Special Article

Asbestos-related Diseases in Thailand: Past Experiences; Current and Future Perspectives

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Background

Asbestos, both in the form of amphibole group and chrysotile, has been imported into Thailand since 1938[1]. In 1995, it became known that the materials are pathogenic, causing asbestosis and mesothelioma[2], the import of amphiboles were banned. This left only chrysotile, the least toxic form of asbestos, remaining in use and available in Thailand.

For certain reasons, during the earlier decades there were strong campaigns against the import of asbestos into the country. Therefore, for the Royal Institute of Thailand, by law having the duty to solve any national scientific problem and to advise the government, took the opportunities to organize academic forums. The themes of which were "Various Views on the Use of asbestos in Thai Industries"[3] held on May 29, 2013, and the subsequent one on "Asbestos Use in Thai Industries and health Impacts"[4] held on April 28, 2014.

The principle objectives of the forums were to hold a joint assembly of individuals concerned to express their views on the use of asbestos. Unfortunately, the first forum had the drawback of having only speakers from a unilateral party. Nevertheless, the first forum and the publication of its proceedings calmed the contradictive atmosphere to some extent and for a period of time.

When the controversy was reborn, The Royal Institute became conscious of a disturbing attitude, so the second forum[4] was organized with the same objectives. Fortunately the second meeting featured many speakers focused on a wider vision. The speakers and participants concentrated on the following topics:

- Despite that chrysotile being noted as a genuine carcinogenic substance, there remain a controversy regarding the occurrence of such hazardous event in Thailand. One speaker described 12 mesothelioma patients that occurred in the period 2004 - 2013, but all of them lacked pathological evidences of asbestos etiology.

- Asbestos exposure occurs during working with asbestos and coping with asbestos products being breaking such as demolishing buildings.

- Chest radiographs shown by speakers may indicate a few cases of persons really having pathological pictures of asbestos etiology.

- Debate of the fundamental diagnosis of asbestos-related diseases based on history of exposure remain unsettle.

- One speaker referred to the etiology of mesothelioma that 80 percent of cases have asbestos etiology, making that among the approximated eighty cases encountered in Thailand, sixty odd cases would have asbestos etiology, as a matter of fact all of them had not a least supporting evidence.

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- Going back to the findings in 330 deceased general patients with 33 percent of asbestos bodies present; among them there were numbers of children as young as 5 months old. The children never worked in the factory using asbestos.

- Suggestions that further research studies must be conducted, particularly pertaining to asbestos biomarkers for the use in identifying exposure persons and diagnosing cases of asbestos-related diseases.

- Asbestos bodies determined from persons' bronchiolar lavage fluids or lung tissues must be analyzed for identifying the type of asbestos whether they are amphibole or chrysotile. Such identification is important regarding the indictment of exposure source and scenario.

- Regarding economy on banning the asbestos for industrial use range in severity of impacts.

- Information from the meeting indicated the negligible incidence of asbestos-related diseases in Thailand.

Past Experiences

Studies on asbestos pollution and asbestos-related health impacts from the date of initial import asbestos for industrial use in Thailand to the present date, i.e. attempts to identify sources of inhaled asbestos pollution by taking air samples from factories where asbestos was used[1, 5 - 7] and from a house during demolishing[8], and on busy streets[9] as well as the incidence of asbestos-related diseases showed negligible results. The first report of a case of asbestosis concomitantly occurred with talc pneumoconiosis appeared in 1976[10, 11], followed by few descriptive cases[12 - 16].

As for mesothelioma, a neoplasm that starts in cells in the linings of certain parts of the body, especially in the thoracic cavity, the abdomen, and around the heart, of which had been claim that about 80 percent of the malignant cases are associated with asbestos exposure occupationally or environmentally[17]; only minor portion of one case/million/year in the general population[18]. Lange JH and colleagues[19] on the other hand noted that not all mineralogical forms of asbestos are in capability of causing this disease as well as other asbestos-related diseases; they cited numerous investigations that there are other exposure agents/substances that appear to be causative for the disease along with idiopathic and familial relationship.

Regarding the incidence of mesothelioma in Thailand, there was a case of the tumor of tunica vaginalis (scrotum) diagnosed from a tissue biopsy at Siriraj Hospital in 1954[20], the first published case of pleural tumor in 1962[21] and three reported cases[22 - 24], adding up with scattered cases in the literature making the total of 80 cases[25]. Most cases had no evidence of asbestos etiology besides the three cases[22 - 24] with histories of working under asbestos environment. Hence the conclusion at that time remained that the industrial use of asbestos materials in Thailand has not cause problem on the Thai lifestyles.

Interestingly, our studies exhibited the finding of asbestos bodies in the autopsy lungs as high as 33 percent[26] and in bronchiolar lavage fluids from seven living persons[27], all of whom had no asbestos-related diseases or evidence of asbestos exposure. Our studies investigated cytokines in the blood with the objective of discovering biomarkers for identifying asbestos exposed persons yielded interesting provisional findings but awaiting further study in confirmation.[28, 29]

Current Perspectives

For earlier cases of mesothelioma, the diagnosis was made by pathological demonstration without asbestos fibers or bodies noted. Such phenomenon had been disputed over the etiology. Recently, there was a report of a mesothelioma case having asbestos bodies in the lung[30]. The case was a foreigner who had exposed asbestos in England 20 years previously and became ill recently while living

in Thailand. The history of the case was conformed to the long incubation period of mesothelioma genesis. The presence of asbestos bodies in this patient rather suggests recent exposure to the atmospheric asbestos pollution in Thailand.

An interesting event in this period was the finding in Incharoen's study of asbestos bodies in deceased lungs[31], which showed higher prevalence of cases than in Sriumpai's findings[26] 40 years ago. Such findings emphasized the persistence of atmospheric pollution in Thailand.

Future Perspectives

In the past four decades since the discovery of gene and the birth of molecular biology, studies of many diseases, especially cancers, are based on the premise of genetic origin. This began to change following the development of gene sequencing and the studies have been devoted to the whole genome sequencing. Next generation sequencing (NGS) is becoming a powerful technology for studying the system biology of health and diseases.

From a brief literature review[32], it is observed that most people exposed to asbestos, even in large amounts, do not get mesothelioma. Additionally, researchers have found several other factors that increase a person's risk of mesothelioma, apart from age, gender and race. Molecular genetic analysis has revealed several key genetic alterations which are responsible for the development and progression of mesothelioma, including cyclin-dependent kinase inhibitor 2A alternative reading frame *(CDKN2A/ARF),* neurofibromatosis type 2 *(NF2)* and *BRCA1*-associated protein-1 *(BAP1)* genes, which are the most frequency mutated tumor suppressor genes in mesothelioma cells. BAP1 is the gene that normally keeps cell growth under control; it is involved in histone modification and its inactivation induces the disturbance of global gene expression profiling and mesothelioma susceptibility. In addition, DNA methylation with up-regulation of epidermal growth factor receptor (EGFR) also plays an important role in the development of malignant pleural mesothelioma.

Furthermore, Raphael Bueno et colleagues' comprehensive genomic analysis of malignant pleural mesothelioma[33, 34] identifies recurrent mutations, gene fusions and splicing alterations in representing the hallmark event of mesothelioma incidence and reflecting the environmental influence. Their studies provided interesting findings on how asbestos-based pathogenesis occurs.

Apart from pathogenetic aspect of malignant pleural mesothelioma (MPM), insight into antitumor targets is currently of interest though still controversial. Focusing on the molecular mechanisms underlying the antiproliferative and pro-apoptotic effects of EGFR-TKIs, it is noted that gefitinib induced the formation and stabilization of inactive EGFR homodimers and inhibited MPM cell growth and survival, preventing EGF-dependent activation of ERK1/2 pathway by blocking EGFR-TK phosphorylation and stabilizing inactive EGFR dimers[35, 36].

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Further Readings

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