

Prevalence of Arnold Nerve Reflex in Adults and Children With Chronic Cough

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Q1 Q2 Peter V. Dicpinigaitis, MD, FCCP; Ahmad Kantar, MD, PhD; Oladunni Enilari, MD; and Francesco Paravati, MD

BACKGROUND: Cough originates from stimulation of structures innervated by the vagus nerve, including the airways and distal esophagus. Arnold nerve reflex describes the induction of cough by stimulation of the external auditory canal, which is innervated by the auricular branch of the vagus. Historically, the prevalence of this reflex has been reported in the range of 2% to 3% on the basis of studies of outpatients in otolaryngology practices, but has not been investigated in healthy volunteers or in patients with chronic cough.

METHODS: Two hundred adults and 100 children with chronic cough, as well as 100 adult and 100 pediatric volunteers, underwent evaluation consisting of stimulation of the external auditory canal of each ear with a cotton-tipped applicator. Cough occurring within 10 seconds of stimulation was considered induced by the intervention.

RESULTS: Arnold nerve reflex was present in 25.5% of adults and 3% of children with chronic cough. The prevalence of the reflex was 2% among healthy adults and children. In adults with chronic cough, Arnold nerve reflex was observed more commonly in women (31.6%) than men (12.5%) and was unilateral in the majority of patients (90.2%).

CONCLUSIONS: The greater than 12 fold prevalence of Arnold nerve reflex in adults with chronic cough compared with healthy volunteers supports the concept of cough hypersensitivity syndrome (CHS), in which vagal hypersensitivity is proposed to underlie chronic refractory cough. The absence of increased prevalence among children with chronic cough suggests that cough hypersensitivity syndrome is an acquired condition, perhaps triggered by viral respiratory infection or other environmental factor. CHEST 2017; ■(■):■-■

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KEY WORDS: airway hyperresponsiveness; cough; sex

ABBREVIATIONS: CHS = cough hypersensitivity syndrome; UTC = urge-to-cough

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FUNDING/SUPPORT: The authors have reported to CHEST that no funding was received for this study. Q4

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DOI: <https://doi.org/10.1016/j.chest.2017.11.019>

In animals and man, cough can only be induced by stimulation of a structure innervated by the vagus nerve or one of its branches.¹ These include the upper and lower airways and the distal esophagus. The auricular branch of the vagus nerve (Arnold nerve) supplies the external acoustic meatus (auditory canal) (Figs 1, 2).

Induction of cough by manipulation of the ear is known as Arnold's nerve reflex or the ear-cough reflex. Three previous studies²⁻⁴ evaluating a total of 1702 outpatients presenting to an otorhinolaryngologist revealed a prevalence of Arnold nerve reflex of 2.6%. To our knowledge, the prevalence of the ear-cough reflex in healthy volunteers and in patients with chronic cough has not been investigated previously.

The concept of the cough hypersensitivity syndrome (CHS) has been proposed.⁵⁻⁷ The premise of CHS

invokes hypersensitivity of the vagus nerve as the mechanism underlying chronic, refractory cough, in that patients with chronic cough respond to common triggers that do not result in cough in the general population. Such triggers include postnasal drip syndrome, airway inflammation, acid or nonacid reflux, exposure to cold air and/or strong scents, prolonged talking, and laughter.

If hypersensitization of the vagus nerve and its branches does indeed underlie chronic refractory cough, then an increased prevalence of Arnold nerve reflex may be expected in such patients. The aim of this study therefore was to evaluate the prevalence of Arnold nerve reflex in adult and pediatric patients with chronic cough, relative to populations of healthy children and adults.

Methods

Subjects

Adult subject populations comprised 200 consecutive patients presenting for evaluation of chronic cough (defined as cough duration > 8 weeks) to a subspecialty cough center (Montefiore Cough Center, Bronx, NY) as well as 100 healthy nonsmokers without history of respiratory disease or recent (> 4 weeks) acute viral upper respiratory tract infection (common cold) or symptoms of seasonal allergies.

Pediatric subject populations were composed of 100 consecutive patients presenting for evaluation of chronic cough (defined as cough duration > 4 weeks) to a subspecialty clinic (Pediatric Cough and Asthma Center, University and Research Hospitals, Istituti Ospedalieri Bergamaschi, Bergamo, Italy; and Pediatric Unit, San Giovanni di Dio Hospital, Crotone, Italy) as well as 100 consecutive healthy children presenting for routine pediatric office visits.

Approval for this study was obtained from the institutional review boards of the Albert Einstein College of Medicine (Bronx, NY; institutional review board No. 2017-7531) and the local unit of the regional ethical committee, Catanzaro-Calabria region, Italy.

Study Methods

In addition to routine physical examination, patients were evaluated for the presence of Arnold nerve reflex by insertion of a cotton-tipped applicator (Q-tip; cotton bud) approximately 3 to 5 mm into the external auditory canal of each ear and mechanical stimulation of its circumference over a period of 2 to 3 s. To maintain uniformity, we arbitrarily tested the left ear first, followed by the right. Cough occurring within 10 s of stimulation was considered to be induced by the intervention. All evaluations were performed by one of the four coauthors of this report, two in the United States (P. V. D. and O. E.) and two in Italy (A. K. and F. P.).

Results

The 200 adult patients with chronic cough evaluated included 136 women (68%) and 64 men (32%). Mean age for the total group was 59.2 ± 13.7 (SD) years; for women, 58.6 ± 13.7 years and for men 60.6 ± 13.7 years. Fifty-one patients (25.5%) demonstrated a positive Arnold nerve reflex (Fig 3). This finding was observed much more commonly in women (43 of 136, 31.6%) than in men (8 of 64, 12.5%). Furthermore, the presence of Arnold nerve reflex was almost uniformly unilateral (90.2%), being present on the right side only in 24 of 51 subjects (47.1%), left side in 22 subjects only (43.1%), and bilateral in 5 (9.8%) patients only. In the vast majority of subjects (> 90%), the Arnold nerve reflex response was observed either instantaneously or within 5 s. In two (1%) patients, an urge-to-cough (UTC) sensation without an associated motor cough was

induced by stimulation of the external auditory canal. Five of 46 (10.9%) subjects with unilateral Arnold nerve reflex experienced contralateral UTC upon stimulation of the ear.

Twenty-eight (14%) of the 200 patients with chronic cough reported a recollection of an ear-cough reflex event at least once in the past when questioned by the investigator. Of those 28 patients, 22 (78.6%) demonstrated the reflex on examination. Of those patients demonstrating an Arnold nerve reflex, 23 of 51 (45.1%) recalled experiencing this phenomenon before evaluation.

Comparison of the adult chronic cough subjects with and without a positive Arnold nerve reflex revealed no significant age difference: mean ages for the two groups were 62.1 ± 11.5 (SD) years and 58.3 ± 14.3 years,

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