Friday, October 20, 2006

Friday, October 20, 2006 **8:00–10:05**

ORAL SESSION

Epidemiology I

32 South Africa: The first link between asbestos and mesothelioma, but not the last word?

J. teWaterNaude, R. Abratt, J. Myers. *University of Cape Town, Cape Town, South Africa*

The link between asbestos and mesothelioma was established by the South Africans Wagner, Marchand and importantly Sleggs, whose clinical acumen recognised both the association and that the entity was separate from fulminant tuberculosis. All three main commercial types of asbestos were mined in South Africa – white chrysotile, blue crocidolite and brown amosite, the latter two being particularly mesotheliomagenic. Peak production occurred in 1975, with more than 97% of the global crocidolite and all of the amosite (an acronym for Asbestos Mines of South Africa) produced by South Africa. A rapid decline and closure of these mines occurred within 20 years. More than 90% of all 10.2 million tons of asbestos produced in South Africa was exported, and to 70 countries at peak.

The mesotheliomagenicity of the different fibre types is crocidolite $>$ amosite $>$ chrysotile. The rarity of mesothelioma in chrysotile exposed workers may occur because the chrysotile contains little tremolite, a pattern which repeats in neighbouring Swaziland and Zimbabwe. While data on incidence is sparse, our best information indicates that about 75% of mesothelioma cases are occupational, with 25% associated with environmental exposure. The mining/industrial split is 45/55. The measured incidence in Prieska, a crocidolite mining town, is similar to that of Wittenoom in Australia. There is an ongoing under-diagnosis of mesothelioma in black workers, because being largely rural and poor, they have lesser access to diagnostic and therapeutic services, and also because of the masking effect of tuberculosis (worsened by the HIV pandemic), which harks back to the experience of Sleggs.

Recent litigation settlements in South African courts – first with individual claimants and later with two larger class action suits - have established significant compensation funds of $\sim$ USD 100 million for asbestos-related diseases. With South Africa being the first link and having exported most of its asbestos, we are still hearing the last words as export destinations are experiencing their own epidemics of mesothelioma.

33 The mesothelioma epidemic: Occupational, environmental and spontaneous cases

J. Peto[1], C. Rake[2], C. Gilham[2], J. Hodgson[3]. *[1]London School of Hygiene and Tropical Medicine, London, UK; [2]Institute of Cancer Research, Sutton, UK; [3]Health and Safety Executive, Bootle, UK*

Background: Asbestos use fell abruptly in Britain around 1980, but there are now 1,900 mesothelioma deaths per year, slightly more than melanoma and almost twice the number for cervical cancer. The total number of British mesothelioma deaths is predicted to be about 90,000, most of which are still to occur, with 250,000 throughout Western Europe.

Methods: We have interviewed 624 mesothelioma patients (513 men, 111 women), 425 resected lung cancers (294 men, 131 women), and 1,420 population controls (1,112 men, 308 women) to obtain lifetime occupational and residential histories.

Results: Defining the reference group as $<$5 years of low-risk industrial work, odds ratios (95% CI) for 5+ years of exposure before age 35 years were 33.8 (17.0-67.2) for carpenters, 12.2 (7.2-20.8) for plumbers, electricians, painters and decorators, 3.9 (2.0-7.8) for other construction workers, and 12.8 (7.2-22.6) for other recognized high-risk occupations. The male mesothelioma rate was much lower in other occupations, corresponding to a lifetime risk of the order of 1 in 600 men in the reference group.

Conclusions: The lifetime mesothelioma risk for men born before about 1950 will thus be about 5% for carpenters, 2% for other high-risk occupations and almost 1% in general construction. Lung samples obtained from the resected lung cancers and at post-mortem from mesothelioma patients we have interviewed will define the relationship between lung fibre burden and mesothelioma risk. These data, together with lung samples obtained from young construction workers undergoing surgery for pneumothorax, will determine the risks caused by current exposures. Most female mesotheliomas have no known exposure, so the fivefold increase in female rates since the 1960s may be due largely to environmental exposure. The effects of brief and prolonged chrysotile exposure will be discussed in relation to these findings, and to developing countries where uncontrolled asbestos use is still widespread.

34 The global asbestos epidemic and its reflections in the recent Japanese experience

R-T. Lin, K. Takahashi. *Department of Environmental Epidemiology, UOEH, Kitakyushu, Japan*

Background: Japan experienced an “asbestos-panic” this past year, triggered by news that a major company was responsible for scores of asbestos-related disease (ARD) cases among former employees. Social criticism gained momentum as it became apparent that many residential victims (without job exposure) were also involved. Many other companies having used asbestos came forward to disclose their responsible share of ARDs. Administration faced allegations that control measures lagged behind Western countries: e.g., crocidolite and amosite was banned in 1995; chrysotile was banned in 2004 “in principle.” The consumption curve of asbestos in Japan trailed that of many Western countries, concurrent with the “economic catch-up period,” and lingered into the late 1990s. Consequently, mesothelioma mortality started to show an upsurge fairly recently (953 deaths or 7.6 per million in 2004). The recent Japanese experience is likely to be a reflection of the global asbestos epidemic.

Methods: We explored the global situation by 1) conducting an ecological study of national-level data between historical asbestos consumption and recent mortality rates of ARDs [mesothelioma (m), pleural m, peritoneal m, and asbestosis]. There is concern that, as regards ARDs, industrializing countries may be following the paths of industrialized countries. To address this issue, we followed-up on the above global analyses by 2) assessing the time-trend patterns of historical asbestos consumption and their relation to the time-trend patterns of ARDs.

Results: 1) Clear and plausible correlations were found between the two sets (consumption and mortality) of cross-sectional national data, which were marked for mesothelioma in both sexes and male asbestosis (Lancet, in press). 2) Preliminary results suggest that the global asbestos epidemic is indeed unfolding, but in a manner that can be characterized by distinctive historical time-patterns of consumption (to be submitted).

Conclusions: The burden of ARDs, which has been/is becoming apparent among industrialized countries, will likely shift towards the industrializing countries in a sequential manner.

35 Risk of pleural mesothelioma: A French population-based case-control study (1998-2002)

P. Rolland[1,2], S. Ducamp, C. Gramond[1,2], F. Galateau-Sallé[3], J.C. Pairon[4], P. Astoul[5], S. Chamming's[4], A. Gilg Soit Ilg[1], E. Imbernon[1], M. Goldberg[1], P. Brochard[2]. *[1]Institut de Veille Sanitaire, Saint-Maurice, France; [2]Université Bordeaux 2, Bordeaux Cedex, France; [3]Centre Hospitalier Universitaire, Caen, France; [4]Institut Interuniversitaire de Médecine du Travail, Paris, France; [5]Hôpital Sainte-Marguerite, Marseille, France*

Background: In industrialised countries, asbestos has been widely used for decades and occupational exposure to asbestos has been identified as the most important risk factor for pleural mesothelioma. The aims of this study are to analyse the risk of mesothelioma according to occupations and industries, to estimate the attributable risk to asbestos exposure, and to research other factors (synthetic fibres, ionizing radiations, SV40 virus, previous diseases). Only results on occupational exposure are presented in this report.

Methods: A population-based case-control study was conducted between 1998 and 2002 in 19 French districts, within the National mesothelioma surveillance program (covering 25% of the French population). This report is based on 467 cases histologically confirmed (80% males, 41-93 years old) and 868 controls matched for sex, age and district. Data were collected by trained interviewers with a standardised questionnaire, and lifetime occupational exposure was as-

sessed by experts. Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CIs).
Results: Among men, the highest risks were observed for the occupations of plumbers, pipe-fitters, sheet-metal workers, and for the industries of ship repair, asbestos products, metal products, and construction. A significant dose-response relationship was found between cumulative occupational asbestos exposure and pleural mesothelioma, even for the lowest exposure category >0-0.07 fibres/ml-years (OR 2.8, 95% CI 1.7-4.7). The attributable risk for occupational asbestos exposure was 83.5% (95% CI 77.2-89.8%) for men and 41.9% (95% CI 29.8-54.0%) for women.
Conclusions: This report enabled us to classify occupations and industries according to the risk of pleural mesothelioma, it provides guidance for preventive actions among specific groups of workers, and allows a continuous evaluation of their efficiency. The analyses are ongoing with a focus on non-occupational exposed subjects to asbestos (women in particular).

36 Health effects among World Trade Center responders

S.M. Levin, R. Herbert, J. Moline. *Mount Sinai School of Medicine, New York, USA*

Background: Responders to the World Trade Center disaster on 9/11 and in subsequent months were exposed to a wide range of physical and chemical hazards and to psychological stressors. Anecdotal clinical evidence suggested that many developed aerodigestive disorders and psychological sequelae.
Methods: Over 16,000 rescue and recovery workers have undergone clinical evaluation with the use of a standardized assessment protocol that includes pre- and post-bronchodilator spirometry.
Results: High rates of persistent upper and lower airway abnormalities, gastroesophageal reflux, and post-traumatic stress and depression have been identified among the examinees.
Conclusions: WTC-related exposures encountered by WTC responders caused upper and lower respiratory abnormalities, GERDS, and psychological sequela that are highly prevalent and persistent. Exposure to asbestos in the rubble and settled dust, especially among specific categories of responders, poses a risk of mesothelioma in the future, the magnitude of which is uncertain.

37 Pleural abnormalities and exposure to asbestos-contaminated vermiculite from Libby, Montana: A twenty year follow-up study

J.E. Lockey, A.M. Rohs, K. Dunning, T. Hilbert, R. Shipley, C. Meyer, J. Wiot, R. Shukla. *University of Cincinnati, Cincinnati, USA*

Background: Vermiculite mined in Libby, Montana was shown to be contaminated with asbestiform fibers, best described as tremolite-actinolite-richterite-winchite transition fiber. This study is a follow up investigation of a 1980 cross-sectional study of 513 workers exposed predominantly to Libby vermiculite ore. The rationale was to determine the long-term pulmonary effects of exposure to Libby vermiculite used in a secondary manufacturing setting.
Methods: Of the original 513 workers, 82 were deceased and eight could not be located. Of the remaining 423, 70.4% (298) participated in the study, 11.6% (49) refused, and 18.0% (76) did not respond. Of the 298 participants, 94% (280) completed both the radiograph and the interview for inclusion in this analysis. Primary outcomes were pleural and interstitial changes as determined from chest radiography. Pleural thickening was defined as unilateral or bilateral thickening, excluding solitary blunting of the costophrenic angle(s). Parenchymal changes were defined as irregular opacities with a profusion category >1/0. Chest radiographs were interpreted by three board certified radiologists (B readers). For a radiograph to be classified as abnormal, two of the three B readers must agree. Exposure to vermiculite ore was defined cumulatively (fiber/cc/years).
Results: Initial analysis of the first 194 participants indicated an increase in the number of workers with pleural changes. Pleural plaques were identified in 25% compared to 4% in the original 1980 cohort. Final results will be presented examining the association of pleura and interstitial findings with exposure indices.
Conclusions: Vermiculite contaminated with asbestiform fibers has the propensity to cause an increase in pleural changes at low exposure levels. The public health implications of these preliminary findings are important in view of the national distribution of the Libby vermiculite ore for home and commercial uses.
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38 Mesothelioma update for Libby, Montana: Occupational and non-occupational

B.W. Case. *McGill University, Montreal, Canada*

Background: In 1986, a McGill University study of vermiculite miners/millers in Libby, Montana reported 4 mesothelioma cases in workers hired before 1965. In 2004 mortality was updated to 1999, adding 8 deaths. No study including workers after 1965 or any para-occupational or non-occupational mesothelioma in Libby has been published previously.
Methods: Case data for mesothelioma in Libby was obtained from 3 sources: a) the published McDonald (McGill) (1986, 2004) follow-up studies of W.R. Grace workers at Libby, Montana; b) Information from attorneys representing mesothelioma victims and c) Dr. Brad Black on case numbers, occupational/non-occupational origin and basis of diagnosis at the CARD clinic at Libby, which began in 2000. There is no overlap between the latter and the published studies. Information obtained included years of work at the mine or mill (if any); pathology reports and death certificates.
Results: Four occupational cases were found additional to the 12 published who started work before 1965. One worked for only 6 weeks and 3 died later than 1999. Mesothelioma proportional mortality among workers is over 5%; a proportion seen previously only in crocidolite asbestos miners/millers and amosite-exposed insulation workers. Three more cases were diagnosed among those who began work after 1965, for a total of 19 to date. Ten non-occupational cases were identified; for 7 diagnosed after 2000, (6 confirmed pathologically, 1 clinically) there was also no history of living with a worker. Latency averaged 35 years from first exposure in workers. Latency in non-occupational cases, if equated with time of residence in Libby, exceeds this. Non-occupational cases incident earlier than 2000, while likely, have never been fully ascertained.
Conclusions: Mesothelioma in Libby workers and those without occupational exposure has been under-estimated. Caused by "Libby amphibole", it has ominous implications for known continuing amphibole exposure sources throughout the USA, including widely distributed waste products and "naturally-occurring" amphiboles not commercially exploited.

Friday, October 20, 2006 10:30–12:20

ORAL SESSION

Epidemiology II

39 Australia: Wittenoom and beyond

N. de Klerk[1], B. Musk[2]. *[1]University of Western Australia, Perth, Australia; [2]Sir Charles Gairdner Hospital, Perth, Australia*

Background: The epidemic of mesothelioma in Australia was initially driven by the crocidolite mine and mill at Wittenoom in Western Australia where long-established asbestos hygiene principles and regulations were routinely ignored. Australia was also the largest per capita user of asbestos in the 1950s, resulting in the highest rate of mesothelioma in the world in the 1990s and beyond.
Methods: Rates of mesothelioma in different Australian states over time and overall consumption of asbestos were examined, and different sources of exposure to asbestos were described.
Results: Rates of mesothelioma in Australia appear to be leveling off while use of asbestos has declined. Importation of new asbestos into Australia was finally banned at the end of 2003, but the vast quantities of materials from previous use still remain. Australia's chief manufacturer of asbestos products during the last century tried to avoid its future liabilities by transferring its operations to the Netherlands, but was shamed into establishing a more realistic compensation fund. While the mesothelioma surveillance of the National Occupational Health and Safety Commission appears to have lost impetus, the National Health and Medical Research Council of Australia has recently set aside substantial funds for asbestos-related disease research.
Conclusions: Given that the highest future exposures to asbestos are likely to occur among workers in small demolition and removal operations, the dismantling of workers' protection regulations for small business, through Australia's "new" industrial relations legislation, is likely to result in future high rates of mesothelioma lasting well into this new century.

40 Age and sex differences in malignant mesothelioma after residential exposure to blue asbestos (crocidolite)

A. Reid[1], G. Berry[2], N. de Klerk[1], J. Heyworth, A.W. Musk[1]. *[1]University of Western Australia, Crawley, Australia; [2]University of Sydney, Sydney, Australia*

Background: Blue asbestos (crocidolite) was mined and milled at Wittenoom,