

## EFFECT OF COLD CHALLENGE ON ALVEOLAR CAPILLARY BLOOD VOLUME IN NORMAL INDIVIDUALS

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**Abstract :** The effect of immersion of both the hands and the feet in water at 10°C on lung transfer factor for carbon monoxide (Tlco) and on pulmonary capillary blood volume (Vc) was investigated in 20 normal young adult males immediately, 60 min and 120 min after the end of the cold challenge. Vc was significantly reduced immediately and the reduction was aggravated at 60 min. Tlco was significantly reduced only at 60 min. All the values returned to baseline at 120 min. It is concluded that the cold-induced changes in Tlco and Vc are physiological responses and not unique to patients with Raynaud's phenomenon as suggested by some workers.

**Key words :** Cold Tlco Vc Vasospasm

### INTRODUCTION

In the absence of any direct demonstration of alveolar capillary blood volume, its existence has been inferred from indirect evidence like perfusion lung scan (1), or measurements of pulmonary arterial resistance (2). The ability to easily and reproducibly measure diffusion capacity provides another tool with the capability of measuring the changes in alveolar vascular blood volume (3). In response to cold pressor test, reduced values of lung transfer factor for carbon monoxide (Tlco) as well as one of its components, namely, alveolar capillary blood volume (Vc), have been observed in patients exhibiting Raynaud's phenomenon but not in normal individuals (4, 5). The cold induced reduction in Tlco and Vc has been attributed to pulmonary vasospasm which was considered unique to patients exhibiting Raynaud's phenomenon and not a physiological response to cold (4, 5). In these studies, the cold challenge consisted of immersion of one of or both the hands in cold water at 15°C. The present study was conducted in order to observe whether a greater cold challenge i.e. immersion of both the hands as well as the feet in water at 10°C in normal individuals produces any effect on Tlco and its components i.e.

diffusion capacity of the alveolar capillary membrane (Dm) and alveolar capillary blood volume (Vc.)

### METHODS

Twenty five healthy non-smoker male volunteers (aged 25-35 years) were investigated, during summer months, between 9.00 a.m. and 12.00 noon, after a light breakfast. Room temperature was maintained at 22-26°C. To eliminate fear and apprehension, the procedure to be adopted was explained in detail to each subject. Morgan transfer test model 'C' and computer magna 88 (PK Morgan Ltd, Kent, U.K.) were used to study and analyse different parameters of pulmonary function i.e. forced vital capacity (FVC), forced expiratory volume first Sec., percent of FVC (FEV<sub>1</sub>/FVC %) and lung transfer factor for carbon monoxide (Tlco) by the methods of Cotes (3).

For the estimation of Tlco, the subjects performed two trials of single breath manoeuvre. It consisted of rapid inhalation from residual volume (RV) to total lung capacity (TLC) of test gases, breath holding at TLC for 9 Sec followed by rapid exhalation to RV. Tlco was measured at two stages, TIH measured using high O<sub>2</sub> (85%) and TIL measured

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with low O<sub>2</sub> (18%) in test gases, to derive Dm and Vc from graphical recording as described by Cotes (3). The average of the two measurements (of TIH or TIL) by the two single breath manoeuvres was taken as a single observation. The results of the two manoeuvres agreed within 10% or 2 ml/mmHg/min of each other. Haemoglobin of each subject was measured by photoloric cyanmethaemoglobin method (6) and used in the computerised calculation of Tlco. Tlco measured with 18% oxygen was corrected to Tlco<sub>120</sub> as described by Mahajan et al (7) to express Tlco at PAO<sub>2</sub> of 120 mm Hg. Corrected Tlco<sub>120</sub> = Tlco (measured) [1+0.0045 (PAO<sub>2</sub>-120)]. Application of correction for back pressure of CO was not required.

After recording the baseline blood pressure (BP), ventilatory and diffusion functions of the lungs, the cold pressor test was performed in 20 subject (group I). The seated subject immersed both the hands (upto the wrist joint) and both the feet (upto the ankle joint) in water at 10°C for 2 minutes.

Diffusion function (Tlco, Dm, Vc) were re-assessed immediately (0 min), 60 min and 120 min, after removal of the hands and feet from cold water.

Group II subjects (n=5) were not exposed to the cold challenge but their diffusion functions were measured at similar time intervals as in group I subjects. The paired 't' test was used to compare the results in a group.

## RESULTS

Baseline pulmonary function tests (ventilatory and diffusion studies) of both groups I and II subjects were within normal limits. The effect of cold pressor test on Tlco, Dm, Vc and blood pressure of the subjects is given in Table I. Compared to the baseline values, exposure of group I subjects to cold challenge produced a significant increase in systolic blood pressure at 0 min but no difference was observed at 60 and 120 min. Vc decreased significantly (P<0.05) at 0 min but the maximum decrease was

TABLE I : Effect of Cold Pressor test on pulmonary diffusion functions and blood pressure.

	Baseline	Cold Pressor test			P Value		
	(1)	0 min (2)	60 min (3)	120 min (4)	(1) Vs (2)	(1) Vs (3)	(1) Vs (4)
Tlco (ml/min/mmHg)	30.35±1.01	29.38±0.77	26.70±1.02	29.40±1.03	NS	<.01	NS
Dm (ml/min/mmHg)	56.93±2.68	57.50±2.50	54.38±2.54	54.80±2.61	NS	NS	NS
Vc (ml)	70.69±2.06	65.57±3.26	62.09±2.44	68.90±3.87	<0.5	<.01	NS
Blood Pressure (mmHg)							
Systolic	124±2.06	130±3.89	123±1.54	120±2.06	<.05	NS	NS
Diastolic	80±1.03	82±0.77	80±0.79	80±0.79	NS	NS	NS

Values are Mean ± SE, NS = Not significant, n = 20

TABLE II : Results of Pulmonary diffusion functions and blood pressure estimations in control subjects recorded at different time intervals.

	Baseline	2 min	60 min	120 min
Tlco (ml/min/mmHg)	29.98±1.49	28.90±1.84	28.78±1.78	29.12±1.77
Dm (ml/min/mmHg)	60.21±5.26	58.40±4.46	58.20±4.86	58.00±4.15
Vc (ml)	68.40±4.45	66.79±3.56	70.72±4.82	70.08±5.33
Blood Pressure (mmHg)				
Systolic	126±1.98	124±1.00	128±2.0	124±97
Diastolic	82±0.81	80±0.77	80±0.79	80±0.77

Values are Mean ± SE; n=5

observed at 60 min ( $P < 0.01$ ). On the other hand a significant decrease in  $Tlco$  ( $P < 0.01$ ) was observed only 60 minutes after the end of cold challenge. None of the subjects developed erythema, blanching or cyanosis during the test. In 5 control subjects (group II) not exposed to the cold pressor test, repeated estimations of  $Tlco$ ,  $Dm$ ,  $Vc$  and blood pressure at similar time intervals (Table II) revealed no change from baseline values ( $P > 0.05$  in all the parameters).

### DISCUSSIONS

The cold pressor test evokes widespread cutaneous vasoconstriction (8). However, the effect of exposure to cold on pulmonary circulation is not well documented, possibly because of the difficulties involved in the study of the lesser circulation. Some recent reports have suggested a decrease in alveolar capillary blood volume leading to decrease in  $Tlco$ , in patients of Raynaud's phenomenon on exposure to a cold challenge of  $15^{\circ}C$ . The present study demonstrates that even in normal individuals, a slightly greater cold challenge i.e. immersion of both the hands and feet in water at  $10^{\circ}C$  for 2 minutes produces a decrease in  $Tlco$  as well as  $Vc$  with no change in  $Dm$ . It is interesting to note that the decrease in  $Vc$  was observed immediately after the end of the cold challenge and that the decrease was further aggravated one hour later when a significant decrease in  $Tlco$  was also apparent (Table I). These changes could not be attributed to any diurnal variation in  $Vc$  (9) since there was no significant change in  $Tlco$  or  $Vc$  in 5 subjects investigated at same time intervals without application of cold challenge (Table II).

In patients exhibiting Raynaud's phenomenon, the decrease in  $Tlco$  has been attributed to cold-induced intense spasm in the pulmonary vessels. Pulmonary vessels, no doubt have a sympathetic inner-

vation and constrict in response to an increase in circulating catecholamines (10). However, there is no evidence that cutaneous and pulmonary vessels have structural or functional similarity (10). Moreover all the systemic vessels do not react similarly to cold. During the cold pressor test in normal individuals, vasoconstriction has been observed in digital arteries (11) but not in the coronary (12) or the renal vessels (13). Similarly although increase in adrenal medullary discharge does occur on chronic exposure to cold (14), no change in plasma noradrenaline level has been observed during the cold pressor test (15). Moreover the slowness with which changes in  $Vc$  and  $Tlco$  developed (Table I) suggest the fluid shift (16) rather than pulmonary vasospasm a more likely mechanism. In patients exhibiting Raynaud's phenomenon subjected to the cold pressor test,  $Vc$  and  $Tlco$  were reported as increased by workers who measured them during the exposure to cold (17) but decreased values lasting upto 120 minutes were reported by workers who measured them after the end of the cold challenge (4, 5). It seems that the cold challenge produces a widespread cutaneous vasoconstriction leading to a shift of blood into pulmonary circulation which results in a transient increase in  $Vc$  and  $Tlco$ . The subsequent decrease in  $Vc$  and therefore in  $Tlco$  could be due to a slow and sustained compensatory reaction of pulmonary vessels to central circulatory overload. However, further work is required to elucidate the exact mechanism of the decrease in  $Vc$  following a cold challenge observed in normal individuals in this work and in patients exhibiting Raynaud's phenomenon by many other workers (4, 5).

To conclude, results of this study suggest that the cold induced changes in diffusion capacity and alveolar capillary blood volume are physiological responses and not unique to patients with Raynaud's phenomenon.

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