Cómo evaluamos los fundamentos de estos datos?

**Levels of evidence**

**Level I:** At least one properly conducted randomized controlled trial, systematic review, or meta-analysis

**Level II:** Other comparison trials, non-randomized, cohort, case-control, or epidemiologic studies, and preferably more than one study

**Level III:** Expert opinion or consensus statements

Pero...
An Official ATS Statement: Grading the Quality of Evidence and Strength of Recommendations in ATS Guidelines and Recommendations

The Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) working group has conducted a review of existing grading systems and developed a system for grading the quality of evidence and strength of recommendations of CPGs that addresses disadvantages of prior systems. These disadvantages include the lack of separation between quality of evidence and strength of recommendation, the lack of transparency about judgments, and the lack of explicit acknowledgment of values and preferences.

GRADE

Grading of Recommendations
Assessment
Development and Evaluation

Recommendations (2 levels)
Strong
Weak

Quality of evidence (4 levels)
High
Moderate
Low
Very low

Dr Maximiliano Gómez
Diciembre 2008
www.rincondealergia.org


Figure 1. The Montreal definition of gastroesophageal reflux disease and its constituent syndromes: Gastroesophageal reflux disease is a condition that develops when the reflux of gastric content causes troublesome symptoms or complications.

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- The common co-existence of cough and GORD is well established. By chance alone the occurrence of these as independent events may be as high as 5% of the general population. Ascertaining cause and effect is however more difficult. Although some patients may have resolution of chronic cough with therapies for GORD there is still insufficient evidence to determine whether GORD is a common cause of chronic cough.

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...extraoesophageal spectrum of reflux-induced disease.  
Coughing (22.5% vs 11%)

- Only 1 of 8 patients responded to omeprazole treatment during 12-week, compared with none of 9 in placebo. A crossover study investigating omeprazole in 29 subjects with GOR-related chronic cough showed a reduction in cough in 12 patients receiving placebo and then omeprazole ($P < 0.05$), although an apparent carry-over effect in those receiving omeprazole and then placebo led to the original crossover design not being used in the data analysis.

- Pathogenic mechanisms. Similarly to asthma, cough may be induced by an oesophageal-tracheobronchial reflex in response to acid in the oesophagus, or by aspiration of oesophageal contents into the larynx and tracheobronchial tree. There is also evidence that cough may stimulate GOR, perhaps as a result of an increased pressure gradient between the thorax and abdomen.
...extraesophageal spectrum of reflux-induced disease.
Laryngitis (23.5% vs 11%)

- Pathogenic mechanisms. Chronic coughing and throat clearing, as well as laryngeal damage may occur via access of refluxate to the larynx and surrounding tissue, or by vagally-mediated reflexes stimulated by acid in the distal esophagus.
- Long-term pantoprazole therapy provided no advantage over placebo with respect to symptomatic improvement of laryngitis (n = 21).

Kempainen RR et al. High Prevalence of Proximal and Distal Gastroesophageal Reflux Disease in Advanced COPD. Chest 2007;131;1666-1671

- COPD pt particularly vulnerable to reflux. Exaggerated intrathoracic pressure shifts, increased frequency of cough, diaphragmatic flattening, and use of 2-agonists exacerbate reflux.
- 41 severe COPD pt (xFEV1; 24%); dual-probe 24-h esophageal pH monitoring
- Prevalence of GERD was 57%. Elevated distal and proximal reflux were present in 41% and 46%. Most patients with GERD were not receiving acid blockers, and only 1/3 reported heartburn and/or acid regurgitation during the pH study. Only higher body mass index was predictive of reflux on regression analysis (OR, 1.2; 95% CI, 1.0 - 1.5; p 0.05).
...extraoesophageal spectrum of reflux-induced disease.  
Asthma (26% vs 20%)

- Low pH or distension of the oesophagus can lead to bronchospasm via vagal reflexes.
- Alternatively, bronchospasm may be induced by the aspiration of refluxate. These mechanisms may be more active during sleep.
- Asthma or COPD could stimulate GOR, as a result of a cough increasing the pressure gradient across the diaphragm, or the effect of asthma medications on lower oesophageal sphincter pressure and gastric acid secretion. These mechanisms gain support from studies showing an increased risk of GORD in patients with a prior diagnosis of asthma (OR 3.2; 95% CI 2.6–4.0) or COPD (OR 1.3; 95% CI 1.0–1.8)

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- Twenty-eight studies. GORD in asthma patients was 59.2%, in controls 38.1%. In patients with asthma, the average prevalence of abnormal oesophageal pH, oesophagitis and hiatal hernia was 50.9%, 37.3% and 51.2%, respectively.
- Asthma in individuals with GORD was 4.6%, in controls 3.9%. Odds ratios 5.5 (95% CI 1.9–15.8) for GORD symptoms in asthma, and 2.3 (95% CI 1.8–2.8) for asthma in GORD.
- One longitudinal study showed a significant association between a diagnosis of asthma and a subsequent diagnosis of GORD (relative risk 1.5; 95% CI 1.2–1.8), whereas two studies that assessed whether GORD precedes asthma gave inconsistent results.
7 cross-sectional studies; prevalence asthma in GORD pt. OR 2.26 (95% CI 1.813–2.834).

Sharma B et al. Effect of omeprazole and domperidone on adult asthmatics with gastroesophageal reflux.

- 198 asthmatics + gastroesophageal reflux diagnosed by 24-h esophageal pH monitoring.
- Ome 20 mg 2/d and Dom 10 mg 3/d or placebo for 16 wk (1:1 double-blind randomization).
- Spirometry.
- Primary outcome measures: asthma symptoms; daily reflux symptoms, albuterol use, PEFR, post B2 FEV1 and FVC as secondary outcomes.
Sharma B et al. Effect of omeprazole and domperidone on adult asthmatics with gastroesophageal reflux.
World J Gastroenterol 2007 March 21; 13(11): 1706-1710

- significant reduction in daytime asthma symptom score (17.4% vs 8.9%), nighttime asthma symptom score (19.6% vs 5.4%), reflux symptom score (8.7% vs 1.6%) and rescue medication use (23.2% vs 3.1%) after antireflux therapy compared to mean change in placebo group (P < 0.001).

- There was significant improvement in morning PEFR (7.9% vs 0.2%), evening PEFR (9.8% vs 0.5%), FEV1 (11.1% vs 3.78%) and FVC (9.3% vs 1.52%) (P < 0.01).

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- two meta-analyses (1998 and 2000)
- anti-reflux therapy in patients with asthma
- objective improvement in respiratory symptoms of patients: only discrete or no detectable improvement in pulmonary function.
- Another systematic review, it was concluded that GERD treatment resulted in no consistent benefit for patients with asthma.
- The role of GERD as an aggravating factor for asthma is still controversial, despite the well-known association between these diseases. The same is true regarding the treatment of reflux in patients with asthma.

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- **Asthma + GERD** (using 24-h pH-metry), evaluated by quality of life questionnaires, respiratory and digestive symptoms. Esophageal manometry, spirometry and PEF.
- 49 pt. clinical randomized double-blind placebo-controlled study, 40 mg/day of pantoprazol for 12 consecutive weeks.
- **Results**: 44pt (n = 22 per group). Significant improvement in scores for respiratory symptoms and quality of life only in pantoprazol (p = 0.01 and p = 0.001, respectively). No respiratory function parameters changed in either group.
- **Conclusions**: effective treatment of GERD improved patient quality of life, and symptoms of asthma significantly decreased. There were no changes in pulmonary function parameters.

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- Cada estudio escala de Jadad de 0 a 8 puntos, acompañada por una calificación separada del procedimiento de asignación donde A indica cegamiento correcto, B poco claro y C un procedimiento de asignación inadecuado.
- Nueve de los 12 estudios utilizaron procedimientos de asignación cegados. El rango de las calificaciones de Jadad fue (4 a 7), el modo 7 y el promedio 6,4, lo que indica solamente una mínima oportunidad de sesgo entre estos estudios.

Criterios de diagnóstico del RGE:
- historia de los síntomas
- endoscopía
- manometría
- prueba de perfusión de ácido
- monitorización de pH durante 24 horas
- motilidad esofágica
Todos los estudios emplearon más de uno
Tratamiento médico del RGE versus placebo.
Mejoría en sibilancias

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Diciembre 2008

Tratamiento médico del RGE versus placebo.
Uso de salbutamol rescate

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Diciembre 2008
Tratamiento médico del RGE versus placebo. 
PC20 Metacolina

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Gibson PG, Henry RL, Coughlan JL. Tratamiento del reflujo gastroesofágico para el asma en adultos y niños. 

**Implicaciones para la práctica:**

- En sujetos que tenían tanto asma como RGE, el tratamiento para el RGE no produjo una mejoría consistente en los síntomas del asma. Se informó que un subgrupo de sujetos obtuvo beneficio pero parece difícil poder pronosticar los entrevistados.

- En este momento no es posible recomendar el tratamiento médico del RGE como medio para controlar el asma.
Gibson PG, Henry RL, Coughlan JL. Tratamiento del reflejo gastroesofágico para el asma en adultos y niños. 

Implicancias para la investigación:

- Se recomienda que se realicen estudios futuros para identificar el tratamiento óptimo del RGE para el asma, las dosis óptimas de fármacos y la duración del tratamiento.
- Estos estudios deberían tener la duración adecuada y las mediciones se deberían efectuar en el período tardío del tratamiento y no durante todo el curso del tratamiento.
- También se debería considerar el reclutamiento de participantes con asma inducido por RGE comprobado.