Inside this issue: Environmental and Occupational Health

Familial malignant mesothelioma: A population-based study in Central Italy (1980-2012). 2

Genetic variants associated with increased risk of malignant pleural mesothelioma: a genome-wide association study. 2

Well-differentiated papillary mesothelioma: clustering in a Portuguese family with a germline BAP1 mutation. 3

Specific inhalation challenge in the diagnosis of occupational asthma: consensus statement. 3

Cadmium exposure and cancer mortality in a prospective cohort: the strong heart study. 4

Nickel accumulation in lung tissues is associated with increased risk of p53 mutation in lung cancer patients. 4

Chest computed tomography screening for lung cancer in asbestos occupational exposure: a systematic review and meta-analysis. 5

Exposure-response estimates for diesel engine exhaust and lung cancer mortality based on data from three occupational cohorts. 5

The effects of PM2.5 and its components from indoor and outdoor sources on cough and wheeze symptoms in asthmatic children. 6

Pesticides and other occupational exposures are associated with airway obstruction: the Life Lines cohort study. 6

Combined effect of smoking and occupational exposure to dusts, gases or fumes on the incidence of COPD. 7

Papers selected and commented on by
Prof Ryuji Ieki, Dr Kozo Kuribayashi and Prof Takashi Nakano,
Division of Respiratory Medicine,
Dept of Internal Medicine,
Hyogo College of Medicine,
Japan
Contact: Takashi Nakano, email: t-nakano@hyo-med.ac.jp
**Familial malignant mesothelioma: A population-based study in Central Italy (1980-2012).**

Authors: Ascoli V et al.
Comment: In this study, among 997 incident mesotheliomas recorded in a 32-year-period (1980-2012), 13 clusters and 34 familial cases were detected, accounting for 3.4% of all mesotheliomas. The study showed that the most common clusters were those with affected siblings and unaffected parents. Asbestos exposure was occupational (n=7 clusters), household (n=2), environmental (n=1), or not attributable for insufficient information (n=3). The results suggest potential genetic recessive effects in mesothelioma that interact with asbestos exposure, but it is not possible to estimate the specific proportion attributable to each of these components.

---

**Genetic variants associated with increased risk of malignant pleural mesothelioma: a genome-wide association study.**

Authors: Matullo G et al.
URL: [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3634031/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3634031/)
Comment: The aim of this study was to identify the genetic risk factors that may contribute to the development of MPM. The authors conducted a genome-wide association study in Italy, among 407 MPM cases and 389 controls with a complete history of asbestos exposure. A replication study was also undertaken and included 428 MPM cases and 269 controls from Australia. Most of these SNPs were located in regions reported to harbor aberrant alterations in mesothelioma (SLC7A14, THRB, CEBP350, ADAMTS2, ETV1, PVT1 and MMP14 genes), causing at most a 2-3-fold increase in MPM risk. The Australian replication study showed significant associations in five of these chromosomal regions (3q26.2, 4q32.1, 7p22.2, 14q11.2, 15q14). These results showed that genetic risk factors may play an additional role in the development of MPM.
Well-differentiated papillary mesothelioma: clustering in a Portuguese family with a germline BAP1 mutation.

Authors: Ribeiro C et al.
URL: http://annonc.oxfordjournals.org/content/24/8/2147.long
Comment: Well-differentiated papillary mesothelioma (WDPM) is a rare variant of epithelioid mesothelioma and is considered to be associated with good prognosis due to its clinically indolent behavior and long survival. Most reported cases involve the peritoneum of women at reproductive age with no history of exposure to asbestos, with pleural involvement being less common. The authors describe two cases of WDPM in women of the same family (siblings). After the concurrent diagnosis of WDPM and uveal melanoma, genetic diagnosis was carried out taking into consideration that these two malignancies were recently associated with hereditary BAP1 gene mutations and it was positive for both the patients. This is the first description of WDPM in two siblings who also presented with a germline BAP1 mutation.

Specific inhalation challenge in the diagnosis of occupational asthma: consensus statement.

Authors: Vandenplas O et al.
Reference: Eur Respir J. 2014 Mar 6. [Epub ahead of print]
URL: http://erj.ersjournals.com/content/43/6/1573.long
Comment: This consensus statement provides practical recommendations for specific inhalation challenge (SIC) in the diagnosis of occupational asthma. This article details each step of a SIC, including safety requirements, techniques for delivering agents, and methods for assessing and interpreting bronchial responses. Testing should only be carried out in hospitals where physicians and healthcare professionals have appropriate expertise. Tests should always include a control challenge, a gradual increase of exposure to the suspected agent, and close monitoring of the patient during the challenge and for at least 6 h afterwards. A positive response is defined by a fall in forced expiratory volume in 1 s ≥15% from baseline. The sensitivity and specificity of SIC are high but not easily quantified, as the method is usually used as the reference standard for the diagnosis of occupational asthma.
Cadmium exposure and cancer mortality in a prospective cohort: the strong heart study.

Authors: García-Esquinases E et al.
Reference: Environ Health Perspect. 2014; 122:363-370
URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3984227/
Comment: Cadmium (Cd) is known as a human carcinogen. This Study was a prospective cohort study of 3,792 men and women 45-74 years of age who were followed for up to 20 years. Baseline urinary Cd (U-Cd) was measured using inductively coupled plasma mass spectrometry. The authors assessed cancer events by annual mortality surveillance. Low-to-moderate Cd exposure was prospectively associated with total cancer mortality and with mortality from cancers of the lung and pancreas. The implementation of population-based preventive measures to decrease Cd exposure could contribute to reducing the burden of cancer.

Nickel accumulation in lung tissues is associated with increased risk of p53 mutation in lung cancer patients.

Authors: Chiou YH et al.
Comment: Many studies have examined the associations between occupational exposure to nickel compounds and lung cancer. This study assessed whether nickel exposure increased the occurrence of p53 mutations due to DNA repair inhibition by nickel. They conducted the host cell reactivation assay in A549 and H1975 lung cancer cells and showed that the DNA repair activity was reduced by nickel chloride in a dose-dependent manner. This was associated with elevated production of hydrogen peroxide-induced 8-oxo-deoxyguanosine. Therefore, increased risk of p53 mutation due to defective DNA repair caused by high nickel levels in lung tissues may be one mechanism by which nickel exposure contributes to lung cancer development.
Chest computed tomography screening for lung cancer in asbestos occupational exposure: a systematic review and meta-analysis.

Authors: Ollier M Jr, et al.
URL: http://journal.publications.chestnet.org/article.aspx?articleid=1819314
Comment: Lung cancer is the frequent malignant asbestos-related pathology and remains the most fatal cancer of industrialized countries. This study aimed to determine whether CT screening in asbestos-exposed workers is effective in detecting asymptomatic lung cancer using a systematic review and meta-analysis and reviewed all cohort studies involving chest CT screening in former asbestos-exposed workers. The prevalence of all lung cancers detected by CT screening in asbestos-exposed workers was 1.1% (CI 95%: 0.6%-1.8%). Detection of lung cancer in asbestos-exposed workers using CT is at least equal to the prevalence in heavy smokers (1%; 95%CI: 0.09%-1.1%) (Aberle et al., N Engl J Med, 2011), and also shared a similar proportion of stage 1 diagnoses.

Exposure-response estimates for diesel engine exhaust and lung cancer mortality based on data from three occupational cohorts.

Authors: Vermeulen R. et al.
URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3915263/
Comment: Many studies have been discussing engine exhaust and lung cancer. This study conducted a meta-regression of lung cancer mortality and cumulative exposure to elemental carbon (EC), a proxy measure of diesel engine exhaust (DEE), based on relative risk (RR) estimates reported by three large occupational cohort studies. They estimated a RR of 0.00098 (95% CI: 0.00055, 0.0014) for lung cancer mortality with each 1-µg/m3-year increase in cumulative EC based on a linear meta-regression model. Corresponding RRs for the individual studies ranged from 0.00061 to 0.0012. Estimated numbers of excess lung cancer deaths through 80 years of age for lifetime occupational exposures of 1, 10, and 25 µg/m3 EC were 17, 200, and 689 per 10,000, respectively. For lifetime environmental exposure to 0.8 µg/m3 EC, they estimated 21 excess lung cancer deaths per 10,000.
The effects of PM2.5 and its components from indoor and outdoor sources on cough and wheeze symptoms in asthmatic children.

Authors: Habre R. et al.
URL: http://www.nature.com/jes/journal/v24/n4/full/jes201421a.html
Comment: Mixed proportional odds models for an ordinal response were used to relate daily cough and wheeze scores to PM2.5 exposures. The odds ratio associated with being above a given symptom score for a SD increase in PM2.5 from indoor sources (PMIS) was 1.24 (95% confidence interval: 0.92-1.68) for cough and 1.63 (1.11-2.39) for wheeze. Cough was associated with indoor PM2.5 components from outdoor sources (denoted with subscript "OS") bromine (BrOS: 1.32, 1.05-1.67), chlorine (ClOS: 1.27, 1.02-1.59) and pyrolyzed organic carbon (OPOS: 1.49, 1.12-1.99). The highest effects were seen in the winter for cough with sulfur (SOS: 2.28, 1.01-5.16) and wheeze with organic carbon fraction 2 (OC2OS: 7.46, 1.19-46.60). These results indicate that exposure to components originating from outdoor sources of photochemical, diesel and fuel oil combustion is associated with symptom's exacerbation, especially in the winter.

Pesticides and other occupational exposures are associated with airway obstruction: the Life Lines cohort study.

Authors: de Jong K. et al.
URL: http://oem.bmj.com/content/71/2/88.long
Comment: Exposure to vapors, gases, dusts and fumes (VGDF) have been associated with a two- to threefold higher COPD risk. This study was included 11851 subjects aged 18-89 years from the Life Lines cohort study. Additionally, they stratified by smoking status and gender and tested for interaction. A second general population cohort (n=2364) was used to verify their initial findings. Occupational exposure to VGDF and pesticides was associated with a lower level of FEV(1) and FEV(1)/FVC and with a higher prevalence of mild and moderate/severe airway obstruction in the two general populations investigated. There were no associations with exposure to solvents. Occupational exposure to both VGDF and pesticides is associated with airway obstruction in the general population.
**Combined effect of smoking and occupational exposure to dusts, gases or fumes on the incidence of COPD.**

**Authors:** Pallasaho P. et al.


**Comment:** This study was performed a longitudinal 11-year follow-up postal survey. Participants of the first postal questionnaire were invited to this follow-up survey in 2007 with 4302 (78%) answers obtained. Cumulative incidence of COPD in 11 years was 3.43% corresponding to an incidence rate of 3.17/1000/year after exclusion of those with self-reported physician-diagnosed COPD and ever COPD in 1996. Smoking and age were associated with incident COPD. Reported family history of COPD increased the cumulative incidence to 8.55% vs 3.04% among those without a family history (p < 0.001). In multivariate analysis, significant independent risk factors for incident COPD were: current smoking in 1996 (OR 4.40 [95% CI 2.89 -6.71]), age over 50 (OR 3.42 [2.22-5.26]), family history of COPD (OR 2.08 [1.27-3.43]), ever asthma (OR 2.28 [1.35-3.86]), and self-reported OE (OR 2.14 [1.50-3.05]).