Results We studied 20 treatment resistant CC, 18 stable mild/moderate A and 20 HC subjects, matched for gender (M:F 10:10, 9:9,10:10, respectively), age [mean (±SD) 57.1 years (±15.7), 51.7 years (±13.5), 58.8 years (±13.5); p=0.17], and lung function [3.02L (±0.98), 2.96L (±1.10), 3.20L (±0.99); p=0.72]. CC had significantly greater UTC intensity (p=0.006, see Abstract S116 Figure 1) and cough responses (p=0.002) compared to HC. Females had significantly greater UTC (p=0.001) and cough responses (p<0.001) compared to males. There was no significant difference in UTC intensity (p=0.449) or cough responses (p=0.997) between A and HC.

Conclusions In a randomised double-blind capsaicin cough challenge:

- Chronic cough patients perceive a more intense UTC sensation and also demonstrate a greater magnitude of cough response than healthy controls.
- Females perceive a more intense UTC sensation than males.

These findings suggest both a heightened sensory experience in addition to an excessive motor response in patients with chronic cough. This data could be explained by sensitisation of afferent pathways (ie, peripheral and/or central sensitisation) but also by impaired inhibitory control mechanisms.

S117 4 H COUGH FREQUENCY MONITORING WITH THE LEICESTER COUGH MONITOR

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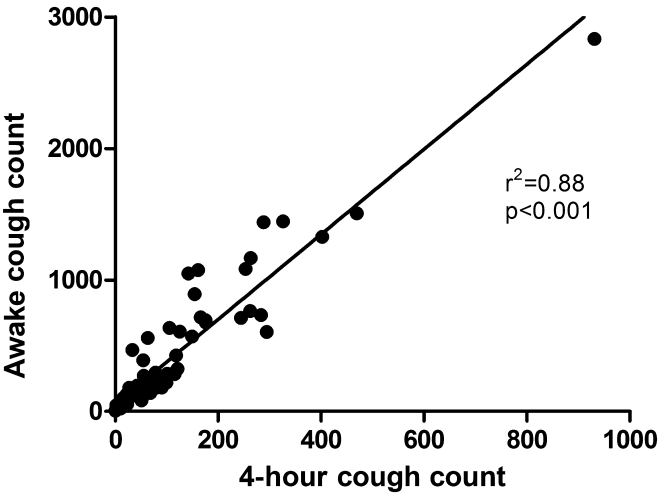
[1]K K Lee, [1]A Savani, [1]S Matos, [1]C Woods, [2]I D Pavord, [1]S S Birring. *[1]King's College Hospital, London, UK; [2]Glenfield Hospital, Leicester, UK*

Introduction The Leicester Cough Monitor (LCM) is a validated 24-h automated cough frequency monitor. Shorter recordings are more convenient for patients and take less time to analyse but their validity for assessing cough is not known. We assessed the relationship between short duration and 24-h recordings.

Methods 100 patients (57 females) with chronic cough underwent 24-h ambulatory cough frequency monitoring with the LCM. Patients completed diaries to identify awake and sleep periods. Cough frequency was determined by automated analysis and presented as 24-h cough frequency (CF_{24}), awake cough frequency, sleep cough frequency, and short duration (1–6 h). Subjective cough severity was assessed by cough visual analogue scale and quality of life questionnaire (Leicester Cough Questionnaire, LCQ). The optimal short cough recording duration was determined by assessing its relationship with awake cough frequency and subjective cough severity. The responsiveness of short duration recordings was tested in 20 patients undergoing trials of therapy.



Abstract S117 Figure 1 Relationship between 4-h cough counts and awake cough counts.

Results The median (IQR) 24-h cough frequency was 11.5 (5.8 to 26.6) coughs/h, awake cough frequency 13.2 (7.6 to 37.5) coughs/h and sleep cough frequency 4.2 (1.0 to 9.2) coughs/h. 4-h cough counts correlated strongly with both awake and 24-h cough counts; r^2=0.88 and r^2=0.87 respectively (Abstract S117 Figure 1). There was a moderate relationship between 4-h cough frequency (CF_4) and LCQ and cough VAS (r=−0.48, p<0.001 and 0.49, p<0.001) which was comparable to that between awake cough frequency and LCQ and cough VAS. The effect size of change in CF_4 after therapeutic trials was 0.55.

Conclusions Shorter duration cough frequency recordings with the LCM accurately reflect daytime and 24-h cough frequency in patients with chronic cough. They can be used to assess daytime cough frequency and the response to trials of therapy.

S118 ACUTE HEMISPHERIC STROKE PATIENTS HAVE REDUCED FUNCTIONAL RESIDUAL CAPACITY AND COUGH FLOW RATES

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P R Rao, K W Ward, C R Reilly, G R Rafferty, J Moxham. *King's College London, London, UK*

Introduction Cough is a complex manoeuvre, requiring coordinated action of the respiratory and upperairway musculature. The mechanisms of impaired cough following hemispheric stroke are unclear. Reduced functional residual capacity (FRC) may impair cough due to the effect of lung volume on the length and pressure generating capacity of the expiratory muscles. We compared FRC (primary outcome) and peak cough flowrate for voluntary cough (PCFR, secondary outcome) in stroke patients and healthy controls.

Methods 27patients and 30 healthy controls were studied. Stroke patients were within 2 weeks of first-ever middle cerebral artery infarct. Stroke severity was scored by a clinician (NIHSS score, worst=31). FRC was measured by helium dilution using a dry rolling seal spirometre. To measure PCFR, subjects wore a tight-fitting facemask and were asked to cough forcefully into the spirometre. During these measurements, the volume inspired before the cough manoeuvre was also recorded. Measurements were performed in a chair with the back reclined to 45°, mimicking patient position in hospital. FRC and PCFR data were expressed as % predicted.[1]

Results Patients' median NIHSS score was 4 (IQR 2–6) reflecting mild disability. FRC % predicted, the volume inspired before cough and PCFR were significantly reduced in patients. Both FRC and the volume inspired before cough were significant predictors of PCFR.

Conclusions FRC (% predicted), the volume inspired before cough and PCFR were significantly reduced in acute hemispheric stroke patients. Higher peak cough flow rates are associated with greater lung volume prior to cough. Interventions that increase FRC, for example, continuous positive airway pressure and upright sitting may improve cough function in stroke patients.

Abstract 118 Table 1

		Stroke	Control	Difference (95% CI)	p Value
Number of participants		27	30		
Age (years)	Mean	68	58	10	0.001
	SD	11	11	4 to 16	
Sex	Male/female	17/27	15/15	0.13	0.420†
	Proportion male	0.63	0.50	−0.12 to 0.36	
Height (centimetres)	Mean	169.6	169.7	−0.1	0.997
	SD	7.9	12.2	−5.6 to 5.6	
O_2 saturations breathing air (%)	Median	97	97	0	0.660*
	IQR	92 to 98	95 to 98	−1 to 1	
Smoking	Number ever/ never smoked	13/14	12/18	0.1	0.599†
	Proportion ever smoked	0.30	0.40	−0.2 to 0.3	
Functional residual capacity (litres)	Median	2.500	2.780	−0.270	0.003*
	IQR	2.323 to 3.601	2.258 to 2.898	−0.710 to 0.115	
Functional residual capacity (% predicted)	Median	76.0	90.0	−14.0	<0.001*
	IQR	66.5 to 89.5	79.8 to 105.0	−22.0 to −5.0	
Peak cough flow rate (litres/min)	Mean	297	380	−83	0.019
	SD	133	121	−153 to −14	
Peak cough flow rate (% predicted PEF)	Mean	61.2	86.3	−25.1	<0.001
	SD	32.6	17.3	−38.8 to −11.4	
Volume inspired before cough (litres)	Mean	2.219	3.409	−1.190	<0.001
	SD	0.828	0.720	−1.715 to 0.665	
Volume Inspired before cough (% predicted VC)	Mean	64.3	94.6	−30.1	<0.001
	SD	19.5	15.6	−42.2 to 18.5	

p Values calculated using t tests except.
*p Value calculated using Mann–Whitney U test.
†p Value calculated using Fisher's exact test.
PEF, peak expiratory flow rate; O_2, oxygen.

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S119 VARIATION IN PHARYNGEAL PH IN THE DIAGNOSIS OF AIRWAY REFLUX

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I D Molyneux, W Jackson, A H Morice. *Castle Hill Hospital, Cottingham, UK*

Introduction and objectives Reflux of gastric contents to the laryngopharynx has been implicated in the pathogenesis of chronic cough and may exacerbate other respiratory conditions. Direct measurement of pharyngeal pH is available but standard analysis relies on the pH crossing a lower threshold. Non-acid gaseous reflux may cause respiratory symptoms without producing a significant drop in pharyngeal pH. We theorised that variation in pharyngeal pH might be a useful marker of airway reflux.

Methods Measurements of pH in the pharynx over 24 h were made in patients with a variety of respiratory diagnoses suspected to have reflux contributing to their symptoms. Diagnoses included chronic cough, cystic fibrosis and asthma. Results were analysed using a predefined, threshold-based scoring system and our novel system based on variation in pH. Comparison was also made with oesophageal physiology where available.

Results 60 studies were performed on 58 patients; median age 48 years (range 17–81). 43 studies had an abnormal threshold score. 31 patients had an abnormal variation score (>30 events per hour). Both were positive in 21 patients and both negative in 7. Cough symptom scores were similarly high in patients with abnormal variation to those with abnormal threshold scores (mean 34.7 and 38.3 respectively) and higher than patients with both negative (23.0; n/s). Cough patients who had undergone fundoplication demonstrated less variation than those who had not (mean events 55 per hour vs 115; n/s). Asthma patients had similar overall variation to other groups but had higher numbers of events over fewer peak hours (468 vs 368 events per peak hour; p=0.08) with the opposite seen in cystic fibrosis patients (276; p=0.26). Of 25 patients with an abnormal pharyngeal study and an oesophageal study available, 15 had normal oesophageal studies.

Conclusions These results show that the interaction between pharyngeal pH and airway symptoms is complex, not easily assessed using a pH threshold alone and not well correlated with oesophageal physiology. Assessment of variation suggests different patterns of reflux may relate to disease phenotypes. The ideal analysis should include correlation of clinical symptoms with peaks in variation and pH threshold events.

Inflammation: an important regulator of the fibrotic response

S120 IL-1 IS A KEY EPITHELIAL ALARMIN WHICH PROMOTES FIBROBLAST ACTIVATION

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M I Suwara, L A Borthwick, J Mann, A J Fisher, D A Mann. *Newcastle University, Newcastle upon Tyne, UK*

Background Alarmins are molecular 'danger signals' released by injured cells that can contribute to the innate immune response by activating immune cells via multiple receptors including Toll-like receptors (TLR), Nod-like receptors (NLR) and the receptor for advanced glycationend products (RAGE). Pulmonary fibrosis is associated with the upregulation of alarmins such as Interleukin 1 α (IL-1α) and High mobility group box 1 (HMGB1) in bronchoalveolar lavage fluid (BAL), however it remains unclear whether alarmins can contribute directly to the fibrogenic process by interacting with fibroblasts. We hypothesised that alarmins released from damaged epithelial cells act as damage associated molecular patterns (DAMPs) which are recognised by fibroblasts and lead to their activation.

Methods The 16HBE14o- human bronchial epithelial cell line was damaged by hydrogen peroxide (H_2O_2) induced oxidative stress and alarmin release (Heat Shock Protein 60 (HSP-60), HMGB1, IL-1α) measured via ELISA. MRC5 human lung fibroblasts were treated with media from damaged lung epithelia and cell proliferation (XTT proliferation assay), phosphorylation of downstream TLR signalling molecules (interleukin 1 receptor associated kinase 1 (IRAK1), TGFβ associated kinase 1 (TAK1)—western blotting) and gene expression of proinflammatory cytokines (interleukin 6 (IL-6) and Interferon β (IFNβ)—qRT-PCR) assessed.

Results Conditioned media from 16HBE14o- cells damaged with 200 μM H_2O_2 contained elevated concentrations of HSP-60 (16.7 vs 0.64 ng/ml; p<0.05, n=3), HMGB1 (71 vs 12 ng/ml; p<0.001, n=3) and IL-1α (434 vs 130 pg/ml; p<0.001, n=3) compared to untreated controls. Treatment of MRC5 cells with media from damaged lung epithelia enhanced cell proliferation by 29% (p<0.01, n=3), increased TAK1 and IRAK1 phosphorylation and increased IL-6 and IFNβ gene expression 2.7-fold (p<0.001, n=3) and threefold (p<0.001, n=3) respectively. Blocking IL-1R (500 ng/ml of IL-1R antagonist (IL-1Ra)) diminished IL-6 (85%; p<0.01, n=3) and IFNβ (34%; p<0.05, n=3) gene expression compared to treatment with conditioned media from damaged cells alone.

Conclusions The results suggest that alarmins such as the intrerleukin-1 family, released by damaged human lung epithelia may be