

Supplementary information for the online depository

The single-breath method

Once the mouthpiece was in place, a few tidal breaths were recorded to establish a stable end-expiratory baseline. The subjects were then asked to exhale to residual volume (RV) where gas supply was switched to the test gas, containing a mixture of 0.3% carbon monoxide (CO), 0.3 % methane (CH₄), 0.3% acetylene (C₂H₂) and 21 % O₂, balanced with nitrogen. The subjects then inhaled rapidly to total lung capacity (TLC). After 10 seconds of breath-holding, the subjects exhaled smoothly with no hesitation or interruption. A mid-expiratory sample of alveolar gas was collected and analysed, discarding the initial volume to clear anatomical and mechanical dead space. Methane was the inert gas used to estimate alveolar lung volume (VA). The criteria for an acceptable manoeuvre were inspiratory volume of at least 90% of vital capacity (VC), inspiration time within 2.5 seconds, and breath-holding time of 10± 2 seconds. When two acceptable manoeuvres were obtained with values no more than 10% apart, their mean values were recorded for further analysis. A maximum of 4 attempts at intervals of minimum 5 minutes were allowed. If only one acceptable manoeuvre was obtained, that value was recorded. Data from a few cases with smooth curves within time limits and inspiratory volumes below, but close to 90% of VC were accepted. DL,CO, VA and DL,CO corrected for VA (KCO) were recorded.

The intra-breath method

This technique is based on measurement throughout a single expiration. The subjects exhaled to RV where the mouthpiece was switched to the test gas containing 0.3% CO, 0.3% CH₄, 0.3% C₂H₂ and 21% O₂ balanced with nitrogen. The subjects then inhaled to TLC, and after a short breath-holding period, exhaled slowly at a targeted flow of 0.5 L/s until the computer ended the test. An acceptable manoeuvre required that the inspired volume should be ≥ 90%

of the VC and the inspiratory time ≤ 2.5 seconds. The same rules as for SB-DL,CO were applied for reproducibility, and the same variables were recorded.

Adjustment for haemoglobin

DL,CO and KCO were corrected for haemoglobin concentration (Hb) [27], measured in venous blood samples from all but five and four participants of the 1982-85 and 1991-92 cohorts, respectively. For these nine subjects, the average Hb concentration, calculated for each sex in each subgroup in both birth-cohorts, was used for corrections.