

This Week's Citation Classic

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Hogg J C, Macklem P T & Thurlbeck W M. Site and nature of airway obstruction in chronic obstructive lung disease. *N. Engl. J. Med.* 278:1355-60, 1968.
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A small catheter was wedged in 2 mm airways to measure central and peripheral airways resistance. We found that peripheral airways resistance accounted for 25 percent of total in normal lungs and that it was increased from four to 40 times in lungs with obstructive pulmonary disease. The fact that peripheral airways resistance is small in normal lungs and greatly increased in diseased lungs suggests that significant small airways disease may be present and undetected during the transition from healthy to diseased lungs. [The SCIP® indicates that this paper has been cited in over 340 publications since 1968.]

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"Our study was based on some fundamental observations made on airways resistance by Peter Macklem and Jerry Mead working at the Harvard School of Public Health in Boston. Macklem had been interested in measuring bronchial pressures for some time and had obtained some interesting data during bronchoscopy by using a small tube which he pushed down the bronchoscope. He tells me that while he was a fellow in Mead's laboratory, Mead got the idea for the retrograde catheter while they were discussing the problems of measuring pressure in the bronchial tree. The methodology is based on a somewhat similar technique used by Colin Caro¹ to measure pressure in the pulmonary vascular bed and involves introducing a catheter in a retrograde fashion. This simply means that a catheter is pushed down into the tracheobronchial tree as far as it can go and a thin piano wire is pushed through that catheter until it breaks through the pleural surface. The original catheter is then removed and a new catheter is fastened to the piano wire extending from the trachea and pulled down the tracheobronchial

tree in a retrograde fashion until it comes through the pleural surface. This meant that the pressure drop along the airways could be partitioned accurately for the first time. Macklem and Mead exploited this new technique and published a classic physiological paper in 1967.²

"Macklem completed his fellowship in Mead's laboratory and returned to Montreal where I joined him as his postdoctoral fellow in 1966. I was actually an MRC postdoctoral research fellow in the department of pathology at McGill University, but, as Thurlbeck, who was my immediate supervisor, and Macklem were great friends, I had the opportunity to work on a joint project. As the Macklem and Mead technique is unsuitable for living patients, the obvious thing to do was to study postmortem lungs. I carried out a study in Macklem and Thurlbeck's laboratory from 1966 until 1968 where we used the technique to partition airways resistance in normal lungs and in the lungs from patients with chronic bronchitis and emphysema. The data showed that the distribution of airways resistance in the human lung was similar to that in the dog and showed that the major site of airways obstruction in the lungs of patients with chronic obstructive pulmonary disease was in the peripheral airways.

"When we wrote up our first paper, we submitted it to *Lancet* and it was rejected by return mail. We then submitted it to the *New England Journal of Medicine* where it was returned with a long letter from Ingelfinger, the then-editor. The paper was revised and resubmitted and was eventually published in 1968. The paper itself has taught me a great deal. First of all, it was a great experience to work with Macklem and Thurlbeck and the excitement of the project made me decide on a career in research. The rejection from *Lancet*, while devastating at that time, has become a less painful memory. The lesson for the young investigator in this situation is not to give up in the face of a rejected manuscript.

"The fact that the work has become highly cited is of course gratifying. However, the reason for this is primarily because it provided measurements of the distribution of resistance in both normal and diseased lungs. The concept that the peripheral airways are a major site of obstruction had been speculated about since the time of Laennec and our data simply provided important supporting evidence for this concept.

"A recent book in this field is *The Lung in the Transition between Health and Disease*.³

1. Caro C G & McDonald D A. The relation between pulsatile pressure and flow in the pulmonary vascular bed. *J. Physiol.*—London 157:426-53, 1961.
2. Macklem P T & Mead J. Resistance of central and peripheral airways measured by a retrograde catheter. *J. Appl. Physiol.* 22:395-401, 1967.
3. Macklem P T & Permutt S, eds. *The lung in the transition between health and disease*. New York: Dekker, 1979. 435 p.