Inhaled particle deposition and body habitus

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Abstract

As a result of the intrapleural pressure gradient that exists in the human lung, both ventilation and particle deposition increase from apex to base. Since the intrapleural gradient varies with the height of the subject, it was decided to compare regional particle deposition in tall, short, and obese subjects to ascertain whether it was influenced by height and weight. Surprisingly, deposition in the vertical plane was not significantly influenced by the height of the subject when corrected for ventilated lung volume. In addition, it was shown that in obese subjects there was increased deposition in the middle zones relative to the apices and bases. This finding persisted after correction for ventilated lung volume and differential attenuation resulting from non-uniform thickness of the fat layer in the obese subject's chest. In the tall and short groups there was a consistent pattern in the concentric deposition of particles with there being a gradient from the central or hilar region to the periphery of the lungs, with the latter showing the most deposition.

It has been claimed that the likelihood of uranium miners developing bronchial carcinoma and of chrysotile asbestos miners developing radiographic evidence of asbestosis varies according to bodily habitus.^{1,2} In both instances those of short stature were thought to be at greater risk.

Gerrity *et al* using a mathematical model predicted that the smaller dimensions of the airways of short people result in greater particle deposition in the large airways.³ Thus the bronchial epithelium of short subjects may be exposed to a greater concentration of carcinogenic or otherwise toxic inhaled particles than that of their taller coworkers. Becklake *et al* speculated that it is the shorter trachea of short asbestos miners that predisposes them to develop asbestosis.²

The deposition of inhaled particles is influenced by many factors. These include the size and density of the particle, its hygroscopicity and electrical charge, posture, exercise, breathing pattern, and the geometry of the airways. Regional differences in particle deposition throughout the lungs have been shown to occur and depend in the main on the same factors that influence regional ventilation.⁴⁻⁸ Prominent among the factors determining regional ventilation is apex to base intrapleural pressure gradient.^{6,9} This is greater in tall individuals than those of shorter stature. Morbid obesity has also been shown to alter regional ventilation. Thus Holley *et al* showed decreased basal ventilation and relative redistribution to the upper zones in obese subjects.¹⁰

Thus differences in bodily habitus might affect inhaled particle deposition both through inherent differences in airways geometry and through differences in regional ventilation. We decided, therefore, to examine the deposition of inhaled particles in subjects grouped according to height and body weight.

Methods

SUBJECTS

The study included 27 subjects, 20 of whom were normal volunteers whereas seven were patients with morbid obesity. The protocol and consent form for the study were approved by the Health Sciences Standing Committee on Human Research of the University of Western Ontario. All subjects freely gave their informed consent.

The subjects were divided into three groups; tall ($n = 10$), short ($n = 10$), and obese ($n = 7$). The physical characteristics of the three groups are summarised in table 1. The mean height of the short group was significantly less than that of the tall group ($p < 0.001$) and the obese group was significantly heavier than the other two ($p < 0.001$). None of the subjects was a smoker and all denied symptoms and previous illnesses suggesting any underlying chest disease.

PARTICLE DEPOSITION AND REGIONAL VENTILATION

Subjects underwent paired studies of ventilation with ¹³³Xe followed by particle deposition with ^{99m}Tc sulphur colloid and administered to subjects as previously described.⁶ Aerosol particle size was measured at the mouth using an Anderson sampler that showed the particles to have a mass median

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Table 1 Subject details

	Short (n = 10)	Tall (n = 10)	Obese (n = 7)
Men:women	2:8	5:5	3:4
Age (y ± ISD)	31.3 (± 11.2)	28.8 (± 5.16)	43.4 (± 12.3)
Height (cm ± ISD)	156.1 (± 6.13)	179.1 (± 7.93)	164 (± 9.14)
Weight (kg ± ISD)	54.4 (± 11.0)	68.1 (± 26.6)	148.2 (± 36.9)

diameter of 0.71 microns with a geometric standard deviation of 1.33.¹¹ Subjects were required to breathe at tidal volume through a mouthpiece while wearing a nose clip. Minute ventilation was measured with a Wright spirometer. The aerosol mixture was breathed for a period of 120 seconds. Immediately afterwards, a posterior scintigraphic image of the chest was obtained using a gamma camera on line to a computer system. The scan was repeated 24 hours later to determine what proportion of the inhaled activity remained and had, therefore, been deposited beyond the mucociliary escalator in alveoli and non-ciliated airways.

¹³³XE STUDIES OF LUNG VOLUME

Subjects breathed through a closed system from a 15 l reservoir to which had been added 15 to 20 mCi ¹³³Xe. Rebreathing continued for 300 seconds during which time the FIO₂ and PCO₂ were maintained at normal levels. In all subjects lung activity approached equilibrium well within the period of rebreathing. Images were recorded continuously at a framing rate of 12/min in the posterior view with the subjects sitting with their backs against the face of the gamma camera.

DATA ANALYSIS

The scintigraphic data were presented on an interactive video screen in a 64 × 64 matrix. The lung activity in each five second frame of the ¹³³Xe study was displayed graphically and a frame selected at a point where equilibrium was approached. In practice the frame at 100 seconds was commonly selected for the equilibrium (regional lung volume) image. This technique differs from our previous method⁶ in which a single exponential function was fitted to the initial portion of the washin curve in order to predict the activity at equilibrium free from the complicating effect of ¹³³Xe in the fat of the chest wall.¹²

The ^{99m}Tc image obtained immediately after inhalation of the radioaerosol was then brought to the screen and its position adjusted so as to coincide precisely with that of the ¹³³Xe equilibrium image. Perfect registration of the two images was achieved by aligning radioactive markers placed on the body surface during imaging when the two images were

superimposed. The ^{99m}Tc particle deposition image was then divided by the ¹³³Xe lung volume image to give a particle distribution image corrected for ventilated lung volume.

Three horizontal (upper, middle, and lower) and three radial (central, intermediate, and outer) regions of interest were drawn for each lung as described previously and illustrated in fig 1.⁶ The regions were superimposed on the corrected particle distribution image. The index of deposition for each region was obtained as follows:

$$\text{IDn} = \frac{\text{Activity in region n}}{\text{Activity in total lung}}$$

Again the technique differs slightly from that which we used previously in which IDn was derived after dividing the particle deposition image by the lung volume image region by region rather than pixel by pixel.⁶ Comparison of indices of deposition calculated in the same subjects by the two methods showed that neither this nor the previous modification in the method of analysis produced any significant difference and the improvement in speed and convenience of the modified method of analysis was judged worth while.

SPIROMETRY AND ANTHROPOMETRY

Spirometry was performed on all subjects and the results are shown in table 2. Standard posteroanterior and lateral chest radiographs were obtained and tracheal dimensions were estimated using the methods of Breatnach *et al*¹³ and Becklake *et al*.² Results are reported in table 3.

Ultrasound scans were performed to measure the thickness of chest wall fat.

CORRECTION FOR FAT ATTENUATION

Two methods were used to gain knowledge of the

Figure 1 Method of dividing lung fields into central, intermediate, and outer zones and into upper, mid, and lower zones (posteroanterior view). Lower limit of lung was defined by horizontal line drawn at upper limit of diaphragmatic dome. Vertical height was then divided equally so as to form three zones. Hilum was located at midpoint of vertical height. Central, intermediate, and outer zones were defined by dividing distance at limit of lower zone as shown.

Table 2 Details of forced vital capacity (FVC), minute ventilation (Vm), and tidal volume (Vt)

	Short (n = 10)	Tall (n = 10)	Obese (n = 7)
FVC (l)	3.66	5.3	3.55
(± 1SD)	(± 0.6)	(± 1.1)	(± 0.9)
Vm (l)	10.0	11.4	11.4
(± 1SD)	(± 2.4)	(± 2.12)	(± 4.4)
Vt (l)	0.757	0.858	0.814
(± 1SD)	(± 119)	(± 215)	(± 122)

effect of attenuation by chest wall fat of emergent gamma rays of ^{133}Xe and $^{99\text{m}}\text{Tc}$ and consequent distortion of regional particle deposition results.

Figure 2 shows how a paraffin wedge was interposed between the posterior chest wall of obese subjects and the gamma camera in such a way as to simulate a relatively even thickness of fat over the whole of the chest wall. $^{99\text{m}}\text{Tc}$ and ^{133}Xe images were obtained with and without the wedge in place and the regional indices of deposition calculated as before. The results are shown in fig 3. The effect of a wedge of paraffin wax of known dimensions was measured by recording gamma camera images with and without the wedge in place (fig 2). The other method depended on applying a correction for the measured fat thickness using a figure for human fat for the half value layer.

RADIATION DOSE

Radiation dose received by the subjects was calculated at about 0.12 rem comprised of 0.05 rem for each of the ^{133}Xe and $^{99\text{m}}\text{Tc}$ scans and 0.02 rem for the radiographs. All values are in effective dose equivalents.

STATISTICAL SIGNIFICANCE

Statistical differences between the various sets of observations were determined using the Student *t* test. Only when *p* was 0.05 or less were the differences accepted as significant.

Results

SPIROMETRY AND BREATHING PATTERNS

Table 2 shows the mean forced vital capacity (FVC), minute ventilation, and tidal volumes for all groups of subjects. FVC was significantly lower in the short and the obese than in the tall. Variation in minute volume and tidal volume did not reach significance.

Table 3 Tracheal measurement

	Short	Tall	Obese
Glottis—right upper lobe bronchus (cm) ²	13.7 (± 1.2)	14.6 (± 1.29)	11.6 (± 1.3)
Clavicle—carina (cm) ²	7.7 (± 1.3)	8.3 (± 0.7)	6.2 (± 0.9)
Tracheal width AP radiograph (mm) ¹³	16.4 (± 1.6)	16.8 (± 2.0)	17.1 (± 1.1)
Tracheal width lateral radiograph (mm)	17.7 (± 1.9)	19.0 (± 2.5)	18.3 (± 2.3)

Figure 2 Diagrammatic representation of fat distribution (lateral view) in obese subjects with wax wedge in situ.

TRACHEAL DIMENSIONS

Tracheal dimensions are summarised in table 3. No significant differences exist between tall and short individuals. When the method of Becklake *et al* was used, glottis to right upper lobe bronchus lengths were significantly longer for both tall and short than for the obese ($p < 0.01$).² Tracheal width by the method of Breatnach *et al* gave a mean value for the short subjects that was smaller than that for the tall and for the obese but the differences did not reach significance.¹³

REGIONAL PARTICLE DEPOSITION

All individuals and all three groups showed the expected gradient of regional particle deposition increasing from the apex to the base as seen in fig 4. Lower zone deposition was significantly greater than upper zone deposition in each group ($p < 0.001$). The obese subjects showed relatively more deposition in the middle zone and less in the lower zone than the tall and short subjects. In tall and short individuals there was a gradient of increasing deposition from the central through the intermediate to the outer zones. Deposition at the periphery was significantly greater than centrally ($p < 0.01$) (fig 5). In the obese subjects, however, deposition was greatest in the intermediate zone.

CHEST WALL FAT

In the obese fat thickness on the posterior chest wall varied from 4.2 (± 0.9 SD) cm at the apex to 6.6 (± 1.3 SD) cm over the base. By contrast, fat thickness in the tall and the short was uniform over the posterior chest wall.

CORRECTION FOR NON-UNIFORM FAT DISTRIBUTION IN THE OBSE

With the paraffin wax wedge in place the increased deposition in the middle zone apparently became

Figure 3 Indices for deposition in obese subjects with and without wedge in situ (vertical plane: apex to base).

even more pronounced with the index of deposition increasing from 106 ± 10.3 SD to 120 ± 9.7 SD ($p < 0.001$). The index of deposition at the base remained unchanged and that at the apex fell by an insignificant amount.

Correction of the $^{99m}\text{Tc}/^{133}\text{Xe}$ image for fat attenuation using the measured fat thickness for each horizontal zone using the half value layer for human fat again exaggerated the mid zone deposition but the lower zone index of deposition remained slightly but not significantly higher than that of the middle zone. The relative shift of particle deposition to the middle zone in the obese may be assumed to be a real phenomenon and not an artifact caused by the non-uniform distribution of chest wall fat frequently seen in the obese.

RESIDUAL ACTIVITY AT 24 HOURS

Lung activity was calculated for all subjects from the scan taken 24 hours after inhalation of the ^{99m}Tc aerosol after correction for radioactive decay in the interim. Over 90% of the original activity remained

Figure 4 Indices for zonal deposition in short, tall, and obese subjects (vertical plane: apex to base).

in the lungs in all subjects indicating that this proportion of deposited particles had been deposited distal to the mucociliary escalator.

Discussion

The expected pattern of particle deposition—namely, an increasing deposition per unit volume of lung from apex to base—was seen in tall and short

Figure 5 Indices for zonal deposition in short, tall, and obese subjects (horizontal plane: hilum to periphery).

normal subjects. The same overall pattern was present in the obese subjects but differed significantly in the relative diversion of deposition to the middle zone.

The pattern of predominant deposition of particles in peripheral rather than central zones in normal subjects differed from that previously reported from our group.⁶ In both the present and the previous studies the nature of the particles and their size was essentially identical, and in both instances more than 90% of deposition took place distal to the mucociliary escalator.

Some of the raw data from the original study were available on magnetic tape and it proved possible to analyse the data from several individuals both by the original method and by the slightly modified method reported here. Unfortunately this did not show the reason for the discrepancy. The original studies for the most part still gave regional indices of deposition favouring the central zones, whether they were analysed by the original or the present method. Similarly the recent studies gave consistent results differing by no more than 3% according to the method of analysis. This seems to exclude a transcription error whereby central zone data and outer zone data might have been transposed at a late stage in the previous work. Higher respiratory rates in the previous study might have explained the difference but breathing patterns were similar in the two studies.

Two potentially important modifications have taken place in the apparatus used to generate and deliver the radioaerosol over the eight years separating the two studies. The settling bag is no longer interposed between the nebuliser and the mouthpiece. Air flow through the nebuliser, previously continuous, is now pulsed to deliver a bolus of radioaerosol to coincide with the patient's inspiratory effort. A limited study in which aerosol was administered to the same subject first in a continuous and then in a pulsed fashion failed to show any difference in regional deposition. Thus the discrepancy remains unexplained. We believe that since the periphery of the lung contains more alveoli per unit volume than does the central zone the deposition of submicron particles should be greater peripherally.

We failed to show any significant difference in pattern of particle deposition between tall and short subjects. The apex to base gradient in regional index of deposition was greater in the tall than in the short, but the difference did not achieve statistical significance. It may be that any effect of height on the incidence of bronchial carcinoma in uranium miners¹ or asbestosis in chrysotile workers² is due to factors other than the preferential deposition of particles at some particular site in the lung.

If the observations of Archer¹ and Becklake *et al*² are substantiated and the association between short

stature and disease is confirmed alternative explanations such as altered clearance rates in short individuals or concentration of cleared material at certain sites may be responsible. It should also be observed that the present studies were carried out at tidal respiration in the sitting position. It is quite possible that particle deposition would have been different under working conditions when pattern and depth of respiration and posture may differ significantly.

In the case of asbestosis it is important to consider that the short stature and excess fat of certain of the miners may have caused an altered appearance and hence overreading of their chest radiographs.¹⁴ In the present study the apparent difference in tracheal dimensions between the obese and both tall and short subjects may be artifactual since it seems unlikely that obesity per se would cause alterations in tracheal anatomy. Moreover, precise definition of the bifurcation may have been more difficult in the obese and excess abdominal fat may have interfered with diaphragmatic excursion during inspiration hence lessening the normal descent of the trachea.

The question of potential artifact affects several aspects of the present study and illustrates the difficulty in answering the apparently simple question "Does bodily habitus alter regional deposition of inhaled particles?" The attenuation of emergent gamma rays, and particularly the differential attenuation of the 80 keV emission of ¹³³Xe and 140 keV emission of ^{99m}Tc has already been discussed. There could, however, be an additional effect due to the tangential pathway of gamma rays originating in the periphery of the lung through body wall fat as opposed to the shorter pathway of gamma rays originating centrally. The phenomenon might be analogous to that in which a pleural effusion appears to rise in the axilla on a chest radiograph because of the greater attenuation of peripheral x rays. Could such a phenomenon explain the shift to intermediate radial zone deposition in the obese subjects? Were this so, it would require a greater effect on the higher energy ^{99m}Tc emission than that on ¹³³Xe and as such this appears unlikely.

When the equilibrium ¹³³Xe lung image was obtained there would have been ¹³³Xe activity in the chest wall overlying the lung. This would have been interpreted as coming from the lung, and because of its nearness to the gamma camera the artifact it created would have been larger than anticipated from the concentration of ¹³³Xe alone. In both tall and short subjects the chest wall thickness, and particularly the fat thickness, was relatively uniform from apex to base although relative to lung thickness at the same level was greatest at the apex. Fat thickness increased from above downwards in the obese. The effect of this would have been to increase apparent lung volume at the base and hence would

tend to obscure the observed increased particle deposition in the lower zones. It is thus most improbable that ^{133}Xe in the chest wall could explain the shift of particle deposition to the middle zones. This statement is supported by the negligible differences in regional deposition indices when the lung volume image was calculated from the first few frames of washin¹² rather than observed directly at equilibrium.

Artifact could also arise from ^{133}Xe and $^{99\text{m}}\text{Tc}$ activity in one lung zone being attributed to the adjacent zone because of scattering of the emergent gamma rays on their pathway to detection in the gamma camera. Because of the pulse height analyser windows used, this scattering effect would be more pronounced for ^{133}Xe (lung volume image) than for $^{99\text{m}}\text{Tc}$ (deposition image). Nevertheless, it is improbable that this phenomenon could have any systematic effect in producing or masking real regional differences when comparisons were made between individuals studied in exactly the same fashion.

We therefore conclude that the potential artifacts inherent in the technique of investigation are insufficient to be responsible for or to mask the gradients of particle deposition per unit volume of lung which increase from upper to lower horizontal zones and from inner to outer radial zones. These are present in normal subjects regardless of height. In the obese the underlying pattern of particle deposition is modified by relative diversion of particles to the vertical horizontal zone and the intermediate radial zone, at least at tidal breathing.

The study does not provide evidence for a mechanism explaining the suggested greater risk of developing disease related to the inhalation of toxic particles in workers of short stature. It may, however, be worth while to look for any difference in the

incidence of such diseases between obese workers and their non-obese colleagues.

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