

## Research article

# EFFECTS OF A BASKETBALL ACTIVITY ON LUNG CAPILLARY BLOOD VOLUME AND MEMBRANE DIFFUSING CAPACITY, MEASURED BY NO/CO TRANSFER IN CHILDREN

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### ABSTRACT

In both children and adults, acute exercise increases lung capillary blood volume ( $V_c$ ) and membrane factor ( $Dm_{CO}$ ). We sought to determine whether basketball training affected this adaptation to exercise in children. The purpose of this study was to determine the effects of two years sport activity on the components of pulmonary gas transfer in children. Over a 2-yr period, we retested 60 nine year old boys who were initially separated in two groups: 30 basketball players (P) ( $9.0 \pm 1.0$  yrs;  $35.0 \pm 5.2$  kg;  $1.43 \pm 0.05$  m), and matched non players controls (C) ( $8.9 \pm 1.0$  yrs;  $35.0 \pm 6.0$  kg;  $1.44 \pm 0.06$  m) who did not perform any extracurricular activity.  $V_c$  and  $Dm_{CO}$  were measured by the NO/CO transfer method at rest and during sub-maximal exercise. Maximal aerobic power and peak power output was 12% higher in the trained group compared to matched controls ( $p < 0.05$ ). Nitric oxide lung transfer ( $TL_{NO}$ ) per unit lung volume and thus,  $Dm_{CO}$  per unit of lung volume (VA) were higher at rest and during exercise in the group which had undergone regular basketball activity compared to matched controls ( $p < 0.05$ ). Neither lung capillary blood volume nor total lung transfer for carbon monoxide ( $TL_{CO}$ ) were significantly different between groups. These results suggest that active sport can alter the properties of the lung alveolo-capillary membrane by improving alveolar membrane conductance in children.

**KEY WORDS:** Membrane diffusing capacity, pulmonary capillary blood volume, alveolar volume, children, NO/CO transfer.

### INTRODUCTION

Pulmonary transfer capacity for CO ( $TL_{CO}$ ) is a widely used test aimed at the estimation of the function of the alveolo-capillary structure. The Roughton and Forster model (1957) allows separating this function in two variables: membrane factor (Dm) and pulmonary capillary blood volume ( $V_c$ ). Membrane factor (Dm) and pulmonary

capillary blood volume ( $V_c$ ) can be estimated by the two-step  $TL_{CO}$  method during which the subject inhales  $O_2$  at different concentrations (Lewis et al., 1958). Membrane factor and lung capillary blood volume have also been measured with the more recent  $TL_{CO/NO}$  technique (Guénard et al., 1987, Moinard and Guénard, 1990). This one step method has been applied to exercise in adults with either the single breath method (Manier et al., 1993; Zavorsky

**Table 1.** Anthropometric characteristics and maximal exercise performances of children. Data are mean ( $\pm$ SD).

	Players Children		Control children	
	<i>test 1</i>	<i>test 2</i>	<i>test 1</i>	<i>test 2</i>
	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>
<b>Age (yrs)</b>	9.0 (1.0)	11.1 (1.0)	8.9 (1.0)	10.9 (1.1)
<b>Weight (kg)</b>	35.0 (5.2) <sup>2</sup>	40.3 (7.5) <sup>1</sup>	35 (6) <sup>4</sup>	39.9 (9.0) <sup>3</sup>
<b>Height (m)</b>	1.43 (.05) <sup>2</sup>	1.50 (.07) <sup>1,4</sup>	1.44 (.06)	1.47 (.9) <sup>2</sup>
<b>BSA (m<sup>2</sup>)</b>	1.03 (.20)	1.31 (.14)	1.03 (.30)	1.28 (.18)
<b>VO<sub>2</sub>max (ml·min<sup>-1</sup>·kg<sup>-1</sup>)</b>	30.5 (7.6) <sup>2</sup>	33.9 (7.6) <sup>1,4</sup>	30.9 (7.6)	29.8 (3.1) <sup>2</sup>
<b>Heart rate (beats·min<sup>-1</sup>)</b>				
Rest	89 (2)	85 (5) <sup>4</sup>	90 (3)	90 (4) <sup>2</sup>
75-85% MAP	167 (7)	173 (7)	170 (4)	181 (5)
Max	192 (4)	199 (2) <sup>4</sup>	189 (6)	193 (2) <sup>2</sup>
<b>Max work load (Watts·kg<sup>-1</sup>)</b>	3.8 (2.0) <sup>2</sup>	3.6 (2.0) <sup>1,4</sup>	3.7 (3.0)	3.4 (1.5) <sup>2</sup>

Superscripts denote the significant ( $p \leq 0.05$ ) differences among the groups and occasions. MAP = maximal aerobic power, Max = maximal.

et al., 2004), the rebreathing method (Tamhane et al., 2001) or the steady state method (Borland et al., 2001). The reaction rate of NO binding to haemoglobin (Hb) being some 280 times faster than that of carbon monoxide, the limitation of NO transfer is due mainly to the membrane component of the transfer.

Basketball is a sport with many very fast changes in metabolic activity requiring rapid adaptation to alterations in oxygen demand which would implicate a specific adaptation of the lung. High-intensity intermittent running has been shown to increase ventilatory performance (forced vital capacity, peak flow, and forced expiratory flow) (Nourry et al., 2005) suggesting that intermittent exercise enhances the respiratory demand as well as it enhances the cardiac demand (Paterson, 1979).

This prompted us to evaluate the effect of two years basketball activity on the transfers of NO and CO in a group of basketball playing children compared with a control group without specific sports activity. Lung transfer components were studied in these children using the TL<sub>CO/NO</sub> single breath method. Lung volume, lung capillary blood volume and membrane factor were calculated at rest and during exercise.

## METHODS

Our study was conducted in a longitudinal period of two years with sixty healthy boys (8-10 years). All were non-smokers with normal lung volumes and flow-volume curves at rest and no history of cardiopulmonary disease or allergy (Table 1 and Table 2). Children who volunteered, with the agreement of the parents, to participate in the study were allocated according to their physical activity. One group consisted of basketball players while the other group was children without specific sport activity. The first 30 children who volunteered to participate in this last group were included. Information regarding past health and activity was obtained from a questionnaire (Ferris, 1978) in order to obtain a socio-economically homogeneous population. Children were selected from the city or the suburbs of Sousse (Tunisia). This lightly industrialized area is only slightly polluted. Tunisia is a melting pot of white populations from the Mediterranean basin. Written informed consent was obtained from all parents and the University ethics committee approved the experimental protocol.

Before the 2-yr period, the subjects were allocated into two groups:

**Table 2.** Lung volumes of the subjects. Data are means ( $\pm$ SD).

	Players Children		Control children		Sylvester et al. 2005 Afro-Caribbean children (n = 80) 9 (4.3-17.8) yrs	Cotes et al. 1973 British boy twins 11.6 (8-16) yrs
	<i>test 1</i>	<i>test 2</i>	<i>test 1</i>	<i>test 2</i>		
	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>		
<b>RV (L)</b>	.80 (.20)	.90 (.27) <sup>1,4</sup>	.87 (.14) <sup>4</sup>	1.20 (.37) <sup>2,3</sup>	.78 (.31)	.62 (.22)
<b>VC (L)</b>	2.10 (.30)	2.50 (.54)	2.20 (.50)	2.20 (.57)	1.92 (.78)	2.43 (.86)
<b>TLC (L)</b>	3.00 (.46)	3.40 (.66)	3.10 (.39)	3.50 (.85)	2.70 (.90)	3.09 (1.10)

RV = residual volume, VC = vital capacity, TLC = total lung capacity. Superscripts denote the significant ( $p \leq 0.05$ ) differences among the groups and occasions.

**Table 3.** Changes from *test 1* to *test 2* in membrane factor for CO ( $Dm_{CO}$ ), lung capillary blood volume ( $V_c$ ), nitric oxide lung transfer ( $TL_{NO}$ ), carbon monoxide lung transfer ( $TL_{CO}$ ) and lung volume ( $VA$ ) at rest and during exercise in Players and Control children. Data are mean  $\pm$  standard deviation (SD).

	Players Children				Control Children			
	<i>test 1</i>		<i>test 2</i>		<i>test 1</i>		<i>test 2</i>	
	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
<b><math>Dm_{CO}</math></b> ( $ml \cdot min^{-1} \cdot mmHg^{-1}$ )	44.1 (5.2)	50.1 †# (6.7)	48.0 * (9.2)	53.2 *†# (11.7)	42.7 (6.5)	49.5 † (9.7)	43.5 * (9.7)	47.4 *† (13.8)
<b><math>V_c</math> (ml)</b>	50 # (4)	53 † (10)	44 # (9)	56 *† (11)	49 (3)	55 † (6)	46 (12)	66 *† (17)
<b><math>TL_{NO}</math></b> ( $ml \cdot min^{-1} \cdot mmHg^{-1}$ )	87 # (5)	99 (10)	95 *# (18)	105 * (23)	84 (5)	98 (7)	86 * (19)	94 * (27)
<b><math>TL_{CO}</math></b> ( $ml \cdot min^{-1} \cdot mmHg^{-1}$ )	15.5 (3.7)	16.7 # (4.5)	16.3 (2.8)	20.0 *# (3.3)	16.2 (1.2)	17.0 (3.2)	16.7 (3.9)	20.9 * (4.6)
<b><math>VA</math></b> (L)	3.0 # (.5)	3.3 †# (.8)	3.4 # (.6)	3.7 *†# (.7)	3.1 # (.4)	3.4 †# (.7)	3.5 # (.8)	3.9 *†# (.8)

\*, † and # denote significant ( $p \leq 0.05$ ) difference between both groups in same test, between rest and exercise in the same group, and between test 1 and test 2, respectively.

*Players (P children):* 30 children who performed basketball training for two hours five times per week during two years, with one month interruption in summer.

*Control (C children):* 30 children participated in normal school physical activities with no extracurricular sporting activity.

Initially (*test 1*) anthropometric data were collected. Maximal  $O_2$  consumption ( $VO_{2max}$ ) and maximal aerobic power (MAP) were determined by a standard protocol. Exercise was performed on a bicycle ergometer (Monark cycle). The child performed unloaded cycling at 60-65 revolutions/min (rpm) for the first minute after which the work rate was increased every minute according to the Cooper and Weiler-Ravell equation (Cooper and Weiler-Ravell, 1984) until maximal oxygen uptake was reached. Oxygen consumption and carbon dioxide production were measured with a MedGraphics CPX (St Paul, MN, USA). The oxygen and carbon dioxide analyzers as well as the flow meter were calibrated before each measurement.

On another day, the transfer of NO and CO were measured. Each child performed three validated transfer measurements: two at rest before exercise and one during exercise at about 75-85% of maximal aerobic power. Exercise was performed as previously using the incremental procedure. The validity of the manoeuvre for the transfer measurement was checked first by looking at the child who should perform the manoeuvre without hesitation, with his mouth tightly closed around the mouth-piece, holding his breath steadily during the preset time. The validity was then checked on the screen looking at the trace depicting changes in volume during the manoeuvre. This trace should be

devoid of pause during the fast inspiration, flat during breath hold and continuous during the fast following expiration. If these criteria were met the results were validated. All children were trained previously to the manoeuvre without inspiring the mixture. If one measurement at rest was not accepted for any reason, another measurement was made after recovery when heart rate had reached its resting value. As the single-breath manoeuvre was difficult to perform during exercise for some children (9/60), they were allowed to interrupt exercise for less than one minute. Measurements were made at the start of the pause. The results of these nine individuals were compared to those of the remaining population. As there were no differences in membrane factor, lung capillary blood volume and lung volume between these individuals and the other children, their results were included in the overall population.

NO and CO transfers, i.e.  $TL_{NO}$  and  $TL_{CO}$ , were measured simultaneously during a single breath manoeuvre (SB) using an automated apparatus (Medisoft Dinant, Belgium). The inhaled mixture was obtained by mixing the gases of two tanks one containing 0.28% CO, 14% He, 21%  $O_2$  balanced with  $N_2$  the other 450 ppm NO in  $N_2$  (Air Liquide Santé, Tunisia). The final concentration of NO in the inspired bag was 40 ppm. The apparatus was calibrated daily with the mixtures contained in the tanks using automated procedures. Linearity of the analyzers was factory checked. The pneumotachograph (PTG) was calibrated with a 2L syringe.

The child breathed through a mouthpiece and a filter connected to the PTG. When needed, he was requested to make a deep expiration. Then at the onset of the next inspiration, a valve opened

**Table 4.** Changes from *test 1* to *test 2* in  $Dm_{CO}/VA$ ,  $Dm_{CO}/Vc$  and  $Vc/VA$  at rest and during in Players and Control Children. Data are means ( $\pm$ SD).

	Players Children				Control Children			
	<i>test 1</i>		<i>test 2</i>		<i>test 1</i>		<i>test 2</i>	
	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
$Dm_{CO}/VA$	14.7 (1.2)	15.2 † (.4)	14.1 * (1.9)	14.4 * (2.7)	13.8 (1.7)	14.6 †# (.8)	12.4 * (2.4)	12.2 *# (3.2)
$Dm_{CO}/Vc$	.87 (.8)	.93 * (.4)	1.1 (.3)	.94 *† (.3)	.86 (.2)	.9 *# (.19)	.94 (.18)	.72 *†# (.3)
$Vc/VA$	16.8 # (2.7)	16.2 (2.5)	12.9 † (3.2)	15.2 † (4.2)	15.9 (1.6)	16.2 (2.5)	13.1 (2.1)	16.1 † (3.4)
$Dm_{CO}/VA$	14.7 (1.2)	15.2 † (.4)	14.1 * (1.9)	14.4 * (2.7)	13.8 (1.7)	14.6 †# (.8)	12.4 * (2.4)	12.2 *# (3.2)

\*, † and # denote significant ( $p \leq 0.05$ ) difference between both groups in same test, between rest and exercise in the same group, and between test 1 and test 2, respectively.

allowing the child to inspire the mixture during a rapid deep inspiration. An apnoea of 4 seconds was then requested followed by a deep expiration. The first 0.6L of expired gas was rejected as the further 0.6L was sampled in a bag which was automatically analyzed for NO, CO and He. The delay to analyse the sample of expired gas was constant, 35s. The lung volume during the apnoea was calculated using the helium dilution technique. The reproducibility of the method was tested in 12 children who performed six consecutive trials on different days.

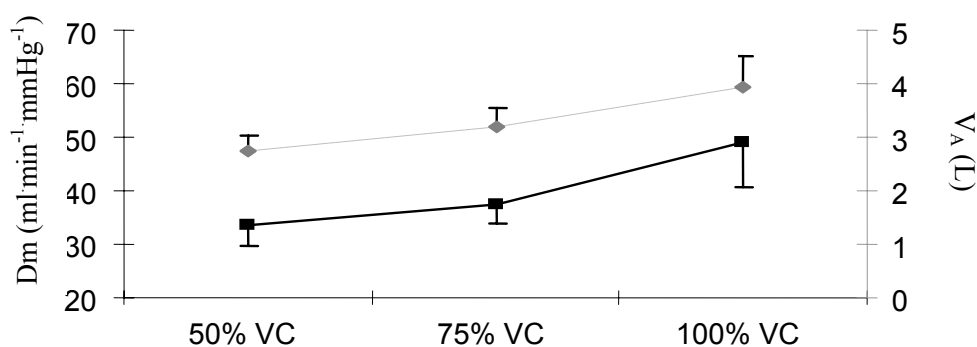
Two years afterwards (*test 2*), the same tests (anthropometric data, maximal  $O_2$  consumption, maximal aerobic power, and NO/CO transfer) were repeated. All of the resting tests and exercise measurements were performed on the same equipment, were calibrated using the identical method, and were measured with the exact same laboratory techniques for the initial and the follow-up tests.

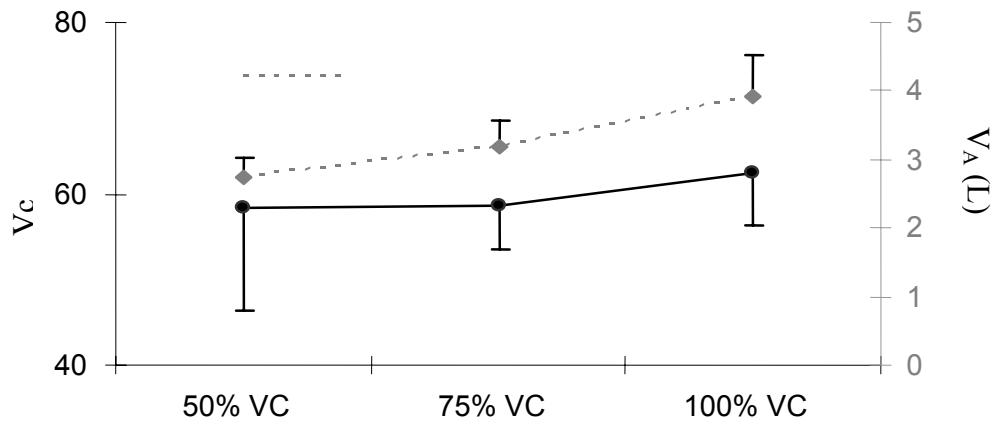
#### Additive protocol: $Dm_{co}$ vs $VA$

In order to check the  $Dm_{co}$  vs  $VA$  relationship in a given individual, 12 basketball-playing children performed at rest on another day,  $TL_{CO/NO}$  manoeuvres at different lung volumes (about 50, 75 and 100% of their vital capacity) (Figure 1). After the deep exhalation, they were requested to fill their lung with the inspired mixture to a preset value indicated on the screen by the operator.

#### Calculations and statistics

Membrane factor ( $Dm_{CO}$ ) and lung capillary blood volume ( $Vc$ ) values were derived from  $TL_{NO}$  and  $TL_{CO}$  values as previously described (Guénard et al., 1987). In brief the reactivity of NO on hemoglobin was considered very high and its inverse negligible, therefore  $TL_{NO}$  value was considered equivalent to  $Dm_{NO}$ .  $Dm_{CO}$  was calculated by estimating the coefficient of proportionality ( $a$ ) of the  $Dm$  values of the two gases to be 1.97. The reactivity of CO with hemoglobin at a  $PO_2$  of 110 mmHg was derived from a work of Forster (1987) in which measurements were done at physiological pH

**Figure 1.** The relationship between membrane factor ( $Dm$ ) and lung volume ( $V_A$ ) at 50, 75 and 100% of vital capacity (VC) in 12 player children. Diamonds indicate lung volume, squares indicate  $Dm$ .



**Figure 2.** The relationship between lung capillary blood volume ( $V_c$ ) and lung volume ( $V_A$ ) at 50, 75 and 100% of vital capacity (VC) in 12 players children. Circles indicate  $V_c$  while diamonds represent  $V_A$ .

the two gases to be 1.97. The reactivity of CO with hemoglobin at a  $PO_2$  of 110 mmHg was derived from a work of Forster (1987) in which measurements were done at physiological pH (Krawiec et al., 1983).

The calculation of  $Dm_{CO}$ , although not necessary, was made to allow comparisons with previous data. Reproducibility of the method was estimated in 12 children who performed the test six times at rest on different days.

Statistical analyses were performed using Statistica 5.0 software'97 edition. Student's t-test for unpaired data was used to identify significant differences between the two groups (players and controls), while paired data analysis was used to compare rest and exercise data. A value of  $p < 0.05$  was considered significant. Mean values are given with the standard deviation ( $\pm SD$ ).

## RESULTS

Data of initial subject's physical characteristics (*test 1*) and of the follow-up study 2 yr later (*test 2*) are shown in Table 1.

Lung volumes in comparisons with literature data (Cotes et al., 1973; Sylvester et al., 2005) are shown in Table 2.

In the 12 children who performed six consecutive trials on different days, the coefficients of variation with their standard deviations were  $2.1 \pm 2.0$ ;  $1.4 \pm 1.3$ ;  $7.3 \pm 4.6$  % for  $V_c$ ,  $TL_{CO}$  and  $TL_{NO}$  respectively.

Initially (*test 1*), lung volume and lung capillary blood volume from both groups did not differ either at rest or during exercise, although they increased significantly in both groups during exercise ( $p < 0.01$ ) (Table 3). Two years later (*test*

2), lung capillary blood volume at rest did not differ between the two groups, but increased significantly from rest to exercise in both groups. The increase in  $V_c$  was greater in the control group.

$V_c/V_A$  ratios in *test 1* were not different between groups either at rest or during exercise, although they increased by 16% in the P children and 22% in the C children from rest to exercise in *test 2* (Table 4). As  $V_A$  increased significantly with age  $V_c$  at rest decrease significantly only in P children between *test 1* and *test 2* and the  $V_c/V_A$  ratio decreased with age.  $Dm_{CO}$  and  $V_A$  increased significantly from rest to exercise in both groups in all conditions. P children increased their  $Dm_{CO}$  significantly during exercise between *test 1* and 2. P children had greater  $Dm_{CO}$  at rest and during exercise in *test 2* than C children.  $Dm_{CO}/V_A$  ratios were higher in the P than in the C children in all paired conditions, however the difference was significant in *test 2* between the two groups. While  $Dm_{CO}/V_A$  increased from rest to exercise in *test 2* in the P children it decreased in the C children (Table 4).  $Dm_{CO}/V_c$  ratios were always higher in the P group than in the C group, the differences were significant during exercise during both tests.

In the 12 subjects who performed measurements of transfers at different lung volumes the relationship between membrane factor and lung volume was linear (Figure 1), the ratios  $Dm_{CO}/V_A$  in ( $\text{min}\cdot\text{mmHg}^{-1}$ ) were not different irrespective of the value of  $V_A$  as a percentage of its maximal value:  $12.2 \pm 1.1$  for lung volume  $54.3 \pm 6.9\%$ ,  $11.8 \pm 0.8$  for lung volume  $73.1 \pm 13.2\%$ ,  $12.4 \pm 1.0$  for lung volume 100%. Compared to the two lower lung volume levels, lung capillary blood volume increased slightly but significantly at 100%  $V_A$  (Figure 2).

## DISCUSSION

This study provides evidence that sporting activity has an influence on the alveolo-capillary membrane properties of children. The main difference was in  $Dm_{CO}$  which was higher during exercise in the P children after a 2 year basketball training period.

### *Methodological points*

$V_c$  and  $Dm$  were calculated using a previously described method in which reactivity of CO for hemoglobin was not taken from the early work of Roughton and Forster (1957) but from the more recent work of Krawiec (1983). The reason for that choice is that the latter work was performed at pH 7.4 as the former was performed at pH 8. As pointed elsewhere (Forster, 1987) the use of this more recent value of the reactivity of CO for hemoglobin leads to 15 to 20% smaller  $V_c$  and 15 to 20% greater  $Dm_{CO}$  values. Choosing the recent equation (Krawiec, 1983) gives results in agreement with the theoretical value of the coefficient  $a$  ( $a = 1.97$ ), as using the early work of Roughton and Forster, 1957 needs to change empirically the value of “ $a$ ” to 2.4 (Hsia, 1995).

$V_c$  depends on hemoglobin (Hb) concentration which was assumed to be normal in our subjects. This concentration was not measured for two reasons. Firstly the University ethics committee did not permit venous puncture in healthy children. Secondly as the children had a similar socio-economic status, as verified by the questionnaire, they had no reason to have great differences in their haemoglobin concentrations. Stam et al. (1994) found in a healthy adult group that Hb concentration had no impact on the mean CO transfer value and its standard deviation, as Hb concentration was normally distributed within a narrow range. The coefficients of variation for lung capillary blood volume were 25% and 15% in the P and C groups respectively, in the range reported in the literature.

### *Experimental results*

*Lung volumes:* The values of lung volume at rest are in agreement with those measured in other populations of children (Hamilton and Andrew, 1976). The P children were a few centimetres taller than the C children, but values of lung volume did not differ between the two. This finding is in agreement with that of Gaultier and Crapo (1997) who found that swimming was the only physical activity leading to a marked increase in lung volumes in children. The increase in lung volume from rest to exercise in both groups of children was attributed to a greater inspiratory drive resulting in a better contraction of respiratory muscles. Changes in

lung or chest mechanics could lead to such an increase, but seems unlikely for such short exercise durations. However, the fact that children have high thoracic compliance (Ingimarsson et al., 2000) would enhance the alterations in maximal lung volume due to changes in inspiratory drive.

*Maximal oxygen consumption:* Maximal oxygen consumption related to body mass in healthy children depends on age, gender and ethnicity (Turley and Wilmore, 1997). Eleven-year-old Negro boys (Maksud et al., 1971) as well as 45 pre-pubertal North American children (Andreacci et al., 2004) or 11-13-year-old Turkish boys (Binyildiz, 1980) had values similar to those reported here. White pre-pubertal American boys had values close to those of our P children ( $33.7 \pm 6.4$  vs  $33.85 \pm 7.6$   $ml \cdot min^{-1} \cdot kg^{-1}$ ) respectively). The difference between the group of children practicing a sport and those who did not (12%) was greater than that reported by Mandigout et al., 2001 for boys (4.6%). The difference between these groups depends on the physical activity of the non-practicing group as well as the type and level of sporting activity of the practicing group.

*Capillary volume:* In *test 2* and at rest,  $V_c/VA$  in both groups of children was around  $13$   $ml \cdot L^{-1}$ , a figure close to that reported by others in young adults (16-20 years):  $14$   $ml \cdot L^{-1}$  by Mahajan et al. (1992). This suggests that lung capillary growth parallels lung parenchyma growth at least between the age of ten and young adulthood. Higher values have been found in adults:  $16.5$   $ml \cdot L^{-1}$  by Manier et al. (1993);  $15.5$   $ml \cdot L^{-1}$  by Zavorsky et al. (2004).

During exercise,  $V_c/VA$  increased by 16% in the player group and 22% in the control group with no significant difference between the two. In adults, the values are dispersed: 10% for 12 professional handball players (Manier et al., 1993), nearly 40% for 18 young adults (Zavorsky et al., 2004) and 70% by Hsia et al. (1995) using a rebreathing method. We will discuss below the possible implication of cardiac blood flow in the dispersion of  $V_c$  values during exercise. The increase in  $V_c$  during exercise has been attributed to the recruitment of capillaries as well as their increase in diameter (Goresky et al., 1975; Hsia et al., 1992; Manier et al., 1993; Wagner et al., 1986; Vaughan et al., 1976). However well correlated to cardiac blood flow,  $Dm_{CO}$  as well as  $V_c$  are not directly dependent on blood flow as shown by Borland et al. (2006) who observed in an analogue model of the lung that neither  $TL_{CO}$  nor  $TL_{NO}$  were blood flow dependent. Exercise by increasing cardiac blood flow ( $Q_c$ ) increases pulmonary arterial pressure ( $P_{pa}$ ) and pulmonary capillary pressure ( $P_{cap}$ ) which would induce an

increase in  $V_c$  by recruitment and distension of capillaries. The link between the increase in  $P_{cap}$  and that in  $V_c$  is rather complex as suggested by Baumgartner et al. (2003) using *in vivo* video microscopic observations. This type of analysis *in vivo* in healthy human is impossible as  $P_{cap}$  can be measured only invasively and no method exists, at this time, to estimate the microscopic distribution of blood flow.

Alveolo capillary membrane:  $Dm_{CO}$  and VA increased significantly from rest to exercise in both groups in all conditions. The P children had higher  $Dm_{CO}/VA$  ratios during exercise than did C children, the ratio was significantly different only in *test 2* (Table 4), i.e. for the same lung volume, P children had 12 to 16% more  $Dm_{CO}$  than did C children.

With the present method,  $Dm_{CO}$  was derived directly from  $TL_{NO}$ . As NO is highly reactive with haemoglobin, its transfer is nearly independent of  $V_c$  but highly dependent on membrane properties.  $Dm$  is a function of membrane thickness and lung surface area. An increase in cardiac blood flow could decrease the thickness of the unstirred plasma layer, close to the capillary wall, which is suspected to increase the effective membrane thickness. However this would hold to be true in both groups and could not explain the difference between the two groups of children. Another attractive hypothesis is that the alveolo-capillary membrane of trained children being submitted to a greater stretch, owing to their greater maximal ventilation, becomes thinner during exercise. Indeed intermittent exercise has been shown to increase respiratory muscle force (Nourry et al., 2005). In this respect it has been shown that an increase in lung stretch induces release of growth factors (Yamamoto et al., 2001) which in turn could increase the surface of the lung.

An increase in lung surface could be due either to an increase in the effective lung surface or to less heterogeneity in the distribution of the perfusion of capillaries leading for a given  $V_c$  to a greater surface of exchange. These two points will be examined successively. An increase in the number of alveoli per unit volume would increase the surface area, which would also increase lung mass. To our knowledge there are no reports of lung mass in children practicing sports. In adults, Manier et al. (1993) reported a lung mass of  $1372 \pm 178$  g in marathon runners at rest and Guénard et al. (1992) reported a lung mass of  $997 \pm 35$  g in 16 healthy, non-sport-practicing adults using the same method and material (tomodensitometry of the lung). Mean lung densities at FRC were significantly different ( $0.37 \pm 0.044$  and  $0.29 \pm 0.064$  respectively).

As it seems that no data exists in the literature on the distribution of perfusion within lung

capillaries the fact that the ratio  $Dm/V_c$  is significantly greater in P than C children during exercise in *test 2* suggest that the distribution of blood in capillaries is more even in P than C children.  $Dm/V_c$  increased insignificantly from rest to exercise in both groups during the first test as, after a 2 yr period, this ratio decreased significantly much less in P children than in C children from rest to exercise (Table 4).

## CONCLUSIONS

In conclusion, player children had greater  $Dm_{CO}/VA$  and  $Dm_{CO}/V_c$  ratios than did control children during exercise. The mechanisms by which basketball playing children were thought to improve lung diffusion are speculative either via an increase in the effective exchanging lung surface area or/and by a decrease in membrane thickness. Further work will be required to determine the kinetics of the alteration in  $Dm$  when children switch from non players to players status or vice-versa.

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## REFERENCES

- Andreacci, J.L., Robertson, R.J., Dube, J.J., Aaron, D.J., Balasekaran, G. and Arslanian, S.A. (2004) Comparison of maximal oxygen consumption between black and white prepubertal and pubertal children. *Pediatric Research* **56**, 706-713.
- Babarskov, E.V., Shulagin, Y.A., Stepanov, E.V., Cherniack, A.V., Aisanov, Z.R. and Chuchalin, A.G. (2004) Caboxyhemoglobin generation in conducting of the single breath diffusing capacity test. *The European Respiratory Journal* **24**(Supl. 48), 404S.
- Baumgartner, W.A., Jaryszack, E.M., Peterson, A.J., Presson, R.G. and Wagner, W.W. (2003) Heterogeneous capillary recruitment among adjoining alveoli. *Journal of Applied Physiology* **95**, 469-476.
- Binyildiz, P.O. (1980) Prediction of maximal oxygen uptake in boys 11-13 years of age. *European Journal of Applied Physiology* **43**, 213-219.
- Borland, C., Dunningham, H., Bottrill, F. and Vuylsteke, A. (2006) Can a membrane oxygenator be a model for lung NO and CO transfer? *Journal of Applied Physiology* **100**, 1527-1538

- Borland, C.D.R., Mist, B., Zammit, M. and Vuylsteke, A. (2001) Steady-State measurement of NO-CO lung diffusing capacity on moderate exercise in men. *Journal of Applied Physiology* **90**, 538-544.
- Cooper, D.M. and Weiler-Ravell, D. (1984) Gas Exchange response to exercise in children. *American Review of Respiratory Disease* **129(Suppl)**, S47-S48.
- Cotes, J.E., Dabbs, J.M., Hall, A.M., Axford, A.T. and Laurence K.M. (1973) Lung volumes, ventilatory capacity, and transfer factor in healthy British boy and girl twins. *Thorax* **28**, 709-715.
- Ferris, B.G. (1978) Epidemiology standardisation project II: Recommended respiratory disease: questionnaire for use with adults and children in epidemiological research. *American Review of Respiratory Disease* **118**, 7-53.
- Forster, R.E. (1987) Diffusion of gases across the alveolar membrane. In: *Handbook of physiology: The respiratory system IV*. Eds: Farhi, L.E. and Tenny, S.M. Bethesda: American Physiological Society. 71-88.
- Gaultier, C.L. and Crapo, R. (1997) Effects of nutrition, growth hormone disturbances, training, altitude and sleep on lung volumes. *European Respiratory Journal* **10**, 2913-2919.
- Goresky, C., Warnica, J., Burgess, J. and Nadeau, B. (1975) Effect of exercise on dilution estimates of extravascular lung water on the carbon monoxide diffusing capacity in normal adults. *Circulation Research* **37**, 379-389.
- Guénard, H., Varène, N. and Vaida, P. (1987) Determination of lung capillary blood volume and membrane diffusing capacity in man by the measurements of NO and CO transfer. *Respiration Physiology* **70**, 113-120.
- Guénard, H., Diallo, M.H.H., Laurent, F. and Vergeret, J. (1992) Lung density and lung mass in emphysema. *Chest* **102**, 198-203.
- Hamilton, P. and Andrew, G.M. (1976) Influence of growth and athletic training on heart and lung functions. *European Journal of Applied Physiology Occupational Physiology* **36**, 27-38.
- Hsia, C.C.W., McBrayer, D.G. and Ramanathan, M. (1995) Reference values of pulmonary diffusing capacity during exercise by a rebreathing technique. *American Journal of Respiratory and Critical Care Medicine* **152**, 658-665.
- Hsia, C.C.W., Ramanathan, M. and Estrera, A.S. (1992) Recruitment of diffusing capacity with exercise in patients after pneumonectomy. *American Review of Respiratory Disease* **145(4 pt1)**, 811-816.
- Ingimarsson, J., Thorsteinsson, A., Larson, A. and Werner, O. (2000) Lung and chest wall mechanics in anesthetized children: Influence of body position. *American Journal of Respiratory and Critical Care Medicine* **162**, 412-417.
- Krawiec, J.A., Forster, R.E., Gottlieb, T.W. and Fish, D. (1983) Rate of CO uptake by human red blood cells. *Federation Proceedings* **42**, 993.
- Lewis, B.M., Lin, T., Noe, F.E. and Komisaruk, R. (1958) The measurement of pulmonary capillary blood volume and pulmonary membrane diffusing capacity in normal subjects: the effects of exercise and position. *Journal of Clinical Investigation* **37**, 1061-1070.
- Mahajan, K.K., Mahajan, S.K. and Mishra, N. (1992) Effect of growth on lung transfer factor and its components. *Indian Journal of Chest Disease & Allied Science* **34(2)**, 77-83.
- Maksud, M.G., Coutts, K.D. and Hamilton, L.H. (1971) Oxygen uptake, ventilation, and heart rate: study in negro children during strenuous exercise. *Archives Environmental Health* **23**, 23-28.
- Mandigout, S., Lecoq, A.M., Courteix, D., Guenon, P. and Obert, P. (2001) Effect of gender in response to an aerobic training programme in prepubertal children. *Acta Paediatrica* **90**, 9-15.
- Manier, G., Moinard, J. and Stoïcheff, H. (1993) Pulmonary diffusing capacity after maximal exercise. *Journal of Applied Physiology* **75**, 2580-2585.
- Moinard, J. and Guénard, H. (1990) Determination of lung capillary blood volume and membrane diffusing capacity in patients with COLD using the NO-CO method. *European Respiratory Journal* **3**, 318-322.
- Nourry, C., Deruelle, F., Guinhouya, C., Baquet, G., Fabre, C., Bart, F., Berthoin, S. and Mucci, P. (2005) High-intensity intermittent running training improves pulmonary function and alters exercise breathing pattern in children. *European Journal of Applied Physiology* **94**, 415-423.
- Paterson, D.H. (1979) Respiratory and cardiovascular aspects of intermittent exercise with regard to ice hockey. *Canadian Journal of Applied Sport Science* **4**, 22-28.
- Roughton, F.J.W. and Forster, R.E. (1957) Relative importance of diffusion and chemical reaction rates in determining rate of exchange of gases in the human lung, with special reference to true diffusing capacity of pulmonary membrane and volume of blood in the capillaries. *Journal of Applied Physiology* **11**, 290-302.
- Stam, H., Hrachovina, V., Stijnen, T. and Versprille, A. (1994) Diffusing capacity dependent on lung volume and age in normal subjects. *Journal of Applied Physiology* **76**, 2356-2363.
- Sylvester, K.P., Milligan, P., Patey, R.A., Rafferty, G.F. and Greenough, A. (2005) Lung volumes in healthy afro-caribbean children aged 4-17 years. *Pediatric Pulmonology* **40**, 109-112.
- Tamhane, R.M., Johnson, R.L. and Hsia, C.C.W. (2001) Pulmonary membrane diffusing capacity and capillary blood volume measured during exercise from nitric oxide uptake. *Chest* **12**, 1850-1856.
- Turley, K.R. and Wilmore, J.H. (1997) Cardiovascular responses to treadmill and cycle ergometer exercise in children and adults. *Journal of Applied Physiology* **83**, 948-957.
- Vaughan, T., DeMarino, E. and Staub, N. (1976) Indicator dilution lung water and capillary blood volume in prolonged heavy exercise in normal



men. *American Review of Respiratory Disease* **113**, 757.

- Wagner, P., Gale, G., Moon, R., Torre-Bueno, J., Stolp, B. and Saltzman, H.A. (1986) Pulmonary gas exchange in humans exercising at sea level and simulated altitude. *Journal of Applied Physiology* **61**, 260-270.
- West, J.B., Dollery, C.T. and Heard, B.E. (1965) Increased pulmonary vascular resistance in the dependant zone of the isolated dog lung caused by perivascular edema. *Circulation Research* **Sep 17**, 191-206.
- Yamamoto, H., Teramoto, H., Uetani, K., Igawa, K. and Shimizu, E. (2001) Stretch induces a growth factor in alveolar cells via protein kinase. *Respiration Physiology* **127**, 105-111.
- Zavorsky, G.S., Badra Quiron, K., Massarelli, P.S. and Lands, L.C. (2004) The relationship between single-breath diffusion capacity of the lung for nitric oxide and carbon monoxide during various exercise intensities. *Chest* **125**, 1019-1027.

#### KEY POINTS

- Trained children had greater  $Dm_{CO}/VA$  and  $Dm_{CO}/Vc$  ratios compared with control children during exercise.
- The mechanisms by which basketball playing children were thought to improve lung diffusion are speculative.
- Further work will be required to determine the kinetics of the alteration in  $Dm$  when children switch from non players to players status or vice-versa.

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