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Transfer factor for CO during exercise in children

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The transfer factor of carbon monoxide (TL_{CO}) has been measured in 40 normal schoolchildren by the steady state method during treadmill exercise. The fractional uptake of CO diminished with increasing oxygen consumption and the nett CO uptake was linearly correlated with oxygen consumption. The TL_{CO} at two work levels was significantly correlated with height and increased moderately with increasing work. The highest values of TL_{CO} during strenuous exercise were approximately three times those reported at rest.

The pulmonary diffusing capacity or transfer factor for carbon monoxide (TL_{CO}) has been studied in adults at rest and on exercise, in health and in disease (Filley, MacIntosh, and Wright, 1954; Bates, 1958). In children, however, we have found only results of measurements at rest (Strang, 1960; Weng and Levison, 1969). The steady state method of measuring pulmonary diffusing capacity, as modified by Bates, Boucot, and Dormer (1955) for assumed respiratory dead space, is a relatively easy test to carry out, especially on exercise. We have therefore used this method to obtain exercise values for TL_{CO} in normal children.

SUBJECTS AND METHODS

Studies were made on 19 boys and 21 girls aged 5 to 16 years (Table I). They were free from any evidence of disease. Each child exercised on a treadmill at two levels of work such as to give pulse rates of 120–160 and 160–210 beats per minute respectively. The appropriate speed and slope for each child was determined in a preliminary experiment. This represented approximately 50% and 80% of their maximum working capacity. The child breathed through a low dead space circuit (53 ml for larger children, 30 ml for smaller children), mixed expired gas being monitored continuously. After 1·5 minutes of exercise approximately 0·04% carbon monoxide was added to the inspired gas. Mixed expired CO_2, O_2, and CO were monitored until steady, which was normally after some 3–4 minutes of exercise. During the next minute of exercise the expired gas was collected in a Tissot spirometer and immediately analysed for CO_2, O_2, and CO. The next work load was begun without pause. Oxygen was analysed with a modified paramagnetic meter and CO_2 and CO with infrared meters. Each instrument was calibrated frequently with known gas mixtures.

TABLE I

DISTRIBUTION OF SUBJECTS BY AGE AND HEIGHT

Age range (yr)	4–5·9	6–7·9	8–9·9	10–11·9	12–13·9	14–15·9
Boys	2	1	5	3	3	5
Girls	2	6	2	3	4	4

Height range (cm)	105–119	120–134	135–149	150–164	165–179
Boys	2	6	3	5	4
Girls	3	6	3	8	–

CALCULATIONS The minute ventilation ($\dot{V}E$), tidal volume (VT), and oxygen consumption (VO_2) were calculated by conventional equations. CO transfer was calculated as follows:

(a) Fractional CO uptake $= \dfrac{FIN_{CO} - FEX_{CO}}{FIN_{CO}} \times 100$

where FIN_{CO} is the inspired fractional CO concentration and FEX_{CO} is the expired fractional CO concentration. No allowance was made for the small difference between inspired and expired volume because this had so small an effect.

(*b*) CO uptake ($\dot{V}_{CO}$) $= \dot{V}E_{STPD} \times (FIN_{CO} - FEX_{CO})$

(*c*) Alveolar CO concentration (FA_{CO}) =

$$\frac{(FEX_{CO} \times V_T) - (FIN_{CO} \times V_D)}{V_T - V_D}$$

where V_D is the dead space calculated from its known relationship to tidal volume and weight in children (Godfrey and Davies, 1970). The instrument dead space was added before inserting into the equation.

(*d*) Carbon monoxide transfer factor TL_{CO} =

$$\frac{\dot{V}_{CO}}{FA_{CO} \times (P_{BAR} - 47) - P_{BACK}}$$

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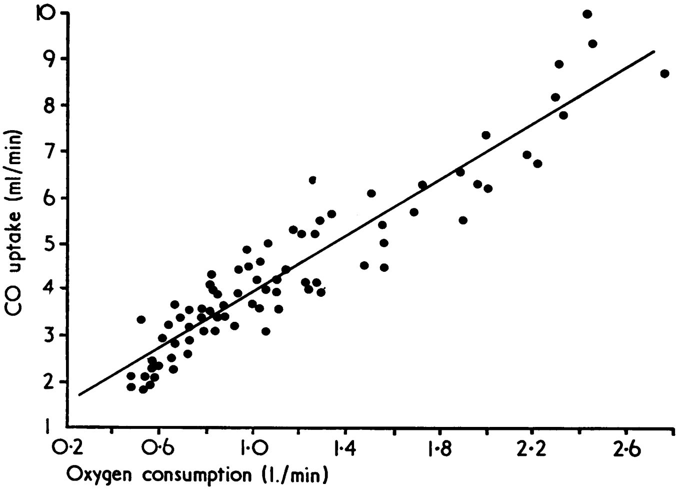

FIG. 1. *Relation of carbon monoxide uptake to oxygen consumption. Their correlation is indicated by the regression line.*

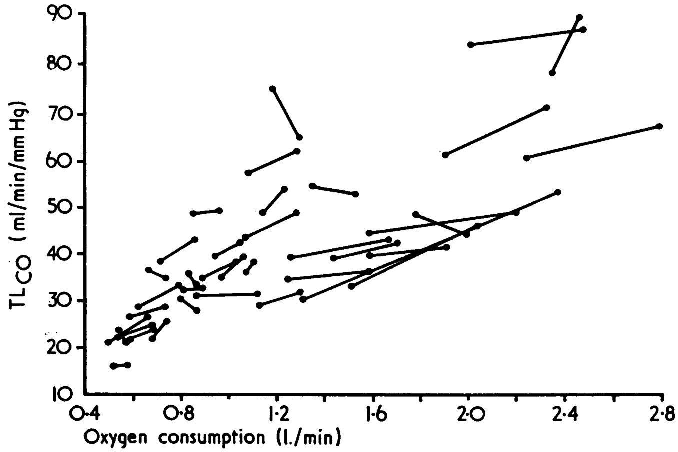

FIG. 2. *Relation of transfer factor* (TL_{CO}) *and oxygen consumption for individual subjects at two work levels.*

where P_{BAR} is the barometric pressure and P_{BACK} is the back pressure of CO in mixed venous blood. The back pressure of carbon monoxide was measured on six subjects by the method outlined by Cotes (1968) and the mean values of 0·7 mmHg for the first work level and 2·1 mmHg for the second work level were applied in all studies since there was very little inter-subject variation.

TABLE II

REGRESSION EQUATIONS FOR RESULTS

Y	B	X	M	SEY	r	n
% CO uptake	−0·00215	$\dot{V}O_2$	48·1	5·3	−0·22	80
$\dot{V}CO$	0·0031	$\dot{V}O_2$	0·86	0·64	0·94	79
TL_{CO} work 1	0·55	Height	−39·6	11·3	0·67	39
TL_{CO} work 2	0·62	Height	−43·5	12·4	0·68	38

Y=dependent variable, B=regression coefficient, X=independent variable, M=intercept on Y axis, SEY=standard error of estimate of Y about regression line, r=correlation coefficient, n=number of subjects. All lines were highly significant ($P<0·0025$). Other symbols as in text. ($\dot{V}CO$, ml/min; TL_{CO}, ml/min/mmHg; $\dot{V}O_2$, ml/min; height, cm)

RESULTS

Fractional CO uptake showed little variation between subjects and the slope of its regression on $\dot{V}_{O_2}$ was very flat though significant (Table II). Nett carbon monoxide uptake ($\dot{V}_{CO}$) was highly correlated with $\dot{V}_{O_2}$ (Fig. 1, Table II).

In any one subject carbon monoxide transfer factor (TL_{CO}) was almost always higher at the greater work level (Fig. 2). A paired *t* test was performed and showed this difference to be small but highly significant (Table III). The TL_{CO} was significantly correlated with height at both work levels (Table II). The results for the highest TL_{CO} obtained in each subject and a regression line for resting studies (Weng and Levison, 1969) are given in Figure 3.

TABLE III

MEAN AND STANDARD ERROR OF MEAN FOR TRANSFER FACTOR VALUES AT TWO WORK LEVELS

TL_{CO}	Work 1	Work 2
Mean	40·4	43·7
S.E.M.	2·5	2·6

n=40
t=3·5018
0·0025>P>0·0005

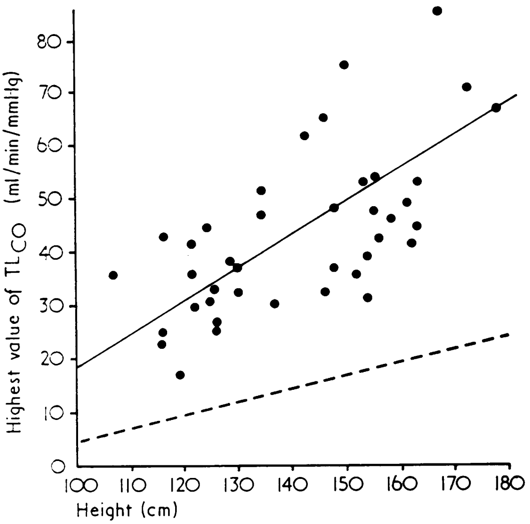

FIG. 3. *Individual relation of transfer factor (TL_{CO}) at the higher rate of exercise to height. The regression is shown by the solid line and may be compared with the regression obtained by Weng and Levison* (1969) *for TL_{CO} at rest shown by the dotted line.*

DISCUSSION

The method of measuring the transfer factor for carbon monoxide by the assumption of a respiratory dead space has been shown by Bates *et al.* (1955) to be valid during exercise because the tidal volume is adequately large. They showed that the discrepancy between measuring TL_{CO} by end-tidal sampling and by assuming a value for dead space was small in these circumstances. This applies all the more to children in whom reliable resting gas collections are difficult to obtain and tidal volume is small.

Our results for fractional CO uptake appear to be in keeping with reports in adults (Filley *et al.*, 1954) assuming reasonable values for the ventilatory equivalent of O_2. The correlation between $\dot{V}_{CO}$ and $\dot{V}_{O_2}$ appears to be the same as for the adults studied by Freyschuss and Holmgren (1965). The absolute levels of CO uptake, however, depend on the inspired CO concentration.

There has been considerable controversy in the literature as to whether or not TL_{CO} reaches a plateau value on exercise and the available evidence has been admirably summarized by Freyschuss and Holmgren (1965). In the present study the TL_{CO} of the second work level showed only a small difference from that of the first work level compared with the larger difference between the expected resting values (dotted line in Fig. 3) and those on exercise. Freyschuss and Holmgren (1965) reported only small changes in TL_{CO} with $\dot{V}_{O_2}$ in women and somewhat larger changes in men and their subjects tended to develop maximal values of TL_{CO} on work which gave pulse rates above 120 beats/minute. This would be equivalent to about 50% of their maximum working capacity—rather lower than the second work level in our children.

The close relationship we observed between our maximum TL_{CO} values and height is also in keeping with their results in adults. They found that TL_{CO} measured at pulse rates greater than 120 were significantly correlated with height.

Based on the results of Weng and Levison (1969) for resting values of TL_{CO} in children, it appears that exercise has increased the TL_{CO} by some three times (Fig. 3) which is rather greater than the increase observed in adults (Filley *et al.*, 1954). We conclude that the TL_{CO} is considerably increased by strenuous exercise in children and that the highest level achieved is related to size.

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