

## China makes impressive achievements in COPD therapy

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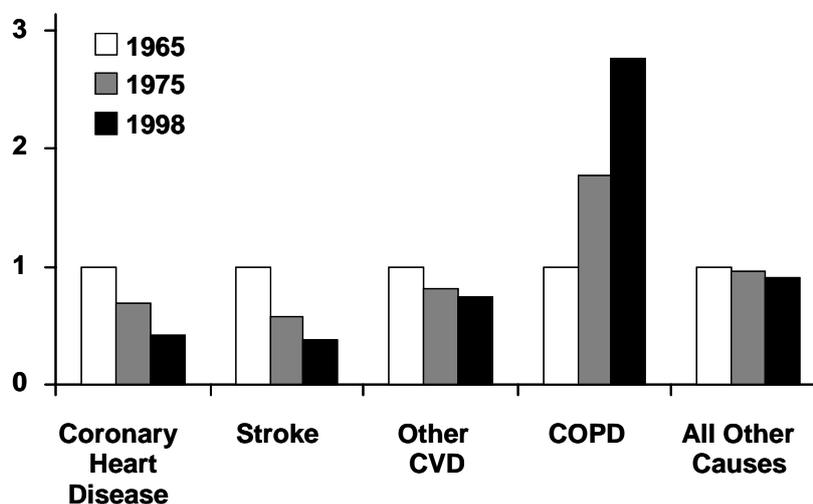
Chronic obstructive pulmonary disease (COPD), a common and frequently occurring lung ailment characterized by obstruction of airflow that interferes with normal breathing, is an overall term for life threatening lung diseases that includes the two conditions of chronic bronchitis and emphysema. The most common symptoms of COPD are breathlessness, or a "need for air," excessive sputum production, and a chronic cough. However, COPD is not just simply a "frequent cough" but often involves lung damage that worsens over time, possibly accelerating deterioration caused by the disease and leading to death.

According to the latest WHO estimates (2007), 210 million people currently suffer from COPD, 3 million died of COPD in 2005, and additional millions are disabled. COPD has been a growing cause of morbidity and mortality worldwide. In the US, for example, the mortality rates for coronary heart disease (CHD) and stroke decreased by 59 and 64 percent, respectively while that for COPD has increased dramatically by 163 percent from 1965-1998, as shown in Figure 1. As a result, the WHO predicts that COPD will become the third leading cause of death worldwide by 2030, particularly in low- and middle-income countries (Data available from <http://www.who.int/respiratory/copden/>).

To date, the pathogenesis of COPD remains somewhat unclear; as a result, the disease is still not curable despite great efforts in seeking effective strategies for COPD treatment and control. However, some potential risk factors have been verified, such as a serious deficiency of  $\alpha_1$ -antitrypsin ( $\alpha_1$ -AT) in the human body, frequent respiratory infections, smoking that includes second-hand or passive exposure, air pollution, occupational dust, chemicals, and poisonous vapors and fumes that irritate or are toxic to bronchial mucosa.

A recent COPD-associated study from China provides encouraging information. According to *China Broadcasting News* from Guangzhou, Zhong Nanshan and his fellow researchers from more than 20 research centers, including the Guangzhou Institute of Respiratory Disease and China Medical University, have achieved exciting results using the mucolytic agent carbocisteine to treat COPD patients ([http://www.cnr.cn/gundong/200806/t20080616\\_504831447.html](http://www.cnr.cn/gundong/200806/t20080616_504831447.html), available as of June 16, 2008).

Zhong is a famous respiratory disease expert and academician of the Chinese Academy of Engineering and president of the Chinese Medical Association (CMA) who has also garnered praise for his significant contribution in fighting Severe Acute Respiratory



**Figure 1.** Percent change in COPD death rates in the US, 1965-1998 (from <http://www.med.monash.edu.au/misc/docs/respiratory-poster-final.pdf>).

Syndrome (SARS) in China. Zhong said less-expensive mucolytics such as carbocisteine could reduce the frequency of self-reported worsening lung damage in approximately 24.5 percent of COPD patients. Furthermore, it significantly improved the quality of life for COPD patients with no obvious adverse effects or toxicity.

Research has demonstrated that pathogenic oxide (e.g. oxygen free radicals), an important pathogenic factor leading to COPD, can affect somatic cells, producing an oxidative stress reaction that results in injury. Therefore, development of effective drugs to counter oxidative stress has become a top priority and an attractive area for drug discovery. Results from Zhong's group also indicated that drugs containing sulfhydryl, usually used as expectorants, counter oxidative stress. However, many difficulties regarding the urgency for prevention and treatment of COPD need to be resolved. These include how to design novel drugs to counter anti-oxidative stress, which drugs containing sulfhydryl should be selected, and the best dosage to administer for them to be effective.

Carbocisteine, a sulfhydryl-containing expectorant with anti-oxidative and anti-inflammatory properties, was selected in order to evaluate its long-term (one year) efficacy and security in terms of reducing acute COPD and improving quality of life; two doses (500 mg) were given three times a day. This study was approved by the local medical ethics committee, and all patients consented to this study and provided informed consent in writing.

Results indicated that mucolytics had clear superiority over conventional therapies such as inhaled corticosteroids, long-acting beta-2 agonists,

and anticholinergics. However, the most significant merit of such drugs is the lower cost of treatment, which was dramatically reduced by up to 3,670 RMB, which was about 85 percent less than that with inhaled corticosteroids. Therefore, "less-expensive mucolytics such as carbocisteine should be recognized as a worthwhile treatment for the long-term management of COPD in the near future," researchers on Zhong's team said, "and this will be exciting news for the majority of COPD patients, and especially for those in low-income countries and regions."

Results of the research, the "Effect of carbocisteine on acute exacerbation of chronic obstructive pulmonary disease (PEACE Study): a randomised placebo-controlled study," were published in the June 14th issue of the respected international medical journal *The Lancet* (Zheng JP, Kang J, Huang SG, et al. *The Lancet* 2008; 371:2013-2018) and have garnered worldwide attention and praise from medical specialists worldwide. Two, Paul Albert and Peter Calverley, commented in an accompanying editorial that this study is particularly prominent in two aspects: (i) it reconsiders the role of existing drugs through rigorous clinical trials, thus offering new insights into COPD care, and (ii) it can greatly reduce the cost of treatment for COPD patients, so that they can benefit from systemic treatment in a standardized way, which is especially suited to low- and middle-income areas in developing countries. Moreover, the journal also held a news conference on the date of publication, providing a special introduction to this exceptional research.

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