Spirometric data and penetration of particles to the alveoli

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ABSTRACT The percentage retention at 24 hours of 4 μm Teflon particles, aerodynamic diameter about 6 μm , was studied in 29 healthy male volunteers. The particles were inhaled at 0.5 l/s with maximally deep breaths. The 24 hour retention correlated significantly with FEV₁ and FVC and persisted when the subjects were divided into different categories according to profession and smoking habits. The results suggest that for exposure to metal particles at a size where impaction is an important deposition mechanism—that is, particles larger than a few microns—workers with large FEV₁ values may run a greater risk of receiving systemic toxic effects than those with small FEV₁ values.

The elimination of intact particles that have settled in the alveolar part of the lung is extremely slow, the most of such particles being removed with a half time in the order of magnitude of one to several years.¹⁻³ The particles are cleared not only by the removal of whole particles but also by dissolution. Dissolution is also an important elimination mechanism for metal particles usually considered insoluble.⁴⁻⁸ For many aerosols of metal particles the fraction deposited in the alveolar part of the lung will enter the bloodstream and may cause systemic toxic effects. For example, less soluble lead particles have been shown to enter the bloodstream rather quickly.⁹ Particles deposited on the tracheobronchial tree are transported by the mucociliary escalator or coughing to the larynx where they are swallowed. As most metals are absorbed into the bloodstream from the gastrointestinal tract to a small degree, less soluble metal particles that are deposited in the tracheobronchial tract will not cause systemic toxic effects.

In an earlier study we found that the 24 hour lung retention of inhaled 4 μm (aerodynamic diameter 6 μm) Teflon particles varied considerably within a group of 10 healthy men, but that the variation of the 24 hour retention was small for each individual.¹⁰ The aim of the present study was to investigate whether there is a correlation between the retention of these Teflon particles after 24 hours and lung function tests such as forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC).

Subjects and methods

Of the 29 healthy men studied, 11 were students and people working at the university and are referred to as "students." Alveolar retention data on 10 of the 11 students have been published previously.¹⁰ Since duplicate measurements were performed in those 10 men, mean values of the two measurements were used. The other 18 men were workers from a battery factory. Table 1 shows age, smoking habits, and spirometric data. Owing to the small number of subjects, two ex-smokers who had stopped smoking two and 22 years before the investigation were included in the non-smoking group. This is justified by the fact that tracheobronchial clearance improves for former smokers three months after they stop smoking and clearance becomes similar to that of non-smokers.¹² Of the 10 smokers, two were pipesmokers, one a combined pipe and cigarette smoker, and seven cigarette smokers. Tobacco consumption expressed as cigarettes a day was: one smoker (3 cigarettes), two smokers (15) and seven smokers (20).

The Teflon particles were produced and labelled with ¹¹¹In (half life 2.83 days) by a spinning disc technique.^{13 14} The students inhaled 4.2 $\pm$ 0.7 and 4.3 $\pm$ 0.8 μm (mean $\pm$ SD) Teflon particles and the workers 3.9 $\pm$ 0.4 μm particles. For details of the exposure technique see Camner and Philipson.¹⁰ The subjects inhaled the test particles with 10-20 maximally deep inhalations. The flow rate was registered on a recorder and by looking at the recorder, the subjects could inhale with a constant flow at about

Table 1 Personal and spirometric data.

	Students		Workers			
	Non-smokers (n = 11)		Non-smokers (n = 8)		Smokers (n = 10)	
	Mean	(SD)	Mean	(SD)	Mean	(SD)
Age (years)	26	(7)	47	(11)	46	(11)
Weight (kg)	76	(6)	82	(11)	75	(10)
Height (cm)	181	(5.6)	172	(6.9)	176	(7.1)
FEV ₁ (l)	5.0	(0.65)	4.1	(0.86)	4.2	(0.93)
FEV ₁ (% of predicted*)	103	(9.8)	111	(16.7)	108	(13.3)
FVC (l)	6.0	(0.75)	5.1	(1.13)	5.5	(0.81)
FVC (% of predicted*)	102	(10.0)	104	(17.7)	107	(9.1)

*According to the formula of Berglund *et al.*¹¹

0.51/s, as trained before exposure. Immediately after inhalation of the test aerosol and after 24 hours (24–26 hours) after the inhalation the radioactivity in the lungs was measured with a profile scanner with two 3 × 2 inches NaI crystals fitted with collimators.^{13 14}

FEV₁ and FVC were measured on the same day as

the inhalation of the test particles with a Vitalograph spirometer with the subject in a standing position.

Results

In the figure the FEV₁ values are plotted against the percentage retention at 24 hours for the students, non-

Correlation between 24 hour lung retention of ¹¹¹In labelled 4 µm Teflon particles in percentage of first observed value and FEV₁. (a) = Non-smoking "students," (b) = non-smoking workers, (c) = smoking workers, (d) = (a) + (b), (e) = (b) + (c), and (f) = (a) + (b) + (c).

Table 2 Correlations between spirometric values (FEV_1 and FVC) and percentage particle retention at 24 hours.

		"Students" (a) (n = 11)	Workers		all non-smokers (a + b) (n = 19)	all workers (b + c) (n = 18)	all subjects (a + b + c) (n = 29)
			Non-smokers (b) (n = 8)	Smokers (c) (n = 10)			
FEV_1 (l)—retention at 24 hrs (%)	Coefficient of correlation (r)	0.76	0.61	0.38	0.75	0.48	0.64
	Slope, %/l	14.1	8.6	4.5	11.7	6.3	9.0
	p Value, diverge from zero	$p < 0.01$	$0.1 < p < 0.2$	$0.2 < p < 0.4$	$p < 0.001$	$p < 0.05$	$p < 0.001$
	1% coincidence interval	(0.89–27.3)	—	—	(4.46–18.94)	—	(3.18–14.1)
FVC (l)—retention at 24 hrs (%)	Coefficient of correlation (r)	0.49	0.60	0.42	0.62	0.52	0.57
	Slope, %/l	7.8	6.4	5.7	8.2	6.2	7.6
	p Value, diverge from zero	$0.1 < p < 0.2$	$0.1 < p < 0.2$	$0.2 < p < 0.4$	$p < 0.01$	$p < 0.05$	$p < 0.001$
	1% coincidence interval	—	—	—	(0.95–15.37)	—	(1.80–13.1)

smoking workers, smoking workers, all non-smokers, all workers, and all subjects. The correlation coefficients, slopes, and p values for the various groups shown in the figure and corresponding data on the correlation between FVC and the percentage particle retention at 24 hours are shown in table 2. Both FEV_1 and FVC correlate significantly with the 24 hour retention for all non-smokers, all smokers, and all subjects ($p < 0.05$). For the students there is also a significant correlation between FEV_1 and the 24 hour retention. There is an overall tendency for a better correlation between FEV_1 and retention than between FVC and retention.

Discussion

Particles deposited in the tracheobronchial tract in some animal experiments have been retained for more than 24 hours. For rabbits, 71% of intratracheally administered Teflon particles deposited at the first bifurcation cleared with a mean half time of 39.0 hours.¹⁵ Using the same inhalation exposure technique as in the present study, however, Camner and Philipson found a similar retention after one and three days,¹⁰ suggesting that there could have been no large fractions which cleared with a half time of about 40 hours. The 24 hour retention represents particles that are cleared slowly from the lung, probably those deposited in the alveolar or non-ciliated part of the lung—the respiratory bronchioli, alveolar ducts, and alveoli.

With the rather large particles inhaled with maximum deep inhalation at 0.5 l/sec, almost all the particles which reached the non-ciliated part of the lung should have been deposited.¹⁶ As the dead space volume is small compared with the inhaled volume (about 5% when 3 l is inhaled), the percentage 24 hour retention should be almost independent of the inhaled volume. Assuming a pause of 2 s after the inhalation

of 4 μ m Teflon particles at 0.5 l/s the percentage of particles deposited in the alveoli is calculated to differ by only 1% between an inhaled volume of 3 l and one of 6 l, using the lung model and equations of the Task Group on Lung Dynamics.¹⁶ Thus differences in inhaled volume have probably not affected the 24 hour retention values in our study to any great degree.

The correlation between the spirometric values and 24 hour retention was studied in a heterogeneous group of healthy male volunteers. When the subjects were divided into groups by profession and smoking habits, all showed similar trends. The smokers had the lowest correlation between the spirometric values and retention. In this group a lower correlation is expected since long term smoking can impair mucociliary transport^{17,18} and this 24 hour retention might include particles in the tracheobronchial tract. Mucociliary clearance has been found to decrease with age.^{19,20} The students in our study were younger than the smoking and non-smoking workers. Nevertheless, there was a similar correlation between FEV_1 or FVC and the 24 hour retention in all three groups. Furthermore, the retention at FEV_1 values of 4 l (estimated from the regression lines) were 39%, 40%, and 43% in the students, non-smoking workers, and smoking workers respectively. Thus it is not probable that age differences have affected our results to any substantial degree.

For the relatively large test particles (ca 6 μ m aerodynamic diameter) inhaled at 0.5 l/s, impaction is an important mechanism for the deposition in the tracheobronchial tract.¹⁶ This implies that subjects with larger bronchial diameters will have a larger fraction deposited in the alveolar part of the lung because the air velocity in the bronchi decreases with increasing diameter. As FVC and especially FEV_1 correlate positively with the dimension of the bronchi, the positive correlation between FEV_1 or FVC and retention is not unreasonable. In patients with airways obstruc-

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tion (and reduced FEV₁) 5 µm polystyrene particles and 3 µm (aerodynamic diameter) albumin particles penetrate the tracheobronchial tract to a lesser degree than in healthy subjects.²¹⁻²⁵ Garrard *et al* studied aerosol deposition in 13 healthy non-smoking subjects using 8.1 µm aerodynamic diameter Fe₂O₃ particles labelled with ^{99m}Tc.²⁶ FEV% correlated with the 24 hour retention (r = 0.45) but FEV₁ did not (r = 0.21). The lack of significant correlation between FEV₁ and the 24 hour retention might be explained by the small 24 hour retention, 12.8 ± 8.6% (mean ± SD) in their study.

In this study and in the study by Camner and Philipson,¹⁰ using the same particles and inhalation pattern, the 24 hour retention varied largely among subjects. As the retention values were reproducible,¹⁰ the differences must be due to individual factors. In real life the amount of particulate material deposited in the alveolar part of the lung depends inter alia on the amount of air inhaled, on the particulate concentration in the air, on whether mouth or nose breathing is used, and on the fraction of particles deposited in the whole lung. Nevertheless, the large differences in the percentage 24 hour retention suggest that under similar conditions, subjects with high retention values will also have a larger amount of deposited particles in the alveoli than subjects with low retention values. This is true when inhaled aerosols consist of relatively large particles, greater than about 2 µm. Impaction is an important mechanism for deposition in the tracheobronchial tract for such particles.¹⁶ In our study artificial conditions were used but in working situations, where tidal volumes are large compared with the dead space, the 24 hour retention will probably not differ much from that in our experiment.

The high correlation between the FEV₁ values and the 24 hour percentage retention suggests that workers with large FEV₁ may be at higher risk of systemic toxic effects from metal particles than their colleagues with lower FEV₁. In epidemiological studies it would be of value if groups with various degrees of exposure had similar FEV₁ values.

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