

This Week's Citation Classic®

Ogilvie C M, Forster R E, Blakemore W S & Morton J W. A standardized breath holding technique for the clinical measurement of the diffusing capacity of the lung for carbon monoxide. *J. Clin. Invest.* 36:1-17, 1957.
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The diffusing capacity of the lung for carbon monoxide was measured in healthy subjects and patients by a modification of Krogh's breath-holding technique. The reproducibility of the method and the technical, physiological, and pathological factors which might influence the result were studied and a formula for the prediction of normal values was derived. [The SC® indicates that this paper has been cited in more than 1,075 publications.]

Measurement of Gas Transfer in the Lung

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The uptake of carbon monoxide during a period of breath-holding was first used as a measure of the diffusing capacity of the lung by Marie Krogh.¹ By including an inert tracer gas (helium) as well as carbon monoxide in the inspired sample, R.E. Forster and his colleagues² were able to calculate what the concentration of carbon monoxide in the expired alveolar sample had been before any had diffused into the blood. This obviated the need to collect two expired samples as in the Krogh method.

I joined Forster in Julius Comroe's laboratory in Philadelphia at the University of Pennsylvania in 1954. Apart from a short period of physiological training with Ronald Christie and David Bates at St. Bartholomew's hospital, my own background was predominantly clinical. I was immediately allotted the task of standardizing this single breath method for clinical use in collaboration with Forster. This entailed an investigation of all the technical and physiological factors that might influence the value obtained, and the derivation of a formula for the prediction of normal values. We then examined the reproducibility of the method in both normal subjects and

patients. We were surprised to find that, despite the large number of variables involved, this was remarkably good; so much so, that when we presented our first results to Comroe, he said that he didn't know what we were measuring but we seemed to be measuring it extremely well. This doubt has persisted to the present day. Even now, in the UK at least, the result of the test is known as the Gas Transfer Factor (rather than the Diffusing Capacity) having regard to the fact that the result is affected by ventilation-perfusion mismatching as well as by impaired diffusion across the alveolar-capillary membrane.

Despite the intellectual discomfort of not knowing exactly what was being measured, the test came into routine clinical use because of its ability to detect changes in the lung parenchyma before other noninvasive methods and because it was simple and painless for patient and operator, taking only seconds to perform. In a *Thorax* editorial marking the first quarter century of the single breath method,³ the main clinical applications of the test were summarized as follows: (a) the identification of an environmental lung hazard and its early detection in individual subjects; (b) monitoring the progress of a lung disease in relation to the need for and response to treatment; and, (c) the differential diagnosis of lung disorders. Under these three headings, respectively, the test has proved especially useful in the assessment of subjects exposed to asbestos, in the early diagnosis of the pulmonary complications of AIDS,⁴ and in differentiating asthma (normal) from emphysema (low), lung hemorrhage (high) from inflammation (low),⁵ and organic from psychogenic causes for dyspnea.

In 1987, an international symposium was convened by the American Thoracic Society to agree on recommendations for a standard technique for the single breath carbon monoxide diffusing capacity.⁶ It is gratifying to know that, after more than 30 years, the test is still in use throughout the world—although it does look from the title of this last publication as if we didn't get it quite right the first time round.

1. Krogh M. Diffusion of gases through the lungs in man. *J. Physiol.* 49:271-300, 1915. (Cited 190 times since 1945.)

2. Forster R E, Fowler W S, Bates D V & Van Lingen B. Absorption of CO by lungs during breath-holding. *J. Clin. Invest.* 33:1135-45, 1954. (Cited 220 times.)

3. Forster R E & Ogilvie C M. The single-breath carbon monoxide transfer test 25 years on: a reappraisal. *Thorax* 38:1-9, 1983.

4. Shaw R J, Roussak C, Forster S M, Harris JRW, Pinching A J & Mitchell D M. Lung function abnormalities in patients infected with human immunodeficiency virus with and without overt pneumonitis. *Thorax* 43:436-40, 1988.

5. Greening A P & Hughes J M B. Serial estimations of carbon monoxide diffusing capacity in intrapulmonary haemorrhage. *Clin. Sci.* 60:507-12, 1981.

6. American Thoracic Society. Single breath carbon monoxide diffusing capacity (transfer factor). Recommendations for a standard technique. *Amer. Rev. Resp. Dis.* 136:1299-307, 1987.

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