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CORRESPONDENCE

Carbon monoxide transfer coefficient (transfer factor/alveolar volume) in females *versus* males

To the Editors:

The single breath transfer factor of the lung for carbon monoxide ($T_{L,CO}$) is derived from the multiple of the carbon monoxide transfer coefficient (K_{CO}) and the alveolar volume (V_A) during breath holding [1]; consequently, the $T_{L,CO}$ is highly dependent on lung size ($\sim V_A$), and thus is smaller in females for a given height and age. Essentially, the K_{CO} is the rate constant for alveolar carbon monoxide uptake (its units are per second or per minute) and may be expected to be the same in males as in females, as it was in the original description of the technique [2]. The published guidelines [3, 4] are not definitive on this point, so we reviewed all studies of reference values for $T_{L,CO}$ and K_{CO}, which have presented data for both males and females.

The European reference values for K_{CO} [3] are derived from the ratio $T_{L,CO}$ predicted/total lung capacity (TLC) predicted. This unusual recommendation arose from correspondence in the *ERJ* [5], which pointed out that the reference equations previously published in 1983 [6] produced values for K_{CO} that were incompatible with those for $T_{L,CO}$. These European Respiratory Society reference values have been quoted in 118 articles published since 1993 (23 in the *ERJ*) and have been adopted elsewhere [7]. The $T_{L,CO}$ values for females were based on a summary equation [6] derived from only five small studies, the most recent being published in 1979. Fortunately, the available database for $T_{L,CO}$ and K_{CO} has now expanded considerably; seven studies that examined both males and females in their chosen populations have been published between 1980 and 1992 (table 1).

In addition, we believe the use of the $T_{L,CO}$ pred/TLC pred ratio is, itself, unjustified. First, because in general it is undesirable to ratio two reference values obtained from different populations; this is compounded in the present instance, when K_{CO} is inevitably measured in every individual in the actual manoeuvre used to obtain $T_{L,CO}$. Secondly, although the original recommendation [18] was that the lung volume during breath-holding ($\sim V_A$) should be measured from the inspired volume preceding the breath hold plus the residual volume (from closed circuit helium dilution), virtually all subsequent population studies (and all those in table 1) have substituted the V_A derived from the dilution of the inhaled marker gas. This single breath V_A, both in the derivation of $T_{L,CO}$ and in the subsequent calculation of T_L/V_A, is always less than TLC, because the anatomic dead space is subtracted from the V_A but not from the TLC, and because gas mixing is often less efficient with a single breath measurement. Hence, using TLC when a single breath V_A has been used to calculate $T_{L,CO}$ will lead to a systematic underestimate of predicted K_{CO}.

Table 1 shows predicted values for K_{CO} at a standard age and height for males and females from 10 studies. Following American Thoracic Society Guidelines [19], we have compared males of 1.75 m stature with females of 1.65 m. When these studies are averaged (without weighting for the different numbers in each study) there is no sex difference for K_{CO} at age 45 yrs, although there is a small (nonsignificant) difference between males and females at 65 yrs. In contrast, from the $T_{L,CO}$ pred/TLC pred ratio [3], the predicted K_{CO} in females at a given age is 5–10% higher than for males, irrespective of whether they are at identical TLC (approximate height for males 1.6 m *versus* 1.8 m for females) or at identical height (approximate TLC for males 6.1 L *versus* 5.1 L for females). Table 1 also shows considerable between-study differences both in mean values and in the age and height coefficients, as is found for most other predicted values for tests of lung function [6]. From first principles, a dependence on height would not be expected, but it has been suggested [16] that in taller people the apices of the lungs may be more poorly perfused relative to the mid and lower

Table 1. – Published population studies of the carbon monoxide transfer coefficient (K_{CO})

Reference	Male					Female				
	n	Age Coeff. per yr	Ht Coeff. per cm	K_{CO} 45 yrs	K_{CO} 65 yrs	n	Age Coeff. per yr	Ht Coeff. per cm	K_{CO} 45 yrs	K_{CO} 65 yrs
[8]	70	-0.03	-0.009	1.81	1.61	72	-0.01	-0.0017	1.88	1.82
[9]	69	-0.03	-0.0353	1.66	1.46	72	-0.01	-0.0396	1.80	1.74
[10]	123	-0.033		1.82	1.62	122	-0.028		1.89	1.69
[11]	74	-0.03	-0.0224	1.59	1.39	130	-0.02	-0.018	1.54	1.41
[12]	80	-0.02	-0.0012	1.65	1.52	291	-0.02	-0.0251	1.58	1.45
[13]	71	-0.04	-0.0235	1.90	1.63	99	-0.03	-0.0278	1.74	1.54
[14]	194	-0.034	-0.0315	1.74#	1.51#	167	-0.026	-0.037	1.75#	1.58#
[15]	83	-0.009		1.68	1.50	96	-0.006		1.67	1.55
[16]	119	-0.008	-0.0067	1.51	1.35	185	-0.008	-0.0017	1.45	1.29
[17]	374	-0.007	-0.0029	1.73¶	1.58¶	129	-0.005	-0.0117	1.70¶	1.52¶
Mean±SD	126			1.71±0.12	1.52±0.10	136			1.70±0.14	1.56±0.16

Age Coeff.: age coefficient; Ht Coeff.: height coefficient. The K_{CO} at age 45 and 65 yrs has been derived from regression equations. Males were 175 cm in height and females were 165 cm. The units for K_{CO} are $mmol \cdot min^{-1} \cdot kPa^{-1} \cdot L^{-1}$ body temperature and ambient pressure, saturated with water vapour (for traditional units, multiply by 3). The data are nonsignificant (paired t-test) for males *versus* females for K_{CO} at 45 and 65 yrs. #: contains a positive exponent for body weight; ¶: contains a negative exponent for V_A.

zones for gravitational reasons; the resulting inhomogeneity in blood flow and blood volume would reduce the measured *K*CO. All published data on changes with age are derived from cross-sectional studies. The only cohort study of >8 yrs of *T*L,CO and *K*CO is that of WATSON *et al.* [20] who followed up, among others, 29 male never-smokers (mean age 37 yrs at start) over a 22-yr period. They found no change in the *K*CO.

We understand that a joint working party of the American Thoracic Society and the European Respiratory Society is currently reviewing reference values for spirometry, lung volumes and the transfer factor. We hope the carbon monoxide transfer coefficient will not be neglected, since the current recommendations are unsatisfactory. Ideally, values for total lung capacity should be obtained from the same individuals used to obtain reference values for the single breath transfer factor of the lung for carbon monoxide and the carbon monoxide transfer coefficient, so that the effects of poor inflation and/or true differences in total lung capacity at a given height and age can be allowed for [17].

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Exhaled breath condensate contains more than only volatiles

To the Editors:

I read with interest the review of WOOD *et al.* [1] on biomarkers of lipid peroxidation. I would like to congratulate the authors on this well-detailed overview of the topic. At the same time I would also like to point out that their statement saying "breath condensate samples…rely on the volatility of the substances being measured" is false. If, by this, the authors mean that only volatile substances can be captured in condensate samples they are misunderstanding this sampling method. The authors may not be familiar with this technique, which may be why they make this comment and also mention that exhaled ethane and penthane are materials being measured in condensate several times in their review. The latter two are present in the gas phase of exhaled breath and are measured directly in the breath and not in the cooled (condensed) sample [2].

The principle of exhaled breath condensate (EBC) collection is cooling the exhaled breath, resulting in a fluid sample that contains evaporated and condensed particles (water, ammonia, *etc.*) plus some droplets from the airway lining fluid. These droplets are released by turbulent airflow, and possibly by other currently not completely understood mechanisms, and can be added to the water vapour from anywhere