Conclusion This small pilot study suggest that opiate sensitive inhibitory mechanisms may have a role in controlling the cough reflex even in healthy subjects.

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P11 THE ROLE OF GABAB RECEPTOR MECHANISMS IN THE HUMAN COUGH REFLUX

Background Chronic cough represents an important unmet clinical need. Gamma-aminobutyric acid is a major inhibitory neurotransmitter in the central nervous system (CNS). GABA_B receptors have been identified peripherally, as well as centrally. Studies in guinea-pigs, have suggested that the activation of GABA_B receptors in the CNS and PNS can inhibit cough. The only clinically available GABA_B agonist is Baclofen, and although it has been shown to suppress cough in animals and humans, it causes drowsiness as it is centrally acting. Lesogaberan, is a novel, predominantly peripherally acting GABA_B agonist.

Objective To determine whether both peripherally acting (Lesogaberan) and centrally acting (Baclofen) GABA_B agonists modulate cough responses to inhaled capsaicin compared with placebo in healthy volunteers.

Methods Single centre, double-blind, double-dummy, three-way crossover trial in healthy controls of Lesogaberan (120 mg MR), Baclofen (40 mg) and placebo. Subjects were treated with single doses of each study medication with a washout period of ≥7 days between doses. Cough responses to inhaled capsaicin were assessed using a novel challenge protocol (1) measured at screening and 2 hrs post dosing (tmax) on each study day. The primary end point was the maximum number of coughs evoked at any concentration of capsaicin (Emax). The secondary end point was the concentration of capsaicin evoking 50% of the maximal response (ED50).

Results There were 15 patients enrolled onto the study with a median age of 29 years old (IQR25–44); 7 female; mean BMI was 24.6 (±3.0).

Lesogaberan treatment was associated with a small, statistically significant increase in Emax (mean 13.4 coughs, 95% CI 10.1–17.9) compared with placebo (11.8, 95% CI 8.8–15.9) (p = 0.04), but had no effect on ED50 (geometric mean 47.4 μM 95% CI 24.4–91.7 vs Placebo 37.6 95% CI 19.2–73.5 p = 0.37), see Figure 1.

In contrast, Baclofen had no significant effect on Emax (11.1, CI8.1–15.4) (p = 0.23), but, ED50 was significantly increased compared with placebo (geometric mean 75.2 μM 95% CI 37.2–151.8 p = 0.002).

Conclusion This data suggests the anti-tussive actions of GABA_B agonists, against capsaicin-induced cough in healthy volunteers, occurs in the central rather than the peripheral nervous system.

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P12 THE USEFULNESS OF HEARTBURN AS A MARKER OF THE SUCCESS OF ACID SUPPRESSION THERAPY IN CHRONIC COUGH

Background A recent retrospective analysis of randomised controlled trials has suggested that patients with chronic cough reporting heartburn are more likely to benefit from acid suppression treatment than those without heartburn. Therefore we set out to investigate the response rate to acid suppression treatment (PPI and or H2 antagonists) in patients attending our specialist cough clinic.

Objective To determine the relationship between reported responses to acid suppression treatment and the presence or absence of heartburn.

Methods We performed a retrospective review of 59 consecutive new referrals to the clinic. The presence or absence of heartburn is collected routinely in our standard clinic proforma. Patients who were treated with acid suppression either at our clinic or previously at another centre were included, together with their reported response to treatment. A Fisher’s exact test was used to assess whether those with heartburn were more likely to report a response of their cough to acid suppression treatment than those without heartburn.

Results Of 59 new referrals (median age 58 (range 26–76), 44 female), 21 (35.6%) reported heartburn, whereas 38 (64.4%) did not. Forty-four subjects had completed a trial of acid suppression therapy; 7 (15.9%) reported a response of their cough to acid suppression treatment. Of those not reporting heartburn, 2/23 (8.7%) reported a response to acid suppression. Although a greater proportion of those with heartburn reported improvement of cough with acid suppression, this did not reach statistical significance (p = 0.23).

Conclusion This data suggests that in the setting of a specialist cough clinic few patients report a response of their cough to...
acid suppression therapy, even in the context of heartburn. However, a larger dataset is required to understand whether those with heartburn might be more likely to respond.

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Abstract P13 Table 1 Prevalence of symptoms amongst the 1394 participants providing complete data

| Year (age in years) | 1966 (20) | 1971 (25) | 1982 (35) | 1989 (43) | 1999 (53) | 2009 (63) |
|---------------------|-----------|-----------|-----------|-----------|-----------|-----------|
| % of Total Population (n=1394) |            |           |           |           |           |           |
| Either symptom       | 8.7%       | 7.8%      | 7.0%      | 9.0%      | 10.3%     | 13.3%     |
| CMH                 | 4.7%       | 4.4%      | 3.9%      | 5.1%      | 5.7%      | 9.0%      |
| CC                  | 4.4%       | 6.0%      | 5.7%      | 7.5%      | 8.8%      | 11.0%     |
| CMH with CC          | 2.5%       | 2.6%      | 2.7%      | 3.7%      | 4.2%      | 6.7%      |
| CMH without CC       | 2.2%       | 1.9%      | 1.2%      | 1.4%      | 1.5%      | 2.3%      |
| No. of study members with CMH | 66          | 62        | 55        | 71        | 80        | 72        |
| % of CMH population with CC | 53.0%     | 58.1%     | 69.1%     | 71.8%     | 73.8%     | 74.4%     |
| % of CMH population without CC | 47.0%     | 41.9%     | 30.9%     | 28.2%     | 26.3%     | 25.6%     |

Basic mechanisms of acute lung injury, interstitial lung disease and PAH

Introduction and objectives Concern about the DNA quality for next-generation sequencing encourages use of dedicated preparative kits. The purpose of this study was to attempt to sequence ten stored DNA samples that had been prepared from human blood using phenol chloroform methods 12–17 years earlier, frozen at -70°C and not subjected to special treatments. Methods The ten DNA samples that had been defrosted on multiple occasions, were defrosted again for library preparations using the Agilent SureSelect Target Enrichment System for Illumina paired-end multiplexed sequencing. Sequencing was performed on an Illumina HiSeq 2000 instrument for 2 × 100 base reads. Sequencing data were processed with RTA version 1.7.45 with default filter and quality settings, aligned to human genome build hg18 using CASAVA Eland pair algorithm, and demultiplexed with CASAVA 1.7. Results All libraries passed stringent quality control steps at each step of library generation. More than 10 Giga bases (Gb) of sequence was generated from each read. High quality scores meant that even the data from the last of the 200 sequencing cycles were usable, with a cycle 200 median Phred score of 25. More than 3.3 million clusters passed filters for each read, and more than 86% of the sequence reads aligned to the human genome. For each sample, approximately 8 million primary sequence reads uniquely mapped to the captured region of interest. Conclusions Extremely high quality DNA sequences can be obtained using stored DNA samples prepared many years earlier, and not subjected to any special treatments in the intervening years. The findings will be of particular importance to research communities where acquisition of new samples is not always possible.