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FOREWORD

The 1979 Symposium on Occupational Safety and Health was presented as the result of cooperation between the National Institute for Occupational Safety and Health (NIOSH) and the American Medical Association (AMA)

The Symposium, held at the NIOSH Educational Resource Center at the University of North Carolina, brought together persons well-known in the field of occupational safety and health. The presentations reflect important issues, research, and the current thinking of those in the field.

Publication of the proceedings makes this information available to thousands of physicians, nurses, industrial hygienists, safety professionals, and students who may not have been able to attend the 39th AMA Congress.

for Anthony Robbins, M.D.
Director, National Institute for
Occupational Safety and Health

PREFACE

This 1979 edition of the Occupational Safety and Health Symposia Proceedings is the fifth in a series beginning in 1975 with which this project officer has been associated. Throughout this period an excellent program of cooperation has prevailed between NIOSH and the officers and staff of the AMA Department of Environmental, Public and Occupational Health. The acclaim with which these proceedings have been received indicates their usefulness to the men and women in the field of occupational safety and health.

With the expansion in 1978 to the University of Arizona, ERC campus, in 1979 to the University of North Carolina, ERC campus, and in 1980 to the University of Utah, ERC campus, the program has continually extended the horizons of students in the field and it has proven to be a stimulus to those already involved on either a full- or part-time basis with occupational safety and health.

NIOSH is concerned with developing new and innovative approaches to improving the delivery of occupational safety and health services to the working men and women of America. This series has helped to accomplish this.

As always, suggestions for agenda items for future symposia are welcome, along with comments to improve the service of NIOSH to occupational safety and health providers and consumers.

Loren L. Hatch, Project Officer

ABSTRACT

This 39th AMA Congress once again endeavored to bring to the awareness of the medical community—the practicing physician, the teacher, the student and other allied health professionals—some of the occupational safety and health concerns of the day.

The meeting opened with addresses that expressed the attitudes and aspirations of both government and the medical profession.

Women in the work force and occupational cancer continue to draw attention; hence, these topics occupied a large share of the program.

Inasmuch as North Carolina is the home of a large number of small plants and industries, there were several papers that reflected the problems either inherent to or handled by such facilities. Of particular note are the discussions on urea-formaldehyde building materials and wood dust, both subjects which are now receiving overdue attention because of their recently discovered adverse health effects.

R. H. Wheater (AMA)
Principal Investigator
and Editor

ACKNOWLEDGEMENTS

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At the University of North Carolina, NIOSH Educational Resource Center, Chapel Hill, special thanks go to David A. Fraser, ScD, ERC Director, Mario Battigelli, MD, and Cynthia Houston, Occupational Health Nurse and others for assistance with the program, and faculty. The smooth operation of the meeting itself was due in no small part to Mss. Rebecca Ulshen and Jan Nordseth. The University Administration is acknowledged for its assistance with housing and for opening their facilities for the Congress. Also to be commended is David S. Thelen, MBA, and Norbert J. Berberich, PhD, who as the NIOSH Training Grant Coordinators were instrumental in arranging for the ERC site location.

The following NIOSH personnel are especially appreciated for their help in preparing these proceedings for publication: Lynne Kallas and Madonna Allen prepared portions of the manuscript and processed the document. Russell Hinton was printing officer, and principal reviewer was Austin Henschel, PhD.

KEYNOTE ADDRESS:
IGNORANCE IS BLISS--AMERICAN MEDICINE AND OCCUPATIONAL HEALTH

Anthony A. Robbins, MD, MPH

I've been in NIOSH slightly under a year now and I've learned a fair bit about being in the federal bureaucracy; yet, it's always nice to get out in the real world. What I've learned in this year leads me to believe that we have reason to be optimistic about where we are going in occupational health.

Over the last two days I have been talking with physicians interested in occupational health from somewhat different worlds. Earlier in the week, I was at the Center for Disease Control in Atlanta, where NIOSH is putting on a training course in occupational medicine for physicians in the Epidemic Intelligence Service. It's a course for epidemiologists with varying degrees of experience who will be conducting field investigations into occupational health problems. Having 50 physicians in one room, all interested in careers in occupational health, was probably the most exciting thing that has happened to me since coming to NIOSH. Occupational health has the greatest opportunity for doing good over the next fifty years, but we have nowhere near the manpower necessary to deal with the size of the problem. The second meeting I had was with the directors of the Educational Resource Centers--twelve universities around the country that are funded by NIOSH to coordinate the training of physicians, nurses, industrial hygienists, safety specialists and a variety of other specialists in occupational health.

No one can read the newspapers or watch television without being impressed by the rapidly rising interest in occupational diseases. The interest grows every day. I don't think the anti-regulatory climate in this country should be confused with a lack of concern on the part of workers and the general public about occupational health problems. In my experience at running state public health programs, I had no end of trouble assuring quality in nursing homes by regulating how to make a bed or how many nurses should be on each floor. Regulation is not always successful in achieving the desired goal. Nevertheless, I see the concern about occupational health growing, and workers and the general public are becoming increasingly well-informed and militant about occupational health problems.

Unfortunately, one of the difficulties I often encounter when I get out of Washington--or even in Washington for that matter--is that the Institute is not really well-known. We are clearly the lesser known partner of the Occupational Safety and Health Act. NIOSH was created to do the research, recommend standards and train manpower. We conduct field investigations and we share with OSHA the right to enter any workplace covered by the OSHAct to investigate the causes of occupational health problems. Because of the current anti-regulatory climate even our right-of-entry is being challenged. In addition to epidemiology, our program includes laboratory research in toxicology, and we are part of the National Toxicology Program in the Department of Health, Education and Welfare. We also are responsible for producing the needed

manpower in the occupational health field.

One thing that we are doing more than ever before is getting our researchers out in the field to look at real problems. In the past we have done about 150 health hazard evaluations each year. We respond to requests from workers, from industry and from other federal agencies. This work also is critically important for research in occupational health, because it generates hypotheses that may be tested more extensively by laboratory research. For example, a union may call and tell us that there is a large number of brain tumors in a group of plants in one community. They ask us to see if that number is excessive and, if so, to find the cause. As you can imagine, that can be a fairly extensive effort. We look at a large number of personnel, medical and death records, trying to figure out how many workers are involved. If there appears to be an occupational health problem, we do the industrial hygiene and the epidemiology to determine the cause. We're usually faced with the complication that most occupational diseases have a long latency period.

Another of our responsibilities is to make recommendations for setting standards to the Occupational Safety and Health Administration. We have found that our recommendations--in the form of criteria documents--are used much more broadly than by regulatory agencies alone. The recommendations usually become standards of good practice long before they are accepted by the regulatory process and become mandatory standards.

Perhaps the single biggest problem in occupational health is the ignorance of both employers and workers about the nature of exposures. A few years ago during a survey of 5,000 workplaces, 70% of the employers were unaware of what was in the various products in their plants. There is little question that the most rapid way, and in some sense the least regulatory way, to bring about a change in this situation is to inform workers and employers about what they are working with. Such a program would include information about certain chemical substances, as well as what can be done to assure a safe level of exposure.

A couple of years ago we recommended that the use of silica for sand blasting be stopped. Silicosis is among the oldest known occupational diseases and is still a problem. Just a few weeks ago, we learned about two plants in southern Illinois that produce silica flour, a powder-like compound. Workers who had been on the job less than 30 months were developing progressive massive silicosis. The workers thought they were dealing with harmless amorphous silica; the material in fact was 98-99% crystalline quartz.

We have also been working on the problem of benzidine dyes. We have to decide whether each of about 100 dyes in the benzidine dye family has to be tested for carcinogenicity or whether we can suggest substitutes on the basis of what we know about a few of the dyes. If we recommend that substitutes be used, we will also recommend that adequate testing of the substitutes must go on.

We have been working with companies and unions in the aluminum industry to protect workers from exposures that occur in the aluminum reduction process. Both the French and Japanese believe that they have adequately enclosed the process and have reduced worker exposure to virtually zero. Thus, we may be able to suggest changes in control technology rather than having to deal with the more complex medical and epidemiological aspects.

I am trying to give a flavor of what occupational health is about. It starts with careful attention to what medical concerns the worker is having. But the solution will come primarily through the application of engineering controls. Any other approach is a mistake. We try to document the best control technology available and demonstrate it as a model for all of the other companies in the field. Once adequate controls are available, they can be required by regulation.

Finally, we have a challenge these days to produce an adequate number of occupational health professionals. There is a particularly critical need for safety specialists with a real academic bent. One of the roadblocks in training occupational health manpower right now comes from the Office of Management and Budget; they question why federal tax dollars should be used to train occupational health professionals, especially when the majority of these professionals are hired by companies that could probably provide the training. We don't have a simple answer. We are trying to arrange with the National Health Service Corps for some sites where occupational health services are lacking. I am very optimistic that this will happen. But what do we do about spending taxpayer's money to train occupational physicians if it is clear that they will go into public service employment? I don't have an answer. There is no question in my mind that this will be a major area of discussion over the next several years. Can we create an environment where physicians and industrial hygienists can work in programs that would not otherwise have occupational health professionals without government help? I hope the answer is, yes. I hope there is a future for these people on labor-management health and safety committees. I hope there is a future in the voluntary consultation programs that OSHA is funding to help business. If we are going to continue to provide occupational health education, we are going to have to develop pay-back programs.

Let me next speculate about the responsibilities or challenges of American medicine in occupational health. It's been a long time since I was a practitioner; although, some might say that being a health commissioner of Vermont is as close to being a general practitioner as you can be in this country. I was trained as an internist and I have fond memories of practicing medicine before I became a bureaucrat. It has always been difficult to arouse practitioners to public health, and particularly to occupational health. First of all, I suggest that organized medicine arouse those sleeping medical schools that have generally ignored occupational health. I say this with more caution now than I would have yesterday, because my colleagues from the ERC's have reported to me a number of optimistic changes. Nevertheless, the average time that medical students spend on occupational health in the US is four hours in four years. This is not an impressive number, except in the negative sense. I would be kidding you to say that I want to teach occupational health to all practitioners in this country. But I do think physicians should have their index of suspicion for occupational health problems raised. I think that medical students ought to know how to take a good occupational history. With a few exceptions, occupational medicine is not a totally different group of diseases and it probably should not be a primary care specialty. This is strictly my own personal view. Most of what you can accomplish in occupational health is to detect the problems at the workplace and then get industry to institute preventive measures. What the doctor can do more than anything else, it seems to me, is to believe that there is such a thing as occupational disease and to learn more about it. We are not going to turn every physician in this country into an occupational health physician. If we can just get every physician to believe in occupational disease and learn something about it, then perhaps workers won't continue to tell me that the doctor is the last person they go to find out whether they might have an occupational health problem.

I should like to see if the resources of the occupational medical profession can be used

to deal with public health problems in a community. This has worked in other public health areas. In the Norfolk area, there are thousands of current and former shipyard employees, many with occupational health problems. I have suggested that there is a responsibility for physicians and public health officials to develop a higher level of understanding among physicians in the community. In communities where there may be a near epidemic of occupational disease, it is important to organize the medical community to do the screening and continuing surveillance, and for them to be able to develop the resources necessary for long-term management of patients who may have been exposed to occupational health hazards of the past. I really think that working with communities on occupational health problems will be very exciting and will be the test of how effectively we can get into the medical practitioner community.

THE PRIVATE PRACTITIONER AND OCCUPATIONAL MEDICINE

Hoyt D. Gardner, MD

It's no secret to anyone in this audience that the relationship between the private practitioner and occupational medicine has not been an especially close one. Rather, that relationship has been something on the order of first cousins who occasionally meet and then go their separate ways. This is not surprising because physicians in private practice—perhaps even more so than their patients--have been transfixed by the scientific and technological wonders of modern medicine. Thus, to some extent limited attention has been paid to external factors in disease causation, including occupational factors.

But strong and growing pressures for change are at work. To begin with, the costs of modern medicine have reached the point that private practice is not all that "private" anymore. Recent opinion polls, for example, demonstrate that public enchantment over the escalating quality of health care is now matched by public disenchantment over the escalating cost of that care. Hence, the socio-economic and political dimensions of health care have been given equal billing with its clinical dimensions. And there have arisen strong pressures for change, including changes in the relationship between the private practitioner and occupational medicine.

The need to moderate health-care costs has led to a re-emphasis of alternatives such as the prevention of disease or injury. This has led to renewed efforts to eliminate the environmental vectors of disease or injury, including those found in the workplace. Thus, occupational medicine has assumed growing importance not only as a specialty in itself, but also in terms of its import to physicians in private practice—or more specifically, to the health of their patients.

There are certain other pressures that are almost sure to make this relationship even closer as time goes by. Not the least among these is regulatory pressure. Certainly the activities of federal agencies such as the EPA and OSHA, not to mention the FDA and the FTC or the Food Safety and Quality Service of the USDA, serve to bring us closer together both as a profession and in our respective practices. I might add that American industry, and businesses large and small, also have been under intense public scrutiny. While those of us in the private sector may often feel like circling our wagons 'round for mutual protection, regulatory pressure does serve as a compelling reason to take mutual action in the resolution of problems common to us and of concern to society.

Less obvious, perhaps, but far more important in the long run, are at least three additional elements that should make consultation between private medicine and occupational medicine more common. First, ample historical precedent exists. Public health measures in general, especially prevention measures, have always played an important role in medicine, including American medicine.

If you'll recall, when the AMA was founded in 1847, it pledged itself to two primary

goals: to promote the art and the science of medicine, and the betterment of public health. Right from the beginning, the AMA devoted considerable time and attention to public health measures, including measures to cope with health hazards posed by the environment.

Among the first committees appointed by the AMA were the Committee on Practical Medicine--to assess the general state of health in the United States—and a Committee on Hygiene whose concerns included the environmental vectors of disease. Now as you can appreciate, very heavy initial emphasis was placed on the collection of statistics including vital statistics essential to the epidemiological approach to disease causation and treatment.

Eventually, these early efforts led to many of the beneficial public health improvements implemented later in the 1800's, including the development of sanitary sewer systems and pure water supplies in towns and cities across the country, and to the establishment of state boards of health.

At the turn of the century, Dr. Walter Reed and his US Army medical team discovered that the Aedes aegypti mosquito was the vector for yellow fever, a discovery that Dr. William Gorgas very shortly put to good use in the construction of the Panama Canal. Meanwhile, the United States was caught up in the Industrial Revolution and the population shift from farm to city. This revolution brought a welcome prosperity to the nation and allowed more Americans to secure the necessities of life, such as proper food and shelter, and an improved state of health.

But industrialization and urbanization also brought the beginnings of those environmental problems that trouble us today. As early as 1895, the Journal of the AMA editorially condemned the pollution of lakes and rivers. By 1900, problems arising from the occupational environment had become evident. Proposals for improvements in occupational health and safety and for the enactment of child labor laws gained added attention.

Problems stemming from urbanization also were evident. Thus, in 1903 an editorial in JAMA attributed a rising suicide rate primarily to "the great increase of urban population...and the increasing stress of modern life." During the early 1900's, automobiles also began to roll off the assembly lines in Detroit, which led the AMA, in 1923, to cite air pollution from automobile exhaust gases as a potential health hazard. The young and vigorous machine-age nation also produced considerable clank and clatter. As an article in our Journal in 1938 observed: "...the multiple and insidious ill effects of noise constitute an inadequately recognized, baneful influence on (the) lives of millions of persons throughout the country."

I could go on and cite numerous other examples of public health improvements that had their beginnings in the first half of this century and which were supported by our profession: the enactment of federal pure food and drug laws and the creation of the forerunner of the FDA, expansion of various disease immunization programs, the development of iodized salt, and the enrichment of food with vitamins and minerals. In any event, there is most definitely solid precedence for physicians in private practice to be concerned with the prevention, as well as the diagnosis and treatment, of health problems. Parenthetically, I wish to say that scientific and technological progress has enhanced our clinical and preventive capabilities. If clinical medicine has been literally revolutionized since the end of World War II, so has preventive medicine. Any number of new preventive capabilities could be cited, ranging from antibiotics, other drugs and

vaccines, to our burgeoning knowledge of genetic factors in disease. And, of course, occupational medicine has taken enormous strides in improving workers safety and injury control.

There are, in fact, strong bonds between occupational medicine and the private practitioner in terms of a dedication to clinical advancement; take, for instance, Drs. Creech and Johnson and their linkage of polyvinyl chloride with angiosarcoma of the liver. All such advances obviously have important implications for medicine in general, for private practitioners and for the health and well-being of the public at large. Which explains why the AMA has been sponsoring these annual Congress on Occupational Health since 1939. Our Department of Environmental, Public and Occupational Health also has helped focus public attention on many other diverse issues, such as the population problem, energy supplies and solid waste management.

I should add that we have supported the major pieces of legislation to protect our environment from air, water and noise pollution. We have, in fact, emphasized that since our environment is a national resource, the federal government has an important role to play in protecting it.

At the same time, however, the AMA has publicly objected to irrational government initiatives. For example, in a statement to the Interagency Regulatory Liaison Group in Washington, we urged that the IRLG be more scientific in its "Scientific Bases for Identification of Potential Carcinogens and Estimation of Risks", and recommended that they appoint a "blue ribbon" panel of leading physicians and other scientists to design and oversee this country's scientific inquiries into the myriad unknowns of the human carcinogenesis problem. We further urged the Group to require more wide-ranging professional peer review and opportunity for comment on the scientific integrity and appropriateness of studies having major regulatory significance.

In any event, I think you'll agree that my remarks demonstrate that there are economic, regulatory, historical and clinical reasons for private practitioners to stress prevention, as well as treatment, of disease. To do so requires the compilation of a complete medical history of the patient, including consultation with occupational medical professionals when appropriate.

There is one additional factor that serves to bring us together. I'm referring to the new and stronger ties between the health care system and business, industry and corporate management. These new ties have come about primarily through two major private sector initiatives to cope with the health-care cost problem--the Voluntary Effort and the deliberations, and subsequent recommendations, of the National Commission on the Cost of Medical Care. As you may recall, the Voluntary Effort was established in 1977 by a coalition of groups, including the AMA and the two largest hospital associations, as well as health insurers, consumers, government, and business and industry. The VE was instrumental in reducing the growth rate of total hospital expenses from 15.6% in 1977 to 12.8% in 1978 and effecting an estimated savings of $1.5 billion. This year, we hope to hold the growth rate to 11.6%, for an estimated savings of $3 billion.

The lion's share of credit for reducing health care costs should go to state and local VE coalitions all across the country. As one indicator of state and local commitment, consider the results of a questionnaire sent to state and local medical societies by the AMA. The questionnaire revealed that: 97% of our state societies are active in the VE; 70% have an organized physician committee for participation in the VE; while a majority of county medical societies also responded affirmatively to both questions.

Local physicians have also responded positively to an AMA plea of June 1978 by Dr. Tom Nesbitt, to bring the annual rate of increase in their own professional fees down to the level of the "all items" component of the Consumer Price Index. For the 12-month period ending in August 1979, the rate of increase in physicians' fees was just 9.6% or 2.2% below the 11.8% increase for "all items." Thus, practicing physicians are fulfilling their cost-containment responsibilities, in their own offices as well as in the hospital.

Furthermore, the AMA is committed to the proposition that the VE must be just one part of an integrated, long-range program of cost containment. This full-scale, long term approach to the cost problem is keyed to the recommendations of the AMA's National Commission on the Cost of Medical Care, which, though sponsored by the AMA, was an independent entity.

Like VE, the Commission also was widely representative of the major institutions in our society and included insurers, consumers, organized labor, government, business and industry. The Commission's 48 major recommendations, most of which have been approved by the AMA's House of Delegates, would instill permanent changes in the health-care economy; such as: greater marketplace choice in the costs and benefits of health-care coverage offered employees and other consumers; consumer sharing in the cost of insured care, with appropriate assistance for the needs of low-income families; fair-market competition between prepaid group practices and other providers and insurance systems; and adjustment of private and government insurance benefit packages "...to provide balanced coverage of alternative services and settings in the provision of health care."

The AMA, then, believes that a concerted, continuing campaign to voluntarily contain health care costs is an absolute imperative, as is the coalition of private sector institutions to shape and sustain this campaign—a coalition that includes business and industry. And let me tell you here and now that this is not just window dressing.

Over the past two years, an AMA-instigated program has taken our officers into the executive suites of more than 75 of the major US corporations to get management views on health care problems—including costs—and to familiarize business leaders with the recommendations of the National Cost Commission. And just three weeks ago, AMA and business leaders met at AMA headquarters to discuss specific plans for an action program through which the business community and local medical societies can mutually resolve some of the problems that exist. I should add that these problems are not related to cost alone, but involve issues such as access to care, employee time loss and employee rehabilitation.

In any case, it should be abundantly clear that these new avenues of communication and cooperation can be used to reach other mutual goals, including those of occupational medicine. As a matter of fact, the Commission's recommendations also stress the crucial value of preventive measures, including the early detection and resolution of developing health programs ,and the necessity to motivate the public to adopt more healthful lifestyles.

In closing, I think you must agree that the relationship between the private practitioners and occupational medicine will become closer and more constructive as time goes by. Not only will the new relationship be in our own best interests, but it will also be in the best interests of our patients and our society as well.

NIOSH TODAY

Marshall E. LaNier, MS

This is the first time in three years that I have participated actively in this program. Each time, knowing that the audience is made up largely of physicians, I wonder what I can discuss. Today I have selected two items, both of which are connected with information that I think will be of interest.

REGISTRY OF TOXIC EFFECTS OF CHEMICAL SUBSTANCES

Section 26 of the OSHAct states that NIOSH shall develop a toxic substance list and report on this to Congress. Some three or four years ago, we changed the name of the list to the Registry of Toxic Effects of Chemical Substances (RTECS). At present, there are some 38,000 substances on this list, including many reported in studies on carcinogenicity, teratogenicity and mutagenicity of various substances. We have continually tried to add some feature to the list each year to make it more valuable to researchers. During the past year we have added primary skin and eye irritation data done by the Draize method, as well as in vitro mutagenicity data from the Ames test. The Registry tracks fairly closely with the bioassay program of the National Cancer Institute in all testing phases of carcinogenicity; reports are filed whether the results be positive or negative. By and large, the Registry does not contain a lot of negative data. The International Agency for Research on Cancer monographs and their conclusions are also included. Roughly 3700 reviews are cited, with all of the citations to the original literature from which the data were taken. Generally, the originals are available in most university libraries; should there be a particular citation that is difficult to locate, you may contact us and we will provide it to you.

One feature of the Registry that users have found convenient is the cross-referencing of chemical names—there are roughly 95,000 cross-reference entries. Thus, a chemical can be found under its Chemical Abstract's nomenclature as well as by any of a number of common synonyms that are used in industry to identify the substance.

We have attempted to make the Registry available in as many formats as possible to foster its widest dissemination. For those who need the most up-to-date information, there is a microfilm update which is automatically mailed out to all Government Printing Office (GPO) subscribers of the paper copy for a fee of $14/year. Two years ago, we put the computerized file on-line at the National Library of Medicine (NLM). I understand it was the second most used data base of the NLM during the last quarter; this makes us feel very good about the total system. Also, the National Institutes of Health, EPA, and Chemical Information System have RTECS on-line. I certainly hope that we can continue to make it one of the largest sources of toxic substance information in the world.

NIOSHTIC

Another system called NIOSHTIC (National Institute for Occupational Safety and

Health Technical Information Center) that I think will be of benefit to physicians is our bibliographic data base. Among the approximately 70,000 references are some of the health hazard evaluation reports (mentioned earlier by Dr. Robbins) that could be useful in specific businesses. This data base is unique, in that it is retrospective, going back to the early 1900's as well as being specific to occupational health. Thus, many medical reports of occupational disease, case histories, toxicological findings, methods of analysis, and other reports are indexed and are available to the interested researcher. The system is designed to allow free text search with a reasonably controllable vocabulary so that a limited number of articles germane to the subject desired can be accessed. Of interest to the occupational physician, are the extensive literature references contained in NIOSHTIC relative to specific industries.

Input from the International Labor Office (Geneva) is included in NIOSHTIC system. NIOSHTIC also contains citations from the CIS of the International Labor Organization, thus giving worldwide scope to the reports of occupational effects of chemicals, heat stress, noise, and other physical and chemical hazards which affect health in the workplace. At present, NIOSHTIC is not available to the public as is RTECS, but efforts are underway to accomplish this. Searches of NIOSHTIC are available through the Clearinghouse for Occupational Safety and Health Information, another service that my Division offers to the physician.

The Clearinghouse accepts questions of an occupational health nature from anyone and attempts to provide an answer in sufficient detail relative to meet the needs of the requestor. We encourage your questions, both specific and general. We will attempt to provide appropriate answers, references and information to facilitate your work. The Clearinghouse can be reached by calling: 513/684-8326 or by writing:

Clearinghouse for Occupational Safety and
Health Information
4676 Columbia Parkway
Cincinnati, Ohio 45226

The files I have described contain toxicity data and occupational health bibliographic references. This includes NIOSH Sampling and Analytical Procedures for Toxic Chemicals found in the workplace. Most of all of these methods are designed for personal air monitoring to determine exposure of individual workers. A research service through the Clearinghouse will not answer every question you might pose. We realize that much is yet to be discovered relative to the causes of occupational diseases and man's interaction with chemicals. NIOSH maintains constant contact with research centers in universities, industry, private groups and other governmental agencies in an effort to keep abreast of the continuing development of knowledge relative to occupational health and well-being. In addition to attempting to provide a sophisticated and well-founded information service to help you in your information needs, we solicit any information you may develop which could be of general value to the occupational health community. Any information that could be input to our data bases would be a benefit to all.

WOMEN IN TODAY'S LABOR FORCE

Physical Fitness and Safety—What Are the Results for Women?

Mary L. Tenopyr, PhD

As most of you are aware, attempts to predict safety behavior on the basis of physical characteristics have had a relatively dismal history. There are, however, some exceptions. For example, Kephart and Tiffen found vision related to accident frequency. Other investigators have found relationships between age and accidents and between perceptual and motor factors and accidents. One reason for the failure of physical characteristics to be predictive is merely the way people were selected for jobs before the advent of equal employment opportunity policies. In the old days, no one would think of putting a 5'2" person weighing 100 pounds on a heavy equipment operator's job. Through formal or informal procedures, we have always hired the hulk. Anyone familiar with statistics knows that statistically meaningful predictions are not possible if the range of values of the predictor is curtailed. In other words, we screened out everybody who was not likely to be physically fit; there was no range in physical characteristics remaining in the people selected for the job. Besides hiring practices, termination procedures contributed to the limited range of physical variability. If a white male could not "cut it" in training or in the early stages of work on a physically demanding job, he was out. With equal employment opportunity and restrictive union agreements, we are less prone to terminate people.

When AT&T signed its well-known consent decree with the Government in 1973, the company had few females or persons of small stature in physically demanding jobs. As would be expected, equipment, work procedures and training had been designed with the person of large stature in mind. For example, most of our telephone poles were not stepped—ie, the poles did not have iron bars on which to climb. Or if they were stepped, the steps were spaced for a large person. Our vans were designed such that persons of large stature were required to reach and remove the work equipment. Needless to say, the cost of modifying all the telephone poles and the largest private fleet of motor vehicles in the US would be staggering. The original consent decree goal for placement in outside craft jobs—involving pole climbing, ladder handling and van driving—was 19% for females. Few changes were made in equipment, personal gear, training and work procedures as we started placing women in these outside craft jobs . Not surprisingly, in the first two years that the consent decree was in effect: more women than men reported difficult physical demands of training (28% for women vs 4% for men; 33% of the women were more likely to be very tired at the end of the day vs 10% for men). The dropout rate in training was 24% for women as compared to 2% for men; after six months, 43% of the women had left outside craft work whereas only 8% of the males had left--in other words, we were losing almost half of the women within six months. Most significantly, 51% of the women reported falls while they were climbing or working on poles vs 32% for men. These results are dramatically supported by Bell System accident statistics reports for 1977, which showed a rate of 7.0 pole climbing accidents for 100 female outside craft employees as opposed to 0.77 for 100 male outside craft employees. That's about a 10-1 ratio.

Our first study, to determine whether the use of physical tests would contribute to safe behavior in pole climbing, was initiated in 1974. Results of the studies are reported by Riley, RR, Zedek S and Tenopyr MN in the June issue of The Journal of Applied Psychology. In conducting the study, we were--as we are now--faced with a society that generally opposed tests and where there were severe restrictions as a result of government regulation and court decisions. In fact, government regulation of testing (not only psychological but also medical) practically dictates every research and development procedure that is used for employee selection in order that the procedure not have an adverse impact on any race, ethnic or sex group. Thus, if one group fails at a higher rate than another group, that procedure must be shown to be job-related. Obviously, physical tests are likely to screen out more women than men, so we had to prove that our physical tests were job-related or "valid."

There are two feasible methods for showing the validity of physical tests. The first is called "content validation." Here, on the basis of thorough job analyses, tests are developed on the basis of job demand. Tests are termed "content valid" if they can be shown to be a representative sample of the actual job tasks. For example, carrying a dummy down a ladder is a content valid test for firemen. For our purposes, we did not think that content validation was the most appropriate strategy. First, physical tests based on job analysis have not fared well in the courts--physical tests used in police and fire departments are under heavy fire. Secondly, there are real difficulties in simulating pole climbing work without risking serious injuries in the company medical office or testing office. Thus we chose a strategy that is technically known as "predictive criterion-related validity." The test is given during the employment process--the results cannot be used to select workers; employees are followed after they are on the job, using job training or job performance results as criteria. The statistical relationship between test results and criteria are then determined.

There are some obvious disadvantages to the predictive method; in particular, such studies require considerable time. When safety is involved, there is a real ethical dilemma about whether to follow the government regulations to-the-letter to prevent charges of discrimination, or to use shortcut methods in the hope of preventing an accident during the course of the study. With considerable misgiving, we chose the long predictive study. We concluded that discrimination charges might prevent us from using any quick test, and more accidents might occur in the long run.

The first phase was a job analysis conducted at the Pacific Telephone and Telegraph Company in July 1974. This analysis had two purposes: 1) to identify the critical tasks in telephone outside craft positions so that we could develop criteria closely related to job tasks, and 2) to aid in selecting the tests that would be tried out in the study, thereby limiting the range of alternate tests we would have to examine.

Government regulations, incidentally, require not only that the tests are job-related, but also that all suitable alternative tests or other selection procedures are studied. The jobs we chose for study were: installer repair technician, cable splicing technician and outside craft technician (formerly linemen). The criteria measures were the trainers' assessments of the safety of the performance of six training tasks: pole testing, throwing a rope around the pole and pulling to see if the rope will hold one's weight; climbing stepped poles; placing a 28 ft ladder on strand-one running between telephone poles; placing a 28 ft ladder on a building; climbing unstepped poles with a safety belt; and climbing unstepped poles and removing a drop wire. These tasks were common to all jobs and were found in the job analysis to be highly important for all three jobs. We used the sum of the ratings on the six tasks as one criterion and tenure

as the second criterion. The test procedures on the basis of job analysis were: grip strength (using a dynamometer); dynamic trunk strength (the number of situps achieved in 30 sec with a 10 lb weight held behind the head); reaction time (average response in milliseconds to one of three visual stimuli); dynamic arm strength (number of revolutions per 60 sec by hand pedaling a bicycle ergometer--resistance on the ergometer was set at 3 Kg); gross body equilibrium-balance (the total time in seconds of balancing on one foot on a 3/4" balance beam); static strength (average force over three trials of pulling a cable across the chest); stamina (total time for stepping up and down on a high bench, timed to a metronome set at 0.5 beats per sec); the Harvard Step Index (a function of total time achieved and recovery heart rate); extent flexibility (a trunk flexibility test); and body fat (measured by a typical skin fold). In addition, we got resting heart rates, weight, arm span and arm reach. Our sample consisted of 83 males and 45 females—including 89 whites, 21 hispanic, 5 blacks, 8 orientals and 1 "other." The two most valid measures for predicting safety of performance were the dynamic arm strength and reaction time; dynamic arm strength was also the best predictor of tenure. Through some detailed procedures, we found that two tests in combination—dynamic arm strength and reaction time—were equally valid for both males and females. This roughly means that both males and females use the same abilities to do the job. We also found that the tests were fair for both sexes; ie, low scorers of either sex tended to be poor performers and high scorers of either sex tended to be good, safe job performers. We implemented this two-test data in Pacific Telephone and proceeded on a second study.

While the Pacific study was being conducted, our training people were attempting to develop a self-paced climbing and ladder handling course for the benefit of small statured workers. This course was divided into six parts: ladder handling, introduction to pole climbing, climbing fundamentals, basic climbing skills, development of climbing skills and avoidance of climbing hazards. Each trainee had to pass a mastery test before proceeding. Since unlimited practice was allowed in each training phase, the time to complete training—varying from several days to several weeks—was the most appropriate measure of trainability. Other criteria were dropouts for physical reasons, field observations (after completion of training and four weeks later) and finally accidents in pole climbing. Accident data were collected for six months in both the second sample and the Pacific study. The second study—conducted in Dallas, Louisville, Portland, San Antonio, San Jose and Seattle—consisted of 78 females and 132 males (including 35 blacks, 18 Spanish and 157 non-minority employees). The results indicated that males outperformed females on all of the physical measures except the extent flexibility test; they also outperformed females on all four criterion measures.

The typical validity coefficient or coefficient of correlation between a test and an industrial criterion is usually about 0.30 for an aptitude test, but we predicted time to complete training with the validity of 0.46. We predicted training dropout with a validity of 0.38; fear of review errors with a -0.36. We cross-validated our results applying them to our data from the first study and predicted that the criteria in that study with a 0.31, turnover 0.33 and accidents for the total sample -0.15. The correlation with accidents is modest but statistically significant. It should be noted, however, that there are several factors that limit the size of the correlation coefficient, especially the unreliability of accident behavior. It is well known that unreliability of a criterion reduces its predictability. Also, since the tests correlate with dropout in training and turnover, it is likely that many of those most apt to have accidents were simply not on the job.

The three-test battery was put into effect in the Bell System in mid-1978.

Approximately 95% of the males and 50% of the female job candidates passed. We could have set a relatively high passing score, selected the top 10 or 20%, and perhaps done a better job of predicting safety behavior in pole climbing. For "affirmative action" purposes, however, we set a relatively low passing score and passed 95% of the men and 50% of the women.

Although the results of the study clearly indicate that physical tests can be predictive of safe behavior, they highlight many needs. We must know much more about various physical abilities and their corollaries to job performance. Unless we have a better understanding of these abilities, we will have to go through elaborate and time-consuming processes to determine which abilities are necessary for a given job. Furthermore, we need a multi-disciplinary approach to the problems affecting safe job behavior. In particular, we should include psychologists with the safety engineers, human factor specialists and physicians in the selection process.

WOMEN IN TODAY'S LABOR FORCE

A Woman's View of Women at Work

Nancy Milio, PhD

Are women to be liberated, only to take on the poorer health common among men? By the turn of the next century, the relative health of women is projected to decline as they increasingly enter the world of paid work and their lives take on some of the advantages and the problems that traditionally have belonged to men. Women's mortality rates from heart and respiratory diseases, for example, are expected to be higher than in the mid-1970's, while the rates for men will be lower. They will die more often from liver cirrhosis at a pace almost equal to that of men. And they will not experience improvements from vascular and digestive conditions as much as men (1). Whether or not these shifts occur will be due in part to those who have professional and institutional responsibility for occupational health. For women more than ever will play out their lives in occupational arenas.

More than half of all women age 16 or more were in the labor force by 1978. Almost 54% of them were married and living with their husbands; one in five of those couples had children under age 6. The rest of the female work force was about equally divided among divorced, separated or widowed, and single. The women in these nontraditional households formed part of that growing share—40%--of adult Americans who now either live alone or have experienced divorce; this compares with 25% in 1972 (2). Furthermore, better than one in ten women workers are heads of families, two-thirds of them have children under 18 years of age.

In short, well over half of the working women have either shared or sole economic responsibility for themselves and younger dependents as well, the role traditionally that has been held by men. Taken together, these changes in American households are bringing shifts in how much and what kinds of paid work women do, as well as what and how much they can buy.

The patterns developed in recent years in women's personal consumption behavior are well known. For example, about a third of all women now smoke; and among those who are separated and divorced, and those who are employed—especially managers, administrators and blue collar workers—up to 55% are smokers. These statistics parallel those of men (3). More than one in four women are problem or potential problem drinkers (4). The average women weighs as much as 20% above her ideal weight and consumes about 400 calories a day more than she needs (5). While she gets about as much regular exercise as man, she engages less in sports activities (6). These "signs of affluence" are health risks which women, as well as men (though in different degrees), carry with them into the occupational setting.

Women, however, bring with them health risks imposed by low income and poverty more than do men. About 30% are individuals or heads of household living in poverty; their diets are 20-30% deficient in calories and almost 50% are deficient in iron, according to

the Health and Nutrition Survey (7). These women are not only particularly vulnerable to economic inflation and recession, to price rises and poor job opportunities, they are also among the first to experience adverse health consequences--more so, if they are pregnant. The unemployment rate is higher for women than for men, especially if they are black or family heads. The majority are in the low paying occupations—ie, clerical and services work—and earn overall no more that 60% of a man's earnings.

When given the opportunities for comparable jobs, women face the same work environment risks as men: asbestos, toxic chemicals, coal, noise, heavy workloads and rotating workshifts. From 1-2 in 10 are now in hazardous job categories.

Whatever the strains at the job, the constraints on women off-the-job are greater than those of men. Working women are less likely to have a spouse or partner to help care for their children. Even when spouses are present, employed women spend more time each week in unpaid work. Overall, they are left with about six fewer hours of free-time per week for recreation or other leisure activities (8).

The health risks of women at work then are not merely the hazards of the job, but include those risks that are part of what it now means to be an affluent American; for example, overeating, drinking and smoking, and lack of vigorous physical activity. They also include low income, undernutrition and sub-standard living conditions. While women have an increasing economic responsibility for themselves and their families, they are having to assume that responsibility with fewer chances to get and hold a well-paying job and at a higher cost in time to themselves.

It is not surprising that such women tend to overeat, drink and smoke to excess, and have elevated blood pressure and serum cholesterol or other forms of chronic illness (9). This pattern is especially true among women in traditionally "male" occupations or with those who attempt a career and run a household (10).

The final dimension in this composite of health concerns for working women relates to their role in human reproduction. Not only is the state of the women's health important, but the health and welfare of the unborn—a part of about 9% of the female work force—must be considered. Yet in spite of additional types of risks, women are denied the means to deal with them more often than not; for example, maternity benefits under employee health plans provide hospital and medical care and disability payments comparable to nonmaternity health conditions for less than 40% of the covered workers.

This overall picture suggests that the task of protecting and improving the health of women workers calls for programs and policies that can help compensate for their health risks. In the most immediate sense, it means that health practitioners teach and reinforce healthful habits and safety practices, refer persons to community resources for child or prenatal care or food stamp programs, and help women understand their rights and entitlements.

More importantly, the health professional should work with management, unions and other groups to initiate and support workplace programs that will improve health-promoting options. These options may include educational programs, more healthful foods in cafeterias and vending machines, segregated smoking areas, exercise breaks, smoking cessation and weight control clinics, child care arrangements, prenatal and other high-risk monitoring, reduction in environmental safety and health hazards, flexible workday scheduling, equalization of health plan benefits and coverage, and the

extension and improvement of unemployment insurance. Support for such changes at the state and national policy levels and by professional associations and responsible agencies will go far toward easing the development of such programs. Work settings that are most familiar to us ought to lead the way.

Improvements in occupational health need a trade-off between women and men. In fact, those that will aid women will also help men, especially those men who are now at high risk. Furthermore, as household and family patterns continue to change, child care will become a problem for single and married men. And they too will benefit from flexible worktime and maternity leaves.

In summary, a woman's view of women at work is no different than any perspective that seeks to enhance the health of persons at work. It takes into account those health risks that are carried into the job world because of one's social status and inherent living conditions. It views biological vulnerabilities and assets within the composite risks of the worksite. It then attempts to design programs to compensate for cumulated risks and to minimize future risks. Although specific programs will vary because employees' risks differ, the program strategy and the goal--health improvements--are the same.

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QUANTITATIVE DIAGNOSIS IN PULMONARY MEDICINE— MAKING VIRTUE OUT OF NECESSITY

Philip A. Bromberg, MD

Diffuse lung diseases are of particular concern for occupational medicine; the putative disease-causing agents are generally inhaled and those agents that reach all parts of the lung are capable of inducing disease in fairly simultaneous fashion. The defenses of the respiratory system against inhaled gases and particulates are multiple and complex; thus, the effects of noxious agents may never reach the level of detectibility if one relies on pulmonary function measurements. For example, there is good reason to believe that one can detect alterations in enzyme patterns and increased cell turnover in the alveolar lining cells or the airway epithelial cells long before there are clear cut structural or functional changes. These are changes that are perhaps simply a normal or adaptive reaction to an environmental stress; they probably are real changes and we make no pretense about trying to define them by the use of the usual pulmonary function tests. So, there may be a stage in the development of inhalation disease in which the changes are really not detectable by physiologic testing; these changes will have to be detected by other methods-biochemical, cytological or other.

A tremendous number of factors contribute to the well-known variations of individual response to a particular challenge. The efffect of dose is the first thing that we think of. But apart from the effect of dose, we have to be very aware of the pattern of deposition and uptake when the agent is inhaled into the lung. Agents can deposit at any point along the complex branching system of the lung, depending on particle size, solubility and the rapidity of air flow. There are also genetically determined variables that are important. We know, for example, the significance of a smoker being a heterozygote for alpha-1-antitrypsin deficiency; such people appear to be at a higher risk of developing chronic obstructive lung disease. We are also beginning to realize that there is a tremendous influence of HLA-type on the occurrence of diseases like rheumatoid spondilitis. It may be that research will show that certain people are susceptible to a particular dust-related disease while genetically different individuals are not. Nutritional factors and co-intoxicants may also play a role in whether or not an agent manifests toxic effects on the subject. Cigarette smoke, of course, is the prime example of a co-factor. The patient may have other diseases that interact with the inhaled agent. A nice example of this is Kaplan's syndrome; coal miners with rheumatoid arthritis react to coal dust and present a fairly special clinical picture. And finally, the effects of potentially noxious agents on a pre-existent lung disease have to be considered. Thus, these interactions of many factors make the evaluation of clinical data very difficult.

On the other hand, progress in pulmonary function testing has not stood still. The degree of sophistication and the ability to assign an anatomic locus to a particular abnormality of pulmonary function have been improving. In the past ten years or so, a tremendous amount of attention has been placed on the small airways, which in the adult lung are those airways smaller than approximately 2mm in internal diameter. These airways include the bronchi with cartilage in their walls and also the various

levels of the bronchiolar tree. Because they are very numerous--despite their relatively small individual size--they have a large aggregate cross-sectional area; thus, the rate of air flow in any individual airway is extremely low and air flow resistance is almost negligible--it is very difficult to detect a pressure drop during expiration on the order of a millimeter of water. The major drop in pressure in the normal individual occurs in the large airways, the segmental and lobar, and the main bronchi and trachea. The small airways thus have been called a "silent area", and a lot of disease can exist in these small airways without any clear-cut impairment of the standard parameters of spirometric pulmonary function.

It's been tough to prove this hypothesis of the genesis of chronic obstructive lung disease, but it is accepted by most experts in the field. In most cases the small airways are the locus of the initial attack, which is rather prolonged and insidious. Because these airways are so numerous, one can suffer the loss of many of their numbers before obstructive lung disease becomes apparent. It is not surprising that investigators have looked for ways to detect small airways disease.

While measurement of the FEV_1, particularly as a fraction of the total vital capacity, is still a very useful and relatively sensitive test for the presence of diffuse obstructive lung disease, there appear to be better tests. First of all, efforts have been made to use the maximum mid-expiratory flow rate. This flow rate is determined by looking at the middle half of expiration, starting from total lung capacity and going down to residual volume, dividing that volume into halves and quarters and then looking at the middle-half to see how long it takes to expire that middle-half of the air; the slope of the curve is a rate because it is a change of volume with respect to a change in time and is called the "maximum mid-expiratory flow rate."

The test was touted as a very sensitive and useful one for the detection of small airways disease because the site of flow limitation during expiration seems to displace itself deeper and deeper into the airways of the lung as the lung gets smaller, finally reaching the small airways. It was a reasonable idea and it has been pushed as an important improvement in the interpretation of spirograms. Unfortunately, I don't think it is a very good test. If you look at the variation within a subject on repeated trials, you will see that the maximum mid-expiratory flow rate is difficult to reproduce—even very good laboratories can have a range of 20 to 25%--whereas, vital capacity and the vital forced respiratory volume in one second are reasonably reproducible (within 5% on repeated trials at the same sitting). In addition, the inter-subject variability is very substantial.

Researchers interested in lung mechanics are convinced that we're not extracting all of the useable information from the spirogram. They continue to look for new and better indices with which to analyze these curves. Some of these efforts involve complicated computer procedures—for example, the analysis of moments and slope ratios--to break down the curve into a sum of exponential curves, each of which might reflect the rate of emptying of a certain compartment of the lung. These techniques are not marketable, but they are shown to be of value in the early detection of disease--one that will be in the <u>individual</u> as well as in a <u>group</u> of subjects.

A test that seems to have a place in the detection of early disease is the single breath nitrogen test devised by Ward Fowler at the Mayo Clinic about 30 years ago. It consists of the subject taking a full breath of oxygen then continuously measuring the concentration of nitrogen at the mouth while he is slowly expiring. There is a rapid rise in N_2 concentration, which proceeds to a plateau as he continues to breathe out.

Fowler focused on the slope of the plateau, concluding that a slope greater than a certain amount indicated diseased lungs and a maldistribution of air. His conclusions are still valid today. More recently, it has been found that a reproducible rise in nitrogen concentration takes place toward the end of the expiration; the lung volume at which this rise occurred was termed the "closing volume"--this is seemingly the volume of the lung at which airways closure begins. When you reach the residual volume, all your airways are theoretically closed. However, the airways do not close all at once but rather in a staggered sequence, starting with the bases and moving up to the apexes. There is general agreement that if the volume at which airways closure first becomes manifest is higher than it should be for that particular patient, then there is an abnormality or disease in the small airways. In other words, the small airways are closing prematurely at a higher lung volume, giving rise to an elevated closing volume.

Another study—it's new to us but it's been done in Europe for a number of years--is very interesting and of particular interest to occupational medicine. In this study you don't just look at the pulmonary function of a subject sitting in the pulmonary function lab. Instead, you attempt to provoke abnormalities in a subject by exposing him to increasing concentrations of a bronchoconstrictive aerosol—histamine, methacholine and carbachol are most commonly used--and observe the effect of the agent and its concentration on his pulmonary mechanics. The asthmatic displays hyperactivity to the bronchoconstrictor; no one knows what gives the asthmatic that particular proclivity, but we do know that it is possible to induce temporary airway hyperreactivty by histamine challenge.

One drug that is noted for this phenomenon is toluene diisocyanate (TDI); it induces an asthma-like disease in persons who have no asthma history. It would be interesting to know if these subjects had normal histamine reactivity prior to their TDI exposure; in other words, is theirs truly acquired or does TDI bring out a latent tendency. On the other hand, if TDI exposure is discontinued, will these subjects return to a state of normal histamine reactivity? I don't know.

Woodworkers—ie, those exposed to red cedar dust in particular, possibly due to the plicatic acid in the wood—develop enhanced responsiveness to histamine as well as wheezing. After a fairly prolonged withdrawal from exposure, the histamine reactivity returns to normal. In this particular case an industrial exposure can engender a rather prolonged, yet potentially reversible, bronchoconstrictive activity. It might be very interesting to carry out such studies in cotton workers. This is a new approach to pulmonary function--airways function in particular--to quantitate response to provocative tests; I think it's an area that should be of great interest to industrial and occupational physicians who have these kinds of patients.

In the case of cigarette smoking, there is evidence that continued smoking will lead to the progression of abnormal pulmonary function at a more rapid rate than that associated solely with aging. Sir Charles Fletcher in England has led a team of epidemiologists and physicians who have pretty well established that the relationship between cigarette smoking and the development of obstructive lung disease is probably correct. He has further shown that if a cigarette smoker with well-established obstructive lung disease stops smoking, the rate of decline of his pulmonary function reverts to the normal slope; he may, therefore, prolong his useful working life out to age 60 or 65 before there is severe symptomatology and disability. I don't know if there is similar evidence for other potentially toxic agents. For instance, does it make any difference to stop exposure if you have pneumoconiosis with micronodulation and hardly any detectable change in pulmonary function? Again, I'm not sure. The whole field of

epidemiology requires cooperative studies and complicated methodology, which should be of interest to occupational physicians who have access to patients with chemical exposure.

In addition to its manifest advantages, exercise imposes an automatic drive to the respiratory and circulatory systems, which overrides psychologic factors that are so frequently confusing at rest. Exercise testing also provides useful information on the cardiovascular system as well as the respiratory system. And finally, it will indicate the limiting factor of the gas transport system.

In normal individuals the cardiovascular system limits the amount of oxygen that is circulated; thus, exercise in ordinary individuals improves the maximum oxygen consumption by increasing the stroke volume. The respiratory system is not a limiting factor for the ordinary individual; there is normally a nice linear relationship between ventilation and oxygen consumption, with a ratio of about 25:1. At rest the expired ventilation might be 6 liters per minute and the oxygen consumption 0.25 liter per minute thus ventilation:consumption = 24:1. At very heavy exercise, oxygen consumption may rise to 4 liters per minute whereas ventilation will be on the order of 100 liters per minute (again, a ratio of 25:1). The limiting factor is how much blood the heart can pump.

For the patient with obstructive lung disease, the situation is entirely different. These patients have a large fraction of their ventilation devoted to the non-gas exchanging parts of the lungs—ie, dead space ventilation; therefore, they have ratios that are closer to 40:1 or even 50:1. So the best that a poor devil can get out of his 40 liters a minute (ie, 40 breaths per minute at 1 L/breath—pretty good for a patient with obstructive lung disease) is 1 liter per minute of oxygen consumption. Mind you, walking at a normal pace on a level surface requires about 1 liter per minute of oxygen consumption. This man might, therefore, function as a bank president or a professor of medicine, but he certainly will not be able to function in a job where he has to move around, climb steps, etc.

OCCUPATIONAL CANCER

Modifying Factors In Experimental Lung Cancer

David G. Kaufman, MD

Lung cancer is the leading cause of cancer deaths among American men. Cigarette smoking is presumed to be the most significant etiologic factor in this cancer toll. In addition, several occupations have been associated with an excess risk of lung cancer. Examples that are well known to all of you include uranium mining, asbestos production and application, production of bis-chloromethyl ether, coke oven operation, production and polymerization of vinyl chloride, smelting and refining of chrome, nickel, arsenic, etc. It has been shown that some of these occupational exposures when combined with cigarette smoking yield a greater cancer risk than a similar type of exposure in the absence of smoking, suggesting additivity or synergy of their effects. Yet not everyone who is subjected to both cigarette smoke and the occupational exposure develops lung cancer. The variability of the carcinogenic effects, even in individual situations at a very high risk, suggests a biologic variability within the exposed population. This variability may be predicated on several physiologic or biochemical properties of the individual that influences either the actual biological dose or the response to a given exposure. Such factors as extent and duration of smoke inhalation, numbers and types of cigarettes and the distribution of smoking throughout the day may be important.

With regard to occupational exposures: the use of protective equipment, the specific job function, the source or location of the material being used, and even the physical design and ventilation of the worksite may influence risk. Individual characteristics, such as rate of function of pulmonary clearance mechanisms, extent of cellular loss from a given injury, and the rate of repair of self-proliferation, capacity for cellular DNA repair, and nutritional and immunologic status may further influence individual risk. And since genetic diseases that predispose to cancer development are known, it is conceivable that the variability of these capacities may be genetically determined. Previous disease or intercurrent illnesses can also increase the risk of respiratory tract cancer.

Because individuality and variability are hallmarks of the human race, it is difficult to isolate the specific effects of the plausible variables to determine if and how they contribute to the risk. For these reasons we turn to experimental models of human cancer—especially, human lung cancer--to gain further understanding. There are several experimental models for respiratory tract carcinogenesis. Each has its strengths and weaknesses. I've chosen to begin this discussion with one that I am most familiar with.

One of the early lessons in experimental chemical carcinogenesis studies was that tumors take a long time to develop, just like human cancers. Toxicity of the carcinogens and intercurrent infections of the animals hampered early efforts. Thus development of what was to become a very widely used model for respiratory carcinogenesis was marked by two significant advances; first, the Syrian golden

hamster. These animals were found to be resistant to the epizootic chronic respiratory infections of conventional rodents. They don't develop spontaneous lung tumors and they are relatively tolerant to instillations of carcinogens into the respiratory tract. Secondly, the carcinogen in our studies—usually benzopyrene—are attached to a particulate material such as ferric oxide dust; the mixture is then instilled directly into the respiratory tract. The result of the new methodology was that tumors developed in the respiratory tract. Furthermore, the animal tumors resemble—in morphology and location—the majority of tumors found in the human respiratory tract. Then too, the tumors appear to develop as a result of a histogenesis process through a sequence of lesions resembling those associated with the tumors of the respiratory tract in humans. And finally, tumor response is reasonably quantitative and reproducible, and the relationship between dose, response and latency is reminiscent of the disease in humans.

In practice, benzopyrene is physically adsorbed onto iron oxide particles suspended in saline. The suspension is injected by syringe into the trachea of the experimental animals. Particles of iron oxide/benzopyrene become distributed throughout the lung. A single injection of the mixture has a toxic effect on tracheo-bronchial epithelium. There is a selective loss of ciliated cells from the epithelium initially; an early response involves basal cell hyperplasia with an increase in the number of basal cells as well as simplification of the overlying epithelium followed by non-keratinizing squamous metaplasias. With continuing injections, a large area of tissue becomes squamous metaplastic with distinct keratinization at its surface. For the most part, these are reversible lesions. Continuing treatment leads to damage of the respiratory epithelium and simplification of the epithelium with toxic changes in the nuclei. Basal cell hyperplasia and focal areas seem to grow extensively. Basal expansion progresses from a relatively well-ordered and reasonably differentiated stage to extensive lesions with many fewer superficial differentiated cells. In time, the entire thickness of the epithelium is composed of basaloid cells that represent an in situ carcinoma. Malignant cells in an early, small evasive lesion show rather limited suffusion through the underlying stroma. As time and treatment progress, there is more extensive infiltration throughout the underlying stroma. Even where the malignant tumor is localized, the entire underlying soft tissue becomes suffused with malignant cells.

One question of technical importance is related to the role of dust particles in the experiment. To address this issue, studies were made in which benzopyrene was mixed with dust by alternate methods. The results showed an increased risk of tumor induction when there was an actual physical association (by grinding) between the carcinogen and the particles, as opposed to simply mixing benzopyrene with the particles or to benzopyrene alone. Adding additional dust didn't seem to affect the outcome. Other particles (such as carbon and nickel) were also compared to ferric oxide. There was a much higher tumor incidence with carbon than with ferric oxide. Perhaps the surface adsorptive characteristics of the particles are a factor. It has been hypothesized that the particles slow the clearance from the respiratory tract, thus increasing the carcinogen dose acting on the respiratory tract. Experimental studies that have evaluated the clearance of carcinogen from the respiratory tract tend to support this role for the particles. It is conceivable, therefore, that conditions that are apt to reduce the clearance of materials out of the lung contribute to the effect of the dose of carcinogen. Cancer risks might then be lowered by altering contributory factors as well as acting on the carcinogen itself.

Hence, several anesthetic agents were evaluated to determine if there might be a simpler way to anesthetize animals in these studies. Ether has generally been avoided

because it is a pulmonary irritant. Sodium barbitol is typically used as a parenteral solution; it yields deep anesthesia and reduces respiratory rate without irritation to the respiratory tract. Methoxyflurane is an inhalation anesthetic which also does not cause pulmonary irritation and is effective as a moderate level anesthesic, causing less reduction of the ventilatory rate and a more rapid rate of recovery.

Groups of hamsters treated with benzopyrene/ferric oxide while anesthesized by these various agents were compared; for the most part, hamsters treated with either barbitol or ether gave a higher incidence of tumors than those given methoxyflurane. Since both ether and barbitol gave a deeper level of anesthesia than methoxyflurane, it was thought that they might cause a reduced clearance rate for the carcinogen mixture. Again, if the carcinogen mixture is removed more slowly from the respiratory tract, then the integral of dose with time of exposure is greater for ether and barbitol than for methoxyflurane; this is the equivalent of giving a larger dose of carcinogen. Again, there is the suggestion that the state of pulmonary function as it affects clearance of carcinogens influences the carcinogenic risk in the experimental animals.

Another factor that has been shown to influence lung cancer incidence in humans is one's concurrent exposure to more than one carcinogen. Experimental studies have examined interactions between carcinogenic treatments under the controlled conditions of an animal study. In each case benzopyrene was adsorbed on ferric oxide particles in one of the treatments. Other co-carcinogens included diethylnitrosamine, which is a metabolically activated carcinogen with great organ specificity for the respiratory tract; methylnitrosourea, which need not be metabolized to be active and is not specific for the lung; and polonium-210, an alpha-particle emitter. Hamsters that received small doses of benzopyrene adsorbed on ferric oxide displayed a very low incidence of malignant tumors. When a benzopyrene/ferric oxide treatment was followed by subcutaneous injections of diethylnitrosamine, malignant tumors occurred earlier and in significantly greater numbers. Note that diethylnitrosamine per se did not yield malignancies.

In the second study with benzopyrene/ferric oxide followed by methylnitrosourea, there was a greater tumor response than that produced by either agent alone; the individual agents actually gave rather low tumor incidences. When the results of these two treatments were reevaluated, it was observed that the tumor incidences exceeded the expected interaction of the two carcinogens acting alone. This suggests a non-additive effect if it occurred in a linear dose-response relationship. However, this type of study does not distinguish an additive response from a synergistic effect on a non-linear dose response curve.

The third experiment employed benzopyrene/ferric oxide with polonium-210. Here there was a slightly increased tumor incidence which appeared to be a simple additive effect. If we consider all these interactions, they suggest that:

> Carcinogen interactions can be studied by experimental model systems.
>
> Interactions are not simple; they may vary according to the specific agents and with such factors as the sequence of the agents and their timing.
>
> The experimental model offers an opportunity to study these effects as they may bear upon human exposures to multiple agents. Reasonable methods may then be developed for reducing lung cancer deaths by eliminating or modifying the most critical points of the exposure equation without necessarily having to avoid exposures to all possible carcinogens.

Other factors may also modify tumor incidences. For example, if vitamin A-deficient animals have increased carcinogen binding to DNA within the respiratory tract, they also get more lung tumors. Human epidemiologic studies also have shown that men who eat a diet relatively deficient in vitamin A have an increased risk of lung cancer. Thus, vitamin A deficiency appears to be a predisposing condition for tumor development in the respiratory tract. On the other hand, animals supplemented with high doses of vitamin A after benzopyrene treatment developed fewer tumors than those treated with benzopyrene alone. Let me warn, however, that both natural vitamin A and the vitamin A tablets sold over-the-counter are highly toxic if taken in large doses, and may even be fatal. Studies are underway to develop vitamin A analogues having beneficial anti-cancer effects and lessened toxicity.

Related studies of the chemical prevention of carcinogenesis have evaluated other antioxidants, such as butylated hydroxytoluene, butylated hydroxyinositol and disulfuram (or antabuse). Experimental studies of peripheral lung adenocarcinomas and adenomas with mice is not the exact equivalent of the majority of lung cancers in man. It's been found that chronic treatment with these antioxidants in the diet reduces lung tumor incidence. The lung tumor response can also be modified in the hamster model by influencing the immune system of the animal. We have treated hamsters with benzopyrene/ferric oxide and immediately thereafter immunized them with isolated cell walls of the BCG bacillus. Inoculations yielded a substantial, non-specific immune stimulation in the treated animals. Moreover, the immunized hamsters developed fewer lung tumors than those not immunized.

Thus, modification of activity of the cellular immune system may also influence tumor responses. We have learned that the rate of induction of lung cancer is predicated upon a complex interaction between the exposure to various carcinogenic factors and host factors. The somewhat disparate list of factors that are able to modify experimental models of carcinogenesis is indicative of the wide range of individual factors that influence the tumor development.

When the problem is looked at holistically, it's not surprising that a single, simple theme doesn't emerge. The phenomenologic studies do contribute to our understanding of the carcinogenesis process. Three distinguishable elements in the process can be identified: exposure, susceptibility and modulation. Factors such as attachment of carcinogen to particles, dose of exposure and multiple exposures influence the quantity of carcinogenic insult that is encountered by the individual, and by reduction of exposures one can hope to reduce the toll of cancers. Dietary supplements of antioxidants may reduce one's susceptibility and reduce the initiated cancer cell quantity. Measurable tumor response in animals and perhaps in man may be modulated. Many factors, such as continued carcinogen exposure, repetitive injury or tumor promotion, may increase the number of tumors that actively grow and appear clinically, or they may even reduce the latency period for tumor initiation. One can not uncritically apply these experimental results; however, they do help to identify more profitable epidemiologic studies, suggest changes in environmental or industrial control, guide careful development of chemo-preventive procedures and, hopefully, help us to bring lung cancer under control.

OCCUPATIONAL CANCER

Lung Cancer—A Lesson from Experiments—Pathogenesis of Lung Cancer as Viewed by the Researcher

Paul Nettesheim, MD

We shall never be able to remove carcinogens completely from man's environment. Carcinogens are not an invention of modern society—man and other animals have always lived with carcinogens.

These are factual statements, but they are sometimes forgotten and perhaps never known by some people. Modern society continues to add new carcinogens to the already existing burden. I am referring to the incomplete combustion of carbonaceous materials resulting in emission of benzopyrene. There is no question that our first and foremost responsibility as physicians is to identify the source of carcinogen exposure and then reduce that exposure to a minimum. To completely eliminate carcinogen exposure in all instances will turn out to be unfeasible, just as we will not be able to remove carcinogens completely from our food and air. We may have to accept a certain level of exposure as unavoidable. We must also face the fact that some individuals will be at greater risk than others due to their genetic dispositions, predisposing illnesses, concomitant insults, etc.

How might we then establish that a certain exposure level will be safe? I doubt that today's tests will allow us to make more than an educated guess. Is there a real possibility that we shall be able to identify individuals who are exceptionally susceptible to a certain level of exposure? Are there early warning signals to indicate that a disease process is beginning and will develop further if exposure continues?

The research that we are conducting is aimed at identifying the very earliest changes that are induced by a carcinogen, changes that can be seen months and years before the first cancer cells appear. The advantage of working with laboratory animals is that many of the diseases in animals are similar to those in humans and the time spans are much shorter; a process that takes a decade or two in humans will develop in animals in a few months or a year.

As you are aware, there is a long, silent latency period between one's first exposure to a carcinogen and the development of cancer. Usually the critical carcinogenic dose that will induce cancer is acquired through multiple, repeated exposures over extended periods of time. In most cases, many years elapse before the critical dose is accumulated. Evolution of cancer, even when the critical dose has occurred, stretches over many years.

The main objective of our studies was to detect the precursors of cancer cells. To approach the problem, we had to develop an experimental model that would allow us to expose a preselected piece of airway mucosa to a known dose of carcinogen at a known

dose rate. We chose rat trachea because it is small and anatomically similar to the human bronchus; it is also an easily accessible piece of tissue. Instead of working with the trachea in situ, we decided to transplant the trachea from a normal animal to an isogenic host (to avoid immunological rejection) and use the transplant as the target organ. Those tracheal grafts became established very rapidly, and microscopically they are almost indistinguishable from the normal tracheas. After about 3-4 weeks, when the transplant was established, a pellet containing the test carcinogen was inserted into the transplant. By suitably modifying the matrix of the pellet, the release rate of the carcinogen—hence its dose rate—could be controlled. The mucociliary epithelium of the airway soon changed from a mucus-producing epithelium to a skin-like squamous epithelium. Eventually the invading cancer destroyed the graft. Various types of lesions, similar to those found in humans, have been seen and induced in the tracheal transplant.

Because clinicians and diagnosticians have suspected that the dysplastic lesions are preneoplastic lesions and are precursors of cancer, we decided to find out what we could about them. The evidence is only statistical—there is no real hard evidence—that either some or all of these dysplastic lesions are indeed precursors of cancer.

When we looked more closely at these and also less advanced lesions, we found three important things:

> In normal tracheal epithelium, or hyperplastic epithelium, the site of self-renewal and proliferation is the basal layer of the epithelium. In the dysplastic lesion, proliferation (as evidenced by DNA synthesis) also occurs in suprabasal layers, which indicates that maturation is impaired in this lesion.
>
> Another abnormal feature of this lesion (as detected by morphometric measurements) is the presence of cells with high nuclear cytoplasmic ratios in the basal, the intermediate and in the superficial cell layers. In contrast, normal stratified epithelium cells (such as the normal squamous epithelium of the esophagus) have high nuclear cytoplasmic ratios only in the basal and parabasal layers; cells in the intermediate and superficial layers have low nuclear cytoplasmic ratios. This also indicates a severe disturbance of maturation and differentiation of the cell population. The "dark cell," which has been observed in skin carcinogenesis, also appears in the dysplastic lesion.

We then decided to determine the fate of the induced dysplastic lesions. The experiment is very simple, involving many tracheal transplants exposed for a short period of time (ie, 4 weeks) to a known dose (165 ug) of dimethylbenzanthracene (DMBA); we removed the carcinogen after 4 weeks and began sampling to determine:

> the evolution and fate of the lesions and
> what types of lesions developed as a function of time.

We sampled 50 tracheas every two or three months for twelve months. In addition, 80 tracheas with the same type of exposure were allowed to stay in place until the tumors developed; that study went on for 2.5 years, giving us a cumulative tumor incidence of 10% in 2.5 years. In other words, a carcinogen dose that is low in terms of tumor induction gave only a 10% cancer incidence. Four months after cessation of carcinogen exposure, we observed the denovo formation of dysplastic lesions. A peak is reached at

4 months; thereafter, the number of dysplastic lesions decreases for both mild and moderate dysplasias. Severe dysplasias, which contain carcinoma in situ, remain constant. Regardless of whether you're looking at all or any specific one of the different types, the number of dysplasias is higher at any given time than the number of cancers that ultimately result. Thus, while any of these dysplasias may become cancerous, the majority of them never do. As a matter of fact, the majority of them reverse unless some other events occur; even some of the severe dysplasias--including the carcinomas in situ--will ultimately disappear.

Are these lesions then precursors of cancer? It appears that the epithelium is healing, or that the carcinogenic insult is healing. Either these lesions are late manifestations of carcinogen toxicity that have nothing to do with carcinogenesis, or they are aborted neoplasias. And inasmuch as their proliferative rate is far above normal, they do have some similarity to neoplastic lesions. While this experiment tells us that many dysplasias do not become cancerous, it does not tell us which ones or if any of them do. One might be tempted to say that the mucosa is healing. And when you look at some of the older literature, the morphological abnormalities of the tracheo-bronchial tree in ex-smokers subsides as a function of the time following cessation of smoking. One might be tempted to think that the effect of the carcinogenic insult recedes with time. However, we have some evidence to suggest that that is not true.

Using the same model, we exposed tracheas to low doses of DMBA for 4 weeks. After that we inserted a non-carcinogenic dose of chrysotile asbestos into half of the tracheas. At the high DMBA dose there is no difference (9 out of 40 vs 7 out of 38) between tissues treated with asbestos and those not treated. At 50 and 25 ug of DMBA, however, the non-carcinogenic dose of asbestos dramatically increases the expression of the preceding DMBA insult. Similar experiments with other non-carcinogenic agents (eg, 12-O-tetradecanoyl-phorbol-13-acetate, or TPA) produce the same results--ie, 4- to 5-fold overall enhancement of tumor response due to the promoting agent.

In still another study, we immuno-suppressed the animals temporarily during the first 3 to 4 months of the tumor induction time. These animals developed a larger incidence of cancer. The results suggest that there are more carcinogen-altered cells sitting in a carcinogen exposed organ than are normally expressed. When injuries or permissive host environments occur, however, these hidden cells express their neoplastic potential. We learned from this immunological study that there may be an early marker. Inasmuch as the tumors only begin to develop after about a year, the host may be recognizing early carcinogen-altered cells—ie, precursors—that are not yet cancer cells. But there are limitations to the morphologic studies: In order to detect the cells, one has to take them, stain them, etc; and in the process, they are killed. Therefore, it's impossible to determine what a cell, or group of cells, would have done had it survived. Some means must be developed whereby we can follow the originally exposed cell population through a long series of cell generations. Since the universal characteristic of cancer is uninhibited, unregulated growth, the disturbance of growth control might serve as an early biological marker of the precursors of cancer cells. If we can develop the appropriate system, we might be able to detect the disturbance.

We therefore examined the growth characteristics of normal tracheal mucosa in vitro. Tracheal epithelium grown in vitro as primary culture will do very well for a few weeks; it will then die out. However, tracheal epithelium that has been exposed to carcinogen in vivo and then placed in a culture dish does several very exciting things. This epithelium not only survives for a few weeks, but it thrives and continues to proliferate in the dish. When we made subcultures from the original primary cell culture, we found

we could easily establish cell lines which have survived to this day after several years. In short, the carcinogen-exposed cells had a drastically altered survival and proliferation capacity in vitro that could be measured. The cell line becomes malignant somewhere between 200 and 500 days. These cell lines are not malignant for a long time; some of them, however, after 200 days and others after 500 days will become malignant. If they are inoculated into an animal they will form a cancer, usually an invasive squamous cell carcinoma. These carcinogen-altered cells can be observed in vitro as they progress to a neoplastic state.

The next questions we asked were:

How many cells are altered by the carcinogen?
Does that number increase or decrease with time?
What's the fate of these cells?
Can we detect different levels of altered growth capacity?

We developed an in vitro assay--the epithelial focus assay--in which we examined in vitro-exposed tracheal epithelium for its capacity to form a proliferating epithelial focus in vitro; if the cells grow in agarose, they may be considered as tumorigenic.

The epithelial cells were next subjected to three different tests:

whether they can form epithelial foci,
whether the epithelial foci can be subcultured (cell lines), and
whether the cells derived from the epithelial foci become neoplastic.

We found that the number of epithelial foci and neoplastic epithelial foci increased with time after the end of exposure. At 8 months, 80% of all tracheas contained cells with neoplastic potential. Let me remind you that this experiment was done at a carcinogen dose level that induced tracheal carcinomas only in 10% of the tracheas at 2.5 years. This study thus supports the earlier conclusion: There are many more cells with neoplastic potential in carcinogen exposed organs than the tumor response would suggest. These "hidden" neoplastic cells only express their tumorigenic potential when permissive or promoting conditions prevail.

OCCUPATIONAL CANCER

Cytology in Industrial Applications

Charles N. Carney, MD

The main objective of cytology in the industrial setting is the detection of cancer and pre-cancer, chiefly of the lung. The ideal cancer-detection program should discover the cases of invasive or late cancer in the early phase. Assuming that all exposed individuals continue to be screened on a regular basis, the remainder of the program should detect cancers in their developmental or in situ stages for confident cure.

The Philadelphia and London projects which screened for early lung cancer by x-ray in the 1950s and '60s failed to significantly reduce the mortality from lung cancer, although early cases were detected (1-3). The investigators of these projects and other investigators have concluded that most patients with a roentgenographically invisible lung neoplasm will develop a visible lesion within 6 to 12 months, at which time the tumor is at least 1 cm in diameter and is comprised of one billion cells (4-6). At this stage it is too late to improve prognosis significantly. Our most compelling task then is to detect the invisible lesions with the microscope.
Detection rates depend on:

the nature and number of specimens,
the method of specimen preparation and its quality, and
the proficiency of the cytology laboratory.

The **nature and the quality of the specimen** is basically the responsibility of the physician. He should explain to the patient the proper technique for acquiring sputum. It is important to do this without frightening the individual, since undue anxiety at the prospect of having cancer may result in a nervous, uncooperative patient and unsatisfactory specimens. Early-morning, "deep-cough" sputum is the only practical specimen for the out-patient. On arising, the screenee should first clean and rinse the teeth and mouth to eliminate food fragments and loose squamous cells from the upper tract. After about five deep breaths and at the height of inspiration of the last breath, he produces an explosive cough by tightening the abdominal muscles and expectorating into a shallow, wide-mouth jar. A fresh, unfixed, specimen thus procured is a very desirable specimen since cellular outlines and detail are well preserved. Unfortunately, it must be delivered immediately to the cytology laboratory. (Cells in unfixed sputum may remain in good condition for several hours, but it is best not to give the patient the option of holding it that long.) Another disadvantage is that the mucus will cause some areas of the smear to be too thick for adequate assessment of cells caught within the mucus. For the patient who cannot cough and produce satisfactory sputum, aerosol induction is advised; several methods for this are described in the literature (7-13). Chest wall percussion (14) and postural drainage (15) techniques are usually unnecessary in the industrial patient, although they may be of value in one with symptomatic disease.

For the out-patient, it is preferable that he expectorate into a jar half-filled with Saccomanno fixative (16), a mixture of 50% ethanol and 2% Carbowax. The fixative allows the patient to collect specimens at home on three to five consecutive mornings; the method has the disadvantage, however, of making the preparation of the smear somewhat cumbersome and it introduces microscopic artifacts. These artifacts are not serious but they might not be familiar to many cytodiagnosticians. A satisfactory specimen is one that contains adequate cellular material from the lung. At the very least, pulmonary macrophages should be present—though they are not siginificant to the evaluation—and ideally, there should be bronchial epithelium.

Several studies have shown the value of multiple specimens for cancer detection (17-19). The detection rate is about 40% with one specimen; the rate increases to about 80% for three specimens and 90% for five. It is recommended, therefore, that the high-risk industrial employee collect five consecutive sputum samples in a half-filled container of Saccomanno fixative. The container may be retained until it is convenient for delivery to the laboratory.

Specimen preparation and laboratory proficiency depend on effective quality control, which is the responsibility of the cytology personnel. Fresh, unfixed sputum is selected for smearing between two glass slides by picking out whitish, opaque or bloody areas or tissue pieces. The smears are fixed immediately without air-drying by rapid immersion in 95% ethanol. Saccomanno specimens are placed in a blender for several seconds to break up the mucus. The blend is then centrifuged and smears are made from the sediment.

Proficiency varies from laboratory to laboratory, depending on how each acquires and utilizes follow-up information. Overall, the more proficient laboratories should detect about 80% of lung cancers (20). Regardless of the laboratory's record of proficiency, a single diagnosis of malignancy should always be confirmed by a second diagnosis to rule out laboratory error.

Data from screening programs of high-risk persons indicate what we may expect in screening for lung cancer in industry.

Uranium - In the 1950s and '60s, a sputum screening program for 3,557 uranium miners (smokers and non-smokers) detected 1% in situ and 4% invasive carcinomas. A similiar detection rate occurred in the control group of smoking non-miners. The two groups differed in that smoking miners developed cancer 10 years earlier than the smoking non-miners (21).

Asbestos - A screening project is currently underway at the asbestos plant in Tyler, Texas. The preliminary report indicates that 2 out of 554 former asbestos workers (ie, 0.4%) had occult, invasive lung cancer and 18 (3.2%) had severe atypia (22).

Cigarettes - A third screening program is for volunteers who are heavy cigarette smokers; it is a major project called the National Lung Cancer Cooperative Study and is sponsored by the National Cancer Institute. It is currently being conducted at Mayo Clinic, Memorial Sloan-Kettering Institute for Cancer Research and Johns Hopkins University Medical School. The prevalence and incidence rates for all carcinomas, in situ and invasive, are summarized in Table 1.

TABLE 1 - Results of the National Lung Cancer Cooperative Study, as of 1977 (23,25,36)

	Mayo	Kettering	Hopkins
Prevalence rates, all carcinomas	8/1000 (0.80%)	4.6/1000 (0.46%)	6.5/1000 (0.65%)
Subsequent incidence rates, new carcinomas	(from all 3 institutions) (0.4-0.5%)		

The cited incidence rate of 0.4-0.5% corresponds to the current lung cancer mortality rate of 38 per 100,000* (assuming that approximately 10% of the population are heavy smokers and that lung cancer mortality rate can be roughly equated with incidence rate). The survival rates are encouraging for those patients who were discovered with early asymptomatic carcinoma (in situ or with focal invasion)—85% survive 3 years. The remaining asymptomatic patients with later disease have a worse prognosis—15% survive 3 years (23).

Similar screening in the future apparently will depend on a balance between the tremendous expense of funding such projects and the undeniable medical and ethical contention that the only effective control of lung cancer—short of removing carcinogens from the environment—is early detection and therapy.

In industry, cytologic surveillance could be done in a manner similar to the National Lung Cancer Study. For those known and suspected industrial carcinogens, see Table 2. We believe that uranium and asbestos workers and those exposed to benzo(a)pyrene certainly should be screened. Whether it is feasible and practical to do so in other industries depends on fiscal factors and health and safety mandates for the employees.

*North Carolina Division of Health Services, Public Health Statistics Branch, 1978.

TABLE 2 - Industrial Agents Associated with Lung Cancer*

	Typical exposures
acrylonitrile	acrylic fiber/textile & resin production; fumigation
arsenic	very numerous
asbestos	numerous
benzo(a)pyrene	cigarette smoke, coke oven emissions
beryllium	numerous
bis-chloromethyl ether (BCME)	organic chemical production, ion-exchange plants
chloromethyl methyl ether (CMME)	organic chemical production
chromium and chromates	numerous
hematite	hematite mining
nickel and its compounds	numerous
soot, tars and oils	numerous
uranium and radon	underground mining
vinyl chloride	polyvinyl chloride (PVC) resin & rubber plants, organic chemical production

*Modified from Schottenfeld, D et al. 1979. Cancer **29**:144

There is a reasonable certainty that lung cancer and other cancers undergo a developmental sequence. Auerbach et al (24) did a systematic autopsy study in which they mapped epithelial changes in the bronchi of cigarette smokers, including those with lung cancer. Three changes were observed in bronchial epithelium: hyperplasia, loss of cilia and the presence of atypical cells. Any or all of these changes were more pronounced in smokers than in non-smokers. It was concluded, therefore, that a pathogenetic, developmental sequence precedes invasive lung cancer.

Saccomanno and his co-workers (21), while engaged in the uranium project, proposed a sequence that begins with squamous metaplasia and proceeds through atypical metaplasia to carcinoma in situ, and ultimately invasive carcinoma. The development from squamous metaplasia to invasive carcinoma in their work took 5-15 years. However, the Sloan-Kettering group has advanced another theory based on their study of nine occult cancers detected cytologically in the National Cancer Cooperative Study. The tumors were localized then resected, and multiple tissue sections of bronchi were examined. These researchers proposed that carcinoma begins as basal cell atypia without regard for either preexisting squamous metaplasia or basal cell hyperplasia (25). Therefore, the exact nature of sequential development of human bronchogenic carcinoma remains somewhat unsettled.

In hamsters, tumor induction by benzo(a)pyrene has been demonstrated to proceed through squamous metaplasia of mucous cells to anaplasia and invasion by the metaplastic cells (26,27,32,34). There is strong ultrastructural evidence that this may also be the situation in man. Thus, another developmental theory has been proposed:

The early stage is the proliferation of mucous cells from basal cells, with late conversion of mucous cells to squamous cells with atypia and eventually malignant invasion (31,33).

Whatever the histogenetic sequence of bronchogenic carcinoma is, there is general agreement on the diagnostic criteria for exfoliated atypical cells in sputum. Squamous metaplasia is represented by groups of generally angular cells which are somewhat larger than bronchial basal cells and with acidophilic, frequently glassy, cytoplasm. With increasing degrees of atypical metaplasia, there are increased nuclear hyperchromasia, irregular nuclear shapes, irregular chromatin distribution and occasionally very dense nuclei. Nucleoli tend to occur in the more severe atypias. The cytoplasm is usually eosinophilic or orangeophilic (keratinized), more so than in non-atypical squamous metaplasia, but it may be basophilic. In the most advanced in situ atypia (carcinoma in situ), cells are more likely to occur singly. Again, the nuclei possess marked atypicalities and are markedly enlarged in proportion to the cytoplasm; however, the cells themselves may be quite small.

Cells of invasive squamous cell carcinoma occur singly for the most part and usually reveal considerable variation and irregularity in size and shape, even to the point of being bizarre. Abundant keratination is very common. Many cells will be degenerative or necrotic; in such an instance, the only clue in sputum to an invasive carcinoma is a streak of necrotic material containing outlines of degenerated anucleate cells with abnormal shapes.

Squamous cell carcinoma has generally been regarded as the most common type of lung cancer; however, there is an increasing awareness of the frequency of adenosquamous carcinoma—up to as much as 50% of the lung tumors (28-34). The ultrastructural study, which proposed the above sequence of events in the development of lung cancer, also demonstrated a combined adenosquamous carcinoma wherein the mucous cells retain some of their mucinous properties as they progress down the line (31-34). Then too, the mucinous cells may skip the squamous metaplasia stage and progress to pure adenocarcinoma, which appears to be increasing in incidence (33). This proposed sequence bears resemblance to Auerbach's finding in smoker's bronchi (24), although he did not develop a specific sequence pattern. Developmental sequences for adenosquamous carcinoma and pure adenocarcinoma as reflected in exfoliated cells in the human has not been demonstrated and will be an interesting challenge.

The other two major types of bronchogenic carcinoma are the large cell and small cell, undifferentiated carcinomas. Large cell undifferentiated carcinoma is the designation for a heterogeneous group of poorly differentiated tumors in the squamous, adeno and adenosquamous family. Ultrastructure frequently detects differentiating features, which allows us to re-classify such a tumor as a poorly differentiated squamous cell carcinoma. Therefore, the developmental scheme for large cell undifferentiated carcinoma is probably not significantly different from the one just discussed.

Small cell undifferentiated carcinoma—frequently referred to as oatcell carcinoma--has suffered through years of confusing terminology and subtyping; the situation now appears to be clearing up. The etiology of this tumor is unknown; although, a few such tumors were recognized in the smoking uranium miners and one has also developed in a hamster exposed to benzo(a)pyrene. There is strong evidence that many of these highly lethal tumors are actually more malignant variants of the less aggressive bronchial carcinoid, which has its early growth phase in the deep mucosa and submucosa. If such is the case, there may be little hope for the early detection of small cell tumors by exfoliative cytology.

When and how does one take clinical action on the finding of early or developing lung cancer? Several diagnostic problems must be recognized and seriously considered at this point. First, the difference in what is "severe atypia" and "carcinoma in situ" is usually a personal preference of the pathologist; the two may even be considered equal. Each condition represents serious bronchial epithelial disease and indicates the need for a definite management protocol. Less has been learned about the developmental sequence of lung cancer in contrast to cervical cancer, mainly because of the relative inaccessibility of the bronchi; systematic and comprehensive studies of the bronchi are inconvenient. However, the progression of developing carcinoma in both organs appears remarkably similar. Most uncertain is the time required for severe atypia in the lung to progress to invasive cancer. A few, long-term clinical observations of patients with untreated, severe, bronchial atypia have been made (23); these suggest that the progression may be a few years longer in the lung than in the cervix. Thus, once severe atypia or carcinoma in situ is diagnosed, the when and how of clinical management should be tempered by extenuating circumstances of the individual patient.

A second point to consider before beginning therapy is that the diagnosis of severe atypia in sputum is only preliminary. Fiber-optic bronchoscopy, bronchial brushing and biopsy are essential to localize the lesion. Furthermore, there may be more than one bronchial lesion, emphasizing the need for multiple and systematic bronchial study. One should also realize that a radiographic mass in a patient with severe atypia may be a benign, unrelated lesion.

And thirdly, severe atypia or malignant cells in sputum does not necessarily indicate a lesion in the lung unless lesions in the upper respiratory tract, mouth and pharnyx have been excluded.

In conclusion, cytodiagnosis of sputum, when properly carried out, is readily applicable to industrial screening. In the hands of skillful staff, it is the most reliable and only feasible method for the detection of early curable lung cancer.

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OCCUPATIONAL CANCER

Early Diagnosis of Lung Cancer

William Weiss, MD

INTRODUCTION

If early diagnosis of a disease is taken to mean that an incurable illness is converted to a curable one, then it is clear that more than 90% of the people who develop lung cancer are not diagnosed early. Even chest surgeons have stopped exhorting their colleagues to find this disease earlier, for our current methods of detecting the disease as well as the type of host who is prone to develop this dread malignancy are inadequate.

The clinical diagnostic methods that are available include the time-honored history and physical examination, the chest roentgenogram, cytologic study of sputum, bronchoscopy, biopsy of accessible lesions (including the method of mediastinoscopy) and thoracotomy. I have listed these in increasing order of technologic sophistication. With the exception of the least expensive chest film and cytologic examination of sputum, these methods also are listed in order of increasing cost.

If we wait for the patient to seek medical attention, his 5-year cure rate for lung cancer—from experience—will be less than 10%. Therefore, efforts have been directed at screening large populations in order to diagnose a larger proportion of cases early enough to improve the cure rate.

SCREENING FOR LUNG CANCER

A useful screening procedure should be simple, inexpensive, convenient, reliable, sensitive and specific. In addition, it should provide a significant yield of curable disease, improve the cure rate and have a favorable cost-to-benefit ratio. The only procedure that has been adequately and repeatedly tested for lung cancer so far is the semiannual chest roentgenogram (1-4), beginning with the Philadelphia Pulmonary Neoplasm Research Project (PNRP) (1). The semiannual chest film is simple, inexpensive, convenient and fairly reliable. While its specificity is good, sensitivity is low, the yield of curable disease is poor and it provides very little improvement in the cure rate. Finally, the cost-to-benefit ratio does not seem to be favorable, but this is a societal rather than scientific judgment.

Semiannual questionnaires about respiratory symptoms were evaluated in the PNRP; the unpublished data have shown that symptoms are insensitive, nonspecific or both. Semiannual sputum cytologic examinations have been studied in only one uncontrolled investigation (4); the results were bad. Controlled studies of cytologic screening at 4-month intervals are in progress (5-6). Although it is too early to assess them, a presentation by Robert Fontana, MD on the Mayo Lung Project (from the State-of-the-Art Conference on Screening for Lung Cancer, sponsored by the National Cancer

Institute in Reston, Virginia, September, 1978) indicates no significant impact on the lung cancer mortality rate. Since sputum cytologic examinations at 4-month intervals cannot presently be evaluated, this discussion will be limited to an assessment of the semiannual chest film and the reasons for its failure.

EFFICACY OF THE SEMIANNUAL CHEST FILM

Estimates of sensitivity and specificity of this procedure have been made in two investigations. The American Cancer Society-Veterans Administration study (4) of approximately 14,000 older men in domiciliary homes, estimated the sensitivity of the chest x-ray to be 42% and specificity at 98%. In the PNRP, unpublished data indicate a sensitivity of 61% in 121 cases of lung cancer (72% in 67 complaint cases) and specificity of 96%; this study took a systematic sample of 97 men from among 5,906 who did not develop lung cancer in the 10-year observation period. These figures show that sensitivity is not very good and, what is worse, the ratio of false positives to true positives is about 3:1 or higher; thus, many men who do not have lung cancer are subjected to clinical evaluation and its attendant anxiety.

The ultimate test of a screening procedure depends on how it affects the cure rate and the population mortality rate; a controlled trial is required in which a screened population is compared with an unscreened, radomized population of similar characteristics. Only Brett (2) has evaluated the semiannual chest film with a controlled trial and it could be criticized because the two populations were not obtained by randomization. Be that as it may, the 5-year survival rate of men with lung cancer in his screened group was 15% vs 6% in the control group (Table 1), a difference which was not statistically significant at the 0.05 level.

TABLE 1. - Results of a 3-year Study of Semiannual Chest X-ray Screening Among Industrial Workers Aged 40-65 in NW London (2)

Characteristic	Screened	Unscreened
Population size	29,723	25,311
No. developed lung cancer	101	77
Lung cancers resected	44%	29%
Cases with 5-yr survival	15%*	6%*
Lung cancer mortality rate (per 1,000/yr)	0.7	0.8

* chi-square, Yates' correction = 2.28, df=1,"p" less than 0.05

Even if the difference were statistically significant, it would have to be interpreted in the light of the "lead-time" afforded by screening. Lead-time is the interval between the time the cancer is detected by the screen and when it would have been found without screening. If this interval becomes part of the survival time, then the screened cases will appear to have better results even though death has not been deferred. To

evaluate the contribution of lead-time to the survival rate, we need to know the length of the lead-time. There are no good data, yet some unpublished data from the PNRP suggest that the median lead-time is more than one year and it varies tremendously according to the growth rate of the individual cancer.

In view of the problem with lead-time and other problems regarding the type of disease uncovered by screening—which might result in the inclusion of a disproportionate percentage of favorable cases—the screening procedure should have a significant impact on the population mortality rate for lung cancer if it is to be considered effective. In Brett's controlled study, there was little impact on the annual mortality rate: 0.7/1,000 in the screened group vs 0.8/1,000 in the control group. This poor result is supported by equally poor figures in the other three studies; therefore, it can be concluded that semiannual chest x-rays have very little value in screening for lung cancer.

There are five reasons for the failure of the semiannual chest film: the nature of lung cancer, the nature of the host, the peculiarities of the patient with lung cancer, the nature of current medical practice and the multifocal nature of lung cancer.

The nature of lung cancer — Experience shows that this cancer is a particularly vicious tumor. Most cases have a short volume doubling time (ie, rapid growth rate) as shown in Table 2

TABLE 2 - Distribution of Tumor Volume Doubling Times of Lung Cancers Appearing as Round Lesions on Serial Chest Films (7)

Doubling time, months	Number (%)
0-	1 (2)
1-	5 (0)
2-	9 (17)
3-	7 (13)
4-	8 (15)
5-	7 (13)
6-	4 (8)
7-	3 (6)
8-	2 (4)
9-	2 (4)
10-	2 (4)
11-	1 (2)
12+	1 (2)
Total	52 (100)

and it metastasizes early (Table 3).

TABLE 3 - Prevalence of Metastases at Autopsy by Interval From Resection to Death in 125 Men with Resected Lung Cancer (8)

Interval, months	No. of cases	No. of metastases (%)
1	44	16 (44)
2-5	27	18 (67)
6-11	20	17 (85)
12+	34	28 (82)
Total	125	79 (63)

Doubling time is inversely related to survival (Table 4).

TABLE 4 - Survival By Tumor Doubling Time in 20 Men with Round Lung Cancers Subjected to Resection (9)

Doubling time	No. of cases	Median survival, months
0.9-2.9 mos.	7	32
3.0-6.9	7	40
7.0-10.0	6	71

Furthermore, lung cancers usually are not detected until they are at least one centimeter in diameter and often larger (7). A majority of lung cancers whose growth rates have been measured have doubling times of less than 6 months (Table 2); therefore, during a 6-month interval between screenings, most tumors double in volume from one to more than six times, and a cancer that is missed at one examination may be quite large at the next (10). Studies of rates of cancer growth suggest that by the time a tumor reaches a diameter of 1 cm, the tumor has passed through the first two-thirds to three-fourths of its lifetime (7,9,10).

The nature of the host — Noncompliance with procedure is a serious obstacle to the success of any screening program and man is not noted for his response to such efforts. In the PNRP we found that the average probability of a patient having two consecutive semiannual chest films was 57%; at the end of 10 years only 18.5% of those who were still eligible (ie, those who were still alive and in contact with the project) had made early scheduled visits (11). And worse, the risk of lung cancer was higher in noncompliant men than in compliant ones (Table 5) (12), a phenomenon which was not limited to the risk of lung cancer but involved the risk of death regardless of cause.

TABLE 5 - Probability of Older Men Developing Lung Cancer in the Second Through Tenth Years of Observation, by Degree of Compliance in the First Year (12).

Compliance*	Number	(%)	Developed lung cancer	(% prob.**)
yes	4,302	(73)	73	(1.98)
no	1,562	(27)	45	(3.48)
Total	5,864	(100)	118	(2.36)

* made 2nd semiannual visit in first year
** computed by actuarial method; adjusted for age, race and smoking habits at start of observation ("p" less than 0.01)

The peculiarities of the patient with lung cancer — People who develop this disease tend to be elderly. The median age of men with this disease in the PNRP was 64 and this was not attributable to any maldistribution by age of the 6,027 men in the project; indeed, the study population tended to be slightly younger than the male population of Philadelphia at the time our group was assembled (13).

Inasmuch as 25% of the lung cancer cases were aged 70 or over, we have learned to be cautious about recommending major chest surgery in such men because the postoperative risk exceeded the 5-year cure rate of such individuals in Philadelphia teaching hospitals during the time of the project (Table 6) (14).

TABLE 6 - Operative Death and 5-year Survival Rates Among 968 Men Operated on for Lung Cancer* by Age in Philadelphia Teaching Hospitals, 1956-65 (14)

Age	Distribution	Operative deaths**	5-year survival
50	15.6%	9.3%	18.7%
50-59	35.9	9.5	14.4
60-69	38.4	12.9	13.7
70+	10.1	19.4	12.2
Total	100.0%	11.8%	14.6%

* includes thoractomies with and without resections
** within 30 days

In addition, many patients with lung cancer are poor risks for thoracic surgery because

they have other serious diseases associated with advanced age or smoking; particularly, chronic obstructive lung disease. We have noted that the risk of lung cancer is also higher in men with chronic cough than in those without this symptom of chronic obstructive lung disease (Table 7) (12).

TABLE 7 - Probability of Older Men Developing Lung Cancer in 10 Years by Presence or Absence of Chronic Cough at the Start of Observation (12)

Chronic cough	Number (%)	Developed lung cancer* (%)
yes	1,756 (29)	58 (2.98)
no	4,271 (71)	63 (2.05)
Total	6,027 (100)	121 (2.41)

* computed by actuarial method and adjusted for age, race and smoking habits at start of observation ("p" less than 0.05)

The nature of current medical practice — Not all physicians who are charged with the care of patients with lung cancer are equipped to provide the best management. In the PNRP, delay was attributable to the patient's physician in 6% of the cases.

The multifocal nature of lung cancer — Even after we have successfully treated a small proportion of people with lung cancer, there are still some who will develop a second lung cancer; especially, those who continue to smoke. The prognosis for them is not as good the second time (15). The explanation for this propensity for a second tumor is readily apparent from Auerbach's extensive studies of the bronchial mucosa (16) and is to be expected a priori since cigarette smoke and industrial carcinogens bathe the mucosa of the entire bronchial tree.

CONCLUSIONS

While the periodic chest roentgenogram has many of the characteristics of a good screening instrument, it is not adequate to reduce the mortality rate of bronchogenic carcinoma in populations at risk. Some of this failure is due to inadequacy of the screening method itself, but failure is due as well to the character of the disease, the nature of the host, current medical practice and available therapy. If screening is to have an impact on this disease in the global population at risk, it must deal with numerous problems that are unrelated to the particular screening method.

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OCCUPATIONAL CANCER

Diagnosis of Paranasal Sinus Carcinoma

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Paranasal sinus malignancies account for approximately 3% of all cancers that originate in the upper respiratory and digestive tracts and less than 1% of all malignancies in the United States (1). Partly because of their rarity, these cancers present serious difficulties in diagnosis and treatment, and they call for carefully coordinated efforts among primary care physicians, dentists, surgeons, radiologists and radiotherapists. In addition, paranasal sinus—cancer along with lung and certain other cancers--has been shown to be associated with certain occupations, particularly those involving wood, nickel and chromium.

The troublesome facts are these: Less than 40% of the patients with advanced sinus cancer will survive five years, nearly half will die within two years of their disease (2). In the most advanced stage, less than 10% will live beyond five years and most of these will succumb within 18 months (3). As is true with most malignancies, the earlier stages of paranasal sinus cancer are more curable; however, less than one third of patients with sinus cancer appear for treatment at the earlier stages (2-7). Thirdly, the relatively low incidence of the disease makes identification of the etiologic factors--hence prevention of the disease—very difficult.

Earlier diagnosis seems most likely to improve survival for those with the disease, though better treatment and effective preventive measures are needed if maximal control are to be achieved. New imaging techniques employing radionuclides, ultrasound, computerized tomography and fiber-optics improve the examination of the sinuses; while better health care delivery—particularly in rural areas—and closer communication between primary care physicians and medical centers afford additional possibilities for earlier detection of sinus cancer.

ANATOMY

The paranasal sinuses occupy the space that develops during childhood as the brain, eyes, and food and air passages move away from one another to produce the distinctly adult facial configuration. Each individual sinus is an air space within bone lined by ciliated respiratory epithelium and communicating with the upper air passages by a single small opening. Air exchange via the opening takes place by passive diffusion; however, mucus carrying surface debris and waste products is swept by the respiratory cilia in a spiral path toward the sinus ostium. Disruption of the ciliary action by infection, allergy or trauma leads to stasis of the mucous blanket and the entrapped foreign material may play a role in the malignant transformation of the underlying mucosa.

There are four sinus groups, usually paired: maxillary, frontal, sphenoid and ethmoid; the last one consists of eight to ten separate small sinuses on each side of the nose

between the air passages and the orbit.

The maxillary sinuses are nearly pyramidal in shape with their bases forming the lateral walls of the nose and the apices extending into the zygomatic bone. The superior and posterior aspects of the bases are directly adjacent to the ethmoid sinuses. The remaining three sides of the pyramids are formed by thin bone facing the orbit, the face and the infra-temporal fossa and base of the skull. The lowest edges of the pyramids are the upper alveolar ridges of the oral cavity which support the posterior maxillary teeth.

The ethmoid sinuses resemble a number of balloons placed in rectangular boxes and which are inflated through stems projecting through the medial walls of the boxes that face the nasal cavity on either side. The remaining walls face the orbit (lateral), anterior cranial fossa and frontal sinuses (superior), sphenoid sinuses (posterior), maxillary sinuses (inferior-lateral) and external nose (anterior).

The frontal sinuses are actually an extension of the ethmoid system into the frontal bone and do not always develop. When present, they are tightly sandwiched between the forehead and the anterior cranial fossa.

The sphenoid sinuses are often asymmetrical and occupy the central portion of the sphenoid bone above and behind the nasopharynx and beneath the sella turcica. Intimately associated with their lateral walls are the optic and maxillary nerves and the nerve of the pterygoid canal, the carotid artery and the cavernous sinuses.

The maxillary sinus is the largest and is most frequently the primary site of a malignant change. The North Carolina Memorial Hospital Cancer Data Base contains 73 patients with paranasal sinus cancer seen since 1952; 62 (85%) of these tumors are believed to have originated in the maxillary sinus. Ethmoid sinus cancer runs a distant second, occurring in 10 patients (14%); primary frontal and sphenoid tumors are extremely rare, frontal sinus cancer occurring once only and sphenoid sinus cancer not at all in our series. Secondary involvement of these sinuses by tumor is much more likely to be the case to their close proximity to the maxillary and ethmoid sinuses and to the nasopharynx.

SIGNS/SYMPTOMS

The signs and symptoms of paranasal sinus cancers relate directly to their anatomical location. Chaudhry et al (8) have classified the symptoms of maxillary cancer into oral, nasal, ocular, facial and neurological groups (Table 1). In our series of maxillary cancers (Table 2), facial symptoms predominated, occurring in 76% of cases and representing the initial complaint in 44%. The most frequent symptoms were swelling and pain localized to the cheek, the latter more likely to be the first symptom. A few patients also experienced facial numbness and/or paresthesias during the onset of the disease.

Nasal symptoms were also important in signalling the presence of maxillary cancer, occurring in 73% of the cases and in 36% as the first sign of disease. Nasal obstruction was the predominant initial symptom (25%), though epistaxis eventually occurred in an equal number before the diagnosis was established. Oral symptoms occurred in 48%, with either oral pain or a painless oral mass as the most frequent initial sign of disease. A few patients initially noticed a bloody or foul oral discharge. Trismus, loose teeth and fistula formation with the maxillary antrum were never first signs; trismus

generally signified far advanced disease.

Ocular symptoms occurred in 31% of the maxillary cancers and represented the first sign of disease in 14%. The predominant complaints were orbital swelling and/or proptosis, while some patients complained of orbital pain or paresthesias, visual changes and epiphora. Neurological symptoms, aside from the paresthesias already mentioned, did not play a significant role. Five patients (8%) with maxillary cancer had a neck mass as the first sign of disease. Severe weight loss--never an initial event--occurred in 20% by the time the diagnosis was made.

In 80% of the maxillary cancer cases, the following complaints were part of the initial complex of symptoms: nasal obstruction, facial pain, facial swelling, oral pain, epistaxis and orbital swelling/proptosis. The onset of cancer was heralded by only one of these complaints in 60% of the cases. Due to the small number of patients with ethmoid cancer, it is difficult to generalize accurately about presenting symptoms (Table 3). Epistaxis was part of the initial symptom complex in three of the ten and the only sign of disease in two. Facial swelling was the sole sign of the onset of disease in one patient, though pain subsequently developed prior to diagnosis. In another case the sole sign of disease was facial pain associated with numbness of the face.

DIAGNOSIS

The diagnosis of paranasal sinus cancer depends upon:

> the presentation of the symptomatic patient to a suitable medical or dental facility, where
>
> the diagnosis of cancer as the probable cause of symptoms can be diagnosed and the disease localized to a discrete anatomical area and
>
> appropriate tissue can be obtained for histological confirmation.

Most recent advances in diagnostic ability differentiate the malignant process from benign disease with similar symptoms and localize the disease for biopsy. The basis of good diagnosis, however, still rests on taking a careful history and the performance of a thorough physical examination, including inspection of the nasal, oral and pharyngeal passages, a cranial nerve examination and palpation of the neck for possible metastatic disease. Plain film radiographs of the sinuses in five views (ie, Caldwell, Waters, exaggerated Waters, lateral and submental-vertex) should also be taken, particularly if transillumination of the sinuses reveals any opacity or asymmetry.

The oldest "new" technique now in widespread use is a telescopic inspection of the upper airway passages. Requiring only topical anesthesia, visual examination of the interior of the nose and nasopharynx can be done with a minimum of equipment and time in the out-patient clinic. Fiberoptics have greatly improved the illumination for telescopic examination, and coupled with the newer quartz rod instruments, an image is obtained that is suitable for photographic documentation.

A telescopic inspection technique for the interior of the maxillary sinus, coupled with biopsy and/or aspiration of fluid for cytologic examination, has been described by Willemot (9). Under local anesthesia, the sinus is approached through a small puncture and any suspicious areas can be biopsied under direct vision. In most cases, the telescope is introduced through the inferior nasal meatus, while the biopsy instrument

passes through a separate puncture in the canine fossa.

The most recent technical advances involve indirect examination of the sinuses by "imaging" techniques of the radiologist. Hypocycloidal tomography and, more recently, computerized tomography provide detailed images of the bony walls and soft tissue compartments surrounding the sinuses, and an accurate delineation of the extent of disease.

Gallium-67 scanning has been reported by Higashi et al (10) to be of use in patients in whom the physical and radiographic findings are equivocal for carcinoma vs chronic sinusitis. The technique requires a 2mCi injection of gallium-67 citrate with scanning in the anterior and lateral projections 48 hours later. Of 25 patients examined, all of whom had equivocal physical and plain radiographic findings, 18 had carcinoma that was confirmed by a subsequent biopsy; all 18 had positive gallium scans. Of the remaining seven patients, who were shown later to have chronic sinusitis, only two had equivocal or positive scans.

Another isotope technique has been reported by Perrin et al (11) using labelled bleomycin, an antineoplastic agent with an affinity for malignant epidermoid cells. Since the majority of paranasal sinus cancers are of this cell type, the technique may theoretically localize not only the primary tumor but also occult regional nodal metastases. However, the labelled drug is expensive to produce and of limited availability, and it has had no systematic trial in these cancers.

Beck and Mann (12) have reported the use of ultrasound scanning to differentiate chronic sinusitis from maxillary cancer in more than 2,000 patients. They used both unidimensional and bidimensional scanning techniques, the latter supplementing the former in doubtful cases. Differentiation between the normal air-containing sinus and a sinus containing pathological secretions or tumor had a margin of error of less than 5%; thus, ultrasound was most useful in cases with an equivocal radiographic appearance. Ultrasonography could also distinguish between maxillary solid tumors and fluid secretions or fluid-filled cysts within the sinus, but benign conditions of a more solid nature—such as an organizing hematoma—appeared very similar to a tumor. The greatest usefulness for the technique, according to Beck et al, was to distinguish the air-filled sinus (which appears opacified on conventional plain radiography) from the sinus filled with tumor or other solid material and having the same radiographic appearance.

If paranasal sinus carcinoma is to be diagnosed earlier, specific levels of potential failure in the diagnostic process must be identified and their roles in delaying diagnosis established. Three levels conceivably have the potential for failure within our institutional referral system:

> the patient fails to seek professional help soon after the onset of the initial symptoms;
>
> the physician, dentist or nurse who first sees the patient fails to make the probable diagnosis of cancer;
>
> also, specialists fail to identify the cancer, including failure of the pathologist to make an accurate histological diagnosis.

To illustrate failure at the first level, we investigated the duration of symptoms prior

to definitive diagnosis for our patients: The median duration of symptoms was five months, while only 30% were diagnosed within two months of symptom onset; delays of a year or more were recorded for 23%. Unfortunately, since the date of the initial visit at the primary care level was only rarely recorded, we could not determine that part of the delay was caused by the patient's inability or unwillingness to seek medical help.

Some of the data in our series appears to suggest the primary care level as a significant point of failure. In nearly half (47%) of the cases that were ultimately referred to our hospital, the tumor was overlooked and the patient was treated in a symptomatic fashion. Again, without the date of the initial visit, it is impossible to determine how much of a delay symptomatic therapy actually caused. However, it was noted that none of the six patients with the earliest stage of disease at the time of diagnosis had received symptomatic therapy.

Then too, most patients (72%) presenting for special diagnostic evaluation required only a simple nasal, oral or transcutaneous biopsy to confirm the diagnosis of cancer. These patients, judging from the mode of biopsy, had gross disease that was within relatively easy access to the examiner. These same patients could have been diagnosed earlier if specialized diagnostic techniques had been used soon after the onset of symptoms or when the disease was in a more occult form.

These observations do not exclude failure at the level of special diagnosis. However, since only a small number of patients (15) arrived at that level with relatively hidden disease—ie, biopsy only by means of a Caldwell-Luc antrostomy—it could be said that the potential for failure at this level had never really been tested.

Only one failure attributable to an error in histological diagnosis could be identified. That patient had had a maxillary cyst removed four years prior to admission to our institution; on re-examination of the specimen, a small focus of carcinoma in the cyst wall was identified.

It might be said that a very obvious failure had occurred at the special diagnostic level (level 3) in that the tools and skills for early diagnosis were not available when they were most needed. Those of us with those tools and skills must acknowledge responsibility if they are not used.

In our situation, then, the primary task seems to be the dissemination of certain technical skills as well as knowledge. Clear identification of primary symptom complexes, improvement in routine physical examination techniques and the early use of diagnostic radiographs would all contribute to earlier detection, as would greater accessibility to sophisticated diagnostic tools. A program that would place such techniques that are proven to be useful—eliminating those that are prohibitively expensive or impractical—in the hands of local health care deliverers would move the special diagnostic level closer to the point where it could do the most good.

Such efforts must also be complemented by much broader approaches to the overall problem; for example,

improved patient education through such agencies as the American Cancer Society,

accessible primary health care (a major need in any setting with a large, isolated rural population),

improved communication between primary care facilities and the large diagnostic and treatment centers and

improved data collection through the auspices of a statewide population based cancer registry.

In summary, the earlier diagnosis of paranasal sinus cancer is a practical goal that should provide improved patient survival and lessened morbidity. Close cooperation among a variety of health professionals and others dedicated to improving health care at several levels of involvement will be required. Those of us who possess special knowledge of the disease should not place sole responsibility for late diagnosis on the patient or the local practitioner. In fact, considering the rarity of the disease, it is likely that we are the only ones who are aware of the specific problems of diagnosis; certainly we are the only ones who possess the information that is required to initiate solutions.

TABLE 1 - Symptoms of Maxillary Cancer, Classification

Oral	
	Mass lesion or ulcer
	Dental pain
	Bloody or foul discharge
	Loose teeth
	Trismus
Nasal	
	Airway obstruction
	Epistaxis
	Blood-streaked or foul discharge
Ocular	
	Swelling/proptosis
	Pain/paresthesias
	Change in vision
	Epiphora
Facial	
	Swelling
	Numbness of the cheek
Neurological	
	Facial nerve palsy
	Meningeal irritation

TABLE 2 - Symptoms of Maxillary Cancer,
Time of Occurrence (N=59)

Facial swelling	34% at any time	19% initially
Facial pain	31	20
Nasal obstruction	31	25
Epistaxis	25	8
Orbital swelling/proptosis	17	8
Oral mass or ulcer	17	7
Dental pain	14	10
Cheek numbness	8	5
Oral discharge	7	7
Nasal discharge	7	2
Change in vision	7	2
Trismus	5	0
Loose teeth	3	0
Epiphora	1	0

TABLE 3 - Symptoms of Ethmoid Cancer, Time of Occurrence (N=10)

Epistaxis	40% at any time	30% initially
Nasal discharge	40	30
Nasal obstruction	20	20
Facial pain	20	20
Facial swelling	20	20
Facial numbness	20	20
Orbital pain or paresthesias	10	10
Change in vision	10	0

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SMALL PLANTS AND THEIR MEDICAL PROBLEMS— THE FURNITURE INDUSTRY

Respiratory Health Effects of Isocyanates

Hans Weill, MD

Occupational asthma has become well-recognized in association with organic dust exposure. There is now an interest in the capability of simple chemicals to induce bronchospasm in a susceptible portion of the work population.

A little more than five years ago it was our good fortune to study an industrial population both before exposure and in a follow-up five years after exposure. We were called in prior to the opening of a new plant that was to manufacture toluene diisocyanate. There was a genuine effort by the medical department of the plant to exclude individuals having a history of asthma or allergy; but, as you will see, that is very difficult—probably impossible—to do clinically. Nonetheless, we suspected that there were some people who would become intolerant; we wanted to find out from those people what causes this intolerance and what might we do to deal with the mechanism. We also hoped to address the question concerning a general effect of TDI on respiratory health; in other words, is there an irritant effect on the airways that can be associated with early development of bronchitis or other airways' problems quite apart from susceptibility or sensitization? We borrowed from the United Kingdom their new methodology for measuring airborne concentrations of TDI vapor. It's a physico-chemical method wherein a chemically impregnated tape-cassette unit permits 8-hour continuous monitoring of TDI vapor.

As one might anticipate, about 5% of the exposed population did indeed become intolerant of TDI. This percentage is consistent with the other limited data in the literature. Some of these people were smokers. Some had an atopic history, some had positive skin tests to the ordinary environmental irritants, some had a known major exposure that had been recognized a week or so earlier, some developed symptoms very shortly after an exposure and some took months. Very few additional people out of a total of 12 have become susceptible in this cohort over the 5-year period. Most of the people develop their symptoms in the first year of exposure. In many cases the clinical picture of susceptibility to sensitization was not entirely convincing or clear; thus, we performed inhalation provocative challenge testing, first using very low doses 0.005 ppm and then going to doses of 0.01 and 0.02 ppm. Contrary to some investigators, we never exposed anyone to concentrations either above the threshold limit value of 0.02 ppm or above those levels that were actually found in the plant. In the population that was believed to be active, we got positive results and usually one of several patterns emerged. Either they had an immediate drop in ventilatory capacity—ie, expiratory airway flow—with prompt reversibility, there was a late response (within 4, 6 or 8 hours) or there might be a gradual decline in ventilatory capacity. All occupational asthmas that I'm aware of characteristically have a dual response—ie, an immediate drop in flow and then a late drop; usually the late drop is slow to emerge. In three individuals there seemed to be a dose-response relationship. As in other types of

occupational asthma, these persons' reactions were blocked by the pre-treatment with cromolyn sodium. That doesn't mean that reactive individuals should be kept in a TDI environment, having to take this medication everyday, but at least there is an available remedy for the occasional problem and it's a good thing to know.

Usually substances like TDI don't cause IgE-mediated, immediate type, reagin-mediated asthma unless the substance binds with protein. We did bind TDI with human serum albumin and employed it on our population. The RAST test, used to measure specific IgE, indicated that IgE antibodies were not present in significant quantity. Cells were not stimulated normally by isoproterenol to release cyclic AMP—which has a bronchodilator effect—in the presence of TDI. TDI at certain concentrations acts as a partial agonist on lymphocytes to stimulate the release of cyclic AMP; at lower concentrations it can block the release. This was the first evidence that something may be awry in the adrenergic function of cells when TDI is present. Persons who had a good clinical picture and were positive on challenge with TDI differed from controls in their responsiveness to methacholine, a nonspecific bronchoconstrictor. Something seems to happen to the cells of TDI-reactors in that there is a flattened dose-response relationship to release of cyclic AMP by the materials that are known to stimulate this release.

Recently, Dr. Yves Alarie at the University of Pittsburgh has developed what he believes is a suitable in vitro test procedure for TDI sensitivity using a normal isocyanate (TMI) together with the RAST test. He claims a rather high specificity for the test, but Dr. Brian Butcher (of Tulane) has found that only about 15% of his reactors had a positive RAST using Alarie's allergen. Inasmuch as we were not able to confirm Alarie's work, we are rather uncertain about the possibility of this test.

A 5-year longitudinal study dealing with the epidemiology, dose vs biologic response (measured serially with lung function), questionnaires, etc, has been completed and the final report will be available shortly from NIOSH. Longitudinal studies such as this are going to be conducted more frequently as various populations are studied over the course of time.

We have had an enviable opportunity in working with a "virgin" population, one that could be assessesd prior to TDI exposure as well as over a period of time subsequent to exposure. There are some problems in any longitudinal study; the analytical part of our study was difficult, but we are convinced that the data are good and valid, and they provide some insight into the longitudinal course of workers exposed in this chemical setting. TDI was certainly not the only chemical produced or airborne in the work environment, yet we feel reasonably sure that the disease symptoms were TDI-related.

Throughout the 5-year period of the study, TDI concentrations fluctuated; at times they were higher than the current TLV for short periods. During a plant or process overhaul, exposures were particularly likely to be elevated. It's important to recognize that TDI-intolerant people shouldn't be in such areas during these episodes. The exposures seemed to have no systematic trend but had a random variation.

The annual declines in FEV_1, FEV% (ie, the ratio) and the FEV midflow ($FEV_{25/75}$) are significantly related to TDI dose after controlling for smoking and atopic status. Dose is measured either by cumulative exposure or according to the exposure time spent above a certain peak level. In both instances, those in the higher exposure groups had a significantly greater decline. The FEV_1 annual decline and FEV% for the higher exposure category was not significantly different from predicted annual declines for

members of the general population. They are, however, significantly greater than the annual declines in the lower exposure groups. Both the $FEV_{25/75}$ and the FEV_{50} were significantly greater than expected in both exposure categories. This is not an exposure-related effect but was found in the total chemical manufacturing cohort; these values were higher annual changes if compared to cross-sectional predicted data. The diffusion constant was greater than expected, but there was a negative correlation that was very hard to explain. TDI dose, measured either cumulatively or at peak exposures, gave the same thing in terms of correlation with lung function change. FEV_1, FEC, RV and RV_2 showed changes that were significantly related to smoking. The prevalence of both bronchitis and dyspnea increased greater in the high exposure (cumulative) group than in the low groups; these differences, however, were not statistically significant.

Neither atopy nor smoking served to identify persons who might be at high risk of developing TDI sensitivity. Some TDI reactors failed to attain pre-exposure or pre-sensitization values (ie, FEV_1, $FEV_{25/75}$) despite their transfer to other areas in the chemical complex. Every effort was made to put them as far away from TDI as possible, but it is difficult to remain upwind of all emissions in a complex chemical plant. There is also persuasive evidence that some people have the clinical picture of sensitization but without a positive reaction to inhalation provocative testing.

SMALL PLANTS AND THEIR MEDICAL PROBLEMS— THE FURNITURE INDUSTRY

The Environmental Problems of Urea-Formaldehyde Structures— Formaldehyde Exposure In Mobile Homes

Peter A. Breysse

Over the past few years, the Department of Environmental Health, School of Public Health and Community Medicine of the University of Washington has been receiving an increasing number of complaints of illness from persons who reside in mobile homes; the problem is also appearing to a lesser extent in conventional homes. Our investigations have pointed to atmospheric concentrations of formaldehyde as the most likely cause of these complaints.

Formaldehyde is utilized in the manufacture of a variety of commercial products, the most significant of these involves the production of phenolic, melamine and urea formaldehyde resins (1). Formaldehyde is also used in agriculture, for chemical analysis, in concrete and plaster, in cosmetics and deodorants, in disinfectants and fumigants, in dyes, in hydrocarbon products for leather tanning, in paper manufacture, in photography, in solvents and plasticizers for rubber production, in starch, in wood, in textiles and in embalming fluid. It is also a product of combustion found in automotive exhaust and in cigarette smoke.

TOXICITY

Recently, three important documents have been published that deal with the health effects of formaldehyde (1-3). Table 1—taken from the NIOSH criteria document—summarizes the human responses to exposures of less than 3 ppm of HCHO in the ambient air.

TABLE 1 -- Dose-Response Relationship Following Human Exposure to Airborne Formaldehyde (below 3 ppm)

Concentration	Exposure	Number	Responses
0.3-2.7 ppm	8 hr/d	Many	Annoying odor, constant prickling irritation of the mucous membranes, disturbed sleep, thirst, heavy tearing (odor subsided during day, but returned at start of next shift)
0.9-2.7	hrs	Many	Tearing of eyes and irritation of nasal passages and throat (irritant effects were greatest at very beginning of workday and after lunch)
0.9-1.6	8 hr/d	2	Itching eyes, dry and sore throats, disturbed sleep, and unusual thirst upon awakening in the morning
1.4	mins	12	Eye sensitivity to light lowered in unacclimated group
1.0	mins	Many	Increased worker complaints
0.8	mins	12	Altered functional state of cerebral cortex
0.8	daily	?	Equilibrium and olfactory sensation shifts; irritation of upper respiratory tract and eyes in most sensitive individuals; enhancement of alpha-rhythms
0.3-0.5	5 min	12	Increased blink rate, rhythms proportional to formaldehyde concentration
0.05-0.5	5 min	12	Eye irritation range in unacclimated group
0.13-0.45	?	Many	Complaints of temporary eye and upper respiratory tract irritation

A report prepared for the Environmental Protection Agency (1) details the known toxicity of formaldehyde to humans and other mammals:

Toxicity to Humans

Epidemiology

Non-lethal doses of formaldehyde vapors generally irritate the mucous membranes of the eyes and upper respiratory tract. Skin irritation can occur in sensitive individuals. Both severity of irritation and types of symptom relate to formaldeyde concentration as well as the individual's sensitivity.

Toxicity to Mammals

Subacute/chronic Toxicity

Some long-term exposure studies suggest definite non-physiological changes, including slight variations in vitamin C metabolism and changes in neurons.

Concentrations below 1 ppm may result in biochemical and tissue changes in animals even though no outward signs of illness are apparent.

Teratogenicity and Mutagenicity

Present data do not adequately demonstrate that formaldehyde is teratogenic or mutagenic in animals; however it is expected that some histological changes of unknown significance may occur to the embryo exposed to formaldehyde in utero.

Carcinogenicity

Animal data indicate that formaldehyde is unlikely to be a strong carcinogen. Bacterial strains for current tests, however, have shown formaldehyde to be a mutagen in a number of systems.

Behavior - Symptomology

Sublethal atmospheric concentrations of formaldehyde have elicited coughing, sneezing, eye irritation, salivation, slowed respiration and loss of appetite.

Possible Synergistic Effects

Guinea pigs exposed to a combination of formaldehyde and sodium chloride aerosol showed a response that was greater than that for formaldehyde alone. Aerosol inhalation in the absence of formaldehyde evoked no response.

Formaldehyde and a number of other aldehydes are considered to be important constituents of photochemical smog (3). Typical concentrations of both formaldehyde and higher aldehydes have been reported as high as 0.04 ppm.

Furthermore, the National Research Council (4) reports that peroxyacyl nitrate (PAN) and peroxybenzoyl nitrate (PBzN) (both photochemical oxidants) together with photochemically produced formaldehyde and acrolein are the primary eye irritants. NRC concluded that aldehyde exposure in Los Angeles has been high enough to cause non-disease effects.

The USDA's annoted bibliography (5) concerning formaldehyde in wood products indicated possible effects on human performance as reported by Freeman and Grendan.

Formaldehyde Emission - Particle Board - Plywood

Particle board and chipboard are formed by impregnating wood chips or sawdust with a synthetic resin, usually urea-formaldehyde, and subjecting the mixture to high pressure.

Plywood is produced by bonding various layers of wood veneer with a synthetic adhesive under increased temperature and pressure. More than 95% of the hardwood plywood production utilizes urea-formaldehyde as the bonding agent (6). In addition, some of the finishes that are applied to the plywood panels may also contain formaldehyde.

Formaldehyde emissions from UF-bonded chipboard and particle board stem from unreacted formaldehyde that remains in the product after manufacture, as well as from the subsequent breakdown of the urea-formaldehyde resin by their reaction with moisture and heat (7). Some gaseous formaldehyde escapes from plywood during its pressing; small amounts are, however, given off afterwards during subsequent storage, sanding, trimming, etc, of the material (8). The extent of emissions and degree of concentration build-up of formaldehyde from both particle board and plywood depend upon a number of factors; for example,

the amount of free formaldehyde remaining in the panels,

the volume of panels in an enclosed space relative to the volume of that space,

the area of exposed surface of the panels,

the temperature and humidity and rate of diffusion of formaldehyde from the panel and

the amount of ventilation available to the enclosed space.

Evidence that particle board and chipboard could give off formaldehyde gas came to light in March of 1961 (9) when a number of investigations were conducted in response to complaints of eye and upper respiratory irritation.

Then about five years ago, an investigation was prompted by an infant that experienced chronic irritation of the eyes and respiratory tract as soon as it was taken from the maternity ward to a mobile home. Formaldehyde concentrations of 0.76 ppm in the bedroom and 1.41 ppm in the bathroom were evident.

Later, a request for assistance was received from a man also living in a mobile home; he had been having irritation of the eyes and a general feeling of ill health, which symptoms abated when he left for a weekend and reappeared shortly after his return. Environmental samples collected on three different occasions indicated the following:

Date	Sample Location	Concn.
10-7-75	Kitchen	1.3 ppm
	Master bedroom	1.3
12-19-75	Living room	0.87
	Master bedroom	0.87
7-27-76	Kitchen	0.64
	Master bedroom	0.93

Recalling the past problems associated with formaldeyde emissions from particle board and plywood and with the rapidly increasing sales of mobile homes and recreation vehicles adding additional impetus, a more extensive investigation of this problem was begun.

Various methods of sampling and analysis for formaldehyde were reviewed and it was decided to utilize the chromotropic acid method recommended by NIOSH (2).

Samples were collected in a midget impringer containing 10 ml of distilled water at a sampling rate of 1 Lpm. Sampling times ranged from 35 to 60 minutes. In most mobile homes, two samples were collected—one in a bedroom and the other in the living room or kitchen. It should be mentioned that the NIOSH method recommended the use of two impringers in series since the collection efficiency of one impringer is approximately 80%. For this study only one impringer was used and no corrections were made in the results.

To date, 334 mobile homes in which one or more individuals have experienced health problems have been surveyed. Formaldehyde concentrations (Table 2) ranged from a high of 1.77 ppm down to 0.03 ppm. Of the 608 samples collected, 66% were between 0.1 and 0.49 ppm while 21% were 0.5 ppm or greater.

A total of 523 individuals, including 240 adult females, 184 adult males and 99 children (under 19 years of age) were affected. The most prevalent symptoms (Table 3) were eye (58% of the adults and 41% of the children) and throat (66% of the adults and 62% of the children) irritation. In addition, 33% of the children were reported to experience chronic cough or cold symptoms. Of particular interest are the relatively large numbers of persons reporting chronic headache and memory lapse or drowsiness and to a lesser extent chronic nausea. A smaller number of the elderly experienced chest pains and heart attacks after having moved into mobile homes.

TABLE 2 - Formaldehyde Concentration in Mobile Homes

Concentration	Kitchen	Bedroom	Other	Total
1.0 ppm	7	7	2	16
0.5 - 0.99	53	44	15	112
0.1 - 0.49	198	161	48	407
0.1	34	36	3	73
Total	292	248	68	608

TABLE 3 - Symptomatic Complaints

	Female (240)		Male (184)		Child (99)	
	No.	%	No.	%	No.	%
Irritation						
eyes	150	62	98	53	41	41
nose	18	8	14	8	11	11
throat	160	67	120	65	62	63
Chronic cold/cough	21	9	18	10	33	33
Difficult breathing	15	6	9	5	1	1
Chronic headache	103	43	65	35	16	16
Chronic nausea	25	10	13	7	5	5
Chronic sneezing	3	1	2	1	1	1
Skin rash	11	5	3	2	1	1
Allergies	7	3	4	2	5	5
Sinus problems	11	5	9	5	5	5
Emphysema	5	2	8	4	0	0
Chest pains	14	6	9	5	0	0
Heart trouble	2	1	3	2	0	0
Heart attack	4	2	3	2	0	0
Memory lapse or drowsiness	62	25	38	20	7	7

Of course, all of the above symptoms could very well result from other causes; however, all of these people indicated that they experienced relief whenever they left their homes on weekends or on vacations. Many of the respondents mentioned that they were being treated by their doctors without any significant relief; a few were accused of being hypochondriacs by either their doctors, spouses or associates. Those who had suffered over the long periods of time often developed acute mental depression.

There is no doubt that the presence of formaldehyde in living areas is an urgent medical concern. The problem may be more serious in mobile homes than conventional homes since the former utilize much more plywood and particle board per volume of space and they are of much tighter construction.

While the literature is vague about permanent health damage and long-term effects are unknown, one must keep in mind that sensitization to formaldehyde can lead to allergic reactions. For such persons, the effect or damage is permanent.

It also is important to consider the prolonged exposure of young children; especially newborn infants, for they spend most of their first year of life indoors. In addition, damage to the developing fetus by exposure of pregnant females deserves consideration.

Many of the people who live in mobile homes are retired and over sixty years of age. These individuals are highly susceptible to formaldehyde because they have an increased incidence of allergies, emphysema, bronchitis and heart disease. Also individuals who have just returned home after open heart surgery may have delayed recovery or complications if they are continously exposed to formaldehyde.

The only standards for formaldehyde to date are associated with the work place. The standard of 1967, for example, provides for a maximum peak concentration of 10 ppm for a total of no more than 30 minutes during an 8-hour work period, with an acceptable 8-hour time weighted average of 3 ppm. The American Conference of Governmental Industrial Hygienists (ACGIH) (11), on the other hand, has recommended an 8-hour ceiling limit of 2 ppm. Recently, NIOSH (2) has proposed that no employee be exposed to formaldehyde at a concentration greater than 1 ppm for any 30-minute sampling period.

On the community level, the American Industrial Hygiene Association (12) has recommended a maximum concentration of 0.1 ppm, which is similar to that adopted in July 1978 by the Netherlands (13).

Control of formaldehyde emissions is difficult. Absorbent chemicals and deodorants have been tried with little or no success, while attempts have been made to seal the plywood and particle board. Yet air samples collected before and after the treatments indicated a relatively insignificant lowering of the atmospheric formaldehyde levels. Attempts to "boil out" the formaldehyde by closing up a home for the weekend and turning up the heat failed to solve the problem. Washing down the walls with ammonia and the discharge of ozone into the interior have not provided any lasting relief. Flow-through ventilation without recirculation appears to be the only reasonable way to minimize indoor atmospheric concentration of formaldehyde in mobile homes; heating and cooling expenses would be increased.

But workplace standards cannot be used for the home environment. First of all, work standards are based on an 8-10 hour work day, 40-hour work week, while the public can be exposed up to 24 hours a day in their homes. Secondly, work standards deal with

adults who are in reasonably good health. The home environment, on the other hand, may contain newborn infants and young children, elderly people with respiratory diseases and heart trouble, pregnant females, hypersensitive and allergic individuals, and people with various other kinds of illnesses.

Attempts to set a standard that would cover all of the above conditions would be extremely complicated. More importantly, enforcement would be impossible. Even if it were possible to develop an atmospheric standard for the home environment, how would it regulate the many thousands of mobile homes that already have been purchased?

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SMALL PLANTS AND THEIR MEDICAL PROBLEMS--
THE FURNITURE INDUSTRY

Industrial Hygiene Aspects of the Furniture Manufacturing Industry

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The furniture industry covers a wide variety of processes and types of products, including household, office and institutional furniture, and partitions and various fixtures. Household furnishings account for about 66% of the sales, numbers of establishments, employment, etc. The household furniture portion can very appropriately be called a small industry. In 1978, there were about 5,370 of these establishments, most companies with only one location. These establishments employed about 320,000 workers, the average plant having around 60 employees and the largest companies with fewer than 7,500 in the furniture portion. Except where furniture manufacturing is a subsidiary or a division of a larger company, there are no full-time industrial physicians or industrial hygienists employed, though a few of the larger plants have safety engineers or safety managers and nurses.

Two broad categories of household furniture are produced--case goods and upholstered goods. The manufacture of case goods involves three basic operations: mill work, assembly and finishing; whereas, upholstered goods manufacturing involves cutting, sewing, spring-up and upholstering. Preparatory to mill work, the lumber is air- and kiln-dried to a moisture content of 6-8% then cut and planed to rough dimensions. Large panels and turnings are cut, glued and planed. Individual parts are cut, mitered, molded, turned, routed and shaped in the finish mill area, then taken to the assembly area where they are sanded, polished and glued together. Parts are stacked everywhere around the plant; it is not surprising then that low back pain--from pushing these parts around on rough wooden floors--is prevalent. After assembly, there is further hand sanding and the addition of ancillary components, such as drawers, mirrors and hardware. Stains, fillers, sealers and finishes are applied in a finishing area after which the pieces are packaged for shipping.

Potential health hazards are present at every step in the process. The primary industrial hygiene concerns are noise, solvent vapor and inadequate ventilation. Other potential hazards are wood dust and formaldehyde.

Not all lumber is pre-treated, but white pine is attacked by a fungus during warm weather storage. The resulting blue stain can be prevented by dipping the lumber in a mixture of sodium pentachlorophenate and sodium azide. In addition to its toxicity, sodium azide reacts with certain metals to form explosive and shock-sensitive metal azides. Sodium pentachlorophenate, on the other hand, penetrates even the intact skin and also causes dermatitis.

Fiber board and particle board, used very extensively in furniture manufacturing, are made primarily with urea-formaldehyde glue. And as pointed out by Mr. Breysse, these

boards continue to release formaldehyde long after their manufacture at a rate that depends on the ambient temperature. Thus, storage warehouses for such material must be well-ventilated, especially during summer months. Many large panels are made in the same way as plywood room paneling, by gluing veneer to each side of a rigid core in a veneer press using urea-formaldehyde glue. As the panels are heated in the press, formaldehyde is released. Thus, press operators very often experience eye, nose and throat irritation. Freshly veneered cores continue to release formaldehyde until they are cool. Experience indicates that local exhaust ventilation is the only feasible way to reduce employee exposure. Local exhaust systems must be provided for both the veneer press and the stacks of panels off-loaded by the operator.

As previously mentioned, a major health hazard in the furniture industry is noise. Hearing conservation programs are a requisite for employees in the mill work area, where noise levels exceed 90 dB(A). Engineering controls for the saws, planers, molders, shapers, tenoners and other pieces of wood working equipment are evolving slowly. Successful noise reduction is achieved with enclosures on the planers, molders and tenoners, but changes in geometry of the saw blade also effectively reduce noise generation; likewise, saw guards can be lined with acoustic foam. Special attention has also been given to the re-design of air nozzles used to blow off dust particles. Meanwhile, it is still necessary that employees use personal protective equipment.

Wood dust is created in abundance and in most areas of the plant. Much of the dust that is very fine and respirable is generated by operations such as sanding; elsewhere, the particles tend to be large. Little attention has been given to the industrial hygiene of wood dust, inasmuch as domestic woods are largely used in the US. Attention is now being given with the recent implication of wood dust to nasal cancer in furniture workers. Lung deposition characteristics cannot be predicted nor can representative air sampling methods be established for the dust because little is known about the particle size distribution in the manufacture of furniture. Preliminarily, the smallest wood particles are produced by sanding and these are 10 micrometers in aerodynamic diameter. If confirmed, the primary site of deposition after inhalation will be the nose and the throat, and the air sampling method of choice will be a total dust sample. If wood dust is determined to be a significant health hazard, local exhaust ventilation will be required at the source. Dust collection systems are presently used; however, the primary concern is for machine maintenance and housekeeping, not to maintain low levels of atmospheric dust. Oftentimes, these systems are starved for makeup-air and the inside of the building is at a negative pressure. Attention should be focused on the location of the exhaust intakes and provision for makeup-air.

Finishing wooden furniture often requires fifteen or more steps, the majority of which involve spraying various finishing materials—stain, filler, sealer and lacquer—onto the furniture. The remaining steps include wiping and sanding between spray applications. Spraying is usually done inside a spray booth with handheld spray guns. The employee's primary exposure is the inhalation of volatile solvents from the finishing materials. Wiping and sanding is done outside the spray booths; these workers also breathe solvent vapors, but their biggest risk is dermatitis—the dry, fissured type—from contact with the finishing materials.

Finishing materials contain a variety of chemicals. Non-volatile components consist primarily of nitrocellulose lacquer, amino resins and pigments. Numerous volatile solvents are used; most, if inhaled, have similar physiologic effects—ie, slight respiratory irritation, central nervous system depression and possible liver or kidney damage from continued overexposure. Benzene and methyl n-butyl ketone are no longer used.

To determine a worker's exposure to these solvents is an analyst's nightmare. EPA's air quality standards for photochemically reactive hydrocarbons require that no individual solvent may constitute more than 20% of the total volatile portion of a given product. Thus, a typical formulation will have at least five different solvents and oftentimes many more. And though air samples are easy to collect (over activated charcoal), their quantitative determination is time-consuming and difficult because of the complexity of the mixture. The concentration of each solvent must be known in order to judge an overexposure, since effects are additive.

Finishing rooms are generally maintained at a positive pressure with respect to other plant areas to prevent dust contamination. This measure also assures adequate make-up air for the spray booths. Well-designed booths provide make-up air from behind the worker and through perforated panels for good distribution; such booths appear to provide adequate protection. Overexposures otherwise result from poor work practices, such as spraying outside the booth or standing between the exhaust intake and the piece being sprayed.

Personal protection against solvent dermatitis, especially for those persons who wipe the finish, consists of chemical-resistant gloves, aprons and clothing. Barrier creams and good personal hygiene are also helpful, but silicone creams must be avoided because of their damaging effect on the finish.

Microwave and infrared radiation hazards attend the ovens that are used to cure the adhesives; however, these ovens are generally quite well shielded and there is little employee exposure.

Another minor operation that poses a hazard is the manufacture and repair of saw blades. Carbide tips are soldered to the blades with silver solder, which poses two potential problems: Cadmium can be eliminated with a solder that is free of cadmium, while silver fumes are controlled by local exhaust ventilation.

There are few additional problems in the manufacture of upholstered furniture, except for the dust from cotton batting. Upholsterers are given pulmonary function tests and respiratory questionnaires. We have seen an occasional case of dermatitis, which was attributable to the fabric; in one case the fire retardant was responsible. Such incidents are rare because the upholsterer contacts only a small area of fabric and potent dermatological agents are not normally used.

Some furniture contains plastic hardware, carvings, etc. Employees who make these plastic parts—generally of polystyrene and rigid polyurethane—are exposed to diphenylmethane diisocyanate (MDI), styrene, diatomateous earth, silica and methylethylketone peroxide. Styrene and MEK peroxide irritate the skin and respiratory tract; MDI, like TDI, is a respiratory sensitizer at low concentrations. It is customary to use the pre-polymerized MDI, which has a lower vapor pressure and is less likely to become airborne.

SMALL PLANTS AND THEIR MEDICAL PROBLEMS— THE FURNITURE INDUSTRY

Health Effects of Wood Dust

John F. Gamble, PhD

Throughout his history man has had daily contact with plants and he has learned to recognize and avoid the harmful species. The first reference of adverse skin reaction to a plant—probably the pokeberry—was in the 28th century BC in China. Up to 1900 AD, there were almost 300 references in the literature of adverse skin reactions from contact with plants; most of these reactions were caused by flowering plants, not trees or wood. Skin irritation from plants is caused primarily by coarse hairs and spicules—for example, the T-shaped hairs on red-twigged dogwood and the hairs on fig leaves—which produce an erythema when the leaf is rubbed on the skin in the long axis of the hairs.

Although holly (Ilex sp.) has a spiny leaf, it has not been reported as a cause of irritant dermatitis. The leaves of white cedar and juniper, on the other hand, and leaf hairs of the plane tree (a European relative of the sycamore) can produce conjunctival and respiratory irritation. The leaf hairs of the elm (Ulnus) are reported to cause skin irritation (4). Some plants, such as the common English nettle and elm trees (which are in the nettle family), have specialized glandular hairs containing histamine and acetylcholine and can produce skin irritation. Buttercups, on the other hand, contain a lactone that produces blisters, and the essential oils in citrus fruits and the sap of fig trees have photodermatitic effects. Perhaps the most familiar allergic dermatitis is caused by poison ivy in which urushiol is the irritant (1,2).

The adverse health effects of wood and wood dust are less commonly noted than those I have just mentioned. Dermatitis from the Japanese lacquer tree—also caused by urushiol—was known in China as early as the 7th century AD. In the 17th century, the sap of the possumwood was said to cause blindness (2); the sap also contains a chemical substance that has been used as a fish poison (3). French soldiers in Napoleonic time reportedly became ill after eating foods that were cooked on spits of oleander wood; and there are references of similar events among barbecuers in California and Florida (4). All parts of the oleander contain glycosides that resemble digitalis in physiological action (3).

Manzanilla is perhaps the most notorious of all irritant trees. It grows along the seashore in Florida, South America, Central America and the West Indies; the tree has been largely eliminated in southern Florida except for the Everglades National Park. All parts of this tree are toxic, including the fruit. Some of the legends portend death to those who sleep under its shade. Direct contact of the conjunctiva with the wood, contaminated fingers or with water dripping from the tree can produce conjunctivitis, burning pain, photophobia, intense tearing, edema and complete closing of the eyelids. After 1-2 hours of dermal exposure there may be redness with smarting and burning; after 24-hours, vesicles appear that resemble 2nd degree burns. Biting the fruit without

swallowing will result in no more than soreness of the mouth and excessive salivation; if you swallow, the symptoms will include vomiting, difficulty in swallowing, pains in the mouth and abdomen, and bradycardia. Moderate inhalation of the wood dust produces cough, while more severe exposure may cause naso-pharyngitis, laryngitis and bronchitis (2,5).

The first occupational reference to wood dust was in the 18th century when Ramazzini (6) reported nose and eye irritations in pit sawyers. He didn't specify any particular wood except to mention that a cypress odor gave some woodturners headaches. In 1902 there were reports of coryzal symptoms from redwood, and throat and eye irritation from a boxwood substitute (4). Three years later there was an epidemic of such severity among Lancashire shuttle-makers using African boxwood (4,7) that the men refused to work with the wood—37 out of 112 were affected: 34 had difficult breathing; 10 had headaches; 17 had somnolence, laziness or dopiness; 14 had rhinitis; 9 had running of the eyes; 6 had sneezing; 6 had coughing; there were 4 with chest tightness and 3 with slight dyspnea; 2 had loss of appetite; 1 had nausea and vomiting; and 1 became faint. The somnolence, headaches, dyspnea and faintness were thought to be due to an alkaloid in the wood—probably quebrachamine (4), a curare-like compound—that induces a gradual slowing of the heartbeat (7). In 1906, English workmen who became ill from exposure to Gonioma (ie, S. African boxwood) were eligible for workmen's compensation; since then, this species has been replaced largely by other woods.

Another troublesome tropical African wood is Iroko (Chlorophora excelsa), which resembles teak. It is often substituted for teak and can cause epidemics of severe dermatitis, particularly during hot, humid weather or when the wood is wet. Its dust may both irritate and sensitize—the sensitizer is chlorophorin, an oxystilbene—as patients may have both severe dermatitis and/or severe respiratory symptoms (ie, obstructive rhinitis and/or asthma) (2,4,7,8). In 1941 an epidemic was reported (8) in which 50 men were working with wet Iroko logs. All suffered irritation of the exposed skin, while 9 had intense irritation of the covered skin, marked edema of the face with eye irritation, acute coryza with mild headache and mild pharyngitis or chest symptoms (ie, constriction, dry cough and dyspnea that simulated asthma). Iroko is one of the six commonest causes of dermatitis in France to this day.

The adverse effects of exotic woods are generally more severe than those of woods that grow in temperate climates; the systemic effects are often toxic and the sensitizers are more potent. One possible explanation is that their extractives or accessory substances—which serve to protect the tree against bacteria, fungi, insects and other animals—are also toxic to man. Except for manzanilla (ie, Hippomane manchinella), no systemic effects have been reported for American woods.

Most of the emphasis in the literature deals with the exotic species, yet most of the wood used in the US is native—less than 5% of the exotic hardwoods are imported into this country. By volume of use, pine and Douglas fir are our major softwoods. These, together with oak (the major hardwood), comprise better than 50% of the wood that is used in the US (Tables 1 and 2).

There is evidence of contact dermatitis, however, from exposure to a number of native American woods (Table 3). Cedar—ie, incense (9), Port Orford (2), Virginia pencil or eastern red, white (2,4) and western red (10)—pine (4,11), Douglas fir (4,12), fir (4), hemlock (13), spruce (4) and poplar (14) are definitely associated. Incense cedar (Calocedrus decurrens) and Virginia pencil cedar, or eastern red cedar (Juniperus

virginiana), are officially recognized causes of dermatitis in the German pencil industry (4). Unconfirmed cases of contact dermatitis have been reported from acacia, alder, beech, birch, chestnut, cypress, dogwood, maple and redwood (15).

TABLE 1 - Volume of Use and Decay-Resistance of Native US Softwoods*

Over 5 billion bd ft:	
Douglas fir (*Pseudotsuga menziesii*)	medium
Pine (Southern yellow) (*Pinus* sp. - 6 species)	medium-low
1.0-4.9 billion bd ft:	
Fir (*Abies* sp. - 8 species)	low
Hemlock (*Tsuga* sp. - 3 species)	low
Ponderosa pine (*Pinus ponderosa*)	low
Redwood (*Sequoia sempervirens*)	high
500-999 million bd ft:	
Western red cedar (*Thuja plicata*)	high
Pine (jack, lodgepole) (*Pinus* sp. - 2 species)	low
Northern white pine (*P. strobus*)	medium
100-499 million bd ft:	
Incense cedar (*Libocedrus decurrens*)	high
Cedar (northern & southern white, Port Orford) (*Thuja occidentalis*, *Chamaecyparis* sp. - 2 species)	high
Cypress (red, yellow, white) (*Taxodium distichum*)	medium
Western larch (*Larix occidentalis*)	medium
Idaho white pine (*Pinus monticola*)	low
Norway pine (*P. resinosa*)	medium
Sugar pine (*P. lambertiana*	low
Spruce (eastern, Engelmannn) (*Picea* sp. - 5 species)	low
Sitka spruce (*P. sitchensis*)	low
50-99 million bd ft:	
Alaska cedar (*Chamaecyparis nootkadensis*)	high
Eastern red cedar (*Juniperus virginian*)	high
Tamarack (*Larix larcina*)	medium

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*Current Industrial Report for Lumber Production and Mill Stocks (1977). Bureau of the Census. (Does not include plywood, posts, pulp, particle board, etc.)

TABLE 2 - Volume of Use and Decay-Resistance of Native US Hardwoods*

Over 1 billion bd ft:	
Red oak (*Quercus* sp. - 14 species)	medium-low
White oak (*Quercus* sp. - 16 species)	high-med.
500-999 million bd ft:	
Poplar (*Liriodendron tulipfera*)	low
100-499 million bd ft:	
Red alder (*Alnus rubra*)	low
Ash (*Fraxinus* sp. - 5 species)	low
Aspen (*Populus* sp. - 2 species)	low
Beech (*Fagus grandifola*)	low
Rock elm (*Ulmus* sp. - 4 species)	low
Gum (*Liquidamber styraciflua*)	low
Hickory (*Carya* sp. - 4 species)	low
Hard maple (*Acer* sp. - 2 species)	low
Maple (Oregon, soft) (*Acer* sp. - 3 species)	low
Tupelo (*Nyssa* sp. - 3 species)	?
50-99 million bd ft:	
Basswood (*Tilia* sp. - 2 species)	low
Birch (*Betula* sp. - 5 species)	low
Cottonwood (*Populus* sp. - 3 species)	low
Locust (*Robinia pseudoacacia*, *Gleditsia triananthos*)	medium
Pecan (*Carya* sp. - 4 species)	low
Sycamore (*Plantanus occidentalis*)	?
10-43 million bd ft:	
Walnut (*Juglan nigra*)	high
Soft elm (*Ulmus* sp. - 2 species)	low
Cherry (*Prunus serotina*)	high
Hackberry (*Celtis* sp. - 2 species)	low
Willow (*Salix* sp. - 2 species)	low
Butternut (*Juglan cinerea*)	low
1-3 million bd ft:	
Box elder (*Acer negundo*)	low
Buckeye (*Aesculus* sp. - 2 species)	low
Cucumber (*Magnolia acuminata*)	low
Dogwood (*Cornus* sp. - 2 species)	low
Magnolia (*Magnolia* sp. - 2 species)	low
Osage orange (*Maclura pomifera*)	high
Sassafras (*Sassafras albidum*)	high

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*Current Industrial Report for Lumber Production and Mill Stocks (1977). Bureau of the Census. (Does not include plywood, posts, pulp, particle board, etc.)

TABLE 3 - American Species Causing Contact Dermatitis

Thuja plicata - Western red cedar
One case of allergic contact dermatitis (10)

Juniperus - Juniper, eastern red cedar
Cause of dermatitis in German pencil industry (9)

Libocedrus - Incense cedar
Two cases reacted to thymoquinone and hydrothymoquinone; could also be irritant; cause of dermatitis in German pencil industry (9)

Chamaecyparis lawsoniaries - Port Orford cedar
Unconvincing evidence (4)

Thuja occidentalis - White cedar
A 1926 description of dermatitis (4)

Pinus sp. - Pine
Relatively uncommon; sensitization mostly in non-American species (4,13)

Picea sp. - Spruce
Possible sensitization to hydrostilbenes as cross-reaction with stilbesterol (2,4)

Pseudotsuga mensiesii - Douglas fir
Three cases with + patch test; two had prior skin disease, two had no dust exposure (4,12)

Abies sp. - Fir
8/125 persons had + patch test, significant in 4/8; needles are common irritant (13)

Tsuga sp. - Hemlock
+ patch test in 1/125 foresters with dermatitis (13)

Populus - Poplar
One atypical case of allergic contact dermatitis; + patch test may be irritation (14)

Prosopis sp. - Mesquite
Not commonly used, except as fuel (14)

Irritant dermatitis primarily affects exposed surfaces; however, the dust may lodge on the eyelids, face, neck and moist skin folds (such as genital areas) and irritate them as well. On the other hand, high humidity in the Pacific Northwest is thought to increase the susceptibility to low-level irritants (eg, in wood, bark and needles) among forest workers, loggers, pond men and lumber handlers and is believed to be the critical factor in the induction of dermatitis among these workers (12). Splinter wounds from Douglas fir and Port Orford cedar heal slowly (2,4). Dermatitis does not seem to be as much of a problem with western red cedar as does asthma--only one case of allergic contact dematitis has been reported.

Up to the present time, asthma and rhinitis have been confirmed in over a dozen species of wood, most of which are exotic types (Table 4). The best known and most studied—including epidemiologic investigations—is an American species called western red cedar (Thuja plicata). It was reported in Japan as early as 1923, but has been well described only within the last 20 years. beta-Thujaplicin is the sensitizer in western red cedar and incense cedar. It's interesting that there are two different sensitizers in western red cedar, one for the skin (beta-thujaplicin) and one for the respiratory system (plicatic acid). Plicatic acid is also a strong organic acid, so it can act as a primary irritant. Except for some of the cancer studies, this is the only wood for which there are specific epidemiological studies.

Some of the symptoms of western red cedar exposure may take weeks or months to develop (Table 5). These symptoms--which usually appear before pulmonary function is affected—include eye and nasal irritation, nasal obstruction, sneezing, coughing, excessive rhinorrhea and chest tightness; symptomatic people generally maintain a normal baseline pulmonary function--at least in the early stages. Symptoms tend to worsen at night, but as exposure increases the symptoms move closer to the onset of exposure. Thus, if one is making a case study, he may get some individuals who have a late response, some who have an early response and some with both early and late responses. Long exposures more often give a dual response, while minor exposures usually tend toward the late response. In those individuals having western cedar asthma, the chest radiograph is normal and there is usually no relationship between skin testing and respiratory sensitivity. (A few studies in Japan have noticed some relationship between skin testing and respiratory effects, but in this country that has not been noted.) There are usually no precipitating antibodies in sensitized individuals and no apparent relationship between smoking and atopic status. In fact, there seem to be more non-smokers and ex-smokers in the case reports. Whether these people are more susceptible or this is a matter of selection, we do not know. The effects of the exposures appear to be reversible if there is no immediate reaction. If both late and early responses are evident, reversibility is less likely.

TABLE 4 - Asthma and/or Rhinitis Due to Wood Dust

Thuja (native US species) - Western red cedar, arborvitae
Immediate, late and dual reactions; confirmed by bronchial challenge (16-23)

Quercus (native US species) - Oak
Confirmed by bronchial challenge (24)

Chamaecyparis (native US species) - Port Orford cedar
Old report of asthma in woodworkers (2,4)

Hippomane (native US species) - Manzanilla, beach apple
Rhinitis; not widely used (2,4,5)

Sequoia (native US species) - Redwood
Two case reports with dual reaction; confirmed by bronchial challenge (25)

Chlorophora - Iroko, African teak
Chlorophorin is sensitizer for dermatitis; cause of industrial asthma in Belgium (2,4)

Pericopsis - Afromosia
Can produce skin and respiratory irritation, asthma and systemic symptoms (2,4)

Pterocarpus - Kejaat, African teak
Dust causes dermatitis and respiratory symptoms (26)

Dalbergia - Rosewood, cocobolo
Many members of this genus cause allergic contact dermatitis (27)

Gossweilerodendron - Nigerian cedar, Agba
Possible case of asthma (4)

Citrus - Orangewood
One unconfirmed case (2,4)

Khaya - African mahogany
Confirmed by bronchial challenge and precipitating antibody; genus could be Swietenia (4,24,27,28)

Triplochiton - Obeche, African whitewood
Confirmed by skin and inhalation test (4)

Cedra - Cedar of Lebanon
Six case reports of asthma and rhinitis (29)

Gonystylus - Ramin
Reports of asthma and dermatitis; case of extrinsic allergic alveolitis syndrome, but challenge gave reduced FEV_1 and transfer factor in 6-8 hrs (30)

Microberlinia - African zebrawood
One case of asthma with dual reaction, confirmed by challenge and immediate skin test reactivity (31)

Pouteria - Abiruana
One case with immediate reaction and one with dual reaction on challenge; both + skin tests (32)

Buxus - Boxwood
One case of asthma and cough from dust; dual response on challenge; + skin test (33)

TABLE 5 - Characteristics of Western Red Cedar Asthma

Latency - Weeks to months

Symptoms - Tearing and nasal irritation; nasal obstruction; excessive rhinorrhea; sneezing; cough; wheeze; chest tightness

Pulmonary function - Acute airways obstruction (reduced FEV_1 and FEF_{50}), baseline PFT not reduced in early stages

Onset of symptoms & reduced PFT - Symptoms worsen at night, occurring closer to onset of exposure with increasing exposure; same pattern of change in PFT on bronchial challenge, though some persons have immediate response and some have a dual response

Chest radiograph - Normal

Skin test - No relation between skin and respiratory sensitivity

Serology - No precipitating antibodies in sensitized persons

Eosinophilia - Variable increases in sensitized persons

Smoking and atopy - No apparent relation in most studies

Reversibility - May be reversible if no immediate reaction; relief from symptoms over a weekend without exposure

An allergic reaction—by definition—requires a period of previous exposure during which sensitization to the antigen takes place. Continued or additional exposure increases one's sensitivity; fortunately, only a small proportion of the exposed population is affected. The lung and skin contact the antigenic substances most often, but the allergic reaction usually is expressed by the skin. Asthma and/or rhinitis may occur alone or concomitantly with dermatitis. The early stages of allergic dermatitis (dermatitis venenata) are redness, scaling and itching, which signs initially resemble airborne contact dermatitis (4). The hands, forearms, eyelids, face, neck and genitals are affected first. Erythema and irritation may then progress to vesicular dermatitis and on to chronic dermatitis after repeated exposures.

Native American species reported to be sensitizers include: acacia, alder, ash, beech, birch, chestnut, cedar, creosote bush, elm, maple, mesquite, oak, pine, poplar, prune and spruce (14). Allergic contact dermatitis has been confirmed in several varieties of cedar (2,4,9,10), mesquite (2), pine (11), spruce (4), hemlock (13), fir (4), Douglas fir (12) and poplar (14). Skin allergens thus far identified are:

poplar: a labile quinone in the heartwood and a sesquiterpene lactone
pine: pinosylvine, delta-3-carene and coniferylbenzoate
western red cedar: beta-thujaplicin
incense cedar: thymoquinone
liverworts: sesquiterpene lactones
lichens: d-usnic acid

Creosote bush (Dictamnus) has not been confirmed as a skin sensitizer, nor is it a native of North America.

Inhalation of organic particles produces two distinct types of allergic reactions: asthma (and/or rhinitis) and extrinsic allergic alveolitis (or hypersensitivity pneumonitis) (34,35). The most common characteristics of each are summarized in Table 6.

Asthma and rhinitis have been confirmed by bronchial challenge for western red cedar (Thuja plicata) (16-22), redwood (Sequoia sempervirens) (25), and oak (species unknown) (24). Asthma has been reported in woodworkers exposed to Port Orford cedar, but it has not been confirmed by bronchial challenge (36).

Plicatic acid has been identified as the allergen in western red cedar (21). The sensitizers have not been identified for other woods. Skin tests and precipitins were negative for redwood (25) and generally negative for western red cedar (21). The characteristics of western red cedar asthma (summarized in Table 5) are similar to those for redwood asthma. One case of asthma from oak dust produced an immediate reaction (reduced FEV_1, FVC, FEF_{25-75}) on challenge to oak dust and its alcoholic extract, while other wood dusts and a water extract of oak dust were negative. Precipitating antibody against the alcoholic oak extract was found in the serum (24).

The adverse health effects of native American woods—primarily dermatitis and asthma—are summarized in Tables 7 and 8. Most species have no case reports; only western red cedar has been studied in any detail.

There are no reports of asthma or rhinitis from Douglas fir; there are reports of dermatitis, probably by contact rather than by dust. Hemlock is responsible for one case. There are no reports of dermatitis from California redwood, but there are two case reports of asthma. A couple of instances of dermatitis and over 90 cases of asthma have occurred from western red cedar.

TABLE 6 - Comparison Between Occupational Asthma and Extrinsic Allergic Alveolitis (modified from references 34, 35, 37-41)

Asthma (type I)	Extrinsic Allerg. Alv. (III, IV)
Predisposing factors	
Atopy	None known
Region affected	
Airways of lung & bronchi to terminal airways	Mid & terminal airways, also alveolar & interstitial tissue
Onset of symptoms	
Immediate (and/or late)	Usually after 4-6 hours
Systemic reaction	
None	Usual, accompanied by fever, chills, anorexia, tachycardia, tachypnea
Serology	
Elevated IgE antibodies	IgE normal; IgG precipitating antibodies may be present
Eosinophilia	
Common	Transient and uncommon
Skin tests	
Immediate wheal and flare	Edematous reaction after 4-6 hours; skin test of little value--most antigens are local irritants
Sensitivity	
Extreme sensitivity to bronchoconstrictors	
Pulmonary impairment	
Increased air flow resistance (reduced FEV_1)	Reduced FVC and FEV_1, reduced diffusion and compliance
Etiology	
Platinum salts, grain & wood dusts	Fungi, animal proteins (some induce Type I reaction) and thermophylic actinomycetes
Mechanism	
Antigenic: IgE-induced release of pharmacologic mediators from mast cells	Precipitating antigen-antibody complex and complement produce Arthrus skin reaction; Arthrus-type pulmonary lesions have not been observed
Treatment	
Reversed with adrenergic drugs; blocked by cromolyn sodium	May be reversed with steroids, not with bronchodilators

TABLE 7 - Summary of Health Effects of Native US Softwoods

Variety	Dermatitis(n)	Asthma(n)	Comments (ref.)
Douglas fir (*Pseudotsuga*)	+ (3)		Probably by contact rather than by dust (4,12)
Pine (*Pinus*)	+ (2)		Sensitizer is stilbene in turpentine (13)
Fir (*Abies*)	+ (4)		Contact, not dust (13)
Hemlock (*Tsuga*)	+ (1)		(13)
Redwood (*Sequoia*)		+ (2)	Rhinorrhea sneezing, cough, tight chest, dyspnea, dual reaction on challenge. Sequoiosis (allergic alveolitis) also described (25,42)
Incense cedar and eastern red cedar (*Libocedrus* and *Juniperus*)	+ (2)		Sensitizer is thymoquinone; also in coleus, lavender and horsemint (9)
Port Orford cedar (*Chamaecyparis*)	?	?	(4)
Western red cedar (*Thuja*)	+ (1)	+ (90^{+})	"Cedar poisoning" from lichens and liverworts. Plicatic acid causes asthma and rhinitis; beta-thujaplicin is skin sensitizer (16-22,10)
Northern white cedar (*Thuja*)	?		(4)
Larch and tamarack (*Larix*)			"Woodcutters' eczema" in Europe; urticaria in European species (2,4)
Sitka spruce (*Picea*)	+		(2,4)

+ = confirmed by patch test and/or bronchial challenge
(n) = number of cases
? = unconvincing report, unconfirmed by patch test or challenge
(ref.) = reference number(s)

TABLE 8 - Summary of Health Effects of Native US Hardwoods

Variety	Dermatitis(n)	Asthma(n)	Comment (ref.)
Oak (*Quercus*)	?	+ (1)	Sneezing, rhinorrhea, cough, precipitating antibody; immediate reaction on challenge; "woodcutters' eczema" in Europe; adenocarcinoma in European sp. (4,24)
Poplar (*Liriodendron*)	+ (2)		Sensitizer is sesquiterpene lactones (2,14)
Red alder (*Alnus*)	?		Dermatitis from European sp. (14)
Ash (*Fraxinus*)	?		Dermatitis from European sp. (14)
Aspen (*Populus*)	?		"Woodcutters' eczema" in France (36)
Beech (*Fagus*)	?	?	Vasomotor rhinitis; may be adenocarcinoma from European sp. (2,4,14)
Elm (*Ulmus*)	?		"Woodcutters' eczema" in Europe (14)
Maple (*Acer*)	?		"Maple bark strippers' disease", extrinsic allergic alveolitis from fungus (43,15,14)
Basswood (*Tilia*)	?		(2)
Birch (*Betula*)			Irritant and dermatitis in non-native sp. (14)
Locust (*Robinia* and *Gleditsia*)			"Woodcutters' eczema" in Europe (2)
Sycamore (*Platanus*)			"Woodcutters' eczema" in Europe (44)
Walnut and butternut (*Juglans*)			Contact dermatitis and contact sensitivity from European sp. (2)

Cherry (Prunus)	Prune wood may be a skin sensitizer (44)
Hackberry (Celtis)	European sp. are skin, mucosal and respiratory irritants (2,4)
Cucumber and magnolia (Magnolia)	Cross-sensitivity with compositae and sesquiterpene lactones (2)
Holly (Ilex)	"Woodcutters' eczema" in Italy (2)
Oregon myrtle and sassafras (Lauracea)	Sneezing from inhalation of pungent oils (2)

\+ = confirmed by patch test and/or bronchial challenge
(n) = number of cases
? = unconvincing report, unconfirmed by patch test or challenge
(ref.) = reference number(s)

There are many more species of hardwoods than softwoods, although their consumption is less than that of the softwoods. The only confirmed case of asthma from native American hardwoods has involved oak; the species was not identified (24).

Two other diseases that are associated with the wood industry are not caused by either wood or its dust; these are "woodcutters' eczema" and hypersensitivity pneumonitis. Fungi growing on wood bark was suspected of causing dermatitis in 1921; it wasn't until over a quarter of a century later that lichens and liverworts were shown to be the etiologic agents of "woodcutters' eczema" (4). This disease—also called "oak poisoning", "cedar poisoning", "pine poisoning", "spruce dermatitis", "spruce poisoning" and "wood poisoning" (45-49)—occurs only after one has been in a forested area for a day or two; the condition is worse in wet weather and subsides 2-4 weeks after the cessation of exposure (12,45). The respiratory system may be affected as well as the skin. The sensitizers have been identified in the liverworts (sesquiterpene lactones) and lichens (d-usnic acid). The most common cause of dermatitis may be attributed to the liverworts. The lactones in liverworts also cross-react with lactone allergens in the compositae family, among which yellow poplar and magnolia are included. Compositae is also one of the largest families of flowering plants, which may explain the reason for the large amount of "weed dermatitis" that we see. Lichens, which may consist of both fungi and algae, have a wide distribution and grow on trees. Algae too can grow on trees; some algae can cause sensitization, but the specific allergen has not been identified.

Hypersensitivity pneumonitis, or extrinsic allergic alveolitis, is similar to "woodcutters' eczema" in that it is caused by microorganisms growing on the wood. Hence, we have "maple bark strippers disease", "sequoiosis" and "woodpulp workers' disease" (34,37,43).

(See Table 6 for a comparison of occupational asthma and extrinsic allergic alveolitis.) While extrinsic allergic alveolitis may come from fungi and lichens on the wood, it also is associated with fungi on moldy hay, cheese, mushrooms and compost.

Nasal cancer is another disease that has become linked with exposure to wood or wood dust. As much as a 12-fold increase in risk has been found among woodworkers. First reported among furniture makers in the High Wycombe district of England in 1965 (50,51), the association has been confirmed by the authors (52-55) as well as by investigators in other countries—ie, Belgium (56,57,58), France (59,60,57,61), Denmark (62,63), Australia (64), Italy (65) and the United States (53)—more locally, in North Carolina (66). Originally noted in furniture makers, the disease also has been observed among woodworkers outside of the furniture industry (55,67); for example, in the boot and shoe industry (68). A reduced risk was observed in the United States (69,70) and Canada (71,72).

The incidence of these tumors was highest from about 1920-1940, during the advent of power machinery but prior to the use of exhaust ventilation.

In their ecological study of cancer rates in 132 US counties—in which 1% or more of the total population employed in furniture and fixtures manufacturing—Brinton et al (67) found excesses of melanoma (SMR=109) and multiple myeloma (SMR=109) in addition to an excess of nasal cavity and sinus cancers (SMR=119). Out of 19 sites, these were the only SMR's greater than 100. Other mortality ratios were less than 100.

The same investigators—using death certificates—conducted a case-control study (66) of nasal cancer in North Carolina counties, again based on at least 1% of the total population being employed in furniture and fixtures manufacturing. Of the 37 persons who had died from cancer of the nasal cavity and sinuses, there were 22% involved in furniture manufacturing compared to 6.8% of the controls. Those having other exposure to wood (carpenters, sawyers, lumbermen and loggers) were 13.5% vs 9.6% for the controls. The odds ratio in the matched triplet analysis was 4.4 (1.3-5.4 at the 95% confidence interval) for furniture workers and 1.5 (1.4-4.3, 95% confidence interval) for other woodworkers. The histogenesis of 13/37 indicated that: Four tumors were adenocarcinomas, three of which were associated with the furniture industry. Because of the limited amount of occupational data on death certificates, "further study is needed to clarify the risk of nasal cancer in US furniture workers and to identify the specific carcinogens involved" (66).

Milham (69) conducted a proportionate mortality study of men in the forest products industry of Washington State who had died from cancer between 1950 and 1971. He found no excess mortality from either nasal or nasopharyngeal cancer among any of the occupational groups within the industry; the PMR for all malignant neoplasms among loggers and carpenters was 93 and 106, resp., and was no more than 100 for the other groups. The PMR for stomach cancer was slightly increased in all groups. PMR's for Hodgkin's disease, multiple myeloma and leukemia were generally higher in all occupations except loggers, sawmill and other mill workers. Milham has suggested that ingested wood particles may cause stomach cancers and that the "physical and chemical breakdown products of wood may be carcinogenic." This conclusion is similar to that of Morton concerning the association between tannins and cancer (73).

Milham (70) also examined the mortality patterns of the AFL-CIO United Brotherhood of Carpenters and Joiners of America; the members of this union were largely construction workers and had been exposed to asbestos. He found high SMR's for

pleural mesothelioma (182—due to asbestos exposure), Hodgkin's disease in men over age 60 (160); lymphosarcoma (168) and lymphatic leukemias in men less than 50 years of age (375). Small elevations were observed for cancer of the lung (100), stomach (112), small intestine (102), and prostate (103). The SMR for all causes was 81, 95 for all malignant neoplasms and 76 for neoplasm of the nasopharynx.

At least 28 compounds of known structure have been identified in 454 species of Spermatophyta and Pteriodophyta (75). These compounds include alkaloids, tannins, nitroso compounds, triterpene glycosides, parascorbic acid, podophyllotoxin, rotenone, safrole and shikimic acid. Several possible human carcinogens from wood have been discovered since 1976; the most likely agents are summarized in Table 9.

TABLE 9 - Possible Carcinogens Found in Wood

Tannins (hydrolyzable and condensed)	In oak (hydrolyzable form occurs primarily in wood, while the condensed form is mainly in the bark), maple bark, birch, beech, sweetgum, horse chestnut, hickory, pecan, butternut, sassafras, hackberry, sycamore, willow, aspen and cottonwood; not in walnut, poplar, box elder, elm, ash and basswood (77)
Sinapaldehyde and coniferaldehyde	3,4,5-trimethoxycinnamaldehyde (TCMA), may be a derivative of sinapaldehyde and coniferaldehyde; has produced nasal squamous carcinomas in rat; sinapaldehyde is found primarily in hardwoods, coniferaldehyde in softwoods; both occur in maple, oak, sweetgum, walnut and butternut (77,78,79,80)
2,6-Dimethoxy-1,4-benzoquinone	Oxidation product of sinapaldehyde; produces carcinomas in animals (79)
Podophyllotoxin	In Juniperus sp. (81)
Quercetin	Mutagenic by Ames test; in oak (heartwood and sapwood), sweetgum and Osage orange (heartwood) (77,82)
Safrole	Weak hepatocarcinogen; converts to proximate carcinogen, 1-hydroxysafrole; found primarily in root bark of sassafras (77,78)

Tannins are generally found in heartwood and outer bark. Being polyphenols, they are capable of forming multiple hydrogen bonds with proteins, which property makes them useful in the tanning industry (77). Structurally, they are of two types:

> **Hydrolyzable** - As esters of a sugar (usually glucose) with one or more gallic acid groups, they are readily hydrolyzed by acids or enzymes to the sugar and the phenolic acid moiety (eg, gallic or ellagic acid). These tannins are known as tannic acid and are usually obtained commercially from nutgall. Tannic acid has been topically applied to burns; however, patients so treated often develop liver necrosis. Animal studies have since shown that tannic acid is an hepatocarcinogen, as well as an oncogenic promoter of 2-acetylaminofluorene (77,81).
>
> **Condensed** - These flavanoid polymers contain only phenolic moieties and polymerize rather than hydrolyze in acid solution. The flavanoid precursors account for most of the yellow, red and blue colors in flowers and fruits. Condensed tannins and related polyflavanoids are quite common extractives, particularly in bark (77).

Morton (83) has suggested that the excessive incidence of esophageal cancer in Curacao and South Carolina may be due to the unusually large dietary intake of condensed tannins and anthocyanins from tea, herbal remedies, wine, peanuts, and the like. Plant extracts rich in phenols (especially, the catechin type of condensed tannins and related anthocyanins) have produced tumors in rats. No tumors were evident from a tannin-free extract (74,75,83). Tannin-containing extracts from chestnut (Castonea), valonea (Quercus) and mimosa (Acacia) produced either sarcomas or liver tumors in mice. Hydrolyzable tannins gave only liver tumors, whereas condensed tannins produced both liver tumors and sarcomas at the injection site (75).

TMCA (3,4,5-trimethoxycinnamaldehyde), a p-O-methyl derivative of sinapaldehyde--a lignin found mainly in hardwoods and hardwood smoke—induces a variety of tumors in the rat, including nasal squamous carcinomas. The oxidation product of sinapaldehyde (2,6-dimethoxy-1,4-benzoquinone), also found in wood, induces sarcomas at the site of its subcutaneous injection in rats and mice (79). Coniferaldehyde, along with sinapaldehyde—a normal constituent of lignin--is predominant in softwoods (Juniperus and Larix) but is also present in hardwoods (76,80). TMCA as such is not present in wood lignins, but it may form metabolically and should, therefore, be considered as a wood carcinogen (76,79).

Podophyllotoxin and related lignins have been found in Juniperus virginiana and certain other Juniperus species. It is the active constituent of podophyllin, which has been used as a cathartic, a remedy for condyloma acuminata and as an antitumor agent. Applied to the mouse uterus or given in the diet, it can produce hyperplastic lesions and occasional tumors. It is also the agent in cedar bedding that is likely to cause the increased incidence of spontaneous tumors in mice (78,84).

Quercetin, a flavanoid related to tannins and one of the most common phenolic compounds in vascular plants, has been shown to be mutagenic in Salmonella typhimurium; its mutagenic activity is about tripled in the presence of liver microsomes. Several related flavanoids and flavanoid metabolites, however, show no mutagenic activity either with or without metabolic activation (82).

Safrole is a major constituent of the oil of sassafrass and a very minor constituent of

many other wood species. It was long used in soft drinks (root beer and sarsaparilla), candy and baked goods; tea made from the oil was used as a stimulant, diuretic, carminative, diaphoretic, a treatment for bronchitis, a sudorific for colds and as a home remedy or spring tonic. Oil from the root bark of sassafrass is 80% safrole; it was banned by the FDA for use as a food additive when 0.5% safrole was found to produce liver tumors in the rat. The actual carcinogen is probably a metabolic intermediate, such as 1-hydroxysafrole (77,78,85-87).

* * *

In summary, four types of adverse health effects have been shown to be associated with wood or wood dust:

systemic effects (ie, headache, nausea and sleepiness);

irritation, leading primarily to dermatitis;

sensitization (ie, allergic contact dermatitis, rhinitis and asthma) and

cancer (confirmed nasopharyngeal and suspected GI cancers).

Systemic effects are not linked to any commercial North American species. Asthma has been confirmed in three North American species (oak, redwood and western red cedar), dermatitis is certain for 7 species (Douglas fir, pine, fir, hemlock, eastern red cedar, western red cedar and poplar). The prevalence of asthma and dermatitis is unknown; the only epidemiologic studies thus far are those with western red cedar. The association between wood dust and cancer needs further study.

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SMALL PLANTS AND THEIR MEDICAL PROBLEMS—THE FURNITURE INDUSTRY

Small Plant Medical and Nursing Services

Daniel M. Murphy, MD

To review a small plant medical program in 20-30 minutes isn't going to be easy; therefore, I'll try to make it fairly general and give you a birds-eye view of what we have tried to do over a period of 30 years.

When I listen to the discussions of the environmental and industrial hygiene programs of industry, I feel that small plant medical care is still back in the horse and buggy days. This type of medical care has been and probably still is pretty far away from modern day medicine.

Our primary program involves plants that do not have a full-time doctor and, furthermore, these plants may have from a few—10 to 25—up to perhaps 2,000 employees. About a half-dozen of the plants have had nurses on one or more shifts. Our responsibility to the nurses has been somewhat vague and general: ie, what we and the nurses were willing to accept rather than a bonafide contract. We have tried to meet with them for many years on a periodic basis and discuss their problems. Frequently, we had formal presentations concerning diabetes, blood pressure, cardiac disease, etc. We also set up some written orders and reviewed them with each individual nurse, varying the orders according to the particular plant problems and the nurse's desires.

When I first began to work with industry, I would take my reports to the personnel people as an entree to get into the plant and to talk with the workers about their problems. Eventually, we developed an in-plant program, going in for an hour or two, once or twice a week. We conducted follow-ups on persons who had returned to work after illnesses. Our concern was with cardiacs who lived within their means and physical abilities, encouraging them to continue their medical care, diets, exercise programs and medications, and ensuring them that the work they were doing was within their limitations. In many cases there were justifiable and legitimate complaints about undue stress, while some were just an attempt to get out of a disagreeable job. Plant personnel looked to the industrial physician for an objective evaluation of the situation.

Most small plant programs are handled in our office. Many employers request a pre-employment examination; they are really not sure what they want, they just feel they ought to have a pre-employment examination. When they get the results, they call you and say, "Can I hire him? His vision in one eye is 20/100 and his blood pressure is 190/100." As far as we are concerned, you can hire anybody who can walk, but our job is to examine the man and find out what we can about his physical disabilities and how they might affect him as far as his ability to do a specific job, his restrictions on the job, how he might be an absentee problem, whether he might have some difficulty that could interfere with the company's group insurance program, etc. We give the employer that information and let him make the decision.

Another major medical evaluation that we make for the small plant is to determine whether or not a disabled worker is unable to work or should return to work. Some employers want the personal physician's evaluation of the employee to remain inviolate, while others—probably rightly so—feel they should have a second evaluation. On one occasion I received a woman who had had an inguinal or femoral hernia operation; I examined her about 10 weeks after surgery to see if she could go back to work. She didn't feel she could and her physician said that he didn't want her lifting a pencil for 12 weeks after surgery. I also had a man off work who was getting dialysis while waiting for a kidney. We put him back to work without any difficulty. Frequently, a worker will go off sick, get an examination, then be told that he needs surgery. Meanwhile, he sits at home waiting for his surgery schedule. If we can get him back to work while he's waiting, the employer is much better off. If it is at all possible, we check with the personal physician when we feel that a worker should be able to return to work. We try to get the doctor to agree that the patient ought to be at work. Surprisingly, the physicians are usually more than willing to go along with us; they want to shift the blame for their patient going back to work to somebody else and they don't want to upset the doctor-patient relationship.

More recently, we've had difficulties dealing with the disabilities of pregnancy. Employees—and many of our ob/gyn men—feel that pregnancy qualifies for disability benefits. We do not agree, but we do feel that there must be a disability if a complication arises out of the pregnancy. We have sent copies of the "Guidelines on Pregnancy and Work" to all ob/gyn men in our area. Major points in the document were underlined and we also indicated to our colleagues that we consider disabilities of pregnancy based only on the complications, not on the pregnancy itself.

Treatment of occupational injuries and disease, including the determination of whether or not the injury comes under the Workers' Compensation Law, is a major part of our program. I'm sure you are all aware of the problems. Everybody who develops an ache or pain invariably feels it must be related to his work: "My backache of today is undoubtedly due to the load that was lifted two days ago." Employers are certainly allowed to have an independent evaluation; yet it becomes a little difficult if you don't have an exact cause other than work-relatedness to explain the complaint. Many employees are referred to our office by personnel people because of job changes, changes in restrictions and subjective complaints. We have to evaluate their problems fairly and objectively and make sure that we're doing as well as we can. If you do likewise, you will get along pretty well.

Our relationships with the unions have always been reasonably good. Again, if they feel that you are making an honest attempt to evaluate the employee's complaint relative to his job situation, they don't have any real gripe. Sometimes they would like a different answer, but if you are doing everything you can to help protect the health and welfare of the employee's job, they're pretty well satisfied.

We try to make sure that all reports are reviewed with the employees. At least the employees are aware that we are trying to keep them abreast of what is going on. In general though, small plant medical programs and small plant medical care lags. Most employers do what they have to do by law, not what **you** want them to do. Hazards are brought to our attention by employees, personnel people and others, and fires are put out as they arise; we really don't have the time to develop a good crisis or environmental protection program. We do recommend periodic evaluations when we are aware of a chemical exposure; but again, what the employer does is **his** responsibility.

Let me close by saying that:

> Getting a trained occupational health physician into a small plant medical program is like the remark of the caterpillar who was watching butterflies fly off a board, "You'll never get me in one of those things."

ERC SUPPORT FOR SMALL INDUSTRIES

Loren L. Hatch, DO, PhD

First, let me say how proud I am to have been the NIOSH representative for the co-sponsorship of these Congresses for almost five years. By your attendance last year and this, the NIOSH/AMA decision to hold these meetings at NIOSH-funded Educational Resource Centers (ERC's) has proven most rewarding. I am especially pleased to see so many students of all disciplines here this morning.

What can ERC's do for small, local industries? Parenthetically, we might ask, "What can small industries do for their nearby ERC?" Dr. Daniel Murphy has indicated some of the services small businesses need and how difficult it is to raise the consciousness of these businesses to the level of their fiscal needs.

I have met with the people on President Carter's White House Committee on Small Business and attended meetings throughout the country where upwards of 500 small business men and women have voiced their problems. I can say that the common appeal is, "Get the government off our backs and we can make it." This is a definite opening wedge for ERC's, as they can do more than the government with their enhanced credibility for small businesses.

Foremost, in my opinion, is the need for every ERC to develop a clinic-based occupational safety and health (CBOSH) program. This is necessary not only for the university's own employees, but also to serve as a practical resource reference for the entire region. The clinical expertise is already in place.

A CBOSH program can serve to focus the coalition between epidemiology, clinical medicine and nursing, industrial hygiene, safety and research. It can also serve as an excellent training resource for students and graduate health professionals and as an orientation location for business leaders and workers.

A frequent question asked at the small business meeting was, "What is a small business?" My definition is: A small business is any business the owner or manager thinks is a small business. Dr. Eula Bingham, OSHA's Director, has recently appointed Kay Klatt as special assistant for small business. In meetings with her, I have concluded she is in agreement with this definition.

Small industries—whether service or manufacturing—do not have the time, expertise or financial resources to develop access to occupational safety and health services. These three points then, are the routes of access to small industries:

Editor's note: Owing to a lack of time, this part of the program (ie, "ERC Support for Small Industries") was not presented. However, inasmuch as this paper had been prepared and submitted for publication by the author in advance of the meeting, it is being enclosed as a formal part of the Proceedings.

provide the expertise,
replace their time with that of the ERC staff and students, and
obtain the financial resources through a grant or contract mechanism.

I know that is easier for me to **say** than for you to **accomplish.** Some ERC's were recently funded through OSHA's New Directions program, without tremendous success. This is no reason not to try again. Perhaps the next time they should be in direct contact with workers and organized groups of workers. The OSHA Regional Office for New Directions should be able to help with funding and information.

Small plants can help ERC's by allowing access to their places of business and employees, as well as by acquainting students with business responsibilities and problems. One business leader told me that he is required to complete 23 different federal forms; he thought some smart student could combine all of them into one, since most of the information was repetitious. Wouldn't that make a nice master's thesis?

Dr. Weill and Mr. Breysse suggested earlier the importance of a good baseline occupational toxic exposure history on all workers. I have developed a model history form for this in my new book, THE OCCUPATIONAL PHYSICIAN IN INDUSTRY, which I hope will be published soon. Wouldn't this make a good project--for a student to go out and take baseline histories of past worker exposures?

What about farmers in ERC areas? All farmers regardless of their acreage think of themselves as small business. Almost anything you do for them is appreciated.

A little innovative initiative will produce a number of low cost, little labor, short time activities for students that will benefit the ERC as well as small businesses. For instance,

> OSH record systems, preventive health services, hypertension, weight maintenance (nutrition), immunization, tuberculosis testing, occupational and reproductive history taking, work-site assessment (walk-through plant surveys), safety meetings, food and water inspections, first-aid training, and interpretation of federal, state, and local regulations affecting small businesses.

These are only a few of the relatively "easy" projects that will develop leadership and familiarization with the work environment. All health professionals need to take off their white uniforms and business clothes and learn first-hand the conditions under which 90% of American workers labor.

My last suggestion for ERC's is to develop out-reach programs with academic credit for physicians, nurses, industrial hygienists, safety professionals, business leaders and labor leaders. These individuals should first be given academic credit for what they already know and then by attending classes at night and on weekends in high schools, at the plant site, hotels--anywhere--they can develop academic expertise in the field of occupational safety and health. This is the fastest way to increase and update professional knowledge. After all, isn't education what colleges and universities do best?

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