

SELECT REPORTS FROM THE DIRECTIONS AND NEEDS IN ASBESTOS RESEARCH
CONFERENCE, MISSOULA, MONTANA

Directions and Needs in Asbestos Research: New Insights: Conference Summary

Jean C. Pfau, Mark Pershouse, and Elizabeth A. Putnam

*Center for Environmental Health Sciences, Department of Biomedical and Pharmaceutical Sciences,
University of Montana, Missoula, Montana, USA*

The Center for Environmental Health Sciences (CEHS) Conference, entitled “Directions and Needs in Asbestos Research: New Insights,” was held at the University of Montana in Missoula. Researchers, physicians, health care workers, and federal agency representatives from around the country met for a cross-disciplinary exploration of many issues related to asbestos research. Topics included community and psychosocial issues in biomedical research, asbestos exposure assessment, assessment and mechanisms of asbestos related diseases, and new research directions. This meeting report is a summary of the conference presentations, and of the topics identified for future research directions. This conference was a follow-up to one hosted by the CEHS in June 2002, and continued to take advantage of opportunities to work with a unique population in Libby MT, where significant asbestos exposures have occurred due to the mining of asbestos-contaminated vermiculite. The goals of this conference were to bring together experts from diverse fields to identify progress made since the last conference and to develop new research avenues that would allow us to address the research needs in emerging asbestos-exposed populations. Participants indicated that these objectives were met, and expressed enthusiasm for follow-up conferences to maintain the dialog that has been established regarding directions and needs in asbestos research. Selected papers from the conference are presented here.

Keywords conference, asbestos, mesothelioma, asbestosis, research translation, Libby MT, exposure assessment

Received 28 December 2007; accepted 25 March 2008.

We gratefully acknowledge Beverly Young, USFS, Region 1, for facilitating the open forum. This conference was supported through grants from NIEHS (R13 ES014289-01), NSF EPSCoR (Grant # 0346458), the Montana Board of Research and Commercialization Technology (Grant # 04-06), and was sponsored by the University of Montana CEHS (NCRP P20RR017670), the Department of Biomedical & Pharmaceutical Sciences, and the College of Health Professions & Biomedical Sciences.

Address correspondence to Jean C. Pfau, Center for Environmental Health Sciences, SB154, Department of Biomedical & Pharmaceutical Sciences, The University of Montana, Missoula MT 59812, USA; e-mail: Jean.pfau@umontana.edu

CONFERENCE OVERVIEW

The University of Montana’s Center for Environmental Health Sciences (CEHS) was pleased to host a highly informative and cross-discipline conference, entitled “Directions and Needs in Asbestos Research: New Insights.” A previous CEHS-hosted conference in June of 2002 initiated a critical dialog between experts in many disciplines relating to asbestos research and set the stage for future interactions. Important advances in these areas of research in the wake of the 2002 meetings emphasized the need for a follow-up conference. The major objective of this conference was to provide an international forum for the exchange of information between experts from diverse fields in order to identify progress made in the intervening years and to develop new research avenues that would allow us to address the research needs in emerging asbestos-exposed populations. As the medical community realizes that asbestos-related disease is not a thing of the past, the research community is realizing that exposures are ongoing, insidious, and widespread. With asbestos-contaminated insulation in an estimated 15-30 million homes in the United States, the study of asbestos-related issues is an essential part not only of occupational medicine and environmental biomedical research but also for ensuring public health.

Technically, the term “asbestos” refers to the regulated, complex group of naturally occurring hydrated mineral silicates that includes both serpentine (chrysotile) and straight fibers (such as crocidolite). They are characterized by fibers or bundles of fine single crystal fibrils, and are very similar in many ways to a large group of unregulated silicate fibers that are generally referred to as “amphiboles.” The primary exposure pathways for all of these materials include inhalation, accidental ingestion, or dermal; and the possibility of differential health effects is a challenging but essential research question. While “asbestos” is a specific, regulatory term, it is commonly used as a generic term for all of the hydrated mineral silicate fibers, even in the scientific community. Therefore, in this Overview and throughout the conference, the term “asbestos” is used even when referring to the unregulated amphiboles.

The northwestern Montana community of Libby provides a unique opportunity to bring together the many disciplines needed to effectively study asbestos and its health risks. Significant exposures to asbestos occurred over several decades in Libby due to the mining of amphibole-contaminated vermiculite from Zonolite Mountain, just 7 miles from Libby, and the use of that material in many applications throughout the community. There has been considerable confusion and debate about the type of material found in Zonolite Mountain, although the fibers have been unambiguously classified in the “amphibole” family. This makes it somewhat unique from chrysotile asbestos, which has been more intensively studied due to its widespread commercial use. Some of the papers presented at the Conference provided critical new information about the unique chemistry, mineralogy and properties of the Libby amphibole, and highlight the need to clarify its toxicity in view of those properties. Other papers focus on specific well-characterized fibers for which specific research questions have been posed as representative of the global issues involving asbestos exposure.

Asbestos-exposed communities, such as Libby MT, tend to be vulnerable and warrant careful study. Their vulnerability stems from the tremendous emotional and financial impacts, the long latency and chronic nature of the disease processes, the uncertainties regarding exposure levels, and the complexity of the asbestos-related diseases (ARD) and their treatments. Effective understanding of the potential health risk therefore requires significant and on-going interaction of researchers with the community, efforts in education and outreach, and coordination of projects to minimize the impact on exposed populations. Such communication, however, opens up issues of confidentiality, privacy and sharing of information that must be ethical and in accordance with regulations protecting human subjects. New approaches are now available, taking advantage of on-line education techniques and various research-to-community bridges. The risk communication process can be considered successful only to the extent that it improves or increases the base of accurate information that decision makers can use and if it satisfies those involved that they are adequately informed within the limits of available knowledge. Successful risk communication makes for better-informed decision makers, including both individuals and public or private officials.

Asbestos research is also being impacted by new technologies in exposure assessment, improved diagnostic approaches including early detection and management, the explosion in genetic and genomic research strategies, and novel biochemical and molecular research tools. Through integrated sessions, discussion periods after every session, a poster session, and social gatherings, this conference allowed the experts in all of these fields to exchange information and establish collaborations that will dramatically improve our ability to address the complex issues of ARD.

CONFERENCE SUMMARY

The conference, with approximately 75 in attendance, consisted of five thematic sessions, a keynote address, a public

forum, and a poster session. Twenty-two speakers presented informational talks, and each thematic session ended with a discussion session with the session’s speakers serving as a panel to whom questions and comments were addressed (Table 1). The theme of the first session was the challenges faced in conducting biomedical research in asbestos-exposed communities. Presentations emphasized the work in the medical, psychosocial and research outreach fields, and compared the experiences in rural settings to those seen in urban areas. In this way, issues were addressed concerning systematic changes necessary to look at problems from a public health perspective. The need to collaborate at the planning stages of a study among the multiple entities involved in response to community issues was addressed. By developing functional partnerships, researchers will be better equipped to design surveys and questionnaires, minimize the impact of research on the subjects, establish excellent rapport with study populations, and to be able to directly address the needs of the affected communities.

Exposure assessment has been an ongoing roadblock in the understanding of the processes behind ARD development. Among other topics, the second session focused on work undertaken to reconstruct the exposures seen in the Libby area using expertise obtained reconstructing historical exposures in other areas of the country. Data were presented on the presence of amphibole fibers in the bark of trees located near the Libby vermiculite mine site. Gaps in our knowledge were identified by the speakers, including Dr. Vik Kapil (CDC/ATSDR), reporting on questions raised about the health impacts of the Libby amphibole at other sites (National Asbestos Exposure Review sites). In addition, the health effects of low level/short duration exposures and the toxicity of the Libby amphibole were also identified as gaps in our current knowledge.

The keynote speaker was Christopher Hahn, Executive Director of the Mesothelioma Applied Research Foundation. He made an eloquent and moving presentation on the need for additional funding for mesothelioma research to enable the development of new therapies for this currently incurable asbestos-related disease.

Another highlight of the first day of the conference was an “Ask the Experts” public information forum, organized and facilitated by Beverly Young, an asbestos removal expert from the U.S. Forest Service, Region 1. Several conference speakers participated in this session, fielding questions from both the lay public and conference participants. The session was filmed for future release on the local public access channel. Questions posed during this session brought up issues regarding on-going exposures to asbestos from insulation materials and possible environmental deposits or reservoirs of asbestos, how those exposures are being or will be monitored and measured, and what kinds of asbestos would be expected in particular settings. There was considerable discussion regarding the “safe exposure levels” of asbestos, which are dependent on asbestos definitions and on possibly out-dated identification and detection techniques. There was general agreement among the experts that there was no “safe” level of asbestos exposure. The effects of exposures

TABLE 1
Asbestos conference participants and topics, University of Montana

Session/Speaker	Affiliation	Title of Presentation
Community Issues in Biomedical Research		
Ann Cook and Helena Hoas	National Rural Bioethics Project University of Montana, Missoula, MT	Health Research in the Rural Community
Rita Messing	Minnesota Dept of Health St. Paul, MN	Community Asbestos Exposure from a Vermiculite Processing Facility
Patricia Cohan	Center for Asbestos Related Research Libby, MT	Consents: Just Sign on the Dotted Line Protecting and Sharing Information in Small Communities
Tanis Hernandez	Center for Asbestos Related Research Libby, MT	Understanding the Psychosocial Impacts of Asbestos
Helen Clarke	Ethics: A Bridge for Communities & Scientists, University of MT and Libby MT	Community Collaboration
Exposure Assessment		
Tony Ward	CEHS, University of Montana, Missoula, MT	Historical Reconstruction and Current Evaluation of Libby Asbestos Exposures
James S. Webber	Wadsworth Center for Laboratories and Research, Albany, NY	Airborne Asbestos Concentrations Since the Late 1800s: Reconstructions from Lake Sediments
Chris Weis Vikas Kapil	EPA, Region 8, Denver, CO ATSDR, Atlanta, GA	Continuing Asbestos Exposures in the US National Asbestos Exposure Review Sites Update
Curtis Noonan	CEHS, University of Montana, Missoula, MT	Exposure Matrix Development
Keynote Address Christopher Hahn	Mesothelioma Applied Research Foundation, Inc., Santa Barbara, CA	Needs in Mesothelioma Research: The Vision of MARF
Assessment of Asbestos-Related Diseases		
E. Brigitte Gottschall	National Jewish Medical & Research Center, Denver, CO	Chemoprevention in Asbestos-Exposed Workers
Stephen Levin	Mount Sinai School of Medicine, New York, NY	Health Effects Among WTC Responders
Amy Rohs	University of Cincinnati College of Medicine, Cincinnati, OH	Twenty-five Year Follow-up of Pleural Diseases in and Asbestos-Exposed Cohort
Harvey Pass	Wayne State University Medical School Detroit, MI	Pleural Mesothelioma: Early Detection, Diagnosis and Management
Mark Pershous	CEHS, University of Montana, Missoula, MT	The Role of SV40 in Malignant Mesothelioma and Other Human Malignancies
Mechanisms in ARD		
Brooke T. Mossman	University of Vermont, Burlington, VT	Intervention of Cell Signaling Pathways in Asbestos-Induced Responses in the Pathogenesis of Lung Disease and Mesothelioma
Agnes Kane	Brown University, Providence, RI	Animal Models of Malignant Mesothelioma <i>(Continued on next page)</i>

TABLE 1
Asbestos conference participants and topics, University of Montana (*Continued*)

Session/Speaker	Affiliation	Title of Presentation
Tom Hei	Columbia University Health Sciences, New York, NY	The Mutagenicity of Mineral Fibers
Deborah E. Sullivan	Tulane University, New Orleans, LA	The Latent Form of TGF- β is Induced by TNF- α through an ERK-Specific Pathway and is Activated by Asbestos-Derived Reactive Oxygen Species <i>In Vitro</i> and <i>In Vivo</i>
Other Asbestos Mysteries: Directions for Research		
Scott A. Wood	University of Idaho, Moscow, ID	Interactions of Asbestiform Minerals in the Lungs: New Insights from Reaction Path Modeling and Experimental Dissolution Rate Studies
Andrij Holian	CEHS, University of Montana, Missoula, MT	Recognition Mechanisms of Particles by Macrophages
Jean C. Pfau	CEHS, University of Montana, Missoula, MT	Asbestos Exposure and Autoimmune Responses in Mice
Elizabeth A. Putnam	CEHS, University of Montana, Missoula, MT	Gene Expression Changes After Exposure to Six-Mix in a Mouse Model

to asbestos on plants and animals, and whether those might be used as research tools, were discussed as well.

The second day of the conference began with a session on current efforts to investigate cohorts of asbestos-exposed individuals in terms of possible new approaches to prevention, detection, and management of ARD. Potential chemoprevention modalities were presented, and generated much discussion as to the need for a better understanding of the basic mechanisms of disease development to expand the options for successful chemoprevention. The opportunities for surgical success in the treatment of mesothelioma were also presented by Dr. Harvey Pass. An assessment of the health effects among 11,768 non-New York Fire Department workers and volunteers among World Trade Center terrorist attack responders and the potential for disease development was discussed by Dr. Stephen Levin. A substantial proportion of participants experienced new-onset or worsened lower and upper respiratory symptoms, and will require follow-up evaluations. Data from a 25-yr follow-up on those exposed to the Libby amphibole in an Ohio factory was also presented by Dr. Amy Rohs. Discussion revolved around understanding the long-term implications of ARD, and possible options for therapies to offer the patients.

The previous sessions illustrated the need for an improved understanding of basic disease pathways and mechanisms to provide potential therapeutic targets. The fourth session focused on systemic and cellular pathways that might answer those needs, with the MAPK, NF- κ B, and AKT/PKB pathways being identified as targets, as well as the implications of activation of the ERK signaling pathway. Chromosomal changes detected in cells

exposed to amphiboles demonstrate that gross genetic damage is also a possible mechanism that needs further analysis to determine its role in the various manifestations of ARD. In addition, the usefulness of animal models in understanding the pathways involved in ARD development was presented. Identifying these targets is the first step in developing potential therapeutics. Novel mechanisms for drug delivery and results of these studies were presented as well.

The last conference session included demonstration of the fate of fibers in the lung, identification of receptors by which lung immune cells recognize and respond to fibers, and the pathways initiated by those receptors. The polyionic nature of the fibers makes them potential ligands for a variety of scavenging and pattern-recognition receptors, and the overall cellular response will reflect an integration of all receptors that might be affected. The result could be cellular survival decisions and a variety of inflammatory pathways, with the potential for differential outcomes based on subtle fiber differences. In addition, the development of autoimmunity in an animal model after exposure to amphibole fibers expands the possible repertoire of ARD and further illustrates that multiple pathways may be activated by asbestos exposure. Microarray analysis of lung RNA from asbestos-exposed mice demonstrated specific gene expression signatures for individual fiber types, and provides new candidates for genes involved in the asbestos response pathways.

All of these issues help frame directions for asbestos research in the future and pose the challenge to experts in the field to find ways to address the more difficult and as yet answered questions.

CONFERENCE SURVEY REPORT

The consensus of the participants in response to a post-conference survey was that asbestos research has moved forward in the past three years, and that novel investigative methods have produced new information that will impact our understanding of ARD development. The integration of asbestos-exposed communities in both research and outreach efforts is an important goal, and the accessibility of understandable materials for the lay public was emphasized. Participants appreciated the community-focused part of the conference because it brought them back to the “big picture” regarding the impacts of asbestos exposure and to the individuals and communities affected. The development of exposure matrices remains a priority, and the importance of model validation cannot be underestimated. Collaborative efforts in this area will be essential. Discussion of the mixtures that are components of the exposures must be taken into account while these matrices are being developed. Any future epidemiologic analyses of various ARD manifestations being associated with various exposure pathways or asbestos sources will rely heavily on validated approaches to exposure assessment. Finally, if any new research or laboratory technologies can elucidate earlier detection, prevention, or management strategies, these are obvious priorities, since it was made clear that asbestos exposures are widespread and ongoing.

CONCLUSIONS

The experience gained from examination of asbestos exposures in vermiculite mining sites such as Libby MT, various vermiculite and asbestos processing sites, and the World Trade Center are providing new insights and tools that will direct asbestos research in the future. The conference organizers and participants hope and anticipate that this conference will inspire collaborations and on-going communication about asbestos research that will eventually lead to major advances in our understanding of community, exposure, pathophysiologic, and mechanistic issues in asbestos research. The conference had two major objectives: (1) Advancement of the scientific background that will ultimately lead to better prevention or treatment of ARD; and, (2) Building partnerships and collaborations in the areas of asbestos-related research and addressing public health issues. Participants felt that both objectives were met, and collaborative efforts have continued since the end of the conference including education and outreach efforts in Libby, exchange of protocols between research laboratories, and development of collaborative grant applications and clinical research efforts. The value of the conference was demonstrated by the enthusiasm of the participants and the expressed desire to repeat the conference in two years. The following articles were selected from the conference to represent the “Directions and Needs in Asbestos Research: New Insights” in this issue of the *Journal of Immunotoxicology*.

Copyright of Journal of Immunotoxicology is the property of Taylor & Francis Ltd and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.