

# Effect of hyperlipidaemia on pulmonary diffusing capacity for carbon monoxide

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**ABSTRACT** There is conflicting evidence on the effect of hyperlipidaemia on pulmonary diffusing capacity for carbon monoxide (DLCO or TLCO) in man. We have measured the carbon monoxide transfer factor per unit alveolar volume (TLCO/VA or Kco) by the single breath method in 25 patients with hyperlipidaemia, and in three normal subjects before and after infusions of an intravenous fat emulsion, Intralipid. Non-smokers with hyperlipidaemia had normal levels of TLCO/VA, whereas some of the smokers showed a slight reduction. In neither group was there any correlation of TLCO/VA with serum triglyceride or cholesterol concentrations. A reduction in triglyceride concentrations of up to five-fold produced by plasma exchange (three studies in two patients) or by dietary manipulation (one patient) had no significant effect on the levels of TLCO/VA. Intralipid infusion in three normal subjects caused a four- to five-fold increase in serum triglyceride concentration but had no effect on TLCO/VA. We conclude that moderate degrees of hyperlipidaemia have no effect on pulmonary diffusion.

There is conflicting evidence on the effect of hyperlipidaemia on pulmonary diffusing capacity for carbon monoxide (DLCO or TLCO) in man. Enzi *et al* (1976) measured DLCO by the steady state method in 17 patients with hyperlipidaemia and compared the results with normal subjects of the same age, height, and with similar smoking habits. They found DLCO to be significantly lower in the hyperlipidaemic patients, with a negative correlation between plasma triglyceride and DLCO values but no correlation between DLCO and plasma cholesterol. It was surprising, perhaps, that when Newball *et al* (1975) increased or decreased serum triglyceride concentrations (by dietary means) in both normal subjects and hyperlipidaemic patients there was no significant change of DLCO, even at extremes of triglyceride concentration. This was true both for short-term changes in serum triglyceride, such as during oral fat tolerance tests, and for hyperlipidaemic patients observed over longer periods.

The results quoted above were obtained in patients with spontaneously occurring or diet-induced hyperlipidaemia. In addition, small changes in gas exchange have been shown after inducing hyperlipidaemia in normal subjects by

intravenous administration of a fat emulsion. Sundström *et al* (1973) showed a 15% fall in steady state DLCO during infusion of 20% Intralipid, with the DLCO returning to normal by 45 minutes after the end of the infusion. The alveolar-arterial oxygen gradient decreased. Analysis of their results shows considerable inter-subject variation and, as they point out the decrease in DLCO was small and without clinical significance in healthy subjects. Similar changes have been observed by Greene *et al* (1976), who used 10% Intralipid.

The mechanisms concerned in these changes are not understood. In awake sheep, McKeen *et al* (1978) showed that Intralipid infusions caused a rise in pulmonary artery pressure (and vascular resistance), an increase in lymph flow (but no oedema), and a fall in arterial  $PO_2$ . These responses were blocked by prior treatment with indomethacin but not by heparin, which was given to prevent the rise in serum triglyceride concentration. The authors speculated that the arachidonic acid in the infusion might have increased the synthesis of prostacyclic endoperoxides. Diffusion was not measured.

The present study attempts to resolve the issue

of whether hyperlipidaemia (either spontaneous or induced) significantly affects pulmonary diffusing capacity. We have, therefore, measured TLCO in hyperlipidaemic patients, some of whom were studied before and after plasma exchange, and in normal subjects before and after Intralipid infusions.

### Methods

Twenty-five patients attending the lipid clinic at the Hammersmith Hospital were studied. There were 20 men and five women aged from 22–66 years (mean 45). Eight had never smoked, eight had stopped smoking for at least two years, and 14 were either still smoking or had only recently stopped. One of the patients was diabetic and one two months' pregnant; all the patients accepted for the study had normal chest radiographs and an FEV<sub>1</sub>/VC ratio of more than 70%. All the patients attended in the morning after an overnight fast, and blood samples were taken for haemoglobin estimation and serum triglyceride and cholesterol concentrations. Diffusing capacity for carbon monoxide was measured by the single breath method (Ogilvie *et al*, 1957) in the sitting position. The mean of three measurements was taken, corrected for haemoglobin concentration, and results expressed as TLCO/VA or Kco. Predicted values were those of Cotes and Hall (1970).

Three normal male, non-smoking, fasting volunteers were given 200 ml of 20% Intralipid\* by intravenous infusion over 30 minutes. Diffusing capacity, serum lipid concentration, and Hb estimations were performed preinfusion, immediately postinfusion, and serially for up to two hours afterwards. The experiments were repeated on another day under identical conditions, except that each subject was given a 200 ml infusion of intravenous egg lecithin (ie Intralipid without its triglyceride). This constitutes a more appropriate control than either dextrose or saline solutions.

In two patients who were undergoing weekly plasma exchange in an attempt to induce regression of their coronary artery disease, carbon monoxide diffusing capacity, serum triglyceride, cholesterol, and haemoglobin were measured immediately before and after plasma exchange of 3.2 to 4 litres using a plasma protein fraction (PPF) continuous fluid cell separator. Patient 1 had mild type IV hypertriglyceridaemia, whereas patient 2 had familial hypercholesterolaemia, with a type IIb phenotype.

\*Intralipid contains soya bean oil 100 g, egg lecithin 6 g, and glycerol 12.5 g per 500 ml.

### Results

The 25 patients had fasting serum triglyceride concentrations ranging from 1.5 to 30.3 mmol/l (normal range: men <2.0 mmol/l; women <1.5 mmol/l) and a serum cholesterol varying from 3.7–9.9 mmol/l (normal range <6.5 mmol/l). We found no correlation between serum cholesterol and TLCO/VA (fig 1), nor between serum triglyceride and Kco (fig 2). In the non-smoking group all patients had a Kco within the predicted range; among the smokers there was a wider scatter of Kco but still no correlation with serum triglyceride concentration. Serial measurements of diffusing capacity were made on one patient with severe type V hyperlipidaemia whose serum triglyceride concentration was progressively lowered by dietary fat restriction over several weeks. The Kco remained within the predicted range at serum triglyceride concentrations, which varied from 12 to 30 mmol/l (ie from six to 15 times the upper limit of normal).

The results of increasing serum triglyceride concentrations by a fat emulsion load are shown in table 1. Haemoglobin concentrations varied only slightly but each Kco measurement was corrected for the haemoglobin concentration recorded at the same time. After Intralipid, Kco averaged 96% of its initial value. The postinfusion values did not differ significantly from the pre-

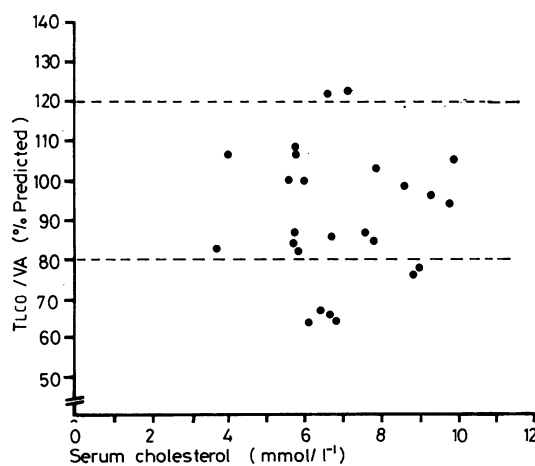


Fig 1 Carbon monoxide uptake (TLCO/VA or Kco) as percentage predicted plotted against serum cholesterol in patients with hyperlipidaemia. Interrupted lines represent predicted range for TLCO/VA (mean  $\pm$  1 SD). Upper limit of normal for serum cholesterol is 6.5 mmol/l. There is no correlation.

Table 1 Serum triglyceride concentrations and changes in CO uptake (Kco) in three normal subjects before and after infusions of fat emulsion and egg lecithin

	Subject A		Subject B		Subject C	
	Serum triglyceride concentration (mmol/l)	Kco (as % initial value)	Serum triglyceride concentration (mmol/l)	Kco (as % initial value)	Serum triglyceride concentration (mmol/l)	Kco (as % initial value)
<b>Fat emulsion</b>						
Preinfusion	0.7	100	1.0	100	1.7	100
End infusion	2.9	100	4.9	89	8.0	98
1 hr postinfusion	1.0	95	2.5	90	7.1	96
2 hr postinfusion					4.2	90
<b>Egg lecithin</b>						
Preinfusion	1.0	100	0.9	100	1.2	100
End infusion	0.9	118	1.0	104	1.3	103
1 h postinfusion		101		93		104
2 h postinfusion						109

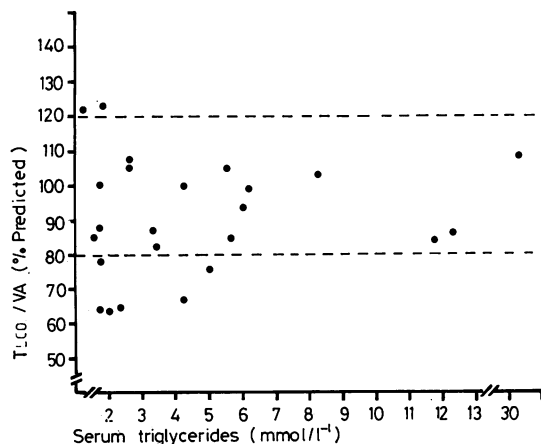


Fig 2 Carbon monoxide uptake as in fig 1 plotted against serum triglyceride concentration for same group of patients. Upper limit of normal for serum triglyceride is 1.5 mmol/l for women and 2.0 for men. Note lack of correlation.

infusion values. Furthermore, when the experiment was repeated with egg lecithin alone, there was again no significant difference between the Kco before and after infusion, nor was there a significant change of Kco in a paired *t* test when the effect of one infusion was matched with the other.

Plasma exchange, which induces a significant fall in plasma triglyceride concentration, was performed on three occasions in two patients. Table 2 shows Kco before and after plasma exchange. There was no correlation between triglyceride concentration and Co uptake. One subject was followed for 93 hours after plasma exchange while the serum triglyceride concentration varied between 37 and 188% of its initial value (fig 3).

There was no statistical correlation between change in triglyceride concentration and change in Kco.

Table 2 Effect of plasma exchange on serum triglyceride concentrations and carbon monoxide uptake (Kco)

	Post-plasma exchange		
	Serum triglyceride		Kco
	Basal level (mmol/l)	% Pre-exchange value	% Pre-exchange value
Patient 1 (1st occasion)	2.7	37	118
Patient 1 (2nd occasion)	1.7	21	91
Patient 2	2.0	45	102

## Discussion

These results do not confirm previous work which suggested an effect of spontaneous hyperlipidaemia on the pulmonary diffusing capacity for carbon monoxide. Nearly all our patients with hyperlipidaemia had normal diffusing capacities; a negative correlation with serum triglyceride concentrations was not seen. Although the triglyceride concentrations were not as high in our patients as in some of those in the Padua series (Enzi *et al*, 1976), a trend would have been expected even with less severe hypertriglyceridaemia. In addition, changes in triglyceride concentration with dietary restriction or plasma exchange were not correlated with changes of diffusing capacity, which is in keeping with the finding of Newball *et al* (1975). The reason for the rise in Kco after plasma-exchange in one patient (fig 3), which was

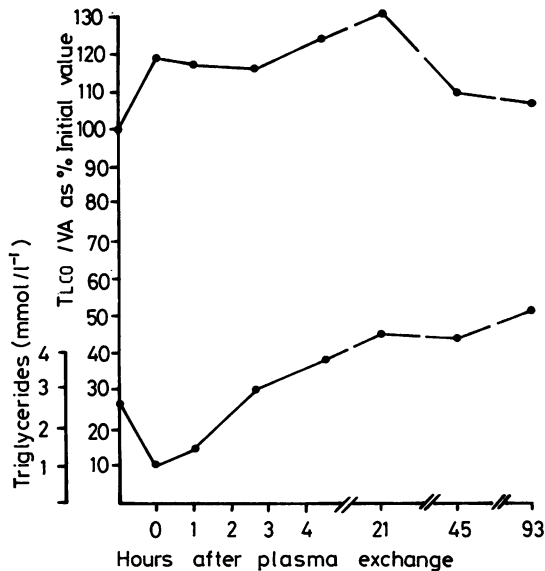


Fig 3 Patient 1. Change of CO uptake (TLCO/VA) and serum triglyceride concentration before and for 93 hours after plasma exchange.

sustained for at least 21 hours, is not clear. A significant fall in plasma viscosity is known to occur after plasma exchange, and this or some other factor may have led to an increase in pulmonary capillary blood volume.

In normal subjects our aim was to exclude the lecithin component of Intralipid as a cause of the reduction of DLCO reported previously (Sundström *et al* (1973); Greene *et al* (1976)). In fact, we were unable to find the small fall in DLCO observed by them. The effect of infusing 200 ml Intralipid in

normal subjects is minimal, and we conclude that moderately raised blood lipid concentrations have no deleterious effects on pulmonary diffusion.

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