Milestones...

in Investigative Pathology

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Asbestos and Mesothelioma


Asbestos) or chrysotile (“white” asbestos) developed pleural types of asbestos. 3 of 50 (6%) rats receiving crocidolite (“blue” asbestos) on rats inoculated in the pleural space with suspensions of different types of asbestos. 3 of 50 (6%) rats receiving crocidolite (“blue” asbestos) or chrysotile (“white” asbestos) developed pleural mesotheliomas. After moving to the UK in 1962, he published data in 1969 on rats inoculated in the pleural space with 20 mg of crocidolite, chrysotile, or amosite fiber suspension, then followed to natural death. 30-40% of amosite-exposed rats, and 50-70% of the crocidolite- and chrysotile- exposed rats, developed pleural mesotheliomata. None of the saline- inoculated controls rats developed mesotheliomas. Rats with mesotheliomas died at 500-750 days of age, whereas control rats died at around 1,000 days. (No statistical testing was performed on the datasets in either the Nature or Br J Ca papers, so take heart, you qualitative types out there.)

Dr. Wagner recognized that pleural inoculation experiments were unrealistic, so he followed up his pleural inoculation experiments with dust aspiration experiments. Exposures mimicked 7 hour/5 day per week work hours. Amosite was the least fibrogenic of the three. As expected, increasing exposure led to increasing fiber load in the lungs. Interestingly, there were marked differences in steady-state fiber load following inhalation of similar amounts of crocidolite and chrysotile dust, indicating difference in dust clearance rates. Although chrysotile was cleared much better than crocidolite, the incidence of mesothelioma (6%) was similar to that seen with high-fiber burden crocidolite (6%). Most mesotheliomas developed after 6 months of dust exposure but, astoundingly, 2 rats exposed for only one day each (one to amosite and one to crocidolite) developed mesotheliomas. Assuming careful control of experimental conditions, these data beg the question of whether there is any risk-free exposure to asbestos dust.

Formal handling of asbestos exposure data in humans was sought by the NIH for a case-control study of mesothelioma patients presenting between 1975 and 1980 from three different populations (LA, NY, and the VA system). Dr. Wagner served as the study Pathologist. Their data showed that "90% of the incidences of pleural mesothelioma among men were directly attributable to past exposures to asbestos." They found an odds ratio of 27-fold for mesotheliomas in individuals with prior asbestos exposure. Statistical analysis confirmed what Dr. Wagner had suspected with that first autopsy.

In summary, Dr. Wagner made the initial association of occupational or environmental exposure to asbestos with subsequent risk for development of mesothelioma. This association required a prepared scientific mind in a region where there was high exposure to the etiologic agent. Following Koch's postulates, he showed that exposure of an animal model to the purified putative etiologic agent increased the incidence of a disease that was rare in the untreated control animals. His experimental work was confirmed by the exposure of humans involved in industries involving insulation and fire retardant materials. Careful history-taking was critical to making the observation, as the delay from exposure to signs/symptoms is measured in decades.
The scientific demonstration of asbestos as the major etiologic agent in mesothelioma prompted marketing of legal recourse to patients receiving this diagnosis. Asbestos has no medicinal value to the human, so our legal system recognized a skewed risk:benefit ratio to asbestos exposure, and proceeded to bankrupt the asbestos industry. Isn't this interesting, that we've witnessed destruction of a legitimate insulation/fire retardant materials industry because its dusty product leads to around 90% of the cases of a rare disease, when we've knowingly tolerated tax revenue subsidy of the growth, processing, and marketing of tobacco, whose dusty product leads to around 90% of the cases of the tobacco-associated common diseases, COPD and primary lung carcinoma?

References: