

have a time association with weakly acidic reflux, either alone or together with acid. The majority of these subjects did not have an increased total number of weakly acidic reflux episodes but they had a positive symptom association probability (SAP), suggesting hypersensitivity to other aspects of the refluxate, either volume or other non-acidic gastric juice components.

In a recent study using the same techniques, we found that 25% of patients with persistent cough despite treatment with proton pump inhibitors (PPI) had a positive SAP for weakly acidic reflux.¹ These data confirm that finding a temporal relation between reflux and cough is a reliable criterion for the diagnosis of reflux induced cough, although perhaps not the sole criterion.

It is true that in the remaining patients, the majority of cough episodes were not time associated to reflux. In some of these patients, cough may have had nothing to do with reflux and in others the mechanism for reflux cough might not have been related to a direct time association. We agree with Benini *et al* that a lower cough threshold induced by repeated reflux possibly features as an additional mechanism of reflux induced cough.

However, we do not think that determining variations in cough threshold after PPI therapy will enable us to identify those patients, for several reasons:

- The hypothesis of a lower cough threshold due to repeated reflux is not only true for acid reflux but can also be applied to weakly acidic reflux. In this case, nociceptor sensitisation might not be reversible with PPI treatment which does not reduce significantly the number of postprandial reflux events with pH >4.²
- It is well known that patients with reflux oesophagitis present a tussive response to minute amounts of inhaled capsaicin. However, exhibiting a lower threshold to inhaled capsaicin is not only limited to patients with reflux but is equally present in patients with asthmatic cough and idiopathic cough. Moreover, other authors in a larger series of patients³ have shown that cough sensitivity to capsaicin did not improve significantly in most patients with asthma or GORD, despite adequate medical treatment. Their conclusion was that the discriminative value of the capsaicin test to differentiate healthy subjects from patients with asthma or reflux was poor.
- It is unlikely that variations in cough threshold after PPI therapy will be a reliable criterion to detect patients with cough in whom the symptom is due to reflux. It has recently been shown in an animal model of allergic airway inflammation that PPI can directly decrease antigen induced cough reflex hypersensitivity by a mechanism other than acid suppression.⁴ This suggests that amelioration of cough threshold with PPI treatment is not necessarily diagnostic for reflux.

Our study presented, for the first time, evidence of a temporal association between weakly acidic reflux and cough. Clinical studies and outcome data will ultimately define the clinical relevance of this time association.

L Dupont, K Blondeau, D Sifrim
Department of Pneumology, KU Leuven, Leuven, Belgium

Correspondence to: Professor L Dupont, Department of Pneumology, KU Leuven, Leuven, Belgium; Lieven.Dupont@uz.kuleuven.ac.be

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Clearance mechanisms of the aperistaltic oesophagus: the “pump gun” hypothesis

We describe the pattern of oesophageal pressure changes noted during high resolution manometry in a patient with achalasia. Our data indicate that longitudinal muscle contraction of the oesophagus is the major mechanism responsible for emptying the oesophageal contents against a poorly relaxing lower oesophageal sphincter. This phenomenon may enable patients with achalasia to empty the oesophagus and thus to relieve discomfort and maintain an adequate nutritional status.

Achalasia (Greek for “lack of relaxation”) is a primary oesophageal motility disorder characterised by the absence of oesophageal peristalsis due to damages of the myenteric plexus. Typically, patients with achalasia report difficulties in swallowing both liquids and solids (dysphagia) but young patients may initially complain of chest pain and regurgitation. These patients have mostly normal endoscopy (that is, no food retention) and initially do not lose weight, which leads to a delay in establishing this diagnosis.

Clearance of the aperistaltic oesophagus of patients with achalasia is thought to occur passively as the hydrostatic pressure of the column built in the oesophagus distends and opens the poorly relaxing lower oesophageal sphincter (LOS). However, patients with achalasia often have a high lower oesophageal sphincter pressure (that is, above 45 mm Hg). For a column of fluid to overcome hydrostatic pressures of this magnitude it would have to exceed 61 cm in height (that is, almost threefold the length of a normal human oesophagus). We hereby show a case which implies that another mechanism may be involved. Our observations are based on changes noted during high resolution manometry testing in a patient with achalasia.

A manometric examination was performed in a 45 year old Caucasian male who had complained for the past three years of difficulty in swallowing both liquids and solids and retrosternal chest pressure after meal intake, to prove the suspected diagnosis of achalasia. Upper endoscopy was normal

and a barium oesophagogram identified a normal sized oesophagus with the typical bird beak appearance at the gastro-oesophageal junction. A 32 channel oesophageal manometry catheter was introduced transnasally and positioned in the oesophagus such that it spanned the entire oesophagus, including both upper and lower oesophageal sphincters. The diagnosis of achalasia was confirmed by the low amplitude mirror image intraoesophageal pressure changes during swallowing of 10 ml of water in the recumbent position, a high LOS resting pressure of 50 mm Hg, and an LOS residual pressures of 11 mm Hg during swallowing. The patient was then asked to sit up and to reproduce his symptoms of retrosternal pressure/pain by repeated swallowing liquid. After 10 water swallows he stopped and reported a sensation of chest fullness. Approximately 10 seconds later he reported increasing discomfort of retrosternal chest pressure immediately followed by the sensation of bolus passage and pressure relief. The pressure recordings during this period are shown in fig 1 and represent the aperistaltic pressure changes during swallowing followed by a brief period of inactivity. After a dry swallow the pressure in the oesophagus increases as the LOS is moving upwards and the fluid column is pressed against the closed upper oesophageal sphincter. Subsequently, the pressure is declining and the lower oesophageal sphincter returns to the initial position.

We interpret these changes as a reflex shortening of the longitudinal oesophageal musculature against the closed upper oesophageal sphincter, resulting in the generation of sufficient pressures to evacuate oesophageal contents into the stomach through the hypertensive and poorly relaxing lower oesophageal sphincter. The presence of this oesophageal propulsive force has been previously described by Winship and Zborlaske¹ as the oesophageal response to acute obstruction. While shortening of the oesophagus during swallowing has previously been documented in normal subjects,^{2,3} this is the first report to describe it in a patient with achalasia. Our observation stimulates questions on the pathophysiology of achalasia and the role of oesophageal longitudinal musculature contraction. This, as we call it, “pump gun” (after the classic side action firearm first patented in Britain by Alexander Bain in 1854) oesophageal emptying, may enable patients with achalasia to clear the oesophagus, relieve pain, and maintain an adequate nutritional status.

R Tutuian, D Pohl

Division of Gastroenterology and Hepatology, Department of Internal Medicine, University Hospital Zurich, Zurich, Switzerland

D O Castell

Division of Gastroenterology-Hepatology, Medical University of South Carolina, Charleston SC, USA

M Fried

Division of Gastroenterology and Hepatology, Department of Internal Medicine, University Hospital Zurich, Zurich, Switzerland

Correspondence to: Dr R Tutuian, University Hospital Zurich, Division of Gastroenterology and Hepatology, Raemistrasse 100, CH-8091 Zurich, Switzerland; radu.tutuian@usz.ch

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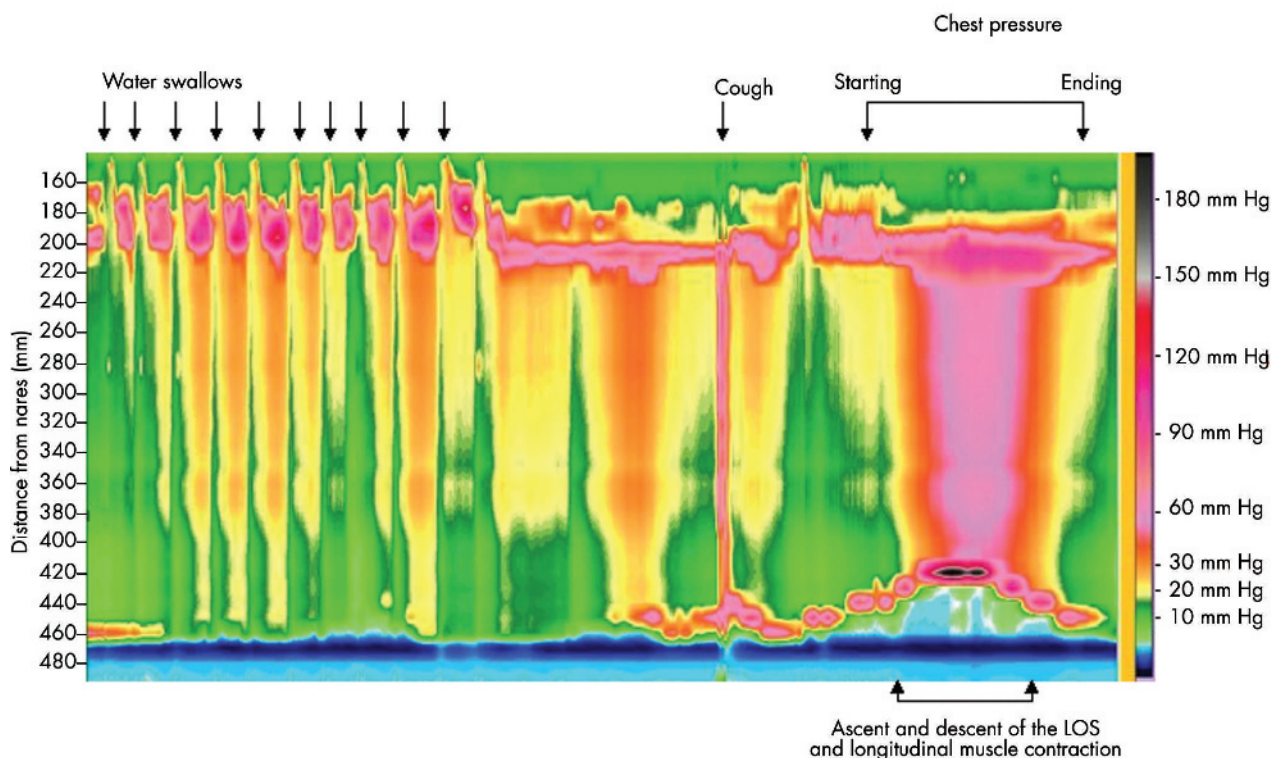


Figure 1 Topographic representation of a high resolution (32 channel) manometric recording of the events of oesophageal filling and emptying in a patient with achalasia. After 10 swallows the oesophagus is filled with water. Elevation of the pressure transition zone corresponding to the lower oesophageal sphincter (LOS) is assumed to be the result of the reflex contraction of the longitudinal musculature of the oesophagus. At the time of rise in intraoesophageal pressure, the patient reports an increase in chest pressure which improves once the oesophageal pressure returns to baseline. During this time the upper oesophageal sphincter (pressure band between 20 and 22 cm from nares) remains closed.

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Does a lower insulin resistance affect antiviral therapy response in patients suffering from HCV related chronic hepatitis?

According to a recently published study (*Gut* 2005;**54**:1003–8), insulin resistance is a worsening factor in hepatitis C virus (HCV) related chronic hepatitis. There is much debate as to whether insulin resistance depends on hepatitis C virus, or vice versa, or whether it is an independent syndrome.

As insulin resistance is the link between obesity, metabolic alterations, and endothelial damage, it is a characteristic feature of the metabolic syndrome. Non-alcoholic steatohepatitis is a recently recognised entity associated with the metabolic syndrome. It frequently overlaps with HCV related chronic hepatitis, sharing some histological features (mainly steatosis).

The aim of our study was to verify the possibility of improving the rate of antiviral

treatment response by ameliorating the metabolic syndrome.¹

Thirty two naïve patients with HCV related chronic hepatitis and metabolic syndrome (assessed using ATP III criteria), genotype 1, aged 44–68 years (16 males), were consecutively enrolled. The population was divided into two groups: 15 patients (group A) were on a strict low calorie diet for three months to achieve a 10% reduction in body mass index (BMI) before starting treatment, whereas 17 were on a free diet for the same period (group B).

All patients were offered standard combined antiviral therapy Peg-interferon alpha 2b 1.5 µg/kg body weight/weekly and ribavirin 1000–1200 µg/daily) for at least three months for non-responders (same virological load before and after) and for 12 months if responders or partial responders (decrease in HCV-RNA ≥ 2 log 10). The results were as follows: homeostasis model of assessment (HOMA) in group A was different before and after weight reduction (4.86 (0.96) v 3.45 (0.66); $p = 0.0018$; paired t test), with 60% and 17.6% of responses in group A and B, respectively ($p = 0.035$; χ^2). The flu-like-syndrome was present in eight patients in group A and in 13 patients in group B.

The low calorie diet was the only parameter differentiating the response rates to antiviral therapy. We speculate that by improving the metabolic syndrome, the decrease in BMI played a key role in reducing the metabolic cofactors and creating a better basis for a good antiviral response. The lower dosages

encouraged better patient compliance to treatment.

G Tarantino, P Conca, M Ariello, M Mastroiolo
Department of Clinical and Experimental Medicine,
Federico II University Medical School of Naples,
Naples, Italy

Correspondence to: Dr G Tarantino, Department of Clinical and Experimental Medicine, Federico II University Medical School of Naples, Via S. Pansini 5 80131, Italy; tarantino@unina.it

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First report of a complete pathological response of a pelvic GIST treated with imatinib as neoadjuvant therapy

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours of the gastrointestinal tract, with approximately 5% being located at the rectum. Up to two thirds of GISTs may have a malignant behaviour, with a high recurrence rate.¹

We report a case of a 68 year old woman with multiple local recurrences of a rectal