S119 INDUCIBLE LARYNGEAL OBSTRUCTION MASQUERADING AS WORK-RELATED ASTHMA: A NEW APPROACH

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Introduction The specific inhalation challenge (SIC) is the reference standard test for diagnosis of occupational asthma in people with immunological sensitisation to a specific agent. In our occupational lung disease clinic, we recognise a separate group of patients who report symptoms consistent with inducible laryngeal obstruction (ILO) triggered by one or more agents which are generally not recognised sensitisers. Symptoms, which include throat and chest tightening, voice change, dyspnoea and wheeze, are frequently misdiagnosed as work-related asthma, "allergy" and even anaphylaxis. In such cases securing the correct diagnosis can avoid unnecessary medication use, excessive health care utilisation and occasionally loss of employment. We have designed a SIC to provide objective confirmation of the diagnosis of ILO in the occupational setting.

Method Patients are carefully selected to undergo ILO-SIC. After histamine challenge testing, spirometry and direct laryngoscopy, they are exposed, in a specialist exposure chamber, to the agent (s) which provoke their symptoms. Each challenge is bespoke according to the patient's triggers, work environment and comorbidities. Exposure is usually continued until the symptoms experienced in the workplace are reproduced, or to a level expected to cause airway irritation in a control individual. Direct laryngoscopy and measurement of spirometry is repeated and any anatomical and physiological changes noted.

Results We have carried out 30 such challenges (90% women; mean age 45 years (SD 9.4)) to date. Agents have included perfumes, household paint and hospital cleaning products. In 87% of cases, we replicated symptoms experienced in the workplace. In 53% of cases, clear changes of ILO were seen. In those with normal laryngoscopy, the SIC is equally useful in reassuring patients that symptoms experienced are not dangerous, nor consistent with anaphylaxis or similar. Following careful explanation of the diagnosis, patients are managed conservatively or referred to specialist physiotherapists or voice therapists if indicated. Asthma treatment can often be withdrawn over time.

Conclusion A precise diagnosis in cases of occupational asthma is key to successful outcome; in this setting, we increasingly see patients with occupational (or other environmental) ILO. ILO-SIC testing in specialist centres can provide objective evidence to assist diagnosis avoiding unnecessary investigation and treatment of other conditions.

S120 ASTHMA IN FIRE FIGHTER APPLICANTS: BURDEN OF DISEASE AND FACTORS PREDICTING SUCCESSFUL APPLICATION

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Asthma is of concern to UK fire services that need to maintain maximal operational capability; current guidance suggests specialist respiratory review of applicants with a history of asthma, including tests of non-specific airway responsiveness. We present

data from our occupational lung disease clinic over a 17 year period.

Between March 1999 and January 2016, 112 firefighters were assessed; 90 of these completed histamine provocation testing allowing measurement of non-specific bronchial hyper-responsiveness using PC20 to histamine. Retrospective case note review was undertaken to look for predictors of PC20 from clinical history in this cohort. Subsequent follow up included recorded outcome of application and reported symptoms on future employment in the fire service.

Unsurprisingly the majority of applicants were male (87.8%, n = 79) and atopic (78.6% n = 66). Around one third had experienced symptoms 27 (31.8) or taken treatment 32 (38.0) in the last year. Most patients were taking no asthma therapy at the time of assessment (64.4%, n = 58) with the majority of those on therapy taking a reliever only (n = 20, 22.2%). Three quarters (75.6%) had normal bronchial reactivity at the time of assessment (PC20 > 16 mg/ml histamine; n = 68) and 85.6% borderline normal airway responsiveness (PC20 > 8 mg/ml histamine; n = 77).

Complete data on follow up was available for 86% of those assessed (n = 90); 64 of these had a recorded PC20. Table 1 shows the predictive factors for successful application in this cohort. Applicants were more likely to be rejected if they were older at time of application; reported recent asthma symptoms or use of treatment in the last year, had a history of childhood asthma or a measured PC20 of less than 16 mg/ml.

The findings of this study suggest that a history of asthma in this occupational group remains a concern to occupational health teams focusing on operational capability of workforces with safety critical roles. Further follow-up of this cohort or a wider prospective study could provide applicants with asthma and their recruiters with useful guidance on individual suitability for employment as a fire fighter.

Abstract S120 Table 1 Characteristics of 64 fire service applicants with asthma who had a known recruitment outcome (excluding those who withdrew application)

	Accepted n = 57	Not accepted (health grounds) n = 7	P value
Male	51 (89.5)	5 (71.4)	0.209
PC 20 ≥ 8	53 (93.0)	3 (42.9)	0.003
PC 20 ≥ 16	47 (82.5)	3 (42.9)	0.036
Recent symptoms	18 (34.6)	6 (85.7)	0.015
Recent treatment	20 (38.5)	6 (100.0)	0.006
Atopic	42 (79.3)	4 (57.1)	0.337
Adult asthma	25 (46.3)	5 (71.4)	0.255
Childhood asthma	42 (77.8)	3 (42.9)	0.070
Age at application	24 (18–46)	31 (24–40)	0.032

S121 THE OCCUPATIONS AT INCREASED COPD RISK IN THE LARGE POPULATION-BASED UK BIOBANK COHORT

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Background Occupational exposures are important and preventable causes of COPD. In a cross-sectional study of current occupation among over 220,000 workers in the UK Biobank cohort (over 500,000 subjects) we previously reported that 14 jobs were associated with increased COPD risk (De Matteis S, et al., OEM, 2016). To progress these findings we developed OSCAR, a new web-based tool for efficient self-reporting and automatic coding of job-histories in large population-based studies. Our aim was to identify the occupations at increased COPD risk taking into account lifetime job-histories in the UK general population.

Methods We administered OSCAR to all UK Biobank participants with an available email address ($n = 324,653$) between June-February 2016. Paid jobs held for at least six months were collected and coded by OSCAR using the UK Standard Occupational Classification (SOC), v.2000. COPD was defined as $FEV_1/FVC < LLN$ based on spirometry performed at recruitment. Prevalence ratios (PRs) for ever-exposure to each of the 353 SOC-coded jobs using lifetime office workers as reference category were estimated using Poisson regression with adjustment for age, sex, recruitment centre and lifetime tobacco smoking. In addition, we used lifetime cumulative job durations to test for exposure-response trends.

Results Among the 116,375 participants who completed OSCAR (response rate: 34%), 94,551 had acceptable and repeatable spirometry data (according to ERS/ATS criteria) and smoking information and were included in the analyses. Taking into account individual lifetime job-histories, 19 jobs significantly increased COPD risk (e.g. 'fishing and agriculture related occupations': PR: 1.69; 95% confidence interval (CI): 1.18–2.42, and 'food, drink and tobacco process operatives': PR: 1.42; 95% CI: 1.02–1.97). The majority were also confirmed by positive exposure-response trends for cumulative years of employment in each job/lifetime.

Conclusions Compared to our previous cross-sectional study, some jobs were confirmed (e.g. 'food, drink and tobacco process operatives', and 'horticultural trades') while others were not (e.g. 'coal miners'), likely due to the few employed in these jobs among the OSCAR responders. OSCAR is still collecting job-histories in the UK Biobank cohort; further analyses on a larger sample, as well analyses restricted to never-smokers and never-asthmatics to investigate the possibility of residual confounding, are planned.

Virtual Smoking: The Risks of the Evil Weeds

S122 EFFECTS OF VAPED E-CIGARETTE LIQUID CONDENSATE UPON HUMAN ALVEOLAR MACROPHAGE FUNCTION. TO VAPE OR NOT TO VAPE THAT IS THE QUESTION?

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Introduction and objectives Electronic cigarette usage or "vaping" has risen exponentially in recent years in smokers and ex-smokers. Published data suggests that vaping e-cigarette liquid (ECL) may not be as benign as propounded by e-cigarette companies which are increasingly owned by "big tobacco". Much of the current literature has focused on the effect of non-vaporised ECL – such studies do not fully reflect the exposure of the user, as the process of vaping causes chemical changes in ECL. To investigate

the effect of unvaped ECL and vaped e-cig condensate (ECVC) using our novel system, with and without nicotine, on alveolar macrophage (AM) viability and immune responses.

Methods We developed a novel method to produce ECVC to allow direct comparison with unvaped ECL. Nicotine concentration as assessed by GFID was 31 mg/ml in ECL and 26 mg/ml in ECVC. AMs were obtained from lung resection tissue and treated with ECVC/ECL $\pm$ nicotine. Cell viability was assessed by cell titre aqueous assay, apoptosis, necrosis and markers of macrophage phenotype (CD68, CD80, CD163, CD206) were assessed by flow cytometry. IL-8 release by AMs was assessed by ELISA.

Results AM culture with ECL or ECVC resulted in dose dependent reduction in cell viability. ECVC was cytotoxic at lower concentrations than ECL (0.8% ECVC vs 5 %ECL, $n = 6$). 24 hour culture with 1% ECVC resulted in a 5fold increase in AM apoptosis and 2 fold increase in necrosis compared with 1%ECL ($p = 0.079$, $n = 5$). Nicotine containing ECVC caused more apoptosis vs nicotine free ECVC (27.2% vs 13.4%, ($p = 0.0079$, $n = 4$). Culture with 0.6%ECVC significantly increased supernatant levels of IL-8 compared with 1% ECL ($p = 0.015$, $n = 4$). ECVC was also found to affect macrophage phenotype, showing both nicotine dependent/independent regulations of markers of macrophage m1/m2 polarisation (CD80 $p = 0.0357$, CD163 $p = 0.0179$, CD206 $p = 0.0357$, $n = 6$).

Conclusions Our novel system creates ECVC which is sterile, minimises loss of nicotine and prevents dilution of the vapour. Vaped E-cigarette condensate is significantly more toxic to AMs than non-vaped e cigarette liquid. Furthermore, ECVC with nicotine is significantly more toxic than ECVC without Nicotine. Effects shown on inflammatory cytokine production and markers of macrophage polarisation indicate both nicotine dependent and independent effects of ECVC on alveolar macrophages.

S123 THE EFFECTS OF ELECTRONIC CIGARETTE FLAVOURINGS ON MACROPHAGE CYTOKINE RELEASE AND PHAGOCYTOSIS

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Background Electronic cigarettes (e-cigarettes) are marketed as an alternative to tobacco cigarettes, but little is known regarding their biological effects. Studies to date have produced varying results, reflecting varying chemical compositions of different e-liquids.

Chronic tobacco smoking is known to alter macrophage function, resulting in impaired bacterial phagocytosis and increased release of cytokines including $TNF\alpha$, CXCL8 and IL-6. To date, there is little understanding of the effects of e-cigarettes on human macrophages. It was hypothesised that e-cigarettes would produce effects on macrophage function comparable to those of tobacco cigarettes.

Methods Six e-liquids were investigated: tobacco-flavoured e-liquid ($\pm$ nicotine), banoffee-pie-flavoured e-liquid ($\pm$ nicotine), e-liquid vehicle (propylene glycol + vegetable glycerine) and nicotine-vehicle solution. Effects of e-cigarette vapour extracts (e-CVEs) were compared with cigarette smoke extract (CSE) from a tobacco cigarette. Monocyte-derived macrophages (MDMs) from healthy subjects ($n = 6$) were cultured for 24 h with e-CVEs or CSE then incubated for 4h with *Streptococcus pneumoniae* or *Haemophilus influenzae*. Cell viability was determined and