

This Week's Citation Classic

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McCarthy D S, Spencer R, Greene R & Milic-Emili J. Measurement of "closing volume" as a simple and sensitive test for early detection of small airway disease. *Amer. J. Med.* 52:747-53, 1972.
[Respiratory Div., Dept. Med., Royal Postgrad. Med. Sch., Hammersmith Hosp., London, England]

Chronic airflow limitation (chronic bronchitis and emphysema), which is largely a disease of cigarette smokers, is a major cause of morbidity and mortality. The closing volume test appears to identify abnormality of the lung function in smokers long before the disease becomes symptomatic or other more routine tests of lung function become abnormal. It is possible that subjects with abnormal closing volumes are destined to develop chronic airflow limitation as a clinical disease. [The *SCF*[®] indicates that this paper has been cited over 295 times since 1972.]

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"Ironic as it might seem, my inspiration came from a stream of tobacco smoke exhaled by a remarkable teacher. His name was J. Milic-Emili, a professor of physiology at McGill University who at the time was spending a sabbatical year at the Royal Postgraduate Medical School situated at Hammersmith Hospital, London, England. At that time he smoked cheroots, a habit he has since abandoned. I was a fellow assigned to him during his sabbatical year. Shortly after his arrival I was summoned to his office. A shaft of sunlight traversed the dimly lit room passing about one foot before his face. After some preliminary pleasantries, he remarked, 'Observe this closely.' He then breathed all the air out of his lungs, filled his mouth with tobacco smoke, and inhaled slowly to maximum lung capacity. He then exhaled slowly

across the shaft of light. I noted the gray shades of smoke but as he approached minimal lung volume, the concentration of smoke increased remarkably. 'That is what I want you to investigate,' he said. The increase in tobacco smoke at low lung volumes was due to airway closure in the dependent lung regions. The lung volume at which airways closed was called the 'closing volume.'¹

"The research reported was conceived because of the need for a simple and sensitive test of lung function to detect presymptomatic airflow limitation in smokers and other subjects at risk to develop lung disease. The alternative tests, at the time, required more subject cooperation, more complex equipment and analysis, and were usually limited to lung function laboratories. The closing volume test on the other hand was a simple test for the subject to perform, it required relatively unsophisticated equipment, and it was suitable for large-scale epidemiological studies. The vital question was and is whether abnormality of closing volume, which occurred frequently in smokers in contradistinction to nonsmokers, predicted the ultimate development of severe chronic airflow limitation in some of these subjects. Clearly this question will require longitudinal studies over many years to provide an answer. Such epidemiological studies have already been established.² If it turns out that closing volume does indeed predict the development of chronic airflow limitation, then a relatively simple test is available which will identify individuals who are at risk to develop significant clinical lung disease hopefully at a stage when the process is reversible."

"The paper was first submitted to *Lancet* in England, but was rejected because of little clinical interest."

1. Dollfuss R E, Milic-Emili J & Bates D V. Regional ventilation of the lung, studies with boluses of ¹³³xenon. *Resp. Physiol.* 2:234-46, 1967.
2. Buist A S, Ghezzo H, Anthonisen N R, Cherniack R M, Ducic S, Macklem P T, Manfreda J, Martin R R, McCarthy D & Ross B B. Relationship between the single breath N₂ test and age, sex, and smoking habit in three North American cities. *Amer. Rev. Resp. Dis.* 120:305-18, 1979.