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Occupational exposure to asthmagens and adult onset wheeze and lung function in people who did not have childhood wheeze: A 50-year cohort study

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ABSTRACT

Background: There are few prospective studies that relate the development of adult respiratory disease with exposure to occupational asthmagens.
Objective: To evaluate the risk of adult onset wheeze (AOW) and obstructive lung function associated with occupational exposures over 50 years.
Methods: A population-based randomly selected cohort of children who had not had asthma or wheezing illness, recruited in 1964 at age 10–15 years, was followed-up in 1989, 1995, 2001 and 2014 by spirometry and respiratory questionnaire. Occupational histories were obtained in 2014 and occupational exposures determined with an asthma-specific job exposure matrix. The risk of AOW and lung function impairment was analysed in subjects without childhood wheeze using logistic regression and linear mixed effects models.
Results: All 237 subjects (mean age: 61 years, 47% male, 52% ever smoked) who took part in the 2014 follow-up had completed spirometry. Among those who did not have childhood wheeze, spirometry was measured in 93 subjects in 1989, in 312 in 1995 and in 270 subjects in 2001 follow-up. For longitudinal analysis of changes in FEV_1 between 1989 and 2014 spirometry records were available on 191 subjects at three time points and on 45 subjects at two time points, with a total number of 663 records. AOW and FEV_1 < LLN were associated with occupational exposure to food-related asthmagens (adjusted odds ratios (adjORs) 95% CI: 2.7 [1.4, 5.1] and 2.9 [1.1, 7.7]) and biocides/fungicides (adjOR 95% CI: 1.8 [1.1, 3.1] and 3.4 [1.1, 10.8]), with evident dose-response effect (p-trends < 0.05). Exposure to food-related asthmagens was also associated with reduced FEV_1, FVC and $FEF_{25–75\%}$ (adjusted regression coefficients 95% CI: −7.2 [−12.0, −2.4], −6.2 [−10.9, −1.4], and −13.3[−23.4, −3.3]). Exposure to wood dust was independently associated with AOW, obstructive lung function and reduced $FEF_{25–75\%}$. Excess FEV_1 decline of 6-8ml/year was observed with occupational exposure to any asthmagen, biocides/fungicides and food-related asthmagens ($p < 0.05$).
Conclusions: This longitudinal study confirmed previous findings of increased risks of adult onset wheezing illness with occupational exposure to specific asthmagens. A novel finding was the identification of food-related asthmagens and biocides/fungicides as potential new occupational risk factors for lung function impairment in adults without childhood wheeze.

1. Introduction

Current evidence suggests that 17% of adult-onset asthma (ERS, 2013) and up to 20% (50% among never smokers) of chronic obstructive pulmonary disease (COPD) (Sigsgaard et al., 2010) can be attributed to work-related exposure. Although the prevalence of asthma in some westernised countries appears to be falling (Asher and Pearce, 2014), the individual and societal burden of asthma remains high. Moreover the worldwide prevalence of asthma and COPD is rising (Anandan et al., 2010; GOLD, 2014), and therefore the search for preventable environmental risk factors remains important.

Studies have shown certain occupational sensitisers to be associated with an increased risk of asthma, e.g. isocyanates, latex (Bakerly et al., 2008), the role of irritant exposures in asthma aetiology is less well established (Brooks and Bernstein, 2011). Most evidence for the association between occupational exposure and respiratory symptoms, ventilatory function impairment and decline comes either from studies that examine specific exposures within single industries or occupational settings (Shi et al., 2010) or from general population cross-sectional (Le Moual et al., 2004; Humerfelt et al., 1993) and case-control (Wang et al., 2010) studies. Such studies have inherent weaknesses, including healthy worker effect, self-selection in job choice, case/control selection

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Table 1
The WHEASE cohort recruitment and follow-up.

Original cohort	
1964	The Medical Research Council random survey of Aberdeen schoolchildren Age 10–15 years 2743 invited, 2511 participated: response rate 92% 121 child asthma, 167 child wheezy bronchitis, 2223 child non–wheezers Spirometry measured in 288 child asthma & wheezy bronchitis
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What Happens Eventually to Asthmatic children: Sociologically and Epidemiologically (WHEASE) cohort	
1989	WHEASE 1 to follow all child asthma and wheeze cases and selected non–wheezers Age 35–40 years 455 traced and invited, 360 participated:response rate 79% Participants included: 97 child asthma, 132 child wheezy bronchitis, 131 child non–wheezers Spirometry measured in 272, including 93 child non–wheezers
1995	WHEASE 2 to follow all child non–wheezers Age 41–46 years 1758 traced and invitedto postal survey, 1542 participatedin postal survey: response rate 88%
	Participants in postal survey: 102 AOW, 1440 never–wheezers Clinical assessment (including spirometry) carried out in 312: 102 AOW and 217 randomly selected never–wheezers
2001	WHEASE 3 to follow all in WHEASE 1 and those with spirometry in WHEASE 2 Age 47–52 years 605 traced and invited, 381 participated: response rate 63% Participants included: 46 child asthma, 65 child wheezy bronchitis, 270 child non–wheezers Spirometry measured in 372, including 270 child non–wheezers
2014	WHEASE 4 to follow all WHEASE 1, 2 & 3 with previously measured spirometry Age 58–64 years 583 traced andinvited, 330 participated: response rate 57% Participants included: 38 child asthma, 53 child wheezy bronchitis, 239 child non–wheezers Spirometry measured in 329, including 239 child non–wheezers Occupational histories collected from 328, including 237 child non–wheezers

bias and the issue of generalisability, which may also preclude causal inference. Another weakness of epidemiological studies is their inability to accurately ascribe exposure measures. A few studies have prospectively examined associations with exposure to specific occupational substances in population-based cohorts, but with relatively short follow-up periods (Lillienberg et al., 2013; Humerfelt et al., 1993; Mehta et al., 2012).

The Aberdeen population-based WHEASE (What Happens Eventually to Asthmatic children: Sociologically and Epidemiologically) cohort study of children recruited in 1964 (Dawson et al., 1969) at age 10–15 years and followed up until 2014 (age 58–64 years) (Tagiyeva et al., 2016) provides a rare opportunity to investigate the effects of lifetime occupational exposures on respiratory morbidity in later life.

The aim of the current study was to investigate, in a community-based setting, whether occupational exposures to known asthmagens, assessed by job exposure matrix (JEM), were related to the development of adult onset wheeze (AOW), spirometry-defined airflow obstruction, or impaired ventilatory function at age 58–64 years and to longitudinal changes in ventilatory function over 25-year follow-up among those who did not have wheezing illness as children.

2. Materials and methods

2.1. Subjects

In 1964, the British Medical Research Council Medical Sociology Research Unit conducted a random community survey of all children attending primary school in the city of Aberdeen, Scotland in 1962 and still resident in Aberdeen at the time of selection. A 1-in-5 random sample was selected totalling 2743 of whom 2511 were interviewed at home with their parents. Amongst the 2511 children aged 10–15 years interviewed, 288 were reported as having had wheeze and