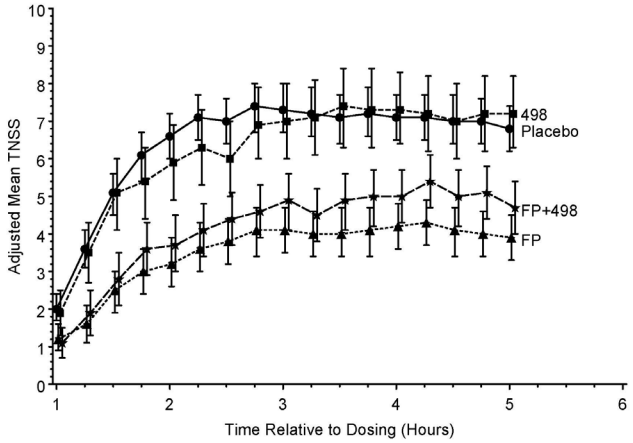
There was no positive impact over FP, or 498 over Placebo, for Diary Card symptoms, RQLQ or Nasal Airflow. Tmax occurred at approximately 5 hrs post dose, in keeping with previous studies. SB705498 was very well tolerated.

Conclusions In a robust clinical model of allergic rhinitis, there was no intrinsic activity demonstrated by SB705498 and no additive effect on a background of intranasal steroids. FP was highly effective in this study. We conclude that despite engagement of the TRPV1 receptor there was no translation to clinical efficacy, suggesting redundancy in symptom pathways.



Abstract P153 Figure 1

P154 TRPV1 IS NOT A TARGET FOR THE TREATMENT OF NON-ALLERGIC RHINITIS: A CLINICAL STUDY

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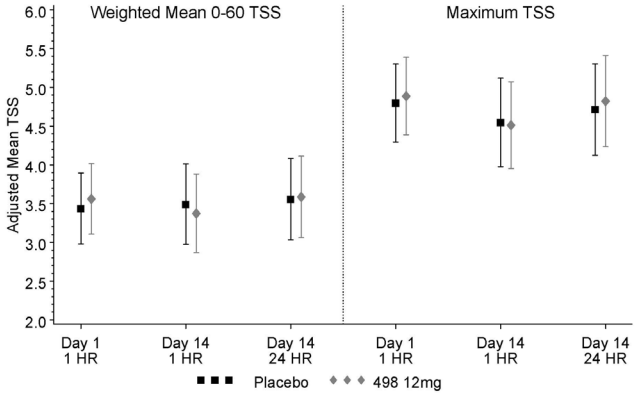
Background TRPV1 is a ligand gated ion channel activated by a range of physiological factors such at Temperature, pH, and osmotic stress. In the nose, the TRPV1-expressing sensory c-fibres are thought to play a key role in the development of nasal hyperresponsiveness resulting in symptoms in NAR patients. We hypothesise that topical antagonism with a selective TRPV1 antagonist would offer substantial symptom control. SB705498 is a potent selective TRPV1 antagonist in animal and human models.

Methods 40 M&F NAR patients were enrolled into a randomised, double-blind, placebo controlled, 2 period crossover study of either 12mg SB705498 i.n. or placebo for 14 days with a 4 week washout. The study was conducted in a validated Environmental Challenge Chamber (Cetero) where patients were exposed to Cold Dry Air (CDA) at 14c, 15% RH, air speed 5 feet/sec. Exposure was over the winter months in Canada. Diary card symptoms were analysed during home dosing on days when the temp was less than 14c. Two chamber sessions of 1hr duration, as well as medical history and neg skin prick testing, at screening were performed to establish a consistent diagnosis with a single challenge on Day 1+1hr, Day14+1hr and Day 14+24hr to establish the drug response. Post dose TSS (rhinorrhoea, congestion, PND), sneezing and ocular symptoms were recorded, as was acoustic rhinomanometry, RQLQ, PK and Safety monitoring.

Results The primary outcome of weighted mean TSS over the challenge period or the maximum TSS was not impacted by administration of SB705498 relative to placebo (see figure). There was no impact on sneezing, ocular symptoms, acoustic rhinimanometry, or RQLQ Compared with placebo, repeated doses of SB705498 did not alleviate TSS triggered by cold in a multistimuli wild type setting. PK analysis supported an o.d. regimen with 2 fold accumulation over the dosing period.

Conclusions In a robust clinical model of non-allergic rhinitis, intranasal SB705498 12mg o.d. for 14 days did not alleviate the symptoms of NAR triggered by the most common provocation agent: Cold Dry Air. We conclude that despite engagement of the TRPV1 receptor there was no translation to clinical efficacy, suggesting redundancy in symptom pathways.



Abstract P154 Figure 1

P155 VISUALISATION OF AIRWAY NERVES IN CHRONIC COUGH: TOWARDS THE IDENTIFICATION OF THE HUMAN 'COUGH RECEPTOR'

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Introduction The spinal and vagal innervation of the respiratory tract is well defined, particularly in animals. These discoveries include the identification of pathways involved in provoking cough and descriptions of the guinea pig 'cough receptor'. However, many of the immunochemical features of the airway afferents described in animals have yet to be defined in humans, yet plasticity of these airway afferents may be important in the pathophysiology of chronic cough.

Objectives To define and characterise the innervation present in bronchoscopic biopsies from patients with chronic cough. We aimed to carry out the first ever whole mount immunohistochemical studies of airway nerves in cough patients, a technique that should improve visualisation of these neuronal structures and their sites of termination.

Methods Biopsy tissue was gifted from patients undergoing clinical investigation for chronic cough. Tissue, sampled from throughout the extrapulmonary airways, was immediately fixed in 4% paraformaldehyde. Non-specific antibody binding was blocked using 10% normal serum and 1% skimmed milk powder, diluted in PBS, before application of primary antibodies. Polyclonal rabbit anti-PGP9.5 (Ultraclone, UK) and monoclonal mouse anti-neurofilament (NF200, Leica Biosystems, UK) were applied at a dilution of 1:1000 and 1:200 respectively. Primary antibody binding was detected using appropriate Alexa-fluor conjugated secondary antibodies and whole mount preparations were visualised using epifluorescence and confocal microscopy. Images of biopsy staining were subject to morphometric analysis.

Results Many epithelial, subepithelial and intramuscular fibres were detected using both antibodies. Co-staining revealed that only PGP9.5 defined pulmonary neuroendocrine cells and better elucidated varicose epithelial fibres. A proportion of all fibre types were

only immunopositive for one marker. Notably NF200 exclusively detected some epithelial fibres and a group of larger diameter neurons (Ø3–6 μm) some of which are consistent with observations of Aδ-fibre airway mechanoreceptors.

Conclusions We have described neuronal structures in whole-mount preparations of tissue from patients suffering from chronic cough. Notably, we described a population of PGP9.5 negative fibres within the airways. Some of these fibres are morphologically consistent with thinly myelinated Aδ-fibres described in animal models as 'cough receptors'. These ongoing studies could help define the plasticity of airway nerves in patients with chronic cough.

P156 OUTCOME AND EXPERIENCE OF LAPROSCOPIC NISSENS FUNDOPLICATION IN ADULT PATIENTS WITH SEVERE ASTHMA AND COUGH WHO HAVE GASTROESOPHAGEAL REFLUX

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Introduction Gastroesophageal reflux (GORD) is an important co-morbidity in patients with asthma.[1] It has a detrimental impact on symptoms with many patients being on oral corticosteroids despite maximal proton pump inhibitor (ppi) therapy.[1] Fundoplication in selected patients with severe asthma has been reported to improve asthma symptoms especially in children.[2]

Birmingham Heartlands Hospital (BHH) is part of Heart of England NHS trust, one of the largest foundation trusts in UK. The Severe and Brittle Asthma Unit which operates from BHH has a policy of referring selected patients for Fundoplication.

Method In this prospective study all patients undergoing laparoscopic fundoplication were followed up for 12 months. All patients had GORD symptoms refractory to ppi therapy and proven reflux on oesophageal manometry. Prior to surgery and at 3 months patients symptoms were assessed with a) Mini asthma quality of life questionnaire (mAQLQ) b) Reflux Cough Questionnaire (RCQ) and c) Cough symptom Score (CSS). Lung function and medication were documented at follow up visits. Wilcoxon signed rank test was used in statistical analyses.

Results Between December 2009 and June 2012 13 patients underwent fundoplication. Patient characteristics are shown below.

Fundoplication significantly improved CSS and RCQ at 3 months from baseline, p=0.002 and p=0.008 respectively. No significant change was seen in mAQLQ or lung function in asthmatic patients.

Conclusions Patients with severe cough and asthmatics with debilitating cough benefit from fundoplication. Asthmatics however have no significant improvement in quality of life scores or pulmonary function in the short term following fundoplication.

References

1. Sontag et al A Am J Gastroenterol. 2003 May; 98(5):987–99.
2. Rothenburg S et al J Pediatric Surg 2012 Jun; 47(6):1101–4.

Abstract P156 Table 1

*Age years	45.8	
M:F	2:11	
*DeMeester Score	59.7	
Diagnosis	Asthma 11	Cough 3
*Spirometry	**Pre**	**Post**
	FEV1 2.2	FEV1 2.15
	FVC 2.83	FVC 2.84
CSS	6.38	5.29
RCQ	50.2	41.6
mAQLQ	3.15	3.52

*mean values

P157 THE LANGUAGE OF COUGH: A FOCUS GROUP STUDY IN RESPIRATORY DISEASES

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Background Little is known about the sensations and triggers that provoke cough in patients, or their preferred language to describe their experiences. We have previously collected a list of descriptors covering the themes of triggers, sensations and secretions, generated from individual interviews in a range of respiratory disorders, with a view to developing a questionnaire.

Aims To take the key descriptors and present these to focus groups diagnosed with chronic cough, COPD, ILD, asthma, and non-CF bronchiectasis.

Methods Five semi-structured focus groups were conducted with 22 participants (7 chronic cough, mean age 67.7 years (range 57–80) 4 female; 5 asthma, age 66 years (60–71) 2 female; 4 COPD, age 68 years (66–73) 2 female; 3 ILD, age 70 years (65–74) 0 female; 3 non-CF bronchiectasis, age 67.3 years (53–77) 2 female). Using simple manifest content analysis, a list of descriptors was derived based on the frequency of use during individual interviews. These were presented to the focus groups, asking them to describe what each word meant to them, the image it conjured up and whether they could identify a most appropriate word.

Results All focus groups favoured the terms 'phlegm' over 'sputum' (which was considered too "clinical"), 'irritation' over the word 'tickle' (which was considered too "gentle") and the 'need to cough' over an 'urge to cough'. In contrast, there were distinct differences in some disease groups for example, all groups, apart from COPD, recognised specific foods and eating as triggers of coughing. Similarly, all groups, apart from asthma, identified specific smells and odours as triggers of coughing. Patients with COPD, ILD and non-CF bronchiectasis related to the word 'crackle', but asthmatics only associated this word with "infection" and chronic cough patients did not identify with this terminology.

Conclusion These focus group discussions would suggest that whilst some descriptors of cough are felt to be universally appropriate, other descriptors and triggers appear to discriminate between diagnoses. This study will inform the language and content of a future questionnaire to categorise patients by the sensations and triggers provoking their cough.

P158 COUGH SOUND INTENSITY: THE DEVELOPMENT OF A NOVEL MEASURE OF COUGH SEVERITY

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Introduction and Objectives Cough sound analysis is currently used for the assessment of cough frequency; it is not known if it could be used to assess cough intensity. We investigated the optimal Cough Sound Intensity (CSI) measure by validating it against peak cough flow rate (PCFR).

Methods 17 (11 female) patients with stable chronic cough and 15 (8 female) healthy subjects underwent simultaneous measurements of peak cough flow rate and cough sound during voluntary coughs using 2 types of microphones. Subjects were asked to cough voluntarily 10 times at 5 incremental thoracic pressures as measured by an oesophageal balloon catheter. Visual feedback was given to patients. A range of CSI parameters were determined from the

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P155 Visualisation of Airway Nerves in Chronic Cough: Towards the Identification of the Human 'Cough Receptor'

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