Results In the 12 patients with data so far available in this study QOL measured by the total SGRQ score correlated significantly with QMVC/BMI (r = -0.75, p = 0.005), FFMI (r = -0.71, p = 0.009) and $USRF_{CSA}$ (r = -0.88, p = 0.0002) (Figure 1A). There was no significant correlation between total SGRQ score and Sensewear measured steps per day (r = -0.62, p = 0.08) (Figure 1B) TEE (r = -0.62, p = 0.08) or AEE (rho = -0.41, p > 0.05) in the 9 patients with data available. Furthermore there was no significant correlation between BNP or resting echocardiographic parameters and total SGRQ QOL

Discussion We have shown that muscle size and function are directly related to QOL in patients with IPAH. This work suggests that muscle function may be an important determinant of QOL in these patients, making it a potential target for therapeutic intervention. Further data is needed to define the association between physical activity and QOL in patients with IPAH.

Cough – mechanisms and therapies

P1 A NOVEL CAPSAICIN COUGH CHALLENGE IN HEALTHY ADULTS; BEYOND THE C5

[1]K Holt, [1]C Gibbard, [2]K Ahern, [1]JA Smith. *[1]University of Manchester, Manchester, UK; [2]University Hospital of South Manchester, Manchester, UK*

10.1136/thoraxjnl-2014-206260.151

Introduction We have developed a novel cough challenge methodology and previously showed that evoked maximal cough responses, defined as E_{max}, better discriminate health from disease than traditional endpoints.[1] It is unclear how other factors influence E_{max} or how it relates to the low cough rates observed in health. We therefore aimed to investigate the variability, repeatability and influences on E_{max} in a larger group of healthy volunteers.

Objective To assess maximum cough responses to capsaicin in a group of healthy adults representing a wide range of ages.

Method Doubling doses of capsaicin 0.49 to 1000[micro]M) were inhaled sequentially up to the maximum tolerated dose. Four inhalations of each dose were administered 30 seconds apart and the number of coughs evoked within 15 seconds was recorded. The maximum number of coughs evoked by any dose of capsaicin (E_{max}) and the dose that elicited half of the E_{max}, defined as ED_{50}, were calculated. General linear models were used to assess the influence of subject demographics on these endpoints.

Results Forty seven healthy volunteers performed the capsaicin challenge; median age 38 years (range 20–74), 17 males, median FEV_1 103% predicted (97–115), median BMI 25.0 (22.2–28.6), and median total cough rate 0.2 c/h (0.0–0.1). The median E_{max} was 11 coughs (IQR, 8–19) with an ED_{50} of 15.6[micro]M (7.8–109.4). The intraclass correlation coefficients for E_{max} and ED_{50} were 0.89 and 0.96 respectively which were highly significant (p < 0.001). Age, gender, FEV_1 and BMI had no significant influence on E_{max}. In contrast, gender (p < 0.001) and BMI (p = 0.029) both significantly influenced ED_{50} explaining 41.7% of the variation. Those subjects with a higher BMI and females tended to have a lower ED_{50}. Objective 24 h cough frequency did not correlate with either E_{max} or ED_{50}.

Conclusion Data collected to date has demonstrated that in healthy volunteers, E_{max} and ED_{50} are stable measures over time however E_{max} has the advantage of being independent of patient factors. Intere stingly, objective cough frequency in healthy volunteers seems to be unrelated to capsaicin evoked coughing.

REFERENCES

J Allergy Clin Immunol. 2013 Oct;132(4):847–55

P2 CHARACTERISATION OF Aδ- AND C-FIBRES INNERVATING GUINEA-PIG AIRWAYS

JJ Adcock, MA Birrell, SA Maher, SJ Bonvini, ED Dubuis, MA Wortley, KE Baker, MG Belvisi. *Imperial College, London, UK*

10.1136/thoraxjnl-2014-206260.152

Introduction and objectives Activation of afferent fibres from the lungs are involved in the cough reflex. *In vitro* studies in guinea-pig have demonstrated that there are various sub-types of Aδ-fibres (RAR's, nociceptive and cough)[1] and C-fibres (either nodose or jugular ganglia derived),[1,2] however, little is known about their equivalent characteristics *in vivo*. This study aims to characterise the responsiveness of airway sensory nerves, *in vivo*, ultimately providing a better insight into understanding the role/contribution of the various types/subtypes of Aδ and C-fibres in airway reflexes such as cough.

Methods Male guinea-pigs were anaesthetized with urethane (i.p. 1.5 g kg^{-1}), paralysed and artificially ventilated via a tracheal cannula. A vagus nerve was isolated: single fibres were identified as originating from Aδ- and C-fibres using several criteria. Action potentials were recorded[3] and agents were administered to the airways by aerosol.

Results Fibre-types were classified according to their conduction velocities (Table 1). All C-fibres examined were activated by capsaicin, whereas in the Aδ-fibres studies there were both capsaicin responsive and non-responsive fibres, irrespective of their CV range. All fibres exposed to CA responded strongly. There were marked differences in the responsiveness to the TRPV4 agonist, GSK1016790A: Aδ-fibres from all subgroups responded vigorously, but the C-fibres examined were not activated. Interestingly, administration of hypotonic solutions activated all of the Aδ-fibres, but had no effect on C-fibres. In contrast, all C-fibres responded to the TRPA1 agonist, acrolein, with no effect on Aδ-fibres.

Conclusion Several vagalafferent nerve subtypes have been identified in guinea-pig airways *in vivo*, although the classification does not appear as obvious to that observed *in vitro*. It is clear that there is a marked variation in their sensitivity to TRP channel agonists, TRPV1, TRPA1 and TRPV4, which have all been shown to evoke cough in a preclinical model in conscious guinea-pigs. It seems probable, therefore, that the different afferent pathways all regulate cough to a greater or lesser degree depending on the nature of the stimulus and underlying cause of the cough.

REFERENCES

1 Canning 2004: *J Physiol*-557 (2):543–558
2 Weigand 2012: *J Physiol*-590, (16):4109–4120
3 Adcock 2003: *Brit J Pharmacol*-138:407–416

Abstract P2 Table 1 Characteristics of vagal afferent neuronal subtypes innervating the airways and lungs of guinea pigs *in vivo*

C-fibres CV = < 1 m s^{-1}	Aδ-fibres CV = 2.3–7.14 m s^{-1}		Aδ-fibres CV = >8 m s^{-1} (Classical RARs)	
Capsaicin- responsive	Capsaicin-responsive (nociceptor)	Capsaicin non-responsive (mechano-receptor?)	Capsaicin-responsive	Capsaicin non-responsive