The CO Single Breath Transfer Factor of the Lung

Generally Acceptable Normal Values

F. Werner and H. Beneken Kolmer

Department of Anesthesiology, Lung Function Laboratory, St. Radboud University Hospital, Nijmegen, The Netherlands

Abstract. The CO single breath method for determining the transfer factor of the lung, $T$, and its component factors, $Dm$ and $Vc$, never gained wide application. The lack of generally accepted normal values has contributed to this. In this paper, based on the results of measurements in 28 normal subjects, it is shown that generally acceptable normal values can be obtained by: 1. determining $T$ at lung volumes above 80% TLC, and 2. expressing $T$, $Dm$, and $Vc$ per unit of alveolar gas volume during breath-holding: $T_{av}$, $Dm_{av}$, and $Vc_{av}$.

Key words: Lung function - Transfer factor - Single breath method - Normal values

Introduction

The transfer factor of the lung, $T$, also called, less correctly (Cotes 1963), the diffusing capacity $D_e$, has been defined as the amount of a gas passing the alveolar-capillary membrane per unit of time and pressure gradient. According to the modern SI system $T$ should be expressed in the units μmol · s⁻¹ · kPa⁻¹; until now, in most papers appearing on this subject, $T$ has been expressed in the units ml · min⁻¹ · mm Hg⁻¹.

The carbon monoxide single breath method, introduced by Krogh (1914), is the oldest known and most extensively studied method for determining $T$. Since then several substantial improvements have been introduced (Forster et al. 1954a, b; Roughton and Forster 1957; Jones and Mead 1961; Cotes 1968), yet the method never gained wide application mainly for two reasons:

1. The wide normal value range of $T$ found by most authors.
2. The lack of generally acceptable normal values.

In this paper it will be shown that these difficulties can be overcome by:

a) Standardizing the alveolar gas volume during breath-holding, $V_{av}$, and
b) Expressing $T$ per unit of $V_{av}$, $T_{av}$.

It will also be shown that the same pertains to the component factors of $T_{av}$, i.e., the transfer factor of the alveolar-capillary membrane, $Dm_{av}$, and the alveolar capillary blood volume, $Vc_{av}$.

Apparatus and Procedure

Basically we used the apparatus, the procedure and formulas described by Cotes (1968), albeit with some modifications (Werner 1979).

The apparatus consisted of:

1. A Resparameter Mark 4 of Morgan. This is a spirometer with kymograph connected to the subject either directly or indirectly via a bag-in-box system. The bag-in-box system contains 2 bags to be filled with the inspiratory gas mixtures, and 2 bags for the collection of alveolar gas samples. The Resparameter also includes a computer-controlled valve system and an analyzing unit for the measurement of He and CO concentrations.
2. An oxygen meter (Teledyne Analytical Instruments) for the measurement of the alveolar oxygen tension ($P_{a,o_2}$) during the different stages of the test.
3. A non-rebreathing system for the wash-in of $O_2$ at the beginning of the test, and a rebreathing system, consisting of a bag filled with $O_2$ and a CO₂ absorber, for the measurement of the CO content of the mixed venous blood ($P_{v,co}$) during the test.

Briefly the procedure was as follows:

a) The subject sits upright, breathing quietly;
b) breathes 100% $O_2$ for 5 min via a non-rebreathing system;
c) rebreathes 100% $O_2$ for 4 min;
d) performs 2 breath-holding manoeuvres with a 4-min interval breathing 100% $O_2$, after inhaling a gas mixture consisting of 0.28% CO and 10% He in $O_2$, to obtain $T_{av}$;
e) breathes air for 10 min;
f) performs 2 breath-holding manoeuvres with a 5-min interval of breathing air, after inhaling a gas mixture consisting of the same percentages of CO and He, completed by 80% $O_2$ in $N_2$, to obtain $T_{av}$.

The breath-holding manoeuvre itself took place as follows. The subject exhales to residual volume, then quickly inhales a present volume of the inspiratory gas mixture, until at least 80% total lung capacity (TLC) has been reached. Now the breath is held for 10 s. During the subsequent rapid expiration an alveolar gas sample (0.6 l) is collected immediately after the dead space has been washed out completely. The breath-holding time at the alveolar level is taken from the moment that the same volume selected for dead space wash-out (0.6 l) has been inspired, until 50% of the sample has been collected (Jones and Mead 1961).
The following formulas were used:

\[ T_{v,CO} = \frac{469.2}{t} \times \ln \frac{F_0 - F_2}{F_1 - F_2} \mu\text{mol} \cdot \text{s}^{-1} \cdot \text{kPa}^{-1} \cdot \text{L}^{-1} \]  

(1)

\[ Dm_v = \frac{T_{v,1} \times T_{v,2} - (P_2 - P_1)}{T_{v,1} \times T_{v,2} - T_{v,1} \times P_2 - T_{v,2} \times P_1 - 7.68} \mu\text{mol} \cdot \text{s}^{-1} \cdot \text{kPa}^{-1} \cdot \text{L}^{-1} \]  

(2)

\[ Vc_v = \frac{7.93 (P_2 - P_1)}{[\text{Hb}] \times (T_{v,1} - T_{v,2})} \times 10^{-3} \text{ mL} \cdot \text{L}^{-1} \]  

(3)

Discussion

1. \( V_A \) Should be More Than 80% TLC

The coefficient of variation for a single measurement on the same day in the same subject is 3.1% for \( T_{v,air} \) and 2.6% for \( T_{v,O_2} \). This is in close agreement with the 2.6% variation of \( T_{air} \) in the study of Cadigan et al. (1961). If no special attention is given to the alveolar volume at which the breath is held, variability of the test appears to be much greater: Cadigan et al. (1961) 10.7%, Ogilvie et al. (1957) 5.8%, and Burrows et al. (1961) 6%.

Krogh (1914) had already shown that \( T_{air} \) varies with the depth of inspiration: with breath-holding at increasing lung volumes \( T_{air} \) changed little until 50% TLC had been reached, but at larger lung volumes \( T_{air} \) increased considerably. Many investigators have confirmed the positive correlation between \( T_{air} \) and the depth of inspiration (Marks et al. 1957; Shephard 1958; Marshall 1958; McGrath and Thomson 1959; Burrows et al. 1961; Apher and Marshall 1961; Cadigan et al. 1961; Hamer 1963; Cotes and Hall 1969; Butner and Fowler 1971; Adaro et al. 1976). The amount of change of \( T_{air} \) as well as the changing pattern seem, however, to be rather variable. Several factors may account for this variability:

a) The \( V_A \) interval was not the same used by all authors.

b) Even a similar absolute change of \( V_A \) does not guarantee a similar proportional change of \( V_A \); differences in case selection with regard to body size may therefore play a role.

c) As shown by Cadigan et al. (1961), different changing patterns of \( T_{air} \) normally occur in different subjects; so in this respect a difference in case selection may also play a role.

Rather little is known about the correlations of the other parameters \( (T_{O_2}, Dm, Vc, T_{v,air}, T_{v,O_2}, Dm_v, Vc_v) \) with the depth of inspiration. Yet, in order to be able to understand the causes of the change of \( T_{air} \) with changing \( V_A \), it is important to know more about these correlations. For this purpose we investigated another three normal subjects. For convenience — numerous breath-holding tests had to be done in each subject — all three were members of the laboratory staff. Altogether 78 measurements were made, 37 with the low \( O_2 \) mixture and 41 with the high \( O_2 \) mixture. All measurements in a single subject were made on the same day with at least 15 min in between to prevent accumulation of a disturbing amount of \( CO \) in the blood. For the calculations of \( Dm_v \) and \( Vc_v \) at different lung volumes the results were arranged in such a way that \( Vc_v \) in every set of values of \( T_{v,air} \) and \( T_{v,O_2} \) never varied by more than 0.35 L on the average by 0.22 L. The final results are shown in Fig. 1. The same kind of investigation was done by Hamer (1963); his results are plotted in the same way in Fig. 2. At first sight it is clear that there is reasonable agreement between the two figures. \( T_{air} \) and \( Dm \) both increase as the lung expands, albeit \( Dm \) increase much more. Above a lung volume of about 80% TLC the increase of both \( T_{air} \) and \( Dm \) appears to occur more steeply in most subjects. The curve of \( Vc \) mirrors those of \( T_{air} \) and \( Dm \) in that \( Vc \) decreases as the lung expands, until at about 80% TLC its decrease diminishes or even is reversed. \( T_{O_2} \) tends also to decrease as the lung expands.

How can we explain these phenomena? According to Roughton and Forster (1957) the value of \( T \) is influenced by the value of \( Dm \) and \( dVc \):

\[
1/T = 1/Dm + 1/dVc
\]  

(4)