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Profile

Zhong Nan-Shan: leader of clinical research in China

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Zheng JP, Kang J, Huang SG, et al. Effect of carbocisteine on acute exacerbation of chronic obstructive pulmonary disease (PEACE Study): a randomised placebo-controlled study. *Lancet* 2008; **371**: 2013–18.

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Explaining the evolution of the PEACE study, Zhong Nan-Shan says the roots of this research lay in the intellectual transformation he experienced on entering British academia in 1979, after an adult life spent surviving China's cultural revolution. "In particular, it taught me how to do research", he says. Zhong says he learned two important things during this time: "Never go to the next step if you have not finished the first step. Never believe that what the authorities say is always correct. Always believe what you have seen for yourself, what you have observed."

The governing philosophy behind the PEACE study was to seek a treatment to manage chronic obstructive pulmonary disease (COPD) effectively, not only clinically but also socially so that those who need treatment will actually be able to afford to use it. Zhong and his team found that carbocisteine effectively prevents COPD exacerbations while costing much less than the standard treatment, corticosteroids and long-acting β_2 agonists. China's transformation into an economic powerhouse has rendered health care, particularly the cost of medications, beyond the reach of the many people without medical insurance. Steroids and β agonists cost about 400 Yuan (US\$58) per month and many patients with COPD simply go without. By contrast, the monthly cost of carbocisteine is about 75 Yuan (\$11) per month, and it was this, along with its antioxidant properties, that made the mucolytic agent worth investigating, says Zhong.

Speaking in his office at the Guangzhou Institute of Respiratory Diseases, in the building where he saw and managed the world's first patient with severe acute respiratory syndrome (SARS), Zhong says his conviction that you must trust your observations and results helped him find ways to manage SARS and to speak out about it, despite working within a bureaucracy unwilling to accept it was confronting a new and serious disease. SARS revealed just how dangerous China's traditionally secretive public-health approach could be. "In some ways the authorities, the bureaucracy, the administration tried to keep it quiet, to say 'oh that's nothing, it's ordinary'. When the reporters asked me if it's under control I said 'No, not yet', because the numbers were still increasing and we didn't know what was causing the disease or how to deal with the disease."

Only when SARS reached Beijing did China's central authorities realise just how badly their bureaucracy had failed them. The Health Minister was sacked and replaced with then Vice-Premier, Wu Yi, who turned the system upside down and asked Zhong to take over as head of the Chinese Medical Association, the umbrella organisation overseeing China's 85 different specialty societies. Zhong says he was unsure, but physicians around the country urged him to accept the position. "Anyway, I've made a big reform—all

the heads of associations have to be elected. Anyone can be elected." Zhong's position as head of the Chinese Medical Association means he now has the power to get the kind of research he wants to do, done. So he had no problem finding 22 collaborating centres nationwide for the PEACE study.

Zhong got his chance to train in the UK—at Edinburgh University and St Bartholomew's Hospital, London—because Deng Xiao Ping, China's reformist leader, decided the best way to build up the health system, in tatters after years of cultural revolution and lack of communication with the outside world, was to send selected doctors overseas to learn from the west. Zhong went to Edinburgh to work with David Flenley, and it was there that he had his "yes I can moment" while researching pulmonary shunts in artificially ventilated patients. "There was a paper published by Dr Kerr from Oxford University in 1975: he found that as the oxygen concentration increased the shunt increased. But I was unable to reproduce his results. I said to Gordon Drummond, maybe I was wrong but he said 'try to find out what's wrong'." Eventually Zhong realised that because he had noticed the electrode measuring oxygen concentrations became unreliable at higher tensions, and had calibrated it to correct this, his results were different from Kerr's. The experience of presenting his findings to colleagues and being given their support was important for Zhong: "I was so happy about that. After that I got my point. Do not always believe that what the authorities say is always correct."

Before his time in the UK, Zhong says that "All I had hoped for was to get my family together". An assistant biochemistry lecturer in Beijing, and son of a famed professor of paediatrics, Zhong was labelled one of the despised intellectuals in the cultural revolution and dispatched to the countryside near the Great Wall, in Hebei, the province surrounding Beijing, to work in kitchens and as a labourer. His wife had just given birth to their first child, but was sent to work in rural Guangdong. Their baby boy was sent to his grandmother. "Every morning I would walk along the Great Wall and think, 'so, I don't know when I can see my family'."

Now aged 72 years Zhong's world is so much wider and opportunities so much greater. Not only that, publication of the PEACE study has made other Chinese clinicians realise that very practical research is valued by the medical world. "This makes a change for Chinese doctors; they say if *The Lancet* can accept such a kind of paper, we can do more clinical research. It seems to us very practical, not very advanced medication, just general medicine, general technique. But it creates new ideas."

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