Protect and serve: community-driven superfund science takes aim at asbestos exposure

As a direct response to local community concerns, **Dr Ian A Blair** and colleagues at the Penn SRP Center are using federal funds to study asbestos exposure pathways that lead to asbestos-related diseases. Dr Blair hopes to identify biomarkers of asbestos exposure with the aim of assessing an individual's risks of developing asbestos-related diseases.

The Center of Excellence in Environmental Toxicology (CEET), part of the Perelman School of Medicine at the University of Pennsylvania, used a $10m grant from the National Institute for Environmental Health Sciences (NIEHS) to set up the Penn Superfund Research and Training Program (SRP) Center: a collaborative reactor for scientists working on superfund research. It brings together all the elements necessary to support world-leading science and has six specific project areas under investigation. Each of the projects addresses a specific community concern.

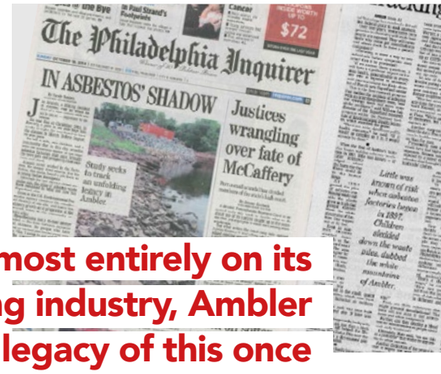
Superfund sites exist across the United States (US), where federal funds are committed to aid the clean-up of sites contaminated by hazardous materials or pollutants. One such site, the BoRit Asbestos site in Ambler, Pennsylvania, is a cause of concern to local communities who are worried about asbestos contamination from lingering industrial waste. A town built almost entirely on its asbestos mining industry, Ambler suffers the legacy of this once promising mineral which became the pariah of twentieth-century industry.

A FELONIOUS FIBRE

Asbestos is a silicate mineral known for its naturally fibrous nature. It was mined extensively in the early twentieth century and used in building materials, as well as many other applications, because of its desirable mechanical properties. Light, strong and resistant to heat, it was often mixed with concrete and other binders to create panels or fittings with these attributes. Each visible fibre, however, is made up of microscopic fibrils, easily shed as the material is worked or degraded and readily inhaled deep into the lungs. Its resistant properties then become a major problem as the body is unable to reject the material. This causes inflammation at the site and can ultimately lead to the development of a cancer known as mesothelioma. Those who worked with the material are most at risk, but family members and communities near mines and industrial processing centres are also affected. Its persistence in the environment and potential for disturbance through human activity are also major factors in its toxic legacy.

PAINSTAKING DETECTIVE WORK

In communities where exposure levels are difficult to assess with any accuracy, a method of calculating individual risk is a vital tool to direct clinical monitoring and follow-up studies. Dr Blair is investigating how approaches used to identify biomarkers in other disease states, such as his pioneering work on Friedreich's ataxia, can be turned to asbestos exposure. Oxidative stress (the response of cells to increased levels of reactive oxygen species) is a prime target and thought to be associated with asbestos exposure. This can be effectively measured in blood samples by analysing metabolites in the serum (the fraction of blood left


The Philadelphia Inquirer

IN ASBESTOS' SHADOW

Justices wrangling over fate of McCaffery

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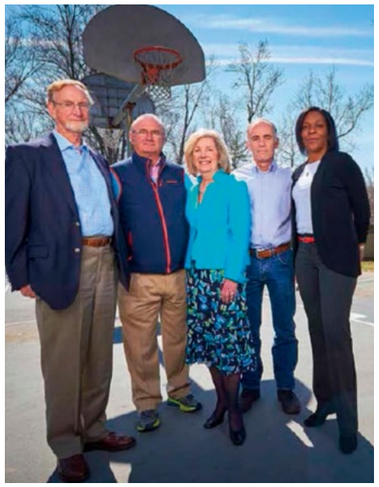

Drs Blair and Emmett with community leaders (Diane Morgan, Bob Adams and Sharon Vargas) at the BoRit Asbestos Superfund Site in Ambler, PA

after it has clotted and the cells have been removed).

Using advanced chromatography techniques and mass spectrometry to separate out the constituents of the samples, the researchers are able to create a series of chromatograms from healthy serum and compare it to that of the disease state. This technique has provided a list of biomarkers which show lack of normal regulation in asbestos-exposed individuals, potentially providing a template against which unconfirmed cases can be assessed.

CALL FOR BACKUP

This is just one of the projects at the SRP which houses six distinct research teams working on different aspects of asbestos toxicity:

- **Project 1**, led by Dr Brenda Casper, researching how plants and fungi can be utilised in the remediation of asbestos contamination in the environment.
- **Project 2**, led by Professors Douglas Jerolmack and Reto Gieré, investigating the mobility and fate of asbestos in the environment to prevent offsite migration.
- **Project 3**, led by Associate Professors Frances Barg and Douglas Wiebe, studying epidemiological and ethnographic data on the incidence of asbestos-related diseases in the community.
- **Project 4**, led by Dr Joseph Testa and Prof Rebecca Simmons, investigating animal models of mesothelioma to understand the genetics of mesothelioma and explore possible remediation strategies.

Figure 1

Penn SRP Center projects addressing the six major concerns of the Ambler Community

Phytoremediation: Project 1	Can asbestos be remediated in situ?
Environmental Science: Project 2	Is asbestos transported through soil and water?
Epidemiology: Project 3	Why is there a cluster of mesothelioma among women in Ambler?
Cancer Genetics: Project 4	Is there a genetic predisposition to asbestos-induced mesothelioma?
Chemoprevention: Project 5	Can asbestos-induced mesothelioma be prevented?
Diagnostics: Project 6	Is there a blood test for asbestos exposure and mesothelioma?

The major benefit of the SRP Center is that researchers working on separate aspects of asbestos remediation, toxicity, and exposure can collaborate effectively

- **Project 5**, led by Associate Professor Melpo Christofidou-Solomidou and Professor Steven Albelda, looking into therapeutic agents for the prevention of mesothelioma in asbestos-exposed individuals.
- **Project 6**, led by Professor Ian Blair and Assistant Professor Anil Vachani, studying biomarkers of asbestos exposure.

This means that Dr Blair's team are not operating alone; the major benefit of the SRP Center is that researchers working on separate aspects of asbestos toxicity can collaborate effectively and share their findings. For example, Project 6 is providing data for Project 4 to use in assessing remediation strategies through animal models of asbestos exposure, while Project 5 uses the same oxidative stress markers identified by the team to investigate the efficacy of flaxseed lignans as potential chemotherapeutic agents.

The Center also brings together data-crunching expertise in the form of the Biostatistics Research Support Core (led by Dr Wei-Ting Hwang), provides administrative functions to free up researchers' time and, perhaps the key component, provides a mechanism for the findings to quickly benefit the local community through the Research Translation Core (headed up by Mr Richard Pepino) and Community Engagement Core (led by Drs Edward Emmett and Fran Barg). There is also a vital training element to the centre (led by Drs Trevor M Penning and Reto Gieré), which gives physicians valuable insight into the causes and treatment of asbestos-related diseases.

SERVING THE WIDER COMMUNITY

This model has shown how research centres, engaging with local communities, can facilitate interdisciplinary collaboration to build creative solutions to local problems with global significance. The problem of asbestos-related diseases, while particularly close to the hearts of the communities around the BoRit site, has international relevance. Due to its ubiquity in twentieth-century construction, populations of previously exposed individuals are common around the world, and in some areas, asbestos extraction and use continues despite the known hazards.

The Penn SRP Center shows how it is possible to produce a truly collaborative research and teaching environment, making it possible to combine effective bi-directional community engagement with innovative scientific research. This in turn produces translational science that can rapidly benefit local communities as well as other populations at risk for exposure and other scientists working in the field.

Q&A

Why was the Penn SRP Center formed?
The National Institute of Environmental Health Science funded the Center of Excellence in Environmental Toxicology (CEET), directed by Dr Trevor Penning, in 2008. The Community Engagement and Outreach Director of the CEET, Dr Edward Emmett, then began participating in the community advisory group in Ambler, PA where there is a Superfund Asbestos site known as the BoRit site. The concerns of the Amber community were too extensive for the CEET to deal with and so Dr Penning invited Dr Blair to form the Penn SRP Center in order to address these concerns. The six projects in the Center came directly from questions posed by the community (see Figure 1).

What are the advantages to this model of research establishment?
Research involves bi-directional knowledge exchange in order that the Penn SRP Center can address the Ambler community concerns. This differs from the traditional model in which researchers simply assume that the community will benefit from their research. Community engagement connects the Penn SRP Center's science with issues that are locally relevant and complements the research strengths and problem-solving goals of the Center.

How will your research help identify at-risk individuals?
Biomarker studies conducted in Project 6 of the Center will identify serum biomarkers of response to asbestos exposure as well as biomarkers for the early detection of mesothelioma. The Amber community is participating in these biomarker studies.

Why are these biomarkers present in asbestos exposure?
Asbestos is a fiber and so exposure cannot be analysed directly in the systemic circulation like a regular chemical. Instead, serum biomarkers of response to asbestos exposure have to be discovered. Asbestos is known to cause oxidative stress and the challenge is to discover biomarkers that differentiate asbestos-induced oxidative stress from other causes of oxidative stress such as cigarette smoking. Asbestos exposure is the major cause of mesothelioma and so biomarkers for the early detection of mesothelioma will also be useful in identifying a prior exposure to asbestos.

What do you hope the centre will achieve for the local community?
The Penn SRP Center provides an independent body for the community members to express concerns that they feel have not been addressed satisfactorily by government agencies. It also provides a resource for medical intervention if a particular community member is concerned about their risk for mesothelioma. Once a serum biomarker of response to asbestos exposure has been validated, it will provide a reliable way for concerned individuals to find out whether or not they been exposed to asbestos.

Detail

RESEARCH OBJECTIVES

Dr Blair's research at the Penn SRP Center aims to identify biomarkers of asbestos exposure. Knowing which biomarkers signal previous asbestos exposure will help practitioners establish whether an individual is at risk of developing asbestos-related diseases.

FUNDING

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COLLABORATORS

From Penn SRP Center: Brenda Casper, PhD; Reto Gieré, PhD; Douglas Jerolmack, PhD; Fran Barg, PhD; Edward Emmett, PhD; Joseph Testa, PhD; Rebecca A Simmons, MD; Melpo Christofidou-Solomidou, PhD; Steven M Albelda, MD; Clementina Mesaros, PhD; Richard Pepino; Wei-Ting Hwang; Trevor M Penning, PhD.
Other key collaborators: David R Lynch, MD, PhD; Garret A FitzGerald, MD, FRS; Kathryn E Wellen; Nathaniel W Snyder, PhD.

BIO

Dr Blair received his PhD in Organic Chemistry in 1971 from Imperial College of Science and Technology, London, under the mentorship of Nobel Laureate Sir Derek H R Barton. He was appointed as the A.N. Richards Professor of Systems Pharmacology and Translational Therapeutics at the University of Pennsylvania in 1997 and Vice-Chair of the Department in 2002. He became Director of the Penn SRP Center in 2014. Dr Blair has published over 370 refereed manuscripts and he has an h-index of 63.

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