Cigarette Smoking and Pulmonary Diffusing Capacity (Transfer Factor)[1-3]

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SUMMARY

Cigarette smoking caused a reduction in the diffusing capacity of the lungs for carbon monoxide and a reduction in coefficient of diffusion of carbon monoxide. This implies that cigarette smoking should be considered in prediction equations. The reduction in the diffusing capacity appeared to be due to a change in the volume of blood in the capillaries. This could account for some of the reversible changes observed in ex-cigarette smokers. The membrane component changed more with age. Prediction formulas were developed for diffusing capacity for the ratio, diffusing capacity/ alveolar volume, based on age, height, and life-time packs smoked.

Introduction

Previous studies by a number of investigators have well documented the deleterious effects of cigarette smoking on various aspects of pulmonary function (1). Most of the functions studied have been the lung volumes or the obstructive components such as forced expiratory volumes or flows; increased alveolar-arterial oxygen differences and altered gas distribution have been described in one group of smokers (2).

In a number of studies (3–12), the effect of cigarette smoking on diffusing capacity of the lungs has been studied. Most investigators have indicated that the diffusing capacity is decreased in smokers as compared with nonsmokers. One group (9), however, believed that the difference was not significant because their predicted values did not differ markedly from the observed value, and another group (10) found no effect of cigarette smoking on the diffusing capacity.

The diffusing capacity is composed of two parts: the membrane component and the volume of blood in the capillaries. The first is the resistance offered by the lung tissues, i.e., alveolar epithelium, capillary endothelium, and interstitial spaces; the second is largely the rate of reaction of carbon monoxide (CO) with hemoglobin and from which the volume of blood in the capillaries can be calculated. In only one of these studies (4) was the membrane component and the volume of blood in the capillaries examined. The results showed a decrease in

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the membrane component with increase in cigarette smoking and no change in the volume of blood in the capillaries.

In 1965, Krumholz and associates (12) reported that the diffusing capacity improved in a group of smokers who had stopped smoking. This implied that there was a reversible aspect of the change. The change, which was a small increase in diffusing capacity after three weeks of abstinence from cigarette smoking, could have resulted from a lowered back pressure of CO in blood. On the other hand, it could have been due to a change either in the membrane component or the volume of blood in the capillaries—both components of the diffusing capacity. Because they had measured the diffusing capacity only while room air was breathed, they were not able to determine whether there had been any change in the membrane component or volume of blood in the capillaries. Another possibility could have been variability of the method because after six weeks of presumed abstinence from smoking there was no difference in the diffusing capacity as compared with that obtained when the subjects were smoking regularly.

The observations of Krumholz and coworkers, however, are supported by those of Martt (5), who noted that ex-smokers had values for diffusing capacity similar to those of persons who had never smoked cigarettes.

When the Berlin, New Hampshire population was resurveyed in 1967, the diffusing capacity was measured while the subjects breathed room air and while they breathed oxygen. Information on cigarette smoking, ages, and heights was also available. The inter-relationship of these factors and the diffusing capacity of the lungs is examined in the present paper.

Materials and Methods

A random subsample from a randomly selected sample of the Berlin, New Hampshire population was selected (13). After their interview and simple tests of pulmonary function, which required 20 minutes to 30 minutes, the subjects were invited to participate in more detailed studies one of which was the single-breath pulmonary diffusing capacity for carbon monoxide ($D_{L_{CO}}$). This was measured first while the subjects breathed a large concentration of oxygen after a seven-minute washout of oxygen breathing and was followed after a five-minute to seven-minute rest period with another measurement on room air. Thus, a minimum of 40 minutes elapsed without cigarette smoking before any measurement was made. Only one measurement was made under each condition. Measurements were made in the sitting position with a nose clip in place. The method for measuring $D_{L_{CO}}$ was the modification by Forster and associates (14) of the Krogh method (15) as standardized by Ogilvie and associates (16) and used a Mark II Resparameter developed by Meade and co-workers (17).

Men and women were studied. Gas mixtures inhaled contained 0.3 per cent CO and 14 per cent to 15 per cent helium in either room air or oxygen. The gas samples were passed through Drierite[5] and Ascarite[6] to remove water vapor and carbon dioxide before analysis. Helium was measured by a thermal conductivity meter[7] that had been calibrated at various oxygen-nitrogen mixtures; CO was measured by an infrared gas meter, and oxygen, by a Pauling oxygen meter.[8]

The membrane component (D_M) and volume of blood in the capillaries (V_c) were calculated from the formulas of Cotes (18).

$$D_M = \frac{D_{L_{air}}\ D_{L_{oxy}}\left(P_{O_{2\,oxy}} - P_{O_{2\,air}}\right) - 0.827\ \dot{V}_{O_2}\left(D_{L_{air}} - D_{L_{oxy}}\right)\times}{D_{L_{oxy}}\ P_{O_{2\,oxy}} - D_{L_{air}}\ P_{O_{2\,air}} - 54.0\left(D_{L_{air}} - D_{L_{oxy}}\right)}$$

$$V_c = \frac{0.593\left(P_{O_{2\,oxy}} - P_{O_{2\,air}}\right) D_{L_{air}}\ D_{L_{oxy}}}{Hgb\%\left(D_{L_{air}} - D_{L_{oxy}}\right)}, \text{ where}$$

DL_{air} and DL_{oxy} represent $D_{L_{CO}}$ observed while breathing air and oxygen, respectively; $P_{O_{2oxy}}$ and $P_{O_{2air}}$ are the $P_{A_{O_2}}$ during breathing of oxygen and air, respectively; Hgb% is the concentration of hemoglobin in per cent of normal; and $\dot{V}_{O_2}$ is the oxygen consumption. The following assumptions were made: Hemoglobin was assumed to be 100 per cent in men and 90 per cent in women; a 10 per cent error (decrease) in this estimate produces an 11 per cent error (in-

[5] W. A. Hammond Drierite Co., Xenia, Ohio.

[6] A.H. Thomas Co., Philadelphia, Pennsylvania.

[7] Cambridge Instrument Co., New York, New York.

[8] Beckman Instruments, Mountainside, New Jersey.

TABLE 1

MEAN FORCED VITAL CAPACITY (FVC), FORCED EXPIRATORY VOLUME IN ONE SECOND (FEV_1), PEAK EXPIRATORY FLOW (PEF), AND HEIGHT OF 142 SUBJECTS IN A SUBSAMPLE, BERLIN, NEW HAMPSHIRE, 1967

Men (70)					Women (72)				
Age (years)	FVC (liter)	FEV_1 (liter)	PEF (liter/min)	Height (m)	Age (years)	FVC (liter)	FEV_1 (liter)	PEF (liter/min)	Height (m)
<45	4.38	3.48	540.9	1.72	<45	3.19	2.69	377.0	1.60
>45	3.44	2.64	449.0	1.69	>45	2.45	2.01	326.1	1.58

crease) in Vc. Oxygen consumption in men was taken to be 300 ml per min and in women, 250 ml per min. A 50-ml error in this estimate produces a one per cent error in DM. Back pressure of CO was not measured but was assumed, as in other studies, to be negligible (6, 11). To ensure that it was as low as possible, the oxygen study was done first. A calculation assuming a 3 per cent carboxyhemoglobin concentration indicated that this would have decreased the DL_{CO} by 2 per cent. In addition, certain criteria were established to ensure comparability of the measurement on oxygen and on room air. These were as follows: (*1*) The values for alveolar volume (VA) calculated from helium dilution during oxygen breathing and during breathing of room air had to agree within 10 per cent. The volume was corrected for the subject's dead space, estimated as one ml per pound of body weight, and the dead space of the apparatus. (*2*) Alveolar volumes had to be equal to or greater than 90 per cent of total lung volume; subjects were required to inhale a volume equal to their vital capacity (VC) less 0.3 liter. (*3*) Breath-holding times were approximately 10 seconds and had to agree within three seconds.

Measurements were also excluded if the subject's VC was less than 1,400 ml, if there was poor cooperation or inability to perform the respiratory maneuvers, or if there was an obvious error during the measurement. Tests in which poor cooperation or obvious errors occurred could occasionally be repeated.

Spirometer temperatures and barometric pressure were recorded so that the DL_{CO} could be expressed at standard temperature and pressure, dry (STPD). Alveolar volumes were calculated from the single-breath helium dilution. Heights were measured using a right angle with the subject standing in stocking feet against a wall and were recorded to the nearest 0.25 inch. Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured on Stead-Wells spirometers.[9] Five trials were made and the average of the last three was used. Volumes were corrected to body temperature and ambient pressure, saturated with water vapor (BTPS). Peak flows were obtained by means of a Wright peak flow meter[10] that had been calibrated against a standard orifice meter, and readings were corrected according to the calibration curve for a given instrument. Five trials were made and the mean of the last three was used. No temperature correction was made.

Information on respiratory symptoms and cigarette smoking habits were obtained by means of a standard questionnaire (19). Ages were taken as of the last birthday.

Results

A total of 203 persons were potential subjects. Some of the difficulties associated with surveys with limited time available and randomly selected samples are indicated by the failure rate. Thirty-five of these were failures, largely due to low VC or poor cooperation; 168 gave acceptable results. Of these, an additional 26 were rejected because the two analyses did not meet the criteria listed. Thus, data from 142 (70 per cent) of the original total could be used to calculate DM and Vc. This group consisted of 70 men and 72 women. The average values for the tests of pulmonary function and heights are shown in table 1.

The DL_{CO} as measured during air breathing, by sex, age, and current cigarette smoking category is presented in table 2. These data are presented graphically in figure 1. Those classified as never smoked or ex-cig-

[9] Warren E. Collins Co., Boston, Massachusetts.

[10] J. J. Monaghan Co., Inc., Denver, Colorado.

TABLE 2

PULMONARY DIFFUSING CAPACITY FOR CARBON MONOXIDE WHILE BREATHING AIR, BY SEX, AGE, AND CURRENT CIGARETTE-SMOKING CATEGORIES

		Current Cigarette-Smoking Category											
		Never Smoked $D_{L_{CO}}$ (ml/min/mm Hg)			Ex-Smoker $D_{L_{CO}}$ (ml/min/mm Hg)			1 to 24 Per Day $D_{L_{CO}}$ (ml/min/mm Hg)			25 or More Per Day $D_{L_{CO}}$ (ml/min/mm Hg)		
Sex	Age (years)	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD
Men	25–44	6	30.27	3.82	4	30.63	1.59	9	26.69	5.76	7	26.86	3.08
Men	45 or older	10	24.14	5.58	15	22.33	6.82	10	19.46*	3.43	9	17.64†	2.49
Women	25–44	6	21.47	3.03	5	22.40	2.14	10	18.41	4.15	3	20.00	3.46
Women	45 or older	31	16.84	3.79	4	17.72	4.42	6	16.07	5.64	7	15.03	5.69

*Versus never smoked, $P < 0.05$.
†Versus never smoked, $P < 0.01$.

arette smokers included a few who smoked a pipe, cigars, or both. In both men and women, there was a decrease in $D_{L_{CO}}$ with increase in age and with increase in cigarette smoking. Ex-cigarette smokers tended to be similar to persons who never smoked. This confirms work that others have reported (5, 9). The effect of back-pressure of CO in smokers was probably small because of the relatively high concentration of CO inhaled.

The relationship with lifetime cigarette smoking (table 3), including the ex-cigarette smokers, was also examined. As with current cigarette smoking, there was a decrease in $D_{L_{CO}}$ with increase in lifetime smoking. When these data were examined, excluding the ex-smokers, the same general trend existed. Because the ex-smokers tended to fall in the two middle categories, these values were slightly lower when they were excluded. When tested for use in prediction formulas, the lifetime smoking was much more significant than the current cigarette smoking. Some of this undoubtedly was due to the extremely long scale used in lifetime smoking, 0 to 20 000 packs.

Similar trends were observed in results obtained after oxygen breathing. Alveolar oxygen tension while subjects breathed a high concentration of oxygen was 573 mm Hg in men and 579 mm Hg in women. These data in conjunction with data obtained while subjects breathed room air were used to calculate D_M and Vc. The results are presented in table 4 for men and women by age groups and current cigarette smoking and graphically in figures 2 and 3. The D_M did not show any consistent change with increased current cigarette smoking whereas it showed a fairly consistent decrease with increased age for the various smoking categories. This change was more marked in men than in women. The Vc, on

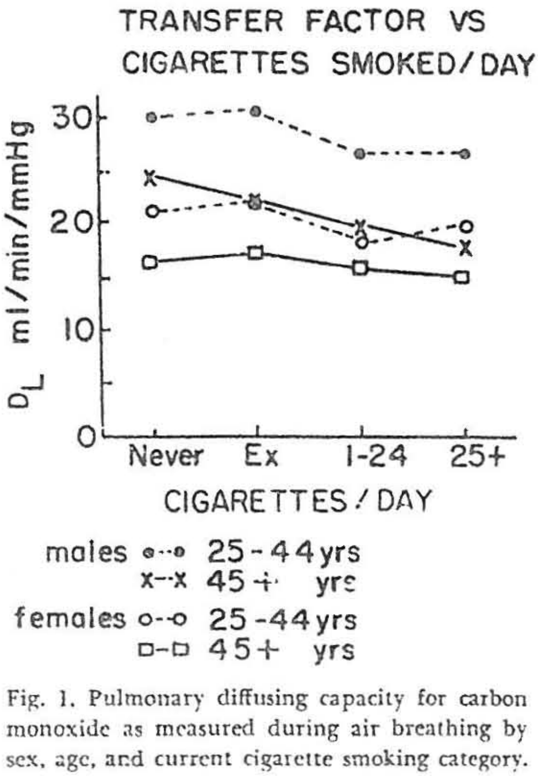

Fig. 1. Pulmonary diffusing capacity for carbon monoxide as measured during air breathing by sex, age, and current cigarette smoking category.

TABLE 3

PULMONARY DIFFUSING CAPACITY FOR CARBON MONOXIDE WHILE BREATHING AIR, BY SEX, AGE, AND LIFETIME CIGARETTE SMOKING CATEGORY (INCLUDING EX-SMOKERS)*

		Lifetime Cigarette Smoking Category											
		0–19 Packs DLCO (ml/min/mm Hg)			30–6,000 Packs DLCO (ml/min/mm Hg)			6,001–12,000 Packs DLCO (ml/min/mm Hg)			12,000 or More Packs DLCO (ml/min/mm Hg)		
Sex	Age	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD
Men	25–44	6	30.27	3.82	7	31.33	1.69	12†	25.23	4.21	1	28.60	–
Men	45 or older	11	24.17	5.30	8	26.34	5.18	7	20.11	2.49	18**	17.35	3.82
Women	25–44	6	21.47	3.03	14	19.61	3.34	4	20.40	5.86	–	–	–
Women	45 or older	31	16.84	3.79	7	16.96	6.05	5	16.76	5.28	5	14.00	4.17

*Mean alveolar oxygen tension: men, 94 mm Hg; women, 98 mm Hg.
†Versus 0 to 19 packs; $P < 0.05$.
**Versus 0 to 19 packs; $P < 0.01$.

the other hand decreased markedly with increased cigarette smoking as well as some change with age. Comparable results are shown in table 5, in which the relationships with lifetime packs smoked are examined.

Discussion

These results are in contrast to those reported by Wilson and co-workers (4), who reported no change in Vc but a decrease in DM in 14 smokers who had been matched for surface area, height, and age. They also eliminated those who had a history of respiratory disease and those with a mixing index greater than 2.5 per cent. They obtained DM and Vc by the graphic method of Roughton and Forster (20). Any or all of these differences in method and selection of subjects could account for the discrepancy. The most probable cause lies in the different selection of subjects; in the present study the selection was random and Wilson and associates had a selected sample with a relatively small number of subjects.

The DM and Vc each constitutes a complex of variables. It is not possible to identify which may have changed or to what degree in this study. Similar results were obtained in a study of shipyard workers (21) where a decrease in Vc with smoking was also noted. Unequal distribution is not an important element in the single breath technique for measuring D_{LCO}. It might have some influence in severely diseased persons. In this population, the severely diseased were probably eliminated by the requirement of VC in excess of 1,400 ml. In addition, the use of the single breath helium dilution method to estimate VA measures the effective VA. In persons with poor distribution and in whom the VA has been measured by another method, larger lung volumes will be used than are actually involved in gas exchange. This would overestimate the diffusing capacity. Again in this population it is believed that values of VA measured by single breath helium dilution were close to those that would be obtained by other methods. Because of the voluntary nature of this study in a general population, the extensive or detailed studies that would be possible in a hospital or clinic setting could not be done.

Because lung volumes are used to calculate D_{LCO}, persons with larger lung volumes usually have higher D_{LCO}; if lung volumes change either with age or smoking habit, it may be important to correct for this. The D_{LCO} can be divided by the VA at which the measurement was made. This is the diffusion coefficient (Kco) and is similar but not identical to the permeability coefficient of Krogh (15). The values of D_{LCO}/VA, i.e., Kco, are shown in tables 6 and 7 for current cigarette smoking and lifetime packs. The relationship of the Kco and current

TABLE 4

MEMBRANE COMPONENT OF PULMONARY DIFFUSING CAPACITY FOR CARBON MONOXIDE (DM) AND VOLUME OF BLOOD IN LUNG CAPILLARIES (Vc), BY SEX, AGE, AND CURRENT CIGARETTE-SMOKING CATEGORIES

		Current Cigarette-Smoking Category											
		Never Smoked			Ex-Smoker			1–24 Per Day			25 or More Per Day		
Sex	Age (years)	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD
DM, ml/min/mm Hg													
Men	25–44	6	46.73	6.07	4	43.95	7.76	9	49.84	16.06	7	55.74	12.51
Men	45 or older	10	34.56*	8.67	15	36.49	14.62	10	43.33	16.68	9	31.83*	8.94
Women	25–44	6	30.12	5.88	5	33.06	5.79	10	26.90	6.39	3	31.97	6.10
Women	45 or older	31	23.70†	6.03	4	33.78	15.71	6	25.72	10.04	7	25.21	7.97
Vc, ml													
Men	25–44	6	75.45	15.47	4	92.00	19.84	9	61.38	25.88	7	49.10**	9.99
Men	45 or older	10	74.99	26.02	15	55.53*,††	18.48	10	33.75**,††	11.14	9	36.48**	20.66
Women	25–44	6	77.20	14.42	5	77.44	36.18	10	57.00††	17.56	3	50.73††	10.68
Women	45 or older	31	60.99	20.75	4	52.88	31.29	6	47.95	25.48	7	39.67††	25.26

*Versus 25–44; P < 0.01.
†Versus 25–44; P < 0.05.
**Versus Never Smoked; P < 0.01.
†† Versus Never Smoked; P < 0.05.

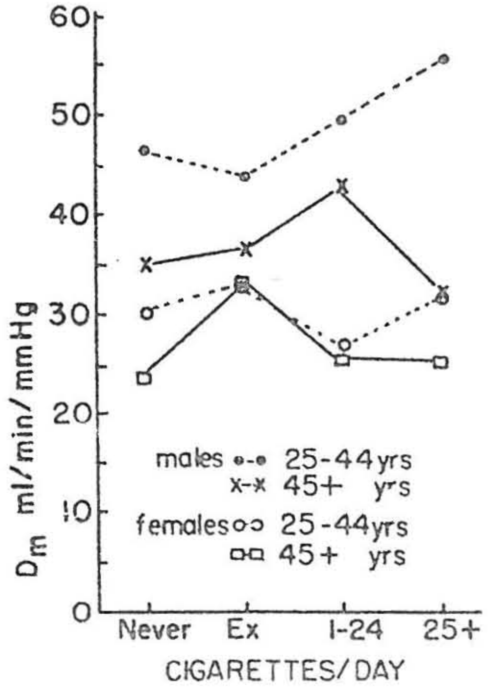

Fig. 2. Membrane component of pulmonary diffusing capacity for carbon monoxide by sex, age, and current cigarette smoking category.

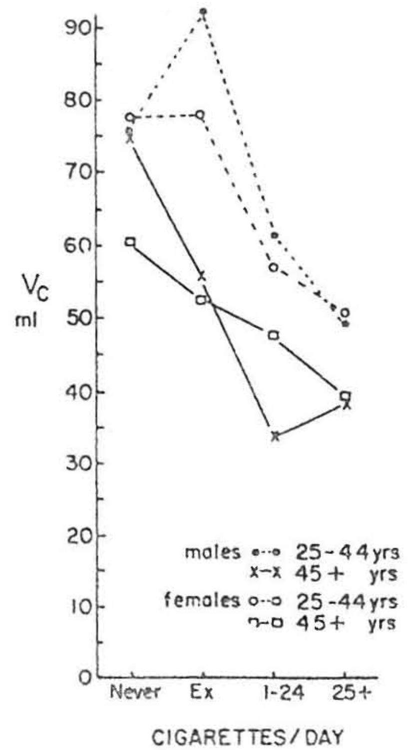

Fig. 3. Volume of blood in lung capillaries by sex, age, and current cigarette smoking category.

TABLE 5

MEMBRANE COMPONENT OF PULMONARY DIFFUSING CAPACITY FOR CARBON MONOXIDE (DM) AND VOLUME OF BLOOD IN LUNG CAPILLARIES (Vc), BY SEX, AGE, AND LIFETIME CIGARETTE-SMOKING

		Lifetime Cigarette-Smoking Category											
		0–19 Packs			20–6,000 Packs			6,001–12,000 Packs			12,000 or More Packs		
Sex	Age *(years)*	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD
DM, ml/min/ mm Hg													
Men	25–44	6	46.73	6.07	7	47.53	7.79	12	51.71	16.48	1	61.40	—
Men	45 or older	11	35.18*	8.48	8	42.38	12.78	7	36.59*	10.48	18	35.03	16.55
Women	25–44	6	30.12	5.88	14	28.78	6.35	4	31.83	7.56			
Women	45 or older	31	23.70*	6.03	7	32.69	13.07	5	23.34	6.21	5	24.08	9.02
Vc, ml													
Men	25–44	6	75.45	15.47	7	87.07	22.51	12	50.06†	15.63	1	53.90	—
Men	45 or older	11	72.74	25.78	8	64.59*	14.93	7	45.47**	21.05	18	35.08†	14.41
Women	25–44	6	77.20	14.42	14	63.46	24.82	4	55.25	24.78			
Women	45 or older	31	60.99	20.75	7	48.79	32.77	5	54.16	24.25	5	32.92**	10.80

*Versus 25–44; $P < 0.05$.
†Versus 0–19 packs; $P < 0.01$.
**Versus 0–19 packs; $P < 0.05$.

cigarette smoking showed a less marked change in the younger age group across the smoking categories. The age effect, however, persisted, and in the older age group there was a definite effect of cigarette smoking and the extremes were significantly different for the older men and women, i.e., never smoked versus 25 and more per day at $P < 0.01$.

Similarly with lifetime packs, there was not much effect in the younger age group; but in the older group, there was an effect

TABLE 6

COEFFICIENT OF PULMONARY DIFFUSION OF CARBON MONOXIDE (KCO), BY SEX, AGE, AND CURRENT CIGARETTE SMOKING CATEGORIES

		Never Smoked KCO *(ml/min/ mm Hg/liter)*			Ex-Smokers KCO *(ml/min/ mm Hg/liter)*			1–24 Per Day KCO *(ml/min/ mm Hg/liter)*			25 or More Per Day KCO *(ml/min/ mm Hg/liter)*		
Sex	Age *(years)*	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD
Men	25–44	6	5.568	0.513	4	5.365	1.099	9	5.492	1.024	7	5.516	0.570
Men	45 or older	10	5.253	0.890	15	4.905	1.439	10	4.328†,**	0.795	9	4.162††,***	0.680
Women	25–44	6	5.600	0.624	5	5.806	0.546	10	5.233	0.807	3	5.840	1.002
Women	45 or older	31	5.541	1.010	4	5.885	1.367	6	4.755	1.273	7	4.371***	0.992

*$KCO = DL_{CO}/VA$.
†Versus 25 to 44 years; $P < 0.05$.
**Versus never smoked; $P < 0.05$
††Versus 25 to 44 years; $P < 0.01$.
***Versus never smoked; $P < 0.01$.

TABLE 7

COEFFICIENT OF PULMONARY DIFFUSION OF CARBON MONOXIDE (KCO) BY SEX, AGE, AND LIFETIME CIGARETTE SMOKING CATEGORIES, INCLUDING EX-SMOKERS

		Lifetime Cigarette Smoking Categories											
		0–19 Packs KCO (ml/min/ mm Hg/liter)			20–6,000 Packs KCO (ml/min/ mm Hg/liter)			6,001–12,000 Packs KCO (ml/min/ mm Hg/liter)			12,000 or More Packs KCO (ml/min/ mm Hg/liter)		
Sex	Age (years)	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD
Men	25–44	6	5.568	0.513	7	5.559	0.883	12	5.515	0.861	1	4.410	–
Men	45 or older	11	5.145	0.916	8	5.818	1.166	7	4.804	0.729	18	3.893*	0.692
Women	25–44	6	5.600	0.624	14	5.534	0.860	4	5.350	0.536			
Women	45 or older	31	5.541	1.010	7	4.963	1.297	5	5.394	1.312	5	4.192†	1.099

*Versus 0–19 packs; $P < 0.01$.
†Versus 0–19 packs; $P < 0.05$.
See table 6 for definition of KCO.

across the smoking categories and the extremes (0 to 19 packs versus 12,000 and more packs) were significantly different ($P < 0.01$) for men and for women ($P < 0.05$).

It is also of interest that the Kco for men and women were remarkably similar. Thus, the lower $D_{L_{CO}}$ measured in women might have been related to their smaller lung volumes. When this was taken into account or when values for $D_{L_{CO}}$ were compared at comparable lung volumes, there was little or no difference between the values of $D_{L_{CO}}$ of men and women.

From these data, prediction formulas have been developed for $D_{L_{CO}}$ during breathing air and for Kco for men and women. In these prediction equations, the use of age and heights were required, but the computer was allowed to decide whether current smoking or lifetime packs added significantly to the prediction equation. The predictions developed are presented in table 8. For both $D_{L_{CO}}$ and Kco, lifetime packs were significant and, in fact, were more so than age or height. In most instances, age was significant, but height tended to be less so, particularly in the equation for the prediction of Kco. Equations are also given without taking into account the smoking effect, to be consistent with other equations in the literature.

These prediction formulas for $D_{L_{CO}}$ predicted values less than those presented in the literature (22), particularly in women. The predicted Kco values, on the other hand, were similar to or slightly larger than those in the literature (22). This could have resulted from using the single-breath helium dilution method to estimate V_A, which in turn could have yielded a smaller V_A than that of other methods. The ratio of the FVC as measured on the spirometer to the V_A as measured by the single-breath helium dilution method was examined. The ratio was 0.79 ± 0.070 (mean ± SD) for men and 0.81 ± 0.089 for women. Because V_A was measured at more than 90 per cent VC, these ratios were of the expected order of magnitude, and men and women yielded similar results. It does not seem, therefore, that the lower $D_{L_{CO}}$ values can be explained by underestimation of V_A. One of the writers (23) has done comparisons of the single-breath helium measurement and helium dilution technique in patients. There was good agreement in the relatively healthy population, but not in persons with severe pulmonary disease. Severely diseased persons did not make up a significant proportion of the present subjects because those with VC less than 1,400 ml were excluded. Therefore it is believed that the present V_A values are valid. No specific answer is avail-

TABLE 8

	Age (*years*)	Height (*m*)	Lifetime Packs	
				A. PREDICTION FORMULAS FOR DL_{CO} IN ADULT MEN AND WOMEN, BREATHING AIR
Men (n=70)	$\bar{X}$ 52.31	1.70	7,882	$DL_{CO} = 9.711 - 0.202\,(\text{age}) + 16.36\,(\text{Ht-M}) - 0.42\left(\text{Lifetime Packs}/1{,}000\right)$
	SD 13.34	0.07	7,544	r = 0.796 SEE = 3.818
Range	25–79	1.44–1.87	0–30, 758	$DL_{CO} = 0.572 - 0.246\,(\text{age}) + 21.16\,(\text{Ht-M})$
				r = 0.625 SEE = 4.894
Women (n=72)	$\bar{X}$ 50.29	1.58	2,892	$DL_{CO} = -0.339 - 0.157\,(\text{age}) + 16.80\,(\text{Ht-M}) - 0.21\left(\text{Lifetime Packs}/1{,}000\right)$
	SD 12.78	0.068	4,938	r = 0.609 SEE = 3.587
Range	24–76	1.37–1.73	0–20, 475	$DL_{CO} = -1.567 - 0.152\,(\text{age}) + 17.06\,(\text{Ht-M})$
				r = 0.562 SEE = 3.715
				B. PREDICTION FORMULAS FOR KCO* IN ADULT MEN AND WOMEN
Men				$KCO = 8.343 - 0.026\,(\text{age}) - 0.9\,(\text{Ht-M}) - 0.06\left(\text{Lifetime Packs}/1{,}000\right)$
				r = 0.518 SEE = 1.069
				$KCO = 6.646 - 0.0327\,(\text{age})$
				r = 0.357 SEE = 1.150
Women				$KCO = 6.381 - 0.011\,(\text{age}) - 0.17\,(\text{Ht-M}) - 0.06\left(\text{Lifetime Packs}/1{,}000\right)$
				r = 0.327 SEE = 0.989
				$KCO = 5.869 - 0.0098\,(\text{age})$
				r = 0.123 SEE = 1.024

*KCO = DL_{CO}/alveolar volume (BTPS).

TABLE 9

RELATIONSHIP OF PULMONARY DIFFUSING CAPACITY FOR CARBON MONOXIDE WHILE BREATHING AIR AND FORCED VITAL CAPACITY, BY SEX

FVC (liter)	Men DLco (ml/min/mm Hg)			Women DLco (ml/min/mm Hg)		
	No.	Mean	SD	No.	Mean	SD
1.0–1.9	–	–	–	8	12.10	2.51
2.0–2.9	10	17.95	4.27	41	16.56	3.44
3.0–3.9	35	21.93	5.08	22	21.65	2.51
4.0–4.9	18	27.51	5.12	1	27.40	
5.0–5.9	6	31.92	1.84			
6.0–6.9	1	28.30				

able as to why these values tended to be less unless this is the case in general populations. Other factors might be difference in smoking habits or small lung volumes as had been noted for this general population (24). Most values reported in the literature have been for selected populations.

When the Kco and DLco were related to various symptoms such as phlegm production, wheezing in chest, or degrees of breathlessness, Kco showed more marked decreases than DLco with increase in symptoms of wheezing in the age group 45 years and older in men and women.

Breathlessness, on the other hand, showed this relationship for men only. It appeared that the symptom of breathlessness might be less reliable in women than in men. A higher prevalence of breathlessness in women as compared with men has been reported previously by Ferris and Anderson (19), Huhti (25), and Payne and Kjelsberg (26), which tends to support this observation.

The relationships of DLco to simple tests of pulmonary function are shown in table 9 for men and women. The values for the various tests have been separated into categories of volume. The DLco in the subjects with those characteristics are tabulated against them. It is apparent, when lung volumes or size are taken into account, in this instance reflected by the FVC, that there was virtually no difference in DLco between normal men and women, or within a sex category. There was an increase in DLco with increase in FVC. Similar but less dramatic association was seen with FEV_1, and peak expiratory flow, as one would expect. showed the poorest association. These data indicate that when comparative studies are made, the size or lung volumes of the two groups should be taken into account. In instances where there is significant disease the ratio of the observed value to a predicted value might be more useful, as has been suggested by Gaensler and Wright (27).

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RESUMEN

El fumar cigarrillos y el factor de transferencia pulmonar (capacidad de difusión)

El fumar cigarrillos causó una reducción en la capacidad de difusión de los pulmones para el monóxido de carbón y una reducción en el coeficiente de difusión del monóxido de carbón. Esto implica que el fumar cigarrillos debería ser considerado en ecuaciones de predicción. La reducción en la capacidad de difusión aparentemente fué debida a un cambio en el volumen de sangre de los capilares. Esta podría ser la razón de los cambios reversibles observados en ex fumadores de cigarrillos. Los componentes de la membrana cambiaron más con la edad. Se desarrollaron formulas de predicción para la capacidad de difusión para el monóxido de carbón para el coeficiente, capacidad de difusión del volumen alveolar, basados en la edad y altura, y paquetes fumados durante la vida.

RESUME

Habitude de fumer la cigarette et facteur de transfert pulmonaire (capacité de diffusion)

L'habitude de fumer la cigarette a entraîné une réduction dans la capacité de diffusion pour le monoxyde de carbone au niveau du poumon, ainsi que la diminution du coefficient de diffusion du monoxyde de carbone. Ceci implique que l'habitude de fumer la cigarette devrait être considérée dans les équations de prédiction. La réduction dans la capacité de diffusion

semble être due à une modification dans le volume du sang dans les capillaires. Ceci pourrait intervenir pour expliquer certaines des modifications réversibles observées chez les anciens fumeurs de cigarettes. La composante de membranes a davantage changé avec l'âge. Des formules de prédiction ont été développées pour la capacité de diffusion pour le monoxyde de carbone, pour le rapport entre la capacité de diffusion et le volume alvéolaire, basées sur l'âge, sur la taille, et sur le nombre de paquets de cigarettes fumés pendant la durée de la vie.

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