

Conclusion The addition of co-trimoxazole therapy to standard treatment for Idiopathic pulmonary fibrosis had no effect on lung function or disease progression but resulted in a fivefold reduction in mortality and was cost-effective at UK thresholds.

Pathophysiology and management of cough

S139 COUGH RESPONSES TO TUSSIVE AGENTS IN HEALTH AND DISEASE

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Introduction Capsaicin or citric acid cough challenges have been used as an objective measure of cough reflex sensitivity for many decades. It remains unclear how the response to these agents differs in different diseases and how the response to one cough challenge agent differs from that to another. Prostaglandin E2 is known to result in cough when given as an inhalational agent, but has not been used as inhalational cough challenge agent.

Objectives To assess the ability of individual challenges and combined challenge responses to discriminate between diagnostic groups and healthy volunteers.

Methods We studied 102 subjects, median age 60.0 years (IQR 51.0–65.0) and 50% female (healthy volunteers n=21, healthy smokers n= 20, COPD n=18, asthma n=22 and chronic cough n=21). A doubling-dose, single inhalation method was used to measure the concentration of capsaicin (CAP), citric acid (CA) and prostaglandin E2 (PGE2) evoking at least 5 coughs (C5) within 15 s of administration, performed at weekly intervals. The operator was blinded to the challenge agent and each challenge contained 3 randomly interspersed placebo inhalations (saline). Data was analysed by multinomial logistic regression with healthy volunteers used as the reference category.

Results Smokers (p=0.03) and COPD patients (p=0.003) had a significantly higher PGE2 logC5 than healthy volunteers. CA logC5 however was significantly lower in asthma (p=0.013), and chronic cough (p=0.001) compared with healthy volunteers. CAP logC5 was also significantly lower in chronic cough (p<0.001) but also in COPD (p=0.035) compared with healthy volunteers. Combining responses to all challenge agents suggested each individual challenge independently predicted the differences between disease groups and healthy volunteers (PGE2 p<0.001, CA p=0.018 and CAP p=0.015).

Conclusions Cough responses to inhalational cough challenges can discriminate healthy controls from airway diseases. Furthermore, cough challenge agents differ in their ability to distinguish health from disease implying different underlying mechanisms drive coughing in these diagnoses. A combination of cough challenge tests appears to be better at discriminating diagnostic groups compared with any individual test in isolation.

S140 PREDICTORS OF 24-H COUGH FREQUENCY IN ACUTE COUGH

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Introduction 24-hour cough frequency monitoring is increasingly being used as an outcome measure to evaluate anti-tussive drugs.

The optimal method of identifying patients with a significant cough frequency for inclusion into clinical trials is not known. We investigated a range of cough assessments screening tools that could be used for this purpose.

Methods 35 healthy subjects with acute cough due to upper respiratory infection (median (IQR) age 31 (23–35) years, 63% female, median (IQR) duration of cough 4 (2–6) days) were recruited as part of a larger study. All subjects underwent ambulatory 24-h cough frequency (CF₂₄) monitoring with the Leicester Cough Monitor, health related quality of life with the Leicester Cough Questionnaire-acute (LCQ) and cough severity visual analogue scale (VAS). Receiver operating characteristic curve analyses were performed for the baseline screening tools LCQ, VAS and cough frequency in first hour (CF₁) to identify patients with CF₂₄=5, =7.5 and =10 coughs/hr.

Results The baseline geometric mean (logSD) CF₂₄ was 14.7 (0.5) coughs/hr, CF₁ 25.9 (0.4) coughs/hr, mean (SEM) VAS 47 (3) mm and LCQ 14.3 (0.7). 4, 6 and 11 patients had CF₂₄ <5, <7.5 and <10 coughs/hr respectively. The area under ROC curve (AUC) for VAS and LCQ for prediction of CF₂₄ were poor, ranging from 0.51 to 0.58 and 0.50 to 0.68 respectively. The mean (SEM) AUC for CF₁ was 0.92 (0.05), 0.79 (0.10) and 0.86 (0.06) for detecting 24-h cough frequency of =5, =7.5 and =10 coughs/hr respectively. The sensitivity and specificity for cough frequency recordings over 1 h to identify patients with significant 24-h cough frequency are presented in Abstract S140 table 1. A good specificity (to exclude patients with low 24-h cough frequency) was achievable at sensitivities ranging from 69 to 87%.

Abstract S140 Table 1 Accuracy of 1-h cough frequency (CF₁) in identifying 24-h cough frequency (CF₂₄)

CF ₂₄ detection level	Specificity (%)	Sensitivity (%)	CF ₁ cut-off level (coughs/hr)	PPV	NPV
>5 coughs/hr	100	87	>12.5	1.00	0.50
>7.5 coughs/hr	83	69	>17.5	0.95	0.36
>10 coughs/hr	92	74	>20.5	0.94	0.65

Conclusion Subjective cough severity and cough-specific quality of life are poor screening tools for predicting objective 24-h cough frequency. However, 1-h cough frequency can be used as a screening tool to identify patients with significant 24-h cough frequency for inclusion into future clinical trials.

S141 TRPA1 EXPRESSION AND CHARACTERISATION IN PATIENTS WITH CHRONIC COUGH

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Introduction and Aims The TRPA1 ion channel is thought to have an important role in the cough reflex. It has been demonstrated that agonisation of TRPA1 receptors by inhalation of cinnamaldehyde, a specific agonist of TRPA1, induces cough in normal human volunteers. We wanted to determine the expression and characterisation of the TRPA1 receptor in human lung tissue.

Methods Bronchial biopsies were obtained from patients with the Cough Hypersensitivity Syndrome on fibre-optic bronchoscopy. Biopsies were obtained from a major bronchus. Lung resection samples were obtained from patients undergoing surgery for lung cancer. Dorsal root ganglia were used as a positive control. These tissue samples were analysed by immunohistochemistry with a specific TRPA1 antibody.

Results Samples from 14 patients (11 males, mean age 56 years) with the Cough Hypersensitivity Syndrome and 10 lung resection samples (6 males, mean age 68 years) were obtained. All the tissue samples stained for TRPA1. The TRPA1 stain was avidly taken up by the bronchial epithelium, smooth muscle bundles and nerve tissue.

Conclusion We have described the distribution of the TRPA1 ion channel in lung tissue. TRPA1 is agonised by several environmental irritants and endogenous mediators of inflammation. The presence of TRPA1 ion channel in bronchial mucosal nerves and epithelium suggests an important role in the cough reflex. The identification of these ion channels on smooth muscle could suggest a role in asthmatic inflammation as well.

S142 INVESTIGATING PATTERNS IN 24 HOURS OF COUGHING

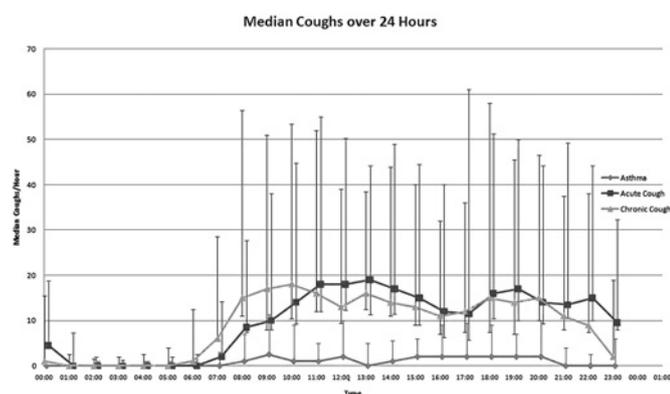
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Introduction and Objectives Ambulatory 24 h cough monitoring is a relatively new technique, and so far few studies have investigated hourly variation in cough frequency. We analysed data from previous studies in three different disease groups to compare patterns throughout the day.

Methods We studied chronic cough (duration >8 weeks) [n=70, median age 58 yrs (IQR 49–64), 67.1% female], acute cough in otherwise healthy volunteers (duration <3 weeks) [n=56, median age 22 yrs (IQR 21–25.5), 62.5% female] and physician diagnosed asthma [n=58, median age 58.5 yrs (IQR 52–67.8), 63.8% female]. Subjects wore a cough monitor (Vitalojak) for 24 h and median numbers of coughs in each hour were manually counted and plotted against the actual time of day.

Results The asthmatic group had significantly lower total cough rates compared with the other groups (geometric mean 2.3 coughs/hr (SD±3.3); chronic cough 13.1 (±2.7); acute cough 8.9 (±2.63); p<0.001). Abstract S142 figure 1 shows the median coughs in each hour of the day (interquartile ranges). The chronic and acute cough groups show a very similar cough frequency and pattern, with two peaks during the daytime, despite substantial variability. The asthma group show a similar pattern but with much lower counts. For all diagnosis coughing practically ceases overnight.



Abstract S142 Figure 1

Conclusions These data suggest that cough frequency in acute and chronic cough are remarkably similar, implying similar mechanisms may be driving coughing in these conditions, unlike in asthma

where cough frequency is much lower. However all groups show similar fluctuations in hour to hour pattern of daytime cough and effective suppression of coughing during sleep, indicating behaviour has an important influence.

S143 THE SENSATIONS PROVOKING COUGH: A QUALITATIVE INVESTIGATION

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Background Little is known about the sensations patients feel prior to or that provoke their cough.

Aims To identify, from the patient's perspective, key descriptors that relate to the sensations provoking cough in patients diagnosed with one of the following: idiopathic cough, asthma, chronic obstructive pulmonary disease (COPD), fibrotic interstitial lung disease (ILD) and cystic fibrosis.

Methods One-to-one, audio recorded, semi-structured interviews were conducted with 34 participants (7 idiopathic cough: age 40–69 years, 5 female, 6 asthma: age 42–65 years, 5 female, 7 COPD: age 52–86 years, 2 female, 7 ILD: age 58–79 years, 3 female, 7 cystic fibrosis: age 20–39 years, 2 female). Words and phrases relating to 1 of 8 top level codes, derived from the interview topic guide (triggers, sensation, sputum, emotion, location, frequency, time and relief) were extracted using simple manifest content analysis. These descriptions were then organised into similar themes. Relationships between the descriptions and themes both within and between the groups were explored.

Results All groups described the sensation of a "tickle" or an "irritation" that was felt most in the throat and upper chest. Cystic fibrosis and COPD participants most commonly described feeling a "need to clear" their airways. The ILD group mostly described a "dry", "tickly" sensation. The idiopathic cough and asthma groups used a very heterogeneous set of terms regarding the sensations provoking their cough. Common across the groups is a hyper-sensitive response to things that may trigger their urge to cough and all groups described coughing as relieving that urge. Emotionally the sensation is associated with negative emotions, however positive feelings were also described; by some who described feeling a need to clear their airways.

Conclusion The extracted list of descriptions has provided some insight into what the sensations provoking cough feel like from patient's perspective and suggest that the sensations felt relate to the pathology of the individual's diagnosis. The distinction between the need to clear and a sensation of a tickle or irritation could be important in understanding the mechanisms driving cough and may be important for the development of targeted interventions.

S144 ACUTE COUGH: A LONGITUDINAL OBSERVATIONAL STUDY

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Introduction Acute cough is a common illness with more than 12 million episodes each year in the UK. More than £100 million is