diseases.

Objectives

The overall objective of this study is to investigate the effects of particles on the metabolism of BaP and the formation of DNA adducts *in vitro*. The proposed hypothesis is that Fe_2O_3 particles can enhance the metabolism of BaP in AM and subsequently facilitate the binding of the BaP metabolites to the DNA of tracheal epithelial cells. The specific aims are as follows: (1) to determine the alteration of basal metabolic activities of AM in response to BaP or BaP–coated particles (Fe_2O_3 and Al_2O_3); (2) to determine the pattern and amount of BaP metabolites, in particular, 7,8–diol–BaP, the precursor of the ultimate carcinogen, in response to radiolabeled BaP or BaP–coated particles in AM; (3) to determine the amount and the profile of DNA adducts in epithelial cells in response to cocultivation of AM which have been treated with BaP or BaP–coated particles.

Methodology

Erythrosin B stain exclusion assay was used to determine the cytotoxicity of BaP–coated particles to AM. Ethyl acetate extraction and HPLC analysis were conducted to determine the pattern and amount of BaP metabolites in the cells. ^{32}P–postlabelling with P1–enhancement was conducted to measure and identify DNA adducts in the cells.

Significant Findings

AM exposed to BaP–coated Fe_2O_3 responded differently than either BaP alone or BaP–coated Al_2O_3. Data indicate that the overall magnitude of total BaP metabolism is higher in Am exposed to BaP–coated Fe_2O_3 than that of either BaP alone or BaP–coated Al_2O_3. The metabolism of BaP in AM can be significantly increased by elevation of the amount of Fe_2O_3 ($p< 0.05$). Addition of Al_2O_3 particles only affect BaP metabolism marginally. Coadministration of both 7,8–benzoflavone (an inhibitor of cytochrome P–450 1A1 and 1A2) and cyclohexene oxide (an inhibitor of epoxide hydrolase) remarkably decreased the metabolism of BaP in AM in the presence of Fe_2O_3(85%), Al_2O_3(76%) or BaP(40%) alone ($p< 0.05$). One of the BaP metabolites, 7,8–dihydrodiol–BaP, is considered to be the precursor to the ultimate carcinogen of BaP. Although the level of these metabolites were low, it was sufficient to produce DNA adducts.

^{32}P–postlabeling of the tracheal epithelial cells (HTE) which were cocultured with AM revealed the quantitative but not qualitative discrepancy of DNA adducts among different treatments. Two adducts with different proportions appeared upon each treatment. The major adduct co–chromatographed with the standard (+)–anti–BPDE–dG on the TLC plate. The other adduct co–migrated with standard (–)–anti–BPDE–dG. The profiles of DNA adducts suggest that the formations of (+)–anti–BPDE–dG and (–)–anti–BPDE–dG involve cytochrome P–450 dependent and independent pathways, respectively. The total adducted adducts and (+)–anti–BPDE–dG appeared to be higher in HTE coincubated with BaP–coated Fe_2O_3 than that of either BaP–coated Al_2O_3 or BaP alone, albeit with no statistical significance. However in the longer–term exposures, these differences may have the potential risk and might be manifested significantly. The other adduct, (–)–anti–BPDE–dG, was significantly higher in the treatment of BaP–coated Fe_2O_3 than that of BaP alone or BaP–coated Al_2O_3 ($p<–0.05$). The adduct levels of HTE in each treatment can be reduced by addition of 7,8–benzoflavone and cyclohexene oxide. The data presented here support the hypothesis that Fe_2O_3 particles can enhance the metabolism of BaP in AM and subsequently facilitate the binding of BaP metabolites to the DNA of tracheal epithelial cells. In parallel with the specific aims, results suggested that the enhancement of BaP metabolism and DNA adduct formation by Fe_2O_3 is modulated by P–450 enzymatic pathway, perhaps non P–450 factors might also be involved.

Molecular Dosimetry for Carcinogens

Suresh P. Krishnan
University of Cincinnati
College of Medicine
Department of Environmental Health
3223 Eden Avenue
Cincinnati, Ohio 45267-0056

Grant Number: *5 R03 OH02880-02*
Start & End Dates: *09/30/91 – 09/29/94*
Funding Level: *$0 ($36,805 Cum)*

Importance to Occupational Safety and Health

Airborne levels of contaminants will not always predict dermal absorption, and in some occupations, dermal absorption may be the main route of exposure for many carcinogens in the workplace. Exposure to complex mixtures containing polycyclic aromatic hydrocarbons e.g., benzo(a)pyrene (BaP) and 7,12 dimethylbenzanthracene [DMBA]; N–heterocyclic aromatics e.g., 7H–dibenz[c,g]carbazole [DBC]; and aromatic amines e.g., 4–aminobiphenyl (4ABP), can cause tumors at the site for BaP, DBC and DMBA or at distant organs (as in the case of aromatic amine–caused bladder cancer or DBC induced liver cancer). Biomarkers sensitive to the effects of compounds absorbed dermally would increase our ability to predict significant exposure and early effect. The aims of our grant are to develop two such markers (DNA adducts and micronuclei (MN) frequencies) for proto–typical occupational carcinogens. This may help identify threshold levels of exposure for individual carcinogens that correspond to the limits of detection for combined adduct and MN measurements in the workplace.

Objectives

The kinetics of DNA adduct levels (^{32}P–postlabeling assay) and MN frequencies (cytochalasin–B blocking method) will be determined in mouse skin and liver for BaP, DBC & 4ABP respectively. Dose–response relationships will be established between carcinogen–DNA adducts and cytogenetic damage as measured by MN frequencies. Appropriate statistical tests wills be conducted to determine the strength of the association between the two biological markers of exposure. Finally, the mechanisms of clastogencity will be evaluated by using an inhibitor of cytochrome P450 to determine if MN formation could be inhibited in mouse skin.

Methodology

The study has been divided into two main parts:

1. Kinetics Study – The kinetics study has been divided into two parts:
   (a) Dose response study (b) Time course study
   This study will allow for observation of repair and determine the times of maximum DNA binding and maximum MN expression.
2. Inhibitor study – An inhibitor of Cytochrome P–450 will be used to determine if MN formation could be inhibited. These experiments will enable us to understand the mechanism of MN formation.

Primary murine keratinocytes will be isolated, under sterile conditions, using established procedures. They will be resuspended in low calcium minimum essential medium and plated on collagen coated microscope sides at a cell density of 3 x 10^6 cells/slide. The cells grown on slides will be used for the MN assay while the cells grown on dishes will be trysinized and stored at –80°C for subsequent DNA isolation and ^{32}P–post labeling. DNA adduct levels will be determined by the ^{32}P–post labeling assay. Micronuclei will be scored in 1000 binucleated cells.

Significant Findings

The procedure (followed in Rebecca Morris' laboratory) for the isolation, establishment and maintenance of mouse leratinocytes was modified and optimized to suit the conditions require for performing the DNA adduct and ^{32}P–postlabeling assay. Immunocytochemical staining of mouse keratinocytes demonstrated that the cells were predominantly mouse keratinocytes. In order to determine the induction of MN in cells that have divided once and only once, MN were scored in binucleated cells.

Experiments were performed to optimize the conditions for obtaining maximal numbers of binucleate (BN) cells [MN were scored in 1000 cytokinesis–blocked binucleate cells]. It has been found that mouse keratinocytes have to be cultured, in the presence of cytochalasin–B, for 72 hours in order to obtain optimal numbers of binucleated cells.

Historical control data [N=11] indicated that the MN values in the controls (15.7+/–4.4) and solvent controls (16.9+/–3.8) were not significantly different form each other. Hence, solvent controls were used in the subsequent experiments performed to determine the association between CA and MN. At the doses ranging between 4.55.0 μg/mouse, BaP did not produce a significant increase in MN over acetone treated controls [*in vivo*]. In addition, this compound

did not produce a significant increase in MN *in vitro* [12 μg – 120 μg/ml of media]. However, adriamycin (*in vitro*) produced a very significant dose–dependent increase in MN when compared to controls (25 ng/ml 99 MN/1000 BN cells; 50 ng/ml 165 MN/1000 BN cells; 100 ng/ml 288 MN/1000 BN cells]. This indicated that mouse keratinocytes had the ability to express MN formation. Furthermore, time course experiments [6, 12, 24 hours] demonstrated that DBC[500 ng/ml] induced MN significantly over solvent controls at all time points tested and MN levels over solvent controls were highest at 24 hours. It was therefore decided to examine the association between CA and MN for DBC as well as DMBA under conditions optimized for the MN assay. Under these conditions, DBC [*in vitro*], an equally significant environmental and occupational pollutant also induced a dose [0.01–1μg/ml] dependent increase in MN [42–90 MN/1000 BHN cells] over solvents controls. Experiments run in parallel demonstrated the fact the DBC induced a significant increase in CA–DNA adducts [17–35; RAL x 10^7] over solvent controls [N=4]. The Pearson's correlation coefficient was 0.66. In addition, there was a good correlation between DMBA adducts [6.7–9.1; RAL x 10^7 and MN [70.7–114.7; N=3] following carcinogen exposure for 24 hours. The Pearson's correlation coefficient was 0.73.

The strength of the statistical association between CA and MN for both compounds, indicated that the two above mentioned end points may be causally related.

Stress Genes as Biomarkers of Mineral Dust Exposure

Cynthia R. Timblin, Ph.D.
University of Vermont
College of Medicine
Department of Pathology
Burlington, Vermont 05405

Grant Number: *1 K01 OH00146-01*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$54,000 ($54,000 Cum)*

Importance to Occupational Safety and Health

Occupational exposure to asbestos or silica is associated with the development of both non–malignant and malignant pulmonary disease. This proposal focuses on the molecular responses of target cells of the lung to asbestos and silica. Considerable evidence indicates that the mechanism of mineral dust toxicity involves the production of active oxygen species (AOS) catalyzed directly on the mineral surface or by phagocytic cells within the lung. Production of AOS in excess of cellular defenses creates an environment of oxidative stress for the cell. The molecular response of cells to stress is a reprogramming of gene expression to meet the new challenges of its' environment. Oxidant–induced genes include: genes encoding antioxidant enzymes, proto–oncogenes (e.g. c–*jun*), *hsp*70, *grp*78, *gadd*45, and *gadd*153. Changes and/or unique patterns of induction using a battery of stress–inducible genes can be used not only to characterize stress–specific or cell type–specific responses, but also to obtain a "fingerprint" in cells which can be used as a biomarker of exposure. Development of biomarkers requires information about the responses of target cells to asbestos, silica, or oxidants and their relationship to cell injury or disease. Measurement of expression of a battery of stress–responsive genes with different cellular functions in pulmonary target cells may identify a set of genes that can be used coordinately as biomarkers of mineral dust–induced injury in man using non–invasive techniques such as BAL.

Objectives

The central hypothesis of this grant is that oxidative stress imposed by mineral dusts elicits a molecular stress response that can be characterized by changes in gene expression. The specific aims are as follows:

1. Define a battery of asbestos and/or silica–induced genes that can be used as biomarkers of mineral dust exposure and disease.
2. Compare asbestos or silica–induced responses to other oxidant–stresses and identify new components in mineral dust–induced toxicity.
3. Examine the role of c–*jun* in mineral dust–induced stress and disease development or progression.

Methodology

The following approaches will be used to address each specific aim:

1. Molecular stress responses of individual target cell types (epithelial, mesothelial), bronchoalveolar lavage (BAL) cells and lung tissues of rats exposed to mineral dusts will be evaluated for alterations in mRNA for the *hsp*70, *grp*78, *gadd*45, and *gadd*153 genes by Northern blot analysis.

2. Cellular signalling pathways activated by asbestos or silica may be comparable to those triggered by other stress–inducing agents. To examine whether pathways overlap, cell cultures (HTE, RPM) will be exposed to low levels of a specific stress agent (e.g.H_2O_2), subsequently challenged with asbestos or silica and the expression of known markers (e.g. c–*jun*, MnSOD, heme oxygenase) of asbestos or silica toxicity examined by Northern blot analysis.
3. Transient transfection assays using the $CaPO_4$ co–precipitation technique have been used to introduce a constitutively expressed c–*jun* construct and two reporter vectors, luciferase and beta–galactosidase into cell cultures of hamster tracheal epithelial (HTE) cells. These transfected cells have been used to examine the induction of c–*jun* dependent gene expression by asbestos and the role of c–*jun* overexpression in cell proliferation and transformation using growth curves, BrdU incorporation and soft agar transformation assays.

Significant Findings

Previously, the laboratory has demonstrated that asbestos causes persistent increases in mRNA levels of c–*jun* and AP–1 DNA binding activity in hamster tracheal epithelial cells, the progenitor cell type of asbestos–induced bronchogenic carcinoma. It has been determined whether asbestos causes transcriptional activation of the c–*jun* gene through an oxidative mechanism. Examinations were conducted to determine whether c–*jun* overexpression is involved in cell proliferation. First, HTE cells were transiently transfected using $CaPO_4$ co–precipitation with a plasmid containing a fragment of the c–*jun* promoter coupled to a luciferase reporter gene. In addition, c–*jun* was overexpressed transiently and effects on cell proliferation and transformation were examined. HTE cells transfected with the *jun*–luciferase construct showed increased luciferase activity when exposed to crocidolite asbestos or H_2O_2. These results demonstrate that asbestos and H_2O_2 activate AP–1 dependent gene transcription. Furthermore, preliminary experiments suggest that overexpression of c–*jun* leads to increased proliferation (measured by BrdU incorporation) and enhanced ability of HTE cells to grow in soft agar, an indication of cellular transformation.

Publications

Timblin CR, Janssen YMW, Mossman BT: Asbestos and H_2O_2 Cause Transcriptional Activation of c–*jun*, A Protooncogene Directly Related To Increased Proliferation and Transformation of Tracheal Epithelial Cells. American Journal of Respiratory and Critical Care Medicine, in press, 1995

Susceptibility to Genetic Damage from Butadiene

Karl T. Kelsey, M.D.
Harvard University
School of Public Health
Occupational Health Program
665 Huntington Avenue
Boston, Massachusetts 02115

Grant Number: *5 K01 OH00110-03*
Start & End Dates: *09/30/91 – 09/29/94*
Funding Level: *$0 ($162,000 Cum)*

Importance to Occupational Safety and Health

In recent years there has been a growing interest in the application of biomarkers in cancer epidemiology. The current research is being conducted with an emphasis on genotoxic and mutagenic markers and the genetic modifiers of sister chromatid exchange induction. Such modifications will likely have relevance for the prevention of occupationally–induced cancers.

Objectives

The objectives of this research were to determine the extent of genotoxicity attributable to 1,3–butadiene exposure in humans in the workplace and to test whether chromosomal sensitivity to diepoxybutane predicts individual susceptibility to genotoxic effects of butadiene exposure. An additional objective was to determine if the previously determined chromosomal sensitivity to metabolites of butadiene are attributable to a discernible metabolic polymorphism.

Methodology

Butadiene workers involved in monomer and polymer production were studied. Exposure was assessed by questionnaire, workplace walk–throughs and personal and area monitoring. Butadiene–exposed workers contributed a blood sample and chromosomal endpoints were analyzed. Individual sensitivity to the cytogenetic effects of diepoxybutane added *in vitro* was assessed. Analysis was completed to determine if individual cytogenetic sensitivity to diepoxybutane predicts the baseline level

of chromosome damage induced by butadiene exposure. In this way, susceptibility to the chromosomal effects of butadiene was examined by looking at chromosomal sensitivity to the butadiene metabolite, diepoxybutane.

Individuals previously phenotyped for cytogenetic sensitivity to butadiene metabolites were re–studied to determine their genotype for a newly described polymorphism in the glutathione S–transferase class theta. Genotype and phenotype were compared to assess the association of the metabolic polymorphism with phenotypic chromosomal sensitivity.

Significant Findings

The field portion of the study has been completed. Exposure to butadiene has been assessed with 8–hour time wait of average personal sampling as well as urine collection and metabolite determination. Significant data has been collected by questionnaire and blood has also been collected. Early analysis of the data reveals baseline cytogenetic changes in the exposed group to be unrelated to time–weighted average measurements of exposure. Urine was collected and there is no relationship between induced cytogenetic damage and urinary measures of exposure to butadiene. However, examination of high SCE frequency cells reveals that there is some relationship between length and the trade and high frequency SCE cells present in workers. Also, one individual who had previously been noted to have a very high HPRT mutant fraction was also sensitive to diepoxybutane *in vitro*.

Thus, the work indicates that acute exposure to 1,3–butadiene was not associated with induction of chromosomal abnormalities. However, tenure in the trade was associated with production of high SCE frequency cells.

It was determined that the homozygous gene deletion in glutathione S–transferase (GST) class theta is responsible for heritable sensitivity to butadiene metabolites. This implies that GST theta detoxifies butadiene metabolites and individuals with this deletion may be susceptible to DNA damage from butadiene exposure.

Companion studies of molecular epidemiology are being carried out using these same techniques. These studies have shown that genetic damage, induced by exposure to radiation results in persistent genetic damage measured as sematic mutations. Further, it's been noted that constitutional heterozygosity for the ataxia–telangiectasia gene results in heterogeneity in the clastogenic response to x–rays in lymphocytes from these individuals. In addition, molecular determination of the heterozygosity in glutathione transferase class μ does not modify venodilatory potency of nitroglycerin in human veins.

Publications

Wiencke JK, Pemble S, Ketterer B, Kelsey KT: Gene Deletion of Glutathione–S–transferase Θ: Correlation with Inducted Genetic Damage and Potential Role in Endogenous Mutagenesis. Cancer Epidemiology, Biomarkers and Prevention, in press, 1995

Wiencke JK, Kelsey KT: Susceptibility To Chromosomal Damage Induction by Metabolites of 1,3–Butadiene and Its Relationship To "Spontaneous" Sister Chromatid Exchange Frequencies in Human Lymphocytes, IARC Monograph (ed. M Sorsa) in press, 1993

Wiencke JK, Kelsey KT: Susceptibility To Induction of Chromosomal Damage by Metabolites of 1,3–Butadiene and Its Relationship To "Spontaneous" Sister Chromatid Exchange Frequencies in Human Lymphocytes, IARC Scientific Publications No. 127, (eds. M Sorsa, K Pelionen, H Vainio, K Hemminki), Lyon, International Agency for Research on Cancer, 1993

Kelsey KT, Bechtold WE, Ward JB, Wiencke JK: Susceptibility to Genetic Damage From Occupational Exposure to Butadiene. Proceedings of the International Symposium on Health Hazards of Butadiene and Styrene, 1993

Wiencke JK, Kelsey KT: Inter–Individual Sensitivity and Cytogenic Response to Diepoxybutane. Proceedings of the International Conference on the Health Hazards of Butadiene and Styrene, 1993

Bechtold WE, Kelsey KT, Ward JB: Measurement of 1,2–Dihydroxy–4–(N–Acetylcysteinyl–S)Butane In A Urine As A Biomarker of Exposure to 1,3–Butadiene. Proceedings of the International Conference on the Health Hazards of Butadiene and Styrene, 1993

Haefeli WE, Srivastava N, Kelsey KT, Wiencke JK, Hoffman BB, Blaschke TF: Glutathione S–transferase Polymorphism Does Not Modify Venodilatory Potency of Nitroglycerin in Human Veins. Clinical Science 53(4):463–468, 1993

Wiencke JK, Wara DW, Little JB, Kelsey KT: Heterogeneity in the Clastogenic Response to X–rays in Lymphocytes from Ataxia–Telangiectasia Heterozygotes and Controls. Cancer Causes and Control 3:237–245, 1993

Cullen MR, Solomon L, Pace PE, Buckley P, Duffy T, McPhedran P, Kelsey KT, Redlich CA: Morphologic Biochemical and Cytogenetic Studies of Bone Marrow and Circulating Blood Cells in Painters

Exposed to Ethylene Glycol Ethers. Environ Res 59:250–264, 1992

Smith CM, Kelsey KT, Christiani DC: Risk Assessment and Occupational Health Overview and Recommendations. New Solutions, Winter:26–38, 1992

Caggana M, Liber HL, Coleman MD, Mauch PM, Clark JR, Kelsey KT: A Prospective Study of *hprt* Mutant and Mutation Frequency in Treated Cancer Patients. Cancer Epidemiology, Biomarkers and Prevention 573–580, 1992

Glycophorin a Biodosimetry in I-131 Treated Patients

William L. Bigbee, Ph.D.
University of Pittsburgh
Graduate School of Public Health
Department of Environmental
and Occupational Health
260 Kappa Drive, RIDC Park
Pittsburgh, Pennsylvania 15238

Grant Number: *1 R01 OH03276-01*
Start & End Dates: *09/30/94 – 09/29/97*
Funding Level: *$77,799 ($77,799 Cum)*

Importance to Occupational Safety and Health

This study is focused on the use of biomarkers, notably the glycophorin A (*GPA*) *in vivo* somatic cell mutation assay, as retrospective biodosimeters of human exposure to ionizing radiation. The results of this study will have direct application in assessing the utility of these methods to reconstruct historical exposures and provide concurrent biomonitoring of workers occupationally exposed to radiation.

Objectives

The principal goal of this project is to use the well calibrated doses of ionizing radiation to the red marrow of patients with thyroid disease treated with I^{131} to more precisely define the low dose and low dose–rate response of the *GPA* assay to ionizing radiation. Use of this medical exposure to determine the shape and magnitude of the dose response and the sensitivity of the assay to low doses of sub–acute exposure to radiation will provide important new data that will be critical in interpreting the results of the assay applied as a biodosimeter in populations occupationally or accidentally exposed to ionizing radiation.

A second goal of the study is to compare the response in the assay in patients who have received very similar red marrow doses in order to evaluate the inter–individual variation in response to ionizing radiation exposure using this biomarker.

A third goal of the study is to collect and cryopreserve viable lymphocytes from these patients as a valuable biological resource for additional lymphocyte–based cytogenetic and mutational biomarker studies of the genetic effects of radiation exposure in humans.

Methodology

The *GPA* assay uses immunolabeling and flow cytometry to enumerate erythrocytes in peripheral blood expressing allele–loss variant phenotypes as a result of gene inactivating somatic mutations that have occurred at the *GPA* locus in erythroid progenitor marrow cells. Previous results obtained for blood samples from individuals who have received whole–body exposures to ionizing radiation have shown the assay is a quantitative retrospective biodosimeter of the persistent effect of radiation exposures that have occurred years to decades previously.

In the present study, time series blood samples are being obtained from patients with thyroid disease, diagnosed with either thyroid cancer or hyperthyroidism, who are treated with I^{131}. Depending on the total dose of I^{131} and the amount and rate of retention of the radionuclide, a patient will receive a whole body exposure of 2 to >100 cGy to the red marrow that can be precisely determined. Blood samples are drawn and analyzed prior to, immediately after, and long–term (up to one year) post–therapy in order to detect and quantitate the induction, accumulation, and long–lived persistence of the radiation–induced somatic mutations detectable with the *GPA* assay.

Significant Findings

Initial preliminary results obtained for six patients studied using the *GPA* assay have shown increases in the frequency of allele–loss variant erythrocytes consistent with immediate and persistent radiation–induced mutations in long–lived marrow erythroid progenitor cells and the 120 day lifetime of circulating erythrocytes. Based on preliminary dosimetry of the I^{131} red marrow doses received by these patients, the observed dose response appears to be one–fourth to one–third of that deduced from previous studies of individuals acutely exposed to external ionizing radiation. The apparent lower slope of the dose response observed in the I^{131} treated

patients may reflect a reduced biological effectiveness of this exposure due to differences in the energy spectra of the γ radiation, internal versus external exposure, and/or protracted versus acute dose rate effects.

Biological Monitoring/Risk Assessment In An Exposed Cohort

George P. Hemstreet, Ph.D.
University of Oklahoma
College of Medicine
Department of Urology
920 Stanton L. Young Blvd., 5SP330
P.O. Box 26901
Oklahoma City, Oklahoma 73190

Grant Number: *5 R01 OH02647-04*
Start & End Dates: *05/01/93 – 04/30/98*
Funding Level: *$342,514 ($1,183,422 Cum)*

Importance to Occupational Safety and Health

Thousands of workers worldwide are at increased risk of bladder cancer because of previous exposure to aromatic amines. These risks have been characterized in the past primarily by epidemiologic means, permitting assessment of risks associated with the cohort as a whole. If markers within the cancer process can be identified, individuals in the exposed cohorts might be differentiated according to risk and targeted for the appropriate intervention. In addition to occupational chemical exposure, other exogenous risk factors and endogenous risk factors influence the estimated relative risk or overall odds of the individual developing bladder cancer. Data on the prevalence of various risk factors and biological markers in exposed cohorts could be used to develop individual risk profiles which could be helpful for determining individual risk in other high–risk cohorts identified by epidemiologic means.

Results of this study of identified high–risk cohorts in China could provide significant new data on early detection of bladder cancer, exogenous and endogenous risk factors associated with the disease, and biological intermediate endpoint markers indicative of bladder cancer risk. These findings could have profound implications for the development and initiation of bladder cancer screening programs in the large number of U.S. industries in which workers are or have been exposed to bladder carcinogens.

Objectives

The primary objectives of this research are to continue screening in a cohort of workers occupationally exposed to benzidine to both develop a bladder cancer screening approach and to reduce the number of deaths and serious morbidity associated with bladder cancer in this cohort. The ultimate aim is to devise a strategy that will detect persons likely to develop dangerous, invasive disease early enough to alter potentially unfavorable outcomes and release those at little elevated risk. The detection window during which this can be achieved with conventional screening techniques is very narrow, but can be widened with new tests based upon detecting the emerging malignant phenotype rather than waiting for frank cancer. The long–term goals are to develop a strategy based upon a combination of biochemical intermediate markers and clinical signs and symptoms, combined with assessments of various exposures to (1) assess the bladder cancer risk faced by an individual and (2) more effectively manage such individuals to minimize their risk.

Methodology

To continue to screen and monitor a cohort of approximately 2,000 Chinese workers exposed to benzidine to identify confirmed and presumptive cases of bladder cancer and conduct a risk factor analysis. This large worker population is located in five cities — Shanghai, Jilin, Tianjin, Chongqing, and Henan – – in the People's Republic of China.

Significant Findings

In a pilot study and the 2–year program which preceded the present study, bladder cancer was detected in its earliest stages prior to detection by conventional cytologic criteria using a biomarker profile consisting of G–actin, a marker for early differentiation changes, the p300 tumor related antigen detected with M344 monoclonal antibody, and abnormal DNA ploidy detected by the presence of cells with >5C DNA. Exposed male workers (1,686) and unexposed male controls (388) matched for age and smoking historyhave been screened. Preliminary statistical analysis of the results from workers in two of the cities using the previously defined panel of biomarkers using both χ^2 and Logistic Regression, identified highly significant correlations ($p < 0.05$ to 0.0001) with duration of benzidine exposure, pack–years smoked, and urinary stasis associated with benign prostatic hypertrophy, all of which are also risk factors for bladder cancer. The currently employed weighted exposure index and hematuria did not correlate with the biomarkers. The current study is designed to assess the bladder cancer risk of

exposed individuals and validate using a panel of biomarkers for risk assessment. The original screening of this cohort has yielded three subject groups. From screening the worker groups in Shanghai and Chongqing, we estimate the numbers in each group (totals of exposed and controls) to be: Group 1 – negative for any biomarkers (about 1500 subjects); Group 2 – positive for one marker (about 400 subjects); and Group 3 – positive for two or more markers (about 150 subjects). Group 1 will be screened every 3 years, Group 2 every year (or five times during the study), and Group 3, the highest risk group, every 6 months (or 10 times during the study). Group 3 will include urological followup, and screening in Groups 2 and 3 will include additional, more specific markers to further stratify risk within the groups and to investigate the relationships among such markers in the carcinogenic process.

Publications

Bi WF, Rao JY, Hemstreet GP, Yin S, Asal NR, Zang M, Min KW, Ma Z, Fang P, Lee E, Li G, Hurst RE, Wu W, Bonner RB, Wang Y, Fradet Y: Field Molecular Epidemiology: Feasibility of Monitoring For the Malignant Bladder Cell Phenotype in a Benzidine–Exposed Occupational Cohort. J Occup Med 35:20–27, 1993

Rao JY, Hemstreet GP, Hurst RE, Bonner RB, Jones PL, Min KW, Fradet Y: Alterations in Phenotypic Biochemical Markers in Bladder Epithelium During Tumorigenesis. Proc Nat Acad Sci, USA 90:8287–8291, 1993

Bonner RB, Hemstreet GP, Fradet Y, Rao JY, Min KW, Hurst RE: Bladder Cancer Risk Assessment With Quantitative Fluorescence Image Analysis of Tumor Markers in Exfoliated Bladder Cells. Cancer 72:2461–2469, 1993

Semen as a Biomarker of Effect Among Lead Exposed Men

Harvey Checkoway, Ph.D.
University of Washington
School of Public Health
and Community Medicine
Department of Environmental Health, SC-34
Seattle, Washington 98195

Grant Number: *5 R03 OH02966-02*
Start & End Dates: *04/01/92 – 10/31/94*
Funding Level: *$0 ($22,828 Cum)*

Importance to Occupational Safety and Health

This study has provided information on some reproductive consequences of occupational lead exposure, and will serve as a model for evaluating the effects of occupational and environmental exposures on male reproductive function.

Objectives

The overall objective of this project was to use semen quality as a biomarker of effect on the male reproductive system resulting from occupational and environmental exposures. Occupational exposure to lead was the focus of this study.

Methodology

A cross–sectional study design was employed to compare semen quality parameters, serum reproductive hormone levels, and reproductive histories among men employed at a large lead–zinc smelter in British Columbia. Study participants were recruited from the entire male employee population by the means of a postal questionnaire. The questionnaire recorded reproductive histories, socio–demographic characteristics, personal habits, such as tobacco and alcohol use, current and past illness, and a range of symptoms potentially related to lead exposure. Of the 2,469 male employees contacted (2,123 current employees and 346 employees laid–off in 1992) 929 returned questionnaires. Of these 152 provided blood and urine samples including 119 who also provided semen samples.

A blood sample was drawn to determine recent lead exposure by measuring blood lead and zinc protoporphyrin levels. A first A.M. void urine sample was obtained for measurement of urinary porphyrins. Aliquots of blood, urine, and semen

were frozen for analysis of other metals including zinc, cadmium, arsenic, copper, and mercury. Work histories and blood lead monitoring data were obtained from the worker health program for all individuals who participated in the study. The average blood lead level during the preceding 10 years was used to estimate chronic lead exposure.

Semen samples were collected at home or on site, and were delivered to the field laboratory within one hour of collection. The semen samples were processed according to the World Health Organization standard protocol recording sperm concentration, count, motility, and morphology. Computer assisted sperm analysis (CASA) techniques for motility were used to determine the motility characteristics of the motile sperm. Aliquots of semen were cryopreserved for a sperm penetration assay and a flow cytometric assay for sperm chromatin structure stability. Serum levels of testosterone, follicle stimulating hormone, and luteinizing hormone were measured to evaluate the effect of lead exposure on the hormonal control of spermatogenesis. The semen quality parameters and reproductive hormone levels were compared between subjects with high, moderate, and low measures of current and chronic lead exposure.

Significant Findings

For blood lead level groups of <15, 15–24, 25–39, ≥40 μg/dl, the geometric mean sperm concentrations were, respectively: 79.1, 56.5, 62.7, and 44.4 million cells/ml, and geometric mean total sperm counts were 186, 153, 137, and 89 million cells. When compared to workers with blood lead levels of <15 μg/dl workers with high current blood lead levels (≥40 μg/dl) had an increased risk of clinically below normal sperm concentration (OR=8.2, 95% CI= 1.2, 57.9) and sperm count (OR=2.6, 95% CI= 0.4, 15.7), based on WHO standards. Among workers with current blood lead levels of <40 μg/dl, the geometric mean sperm concentration, total sperm count, and total motile sperm count decreased as the average blood lead level of the preceding 10 years increased. No consistent associations were observed between lead exposure and computer assisted measures of sperm motility or serum levels of reproductive hormones. This study provides evidence that lead exposure resulting in blood lead levels below current worker protection limits has a direct effect on testicular function as indicated by a suppression in sperm count and concentration.

Organophosphate Neuropathy and Biomarkers of Exposure

James Godbold, Ph.D.
Mount Sinai
School of Medicine
One Gustave L. Levy Place
New York, New York 10029-6754

Grant Number: *5 K01 OH00123-03*
Start & End Dates: *07/01/92 – 07/31/95*
Funding Level: *$54,000 ($161,987 Cum)*

Importance to Occupational Safety and Health

Poisoning with methamidophos and certain other organophosphate insecticides, including chlorpyrifos, has been reported to cause neuropathy. Recent studies suggest that mild and subclinical neuropathy may affect over 25% of all individuals poisoned with methamidophos, an insecticide used widely by hundreds of thousands of farmers throughout the world. Experimental studies suggest that inhibition of the activity of neuropathy target esterase, which can be measured in lymphocytes, is predictive of subsequent neuropathy and that autoantibodies to neurofilament triplet protein are increased in serum of animals with experimentally induced organophosphate induced neuropathy. We propose to validate these assays among a poisoned population. These assays are potentially of use for screening workers exposed to organophosphate neurotoxins, for predicting the clinical sequela among individuals poisoned with methamidophos, chlorpyrifos, and other organophosphate neurotoxins, and as the basis for further exploration of the mechanism of organophosphate neuropathy.

Objectives

The biological hypothesis under study is that there exists a syndrome of persistent subclinical peripheral neuropathy caused by methamidophos or chlorpyrifos, and that this syndrome can be reliably detected by electrophysiologic assessment of sensory and motor function coupled with assessment of serum autoantibodies to nervous system tissue and assessment of exposure through measurement of NTE activity in circulating lymphocytes.

Specific Aims are:

1. Whether inhibition of lymphocyte neuropathy target esterase (NTE) measured in peripheral lymphocytes is a sensitive and specific index of peripheral neurotoxicity and of serum autoantibodies to peripheral nervous system proteins.
2. Whether previous poisoning with methamidophos or chlorpyrifos results in diminished motor and sensory function, as reflected in electrophysiologic studies, pinch strength, and elevated vibrotactile threshold.
3. Whether a dose–response relationship exists between lymphocyte NTE inhibition and motor or sensory function, or serum autoantibodies.
4. Whether there exist threshold levels of methamidophos or chlorpyrifos exposure, below which either sensory or motor neuropathy is no longer evident.

Methodology

The study population consists of 50 patients previously poisoned with neuropathic organophosphates and treated at two teaching hospitals in Nicaragua plus two control groups: (1) patients poisoned with other organophosphates not known to be neurotoxins, and (2) unexposed cattle rancher controls. At the time of acute poisoning, inhibition of neuropathy target esterase (NTE), the putative target enzyme for organophosphate neuropathy, and serum autoantibodies to neurofilament triplet proteins, are measured in peripheral lymphocytes. Severity of poisoning also is evaluated clinically. Before hospital discharge (and before neuropathy is likely to have occurred), vibrotactile threshold, thermal sensory threshold, dynamometric grip and pinch strength, nerve conduction studies, and clinical evaluations are conducted among poisoned and never poisoned patients (cattle rancher controls). Exposure is characterized by patient interview and field visit to the site of poisoning, and by analysis of residue in dermal wipe samples or in field samples, where necessary, to confirm the pesticide responsible for poisoning. All patients are re–examined 6 weeks to 3 months after poisoning, long enough for peripheral neuropathy to develop. Convalescent autoantibodies are measured, and baseline neuropathy target esterase is measured at the time of followup. Neuropathy target esterase will be validated against clinical outcome and serum autoantibodies, and dose–response relationships and possible thresholds of inhibition of NTE, necessary for the development of neuropathy, will be examined by measuring acute and subsequent baseline (percent depression) of neuropathy target esterase. All workers will be re–examined two years after poisoning to evaluate the persistence of neuropathy.

Significant Findings

Of the fifty acutely poisoned patients recruited to date to this cohort, thirty have been poisoned with the peripheral neurotoxins chlorpyrifos or methamidophos. All fifty poisoned patients have been re–examined between 6 weeks and 3 months after acute poisoning. In addition, 20 not poisoned cattle ranchers have had two examinations at similar intervals to the controls. In the poisoned cohort, we have identified one case of profound neuropathy who had markedly depressed neuropathy target esterase at the time of acute poisoning.

Publications

McConnell R, Keifer M, Rosenstock L: Elevated Quantitative Vibrotactile Threshold Among Workers Previously Poisoned With Methamidophos and Other Organophosphate Pesticides. Am J of Indust Med 25:325–334, 1994

Biological Monitoring of Methanol Exposure

Alfred Franzblau, M.D.
University of Michigan
School of Public Health
Department of Environmental and Industrial Health
1420 Washington Heights
Ann Arbor, Michigan 48109-2029

Grant Number: *5 R01 OH03024-02*
Start & End Dates: *02/01/93 – 07/31/95*
Funding Level: *$187,398 ($363,589 Cum)*

Importance to Occupational Safety and Health

Methanol has been selected by the U.S. government as a potential alternative automotive fuel. Usage as an automotive fuel would involve vastly greater opportunities for chronic low–level exposure of workers and consumers to methanol than have existed in the past. Human health effects related to chronic, low–level methanol exposure are largely unknown. There have been no human epidemiological studies focused on the effects of chronic low–level methanol exposure, and results of animal studies are difficult to extrapolate to humans

because of significant difference in the metabolism and toxicity of methanol in most animal models. An essential component of any human epidemiological investigation of the effects of chronic low–level methanol exposure will be exposure assessment of subjects. Methanol is quite well absorbed via all major routes of exposure (gastrointestinal, inhalation, and dermal), so biological indicators of methanol exposure would provide more accurate assessment of the total absorbed dose, in comparison to routine measurements of the airborne concentration of methanol that are usually applied in the industrial setting. Although two approaches to biological monitoring of occupational methanol exposure have been endorsed by the ACGIH the published data supporting these methods are limited, and in some areas, are contradicted by more recent reports. The data and analyses from this study will permit separate, quantitative examination of the major factors which are believed to influence biological indicators of methanol exposure in the occupational setting: airborne concentration of exposure; duration of exposure; level of pulmonary ventilation; and cutaneous exposure.

Objectives

The goal of this research is to identify valid, reproducible, and non invasive methods for biologically monitoring occupational methanol exposure, and to assess quantitatively the impact of exercise and cutaneous methanol exposure on such indices. The underlying approach will be to perform a series of controlled experiments with volunteer subjects. Specific aims are to investigate the:

1. Use of formic acid (formate) in urine as a quantitative biological exposure indicator for exposure of humans to methanol via the inhalation route and via the cutaneous route;
2. Use of methanol in urine as a quantitative biological indicator for exposure of humans to methanol via the inhalation route and via the cutaneous route;
3. Use of methanol in end–expired (alveolar) air as a quantitative biological exposure indicator for exposure of humans to methanol via the inhalation route and via the cutaneous route;
4. Effect of exercise, as measured by the ventilation rate, on formic acid in urine, methanol in urine and methanol in end–expired air when humans are exposed to methanol via the inhalation route.

Methodology

The study has involved two sets of separate human experiments. In the first, paid volunteer subjects underwent controlled exposures to methanol vapor in an exposure chamber. Each subject had 10 separate chamber exposure sessions consisting of 5 different methanol exposure levels, and two levels of exercise/pulmonary ventilation. This is a complete block design experiment in that each subject underwent each combination of 'treatments' (5 levels of methanol exposure and 2 levels of exercise/pulmonary ventilation). Exposure sessions lasted approximately 8 hours. Breath, blood and urine specimens were collected before, during and after exposures. Twelve subjects completed this entire protocol. Methanol in urine and blood, and formic acid in urine were assayed using gas chromatography. Methanol in breath was measured using Fourier transform infrared spectroscopy. Minute ventilation at rest and during controlled exercise was quantitated using standard pulmonary function methods.

The second set of experiments will address dermal methanol exposure and absorption. Each paid volunteer subject will have 5 separate exposure sessions consisting of different durations of controlled dermal exposure to methanol. Again, this is a complete block design experiment. Each level of exposure is a 'treatment', and each subject will complete each 'treatment'. Dermal exposure of one hand to methanol will vary from zero to 16 minutes. Baseline breath, blood and urine specimens will be collected before exposure begins, and will then be repeated at timed intervals for up to 8 hours following cessation of exposure. The goal is for 12 subjects to complete this entire protocol. Methanol in urine and blood, and formic acid in urine will be assayed using gas chromatography. Methanol in breath will be measured using Fourier transform infrared spectroscopy.

Significant Findings

The project started on 2/11/93. The focus of the first year of the project was on writing and validating laboratory protocols for analyses of blood, urine and breath specimens, hiring staff, recruitment of volunteer subjects, and initiation of human experiments.

The inhalation exposures of human subjects were completed during the late summer of 1994. Preliminary analyses of these data indicate the following: (1) Methanol levels in urine and blood rapidly rise following exposure and approach a steady state level after an exposure period of approximately 2 hours; (2) Uptake and metabolic rates calculated from blood and urine data are in rough agreement with results of multicompartment models using parameters obtained from the literature; (3) concentrations of methanol in breath collected while breathing a methanol–contaminated atmosphere do not reflect alveolar air, as demonstrated by very

significant drops in concentrations of methanol in breath upon leaving the exposure chamber, (4) blood and urine concentrations of methanol appear roughly proportional to the methanol exposure level at steady–state; (5) intersubject variability can be high, especially for methanol concentrations in urine and blood levels; (6) In some cases, e.g., low exposure experiments, several pre–exposure tests are needed to determine the absolute level and trend of background levels.

Dermal exposures of human subjects will be completed soon. Data collected so far suggest that blood and breath concentrations of methanol are not in equilibrium for up to 2 hours following cessation of dermal methanol exposure. In settings where there might be opportunities for dermal exposure to methanol, it would be necessary to wait at least two hours to collect breath specimens following cessation of methanol exposure. This prolonged waiting period might serve to decrease the attractiveness of measurement of methanol in breath as a strategy for monitoring occupational methanol exposure.

Publications

Franzblau A, Lee EW, Schreck RM, D'Arcy JB, Santrock J, Levine SP: Absence of Formic Acid Accumulation in Urine Following Five Days of Methanol Exposure. Applied Occup Environ Hyg, in press, 1993

Dose/Response for Styrene Exposures

Stephen M. Rappaport, Ph.D.
University of North Carolina
School of Public Health
Department of Environmental Sciences & Engineering
CB #7400 - Campus
Chapel Hill, North Carolina 27599-7400

Grant Number: *5 R01 OH02221-05*
Start & End Dates: *09/28/86 – 12/27/93*
Funding Level: *$0 ($838,329 Cum)*

Importance to Occupational Safety and Health

The project represents one of the first comprehensive applications of biochemical epidemiology to an occupational cohort. The extensive exposure assessment, performed longitudinally, allows for the correction of biases in any dose–response relationships which are derived from the work. This study design has allowed us to detect elevated levels of SCEs at styrene concentrations below those which had heretofore been reported, even after adjustment for cigarette smoking. The development and application of methods for detecting styrene–7,8–oxide (SO) adducts of DNA (SO–DNA) and the blood proteins, hemoglobin (SO–Hb) and albumin (SO–Alb) will produce important new information concerning the bioavailability of SO in humans exposed to styrene.

Objectives

This study is investigating the linkages between exposure, uptake, and genotoxic response resulting from occupational exposure to styrene in the reinforced–plastics industry. A longitudinal assessment of exposure was completed in which 48 subjects were monitored in a single facility where fiberglass boats were manufactured. The primary purpose of the study is to accurately estimate the airborne exposure and uptake of each individual in the cohort for comparison with several indices of the dose of SO measured in blood samples, i.e., sister–chromatid exchanges (SCEs) in peripheral lymphocytes and the adducts, SO–Hb, SO–Alb and SO–DNA. This would allow exposure– dose–response relationships to be established for styrene and for SO arising from metabolism of styrene *in vivo*. A secondary objective is to correlate the above indices of styrene uptake and genotoxicity with each other in a common pool of samples where exposure had been carefully documented.

Methodology

Each individual's airborne exposure was measured 7 times (shift–long sampling), his/her blood was collected 4 times, and his/her exhaled air was collected up to 25 times over a 12–month period. Exposures were measured with passive monitors. Measurement of styrene in the exhaled air employed a new device which collects styrene from 3 L of mixed exhaled air in a tube containing 200 mg of coconut carbon. Both types of samples were analyzed by solvent desorption/gas chromatography. Blood styrene was measured via the head space technique using standard addition and gas chromatography. SCEs were measured by the standard method. Styrene glycol was measured in the blood by extraction followed by derivitization and gas chromatography with electron–capture detection. SO–DNA is being measured by a modification of the ^{32}P post–labeling technique developed in this study. A new technique has been developed for measuring SO–Hb and SO–Alb, which takes advantage of a metal catalyst (Raney–nickel) to selectively cleave

SO–cysteine adducts to yield 1– and 2–phenylethanol, which are subsequently derivitized and measured by gas chromatography with negative–ion mass spectrometry.

Significant Findings

The exposure assessment was completed with analysis of styrene in all samples of air, exhaled air, and blood. Individual mean exposures ranged between 0.2 and 55 ppm for the 48 subjects with an overall mean of 15.1 ppm. A correlation matrix revealed that all of the biomarkers were significantly correlated with exposure to styrene. The strongest correlation with exposure to styrene was observed for exhaled air ($r=0.91$, $n=48$) followed by styrene in blood ($r=0.81$, $n=48$), styrene glycol in blood ($r=0.73$, $n=48$), SCEs ($r=0.39$, $n=46$), albumin adducts ($r=0.34$, $n=48$), and DNA adducts ($r=0.33$, $n=47$). All of these exposure–biomarker relationships were significant ($p<0.05$). Interestingly, a significant relationship was not found between hemoglobin adducts and exposure to styrene. The only biomarker which was found to be significantly correlated with SCEs was styrene in exhaled air ($r=0.49$, $n=46$). The correlations between SCEs and both exposure to styrene and styrene in exhaled air were still significant after accounting for the number of cigarettes smoked per day by multiple regression analysis. This indicates that styrene exposure below 50 ppm, the current OSHA PEL, contributed to elevated SCEs; such findings of SCEs at these levels of styrene exposure have not been reported before.

We have successfully applied the ^{32}P postlabeling technique to *in vitro* modified samples of nucleosides, DNA, and cells and in samples of human DNA obtained from this study. The results clearly show that five SO–DNA adducts have been detected. Recent work has confirmed the identities of these adducts in the *in vitro* modified samples as products of reaction of SO at N^2–, O^6–, N–7–, and C–8–positions of guanine. Application of the method to the human samples has confirmed the presence of the SO–N^2– adduct of guanine and of an as–yet–unknown adduct associated with styrene exposure.

The methods for measurement of SO–Hb and SO–Alb were first applied to samples of blood which had been modified with SO *in vitro*, and following administration of both SO and styrene to rats *in vivo*. The *in vivo* results suggest that only about 2% of the styrene dose was bioavailable as SO in the blood of rats. Application of the methods to the human samples has shown significant correlation with styrene exposure with SO–Alb but not with SO–Hb as noted above.

Publications

Rappaport SM, Symanski E, Kupper L: The Relationship Between Environmental Monitoring and Biological Markers in Exposure Assessment. Environ Health Perspectives, in press, 1994

Horvath E, Pongracz K, Rappaport SM, Bodell WJ: ^{32}P–Postlabeling Detection of DNA Adducts in Workers Occupationally Exposed to Styrene. Carcinogenesis 15:1309–1315, 1994

Rappaport SM, Ting D, Jin ZL, Yeowell–O'Connell K, Waidyanatha S, McDonald T: Application of Raney Nickel To Measure Adducts of Styrene Oxide with Hemoglobin and Albumin. Chem Res Toxicol 238–244, 1993

Yager J, Paradisin W, Rappaport SM: Sister–Chromatid Exchanges in Lymphocytes are Increased in Relation to Longitudinally Measured Occupational Exposure to Low Concentrations of Styrene. Mut Research 19:155–165, 1993

Compton PJE, Jensen RH, Bigbee WL, Langlois RG, Smith MT, Rappaport SM: Use of the Glycophorin A Human Mutation Assay to Study Workers Exposed to Styrene. Environmental Health Perspectives 99:297–301, 1992

Rappaport SM, Dionne L, Woodlee J, Yager J: The Relationship between Exposure to Styrene, Biomarkers of Exposure and Cytogenetic Response: (Abstract from the Proc of the 8th International Symposium of Epidemiology in Occupational Health, Paris, France, Sept. 10–12, 1991) Revue d'epidemiologie et de Sante Publique 40:S80–S81, 1992

Pongracz K, Kaur S, Burlingame AL, Bodell WJ: Identification of N^2–substituted 2′–deoxyguanosine–3′–phosphate Adducts Detected by ^{32}P–postlabeling of Styrene–Oxide–treated DNA. Carcinogenesis 13(3):315–319, 1992

Rappaport SM, Kure E, Petreas M, Ting DT, Woodlee J: A Field Method for Measurement Vapors In Exhaled Air – Application To Styrene Exposure. Scand J Work Environ Health 17:195–204, 1991

Ting D, Smith MT, Doane–Seltzer P, Woodlee J, Rappaport SM: Measurement of Styrene–Oxide Cysteine Adducts in Hemoglobin by Selective Catalytic Reduction. Advances in Experimental Medical Biology, 283:837–841, 1990 (not peer reviewed)

Ting D, Smith MS, Doane–Setzer P, Rappaport SM: Analysis of Styrene Oxide–Globin Adducts Based Upon Reaction With Raney Nickel. Carcinogenesis 11:755–760, 1990

Yager JW, Paradisn W, Symanski E, Rappaport SM: Sister–Chromatid Exchanges Induced in Peripheral Lymphocytes of Workers Exposed to Low Concentrations of Styrene. Proc of the Fifth International Conference on Environmental Mutagens, (eds. ML Mendelsohn, RJ Albertini), pp. 3470–356, 1989

Selvin S, Rappaport SM: A Note On The Estimation of The Mean From a Lognormal Distribution. Am Ind Hyg Assoc J 50:627–630, 1989

Rappaport SM, Spear RC: Physiological Dampening of Exposure Variability During Brief Periods. Ann Occup Hyg 32:21–33, 1988

Liu SF, Rappaport SM, Pongracz K, Bodell W: Detection of Styrene–Oxide DNA Adducts in Lymphocytes of a Worker Exposed to Styrene. In Methods for Detecting DNA–Damaging Agents in Humans, Appl in Cancer Epidemiology and Prevention (eds. H Bartsch, K Hemminki, IK O'Neill), IARC Sci, Publ #89, Lyon, pp 217–222, 1988

Lui SF, Rappaport SM, Rasmussen J, Bodell WJ: Detection of Styrene–Oxide–DNA Adducts by ^{32}P–Postlabeling. Carcinogenesis 9:1401–1404, 1988

A New Hearing Protector Attenuation Measurement Method

Michael J. Ellenbecker, Sc.D.
University of Massachusetts Lowell
School of Engineering
Department of Work Environment
One University Avenue
Lowell, Massachusetts 01854

Grant Number: *1 R03 OH03249-01*
Start & End Dates: *09/30/94 – 09/29/95*
Funding Level: *$26,362 ($26,362 Cum)*

Importance to Occupational Safety and Health

The degree of protection (attenuation) given by hearing protection devices (HPDs) such as earplugs, earmuffs, and canal caps is generally much less in actual use than in laboratory certification tests upon which HPD ratings are based. Also, the attenuation varies so greatly between individuals that the amount of protection provided to any particular individual is almost completely unknown. As a result, underprotection of workers exposed to high noise levels can often only be detected by subsequent measurement of their hearing loss. Procedures which can readily be used to assess field performance of HPDs would be very useful for worker training and hearing conservation program assessment. The one method currently in use is only applicable to earplugs, shows considerable variance from the standard laboratory method, and must be done in the quiet environment of an audiometric test booth.

Objectives

A new procedure for measuring HPD attenuation is proposed which may be done in moderately noisy environments and could be used for any sort of hearing protector or combination of HPDs. It is a loudness balance technique in which one sound is delivered to the inner ear by a bone–conduction transducer and another sound is delivered externally to the ear and the HPD. By balancing the loudness of the two sounds both with and without the HPD, the attenuation of the HPD may be directly calculated. Preliminary results of this bone conduction loudness balance (BCLB) method indicate that it is a reproducible technique which gives measurements comparable to the standard methods.

The proposed research is intended to develop procedures and instrumentation necessary to use this new technique as an alternative method of HPD attenuation measurement. The method will also be compared to the commonly used procedures for both laboratory and field measurements. A variety of different types of HPD will be evaluated using the procedure to demonstrate its usefulness in actual practice and to provide information on any defects and limitations of the method.

Methodology

Two approaches for implementing the BCLB method will be tested. First, a two–channel diagnostic audiometer with bone conduction capability and automatic alteration of signal presentation will be used for feasibility testing. The primary option to be explored is the use of a personal computer with a commercially available analog–to–digital sound card which can be programmed to produce the proper sequence of noise bands or pure tones. Both of the proposed BCLB test methods will be compared to the laboratory standard threshold difference method and to the common field procedure of threshold difference measurement using headphones.

The proposed test methods will first be evaluated with small panels of volunteers, followed by full–scale testing with twenty paid volunteers (half male and half female). Commercially–available earplugs, earmuffs, and canal caps will be tested. Tests will be performed by Thomas Rimmer, doctoral candidate in the Department of Work Environment, at the Speech and Hearing Clinic of the University of Arkansas at Little Rock, where Mr. Rimmer is a faculty member.

Significant Findings

Preliminary tests of the two BCLB approaches have been completed. Tests with a commercial two–channel audiometer and a single subject confirmed the utility of the technique. Following this success, the personal computer–based system was constructed and found to perform very well. Results with a panel of four volunteers wearing commercially–available earplugs indicate that the BCLB method compares favorably to the standard laboratory and field methods of measuring hearing protector attenuation. Results of these preliminary studies will be included in the referenced journal article now under preparation. The system will now enter full–scale evaluation, as described above.

Application of Neural Networks for Process Fault Diagnosis & Safety

Venkat Venkatasubramanian, Ph.D.
Purdue University
School of Chemical Engineering
Laboratory for Intelligent Process Systems
West LaFayette, Indiana 47907

Grant Number: *5 R01 OH02740-02*
Start & End Dates: *01/01/92 – 12/31/94*
Funding Level: *$0 ($161,706 Cum)*

Importance to Occupational Safety and Health

The study of fault detection and diagnosis is concerned with designing systems that can assist human operators in detecting and diagnosing process failures in order to prevent accidents. As modern chemical plants are extremely complex they are more vulnerable to failures, as witnessed by the recent chemical plant related accidents. Because of this complexity, modern plants are also more difficult to diagnose thus raising serious occupational safety related problems. We are also dealing more with toxic substances, and with the advent of biotechnology and genetic engineering industries, the results of an industrial accident can be quite devastating. Occupational safety and health hazards pose a serious threat to an estimated 80 million workers in the United States. Industrial statistics show that even though major catastrophies and disasters of chemical plants are infrequent, minor accidents are very common, occurring on a day–to–day basis, resulting in many occupational injuries, illnesses, and costing the society billions of dollars every year. During 1983 the Bureau of Labor Statistics has reported over 3000 job–related deaths and estimated 4.9 million job–related injuries and illnesses. It is also estimated that the annual cost to society of work–related injuries, illnesses, and deaths has nearly tripled from $11.5 billion in 1972 to $33.0 billion in 1984.

The proposed project is aimed at the prevention and control of such frequent, day–to–day, accidental events in the industry. The proposed research would lead to a better understanding of the complexities that are involved in the design of intelligent computer systems that can effectively monitor, diagnose, and control chemical plants. In this project, we propose a neural network–based methodology that has considerable potential in the development of such intelligent systems.

Objectives

The major goal of this proposal is to research and demonstrate a novel approach based on *Neural Networks* for the design of chemical process hazard detection, prevention, and control systems. Fault diagnosis using neural networks is achieved by exploiting their non–linear pattern classification properties. This diagnostic ability crucially depends upon the discrimination of decision regions corresponding to various fault classes. The delineation of decision regions for a given number of fault classes, in turn, hinges on several factors, such as the number of input and hidden nodes, the type of activation function employed, noise in sensor measurements, the extent and nature of training, etc. Further, it is also important to examine the ability of neural nets in detecting and diagnosing faults during process transients by extracting key qualitative features of the underlying process trend. In this project, we propose to examine these central issues.

Methodology

We have built a dynamic simulator of a chemical reactor–distillation column system which is used to simulate a wide variety of faults and dynamic process trends. Using this as a test bed, we have been investigating a variety of neural network architectures to analyze their classification characteristics, their ability to deal with dynamic and noisy sensor data and so on.

Significant Findings

In the first year of the project, a hierarchical representation framework was developed that can model process trends at different levels of detail to address the problem of extracting key qualitative features from noisy data to aid in fault diagnosis. We also demonstrated the superiority of ellipsoidal neural nets for representing bounded fault classes. In the second year, two important contributions were made following up on our hierarchical framework. We demonstrated that a properly trained network, using transient sensor data, can detect abnormal process conditions soon after they appear, thus facilitating early diagnosis and supervisory control actions. We also developed a network and problem decomposition scheme to reduce the complexity in large–scale fault diagnosis problems. The technique involves input space reduction through the use of principal component analysis and hidden nodes specialization.

In the current period, we tested these techniques further with the aid of a larger industrial case study that involved a fluidized catalytic cracking process system. The dynamic simulator for this process was developed by researchers at Amoco Chemical

Company. Using this case study, the neural net approach was evaluated in the presence of noisy and uncertain sensory data. This is a very important issue from the industrial perspective. These investigations showed that neural nets are quite noise–tolerant and can diagnose successfully in the presence of upto about 5–10% noise levels. The level of tolerance depends on the importance of the particular sensor and how many other sensor are being consulted by the network. As one can expect, larger amounts of noise lead to a deterioration in the performance of the network. We also developed some preliminary approaches to incorporate a priori probabilities and predefined error bounds into the neural net architecture.

Publications

Rengaswamy R, Venkatasubramanian V: A Syntactic Pattern Recognition Approach to Process Monitoring and Fault Diagnosis. Eng Appln Art Intell, in press, 1995

Kavuri S, Venkatasubramanian V: Neural Network Decomposition Strategies for Large Scale Fault Diagnosis, (eds. Morari and Morris), Special Issue of Intl J Control 59(3):767–792, 1994

Venkatasubramanian V, Rengaswamy R: A Framework for Integrated Process Supervision. Proceedings of ADCHEM'94, Kyoto, Japan, May 1994

Venkatasubramanian V: Integrated Process Supervision: Emerging Trends and Future Directions. Proceedings of Second IFAC International Conference on AI/KBS in Process Control, Lund Institute of Technology, Lund, Sweden, Aug 1994

Kavuri S, Venkatasubramanian V: Using Fuzzy Clustering and Ellipsoidal Units in Neural Networks to Improve Fault Classification. Computers and Chemical Engineering 17(8):765–784, 1993

Safety First: Fault Tree Expert System For Construction

Fabian C. Hadipriono, Dr.Eng.
Ohio State University
School of Engineering
Department of Civil Engineering
470 Hitchcock Hall
2070 Neil Avenue
Columbus, Ohio 43210

Grant Number: *5 K01 OH00115-03*
Start & End Dates: *09/30/92 – 09/29/95*
Funding Level: *$54,000 ($162,000 Cum)*

Importance to Occupational Safety and Health

The project develops a system to improve construction safety by emphasizing the engineering aspects, and further incorporates other aspects pertinent to the engineering control system (e.g., procedural, behavioral, social, and economic aspects). The importance of the work is as follows:

1. The knowledge gained could have a great impact on the way occupational safety and health institutions perform an analysis of a construction accident. These institutions are constantly involved in promoting safety in construction and in performing investigations in the event of construction accidents. The product of our research can be used as an engineering control system and would be of an invaluable aid to these institutions in reaching their objectives.
2. We expect that research results will affect existing procedures and will automate the processing of construction accident information. When completed, our project produces a run–time version of a software for use in micro computers. The system can be stationed centrally or distributed to any construction site. The service life of the system is essentially unlimited.

Objectives

Our objective is to develop SAFETY FIRST, a fault tree expert system for investigating and avoiding construction accidents in the area of construction falls. It is expected that the system could be used to minimize construction accidents and improve construction safety. SAFETY FIRST will provide a heuristic yet systematic approach for investigating the causes of construction accidents and for reducing and

avoiding them, thereby increasing labor safety. The research is intended to accomplish the following:

1. To provide the user a tool with which to investigate a construction accident that has already occurred. The fault tree models will establish all possible causes contributing to the accident (and any combination of these causes), and will rank them in order of importance. Based on evidence gathered from the accident site, the expert system will trace a particular cause and will explain to the user how and why the accident has occurred. The expert system will also recommend ways to avoid this accident in the future.
2. To provide the user with a consulting tool that will explain the contributing causes of potential construction accidents. The fault tree models will show graphically the relationships among these causes and will determine the potential "weak links" that could result in a construction accident. Simulation study by the user using the expert system models will establish which causes are potentially hazardous to the workers. Hence, the system will serve as a tool to warn the user of potential accidents and to suggest applicable precautions.

Methodology

In order to achieve the objectives of our proposed project, we will use and combine two innovative research methods: the fault tree system and the expert system. Fault tree models are employed to represent the knowledge obtained from experts and literature concerning the causal relationships among events/causes that contribute to a construction accident. In simulating the way experts determine the cause of the accident, the expert system accommodates the knowledge for use by safety investigators. The research encompasses the following four major tasks: (1) Knowledge acquisition, (2) Fault tree development, (3) Expert system development, and (4) Validation.

During the knowledge acquisition process, we function as the knowledge engineer who communicate with the experts, gather information from literature, and build the knowledge base. We perform three phases of knowledge acquisition: preliminary discussion, detailed discussion, and organization. Expert knowledge are represented by fault tree models, which show the paths of knowledge an expert takes in reaching a conclusion. Development of fault tree models include fault tree logic evaluation, fault tree modeling, and analyses. The development of the expert system includes knowledge base development and system validation. The knowledge acquired from experts and literature is organized in each path.

The development of SAFETY FIRST consists of the development of system architecture, construction of the knowledge base, and interface with external programs. An expert system shell—LEVEL5 Object—is used to construct SAFETY FIRST. In order to use SAFETY FIRST as a tool for investigating and simulating accidental falls at construction sites, the system is required to have five main components: the knowledge base, the inference engine, the user interface, the external file interface, and the external files. The knowledge base contains knowledge acquired from our experts (a list of experts was presented in the first report). The inference engine infers solutions to causes of construction falls by matching evidence from the user with the appropriate rule in the knowledge base. The user interface allows the user to interact with modules within the SAFETY FIRST, while the external file interface allows additional capability to interact with external files, such as graphic, multi–media, and text files. At the end of project period, SAFETY FIRST will be validated by the knowledge engineer, participating experts, and independent experts.

Significant Findings

Our study reveals that fault tree diagrams can be used not only as a tool to show possible sequential and parallel combinations of causes leading to falls, but they can also be used as a reference point to develop the rules needed to represent experts' knowledge in the system's knowledge base. Furthermore, the use of these fault trees allows the knowledge engineers to easily trace, modify, and refine the rules developed in the knowledge base. In addition, the fault trees can be used as a "road map" of the knowledge path during the validation process.

Furthermore, we found the importance of questions prompted to the user. In our system, these questions were classified into those having a simple YES/NO answer or those with multiple answers that will lead the user to systematically deduce all causes and conclude the cause(s) of the fall. Prompts with a YES/NO answer accommodate the causes of accidents within the questions asked to the user, while prompts with multiple answers accommodate the causes within the answers selected by the user. At this stage, the knowledge base for *floor edge* has been completed and evaluation is being conducted by the users. The evaluation showed the importance of help statements for a user to accurately furnish the information needed by the system. It was noticed that several branches of the knowledge structure are replicable to other construction platforms, such as floor opening, wall opening, etc. Hence, it is reasonable to expect that the development of other knowledge bases will not be as time consuming.

Publications

Hadipriono FC, Fujino T: Fuzzy Fault Tree Analysis for Construction Safety. Proc. of the 1994 International Conference on Information Processing and Management of Uncertainty in Knowledge–Based System, Paris, France, pp. 753–758, July 4–8, 1994

Load Monitoring For Safe Construction

Dryver R. Huston, Ph.D.
University of Vermont
College of Engineering & Mathematics
Department of Mechanical Engineering
Votey Building, Room 201E
Burlington, Vermont 05405-0156

Grant Number: *5 R01 OH03157-02*
Start & End Dates: *09/30/93 – 09/29/96*
Funding Level: *$203,498 ($422,176 Cum)*

Importance to Occupational Safety and Health

This project addresses the problem of occupational safety on construction sites. The specific problem addressed in this study is the prevention of the unexpected collapse of partially constructed facilities, in particular multistory reinforced concrete structures which are built using falsework and shoring structures. Over the past 25 years at least 85 such collapses have been documented and reported. The effects of such a collapse can be catastrophic as evidenced by the 1987 collapse of the L'Ambiance Plaza in Bridgeport, CT in which 28 construction workers were killed.

At present there is little detailed guidance in the construction building codes regulating the design and construction of shoring systems for the construction of reinforced concrete buildings. There are also, at present, very few instruments available that can detect, document and provide a warning for dangerous loading conditions on the shoring systems.

The overall results of this project will be the acquisition of load data on shoring systems during construction which can be used in the development of rational design codes. A subsidiary result will be the development and testing of equipment that can possibly be used to provide a real–time early warning and data logging capability for dangerous loading conditions.

Objectives

The overall goals of this project are to develop and implement real–time load and deflection monitoring instrumentation for buildings during construction, to develop an improved understanding of critical construction loading conditions, and to develop guidelines for safe construction practices specifically associated with multistory reinforced concrete construction. The fundamental hypotheses for this work are (1) that the primary cause of construction failures is inadequacy of the temporary support elements such as vertical shores and lateral bracing, (2) that an investigation of load and deflection histories during actual projects can contribute greatly to our understanding of critical loading conditions, and (3) that this improved understanding and invaluable information can be used as the basis for improved construction procedures and guidelines for safe design and construction.

Methodology

The research plan for this project contains two distinct portions. The first involves taking shoring load data in the laboratory and on at least three building sites. The load data are measured with an array of eight or more three–axis load cells. The three axis load cells enable the measurement of side loads as well as vertical loads. Side loads have been implicated in a number of collapses that involved a loss of lateral stability. The data are gathered and stored on an optical disk drive for further analysis. The second phase will involve a detailed analysis of the data coupled with computer models of the load distribution in curing concrete structures. The data and structural analysis will then be used with various reliability–based techniques to develop proposed guidelines for shoring design. The proposed guidelines will be presented to the cognizant bodies for comment and possible adoption.

Significant Findings

To date measurements have been taken at two construction sites: a federal prison near Beckley, WV and a library storage facility on the University of Vermont campus. Preliminary analysis of the data indicate that routine live loads are about 10–20% of the dead loads and that routine lateral loads are also about 10–20% of the dead loads. The biggest surprise is that nominally identical shoring members that are supposed to receive identical loads have measured variations in dead loads of up to 40%.

Publications

Huston DR, Fuhr PL, Ambrose TP: Structural Safety Alarm Systems using Instrumented Shoring Load Monitoring. Proc SPIE Smart Materials and Structures Conference, San Diego, CA, in press, Feb, 1995

Huston DR, Rosowsky DV, Fuhr PL, Chen WF: Instrumented Shoring for Construction Load Monitoring. Proc ASCE Structures Congress '95, Boston, MA, in press, April, 1995

Ambrose TP, Huston DR, Fuhr PL, Devino EA, Werner MP: Shoring Systems for Construction Load Monitoring. Smart Mater Struc 3:26–34, 1994

Rosowsly DV, Huang YL, Chen WF, Yen T: Modeling Concrete Placement Loads During Construction. Structural Engineering Review 6.2:71–84

Rosowsky D, Huston D, Fuhr P, Chen WF: Measuring Formwork Loads During Construction. Accepted in Concrete International, July, 1994

Huston DR, Fuhr PL, Ambrose TP, Devion EA, Werner MP: Construction Load Monitoring Using Instrumented Shoring. SPIE Vol 2192, No 48, SPIE Smart Structures '94 Conference, Orlando, FL, Feb. 1994

Predictive Models of Solvent Permeation Through CPC

Edward T. Zellers, Ph.D.
University of Michigan
School of Public Health
Department of Environmental and Industrial Health
1420 Washington Heights
Ann Arbor, Michigan 48109-2029

Grant Number: *5 R01 OH03033-02*
Start & End Dates: *12/01/92 – 11/30/95*
Funding Level: *$112,550 ($229,003 Cum)*

Importance to Occupational Safety and Health

Dermatological disease arising from contact with chemicals historically has accounted for a disproportionately large percentage of all cases of chronic occupational illness. Dermal absorption of systemic toxicants is also known to be important for several classes of chemicals and is likely underreported. The use of chemical protective clothing (CPC) is often the only feasible means of protecting workers from dermal contact with toxic chemicals. Yet, our current understanding of the factors affecting the permeation resistance of CPC materials to solvents is very rudimentary. As a result, the protection afforded by a given type of CPC in workplace applications, particularly those involving organic solvents, is rarely known with certainty. This research entails a comprehensive investigation of solvent permeation through CPC and the development of semi–empirical predictive permeation models for solvents and solvent mixtures.

Objectives

The broad goals of this project are to gain improved understanding of the physicochemical factors affecting the permeation of solvents through CPC and to develop broadly applicable models for industrial hygienists to use in selecting CPC when experimental data are not available. More specifically, the project focuses on the development and validation of new models for predicting the equilibrium solubilities and the diffusion coefficients in common CPC materials of a wide range of individual organic solvents and binary solvent mixtures as a function of the type of solvent and CPC material; temperature; and the nature and concentration of co–solvents. This information will then permit accurate prediction of breakthrough times (BT) and steady–state permeation rates (SSPR) as a function of these variables.

Methodology

Immersion and permeation tests are being performed on four types of commercial polymeric CPC materials (i.e., butyl, natural, nitrile and neoprene rubbers) challenged with organic solvents from each of 13 chemical classes. Binary mixtures are being examined with a representative subset of these solvents. Results will provide the basis for the models of equilibrium solubilities, diffusion coefficients and permeation rates. Solubility models based on three–dimensional solubility parameters (3DSP), solvatochromic indices in conjunction with linear solvation free–energy relationships (SCI–LSER), and molecular group contribution (MGC) methods are being investigated. Models for diffusion coefficients rely on empirical correlations of measured values with the physical properties and CPC–interaction strengths of the solvents. Modeled solubility and diffusion coefficient values will be used in Fickian models to obtain estimates of solvent BT and SSPR values.

Significant Findings

Immersion tests have been performed with 53 solvents in each of the four types of gloves at each of three temperatures between 25°C and 45°C. Fractional weight gains ranged from < 1% for ethanol in butyl rubber to > 1,000% for N–methyl–2–pyrrolidone in nitrile. Most (70%) of the combinations tested showed an increase in solubility with increasing temperature, but a significant fraction (30%) showed a decrease. For the vast majority of cases, the change in solubility was < 30% over this temperature range. Immersion testing with binary solvent mixtures is still in progress. Initial results show significant changes in uptake as a function of solvent composition. Results are being analyzed in the context of recently developed models for such systems.

The density of crosslinks in each glove material was determined from stress–strain measurements and from immersion test measurements. Agreement between the two methods was excellent for all of the gloves except nitrile. Values were in the range of $1–3 \times 10^{-4}$ mole/cm^3 for all of the gloves.

The development of solubility models based on 3DSPs required determination of the 3DSPs of the glove materials. The currently accepted method for determining glove 3DSP values based on immersion test results was found to be cumbersome, inefficient and inherently inaccurate. Several alternative methods have been investigated that calculate the glove 3DSPs based on a weighted average of solvent 3DSP values, where the weighting factors reflect solvent size and/or uptake by the glove materials. One additional method is being explored which uses equations derived from the Hildebrand and Flory–Rehner theories of polymer–solvent interactions in a multiple regression model.

Initial testing of the SCI–LSER solubility models has been performed. Solubility estimates within a factor of two of experimental values were obtained for the majority of solvents. Estimates of solubility obtained via the MGC model were within a factor of two of experimental values for only about fifty percent of the solvent–glove combinations.

Duplicate permeation tests have been performed on 158 solvent–glove pairs at 25°C. Most of the BT values were either < 1 hr or > 7 days. Only 14 cases gave BT values between these extremes. Solvents with short BT values invariably had higher SSPR values. Experimental diffusion coefficient values were calculated at breakthrough and at steady–state assuming Fickian diffusion. Thus far, empirical models employing predictor variables that combine an index of plasticization (e.g., the Flory interaction parameter) with an index of solvent size (e.g., molar volume) have provided the best correlations with experimental diffusion coefficients. Models of BT and SSPR are being constructed based on estimated solubility and diffusion coefficient values.

A computerized permeation model developed by other researchers for predicting BT and SSPR values has also been investigated. This model combines MGC–derived solubility values with diffusion coefficient values obtained from correlations with solvent molecular weight in Fickian diffusion equations to estimate BT and SSPR values. Results indicate that useful qualitative guidance in estimating permeation resistance is obtained only for certain solvent–glove combinations with this approach. Best results are obtained for natural rubber.

Low Vibration Hand-Held Tools For Safety and Health

Nisar Shaikh, Ph.D.
Analytic Engineering Company
1590 Finch Way
Sunnyvale, California 94087-4719

Grant Number: *1 R43 OH02793-01A3*
Start & End Dates: *09/30/94 – 03/31/95*
Funding Level: *$68,652 ($68,652 Cum)*

Importance to Occupational Safety and Health

Over a million workers in the U.S. are routinely exposed to vibration from hand–held tools. Prolonged use of these tools causes Raynaud's Disease or Vibration–induced White Finger. For a variety of reasons, the hand–held tools did not get the benefit of technological advances. The construction and heavy machinery industry desperately needs low vibration tools to reduce worker injuries and related liabilities. The work under this grant would generate needed technological innovation for demonstrating the feasibility of a low vibration tool for control and prevention of musculoskeletal disease.

Objectives

This project will conduct much neglected research in hand–held tools through design and development of a chipping tool. Based on the findings, a prototype chipping tool will be fabricated and its performance and vibration levels will be tested. The demonstration of a tool with low vibration and noise will help raise capital for subsequent mass production and marketing.

Methodology

Three innovations are offered to develop necessary technology which will be translated into a prototype through mechanical design: (1) a viable oscillator, (2) a novel construction grade composite material and, (3) a mode de–coupling joint design. The feasibility of a low vibration oscillator has already been demonstrated and the proposed work will devise a viable system through optimization. The elements transmitting impact energy will be studied critically to understand the mechanism leaking vibration to the body. Change of frequency spectrum and efficient cutting mechanisms will alleviate noise and vibration.

Significant Findings

None to date.

Safe Removal of Arsenic Dust From Gallium Arsenide Crystal Pullers

Rowland M. Ware
Ware Technical Service, Inc.
42 Lorraine Road
Westwood, Massachusetts 02090

Grant Number: *1 R43 OH03220-01*
Start & End Dates: *09/30/94 – 03/31/95*
Funding Level: *$75,177 ($75,177 Cum)*

Importance to Occupational Safety and Health

The program is expected to make a major improvement in the safety of operation of Liquid Encapsulated Czochralski crystal pullers used in the growth of gallium arsenide. The hazard is caused by the presence of finely divided arsenic dust on the inside of the pullers after growth. Some of this is believed to convert to arsine. Operators remove the dust by vacuum cleaning and scrubbing with tissues, and hence are exposed to high levels of toxic and carcinogenic material. The improved process is aimed at eliminating this exposure.

Objectives

The main objective is to obtain complete removal and trapping of the arsenic before opening the puller at the end of a crystal growth run.

Methodology

The technique employed is to convert the arsenic *in situ* to arsenic trichloride. The chloride is removed from the puller by a flow of insert gas(argon) and trapped in a dry chemical canister scrubber.

At the end of the crystal growth run the chamber is cooled to a temperature at which the finely divided arsenic dust reacts readily with chlorine but at which attack on the crystal and chamber components is minimal. A flow of a mixture of argon and chlorine is established through the chamber and the resulting $Ar/Cl_2/AsCl_3$ mixture conducted through heated tubing to the chemical scrubber.

Significant Findings

Ideally all the operator will have to do at the end of a crystal growth run is remove the crystal and crucible, and install a new seed and charged crucible for the next run. Apart from the arsenic removal, some modifications to the puller were necessary for this to be possible. The first was a modification to the crucible support system. This was installed and tested. Successful crystal growth showed that this change did not have a deleterious effect on the crystal growth process.

The second modification involves changing the graphite insulation. It has not been possible to test this yet due to poor delivery and unacceptable quality by the vendor.

The removal and trapping of the arsenic using a mixture of 30% Cl_2 in argon was successful.

It was found necessary to replace molybdenum components in the puller due to chlorine attack. The main remaining problem is attack by the chlorine on the crystal and on the stainless steel of the puller. The former is not a serious problem since the weight loss is small. The latter gives rise to deposits of small quantities of iron, nickel and chromium chlorides, unacceptable from considerations of crystal purity. Attempts will be made to reduce this attack by variation of temperature and gas composition.

Lighter Compact Respirators For Toxic Vapor Protection

Clinton E. Brown
Dynaflow, Inc.
7210 Pindell School Road
Fulton, Maryland 20759

Grant Number: *5 R44 OH03011-03*
Start & End Dates: *09/30/93 – 09/29/95*
Funding Level: *$169,290 ($333,748 Cum)*

Importance to Occupational Safety and Health

Respirators for toxic gases are usually of either full face or half face design and utilize two canisters extending out from the cheek area. Workers in toxic atmospheres find current respirators bulky and uncomfortable. If respirators can be made lighter and more compact, their acceptance and use will be enhanced, leading to increased safety in the work place. The current research and development is exploring the use of twoway breathing through an absorbent rather than an adsorbent medium such as activated charcoal. Such a respirator may be worn like a surgical mask or dust mask with substantial savings in weight and bulk.

Objectives

The goal of the research is to develop technology for lighter and more compact respirators using alternating flow and absorbent materials insensitive to the presence of water vapor. The project identifies suitable absorbent polymer and toxic gas pairs or groups that will allow reduction of the weight and size of respirator elements relative to activated charcoal elements in common use today. These materials will be used in a two–way flow breathing mode. Predictive codes for estimating the performance of various absorbent materials relative to selected toxic gases when incorporated in a filter design of specified geometry have been developed and checked out. Experiments to assess performance are being conducted in a test apparatus simulating human breathing. An engineering study will be made to design two–way flow respirators and assess the practical issues of wearer comfort, face seal leakage and methods of mass production.

Methodology

A combined experimental and numerical modeling approach is being utilized to evaluate the influence of various parameters and materials on respirator performance. The predictive numerical code developed computes mass and heat transfer in the absorbent materials using well grounded fundamental physical and chemical relations. Effects of temperature variation are included where they affect the local thermal and mass diffusities as well as the solubility coefficients of the absorbents.

The experimental program provides for testing filter elements of reduced flow through area, but of essentially full scale geometry otherwise. The test apparatus simulates the human breathing cycle and provides for concentration measurements using flame ionization detection in two–way oscillating flow with return flow matched in temperature and humidity to human breath.

Measurements of partition coefficients and diffusivities for the polymer/gas pairs are being made using an equilibrium technique in which permeability is measured for a polymer membrane in a counter flow mass exchanger, and weight gain measurements are used to determine the partition coefficients.

Significant Findings

During the first phase of the research, the feasibility of the two–way flow concept was demonstrated. Experiments were conducted with a high boiling point vapor in an experimental loop which simulates the human breathing cycle and includes a small section of a respirator filter element formed with an absorbent polymer. Measurements were made of the concentrations of the toxic gas simulant exiting the module as a function of time. Comparison of results for operation with two–way oscillatory flow with those of conventional one–way flow show a dramatic increase in the breakthrough time and a large decrease in the concentrations following breakthrough. These experiments demonstrate the feasibility of the new concept and its potential for superior performance relative to conventional respirators such as those using charcoal.

Original simplified test hardware has been upgraded to provide increased test module size and to reduce time lags in the measurements of the exhaust flows. Experiments in progress confirm the projections made. Results of the numerical simulation model developed, which has been expanded to include both heat and mass transfer effects, show similar significant improvements in respirator performance using two–way oscillatory flow over conventional one–way flow. A parametric study conducted with the numerical simulation model determined the influence of various factors such as partition coefficient, diffusivity, geometry and flow velocity on respirator performance.

A number of rubbery polymers having high solubility coefficients for high boiling point vapors

have been identified and their properties measured. Test modules utilizing these polymers have been prepared in various configurations designed to enhance mass transfer and are presently under test.

Relative Health Risks of Diesel Emission Control Systems

Susan T. Bagley, Ph.D.
Michigan Technological University
College of Sciences and Arts
Department of Biological Sciences
1400 Townsend Drive
Houghton, Michigan 49931-1295

Grant Number: *2 R01 OH02611-04*
Start & End Dates: *01/01/89 – 10/31/93*
Funding Level: *$0 ($352,307 Cum)*

Importance to Occupational Safety and Health

Whole diesel exhaust is regarded as a potential occupational carcinogen by the National Institute for Occupational Safety and Health (NIOSH) but the risk of cancer to exposed workers has not been quantitatively defined. One problem encountered in defining risk is the chemical complexity of diesel exhaust, making it difficult to define exposure. Michigan Technological University (MTU) and the Bureau of Mines (BOM) have worked together to define key aspects of the chemical nature and biological activity of diesel particulate matter (DPM) collected in underground mines with and without diesel emissions control devices and DPM and semi–volatile organics collected from a heavy–duty diesel engine operated with and without emission control devices in the laboratory. Together, these data will help evaluate the potential health effects of diesel exhaust and the impact of emission control.

Objectives

The overall objectives of this project were: (1) to obtain estimates of diesel pollutant levels in underground coal mines when DPM emission control devices are not in use, to include polynuclear aromatic hydrocarbons (PAH) and biological activity; (2) to assess the effects of using DPM emission control systems on these pollutants in laboratory tests; and (3) to obtain estimates of the effectiveness of using various DPM emission control devices on these same pollutants in a metal mine and in a coal mine.

Methodology

Samples from four dieselized underground coal mines without DPM control devices were collected by BOM personnel using Hi–volume samplers equipped with inertial impactors to collect size–differentiated particle samples. Particles ≤ 1 m in size were considered to be primarily of diesel origin. Samplers were located at the section intake and in the haulageway near where diesel shuttle cars turned around to dump their loads. The soluble organic fraction (SOF) was removed from the particles on the filters by Soxhlet extraction with dichloromethane. The daily extracts from all filters at each sampling location in a mine were pooled to reflect average levels over each day's sampling period. Samples were also collected and analyzed using similar techniques from: (1) a dieselized metal mine where a catalyzed diesel particle filter (CDPF) and an oxidation catalytic converter (OCC) were used together (in place of an OCC); and (2) a dieselized underground coal mine where a disposable diesel exhaust filter (DDEF) was used.

Laboratory samples were also collected at the BOM in two separate studies: (1) with and without a CDPF; and (2) with and without an OCC. Both filter (DPM) and XAD–2 resin (XAD–2 resin organic component or XOC) samples were collected, with organic material removed from both types of media by Soxhlet extraction with dichloromethane. The CDPF studies were conducted using a low sulfur (0.039 wt.%) fuel. The OCC studies were conducted with six different fuels varying in sulfur and aromatic levels and cetane number.

PAH and nitro–PAH fractions of the SOF and XOC were obtained from a two–column clean–up procedure and analyzed by HPLC with fluorescence detection. The compounds chosen for quantification due to their known or suspected health effects included fluoranthene, chrysene, benz[*a*]anthracene, benzo[*a*]pyrene, 1–nitropyrene, 2–nitrofluorene, and 3–nitrofluoranthene. Sulfate levels were determined by ion chromatography of aqueous extracts from the filters following their Soxhlet extraction for SOF removal. Unfractionated SOF and XOC and some fractions were tested for biological activity using the microsuspension version of the Ames assay.

Significant Findings

Estimates of Diesel Pollutant Levels in Underground Coal Mines – The DPM, PAH, nitro–PAH, and mutagenic activity levels represented potential highest in–mine values that would occur when diesel equipment was operating in a given area. The DPM values (mean/mine range of 0.9 – 1.9 mg/m^3) were typically at the upper end of values obtained with other, more personal–type sampling methods. In most cases, the mine atmosphere levels of DPM, SOF, PAH, and mutagenicity were statistically similar for all four underground coal mines, thus providing a range of values that might be expected to occur when diesel vehicles without DPM emission control devices are operating. Use of the

DDEF in another coal mine resulted in at least 50% reductions in all diesel emissions' concentrations in the haulageways. The differences in levels between the mines were likely related to differences in parameters such as vehicle type, mine ventilation efficiencies, fuel composition, and engine design, operation, and maintenance, with engine operation and maintenance probably being the major factor. The lowest levels of SOF and associated PAH and nitro–PAH were found at the mine with well–maintained engines operating at high loads; the highest levels of these parameters were found at the mine with relatively poorly maintained vehicles spending a considerable amount of time idling.

Laboratory Studies with DPM Emission Control Devices – Laboratory–generated data were found to be reliable for estimating in–mine levels in dieselized underground mines. The data obtained from a transient cycle designed to simulate haulage vehicle operation closely resembled the coal mine data where such haulage vehicles operate. In contrast, the data from a steady–state cycle designed to simulate operation of load–haul–dump vehicles, such as would be used in metal mines, did not as closely resemble the actual data from the coal mines.

When used with a low sulfur (<0.05 wt.%) fuel, it was estimated that use of the tested CDPF in underground mines could result in at least 90% reductions in DPM levels, with comparable effects on other diesel exhaust components. The CDPF was slightly less effective in reducing XOC compared to SOF (99% versus 89%, respectively), although both reductions were significant. The CDPF removal efficiencies for DPM–associated PAH and nitro–PAH were ≥95% for both transient and steady–state operation. Only fluoranthene and pyrene were found with the XOC with or without the CDPF; levels of both were reduced by >85%. Mutagenic activity associated with the particle or vapor phases decreased by approximately 70% with CDPF use. Engine operating conditions were found to have potentially significant effects on most of the diesel emissions.

When used in conjunction with a low sulfur fuel, use of the tested OCC in underground mines could also have a significant impact on reducing DPM levels as well as other emission components. Using a transient test cycle simulating potentially worst case operation of the OCC, from 30 to 70% reductions were found in most of the measured emissions. Some differences in emissions due to fuel composition were also noted.

Effects of a CDPF and an OCC in an Underground Metal Mine – Use of a combined CDPF/OCC in an underground metal mine resulted in approximately 50% reductions in DPM, SOF, PAH, and nitro–PAH concentrations over use of an OCC alone. Mutagenic activity concentrations (revertants/m^3) increased by about 250% with CDPF/OCC use over use of an OCC alone, reflecting over 500% increases in activity on a mass basis (revertants/g).

Publications

Carlson DH, Johnson JH, Bagley ST, Gratz LD: Underground Coal Mine Air Quality in Mines Using Disposable Diesel Exhaust Filter Control Devices. Proc of 4th Symposium on Respirable Dust in the Mineral Industries, Pittsburgh, Pennsylvania, November 8–10, 1994 (for publication in Applied Occupational and Environmental Hygiene)

Johnson JH, Carlson DH, Bagley ST, Gratz LD: Underground Metal Mine Air Quality Measurements to Determine the Control Efficiencies of Combined Catalyzed Diesel Particulate Filter and Oxidation Catalytic Converter Systems. Proc of 4th Symposium on Respirable Dust in the Mineral Industries, Pittsburgh, Pennsylvania, November 8–10, 1994 (for publication in Applied Occupational and Environmental Hygiene)

Cantrell BK, Rubow KL, Watts WF Jr, Bagley ST, Carlson DJ: Pollutant Levels in Underground Coal Mines Using Diesel Equipment. Proc of the 6th US Mine Ventilation Symposium, Society for Mining, Metallurgy, and Exploration, Inc, Salt Lake City, Utah, in press, June 21–23, 1993

Bagley ST, Baumgard KJ, Gratz LD: Polynuclear Aromatic Hydrocarbons and Biological Activity Associated with Diesel Particulate Matter Collected in Underground Coal Mines. Proc of Bureau of Mines Information and Technology Transfer Seminar on Diesels in Underground Mines: Measurement and Control of Particulate Emissions, Bloomington, Minnesota, pp. 40–48, September 29–30, 1992

McClure BT, Bagley ST, Gratz LD: The Influence of an Oxidation Catalytic Converter and Fuel Composition on the Chemical and Biological Characteristics of Diesel Exhaust Emissions. SAE Technical Paper Series No 920854, 1992

Bagley ST, Baumgard KJ, Gratz LD, Bickel KL, Watts WF Jr: Effects of a Catalyzed Diesel Particle Filter on the Chemical Biological Character of Emissions from a Diesel Engine Used in Underground Mines. SAE Transactions 100:1578–1589, (SAE Technical Paper Series No 911840), 1991

Bagley ST, Baumgard KJ, Gratz LD: Comparison of IN–mine and Laboratory–generated Diesel Particulate Matter, Biological Activity, and Polynuclear Aromatic Hydrocarbon Levels. Proc of 3rd Symposium on

Respirable Dust in the Mineral Industries, Pittsburgh, Pennsylvania, 61–70, October 17–19, 1990

Health Care Worker Compliance with Hepatitis B Vaccine

Bradley N. Doebbeling, M.D.
University of Iowa
College of Medicine
Department of Internal Medicine
200 Hawkins Drive, C31 GH
Iowa City, Iowa 52242

Grant Number: *5 K01 OH00131-02*
Start & End Dates: *04/01/93 – 03/31/96*
Funding Level: *$54,000 ($104,956 Cum)*

Importance to Occupational Safety and Health

The overall goal of this study is to evaluate the distribution and determinants of hepatitis B vaccine use and compliance in Iowa hospitals and among Iowa health care workers. This study is designed to identify institutional occupational, and behavioral variables among health care workers that impact on their practice of effective preventive health measures, using compliance with the hepatitis B vaccine as the paradigm.

Objectives

We propose to test the following specific hypotheses:

1. that institutional levels of HBV vaccine compliance are directly related to the type of vaccine implementation program;
2. that high levels of institutional compliance with OSHA's Bloodborne Pathogens Rule will have indirect benefits on the frequency of sharps injuries, cutaneous exposures to blood, TB exposures, and PPD conversions;
3. that the frequency of educational programs is unimportant in determining compliance in individual hospital workers;
4. that institutional factors including provision of the vaccine at the work site, increased access (availability), and documented informed refusal are more important than individual factors in determining individual compliance;
5. that compliance with universal precautions will predict compliance with HBV vaccination; and
6. that social influence and facilitating conditions are extremely important in behavioral models of HCW vaccination behavior.

Methodology

In the first stage, a longitudinal survey of Iowa health care institutions has been performed over a two–year period to define the rates and distribution of hepatitis B vaccine acceptance following implementation of a federal mandate for vaccination. Levels of institutional compliance with OSHA's Bloodborne Pathogens Rule will be categorized and their effect on vaccine compliance and occupational exposures measured. Vaccine acceptance rates among health care workers in different job categories have been determined in institutional assessments at baseline and 24 months later. In the second stage of the study, a stratified random sample of 15 health care workers in each of three occupational categories at 30 general hospitals will be studied to investigate attitudes about vaccination, the effectiveness of different types of vaccination programs, as well as the effect of 0SHA's Bloodborne Pathogens Rule.

Data from individual health care workers will be used to evaluate the relative utility of two theoretical behavioral models in predicting health care worker vaccine acceptance. Multivariate models will be developed to predict individual and institutional acceptance. Additionally, the relative importance of institutional versus individual factors in determining individual hepatitis B vaccine acceptance will be evaluated. In the third year of the study, these models will be validated prospectively in a second sample of workers and unstudied facilities to identify an effective vaccine implementation program for health care facilities.

Significant Findings

The health care facilities studied include the hospitals and the largest chronic care facilities in Iowa in the Iowa Statewide Surveillance System (ISSS). We surveyed 141 ISSS facilities (94% participation) in 1992 prior to OSHA's Bloodborne Pathogens Rule (BPR) becoming enforceable to determine mean institutional vaccination rates (IVR) in different occupational groups. Vaccine delivery program characteristics were categorized according to the following factors: community and hospital demographics, clinical leader involvement, educational and occupational health program characteristics, access to care, and HBV experience.

In 1992, the mean IVR (three or more doses) ranged from 58% among nursing assistants, 59% among physicians and housekeepers, 68% among licensed practical nurses, 74% among registered nurses, and 82% among laboratory workers. Data

regarding rates of vaccination among physicians are limited in that most are not considered hospital employees and records were not available. Vaccine delivery characteristics differed considerably by size of the institution and whether it was located in an urban versus a rural county. For example, vaccine provision at a health fair ($p=0.006$) and provision to physicians at the worksite ($p=0.007$) were significantly different at rural versus urban hospitals. Differences in programs by hospital size included: vaccination records availability in a database ($p=0.035$), and provision to nurses at the worksite ($p<0.0001$).

Regression analysis to predict the facility IVR at baseline identified a six variable model with an adjusted R square of 0.34. The baseline regression model to predict the IVR identified the importance of active encouragement of and participation in vaccination by leaders, invitation by letter to receive the vaccine, the proportion of registered nurses and housekeepers in the workforce, and a requirement of vaccination for workers.

Facilities in the ISSS were surveyed again in 1994, two years after the BPR became enforceable. A total of 116 of 142 facilities participated in the follow–up survey (82% response rate). Initial results demonstrate an increase in the mean IVR for each occupational group, except for laboratory workers and physicians. Verification of the follow–up data is currently being performed. Data collection for the institutional validation study of vaccine provision program characteristics and rates of vaccination in facilities in Virginia is expected to begin shortly. Taken together, these data suggest that an active vaccine implementation program supported by clinical leaders in an institution is independently associated with the institution–wide vaccination rate. Since a requirement of HBV vaccination of workers is also associated with the IVR, the mandatory informed refusal approach of OSHA is expected to be effective in increasing HBV vaccine acceptance among health care workers.

Publications

Doebbeling BN, Wenzel RP: Nosocomial Viral Hepatitis and Infections Transmitted by Blood and Blood Products. In: Principles and Practice of Infectious Diseases, (eds. GL Mandell, JE Bennett, R Dolin), New York: Churchill Livingstone, Inc., 4th Edition, pp 2616–2632, 1995

Diekema DJ, Ferguson KJ, Doebbeling BN: Motivation for Hepatitis B Vaccine Acceptance Among Medical and Physician Assistant Students. J Gen Intem Med, in press, 1995

An Ergonomic Study of Alternative Keyboard Designs

Richard W. Marklin, Ph.D.
Marquette University
College of Engineering
Department of Mechanical and Industrial Engineering
1515 W. Wisconsin Avenue
Milwaukee, Wisconsin 53233

Grant Number: *1 R03 OH03184-01A1*
Start & End Dates: *09/30/94 – 09/29/96*
Funding Level: *$35,638 ($35,638 Cum)*

Importance to Occupational Safety and Health

One of the growing occupationally–related problems in both the manufacturing and service industries is that of hand and wrist cumulative trauma disorders (CTDs), of which carpal tunnel syndrome (CTS) is the most widely publicized. It is widely accepted that CTDs are related to repetitive and/or forceful exertions of the hand and wrist performed in work environments. The incidence and costs of CTDs are rising every year — over 50% of the illnesses reported to the U.S. Government are due to repeated trauma, with an average cost of $20,000.

Hand and wrist CTDs have been troublesome in the clerical service sector in the U.S., which has an employment base of over 18,000,000 (Stat. Abstract of the U.S., 1992). Many clerical workers exert 50,000 to 100,000 key strokes per day. Recently, there has been an onslaught of legal cases against manufacturers of computer keyboards by users who have claimed CTD injuries. While the exact cause of occupationally–induced CTDs in keyboard users is not known, the deviated wrist posture and forearm posture (ulnar deviation and pronation, respectively) dictated by the design of the standard, flat keyboard is often implicated in the etiology of hand and wrist CTDs. In response to this problem, several new alternative keyboard designs have entered the market, each claiming their own keyboard reduces the musculoskeletal stress on the data entry operator. Typically, these alternative keyboards are split into halves and rotated in the horizontal plane to reduce ulnar deviation and are declined in the vertical plane to lessen forearm pronation. However, little quantitative data are available as to whether the

fundamental design of these keyboards actually reduce deviated wrist and forearm posture and lessen musculoskeletal stress.

Objectives

The specific aim of this research study is to determine whether the fundamental designs of alternative keyboards have a beneficial effect on the posture of the wrist and forearm -- i.e. whether alternative keyboards impose less ulnar deviation and forearm pronation on the data entry operator than the conventional, flat keyboard. Another aim of this research is to determine whether the design of the keyboard affects the upper extremity motion patterns of operators in the early stage of CTS differently than healthy operators.

The long-term objective of this research is to improve the safety and health of keyboard operators by reducing the incidence, severity, and costs of musculoskeletal disorders in computer work environments. This research could not only enhance the quality of life of keyboard users, but also reduce health care costs, which would benefit employees, employers, and the national economy.

Methodology

In this study, a combination of electrogoniometers and video equipment will monitor the motion patterns of the finger, wrist, forearm, elbow, shoulder, and neck of 20 subjects with CTS and 20 healthy subjects. Three alternative keyboards and one standard, flat keyboard will be tested.

Significant Findings

None to date.

Encapsulating Protective Clothing: Work Tolerance

Phillip A. Bishop, Ed.D.
University of Alabama
Human Performance Laboratory
Box 870312
Tuscaloosa, Alabama 35487-0312

Grant Number: *5 R01 OH03015-02*
Start & End Dates: *09/15/93 – 09/14/95*
Funding Level: *$152,170 ($305,669 Cum)*

Importance to Occupational Safety and Health

This is the beginning of the second year of a two-year study of the efficacy, stability and generalizability of a prediction model for work tolerance of workers wearing encapsulating protective clothing (PC) in moderate to warm environments. The project is testing and refining a previously developed prediction model to determine the generalizability of this approach to prediction in simulated industrial situations.

Successful completion of this project will contribute to managing personnel engaged in labor requiring encapsulating protective clothing in moderate to warm temperatures. Worker safety will be enhanced, and more efficient work planning can be utilized. Current American Conference of Government Industrial Hygienists TLVs (1988-89 ACGIH, 1990) provide little help to managers and supervisors whose workers utilize PC . Present guidelines are necessarily conservative,but because of the restrictive nature of these guidelines, adherence is sometimes economically very difficult. Consequently many supervisors ignore present guidelines. Workers currently are required to self monitor, which increases safety risks and mitigates effective work management. Additionally this proposed project addresses, in part, 5 of the 12 research needs listed in NIOSH Criteria for a Recommended Standard for Occupational Exposure to Hot Environments, Revised Criteria, 1986. Current guidance for worker safety in PC is limited. The results of this study could be immediately useful in maximizing work productivity while minimizing safety risks.

Objectives

The purposes of the proposed study are to (1) test the generalizability, stability, and validity of, and refine the multiple regression equations developed in the previous study, (Bishop et al, 1994) and (2) Derive new equations as needed for other environments and work conditions.

Both purposes of this study lead to development of a technique for predicting physical work capacity of workers in these situations based upon field measurements gathered in a short–term work task performed in protective clothing in a mild ambient environment. This work will build upon recent work done in our laboratory (Bishop, PA, G Smith, P Ray, J Beaird, and J Smith. Empirical prediction of physiological response to prolonged work in encapsulating protective clothing. Ergonomics (In Press)). This prior study extended earlier work of Kenny et al. (Kenny, WL, Lewis, DA, Anderson, RK, and Kamon, E. A simple test for the prediction of relative heat tolerance, American Industrial Hygiene Association Journal, 47(4) 203–206, 1986), and Shvartz et al. (Shvartz, E, Shibolet, S, Meroz, A, Magazanik, and Y Shapiro. Prediction of heat tolerance from heart rate and rectal temperature in a temperate environment, Journal of Applied Physiology: Respiratory, Environmental, and Exercise Physiology, 43(4), 684–688, 1977) and showed that the work tolerance of 15 subjects wearing protective clothing could be predicted from simple performance measures obtained during bench stepping in a 21°C environment.

Methodology

After medical screening, 50 subjects are being measured during a bench step test of less than 20 minutes duration at room temperature (WBGT = 18°C). Simple data (i.e duration, comfort rating, etc.) from this bench step test is then being used to predict performance on a generic work protocol consisting of 15 minutes of treadmill walking at 3 mph followed by 5 minutes of arm curls with 14.6 kg of weight referred to as "work" hereafter), with this work sequence repeated on separate days in counterbalanced order under these four conditions:

Environment (WBGT °C)	Workload (L/min)
18	VO2=1.0, continuous
18 work, 18 rest	VO2=1.8 for 30 min, rest 30 min (1.8 +.0.2 @ rest yields 1.0)
26 work	VO2=1.0 continuous
26 work, 26 rest	VO2=1.8 for 30 min, rest 30 min (1.8 +.0.2 @ rest)

Models will be derived and tested for generalizability and stability by comparisons of models across subgroups and treatments.

Significant Findings

Data collection has been initiated and approximately 44 subjects have completed all phases of the study. Analyses of these data have not been initiated, but a data base is currently being constructed.

Additional questions regarding aspects of PC tolerance and work capacity are simultaneously being addressed.

Communication with Flat-Attenuation Hearing Protectors

Tomasz R. Letowski, H.D., Ph.D.
USARL, HRED
ATTN: AMSRL-HR-SD
Building 520
APG, Maryland 21005-5425

Grant Number: *1 R01 OH03021-01A1*
Start & End Dates: *09/30/93 – 11/30/94*
Funding Level: *$0 ($114,330 Cum)*

Importance to Occupational Safety and Health

The results of this study are expected to determine noise spectra and ranges of noise levels which are appropriate environments for wearing flat–attenuation hearing protection devices (HPDs). Collected data will also be used to assess efficacy of

various speech communication measures for assessment of HPDs.

Objectives

The proposed study is designed to evaluate the relationship between noise attenuation and speech communication effectiveness resulting from wearing flat–attenuation HPDs in several simulated work environments. Various objective and subjective measures will be compared to assess the amount of noise attenuation by the protectors as well as the effectiveness of speech communication between workers wearing the protectors.

Methodology

Sixty subjects will participate in the study. The following measures will be directly obtained or calculated in the study: (1) real–ear attenuation at threshold, (2) sound pressure level reduction, (3) word recognition score, (4) speech intelligibility rating, (5) double–task performance effectiveness, (6) speech level adjustment, and (7) vocal effort.

Significant Findings

The experimental part of the study has been completed. Thirty normal hearing and 30 hearing impaired hearing subjects participated. We are in the process of coding the data for analysis. No data analysis has been performed so far.

Factors Affecting Respirator Leak Sites and Shapes

Riedar K. Oestenstad, Ph.D.
University of Alabama
School of Public Health
Department of Environmental Health Sciences
UAB Station
Birmingham, Alabama 35294

Grant Number: *5 K01 OH00085-03*
Start & End Dates: *09/28/90 – 01/27/94*
Funding Level: *$0 ($160,373 Cum)*

Importance to Occupational Safety and Health

The results of this study will contribute to the understanding of the distribution of respirator leak sites and shape, and will have both theoretical and practical applications. Knowledge of these parameters may contribute to more accurate theoretical modeling of respirator leakage. Determination of the persistence of streamlining flow at high breathing rates may partially explain the lack of correlation between laboratory and workplace fit factors. Based on the results of the association of anthropometric dimensions with leak sites and respirator fit observed in this study and in our previous work, it appears that the facial dimensions currently used to define half–mask respirator test panels needs to be re–evaluated. These associations could be useful to respirator program administrators in the selection of a model or size of respirator for an individual wearer. They may also contribute to the improvement of facepiece design, thus providing greater protection to the user.

Objectives

The specific objectives of the study were to: (1) determine if leak sites and shapes change between the exercises of a quantitative fit test, (2) determine the variation of leak sites and shapes for multiple fittings of the same respirator on the same subject, (3) determine the distribution of leak sites and shapes for different respirators being worn by the same sample of subjects, (4) more accurately define the characteristics of subjects who show evidence of aerodynamic streamlining under the respirator facepiece, and (5) determine the effect of increased breathing rates on the development of air flow streamlining patterns.

Methodology

The first four objectives were accomplished by performing respirator fit tests on human subjects using a fluorescent whitening agent aerosol. Faceseal leak sites were identified by observation of fluorescence of the aerosol deposited at the site(s) when illuminated by ultraviolet light. Anthropometric facial dimensions of the subjects were also be measured. The fifth objective was accomplished by performing the same tests on a mannequin fitted with a respirator using a breathing simulator. Data was analyzed by conditional logistic regression, multiple linear regression and ANOVA.

Significant Findings

This study resulted in significant findings related to the correlation of facial dimensions and respirator fit, the distribution of leak sites and shapes, facial dimension differences for subjects with specific types of leaks, and the persistence of streamlining patterns at elevated breathing rates. Although seven facial dimensions were found to have significant correlation coefficients with respirator fit, they were poor predictors of fit in both linear and logistic regression models. Correlation was found to be strongly affected by gender. Of the dimensions currently used to define the half–mask respirator test panel, only face length was found to be significantly correlated to fit. Also, neither of the dimensions were included in any of the linear or logistic models for predicting respirator fit.

Analysis of leak site data found a very high proportion of cheek leaks and multiple leaks that included the cheek, and a high proportion of nose leaks. The distribution of leak sites was not affected by gender, respirator brand, or fit test repetition. There was no significant difference between leak shape distributions for gender, respirator brand, or fit test exercise.

Facial dimensions for subjects in leak site categories were significantly different in only one dimension for all subjects and females; however, ten dimensions were significantly different for males. There were few significant differences in the two–way comparisons of dimensions for subjects in a leak site category and their comparison groups. Logistic regression analysis found that subject, test repetition, and respirator brand were not significant in any of the models to predict the probability of a leak at any of the primary sites; and gender was only significant in the model for cheek leaks.

The fit tests on a mannequin fitted with a half–mask respirator over a range of work rates, and corresponding inspiratory flow rates, resulted in less developed visual streamlining patterns at the higher rates. In addition, bias associated with in–facepiece sampling was found to significantly decrease as inspiratory flow rate increased.

Publications

Oestenstad RK, Graffeo JB: Determination of Respirator Fit by an Aerosol Method and a Negative Pressure Method. J Internat Soc Resper Prot 11(3):6–14, 1994

Oestenstad RK, Perkins LL: An Assessment of Critical Anthropometric Dimensions for Predicting the Fit of a Half–Mask Respirator. Am Ind Hyg Assoc J 53:639–644, 1992

Oestenstad RK, Zwissler AM: A Comparison of Fit Provided by Natural and Silicone Rubber of the Same Brand of Half–Mask Respirator. Appl Occ Env Hyg 6:785–789, 1991

Oestenstad RK, Perkins JL, Rose VE: Identification of Faceseal Leak Sites on A Half–Mask Respirator. Am Ind Hyg Assoc J 51:280–284, 1990

Oestenstad RK, Dillon HK, Perkins LL: Distribution of Faceseal Leak Sites on A Half–Mask Respirator and Their Association with Facial Dimensions. Am Ind Hyg Assoc J 51:285–290, 1990

Rose JC, Oestenstad RK, Rose VE: A Comparison of Respirator Fit Factors Determined by Portable Nuclei Counting and Forward Light–Scattering Methods. Appl Occ Env Hyg 5:792–797, 1990

Minimizing Work Schedule Disruption with Bright Light

Scott S. Campbell, Ph.D.
New York Hospital - Cornell Medical Center
Institute of Chronobiology
Department of Psychiatry
21 Bloomingdale Road
White Plains, New York 10605

Grant Number: *5 R01 OH02758-02*
Start & End Dates: *05/01/92 – 04/30/94*
Funding Level: *$0 ($295,783 Cum)*

Importance to Occupational Safety and Health

It is generally acknowledged that almost three–quarters of the 20 million shift workers in the United States suffer from a variety of symptoms associated with the maladjustment of their circadian rhythms to an ever–changing work schedule. The cost of shift work due to accidents, loss of productivity, and increased health care demands is staggering. Recently, the aggregate social cost was

estimated at approximately 70 billion dollars annually. Despite the magnitude of the problem, traditional approaches to reducing the impact of shift work have been largely unsuccessful. The traditional use of hypnotics to treat sleep disturbance in shift work populations is complicated by a number of factors, the most problematic of which are hangover effects on waking function and the potential for abuse. Attempts to implement behavioral strategies that address more closely the etiology of the disturbance have been largely unsuccessful due to compliance problems.

Objectives

In contrast, the use of bright light offers a safe and viable alternative to hypnosis. The approach offers rapid action without the drawbacks associated with pharmacological interventions. There is substantial evidence that exposure to bright light is effective in modifying both the phase and the amplitude of circadian rhythms, which in turn, can improve sleep quality and waking function. This knowledge has already been applied successfully in clinical circadian disorders, but surprisingly, it has not been used to address the problems associated with circadian adaptation to shift work. Because night shift workers are awake, and thus available, to receive light during intervals in which the most robust physiological effects have been demonstrated, they constitute an ideal population for such an approach.

Methodology

In previous studies, we have shown that two distinct components of bright light exposure are effective in alleviating sleep and/or performance deficits associated with rotating shift work. Timed exposure to a 4–hour pulse of very bright light (>6000 lux) on the first night of shift work facilitates adaptation by rapidly shifting circadian phase by up to five hours. Such re–setting of the biological clock improves daytime sleep quality and subsequent on–shift performance. In addition, exposure to ambient light of less intensity (approximately 1000 lux) throughout the night shift results in an immediate enhancement of alertness and performance efficiency. This effect is probably not the consequence of changes in the circadian timing system, but rather the result of a direct cortical activating effect of bright light exposure.

The current study seeks to examine the effects of a light regimen that combines these two components during a simulated shift work protocol. Because middle–aged shift workers suffer most from shift work maladaptation, it is these individuals who are likely to benefit most from the implementation of bright light interventions. As such, we are comparing rates of physiological and behavioral adaptation in 40 to 60 year old subjects in the combined bright light condition and a control conditions. It is expected that these important and necessary laboratory–based, simulated night shift studies will form the basis for subsequent investigations to evaluate the efficacy of such interventions in applied settings.

Significant Findings

Data acquisition is ongoing. The results reported here are from a group of subjects whose data have been fully analyzed. As such, the findings should be considered preliminary.

Bright light had the expected result on the circadian timing system. By the third night of shift work the Active group showed a mean delay in the course of body core temperature of over seven hours, whereas, the Control group exhibited a mean delay of less than four hours. Despite this, there was no significant difference between the Active and Control groups in any measure of sleep quality following light exposure, with both groups exhibiting substantial reductions in the ability to sleep relative to Baseline. Post–hoc *t*-tests revealed significant reductions in sleep efficiency and significant increases in wakefulness after initial sleep onset. In addition, in the Active group, total sleep time declined by an hour. Similarly, analyses revealed that by the third night of shift work, no differences in performance were evident between the Active and Control subjects.

These results suggest that bright light treatment in middle–aged subjects may be less effective than equivalent interventions in younger subjects. It is essential that the issue of possible differential age effects be clarified if bright light interventions are to be of maximum benefit in the applied setting.

Publications

Campbell SS: Effects of Bright Light Exposure on Shift Work Adaptation in Middle–aged Subjects. Sleep Research, in press, 1994

Campbell SS, Dawson D and Zulley J: When The Human Circadian System Is Caught Napping: Evidence For Endogenous Rhythms Close To Twenty–four Hours. Sleep 16(7):638–640, 1993

Campbell SS: Alerting/activating Effects of Light. Sleep, in press, 1993

Campbell SS and Broughton RJ: Declining Body Temperature Prior To Sleep Initiation: Fluffing The Physiological Pillow? Chronobiology International, in press, 1993

Campbell SS: Effects of Sleep and Circadian Rhythms on Performance. In: Handbook of Human Performance, Volume 3, (eds A Smith, D Jones) New York, Academic Press, pp. 195–216, 1992

Effect of VDT Mouse Design on CTD Risk and User Skill

Ann E. Barr
Hospital For Joint Diseases
Occupational & Industrial
Orthopaedic Center
63 Downing Street
New York, New York 10014

Grant Number: *1 R03 OH03260-01*
Start & End Dates: *09/30/94 – 09/29/96*
Funding Level: *$35,900 ($35,900 Cum)*

Importance to Occupational Safety and Health

The biomechanical requirements for electronic mouse operation may be risk factors for cumulative trauma disorder (CTD) of the forearm and wrist and may limit skill acquisition and ultimate skill proficiency among both highly skilled and novice mouse users. No commercially available mouse eliminates all of these constraints, and studies of mouse user proficiency have not adequately assessed skill acquisition, especially with respect to the musculoskeletal system. This study will document the extent of CTD risk factors among occupational mouse users. It will result in a new mouse designed to reduce these risks. It will explore the impact of the constraints of mouse use on the acquisition of a complex functional task. It will investigate the effectiveness of an ergonomic solution intended to balance the problems of worker risk and the upper limits to skilled worker performance. Such knowledge will foster the prevention of CTD in computerized offices and enhance understanding of the limits to skill imposed by constraints in the human–machine interface.

Objectives

The objectives of this study are: (1) evaluate the biomechanical effects of mouse use on the forearm and wrist; (2) design an alternative mouse that reduces the risk of forearm and wrist CTD and to determine the biomechanical effects of mouse design; and (3) determine the effect of mouse design on skill acquisition and proficiency.

The hypotheses to be tested are as follows: (1) use of a standard mouse will be associated with fixed wrist extension, fixed wrist ulnar deviation, use of wrist radial–ulnar deviation for mouse operation, and continuous, submaximal electromyographic (EMG) activity by the forearm pronators and wrist extensors and ulnar deviators; (2) the new mouse design will reduce these biomechanical constraints; (3) novice mouse users will demonstrate an increased rate of skill acquisition with the new mouse design as indicated by improvement over time in the skill level, speed, accuracy, and motor coordination pattern with which a mouse input task is performed; and (4) both highly skilled and novice mouse users will demonstrate better ultimate skill with the new mouse design.

Methodology

One–hundred twenty–five skilled and novice occupational mouse users will be tested five times over seven weeks on a graphical mouse targeting task using a standard mouse and a new mouse designed for this project. 3D kinematics and EMG of the forearm and wrist will be measured on three of the visits. A two factor hierarchial ANOVA will be used to compare ultimate mouse skill across user skill category and mouse design. ANCOVA will be used to compare the rates of mouse skill improvement across user skill category and mouse design. Student's t–tests will be used to compare the fixed postures and ranges of motion required for mouse use across mouse design. Kinematic and EMG patterns will be used to compare changes in motor coordination patterns across skill category and mouse design as follows: (1) the degree of linear coupling

of joint motions will be analyzed by computing the correlation coefficients, r values, for angle–angle diagrams of wrist v. forearm movements for both mouse designs at three points during skill acquisition. The r values will be compared using the χ^2 statistic; (2) the onset of agonist activation and the latency between agonist and antagonist activation, as indicated by onset of EMG, during specific joint motions with each mouse design will be compared by two-way ANOVA for factors test session (three levels) and subject skill category (two levels); and (3) percent agonist-antagonist coactivation, or concontraction, will be calculated for specific joint motions with each mouse design and compared by two-way ANOVA for factors test session and skill category.

Significant Findings

None to date.

Preventing NIHL In Construction Workers

Sally L. Lusk, Ph.D.
University of Michigan
School of Nursing
Department of Health Promotion
& Risk Reduction
400 N. Ingalls, Room 3180
Ann Arbor, Michigan 48109-0482

Grant Number: *5 R01 OH03136-02*
Start & End Dates: *09/30/93 – 09/29/96*
Funding Level: *$256,296 ($434,136 Cum)*

Importance to Occupational Safety and Health

The purpose of this project is to prevent noise–induced hearing loss (NIHL), an irreversible impairment with significant monetary and personal costs, in construction workers through improved training in use of hearing protection (HP). The training will be based on a conceptual model, the Health Promotion Model (HPM) and specific to construction workers (CWs).

The Department of Public Health has estimated that one quarter of the five million CWs in the U.S. are exposed to average daily noise levels above 85 dBA (USDPH, 1988); yet no data regarding prevalence of NIHL or level of use of HP by CWs has been reported. While it is preferable to reduce this noise exposure through engineering controls, it is not feasible to eliminate all harmful noise. However, consistent use of HP equipment prevents NIHL. CWs represent a diverse and mobile population, exposed to various types of noise in conjunction with other safety hazards, on multiple and variable job sites. Therefore, knowledge of the predictors of these workers' use of HP is essential to the design of more effective training programs.

This study will provide needed data covering five different areas: (1) the degree of hazardous noise exposure as perceived by CWs; (2) the frequency of use of HP by CWs; (3) the strongest predictors of use of HP by CWs; (4) recruitment of CWs into research studies through their training programs; and (5) worker behavior related to personal involvement in safety precautions within a comprehensive health promotion framework.

Additionally, the proposed study will result in a customized training program for the prevention of NIHL in CWs through the increased use of personal HP. By developing the individual worker's consistent use of protective equipment, safety measures can be transported from construction site to construction site, despite the limited options for environmental control.

Objectives

This project has four specific aims: (1) identify the most important predictors of CW's use of hearing protection, specifically for carpenters, operating engineers, and plumbers/pipefitters; (2) use the identified predictors of CW's use of HP to adapt the training program already developed for factory workers to the needs of CWs; (3) assess the effect of the training program on CWs' use of HP; and (4) revise the training program as indicated and make it available for general use in training CWs.

Methodology

This study will be conducted with two distinct samples, a regional sample and a national sample, in three phases: (1) a cross–sectional correlational study will identify predictors of selected CWs' use of HP (carpenters, operating engineers, and plumbers/pipefitters); (2) the training program

prepared for factory workers will be revised to incorporate the predictors of CWs' use of HP and pilot–tested with CWs in this region; (3) the effect of the training program on the use of HP will be measured in both the regional and national samples through random assignment of workers to a Solomon Four–Group experimental design.

Significant Findings

Significant findings for the first two specific aims are reviewed in the paragraphs below. The next two specific aims will be completed in 1996.

Aim 1. Identify the most important predictors of CW's use of hearing protection.

Predictors of the use of hearing protection were identified separately for the national sample (n=145) and the regional sample of carpenters, operating engineers, and plumber/pipefitters (n=399). For the regional sample, significant bivariate correlations with use of hearing protection were found for the following components of the model: health competence, a non–clinical conception of health, self–efficacy in the use of hearing protection, situational influences for hearing protection, value of use of hearing protection, benefits of use minus barriers to use of hearing protection and interpersonal influences on use of hearing proteciton. When hearing protection use was regressed on the components of the model, significant predictors were Interpersonal Influences on Hearing Protection, Benefits Minus Barriers, and Value of Use of Hearing Protection (R^2=.35, Adj. R^2=.34). There were some differences among trade groups in the number of these variables that achieved significance.

For the national sample, significant bivariate correlations with use of hearing protection were found for the following components of the model: health competence, a clinical conception of health,a non–clinical conception of health, self–efficacy in the use of hearing protection, situational influences for hearing protection, value of use of hearing protection, benefits of use minus barriers to use of hearing protection and interpersonal influences on use of hearing protection. When hearing protection use was regressed on the components of the model, significant predictors were Situational Influences on Hearing Protection and Interpersonal Influences on Hearing Protection (R^2=.40, Adj. R^2=.35).

Aim 2. Use the identified predictors of CW's use of HP to adapt the training program already developed for factory workers to the needs of CWs.

Using the predictors identified in Aim 1, components of the program developed for factory workers, and advice from consultants and NIOSH staff, a completely new script was developed into a videotape presentation that will form the core of a training program for construction workers. The training program, consisting of the videotape presentation, a trainer–guided practice session with samples of hearing protection and learning tools, and a pamphlet, will be piloted with small groups of CWs representing each of the trade groups by mid December, 1994. Results of the pilot study will influence revisions in the training program prior to implementation in 1995.

Field Validation of Ventilation Troubleshooting Method

Steven E. Guffey, Ph.D.
University of Washington
School of Public Health
Department of Environmental Health, SC-34
Seattle, Washington 98103

Grant Number: *1 R01 OH03165-01*
Start & End Dates: *04/01/94 – 03/31/97*
Funding Level: *$67,618 ($67,618 Cum)*

Importance to Occupational Safety and Health

For ventilation hoods in an exhaust ventilation system to adequately protect workers from airborne contaminants, they must receive at least some minimum level of airflow. The amount and the distribution of the airflow provided by the fan can change in undesirable ways due to damage to the ducts (e.g., from abrasion, metal fatigue, crushing, cutting) and to ill–advised or sloppy modifications of the ducts by maintenance and operating maintenance. Modifications by maintenance and operating maintenance are rarely recorded anywhere, much less in a form useful to someone trying to understand the cause of changes to the system. Visual inspection is inadequate due to the large scale of many systems, the fact that the damage may be inside of opaque

ducts, and the frequently difficult access to ducts. For that reason, engineers and health personnel must rely on measured duct static pressures and velocities to determine when and where change have occurred to a system. This study is intended to test the effectiveness of three strategies used to interpret those measurements. Improvements in "troubleshooting" practices would produce earlier detection and repair of undesirable changes to ventilation systems, which would allow the possibility of reducing the lifetime cumulative exposures of millions of workers.

Objectives

This study examines the relative effectiveness of three "troubleshooting" methods as applied to five operating ventilation systems. Two methods (ACGIH and Hood Static Pressure) represent current practice, and the third (X–Method) has been proposed by the P.I. The measures of effectiveness are the specificity and sensitivity of each method in flagging actual changes to the systems.

Methodology

For each system, every three to four months the airflow and the hood static pressure in each branch duct and the static pressures at the downstream end of each duct is measured. By comparing troubleshooting parameters for a given round of measurements to those determined from the previous round, predictions can be made as to which ducts have experienced a real change using each of the three methods. If any method suggests that a change has occurred to a given duct, the inside of that duct is inspected, any visible change is noted, the obstruction is removed (or attempts are made to restore the duct to its previous condition), and, finally, the airflow and static pressures are remeasured to determine if each of the three methods now suggests that the duct has returned to its previous condition.

Significant Findings

The results so far are inconclusive because not enough time (7 months) has passed to make a substantial number of valid comparisons (samples are made every 3 to 4 months, as proposed). In addition, the project has been plagued with an unexpected problem: the number of insults to the systems has been very high. Had this been expected, it would have been highly desirable since it allows a large number of tests. However, thinking that changes would occur only moderately frequently, a week delay between measurement and analysis was assumed to be acceptable (up to two–weeks delay was proposed). In fact, after two rounds of measurements, changes were so frequent that a decision was made to measure, analyze, and search for changes all on the same day to relate discovered changes with any certainty to changes in troubleshooting parameters. Thus, the first two rounds were of dubious value in testing the three methodologies. On the other hand, the need for speed led to development of much faster data collection and analysis tools an extremely useful side benefit to the study.

Another unexpected problem has been the time delay in gaining effective access to submain ducts. Access hatches are now being installed, so this problem should be much diminished in future rounds. In addition, three new systems have been added at another site to the study. The new systems allow excellent access to submains. The first round of observations has been collected on two of the three new systems. The third will be completed in December.

Training and Medical Surveillance Under the ETO Standard

Anthony D. Lamontagne
Harvard School of Public Health
Department of Environmental Health
665 Huntington Avenue
Boston, Massachusetts 02115

Grant Number: *5 R03 OH03088-02*
Start & End Dates: *08/01/93 – 07/31/95*
Funding Level: *$12,486 ($29,767 Cum)*

Importance to Occupational Safety and Health

This study examines the implementation of OSHA–mandated medical surveillance, exposure monitoring, and worker health & safety training. Historically, training and medical surveillance have been emphasized and studied less than other preventive measures, such as engineering controls, which focuses more directly on the source of exposure. Training and medical surveillance are generally assumed to occur and to have some

preventive impact; however, systematic evaluation of these areas is only recently becoming recognized as a research need. In addition, there has been little study of the implementation of exposure monitoring requirements by workers, supervisors, health and safety staff, and others in industry. This study aims to determine the extent and nature of exposure monitoring activities, the results obtained, and how exposure monitoring results are related to follow–up activities, such as medical surveillance. Systematic study will help to develop untapped preventive potential of exposure monitoring, training, and medical surveillance, fostering the development of a more integrated and balanced approach to hazard control at all levels.

The specific aims of this study are to critically evaluate the implementation of the medical surveillance, exposure monitoring, and training provisions of OSHA's 1984 Ethylene Oxide (EtO) Standard in the hospital setting. The broader goal of this research is to identify strengths and weaknesses of medical surveillance, exposure monitoring, and training implementation in substance–specific OSHA standards in order to provide for more effective practice, enforcement strategies, and policy–making in these areas. The functioning of OSHA's medical surveillance trigger scheme is being evaluated, most importantly to examine the relationships between exposure monitoring results and medical surveillance, and between training and medical surveillance.

Objectives

The following three specific hypotheses, derived directly from the implementation strategies of exposure monitoring–driven substance–specific OSHA health standards are being tested: Hypothesis 1: Exceedance of trigger exposure levels is positively associated with implementation of EtO training; and Hypothesis 2: Exceedance of trigger exposure levels is positively associated with implementation of EtO medical surveillance. Two EtO exposure levels are specified to trigger training and medical surveillance requirements: the Action Level of 0.5 ppm Time–weighted Average (TWA) and the Excursion Limit of 5 ppm TWA per 15 period. Questions being asked are: to what extent are employers in compliance with these requirements and to what extent does exposure monitoring specifically guide employers in the implementation of EtO training and medical surveillance. Hypothesis 3: The implementation of training is positively associated with the implementation of medical surveillance. As stated in current OSHA policy, part of the intent of training is to make workers aware of their rights under a standard, which in turn is presumed to make workers more likely to exercise those rights. A test for association will be conducted which would be consistent with such a causal relationship between training and implementation of medical surveillance.

Methodology

The approach integrates theory and principles from occupational health, health education, and the social sciences with epidemiology and survey research methodology. All Massachusetts hospitals were surveyed by mail to identify EtO users. Of the 159 hospitals in the state, 92 responded as EtO users and 62 as non–users. The response rate for the mailed survey was 97%. EtO users were then administered a 15 minute standardized telephone interview (response rate = 92/92), followed by a standardized 1–2 hour on–site, face–to–face interview with the sterilization department supervisor (response rate = 90/92). Brief questionnaires on the process and findings of EtO medical surveillance exams were mailed to providers wherever EtO medical surveillance was reportedly provided. The medical surveillance provider response rate was 65% (37/57 hospitals where surveillance provided).

Significant Findings

From 1985 to 1993, medical surveillance for EtO exposure was provided one or more times in 62% of EtO–using Massachusetts hospitals. Sixty–five percent of EtO medical surveillance providers reported performance of all five medical surveillance procedures required by OSHA's EtO standard. Medical surveillance provider certification in occupational medicine or nursing, and a greater extent of coverage of written medical surveillance policies were related to higher likelihoods of fulfillment of OSHA required procedures (Relative Risks = 1.6 ($p = 0.04$ one–tailed) and 2.0 ($p = 0.01$), respectively). Twenty–seven percent of medical surveillance providers reported detection of EtO–related symptoms or conditions, ranging from mucous membrane irritation to peripheral neuropathy. These findings reveal widespread implementation of OSHA–mandated EtO medical surveillance, with concomitant incomplete fulfillment of OSHA–specified procedures. From the provider–based survey, we estimate that one or more

workers at 19% of EtO–using Massachusetts hospitals have experienced EtO–related health effects.

Among OSHA's five specified triggers for providing EtO medical surveillance, only accidental worker exposures were related to providing surveillance (RR = 2.56, $p < 0.001$). Exceeding the Action Level for 30 or more days, one of OSHA's EtO triggers that is also used in a number of other standards, was not related to providing surveillance (RR = 0.84, $p = 0.714$). Reports of coverage of EtO medical surveillance issues in worker training were also strongly related with providing EtO medical surveillance (RR = 3.68, $p < 0.001$), supporting OSHA's premise that worker training plays an important role in medical surveillance implementation. Thirdly, the presence of detailed written EtO medical surveillance policies was positively related to providing EtO medical surveillance (RR = 1.81, $p < 0.001$). Each of these three variables also remained significantly related to providing medical surveillance in logistic regression analysis after adjustment for a wide variety of covariates. These findings have implications for improvement of OSHA medical surveillance implementation through revised trigger schemes, improved worker training efforts, and other measures. Findings are also relevant to the future development of medical surveillance and exposure monitoring policies in both substance–specific and generic contexts.

Investigation of ROPS Design For Older Tractors

Paul D. Ayers, Ph.D.
Colorado State University
College of Engineering
Department of Chemical
& Bioresource Engineering
Fort Collins, Colorado 80523

Grant Number: *1 R01 OH03163-01*
Start & End Dates: *06/01/94 – 05/31/97*
Funding Level: *$88,998 ($88,998 Cum)*

Importance to Occupational Safety and Health

Tractor overturns are a major cause of agricultural–worker deaths every year. An estimated 150 – 200 agricultural tractor overturn fatalities occur each year accounting for one out of every seven agricultural work deaths. In addition, other serious non–fatal injuries result from overturns of tractors without roll–over protective structures (ROPS). These deaths and serious injuries may have been prevented if the tractors had been equipped with a rollover protective structure (ROPS) and if the operator was wearing a seat belt.

A ROPS is a protective structure designed to protect the operator in the event of a vehicle overturn. ROPS are designed to absorb energy resulting from the impact of the vehicle (tractor) with the ground surface during an overturn and protect the operator from serious injury.

An agreement between North American tractor manufacturers resulted in all tractors built after 1984 be fitted with ROPS. Also, retrofit ROPS are currently available for tractors that were manufactured with ROPS as an option. Although some tractor manufacturers had ROPS–equipped tractors earlier, many tractors manufactured prior to 1970 did not have ROPS as an option, and thus the axle mounts were not designed to structurally support a ROPS during an overturn. Such tractors will be referred to as pre–ROPS tractors.

An estimated 4.61 million agricultural tractors are utilized in the United States, and 61 percent were manufactured before 1971. For many of these older tractors, ROPS are not available. If ROPS can be mounted to the axles of older tractors, then the control of this potential hazard can be attained. By retrofitting all agricultural tractors in the U.S. with ROPS, an estimated total 2,800 rollover–related fatalities can be prevented.

Objectives

The major hypothesis of this study is that ROPS can be mounted on pre–ROPS tractors and used to protect the operator in the event of an overturn. The specific objective of this project is to use laboratory and field testing of ROPS to develop suitable guidelines so that ROPS can be designed to be mounted on older tractors. These ROPS must meet the requirements stipulated in ASAE S519 "Roll–Over Protective Structures (ROPS) for Wheeled Agricultural Tractors (ISO Compatible)."

Methodology

Existing tractor surveys will be examined to identify the make and model number of pre–ROPS

tractors currently in use in the United States. Known surveys have been conducted in Colorado, West Virginia, Iowa, South Dakota, and Pennsylvania. The program leader of the NIOSH supported Farm Family Surveillance project will be contacted to utilize on–going surveillance results. Additional contacts will be made through NIOSH to obtain appropriate databases. A database of pre–ROPS tractors currently in use will be developed so future research efforts will be able to focus on the most abundant makes and models. Based on previous surveys in Colorado, the pre–ROPS tractors Ford 9N, John Deere Model A, John Deere Model B, and John Deere 730 are most common pre–ROPS tractors utilized.

Investigations will be conducted to categorize the pre–ROPS tractors in terms of similar axle designs and define the major categories of pre–ROPS axle designs. Typically, each major tractor manufacturer has several pre–ROPS axle designs. By separating the pre–ROPS tractors into major axle designs, guidelines may not be needed for each tractor model. It is likely that ROPS design guidelines can be developed for each major axle type with minor modifications for each model tractor.

Design of axle and mounting modifications for each major axle category will be conducted to allow ROPS to be mounted on pre–ROPS tractors. Based on preliminary studies, these modifications may be needed to: (1) support the axle housing or (2) incorporate additional mounting support to attach the ROPS to the tractor frame. Computer–aided design drawing of the design modifications will be developed.

The design modifications will be tested utilizing laboratory and field testing to investigate ROPS design for the major axle categories of pre–ROPS tractors. The testing will be conducted in accordance with ASAE S519. The static ROPS testing apparatus at the Agricultural Engineering Research Center, Colorado State University, will be used to test the ROPS–axle frame combinations.

The major purpose of this project is to develop guidelines for the design of ROPS for pre–ROPS tractors. The design guidelines will concentrate on axle housing support and mounting modifications, and locations for the major axle categories identified for pre–ROPS tractors. The design guidelines will provide tractor and ROPS manufacturers with detailed information on design modifications and test results. The guidelines will address general information on ROPS materials types and sizes, welding, gussetting, mounting (including fasteners and structural support), and seat belt mounting, in addition to the specific information addressing the appropriate axle categories. These preliminary guidelines will presented to tractor and ROPS manufacturers for their critique and recommendations. Final guidelines will be developed and distributed.

Significant Findings

None to date.

Publications

Ayers PD, Dickson M, Warner S: Model to Evaluate Exposure Criteria During Roll–over Protective Structure (ROPS) Testing. Transactions of the ASAE, in press, 1994

Permeation Mechanisms of Pesticides Through Materials

Shane Que Hee, Ph.D.
University of California
School of Public Health
Department of Environmental Health Sciences
10333 Le Conte Avenue
Los Angeles, California 90024-1772

Grant Number: *3 R01 OH02951-02S1*
Start & End Dates: *09/30/92 – 11/30/94*
Funding Level: *$151,876 ($269,507 Cum)*

Importance to Occupational Safety and Health

While permeation characteristics of single specific solvent chemicals through gloves and garments are well documented, those for specific pesticides and for pesticides in their emulsion concentrate forms (regarded as the most hazardous forms to handle), have not been intensively investigated. Emulsion concentrates consist of the active ingredient, organic solvents, surfactants, and other adjuvants, and thus constitute a multi component chemical exposure on inhalation, dermal or ingestion exposure. This is important during spraying, on worker field reentry, and when formulating. When several pesticides are coformulated in blends under small shop conditions, permeation characteristics through gloves and garments may be influenced by the prior and

concurrent handling of the other formulary components.

Objectives

The hypothesis is: the most permeating constituent of the challenge medium containing a pesticidal emulsion concentrate regulates the permeation of the pesticide through glove and garment materials.

The studies will allow selection of the appropriate permeation method, the most protective gloves and garments for these formulations, and development of a predictive model.

Methodology

The initial studies will involve the identification and quantification of the inert components and surfactants/adjuvants in the selected emulsion concentrates. The latter are: captan, chlorpyrifos, 2,4–D (three forms), endosulfan, malathion, methomyl, methyl parathion, and trifluralin. The selected glove materials are: Butyl, Nitrile, Silver Shield, and Viton. The garment materials are: Barricade, two–ply Saranex–Laminated Tyvek 23–P, Chemrel Max, and Teflon/Nomex/Teflon.

Eight–hour screening studies with two ASTM–type permeation techniques will be performed. One technique involves a I–PTC ASTM–type permeation cell and liquid collection system. The other method utilizes a solid silicone sheet collection method. Challenges will be to the neat chemical if liquid, the neat chemical in the major solvent of the formulation in the presence /absence of surfactant/adjuvant, the emulsion concentrate, and to the aqueous emulsion diluted to its highest spraying concentration. Kinetics studies over two–hour periods at three different temperatures will then lead to measurement of breakthrough times, and steady state rates. Shelf–life studies for materials aged 0.5 and 1.0 years after acquisition will also be performed. A predictive permeation model will be developed.

Significant Findings

Work has almost been completed on two malathion emulsion concentrates and on formulations containing chlorpyrifos, methomyl, and endosulfan. The liquid malathion neat chemical is a monopolar ester and thus permeates Nitrile (lag time 50–85 minutes; 0.37– 0.41 $mg/cm^2/min$) and penetrates Latex (causes holes within minutes) but not Viton or Silver Shield over 8 hours. The permeation is antagonized by xylene/trimethyl benzene inert components. Challenges of malathion as aqueous emulsion formulations required optimization of challenge mixing conditions and selection of an inert collection solvent that also permitted solubilization of the malathion. Permeation was still observed at much lower steady state rates and about the same breakthrough times relative to challenges with formulations alone.

Studies with formulations containing endosulfan, chlorpyrifos, malathion, and methomyl have shown that Nitrile is protective for at least two hours, that Butyl does not protect as well, and that Silver Shield and Viton protect at least 8 hours. Lannate had the highest steady state permeation rate. The formulations with endosulfan, malathion, and chlorpyrifos contained mesitylene inert components, but those for lannate had methanol and n–propanol. The latter were responsible for the faster breakthrough times and higher steady state rates for methomyl.

Simple physical parameters and chromatographic rate theory were utilized to construct a theory of permeation that was able to characterize the permeation of challenge mixtures. The permeation data for trimethyl–, methyl ethyl–, and propyl–benzenes were obtained for the first time for interpretation by the new theoretical approach for both neat solvent challenges and pesticidal formulation mixtures.

Data collection will be continued on the phenoxy herbicide 2,4–dichlorophenoxyacetic acid as three separate forms, and on the xylene/ethylbenzene constituents of the inert components.

Evaluation of Respirators for Asbestos Fibers

Yung-Sung Cheng, Ph.D.
Lovelace Biomedical & Environmental Research Institute
Inhalation Toxicology Research Institute
Aerosol Science Group
P.O. Box 5890
Albuquerque, New Mexico 87185

Grant Number: *5 R01 OH02922-02*
Start & End Dates: *09/30/92 – 09/29/95*
Funding Level: *$0 ($357,145 Cum)*

Importance to Occupational Safety and Health

Results from this research will provide quantitative information for determining the performance of respirators against asbestos and manmade fibers. The information can then be used as a basis to evaluate the current NIOSH procedures for certification of respirators for protecting workers exposed to fibers. Improved designs of the respirators and test procedures for NIOSH certification will help to reduce occupational exposures to asbestos and manmade fibers. The effects of electrostatic charges of the respirator cartridges and particles on the filter performance will also be determined. This information will help to evaluate respirator filters using electret material to enhance performance.

Objectives

The goal of this research is to quantify the performance of respirator filters used to protect workers in environments where they are at risk of exposure to asbestos and manmade fibers. Current OSHA guidelines require the use of respirators fitted with high–efficiency filters. These filters must be approved under NIOSH certification criteria based on penetration tests using spherical aerosols. Fiber aerosols are known to have different aerodynamic behaviors than spherical particles and usually carry higher electrostatic charges. Because the carcinogenicities of asbestos and other fibers are known to be due, in part, to fiber dimensions, the efficiency of the respirator filters in relation to fiber dimension is very important. It is difficult to predict how fiber aerosols will penetrate respirator filters based on the NIOSH testing results using spherical particles.

The specific objectives of this study are: (1) to elucidate effects of fiber size, electrostatic charge, and flow rate on fiber aerosol penetration of filter cartridges, (2) to develop a mathematical model for predicting the penetration of fiber aerosols in respirator filters, and (3) to determine the fiber aerosol penetration through leaks in the face seal.

Methodology

Three asbestos fibers with mean diameters ranging from 0.04 to 0.5 μm and aspect ratios from 3 to 60 are used. Both overall and size–specific penetration of fiber aerosols through filters are determined. Based on size–specific fiber penetration information, the effects of particle diameter, length, and flow rate are examined and the filtration mechanisms identified. The dimensions of fibers that most likely penetrate the respirator filter are then determined. Our hypothesis states that electrostatic collection is the main reason for the inconsistent filter performance reported in the literature. This hypothesis is being tested by investigating the effects of electrostatic forces on fiber collection. Filtration models are being developed to predict the penetration of fiber aerosols of given size distributions and electrostatic charges. The study includes four types of filters, each tested at two flow rates: the AO–R57A, a dual cartridge HEPA filter tested at 16 and 42.5 L/min; the MSA–S, a dust and mist filter tested at 16 and 42.5 L/min; the MSA–A power filter tested at 32 and 85 L/min; and the 3M–8710, a low–efficiency disposable face mask filter tested at 32 and 85 L/min. The fibers are tested in both charged and neutralized forms. Filter cartridges are used in an untreated condition directly from the box and in a treated condition which is induced with an antistatic spray.

Significant Findings

1. Measurements on the respirator filters showed that some filters including a filter mask and a filter cartridge for powered respirators had substantial surfaces charges. However, the surface charges disappeared in 38° and 93% RH in 2 days. Our results suggest that the electrostatic charge in some filter cartridges is the major factor for increased collection efficiency. However, the efficiency enhancement due to these

electrostatic charge effects may not be long–lasting when used in certain environments.

2. The collection efficiencies for two high–efficiency filters (AO–R57A and MSA–A) are essentially 100% for all three types of fibers regardless of the electrostatic status presented in the fibers and filters. These results indicate that for these high–efficiency filters, the mechanical deposition processes are sufficient for fiber collection, and the electrostatic forces are not important.
3. The filtration efficiencies for two low–efficiency filters (MSA–S and 3M–8710) indicate that the charged fibers are collected more efficiently, especially before the filter is treated with antistatic spray. When electrical charges are removed from either the filter or the fibers, the filtration efficiency decreases. These results indicate that for low efficiency filters, electrostatic forces are important in enhancing filter performance.
4. The mathematical filtration model for fiber and spherical aerosols shows increased filter collection efficiency for elongated fibers due mainly to the interception mechanism. Because of the long axis, an elongated particle contacted the filter material and is collected. Our model show that this interception effect increases with the aspect ratio. However, the interception effect is only effective for fiber aerosols with a volume equivalent diameter greater than 0.5 μm. For fibers smaller than 0.5 μm, the diffusion deposition mechanism dominates, and the filtration efficiency for fiber aerosols is not enhanced.
5. Preliminary results on the penetration of amosite fibers in a disposable filter show that smaller and thinner fibers penetrate more than longer fibers. For fibers of a given diameter, the collection efficiency increases with increasing fiber length, indicating the importance of the interceptional mechanism.

Publications

Chen BT, Irwin R, Cheng YS, Hoover MD, Yeh HC: Aerodynamic Behavior of Fiber and Disk–Like Particles in a Millikan Cell Apparatus. J Aerosol Science 24:181–195, 1993

Performance of Surgical Masks

Klaus Willeke, Ph.D.
University of Cincinnati
College of Medicine
Department of Environmental Health
Kettering Laboratory
3223 Eden Avenue
Cincinnati, Ohio 45267-0056

Grant Number: *5 R01 OH02948-02*
Start & End Dates: *09/01/92 – 08/31/95*
Funding Level: *$0 ($1,268,484 Cum)*

Importance to Occupational Safety and Health

Results of this study will extend our ability to protect both patients and operating teams from airborne and dispersed bloodborne pathogens. This concern is encouraging the examination of existing respiratory protective devices and the consideration of modifying devices used in industrial settings for use in health–care environments. About 6.9 million health care and other workers in the U.S. are at risk for blood contact at the worksite. The number at risk from aerosol transmission has not been accurately estimated; however, given the variance in mask collection efficiencies, the continued use of new technologies, and the potential for disease transmission, ascertaining the value of current mask protection is important.

Objectives

The objective of the current grant research is to study the performance of masks and respirators currently used or considered for use in the health care industry. The principal aim is to find how the aerosol penetration efficiency of a health–care respirator/mask depends on the size and shape of the test organism and to determine how the collection efficiencies obtained with bacteria differ from those obtained by the use of inert, non–viable test particles currently used to evaluate industrial masks and respirators. The second major aim of this study is the development of a method to dynamically measure the filter penetration efficiency of airborne microorganisms, so that such a method may be considered for the rapid testing of health–care

respirators, if testing with microorganisms is judged necessary by the health–care community.

Methodology

Viable bacteria and inert particles are generated in the laboratory for testing a wide range of available masks. The masks are exposed in a test chamber specifically designed for studies of respiratory protective devices. The aerosols are analyzed physically by aerosol size spectrometry and biologically by sampling the bacteria into bioaerosol samplers. *Pseudomonas fluorescens* ATCC 13525 is used as the principal challenge bacterium. It is grown in tryptic soy agar at 25°C for 25 hours, washed and dispensed in deionized water. The size of this bacterium is approximately 0.5 μm in width and 1.5 μm in length, i.e. it is physically similar to the tuberculosis bacterium. Other test bacteria range in shape from spherical to rod–shaped with a length to diameter aspect ratio exceeding 4. The size–dependent penetration efficiencies of inert and biologically active test aerosols are compared with each other.

Significant Findings

Experiments with inert particles have shown a considerable range in collection efficiency values depending on the mask used. Penetration is highest for submicrometer–sized aerosols, approaching 100% for some masks used. Some industrially used dust–mist–fume respirators have less penetration than the best currently used surgical mask. However, in the presence of a large face–seal leak, the dust–mist–fume mask may not provide any more protection than a surgical mask with a lower filtration efficiency. Due to the higher pressure drop across the dust–mist–fume mask it may even perform worse than the surgical mask, because considerable aerosol flow may be directed through the leak site. Thus, it is concluded that improvements in filtration efficiency in health care masks may necessitate quantitative fit testing to ensure proper fit of the mask to the health care worker's face.

The concentrations of bacteria upstream and downstream of the health–care respirators were measured with an Aerosizer, a relatively new aerodynamic size spectrometer, which was found to effectively and dynamically measure the bacterial concentration over the entire bacterial size range down to 0.5 μm in aerodynamic size. The results indicate that the spherical corn oil particles and the spherical *Streptococcus salivarius* bacteria have the same penetration efficiencies in the size range from 0.9 to 1.7 μm. Rod shaped bacteria penetrate less. The penetration difference between the spherical and rod–shaped bacteria depends on the aspect ratio of the bacteria. For an aspect ratio of 4, the penetration of these elongated bacteria is about half that of spherical ones. Thus, a respirator that collects 95% of rod–shaped microorganisms with an aspect ratio of 4 collects only about 90% of spherical microorganisms or test particles.

Publications

Myojo T, Willeke K, Chen CC: Fit Test for Filtering Facepieces: Search for a Low–Cost, Quantitative Method. Am Ind Hyg Assoc J 55(9):797–805 1994

Krishnan U, Willeke K, Juozaitis A, Lehtimäki, Szewczyk K: Development of a Dichotomous–Flow Quantitative Fit Test for Half–Mask and Full–Facepiece Respirators. Am Ind Hyg Assoc J 55(3):223–229 1994

Krishnan U, Willeke K, Juozaitis A, Myojo T, Talaska G, Shukla R: Variation in Quantitative Respirator Fit Factors due to Fluctuations in Leak Size during Fit Testing. Am Ind Hyg Assoc J 55(4):309–314 1994

Willeke K, Grinshpun S, Quian Y, Donnelly J, Juozaitis A, Ulevicius V: Physical and Biological Aerosol Penetration and Face–Seal Leak Characteristics of Industrial and Health–Care Respirators. J Aerosol Sci 25(1):S569–S570, 1994

Weber A, Willeke K, Marchioni R, Myojo T, McKay R, Donnelly J, Liebhaber F: Aerosol Penetration and Leakage Characteristics of Masks used in the Health Care Industry. Am Journal Infection Control 21(4):167–173, 1993

Chen CC, Lehtimaki M, Willeke K: Loading and Filtration Characteristics of Filtering Facepieces. Am Ind Hyg Assoc J 54(2):51–60, 1993

Chen CC, Willeke K: Aerosol Penetration Through Surgical Masks. AJIC 20(4):177–184, 1992

Willeke K, Chen CC, Myojo T, Weber A, Krishnan U, Juozaitis A, Marchioni R, Lehtimaki M: Filtration, Loading and Faceseal Leakage Characteristics of

Filtering Facepieces. J Aerosol Science 23:S749–S752, 1992

Adsorption of Vapor Mixtures onto Activated Carbon

Patrick N. Breysse, Ph.D.
Johns Hopkins University
School of Hygiene and Public Health
Department of Environmental Health Sciences
615 North Wolfe Street
Baltimore, Maryland 21205

Grant Number: *5 K01 OH00087-03*
Start & End Dates: *09/28/90 – 05/27/94*
Funding Level: *$0 ($162,000 Cum)*

Importance to Occupational Safety and Health

Complex industrial environments typically contain numerous organic vapors and a range of relative humidities. It is not possible to experimentally determine respirator breakthrough performance for every possible combination of vapor mixtures. A fundamental understanding of the physicochemical interaction of adsorption of vapor mixtures is needed in order to properly understand and model activated carbon bed behavior. Data generated by this proposal will be used to evaluate and modify existing respirator service–life models.

Objectives

The purpose of this investigation is to evaluate adsorption of organic vapor mixtures onto activated carbon. Experiments are designed to measure parameters associated with adsorption kinetics and equilibria. Binary vapor mixtures containing a variety of different polarities and functional groups at different humidities will be selected and tested.

Adsorption studies using silica gel are also to be conducted. Adsorption onto silica gel, a polar adsorbent, will help to determine the role of polar forces in adsorption and to evaluate the suitability of silica gel as an adsorbent.

Successful completion of this project will provide a more fundamental understanding of adsorption of complex organic vapor mixtures onto activated carbon and silica gel.

Methodology

Experimental data will be analyzed using parameters of the Dubinin Equilibrium Model and the Wheeler Kinetic Model. These parameters include equilibrium adsorption affinity coefficients and capacities and kinetic rate constants and capacities. Equilibrium and kinetic behavior of vapor mixtures will be evaluated using gas chromatography (GC). Mixed vapor analysis will be conducted using a GC equipped with flame–ionization and photo–ionization detectors in series. The photo–ionization detector (PID) will be used with two different ionization potential lamps, 8.4 and 9.6 eV. Vapor pairs are selected such that the PID will respond to only one of the vapors in the mixture.

Significant Findings

The first phase of this investigation involved the development of the GC/two–detector system. The photo–ionization detector (PID) was installed on the GC. Different ionization potentials were evaluated in order to provide sufficient analytical sensitivity. Vapor pairs to be used to evaluate component polarity effects have been selected and the adsorption system has been tested and calibrated.

Kinetic experiments using paired organic vapors onto activated carbon are complete. Experiments were designed to pair each of two test vapors, p–xylene and pyrrole, with polar and non–polar vapors (toluene and p–dichlorobenzene are non–polar and o–dichlorobenzene and p–fluorotoluene are polar). To account for any boiling point effects, each test vapor is also paired with vapors having a higher and a lower boiling point (the dichlorobenzene isomers have boiling points greater than p–xylene or pyrrole, while toluene and p–fluorotoluene have boiling points less than either test vapor). Comparison of the kinetic adsorption capacities of p–xylene and pyrrole for the different mixtures indicates that the adsorption space occupied by each vapor is reduced based on it's mole fraction in the mixture. The data do not indicate that there are any differences based on whether p–xylene and pyrrole are paired with polar or non–polar vapors. Furthermore the boiling point of the paired vapor does not seem to effect the kinetic adsorption capacity.

Collection of equilibrium adsorption data is 90% complete. Preliminary analysis indicates, similar to the kinetic experiments, that the overall adsorption

space is conserved when isotherms are determined for paired vapors.

Aerosol Penetration Behavior of Respirator Valves

Lisa M. Brosseau, Sc.D.
University of Minnesota
Box 807 UMHC
420 Delaware Street SE
Minneapolis, Minnesota 55455

Grant Number: *5 R03 OH02938-02*
Start & End Dates: *06/01/91 – 02/28/94*
Funding Level: *$0 ($31,198 Cum)*

Importance to Occupational Safety and Health

Properly fitted air purifying respirators must have functioning valves (exhalation and inhalation)in order to provide the protection expected. Inhalation valves open during inhalation and close on exhalation, thus ensuring that a]l expired air exits through the exhalation valve. The exhalation valve, which is the more important of the two in providing protection, closes during inhalation, thus ensuring that all inspired air passes through the filters before being breathed.

The adequate functioning of respirator valves is not often easy to evaluate. Respirators can be visually checked for malfunctioning valves; qualitative checks of their function are also possible. Neither of these methods is done often enough by respirator wearers, and neither guarantees adequate valve functioning. Only by quantitative measurement can the protection of a used respirator be determined, and this is rarely if ever done.

There is not, at present, any easy method by which valve replacement can be predicted. This research will lead to the development of an empirical model derived from experimental results which can be used to predict how often and when respirator valves must be replaced before they fail, given their particular use conditions. This model will be validated by comparison with measurements of used valve behavior.

Objectives

The objectives of this research include:

1. Evaluation of three respirator manufacturers' new exhalation and inhalation valves for particle size–related penetration as valves are stressed by a breathing cycle over an 8–hr period;
2. Evaluation of used valves for particle size–related penetration;
3. Comparison of predictions by an empirical model (developed from experimental data) to measurements of penetration made with used valves;
4. Evaluation of local companies' respirator maintenance practices, particularly as they relate to valve replacement.

Methodology

The experimental portion of this research will stress inhalation and exhalation valves using a breathing machine with humidified and heated exhalation air over an 8–hr period. Periodic measurements of aerosol penetration upstream and downstream of each valve type are made during the test period and recorded by computer, which also controls exhalation air conditions. Measurements of aerosol penetration will be made at several particle sizes, starting at 0.3 μm and extending to 1 μm. Two different work rates will be evaluated. The survey of respirator users has been completed by thirty local companies. Local companies have received new valves, which will used for a time equivalent to 8 hr before evaluation of particle size penetration in the laboratory. A model to describe particle–size related penetration for a given work rate over time will be developed. Model predictions will be compared with results of experiments with used valves.

Significant Findings

Of the 28 companies surveyed on respirator maintenance practices, 60% had workers wearing respirators on a daily basis for a range of aerosol and gas and vapor exposures. All but two of the companies had a formal, written respiratory protection program. In half of the companies the employee was responsible for inspecting the respirator on a daily basis prior to use, for maintaining the respirator as needed, and for replacing valves and filters or cartridges as needed.

In all but three of the companies the person responsible for maintenance received formal training in repair methods. During inspection and maintenance, almost all companies indicated that inspection included a visual check of the harness, face piece, valves, and filters or cartridges; respirators were stored in a bag when not in use. In 60% of the companies cleaning and sanitization were accomplished by wiping or manually washing the respirator. A majority of the companies indicated the service life of their respirators as being about three to four years. Almost all companies indicated that worker training included inspection, cleaning and sanitization, maintenance, storage, and negative and positive pressure tests. Most companies indicated that these items were demonstrated by a trainer, while only half of the companies show videos and have workers practice the items during training Sessions.

For the experiments of valve leakage, two of four conditions have been evaluated to date: high and low flow with a small diameter (0.31 μm) aerosol. While the data have not been completely analyzed, initial evaluation shows that, under high flow conditions, the smaller aerosol may experience penetration up to 20% through exhalation valves and up to 5% through inhalation valves. Under low flow conditions penetration is much less, as expected. For exhalation valves penetration averages about 0.02% and for inhalation valves the 0.31 μm particles experience about 0.005% penetration. Experiments are presently underway for low and high flow conditions with a larger particle size (0.84 μm).

☆ U.S. GOVERNMENT PRINTING OFFICE: 1995: 650-147/20005

Delivering on the Nation's promise:
Safety and health at work for all people
Through research and prevention

DHHS (NIOSH) Publication No. 95-112