Using a multidisciplinary approach to combat the burden of asbestos-related disease

An update from the Asbestos Diseases Research Institute

"the ADRI's focus on epidemiology, biobanking, guidelines, and research into the basic biology of asbestos cancer has led to rapid clinical translation"

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doi: 10.5694/mja15.01209

Australia was the world's highest per capita consumer of asbestos in the previous century. As such, it is considered to be a sentinel site for observing, over time, the deleterious human health, environmental, economic and social effects associated with high levels asbestos exposure.[1] The increasing awareness of the dangers of asbestos among asbestos workers in Australia and the public request for disease-oriented research resulted in the establishment in 2009 of the Asbestos Diseases Research Institute (ADRI), housed in the Bernie Banton Centre on the campus of the Concord Clinical School in Sydney.

The ADRI's most important mission is to improve the grim outlook for patients with asbestos-related diseases. It was decided early on to adopt a multidisciplinary approach with the development of a research program concentrating on epidemiology and prevention of asbestos-related diseases; drafting guidelines for the diagnosis and treatment of malignant pleural mesothelioma (MPM); and establishment of a biobank for research into the biology of mesothelioma, to support the search for novel treatment approaches.

An essential tool for tracking the national mesothelioma epidemic was the re-establishment in 2010 of the Australian Mesothelioma Registry (AMR). The AMR collects fast-track notifications of newly diagnosed mesothelioma cases across the country and invites patients/families to provide information about asbestos exposure. The AMR is a collaborative arrangement between Safe Work Australia, Comcare and the Cancer Institute NSW, with collaboration from the ADRI, Monash University, the University of Sydney, the Hunter Research Foundation, and state and territory cancer registries. ADRI analysis of AMR data suggests that the malignant mesothelioma epidemic is slowing, but the number of older patients diagnosed with MPM is projected to increase until 2020. An increase in the incidence of malignant peritoneal mesothelioma among men up to 2025 is also projected.

In 2010, the ADRI convened a multidisciplinary national team of 50 mesothelioma experts and organised a detailed review of the world literature. Critical appraisal of 1110 publications led to 40 recommendations and 23 clinical practice points. The guidelines were approved by the National Health and Medical Research Council and published in 2013.[2] These formed the basis of an information booklet for patients and carers drafted in cooperation with Cancer Council Australia.[3]

Shortly after the ADRI's establishment, a biobank was set up, supported by an equipment grant from the Cancer Institute NSW and corporate funding. The ADRI biobank has focused on the prospective collection of optimally preserved (fresh-frozen) tissue samples and blood from patients and control individuals, and represents Australia's largest repository of mesothelioma specimens. Fresh-frozen MPM samples have contributed to an intercontinental effort, led by The Cancer Genome Atlas, to picture the most important genetic changes in MPM, leading to a better understanding of the fundamentals of malignant mesothelial growth. Researchers at the ADRI have also made extensive use of formalin-fixed tissues archived by thoracic surgeons at Royal Prince Alfred Hospital. Comparison of tumour and control tissues revealed major changes in the expression of microRNAs, a class of non-coding gene regulators frequently lost in cancer. These changes have potential diagnostic, prognostic and therapeutic implications.

ADRI researchers showed that levels of microRNA-16 (miR-16), a gene known for its tumour suppressor activity, are significantly reduced in mesothelioma tissues. This observation led to additional laboratory experiments using mesothelioma cell cultures and mesothelioma xenograft tumour-bearing mice. In both models, the addition of miR-16 mimics, synthetic versions of these short gene regulators, was able to halt tumour growth.[4] The translation into the clinic was quickly made and a dose-finding (phase I) study was initiated at the end of 2014. This trial is using miR-16-based mimics packaged in nanocells, a unique delivery system developed by Sydney-based biotech company EnGeneIC. The nanocells are targeted with an antibody against the epidermal growth factor receptor. A major clinical response observed in the study — the first to be reported in a patient treated with a microRNA-based therapy — provided a clear indication that the new treatment concept is worth continued investigation, and a phase II study is in preparation.[5]

In a little over 6 years, the ADRI's focus on epidemiology, biobanking, guidelines, and research into the basic biology of asbestos-related diseases has led to rapid clinical translation. It is a good example of how, with sufficient investment, a relatively small, disease-oriented research institute can produce prominent research outcomes within a relatively short time.

Competing interests: No relevant disclosures.

Provenance: Commissioned; not externally peer reviewed. ■

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