

# Recurrent Cough Syncope Due to Pertussis in Adults: Report of Three Cases and Review of the Literature

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## Abstract

Cough syncope, also called “tussive syncope”, is a well-recognized syndrome for about 70 years, in which loss of consciousness usually occurs immediately after a violent cough or prolonged bouts of violent coughing, lasting for seconds with rapid restoration of full consciousness. Its precise pathophysiologic mechanism is not fully understood and remains a matter of debate. Although pertussis is a frequent cause of prolonged cough in adults, still its burden in this age group is under-appreciated and under-diagnosed worldwide. This is well reflected by the fact that despite cough syncope is definitely not rare, until yet only six cases of cough syncope related to pertussis have been reported in the medical literature, one of them by us. We describe additional three adults with recurrent cough syncope due to pertussis who were diagnosed during a period of 3 months which completely resolved by treatment with azithromycin. Diagnosing four cases of cough syncope in adults due to pertussis during a short period in one Department of Internal Medicine, while only five cases were reported from the rest of the world, reflects the great lack of awareness on adult pertussis worldwide. Our four cases indicate that physicians should be much more aware of pertussis as a cause of cough and cough syncope in adults in order to terminate the attacks of cough and cough syncope and its serious complications by adequate antibiotic treatment, as happened with our four patients.

**Keywords:** Cough; Syncope; Pertussis; Adults

## Introduction

Cough syncope is a well-recognized syndrome in which loss of consciousness usually occurs immediately after a violent cough or episode of violent coughing lasting for seconds. The

syndrome is usually characterized by facial congestion, turgidity and cyanosis [1, 2]. It usually occurs while sitting or standing, but may also occur during supine position, and consciousness rapidly recovers completely [2, 3]. A very consistent profile of the typical cough syncope patient is that being of a middle-aged, overweight male smoker with obstructive lung disease [1-3]. A variety of disorders of the respiratory tract, of the central nervous system, cardiovascular system, gastrointestinal system, and other disorders have been associated with the occurrence of cough syncope [1]. To the best of our knowledge, until yet more than 470 adult cases of cough syncope have been reported in the medical literature [1, 4-6].

Although pertussis is a common cause of cough, only six cases of cough syncope related to pertussis have been previously reported in the medical literature [4, 7-10]. In two of them, the diagnosis of pertussis was made without laboratory tests [10], and one of them was recently reported by us [4]. We describe additional three patients from our Department of Internal Medicine with recurrent cough syncope due to pertussis who were diagnosed during a period of 3 months.

## Case Reports

### Case 1

A 59-year-old man was referred to the emergency department (ER) because of paroxysmal episodes of violent non-productive cough immediately accompanied by syncope lasting a few seconds for the last 2 days. Another episode of cough syncope lasting a few seconds was observed in the ER with restoration of full consciousness rapidly. No significant increase or decrease of the heart rate and blood pressure, or significant decrease of oxygen saturation was observed there. The patient was admitted to our Department of Internal Medicine for further observation and investigation. He denied hemoptysis, fever, chills, chest pain, dyspnea, rhinorrhea, sore throat, or paroxysmal nocturnal dyspnea. His other medical history was remarkable for hypertension for the last 18 years, stroke with mild left hemiparesis 16 years ago, and sudden cardiac arrest 14 years ago without apparent cause after extensive investigation. For that he underwent implantation of cardiac pacemaker with defibrillator. His current medications included aspirin, atenolol, and simvastatin.

Physical examination revealed normal heart rate, blood

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pressure, body temperature, and oxygen saturation of 96% on room air. Throat, lungs, heart, and neurological examinations were normal, and no enlarged lymph nodes were palpated. Other physical findings were unremarkable.

Routine hematological and biochemical blood tests revealed normal results. Serologic tests and blood, throat, and sputum cultures for common pathogens were negative. Chest X-ray film, electrocardiogram (ECG), electroencephalogram (EEG), echocardiography, head and neck computerized tomography (CT) scan, and optic fiber laryngoscopy were normal.

In the department, the patient was monitored by continuous ECG, blood pressure, and oxygen saturation recording, during which several episodes of cough syncope were observed. During each episode, no significant changes in his heart rate, blood pressure, and oxygen saturation were observed. Restoration of full consciousness after each episode occurred within seconds. DNA detection by PCR from nasopharyngeal secretions was positive for *Bordetella pertussis*.

The patient was treated orally with azithromycin for 5 days, bringing to a significant gradual clinical improvement. The frequency and intensity of the cough episodes declined, and completely resolved with termination of the syncopal attacks 2 weeks later with addition of doxycycline after azithromycin. No cough or syncope occurred during a follow-up period of 3 months.

## Case 2

A 39-year-old previously healthy woman was admitted to our department with a 2-week history of episodes of dry coughing accompanied with syncope lasting several seconds, with rapid restoration of full consciousness. She denied other respiratory symptoms, fever, chills, or throat and chest pain. She works as a kindergarten teacher, and mentioned that she was in contact with a kid in the kindergarten who was diagnosed with pertussis.

Physical examination revealed normal heart rate, blood pressure and body temperature. Throat, heart, lungs, and neurological examinations were also normal. Other physical findings were unremarkable.

Routine hematologic and biochemical blood tests revealed normal results. Serologic tests and blood, throat and sputum cultures for common pathogens were negative. Chest X-ray film, ECG, and EEG were normal.

In the department, the patient's episodes of cough and cough syncope continued while she was on continuous monitoring of ECG, blood pressure, and oxygen saturation. No significant changes in these parameters were observed during her cough syncope attacks. DNA detection by PCR from nasopharyngeal secretions was positive for *Bordetella pertussis*.

The patient was treated orally with azithromycin for 5 days, bringing to a significant gradual improvement. The cough episodes and syncopal attacks completely resolved 10 days later.

## Case 3

A 70-year-old woman was admitted to our Department of In-

ternal Medicine with a 1-week history of dyspnea and episodes of violent coughing accompanied on the day of admission with syncope, for the first time in her life, lasting less than 1 min. The syncopal attack was accompanied with head injury. She denied fever, chills and chest pain. In the ER, recurrent episode of violent coughing with syncope lasting several seconds was observed while the patient lying down in the bed. Restoration of full consciousness took less than 1 min. Her other medical history included bronchial asthma well controlled with medical treatment, ischemic heart disease, hypercholesterolemia, hypertension, hypothyroidism, and heavy smoking. Her current medications included bisoprolol, valsartan, aspirin, clopidogrel, rosuvastatin, levothyroxine, Montelukast, and budesonide by inhalation.

Physical examination revealed normal heart rate, blood pressure, body temperature, and oxygen saturation of 94% on room air. Lungs examination revealed prolonged expiration with expiratory wheezing. Other physical findings were unremarkable.

Routine hematologic and biochemical blood tests revealed normal results. Serologic tests and blood, throat and sputum cultures for common pathogens were negative. Chest X-ray film, ECG, EEG, and head and neck CT scan were normal.

In the department, a few attacks of cough syncope were observed while the patient was on continuous monitoring of ECG, blood pressure, and oxygen saturation. Oxygen saturation decreased from 95-93% to 86-84% on room air during the episodes of cough syncope. No significant changes in heart rate and blood pressure were observed during these episodes. DNA detection by PCR from nasopharyngeal secretions was positive for *Bordetella pertussis*.

The patient was treated orally with azithromycin for 5 days, inhalation of budesonide and salbutamol, prednisone and her other previous medications. A gradual significant clinical improvement occurred with decline in the intensity and frequency of the coughing episodes until complete resolution of these episodes 1 week later, and termination of the syncopal attacks with termination of azithromycin treatment. No violent episodes of coughing or syncope occurred during a follow-up period of 4 months.

## Discussion

The syndrome of cough syncope, also called "tussive syncope", was first described by Charcot in 1876 under the name "laryngeal vertigo". The term "laryngeal epilepsy" was also used, reflecting initial opinion that this condition was primarily epileptic in nature [11-13]. Only in 1940s, it was recognized to be of syncopal nature [3], where in 1949 the term "tussive syncope" was recommended as a more appropriate term [13]. In 1953, Kerr and Derbes [2] described a series of 40 patients using the term "cough syncope" which has remained the preferred term in the medical literature since.

Syncope is a transient self-limited loss of consciousness due to acute global impairment of cerebral blood flow. The onset is rapid, duration is brief, and recovery is often spontaneous and complete. In cough syncope, loss of consciousness usually

occurs immediately after a cough, and more commonly after prolonged bouts of violent coughing, lasting for seconds with rapid restoration of full consciousness. It more commonly occurs in middle-aged, obese smoker males with obstructive lung disease [1-3]. Until yet, more than 470 cases of cough syncope have been reported in the medical literature [1, 4-6]. This syndrome could be accompanied with significant increase of morbidity and mortality as with any syncope. Numerous motor vehicle accidents resulting from cough syncope have been reported. These reports include the death of two drivers and three pedestrians [1]. It seems likely that the real number of deaths due to cough syncope-related motor vehicle accidents is much more than is reported, particularly if it caused death of the driver, since in this case nobody can know what the cause of the accident was.

The precise pathophysiologic mechanism of cough syncope is not fully understood, and remains a matter of debate [14-20]. Several mechanisms have been proposed in this regard. With continuous coughing, intra-thoracic pressure increases resulting in decrease in venous return, ventricular filling, cardiac output, and blood pressure [15]. Since cough syncope may occur without prolonged period of coughing, it has been suggested that baroreceptor mechanism via a baroreceptor-initiated neural vasodilation-bradycardia reflex, further reducing blood pressure, could be partly responsible for the syncope. Hence, subjects susceptible for cough syncope exhibit greater hypotensive response to transient exaggerated intra-arterial pressure pulses. Both the magnitude and duration of the consequent hypotension are greater than in other fainters, and the hypotensive-triggered compensatory positive chronotropic response is absent or markedly suppressed [14, 15]. Other suggested mechanisms indicates that the increased intra-thoracic pressure during coughing is transmitted to the cerebrospinal fluid, causing an acute pressure increase in the skull, compromising cerebral perfusion and resulting in syncope [16, 21]. Complete atrioventricular block in patients with left bundle branch block [19], carotid sinus hypersensitivity [20], sinus arrest in patients with sick sinus [22], and synergistic effect between jugular venous reflex and plasma endothelin-1 levels [23] have also been suggested. Simultaneous occurrence of multiple pathophysiological processes may be required to induce cough syncope [1]. In our three patients, no significant decrease in blood pressure or heart rate was observed during their syncopal attacks, suggesting that decrease in cerebral perfusion due to increased intra-thoracic pressure seems the likely mechanism for their syncope. In the third patient, decrease of oxygen saturation during her violent coughing may partly participate in the development of cough syncope.

Pertussis continues to be an important public-health issue. Despite widespread vaccination, *Bordetella pertussis* is increasingly identified as a cause of sub-acute and chronic cough in adolescents and adults. The clinical characteristics of pertussis among adults are less obvious than among children. While the clinical presentation in children classically consists of three phases (catarrhal, paroxysmal and convalescent) [24], in adults it is usually a long and mild disease, and may show atypical manifestations with prolonged cough [25]. Therefore, diagnosis of adult pertussis may be complicated by these facts. Furthermore, pertussis in this age group may have been largely

ignored due to lack of awareness on adult pertussis as well as diagnostic facilities and the reliance on clinical diagnosis [26]. From an epidemiological point of view regarding pertussis being important public-health issue, a major role is played by this age group who is a significant source of infection for unvaccinated or incompletely immunized newborns/infants in whom the severity of the disease can be serious [26]. Recently, more sensitive detection methods, including PCRs or serological assays of antibody titers against pertussis antigens, have allowed for a more sensitive measure of pertussis in adults. Using these methods, several studies identified pertussis as a frequent cause of prolonged cough in adults, supporting further the concept that pertussis burden in this age group is under-appreciated and under-diagnosed [26, 27].

Until yet, only six cases of cough syncope related to pertussis have been described in the medical literature [4, 7-10], two of which were not documented by laboratory tests for pertussis [10]. In our medical center, we have the national center for pertussis research and diagnosis, and we are strongly aware to occurrence of this infection in adolescents and adults. Since cough syncope is not rare and cough due to pertussis in the adults is common (recently about 50% of the reported cases), it seems likely that cough syncope due to pertussis is much more than is reported in the medical literature. Diagnosing four cases of cough syncope due to pertussis in adults, the three described herein and the one previously reported [4], in one Department of Internal Medicine during a short period while in the rest of the world only five cases were reported until yet is due to our awareness on pertussis in adults, and reflects the lack of awareness on adult pertussis in most of the world.

In conclusion, although pertussis is increasingly reported as cause of sub-acute and chronic cough in adolescents and adults, in these age groups still pertussis is under-appreciated and under-diagnosed. It seems likely that cough syncope due to pertussis is not rare, and its prevalence is much more than is reported in the medical literature. Diagnosing four cases of cough syncope in adults due to pertussis in one Department of Internal Medicine during a short period should stimulate physicians to be alert to pertussis as being a not uncommon cause of sub-acute and chronic cough with or without syncope in this age group. Increasing the awareness on adult pertussis may prevent recurrent attacks of cough and cough syncope and its severe complications due to pertussis by proper antibiotic treatment as happened with our four patients. It also may decrease significantly this age group as being source of infection with *Bordetella pertussis* for unvaccinated or incompletely immunized newborns/infants in whom the severity of the disease can be serious.

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## Conflicts of Interest

The authors declare no conflicts of interest.

## Author Contributions

All authors contributed significantly to the collection of data and preparing of the manuscript.

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