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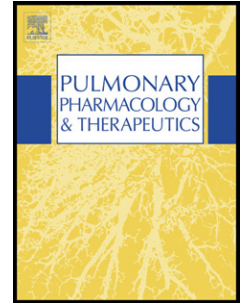
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Patterns of Cough in the Clinic**McGarvey LPA**

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Abstract

Current guidelines for the management of cough highlight the value of a taking a careful history to establish specific features of the cough in particular its duration, typical triggers or aggravants and associated symptoms. Unfortunately the diagnostic yield from a history alone is poor and there is a need to understand the pattern of clinical cough in a more precise way. As the technology to record cough in ambulatory settings becomes more sophisticated so the possibility that precise measurement of the cough frequency, intensity and acoustic characteristics may offer diagnostically valuable information in individual patients becomes a reality. In this article the current knowledge of the clinical patterns of cough is discussed and the potential for new technology to record cough patterns in a meaningful way is considered.

Introduction

Over the last 50 years much effort has been devoted to defining the patterns of experimentally induced cough in the laboratory. This work has provided an important although incomplete understanding of the various neural, motor and acoustic patterns of the cough reflex in animal and human species. The same progress has not been made in understanding the patterns of cough in the clinic which is surprising as cough consistently remains one of the most common reasons why patients seek medical help [1]. This has not been because of a lack of endeavour but rather due to the complexities and nuances that arise when an apparently simple question such as 'What is a cough?' is asked in the context of clinical disease [2]. In a recent article detailing a panel discussion on the 'semantics and types of cough' held at the 5th International Symposium on Cough it was broadly agreed that the pattern of cough in the clinic was one area that justified further consideration [3]. One suggestion from this group was to classify cough under the names eutussia (normal), atussia (absent), dystussia (pathological), hypotussia (weakened) and hypertussia (sensitized). Cough presenting to the clinic is never perceived by the patient as normal and although an absent or weakened cough is clearly associated with pathology this will only be considered briefly in this article. Dystussia as it presents in the clinic is almost invariably associated with hypertussia and this particular pattern of coughing is attracting much interest from clinicians, scientists and the pharmaceutical industry. The enlightened comments arising from the panel discussion mentioned above have provided a template for this article.

Taking a clinical history

Clinicians are readily aware that like patients not all coughs are the same. The idea that identifying specific cough patterns could be of value diagnostically and ultimately therapeutically is attractive. Existing guidelines on the management of cough advocate the value of taking a careful history although one study has suggested that a patient's own description of the pattern (character and timing) of cough is of no diagnostic help [4]. Here we consider the information that can be obtained by directly asking the patient about their cough, the diagnostic value of that information and the potential significance of the typical factors that trigger cough.

Asking the patient

Asking the patient to describe the cough in their own words can be a useful first question. Patients will detail those features that are most bothersome, in particular the frequency, intensity and associated effects such as urinary incontinence and retching or vomiting. Many will also describe a

tickle or irritation in the laryngeal or central chest area which just precedes the cough and which is associated with a need or 'urge' to cough. In addition, asking the patient to provide a brief demonstration of their cough may help to distinguish obvious throat clearing from coughing or if not already apparent reveal a cough with a bizarre and obviously functional or psychogenic quality [5].

Is the patient's description of cough helpful diagnostically?

Although the history may suggest that the cough is directly associated with throat clearing, or the sensation of post nasal drip, or that it occurs mainly at night when supine or after meals, or is made worse with exercise or cold air, this may be misleading: i.e. the symptoms of post-nasal drip in a patient may simply reflect coexistent rhinitis and the absence of dyspepsia does not rule out reflux as the cause of cough. In a study designed to evaluate the utility of the anatomic diagnostic protocol originally conceived by Irwin and colleagues, the positive predictive value (PPV) for the various cough patterns described by patients referred to a specialist clinic was determined [6]. The findings suggested that relying solely on history was useless from a diagnostic perspective. For example, a history of cough triggered by exercise was poorly predictive for asthma. This is not perhaps surprising as recent findings indicate that the cough reflex may actually be desensitized by both exercise and voluntary hyperpnea suggesting the relationship between cough and exercise is rather complex [7]. Frequent throat clearing or the presence of secretions draining at the back of the throat accompanying the cough had a positive predictive value of only 52%. Worsening of cough after meals and/or dyspepsia was even less predictive which contrasts the findings of Everett and Morice who advocate the value of a history in diagnosing GORD associated cough [8]. They used a more refined series of questions including detail on the timing of cough with meals, specific precipitating factors such as phonation (e.g. talking on the telephone) and the presence of associated symptoms (e.g. throat clearing/lump sensation at back of throat) which may explain the greater diagnostic utility. Accurately defining the temporal relationship between cough events and episodes of reflux is likely to improve our understanding of the mechanisms of reflux cough and our ability to make the diagnosis. The accurate recording of cough events will be discussed later in this article.

The pattern of cough intensity variation over time is considered to have diagnostic value particularly in paediatric settings [9]. Children (or more often their parents) describe three typical scenarios; a cough of acute onset usually reaching peak intensity within 2 or 3 days but rather than settling quickly within a week or so it persists for a month or more, only to eventually settle. Recognising this as characteristic of a viral upper respiratory tract infection should reduce the inappropriate prescription of inhaled corticosteroids and/or antibiotics or both [10]. The second pattern in

children is cough of acute onset settling down within a few weeks only to recur again a week later and when this pattern repeats itself with regular frequency over a number of months it prompts parental and physician concern of underlying asthma. This pattern of cough has been termed 'recurrent acute' is felt to represent recurrent respiratory viral infectio . Finally children with cough may present with a persistent non-remitting cough, beginning innocuously and building to a persistent and disruptive cough. A cough with a 'honking' or 'barking' quality and which disappears with sleep is thought to be typical of a psychogenic or habit cough. Such characteristics have been frequently reported in the paediatric literature [11,12]. Recognising the typical sound and behavioural characteristics of a psychogenic cough are more diagnostically useful than the pattern of cough cessation during sleep. The latter is not such a reliable indicator as sleep is known to suppress the cough reflex. In a study of patients with lung disease and nocturnal cough, spontaneous cough was almost abolished during stage 3 and 4 sleep [13].

Cough triggers

Patients who seek medical help for cough frequently report bouts of coughing triggered by relatively innocuous stimuli such as a change in air temperature or exposure to scents and odours suggesting a sensitized cough reflex (hypertussia). The triggering of cough by physical (mechanical and thermal) and chemical stimuli occurs in about two-thirds of patients referred to specialist cough clinics, is more common in females but has no specific diagnostic value [14]. The extent or degree of hypertussia can be measured in a semi-objective way using capsaicin or citric acid cough challenge testing [15]. A hypersensitive cough reflex is a feature in virtually all patients with cough, irrespective of underlying aetiology and elucidating the mechanisms of hypertussia is likely to be of help in the search for new cough therapies. At the moment the influence of the peripheral and central nervous system is an area of intense interest as pharmacological modulation of a number of key sensors and mediators is theoretically possible [16]. In the meantime recognising the existence of 'cough hypersensitive syndrome' which unifies all acute and chronic respiratory diseases where cough is a problem is felt to be an important step forward in reaching the goal of safe and effective treatments for cough [17].

The converse of hypertussia is a weakened or absent cough reflex with resulting risk to the airway from aspiration. This situation is commonly encountered in patients following cerebrovascular accidents but is also a feature in neurological syndromes where the efferent motor pathways responsible for neuromuscular function are deficient [18]. This is not to be confused with a failure of

upper airway protective reflexes. Impairment of the laryngopharyngeal reflexes has been reported in cough patient with documented GORD [19].

Recording the pattern of clinical cough

The ability to reliably and efficiently record cough sounds in an ambulatory setting has relied on modern technological developments although the analysis of cough sounds is not a new science. Yanagihara and colleagues studied the relationship between the change of flow rate and glottal function and the creation of a cough sound [20]. Cough sounds can be studied by recording the acoustic pressure changes associated with cough (tussiphonogram)[21] or alternatively by analysis of sound frequency [22]. Discussion around the mechanistic, diagnostic and prognostic information possible from recording cough patterns follows below:

Do cough patterns provide information on mechanism of cough?

A single definition of cough which satisfies both the scientist and clinician does not exist but there is consensus on the requirement for all researchers to define cough in context of their work (either in the laboratory or clinic) [15]. For the physiologist, the presence of an inspiratory phase preceding the expulsive motor effort distinguishes 'true' cough from an expiration reflex [2]. When clinicians consider cough they focus more on the expiratory effort which may more closely resemble the 'expiration reflex'. Postnasal drip, more recently termed upper airway cough syndrome (UACS) [23] is proposed to cause cough via the mechanical effect of mucus draining down to the larynx triggering an immediate expiratory effort (without a preceding inspiratory phase). Similarly, proximal reflux of gastric contents to the laryngopharyngeal area may trigger an only expiratory reflex so preventing possible lung aspiration associated with an inspiratory effort. In contrast, cough generated by activation of afferent sensory nerves in the lower airway or in extra-pulmonary sites such as the distal oesophagus [24] may trigger a cough with both inspiratory and expiratory phases. This is all somewhat speculative but the ability to record cough and test this theory should be possible.

Technological advances have allowed the recording of cough over longer periods of time. In disease, coughing rarely occurs as single events but in explosive phases following a single breath or interspersed with several breaths and are often termed 'bouts', 'peels' or 'cough epochs'. At least clinically, the issue of whether cough requires the presence of an inspiration phase before expiration becomes semantic and the practical issue of accurate cough counting becomes the priority. Methods have been designed to quantify cough and the recently described 'cough seconds' (i.e. the

number of seconds containing at least one explosive phase) has been shown to correlate well with subjective assessment of cough severity and quality of life [25].

Do cough patterns provide diagnostic information?

Although the presence or absence of mucus (loose or dry cough) can be readily identified just by listening to the cough, humans find it much more difficult to determine any more specific diagnostic information. One study to assess how health care professionals clinically interpret cough sounds highlighted such limitations. In this study the observers were asked to interpret four distinct sounds; an isolated cough, cough with mucus, cough with wheeze and cough with both mucus and wheeze. In addition they were asked to listen to cough sound generated by four common respiratory diseases; idiopathic pulmonary fibrosis, COPD, asthma and laryngitis. The observers were able to discriminate cough with and without mucus but were unable to accurately make a diagnosis from listening to the acoustic properties of the cough [26].

It seems logical that automated methods of cough recording and sound analysis would have a greater capacity than the human ear alone to interpret cough in a diagnostically discriminative way. Analysing the differences in cough sounds in various lung diseases was undertaken by Korpas et al who reported between two and four-fold increases in intensity and duration of the cough sound in severe airway inflammation compared to that recorded in mild bronchitis and healthy subjects [21]. The tussiphonogram has particular value in detecting changes in airway calibre (obstructive lung disease) and the presence of airway mucus in conditions such as chronic bronchitis. Loundon and Baughmann reported a relationship between sputum weight and cough number and intensity [27]. Using Fast Fourier Transform spectrum analysis, Piirla et al were able to discriminate between asthma, chronic bronchitis and tracheobronchial collapse [22].

Do cough patterns provide any prognostic (or phenotypic) information?

In the management of chronic obstructive pulmonary disease (COPD) attention has focused largely on lung function [28]. More recently the predictive value of composite scores which have included factors such as body mass index and severity of breathlessness have been developed [29]. Little attention has been devoted to cough even though productive cough is known to be a predictor of lung function decline in COPD [30] and is related to higher mortality rates [31]. Recognition that cough is associated with a worse outcome in COPD should argue for its inclusion as part of a more complete evaluation of COPD patients. Furthermore, there has been recent attention in identifying subgroups or disease phenotypes in COPD. Roflumilast, a novel selective phosphodiesterase (PDE) IV

inhibitor has been shown to improve lung function and reduce exacerbation frequency and severity but predominately in those patients with cough and phlegm [32]. Identifying treatment responders by accurately recording the presence of cough may prove valuable.

The future for recording cough patterns in the clinical setting

It is not surprising that development of ambulatory cough recording devices is an active and competitive research field [33,34,35]. Despite progress in this area, it is not clear what ambulatory cough recording as it currently exists really tells us about clinical cough. A number of important gaps in knowledge exist the most pertinent of which is how to resolve the poor correlation between recorded cough events and subjective measures of cough severity and quality of life (ref). Clearly not all coughs are of equal importance to the patient; a single intense bout of coughing causing incontinence is of much greater importance to the patient than the many hundreds of low intensity and barely noticeable coughs occurring throughout the day. Therefore recording the number of coughs alone is not the challenge but rather identifying the composites of cough intensity, frequency and duration that are meaningful to patients and are realistic treatment endpoint for new therapies.

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