Prof. Kefang Lai: the diagnosis and treatment of cough in China

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Kefang Lai (Figure 1), PhD, MD, Professor of Internal Medicine, Guangzhou Institute of Respiratory Disease, The First Affiliated Hospital of Guangzhou Medical University. Director of Clinical Research Department, State Key Laboratory of Respiratory Disease. Editorial Board of Chin Asthma J, Chin J Lung Dis, Int J Rerspir Dis. Academic interest: chronic cough and bronchial asthma, chairing several key national science research projects on asthma and chronic cough, including State "863" projects, State "115" Project, National Nature Science Foundation of China, taking the lead in chronic cough field in China with more than 100 papers published. Editor-in-chief of "Chronic Cough", editor of eight books associated with respiratory disease, and chief draftsman for "Guideline of Diagnosis and Management of Cough" in China (2005, 2009).

Figure 1 Prof. Kefang Lai.

JTD: Your research interests lie in the pathogenesis, etiological diagnosis and treatment of chronic cough with unknown causes and bronchial asthma. In your opinion, what significance does this international cough conference have for the academic circle of chronic cough in China?

Prof. Lai: Heretofore, international cough conference has been held in turn in the UK and USA. This is the first time this conference has been held in China, so successful organization of this conference means a lot to us.

Firstly, this conference has certainly promoted mutual understanding and communication between Chinese and foreign experts and it also provides a platform or lays a sound foundation for the future collaborative study on cough.

Secondly, we organized many seminars on various topics of clinic and basic medicine, which helps domestic clinicians and researchers know more about the up-to-date progress made in the cough study, and thereby elevates the diagnostic and therapeutic levels of clinicians for cough in our country.

Thirdly, this international conference in China is a result of joint efforts of experts from China, Europe, USA, Japan and Australia, and also acknowledgement of the accomplishments of Chinese cough study by international experts, which will make the cough study in China take new steps forwards.

JTD: Professor Lai, as the drafter of the first Chinese Guideline for Diagnosis and Management of Cough (hereinafter referred to as "Chinese Guideline"), you gave interpretations of this guideline for adults in the seminar "Guideline for Cough: Consensus and Controversy, Present and Future" in this conference. Would you like to talk about the background for development of this guideline?

Prof. Lai: *Chinese Guideline for Diagnosis and Management of Cough*, published in 2005 (1st edition) and updated in 2009, is the fourth guideline for cough in the world following the corresponding guidelines by the American College of Chest Physicians (ACCP), European Respiratory Society (ERS) and Japanese Respiratory Society.

Why did we need a specially developed guideline for the diagnosis and management of cough? The reasons are as follows:

For one thing, cough is very common in clinic. Patients with symptoms of cough account for almost 1/3 or even more than 1/2 of the visitors in the specialist outpatient clinic. Despite its prevalence, misdiagnosis and mistreatment of cough, especially chronic cough, was very common. Our investigation demonstrated that since in more than 80% of the patients chronic cough was misdiagnosed as chronic bronchitis or chronic pharyngolaryngitis in the past, those patients failed to receive effective treatment. In China, large doses of various antibiotics and antitussives are administrated to patients, but cough symptoms cannot be effectively alleviated and thus severely hinder their work, study and life. When patients cough for a long time, they may fear that others will mistake their condition as an infectious disease, or they may worry that their disease is incurable. The disease places a heavy mental burden on them. Some female patients feel painful, because their long-term cough has induced urinary incontinence. Our data showed a grim situation that as many as 48% of the female patients with chronic cough have cough-induced urinary incontinence. Therefore, chronic cough has greatly affected the quality of life of patients. At least in China, chronic cough is severely afflicted by abuses of antibiotics. Actually, most cases of chronic cough have nothing to do with infection, but doctors in our country tend to use antibiotics and antitussives in clinical practice. Therefore, the high incidence of chronic cough and prevalence of misdiagnosis and mistreatment are the two major background factors for development of the *Chinese Guideline*.

Furthermore, compared with Europe and the USA, studies on chronic cough in China started relatively late, only after 2000. The research achievements we have made over the past years are the foundation of *Chinese Guideline*. It referred to many well-established conclusions in the overseas guidelines, but did not copy them completely because we had included findings of our own. In the section *Common Causes of Chronic Cough* in the guideline of 2005 edition, based on our data on chronic causes in China, eosinophilic bronchitis was first listed as one of the common causes of chronic cough. In addition, bronchial tuberculosis is not rare in China, but some cases of bronchial tuberculosis are likely to be misdiagnosed because they present with no typical symptoms but merely cough. Consequently, bronchial tuberculosis was included as a cause of chronic cough in *Chinese Guideline* in 2005. Atopic cough, as a diagnostic term, was first proposed by Japanese experts, which includes eosinophilic bronchitis in the Japan guideline; however, eosinophilic bronchitis was an independent entry listed in the *Chinese Guideline*, suggesting a difference in the definition of atopic cough between Japan and China. Atopic cough is defined in our country as cough characterized with atopy, no induction of increased sputum eosinophils or bronchial hyperreactivity, and responsiveness to the antihistamines and glucocorticoid treatment. There is no such a concept of atopic cough in Europe and the USA. It may be classified into categories of rhinitis or rhinosinusitis, postnasal drip syndrome. We found that these patients with atopic cough have no signs and symptoms associated with rhinitis or rhinosinusitis, therefore we think the cause of cough in those patients should not be considered as postnasal drip syndrome.

JTD: You have been studying asthma and eosinophilic bronchitis for a long time. Cough variant asthma (CVA) is a common cause for chronic cough. Can you talk something about the differences and associations between cough variant cough, atypical asthma and eosinophilic bronchitis?

Prof. Lai: This is a good question. CVA is a special type of bronchial asthma in which cough is sole or predominant symptom without no obvious wheeze and dyspnea, and spirometry and bronchial reactivity is normal. About 30-40% of CVA patients may develop classic asthma. However, a majority of these patients, 60-70%, stay all along at this special stage or manifestation of CVA. Why do these patients present only with cough but no dyspnea or wheeze? How long should those patients be treated? How to identify the patients who will develop classis asthma? Those questions should be clarified. I think we can study the pathogenesis of these patients, which may find out new strategies of early intervention, or targets of clinical treatment, for classic asthma. The similarities between eosinophilic bronchitis and CVA include eosinophilic airway inflammation, an increase in sputum eosinophils, symptoms of chronic cough and good responsiveness to steroids treatment. There is still no global consensus on whether eosinophilic bronchitis is actually an early stage of bronchial asthma, or whether they are two different diseases. This needs further research. Based on our preliminary finding that eosinophilic bronchitis seldom develops into asthma or airway obstruction, we tend to think that eosinophilic bronchitis is an independent disease.

JTD: Great progress has been made also in the diagnosis and treatment of cough in China, but there are difficulties to be worked out. How will you handle the challenges and opportunities in cough clinics? And what is the direction of the cough study by you and your colleagues in the future?

Prof. Lai: There have been indeed great achievements in the diagnosis and treatment of cough in China over the past 12 years. The proficiency in diagnosis and therapy of chronic cough has been greatly enhanced. Misdiagnosis and mistreatment, especially in large hospitals, have been significantly reduced. We are happy to see that chronic cough has now become one of common concerns of our clinicians. However, there are still some problems in cough to be dealt with, such as the above-mentioned relationships between CVA and classic asthma, between eosinophilic bronchitis and asthma, and their treatment protocols as well. Moreover, we also need to find out the pathogenesis and management of idiopathic cough and refractory cough which are also referred to as cough hypersensitivity syndrome in Europe. One major characteristic of these patients is their increased cough hypersensitivity for which currently there is no effective treatment or medication. Therefore, the mechanisms, pathways and relevant receptors of cough hypersensitivity need further study. We set up a seminar for the discussion of cough hypersensitivity syndrome in this conference. In China, Chinese traditional medicine has long history and rich experience in the treatment of cough and may have efficacy in some cases of refractory cough, but unfortunately, it is still at the stage of experience-based medicine and its symptomatic treatments are not supported by evidence-based study.

JTD: Thank you for your accepting our interview and we do look forward to further progress on the diagnosis and treatment for chronic cough.

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