CASE REPORT

The upper limit of alveolar capillary recruitment in a young man with lung growth impairment

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The upper limit of alveolar capillary recruitment in a young man with lung growth impairment. P.M. Donnelly, B.V. Daxini, P.T.P. Bye. ©ERS Journals Ltd 1994.

ABSTRACT: In order to obtain further insight into the adaptive mechanisms relating to gas exchange in anatomically small lungs, tests of mechanical lung function and gas exchange were made in an active young man, whose lung growth had been severely impaired due to pectus excavatum developed in childhood.

We found our patient to have small (total lung capacity, 59% of predicted) but mechanically normal lungs. He had a normal cardiac output, a normal single-breath diffusing capacity (100% pred), and a high diffusion coefficient (148% pred) associated with a high pulmonary capillary blood volume (131% pred) at rest. Pulmonary distensibility (K) and elastic recoil were normal. During steady-state exercise he was unable to recruit further reserves of pulmonary capillaries, but this was not reflected in a plateau for oxygen consumption, which was presumably the result of an increased pulmonary capillary blood flow rather than volume. The recruitment of pulmonary capillary reserves in this young man has enabled him to maintain a normal maximum exercise capacity. In addition, the high stroke volume and a haemoglobin level in the high normal range (176 g·l⁻¹) may have maintained his maximal exercise function, despite fewer alveolar units.

This study suggests that, contrary to previous findings, loss of a major proportion of lung tissue need not impair exercise capacity. Patients with either small lungs or following pneumonectomy may benefit from physical training sufficient to optimize both an increase in cardiac output and recruitment of their existing alveolar capillary reserves.

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Arterial hypoxaemia and increased alveolar to arterial gradient (A-aDo₂) can result from any combination of ventilation-perfusion inequality, shunt and/or failure of complete transfer of O₂ by diffusion from the alveolus to the pulmonary capillary. During exercise, arterial hypoxaemia has been demonstrated in normal humans at altitude [1], and in some highly trained runners at sea level [2]. In patients with interstitial lung disease, arterial hypoxaemia occurs despite exercise ventilations well above the normal range [3]. In each of the above examples, it has been postulated that diffusion limitation within the lungs plays some role in the incomplete equilibration of oxygen between alveolar gas and end-capillary blood either at rest or during exercise.

Loss of a major portion of lung tissue has been shown to impair exercise capacity [4]. Reductions in ventilatory capacity and cardiac output have been reported in humans after pneumonectomy, but impairment in gas exchange is thought to be mild, until almost two thirds of lung tissue has been removed [4]. Compensation for loss of gas exchange units during exercise can be made through recruitment of existing physiological reserves of diffusing capacity (pulmonary capillaries) in the remaining tissue [5]. No limit to this recruitment with respect to cardiac output has yet been demonstrated in normal subjects.

A recent report in ex-smokers, six months post-pneumonectomy, has shown that the pattern of diffusing capacity of the lungs for carbon monoxide (DLCO) recruitment during exercise was not significantly affected [5]. In seven subjects, there was no evidence that an upper limit of recruitment was approached. However, in one patient studied 8 yrs after lung resection, the predicted recruitment of DLCO during exercise was impaired. In contrast, we report lung function and gas exchange adaptations at rest and during exercise in an active young man, whose lung growth had been severely impaired due to pectus excavatum, developed in childhood. In this man, an upper limit for recruitment of alveolar capillaries has been reached at rest, in association with a normal erect resting cardiac output. Some similarities to our findings have been reported in conditioned foxhounds after pneumonectomy [6].

Case report

A 27 year old nonsmoking male was referred to the Department of Respiratory Medicine for review of the complaint of chest tightness during his regular games of soccer, particularly after sprinting. These symptoms were

not relieved by prematch administration of a beta-agonist aerosol. He did not complain of wheezing. He had a history of childhood "asthma", having been hospitalized overnight at least six times between the ages of 5–9 yrs. At 14 yrs, he had an operation to correct a pectus excavatum deformity. His "asthma" improved in his teenage years; however, his chest tightness recurred at about 19 yrs of age. He did not describe any definite food allergies, and had not suffered from hayfever or any definite eczema. Neither his parents nor his brothers and sisters have suffered from asthma.

He was admitted to hospital in April 1992, with suspected pericarditis, having presented to casualty with pleuritic chest pain. Clinical examination was unremarkable. However a 12-lead electrocardiogram showed sinus rhythm, left atrial enlargement and anterolateral ST elevation. Echocardiogram was normal. At review, a few months later, he remained asymptomatic. A repeat electrocardiogram still showed ST elevation in anterolateral leads, suggestive of early repolarization. M-mode and 2D echocardiography again revealed normal chamber dimensions, normal valves, and good left ventricular contractility. The ejection fraction was estimated to be 56%, and the calculated cardiac output was $4.91 \text{ l} \cdot \text{min}^{-1}$. On treadmill, he exercised for 17.5 min on Bruce protocol (17.0 METS), achieving 96% of his maximal heart rate, with normal haemodynamic responses and no evidence of ischaemia. A chest radiograph showed no focal pulmonary pathology.

The patient was a tall (193 cm) young man of slim build (75 kg). His relative sitting height (0.51 cm) was normal (sitting height/standing height) but his chest width, depth and circumference were less than expected [7] (29 cm, 15 cm and 82 cm, respectively).

On examination, the chest was clear to auscultation. The patient still possessed marked sternal depression. He had a slight flow murmur at the left sternal edge, but no other cardiac abnormality. Blood pressure was 140/85 mmHg. Spirometry revealed a forced expiratory volume in one second (FEV_1) of 3.1 l, and a forced vital capacity (FVC) of 3.5 l. Thus, he had a normal to high FEV_1/FVC ratio (89%), but his vital capacity was 55% of predicted.

He was referred to the pulmonary function laboratory for more detailed testing, including a methacholine challenge for estimation of bronchial reactivity, an 8 min exercise challenge test for asthma, including the last 4 min at a minute ventilation approximately 60% of the patients maximum voluntary ventilation, lung volumes, and DLCO determinations at rest and during exercise. These initial tests showed his bronchial reactivity to be in the borderline "asthmatic" range, with a 20% fall in FEV_1 (0.6 l) following 5 μmol of methacholine inhalation. His asthma exercise challenge test was negative. His spirometry and all subdivisions of lung volume were severely restricted but, most interestingly, he had a normal DLCO (100% pred) with a very high diffusion coefficient for carbon monoxide (Kco) of 148% predicted (table 1). Estimation of pulmonary capillary blood volume (Vc) and pulmonary membrane diffusing capacity (Dm) in the sitting position revealed Vc to be 115 ml

(131% pred) and Dm 96% pred (table 1). Both Vc and Dm were predicted on the basis of the patient's body surface area (BSA) [8]. Haemoglobin concentration was $176 \text{ g} \cdot \text{l}^{-1}$. All determinations for DLCO at rest (during hyperoxia and normoxia) were made at least in duplicate. All measurements were standardized to a haemoglobin of $146 \text{ g} \cdot \text{l}^{-1}$ in agreement with the normal values used [8, 9]. For the calculations of Dm and Vc, the relationship proposed by ROUGHTON and FORSTER [10] was used: $1/\text{DLCO} = 1/\text{Dm} + 1/\text{Vc}$. The 1957 equation (average): $1/\theta = \text{PAO}_2 (\text{mmHg}) \times 0.0058 + 0.73$, where PAO_2 is the partial pressure of oxygen in the alveolar gas, was used to calculate $1/\theta$ (the rate of CO transfer into the blood in $\text{ml} \cdot \text{mmHg}^{-1} \cdot \text{min}^{-1}$ of capillary blood). The close proximity between total lung capacity (TLC) estimated by body plethysmography and the 10 s alveolar volume-body temperature and pressure saturated with water vapour ($\dot{V}_{\text{A}_{\text{BTPS}}}$) during the single-breath manoeuvre, indicated a normal distribution of ventilation in this man (table 1).

On another day, the patient performed an exercise test consisting of 3 min of work at 50, 100 and 125 W, respectively. At the end of each 3 min period, whilst still pedalling, a single-breath estimation of DLCO was made, according to the method of NEVILLE *et al.* [11] (fig. 1).

Table 1. — Spirometry, subdivisions of lung volume, lung mechanics and gas exchange at rest

Index	Value	% pred
$\text{FEV}_1 \text{ l}$	3.15	62
FVC l	3.55	56
$\text{FEV}_1/\text{FVC} \%$	89	110
VC l	3.46	55
TLC l	4.78	59
RV l	1.32	68
RV/TLC %	27	117
FRC l	2.48	61
ERV l	1.16	54
IC l	2.30	57
DLCO $\text{mmol} \cdot \text{min}^{-1} \cdot \text{kPa}^{-1}$	13.15, 14.0	97, 104
Kco $\text{mmol} \cdot \text{min}^{-1} \cdot \text{kPa}^{-1} \cdot \text{l}^{-1}$	2.96, 2.94	148, 147
Vc ml	115	131
Dm $\text{mmol} \cdot \text{min}^{-1} \cdot \text{kPa}^{-1}$	27.1	96
$\text{VA} \text{ l } 10\text{s}$	4.43, 4.75	93, 99% of box TLC
KkPa ⁻¹	1.18	96
Pel_{mi} kPa	3.14	79
Pel_{90} kPa	1.57	92

FEV_1 : forced expiratory volume in one second; FVC: forced vital capacity; FEV_1/FVC : FEV_1 as a percentage of FVC; VC: relaxed vital capacity; TLC: total lung capacity; RV: residual volume; RV/TLC: RV as a percentage of TLC; FRC: functional residual capacity; ERV: expiratory reserve volume; IC: inspiratory capacity; DLCO: diffusing capacity of the lungs for carbon monoxide; Kco: diffusion coefficient ($\text{DLCO}_{\text{STPD}}/\dot{V}_{\text{A}_{\text{BTPS}}}$); Dm: membrane diffusing capacity; Vc: pulmonary capillary blood volume; $\text{VA } 10\text{s}$: alveolar volume measured during single breath DLCO 10s breathhold (using helium) at BTPS; K: an index of alveolar distensibility; Pel_{mi} : elastic recoil pressure of the lungs at maximal inspiration; Pel_{90} : elastic recoil at 90% of maximal inspiration. STPD: standard temperatures and pressure, dry; BTPS: body temperature and pressure, saturated with water vapour; SB: single-breath.

Fig. 1. — a) Single-breath diffusing capacity of the lungs for carbon dioxide ($DLCO_{SB}$); and b) diffusion coefficient for carbon dioxide (Kco) at rest and during steady-state exercise (3 min), plotted against the workload in watts. The duplicate studies were performed four weeks apart (Run I and Run II). Predicted values (slopes) are taken from the data of KENDRIK and LAZLO [9], and have been confirmed in our laboratory using normal subjects of the same age and sex.

In this test, allowance was made for the effect on diffusing capacity of variation in, haemoglobin concentration, in carbon monoxide back pressure, and in alveolar capillary O_2 tension (Pao_2) [9]. The results showed that a plateau for $DLCO$ existed in this man over the range of work loads attempted (fig. 1). He did not exercise higher than 125 W because breathholding for him (as for most subjects) became difficult above that work level. This exercise study was repeated after two months, when he achieved a maximum workload of 150 W, but with a similar outcome (fig. 1).

In order to determine whether a fall in oxyhaemoglobin saturation developed in this man at or near to his maximum work capacity (W_{max}) a progressive (stage 1) exercise test was performed (fig. 2). The patient completed 230 W, before stopping as a result of leg tiredness and slight chest tightness. His haemoglobin oxygen saturation measured by pulse oximetry did not fall below 94% throughout the test. Throughout the test he maintained a normal minute ventilation ($\dot{V}_E$), heart rate (HR), and oxygen consumption ($\dot{V}O_2$) (fig. 2) and oxygen pulse ($\dot{V}O_2$ $l \cdot \text{beat}^{-1}$) at W_{max} was $0.018 l \cdot \text{beat}^{-1}$ (82%),

Fig. 2. — Stage 1 incremental exercise test for the subject with severe pectus excavatum deformity. *: arterial oxygen saturation (SaO_2) determined by oximetry at increasing levels of $\dot{V}O_2$. End-tidal CO_2 tensions (kPa) are in brackets below SaO_2 values; ■: respiratory frequency (f); ●: heart rate (HR); ▲: minute ventilation ($\dot{V}_E$). $\dot{V}O_2$: oxygen consumption at different workloads. Unbroken parallel lines represent the normal range for heart rate from rest to $3.5 l \cdot \text{min}^{-1} \dot{V}O_2$. Broken lines delineate the normal range for $\dot{V}_E$ from rest to $3.5 l \cdot \text{min}^{-1} \dot{V}O_2$. BTPS: body temperature and pressure, saturated with water vapour; STPD: standard temperature and pressure, dry.

the latter being an index of fitness and stroke volume. Ventilation was achieved through a simultaneous increase in both tidal volume (V_T) and breathing frequency (f) (fig. 2). At end-exercise, $\dot{V}_E$ was 88% of his predicted maximum voluntary ventilation (MVV). End-tidal carbon dioxide tension (P_{ETCO_2}) remained constant at 5.6 kPa (42 mmHg) up to 160 W at which point it increased progressively over 2 min to 6.1 kPa (46 mmHg) at 200 W, but fell progressively over 4 min to 5.1 kPa (38 mmHg) at 230 W, probably as a result of an increasing metabolic acid drive to ventilation (fig. 2). The patient did not develop any of the symptoms of exercise-induced asthma following any of the exercise tests performed.

Mechanical lung function tests performed included pulmonary distensibility (K), elastic recoil pressures at maximal and at 90% of maximal inspiration ($Pe_{l_{mi}}$ and $Pe_{l_{90}}$, respectively) (table 1). Methodology and normal predicted values have been reported previously [7, 12].

Discussion

We found our patient to have small (59% pred) but mechanically normal lungs, associated with pectus excavatum and a small thorax, probably the result of asthma in early childhood. In this study, the decreased lung volumes were not due to a decreased alveolar distensibility (K), or to an increased elastic recoil; and, therefore, probably resulted from a decreased alveolar number in association with his small chest and resultant lung growth impairment. Detailed discussion on the relationship between lung volume, chest size and shape, alveolar distensibility and alveolar size and number has been reported in two earlier publications [7, 12].

Despite having small lungs, single-breath DLCO ($DLCO_{SB}$) was maintained at a normal resting level, probably as a result of recruitment of pulmonary capillary reserves. This recruitment of DLCO was confirmed by the high V_c (131% pred). Since V_c reflects stroke volume, all of this man's expected stroke volume has been accommodated in a lung volume only 59% of predicted. It has been reported that pulmonary capillary blood volume is affected by both inflow and outflow pressures, as they influence transcapillary pressure [13]. Although the initial echocardiogram (ECG) in our subject showed evidence of left atrial enlargement, subsequent 2D echocardiography revealed normal chamber dimensions, normal valves, and good left ventricular contractility. Thus, the normal DLCO that we measured (despite fewer alveoli) suggests an increased inflow pressure. During steady-state exercise at increasing workloads, he was unable to recruit further reserves of DLCO (fig. 1). This feature may be a result of the demands of his active lifestyle. In contrast, patients 4–6 months after pneumonectomy usually exhibit 50% reduction in their maximal cardiac output, mainly because of an impaired stroke volume [5]. Many patients lead sedentary lives after pneumonectomy [5], and deconditioning may have been an important contributing factor to explain their reserve capacity for DLCO increase during exercise.

During Stage 1 incremental exercise testing HR, $\dot{V}_E$, $\dot{V}_{O_2}$ and oxygen pulse (stroke volume) were all within the expected range for a subject with normal sized lungs (fig. 2). The haemoglobin level in the high normal range at rest would have benefited O_2 delivery [6]. Minute ventilation was maintained, although end-tidal CO_2 carbon dioxide tension (P_{ETCO_2}) increased from 5.6 kPa (42 mmHg) to 6.1 kPa (46 mmHg) (fig. 2). Thus, although total ventilation was maintained at predicted levels, effective alveolar ventilation and CO_2 exchange were impaired. A correspondingly small decrease in arterial oxygen saturation (Sao_2) was observed over this period (fig. 2). These mild disturbances in gas exchange are probably the result of increasing ventilation perfusion ($\dot{V}_A/\dot{Q}$) inequality during exercise. Similar results have been observed during exercise in conditioned foxhounds following pneumonectomy [6].

CASTILE *et al.* [14] studied lung mechanics and exercise performance in eight male subjects with mild pectus deformities (mean TLC 79% pred). Lung mechanics studies were normal, and did not separate the symptomatic from the asymptomatic patients. Exercise studies showed an abnormal elevation in the work of breathing at high workloads. Tidal volume (V_T) as a percentage of VC was low at 38% mean. In our patient with small lungs, $\dot{V}_{O_2}$ at maximal work capacity was 103% pred, and higher than all the $\dot{V}_{O_2}$ values obtained by CASTILE *et al.* [14] for their patients. In addition, $V_T/VC\%$ for our subject was a normal value at 53% pred. The authors believe that the fitness level of their subject and the resultant recruitment of all the existing alveolar capillaries at rest were responsible for these findings.

BEISER *et al.* [15] demonstrated cardiac output to be reduced during exercise in some subjects with pectus deformities. But we found no evidence for this in the present study.

The chest tightness described during exercise in our subject may be the result of a transiently increased pulmonary artery pressure (Ppa), which subsides when activity is less intense [6]. However, this chest tightness may also be due to his $\dot{V}_E$ approaching his predicted maximum voluntary ventilation (MVV). A period of detraining in this man may reduce his stroke volume, thus allowing for DLCO recruitment during exercise, albeit at a lower activity level.

As far as the authors are aware, this is the first time a fixed DLCO has been described in response to exercise in healthy lungs.

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