

INHALATION RISK AND PARTICLE SIZE IN DUST AND MIST*

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Respiratory Absorption and Elimination

The human respiratory system has long been known to filter the air passing through it. Lord Lister demonstrated that putrefactive organisms were not present in air passing out of the lungs and in 1869 Tyndall (1881) found that air expelled towards the end of a breath failed to produce scattered light near the focus of a light beam and caused the white track of the beam, due to atmospheric dust, to disappear. These early observations are incomplete: as a rule, when dusty air is inhaled, only a proportion of the dust is retained in the body while the rest is expelled. The particles which are left behind deposit in different regions of the breathing tract according to their size. The coarsest get trapped in the nose in normal breathing,

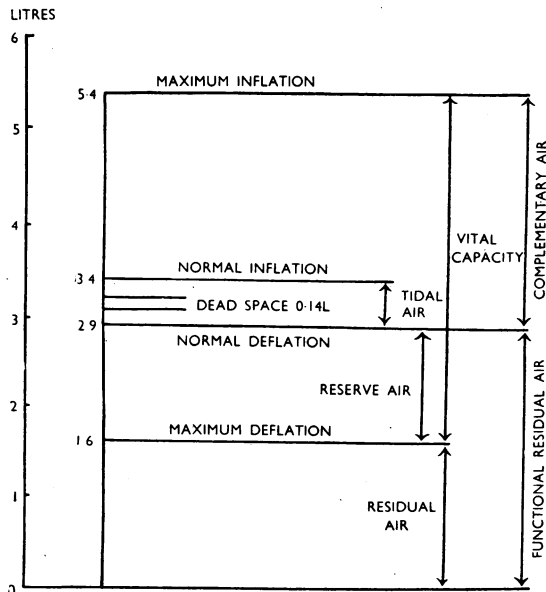


Fig. 1.—Normal volume and nomenclature of human lungs.

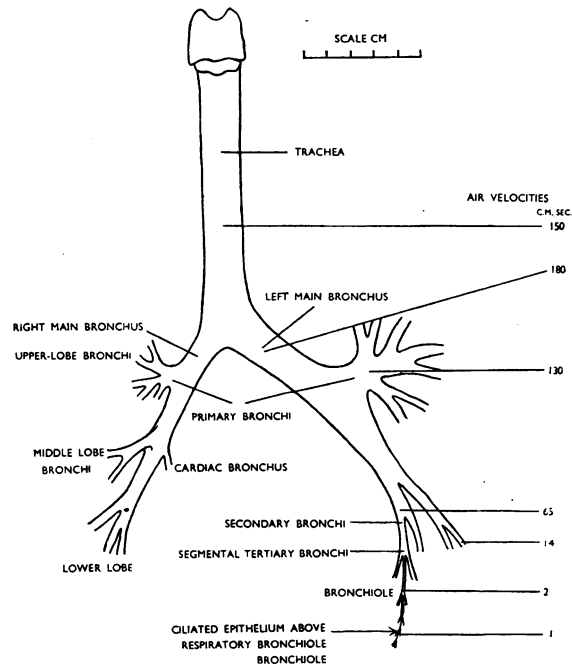


Fig. 2.—Scale diagram of respiratory channels of human lung.

which is always through the nose in contaminated atmospheres, save during heavy exercise. Very fine particles penetrate deeply into the lungs and a considerable number are exhaled.

Fig. 1 is a diagram (based on measurements of Aslett and others, 1939) which shows to scale the volumes of air associated with respiration and explains the usual nomenclature. It can be studied in conjunction with fig. 2, a scale diagram of the human lungs, and the Table, which gives dimensions. Fig. 3 and 4 illustrate the nasal passages.

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The trachea, bronchi, and bronchioles are lined with a continuous ciliated epithelium (fig. 5) which terminates at the entrance to the respiratory bronchioles. The cilia engage with a film of mucus which they keep in steady upwards movement at a rate rising to 3 or 4 cm. per minute in the trachea. Peristaltic movements and coughing may cooperate to provide a mechanism which has been shown by Barclay and others (1942) to be very competent in lifting dust particles up to the pharynx, when they can be swallowed, sneezed out, or expectorated. It is less effective for liquids, which may slip down into the alveoli, though fine mist droplets should be eliminated satisfactorily if the concentration is low. The ciliary movement is ineffective if the mucus is not of the right consistency owing to illness or pharmacological action.

Particles of solid which reach the alveoli are passed into the lymphatic system or ingested by mobile phagocytes which may transport them to the mucus escalator. This process has been reviewed by Robertson (1941).

TABLE
DIMENSIONS OF THE HUMAN LUNG

Part of Lung	Number	Length	Internal Diam.	Volume
Trachea ..	1	12 cm.	1.4-2.0 cm.	14.3 cm. ³
Main bronchi ..	2	2.5-5	1.0-1.6	7.1
Primary bronchi ..	12	3	0.4	4.5
Secondary bronchi ..	100	1.5	0.2	4.6
Tertiary bronchi ..	770	0.5	0.15	7.0
Bronchioles ..	54,000	0.3	0.1-0.2	4.5
Respiratory bronchioles ..	110,000	0.15	0.05-0.1	33
Alveolar ducts ..	26,000,000	0.02	0.02	164
Alveolar sacs ..	52,000,000	0.03	0.03	4,320

A further protective factor, purely physical, was suggested by Aitken (1883-4). Air entering the breathing channels is cooler than the body and relatively dry. A force of thermal repulsion therefore exists to keep particles away from the walls of the channels, and this is supplemented by a continual stream of water molecules, evaporating from the surfaces, which bombard dust particles and tend to drive them back. Thus the retention of fine particles in the lungs would be enhanced by high temperature and humidity.

Site of Action

The respiratory tract is protected with remarkable efficiency against inert, dry solids deposited anywhere save in the very depths of the lung. Elimination is less effective from these alveolar regions, of considerable surface area (some 15m²), which constitute, anatomically, the respiratory unit where oxygen absorption takes place. Liquids, or

suspensions of powder in liquid, may reach the alveoli irrespective of the location of their first contact with the walls of the breathing system. This fact, associated with impairment of the ciliary motion, may explain the occasional deaths reported from exposure to high concentrations of mists which are not highly toxic; especially is this common in the aged. High concentrations of relatively inert dust might equally be dangerous to individuals suffering from loss of function of the ciliated epithelium. Irritant dusts which are too coarsely particulate to reach the alveoli in a healthy subject might, nevertheless, penetrate so far if chemical interference with the mucous blanket should occur.

At the same time it must be remembered that serious symptoms can arise without implication of the alveoli. Water-soluble substances and gases, for example, are rapidly absorbed in the bronchi. Again, small animals can be killed with some gases which operate as systemic poisons. The lungs are unharmed but the nasal passages become inflamed, indicating the site of absorption. Other gases destroy the lungs. The difference depends on solution in the nose. If rapid, and unimpeded by accumulation of reaction products, the poison may be entirely absorbed from the inhaled air while traversing the nose. This is less likely to occur in large animals or man and shows the need for care in estimating dangers to human beings from experiments with small animals. Nevertheless, large liquid or solid particles trapped in the nose could cause local or systemic injury in man without lung damage. Thus, coarsely particulate clouds of arsenicals of the blue cross type, as used by the Germans in the world war 1914-18, produce unpleasant symptoms in the nose. A particle size of about 30 μ (microns) could be obtained by dispersing with explosive or by spraying. On the other hand fine clouds of particles below 1 μ , generated by thermal evaporation, cause acute chest pains and, incidentally, penetrate poor-quality gas masks quite readily.

Men and animals after a lifetime of exposure to wind-blown desert sand have been found to possess lungs unscarred by silicotic lesions, while a few years' exposure to particles of the same chemical constitution, which have been released from sandstone grinding-wheels or in the figuring of millstones, may be disastrous. The difference is due to particle size. Desert sands are very much coarser than the dust released by the vigorous action of tools upon sandstone.

We see, therefore, that particle size is decisive in governing the region of initial deposition in the respiratory tract but that only in certain cases can immunity from hazard be claimed on this basis.

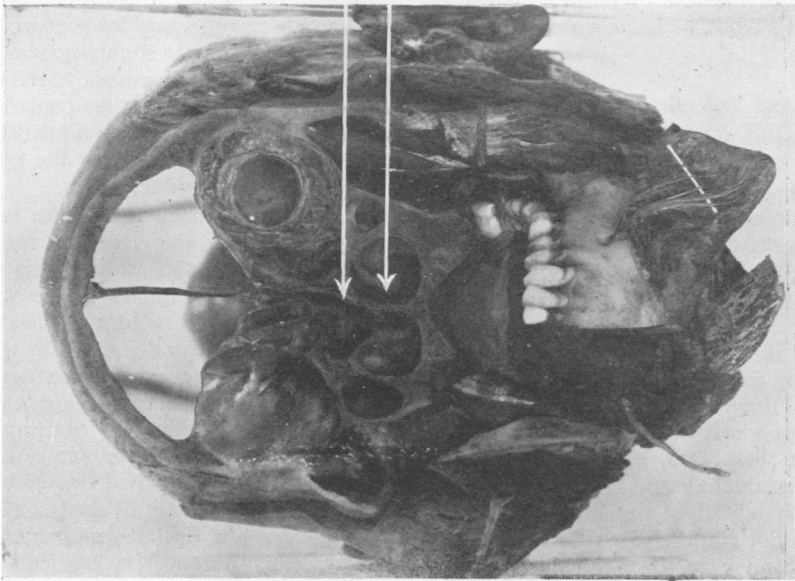


FIG. 4.—Section of human nose.

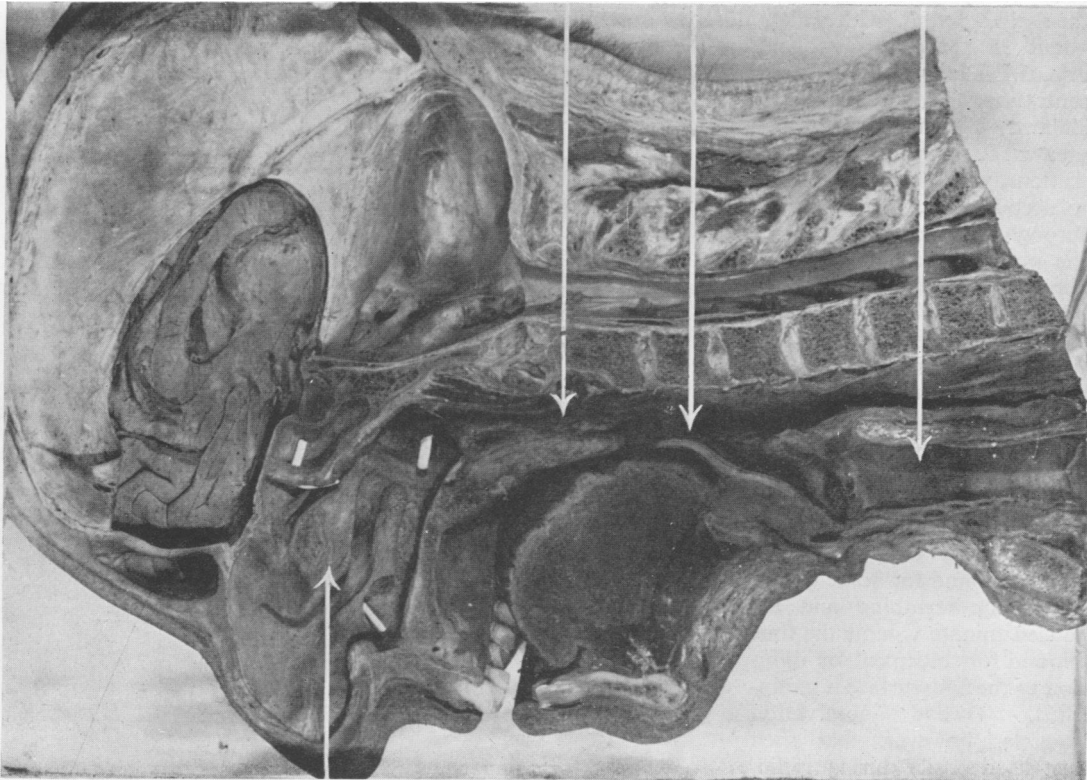


FIG. 3.—Section of human nose and pharynx.

However, an understanding of the role of particle size in a purely mechanical way is of some value in discussing inhalation risks.

Experiments on Inhalation and Retention of Dusts

Following the observations of Lister and Tyndall the dust content of exhaled air was examined more carefully by Owens (1923), using his new dust-counting apparatus. He showed how the retention of dust depended on the method of breathing. A subject breathing dusty air by normal respiration, using his tidal air, had very little dust in the reserve air (fig. 1) when it was sampled after a deep exhalation. On the other hand, if the reserve air was sampled after deep breathing for several cycles, its dust was only reduced to three quarters of the original content of the atmosphere.

The alveolar air, in the first case, was pure because the exchange between tidal air and alveolar air is mainly by diffusion with only slight mechanical mixing, so that particles do not readily gain access to the alveoli. In the second case, deep air is forced in and out and particles are taken right down where some can deposit by sedimentation and Brownian motion.

Early experiments on particle retention were reviewed by Drinker and others (1928), and they themselves found, with widely differing dusts, that about 55 per cent. was held in the respiratory organs. The percentage was independent of concentration. Brown (1931) continued the work and claimed a tendency towards greater retention at low concentrations, which is rather difficult to account for. Breathing in through the mouth instead of the nose caused a decrease of about 10 per cent., which illustrates the greater filtration efficiency of the nose in comparison with the mouth. He also showed during exercise, or when 5 per cent. carbon dioxide was inhaled along with the dust to increase the depth and rate of respiration, that a greater proportion of inhaled dust escaped on breathing out. A similar result is found for some gases; with quick breathing and enhanced minute volume the time allowed for settlement or diffusion to the lung surface is diminished. Owens' observation suggests, however, that such dust as deposits during rapid,

deep breathing may be located where it can do far more damage than higher up, where the prospects of elimination are better. The effect of particle size was not examined in detail, though Brown observed that airborne particles were often aggregates containing numbers of the ultimate grains of dust, and that they were therefore more readily trapped in the upper respiratory passages than individual grains.

Previous workers had assumed their dusts to be completely dispersed, but the large quantities caught in the nasal channels suggest that this was not the case. This criticism applies to the work of Lehmann (1935), who measured the filtration efficiency of the nose and found generally high values, exceeding 80 per cent. in some of his subjects, although the particle sizes quoted in his paper range from 0.2 to 5 μ . Probably his method of sampling did not reveal large aggregates. Lehmann claimed that men suffering from silicosis had less efficient nasal filtration than healthy individuals. Since silicosis is due to very fine dust which penetrates the nose freely, this finding is difficult to interpret.

Tourangeau and Drinker (1937) also measured nasal filtration of limestone dust, using unidirectional flow, and obtained figures below 30 per cent. They demonstrated that nasal filtration efficiency was related to the resistance to air flow through the nose. The particle size is not given but many particles about 10 μ in size must have been present.

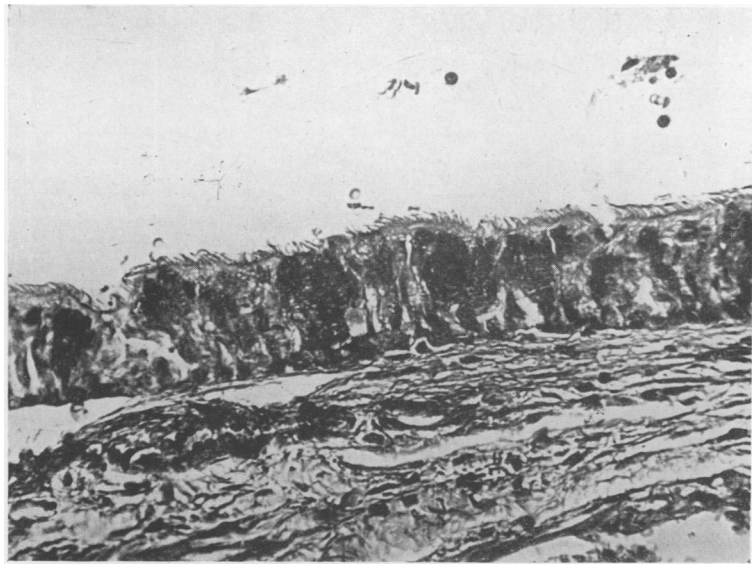


FIG. 5.—Ciliated epithelium from trachea of rabbit ($\times 560$).

The Effect of Particle Size

A theoretical estimate of the removal of airborne particles in the lung was made by Findeisen (1935) and is of great interest. He estimated the dimensions of various parts of the lung and, assuming a constant air flow of 200 c.cm./sec. during inhalation and exhalation, calculated the average air velocity at different points in the breathing tubes from the cross section and volume. His velocities are shown in fig. 2. This made it possible to judge the time which a given element of air spent in traversing the various air passages. The precipitation of particles on to the lung surfaces was considered to take place by four distinct mechanisms, namely: inertia, sedimentation, wall effect, and Brownian motion.

Inertia deposition, or impingement, occurs wherever the air passages change direction; owing to their mass, particles tend to continue moving in a straight line and may therefore come into collision with the bounding surface of the air channel. It is more effective for large, heavy particles and occurs particularly at the angles between bifurcations of the trachea and bronchi. The sensory receptors from which the cough reflex arises are concentrated at these points. Findeisen considered that this led to deposition, principally, for particles greater than 5μ radius at the forks of the primary, secondary, and tertiary bronchi. Impingement is favoured by high air velocity.

Sedimentation operates where air speeds are low, in the deeper parts of the lung; no particles greater than 5μ radius could reach the alveoli because they are removed by impingement or settlement higher up.

Wall effect is due to the particle being comparable in size with the air passage and reduces the effective size of the latter. It is important for elongated particles.

Brownian motion causes particles to diffuse towards a surface on which they precipitate. It is an appreciable factor in alveolar retention for particles below 0.3μ radius and is the cause of the absorption of extremely fine particles in the bronchioles. Elsewhere, diffusion has no significance except for gases and in connexion with the humidification of inspired air.

Since experimental data on lung retention as a function of particle size is now available it is possible to check Findeisen's results and confirm the general accuracy of his views. Brownian motion is dependent only on the size of the particles and must lead to almost complete retention of sufficiently fine clouds. Sedimentation and impingement both increase with the quantity ρr^2 where ρ is the effective density of the particle and r is the radius. Since the particles may be open in struc-

ture, the effective density is often less than that of compact material. Hygroscopic solutions which absorb water may have both ρ , and especially r , increased during their passage into the lung and so have a greater chance of being deposited and a smaller chance of reaching the alveoli. Apart from this, the deposition of particles of different materials will be the same for those sizes over which settlement and impingement are the chief mechanisms if the quantity ρr^2 is held constant.

Experiments on the retention of particles in the lungs have been carried out by Van Wijk and Patterson (1940), by Landahl and Herrmann (1948) and by Wilson and La Mer (1948). The methods used by these workers were quite different.

The first named dispersed a cloud of quartz dust and sampled the original and exhaled clouds by means of thermal precipitators. From comparative size distributions, determined by counting under the microscope, the percentage removed by breathing was calculated as a function of particle size. Since quartz has a density equal to 2.5 these results have been reduced to unit density by multiplying the radius by $\sqrt{2.5}$ so that comparison with the other results and with Findeisen's calculations is facilitated. This is justifiable over most of the range of sizes which they cover where impingement and sedimentation are the principal mechanisms at work. For the smallest sizes it may lead to a slight overestimate of particle retention which is of no significance.

The experiments of Landahl and Herrmann demonstrate that particles of high density are retained to a greater extent and that hygroscopic particles absorb moisture to form drops, which are larger and are more effectively retained than the original particles would have been. Their results for droplets of corn oil of density 0.91 are considered below.

Wilson and La Mer worked with particles of nearly uniform size formed from glycerol by vaporization in a special apparatus. Each particle contained a trace of radioactive sodium Na^{24} . By adjusting the generator, the drop size could be varied from 0.2μ to 2.6μ radius. A number of subjects inhaled the aerosols and measurements were made from which it was possible to deduce the total quantity retained in the respiratory tract and also the amount in the alveoli.

The observations consisted of β and γ ray activity determinations with a Geiger counter. The total retention was estimated from the deposit in filters through which measured volumes of inhaled and exhaled air had been drawn. To find the alveolar retention the counter was screened with a lead shield containing a slot. It was placed

against the chest wall, in the axillary region, with the slot horizontal and cutting across the fifth rib. The β radiation was absorbed by the body but the γ rays penetrated and could be counted. Since the counter was shielded from the upper respiratory tract and was remote from the larger air spaces, the radiation picked up came predominantly from the peripheral portion of the lung near the chest wall. These observations gave information about the relative retention in the alveoli as a function of particle size; to gauge the absolute retention additional measurements were made of count frequency from a standard source and also of counts from blood samples.

The experimental results for total percentage retention, P , are expressed by the following equation:

$$P = 105r^{0.163} - (2.37 - 0.29r)R$$

where r is the particle radius in microns and R is the frequency of respiration, in cycles per minute,

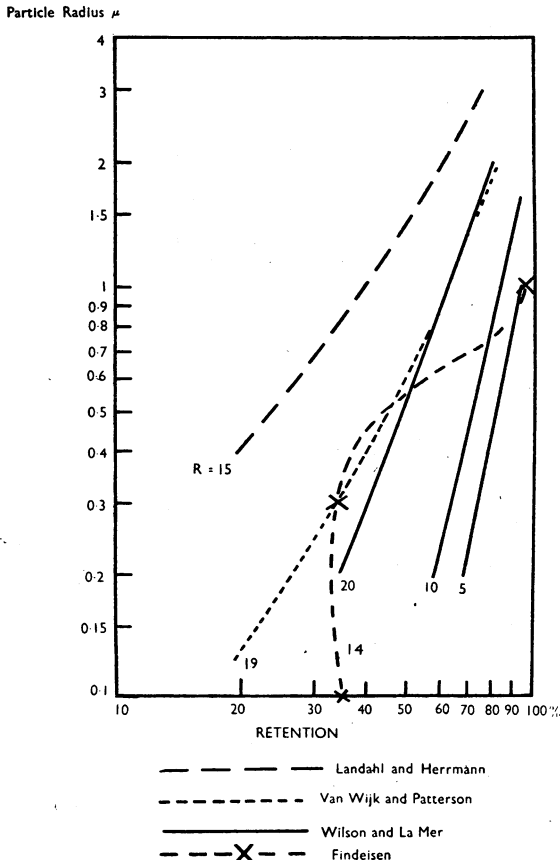


FIG. 6.—Retention of particles of unit density in the lungs. R =breathing cycles/min.

ranging from $5\frac{1}{2}$ to 20. The formula must not be used outside the ranges of the variables covered in the experiments. The term in brackets is given incorrectly in the original paper.

The retention is greater for slow breathing, in agreement with the observations of previous experimenters. It was also noticed that deep inspiration, followed by a brief pause before exhalation, caused a greater retention of small particles. The alveolar retention exhibited two maxima with peaks in the range 0.3 to 1.0 μ radius. The maximum alveolar retention was about 45 per cent. of the inhaled aerosol.

In fig. 6 the theoretical results of Findeisen are exhibited in comparison with the available experimental data. Those of Van Wijk and Patterson and of Landahl and Herrmann have been reduced to particles of unit density as explained above. The experiments of the latter workers included various kinds of particulate material and the results for corn oil were selected for this comparison because the particles are non-hygroscopic, spherical droplets and should be influenced only by mechanical factors. Their subjects breathed 15 cycles per minute using 450 c.cm. tidal air. The lung retention is substantially less than in the other work, and it is suggested that an over-estimate of particle size, which can easily occur with oil droplets, might account for the discrepancy. With other materials higher retentions were measured.

The curve from the results of Van Wijk and Patterson, at 19 cycles per minute, is very close to that of Wilson and La Mer for 20 cycles, while a smooth curve through Findeisen's theoretical points (14 cycles per minute) is also in quite good agreement. Findeisen appears to predict too high a retention for both smaller and larger sizes. According to his theory the retention of particles of 1 μ radius takes place to the extent of 82 per cent. in the alveoli, and 15 per cent. in the bronchioles. However, as we have seen, the exchange between tidal air and alveolar air is quite small in normal respiration, a fact which Findeisen did not take sufficiently into account in his treatment. As a result he reckoned on too great a penetration of 1 μ particles to the alveoli and so overestimated their retention. For the same reason his estimate for the retention of particles about 0.1 μ radius is probably high.

Fig. 7 exhibits a comparison between the average alveolar retention, from the experiments of Wilson and La Mer, and the theoretical alveolar retention according to Findeisen. The experimental data shows the double peak already referred to; in the curves for the seven individual subjects, which are here shown averaged, the peaks were, of course,

more pronounced. Wilson and La Mer consider that their curve includes some deposition in the finer bronchi and bronchioles. Findeisen's computed figures for the alveoli and also for the alveoli plus bronchioles are shown. It seems that Findeisen overestimates retention in the finer air passages for particles of about 1 to 2 μ radius and underestimates retention for radii of the order of 0.4 μ which takes place, in his view, almost entirely in the alveoli. It is probable, therefore, that sedimentation in the fine bronchioles is rather more important than he considered for particles of this size.

On the whole the general picture drawn by Findeisen is well substantiated so it is evident that

Nasal Filtration

Deposition in the nose is mainly due to impingement, owing to the inertia of the particles. This is shown by the increase in retention which follows an increase in the rate of air flow, and has been demonstrated in small animals and man by Davies (1946) and by Boyland and others (1947).

Landahl and Black (1947), and later Landahl and Tracewell (1949), studied the penetration of airborne clouds through the human nose by drawing the cloud up the nose and out through the mouth while the subject held his breath. The particle concentrations in the original and passing clouds were compared by analytical methods. Reduction

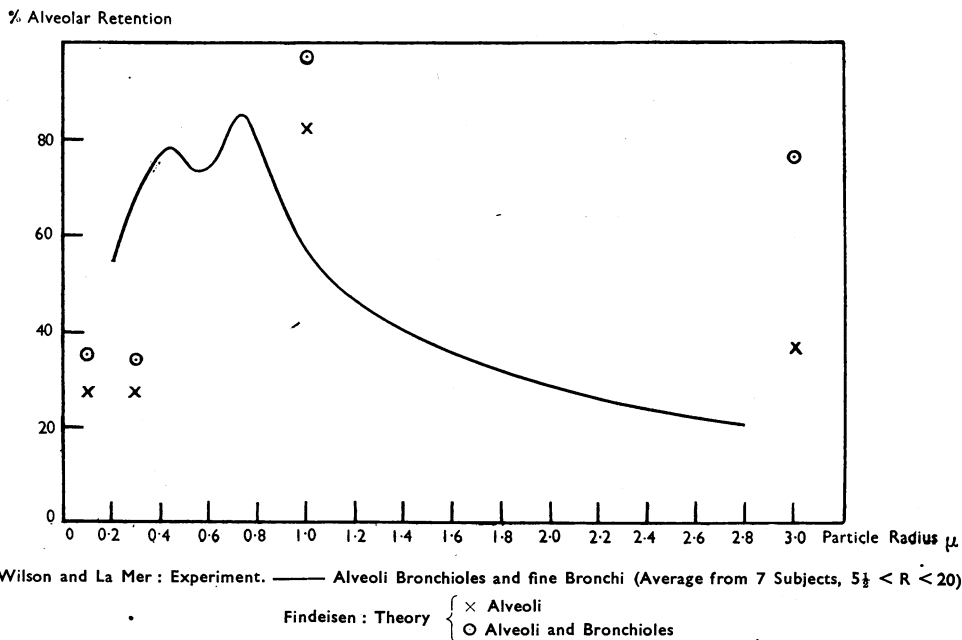


FIG. 7.—Retention of particles in the deep lung.

thermal and evaporative effects, considered by Aitken (1883-4), can be of no great significance in decreasing lung retention.

Landahl and Herrmann show that the minimum retention in the lung takes place for particles about 0.1 to 0.15 μ radius. Retention increases for still smaller particles owing to Brownian motion. Although the minimal retention is quite low the significance of particles of this size may be considerable since they have access to the alveoli. Thus Hatch and Kindsvatter (1947), using fine quartz dust with a median radius of 0.09 μ , determined with the electron microscope, produced lung changes in guinea-pigs after two weeks' exposure to a concentration of 35 mg./m³.

of their findings for different materials to spherical particles of unit density shows that 80 per cent. penetration occurs for particles of radius 0.9 μ , 50 per cent. at 2 μ , and 20 per cent. at 6 μ . Compact spherical particles of high density will be caught more readily in the nose, while loose, flocculant aggregates will penetrate to a greater extent than is suggested by the figures quoted. These must, of course, be subject to considerable variation according both to the individual and to the circumstances. The turbinate bones in the nose are covered with erectile tissue which may become swollen with blood so that they partially block the airways. Cold, dry air promotes this reaction while warm, moist air causes shrinkage. The complexity of

the nasal channels in some small animals, together with the low rate of air flow, leads to the air becoming saturated with moisture during its passage through the nose; this is not the case in man.

Discussion

We have seen that particles down to about 6μ radius are retained in the nose. With mouth breathing they would hardly penetrate deeper than the secondary bronchi. Deposition of these and larger particles is mainly due to impingement. At 2μ radius penetration of the nose is considerable and most particles are deposited by sedimentation in the bronchioles; a small proportion reach the alveoli. Above 2μ scarcely any particles are exhaled. Maximal deposition in the alveoli and fine bronchioles occurs between 0.4 and 0.8μ radius and is also due to sedimentation. Some 80 per cent. of particles of radius 0.1 to 0.15μ are breathed out again, this being the range over which retention is a minimum. Deposition in this range takes place almost entirely in the alveoli. Still smaller particles deposit, on account of their Brownian motion, in the alveoli and bronchioles.

Retention is enhanced by slow breathing because it allows more time for sedimentation of particles on to the surfaces of the bronchioles and alveoli. Alveolar retention is enhanced by deep breathing because exchange between tidal and alveolar air is then more effective.

The figures quoted relate to spherical particles of unit density. For other densities the radii given above should be divided by the square root of the density of the particle which may be several times smaller than the density of the material dispersed. Thus particles of low density penetrate further. This does not apply for very small radii, below 0.1μ , where Brownian motion is important, since this is independent of density. Particles which deviate from spherical shape will penetrate to greater depths, since the surface to mass ratio is greater; clearly, however, this may not be the case for extreme shapes, such as fine fibres, which are readily entangled.

Apart from retention, the solubility of particles is an important factor influencing the risk from dust exposure. Having quartz dust in mind, Hatch and Hemeon (1948) showed the existence of a most dangerous size on the assumption that solubility increases as particle size diminishes. This is in accord with experiment; it is difficult to demonstrate that a pebble of quartz dissolves at all, but finely powdered Si O_2 readily forms a 0.01 per cent. to 0.015 per cent. solution. On combination of this effect with the lung retention factor it was shown that particles of about 0.5μ radius are the

most toxic. A dust with a median number diameter of 0.5μ was twelve times more active than a dust with a 1.5μ median. This calculation was based on alveolar retention. Substances of greater solubility than quartz might be dangerous when deposited in the higher regions of the respiratory tract.

Summary

Particles greater than about 6μ (microns) radius are retained in the nose. With mouth breathing they would not be deposited below the secondary bronchi. Deposition of these and larger particles is mainly due to impingement. At 2μ radius penetration of the nose is considerable and most particles are deposited by sedimentation in the bronchioles; a small proportion reach the alveoli. Above 2μ scarcely any particles are exhaled. Maximal deposition in the alveoli and fine bronchioles occurs between 0.4 and 0.8μ radius and is also due to sedimentation. Some 80 per cent. of particles of radius 0.1 to 0.15μ are breathed out again, this being the range over which retention is a minimum. Deposition in this range takes place entirely in the alveoli. Still smaller particles deposit, on account of their Brownian motion, in the alveoli and bronchioles.

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Particles deposited in the trachea, bronchi, or bronchioles are normally removed by ciliary action; this will not prevent absorption of water-soluble material and may fail through impairment of the ciliated epithelium or the mucus coating due to illness or chemical action. The ciliary mechanism is ineffective for liquids. Elimination from the alveoli is by phagocytes. Although particle size is decisive in governing the region of initial deposi-

tion in the respiratory tract, only in certain cases is it possible to claim immunity from health risk on this basis.

The author has made free use of a private communication from Professor J. H. Gaddum, F.R.S., on the retention of inhaled clouds; he is indebted to W. A. Fell, Esq., and R. H. D. Short, Esq., for the loan of anatomical specimens, and to Dr. T. Bedford for valuable advice and encouragement.

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