DUST SAMPLING AND LUNG DISEASE*

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No instrument for sampling airborne dust or mist collects a sample which is truly representative of all the particles present. There are errors associated with the random variation of the cloud in time and position and instrumental errors due to the act of sucking the cloud into the sampling apparatus or to inherent failings of the dust-separating or measuring mechanism which cannot be entirely eliminated. Fine particles, coarse particles, or both, may be lacking in the final analysis, and the original particles may be changed during collection. In favourable circumstances a fair picture of the airborne dust can be built up by combining several methods of securing samples and using a variety of techniques for their evaluation.

The Principle of Selective Sampling

A laborious reconstruction of the original cloud is seldom necessary for gauging a risk to health. The danger due to a toxic gas is measured by its concentration and the same is true of a cloud of one substance dispersed in particles of uniform size. But it is usual for dust and mist to contain a range of sizes, only some of which need to be sampled accurately because of their greater significance. Unless dangerous particles happen to lie in the coarse end of the size distribution, correlation between health risk and mass of dust is likely to be poor and it will be necessary to investigate microscopically the particle size distribution in the cloud.

On the other hand, the mass of dust in a selected sample, containing only particles in the dangerous size range, may be a good measure of health risk. If the sampling instrument selects this range spontaneously, microscope work is avoided and analysis of the results is reduced to simple weighing. Because of the great simplification which is promised by selection, it is necessary as a preliminary to dust surveys to consider what constitutes the dangerous range of particle size.

The full benefit of selective sampling is gained when the dust is slowly absorbed, or reacts very slowly in the tissues of the body. Ingestion and contamination of the skin and eyes produce no significant pathological effects, and natural elimination from the bronchioles, bronchi, and upper respiratory tract of the larger particles is probably sufficiently rapid and complete to constitute an adequate defence of these regions. Harmful effects, therefore, can be ascribed fairly confidently to particles which are small enough to penetrate deeply into the lungs. Alumina-silica fume and vanadium pentoxide, silica and coal dusts, for example, fall into this category.

The action of reactive or soluble particles of dust or liquid is complicated by the possibilities of evaporation and chemical change in the atmosphere as well as by localized tissue sensitivity. It is impossible to generalize about such particulate clouds beyond saying that mass concentration of total airborne material is likely to be a better measure of health risk than it would be for dusts of the preceding group. This implies that the coarser particles, which contribute largely towards the weight, are likely to be dangerous, although it is by no means certain that symptoms will be confined to the upper respiratory tract, where the larger particles are filtered out, because systemic effects may arise. Conversely, proceeding to particles of molecular dimensions, some gases can cause upper respiratory symptoms due to their rapid absorption, while others produce lung reactions; again, fine particles of tobacco smoke, of sizes which are almost entirely retained in the alveoli and fine bronchioles, are believed to have some association with cancer of the bronchi where their retention factor is very low. In general, it is not safe to assume a simple connexion between the size of particles responsible for lesions and the places where they occur.

It seems, therefore, that the benefits of selective sampling, in which an attempt is made to simplify the investigation of a dust hazard by restricting

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attention to a limited range of particle sizes known to be dangerous, are confined to fields in which the chemical action of the particles is slow; this restriction means that particles which are to be selected by the sampling device should be those which are retained in the human lung for long periods. Particles of very low solubility deposited in the upper respiratory tract, or on any part of the ciliated epithelium of the bronchial tree, will be excreted and can have no conceivable effect on a long term basis.

If the actual sample can be collected or assessed after the elimination of all particles, which would have been deposited during respiration elsewhere than in the alveoli, then the ideal selective sampler has been achieved and the material available for chemical and physical examination will be similar to that which remains in the lung. The need for studying functions of the size distribution would not be entirely removed by such a technique because the toxic effect per particle must depend on weight, surface area, or other factors; nevertheless, it is likely that a relationship between disease incidence and mass of dust in the restricted, "alveolar" sample would be shown.

Gaddum (1941) was probably the first to apply the principle of selective sampling by drawing air into an impinger through a bent glass tube. The coarser of the suspended particles were deposited in the curve of the tube, due to inertia, while the finer ones, being able to sweep round the bend, were collected in the impinger; the dimensions of the apparatus were chosen so that the tube retained particles of sizes which were filterable by the human nose and the impinger collected a "lung" sample. Before discussing sampling methods it is therefore necessary to consider the filtering action of the respiratory tract.

Retention of Dust in the Human Alveoli

Since the publication of the author's review of inhalation risk and particle size (Davies, 1949) several papers have appeared which give important additional information on the access of dust to the alveoli.

There are two distinct experimental methods available for studying this problem. An analysis can be made of air exhaled by living subjects, and its content of particles compared with the quantity inhaled. This technique has been adopted recently by Brown, Cook, Ney, and Hatch (1950), by Dennis and Sawyer (1950), and earlier by van Wijk and Patterson (1940). Alternatively, undissolved dust can be extracted from the lungs of deceased miners and rock workers and its size distribution determined and compared with the size distribution

of airborne dust in their former work places. The latter method has been tried by Gessner, Rüttner, and Bühler (1949), by Bedford and Warner (1950), and by Cartwright and Nagelschmidt (1951).

Some of the particles which are deposited beyond the respiratory bronchioles, where there is no ciliated epithelium, will be taken up by phagocytes, or otherwise penetrate into the lymphatics and will remain available for subsequent extraction and estimation in the lung residue, if they are insoluble. Others, however, will be carried by phagocytes to the ciliated surfaces above the respiratory bronchioles and will be eliminated from lung tissue. The limits of particle size outside which phagocytosis is ineffective are unknown, but they must exist.

The two methods of investigation should yield different results for particles which are neither too large nor too small for effective phagocytosis; exhaled air analysis would record that a greater proportion of these sizes was retained in the lung than did the analysis of lung residues from which material would have been lost by phagocytosis to the ciliated epithelium and possibly by solution.

Particles are deposited in the upper bronchial tubes by impingement, with a gradual transition to sedimentation in the finest bronchioles and alveoli. Since the effectiveness of both these processes is measured by the value of ρd^2 for particles of similar shape, ρ being the density and d the diameter of the particle, it follows that experiments performed with particles having density ρ can be expressed in terms of the diameters of particles of unit density by multiplying the actual diameter by $\sqrt{\rho}$, subject to certain limitations of the breathing pattern which are discussed below. In this paper all the results quoted have been rendered comparable by adjusting the particles sizes to unit density.

The retention of particles between 0.2μ and 1.5μ diameter takes place almost entirely in the alveoli and respiratory bronchioles; this will be termed alveolar retention. Larger particles are distributed throughout the bronchial tree, though it becomes more and more probable with increasing size that they will precipitate before reaching the alveoli.

Brown, Cook, Ney, and Hatch measured the carbon dioxide concentration in expired air simultaneously with their particle analysis; by assuming that the exchange of fine particles between alveolar and tidal air was similar to the exchange of gas, they were able to distinguish alveolar retention of particles. Their curve for maximum alveolar retention has been reduced for density, as explained above, and is plotted on Fig. 1, and the corresponding data for particles retained above the alveoli are shown in Fig. 2. In Fig. 1 the results of van Wijk and Patterson and of Dennis and Sawyer have

FIG. 1.—Alveolar retention of particles of unit density.

also been plotted, using only reduced particle diameters which are less than 2μ . These points fall quite close to the curve of Brown and others, though the points at 1.9μ are high, presumably because some particles are included in the alveolar retention which had actually been deposited above the respiratory bronchioles.

FIG. 2.—Percentage of inhaled dust which is retained above the respiratory bronchioles (unit density).

If the data of Dennis and Sawyer, corrected for alveolar retention according to Brown and others, are plotted it will be seen in Fig. 2 that all the points lie above Brown's curve, though not by a large amount. To bring the points on to the curve it would be necessary to have a greater proportion of alveolar retention than is given by Brown's maximum curve. It should be pointed out that all these workers took averages from a number of separate experiments. Dennis and Sawyer used 25 subjects, Brown and others made 100 tests, and van Wijk and Patterson did 40 experiments.

From their analyses of lung residues, Gessner, Rüttner, and Bühler computed a dust retention curve by assuming that particles between 0.5 and 0.75μ were completely retained. This is not true, even allowing for the high density of their dust, and their retention curve has been adjusted in the light of the air analysis experiments described above so as to make the alveolar retention 52% at 1μ diameter with unit density. The resulting curve is plotted on Fig. 1. This adjustment assumes that both solution of particles and their transport by phagocytes to the

bronchioles are either negligible or independent of particle size over the range investigated. The relationship between air analysis and lung residue experiments is unaffected by phagocytosis to the lymphatic system.

Bedford and Warner, examining lung sections microscopically, separated the particles into coal and non-coal by their appearance, and gave distributions of dust in lung nodules and also in reticulation areas. Averages of the latter have been used as the differences are not significant. Figures from their Table VI have been extracted, and lung dust compared with airborne dust after firing ripping shots for the non-coal particles, and after shots in coal, for the coal dust. Adjustment of lung retention has been made to 52% alveolar retention at 1μ , for particles of unit density, supposing the density of the fine coal particles to be 1.3 g./cc. and the non-coal to be 2.6 g./cc. These points are plotted on Fig. 1. The non-coal particles give points which lie in very good accord with the three air analysis experiments below 1μ and then follow Gessner's curve quite closely up to 4μ . The coal particles also give points which agree with all the other results below 1μ , but above 1μ alveolar retention is much higher than it was for non-coal; it is apparently above the mean curve of Brown and others in the region of 2μ but it is quite close to their curve for larger particles.

The points on Fig. 1 from the work of Cartwright and Nagelschmidt (1951) are taken from Fig. 8 of their paper, and relate to a comparison of trypsin digested lung residues with the mean of three airborne coal dusts from South Wales, not, however, from the actual pits in which the men had worked. Particles were counted and sized under the microscope. Reduction to unit density and 52% retention at 1μ have been carried out as before. These points agree very well with the curve of Brown and his colleagues, from 4μ to 5μ diameter, and though they show a lower retention between 2μ and 4μ , the values are well above the curve of Gessner, Rüttner, and Bühler and the non-coal points of Bedford and Warner.

It is clear that on the basis of the adjustment of lung residue size distribution to 52% alveolar retention at 1μ (unit density) a very good measure of agreement between different laboratories and techniques has been obtained regarding alveolar retention of particles below 1μ diameter, irrespective of the nature of the dust, which rather argues against the possibility that solution was appreciable in the lungs concerned. This in turn suggests that phagocytosis of these very fine particles upwards beyond the respiratory bronchioles is not an important factor. Perhaps they are too small for

the phagocyte to sense, or for the probability of chance encounters to be significant, or even to stimulate the production of phagocytes.

Above 1μ in Fig. 1 implies that clay and quartz particles are retained in the alveoli less abundantly than would be expected from air analysis. This might be explained by the phagocytosis of some of them to the ciliated epithelium. On the other hand, coal dust seems to be retained very much as the experiments of Brown and others indicate, about whose curve the points are fairly evenly spread. Such a difference between coal and quartz, if substantiated, might be accounted for on the hypothesis that coal particles were less effectively transported by phagocytes.

Further analysis of lung residues, and a more accurate correlation with the working environment, is necessary before such ideas can be accepted, particularly in view of the very difficult particle size analysis involved and the uncertainty attached to the separation of lung residues without disturbing the particle size distribution. All the same, it is fair to comment on the remarkable agreement below 1μ and near 5μ because such widely different experimental techniques were employed.

Dependence of Particle Retention on Breathing Rate

We must also consider the possible effects of variation in breathing pattern. For example, in normal respiration, the tidal air is 0.5 litres and the functional residual air is 2.9 litres (Davies, 1949) so that, if all the alveoli worked together, only 15% of the air in an alveolus would be expelled. For maximum respiration, the figures are 3.8 and 1.6 litres, so 70% of the volume of an alveolus is used.

Now alveolar retention depends on the number of particles which reach those regions; this, in turn, is a direct function of the volume of tidal air, T . It is also related to the time they stay there which is an inverse function of respiration frequency, R . Hence, alveolar deposition is measured by the ratio T/R . During heavy work both T and R increase, but the ratio does not change very much. In contrast, impingement of larger particles is favoured by a high value of T and a high air velocity, which is a direct function of the respiratory frequency. Thus, the deposition of particles in the upper lung, due to impingement, is favoured by increasing the product TR , or minute volume, which, of course, increases rapidly when the body demands more oxygen.

As can be seen from Table 1, the values of $100T/R$ covered in the experiments we have been discussing do not vary a great deal, so it is reasonable to expect that the alveolar retention, at least, for sizes below 2μ , will be similar, and our comparison

of these experiments will not be invalidated by differences in the cycle of respiration.

Some idea of the dependence of retention on breathing pattern can be obtained from the theoretical calculations of Landahl (1950) and the experiments of Landahl, Tracewell, and Lassen (1951). Unfortunately, these experiments appear to be marred by an overestimate of particle size by a factor of 2, just as was the case in the earlier experiments of Landahl and Herrmann (1948). Attention was drawn to this discrepancy in the writer's previous paper (Davies, 1949). On Fig. 3 the mean curve of the experiments we have discussed in the last section is plotted. They were done with values of 100T/R between 3.2 and 4.7 (Table 1). The experimental points of Landahl and others, with 100T/R equal to 3 and 12, are shown joined together by a vertical line. Each of these lines falls too far to the right, but, if the particle size is reduced by one half, a curve through the mid-point of the joining lines lies very close to the mean curve of alveolar retention, which it cuts. The minima of the curves occur at the same particle size, while the only marked deviation in trend is above 1.5 μ diameter where upper lung retention has become appreciable.

This defect does not prevent the use of Landahl's

FIG. 3.—Alveolar retention of particles of unit density.

work to demonstrate the effect of breathing pattern. In Table 2 it is shown that alveolar retention is a direct function of 100T/R for particles below 1.9 μ diameter (on Landahl's figure, 3.8 μ) and that the dependence is less for larger particles owing to impingement in the upper bronchial tubes coming into play. Table 3 shows that upper lung retention is almost unchanged as long as the minute volume, TR, is held constant, although wide individual ranges of T and R are covered.

TABLE 1
PATTERN OF RESPIRATION

Experiments	Respiration Frequency (R) (min.)	Tidal Air (T) (litres)	100T/R. (l./min.)	Minute Volume (TR) (l./min.)
Brown and others	15	0.7	4.7	10.5
van Wijk and Patterson	19	0.9	4.7	17
Dennis and Sawyer	15.7	0.68	4.3	10.7
Mining	25	0.8	3.2	20
Hard exercise	30	1.3	4.3	40

TABLE 2
RETENTION OF PARTICLES IN THE LUNG ACCORDING TO THE EXPERIMENTS OF LANDAHL, TRACEWELL, AND LASSEN (1951)

Respiration Frequency (R) (min.)	Tidal Air (T) (litres)	100 T/R	Percentage Retention of Particles of Diameter (μ)*						
			0.11	0.25	0.55	1.4	2.9	3.8	6.3
15	0.45	3	24	22	15	27	52	59	86
7.5	0.9	12	36	32	23	53	69	82	93
5	1.35	27	46	41	32.5	65	81	89	96

* Particle diameters are quoted as published but are probably too large by a factor of 2.

TABLE 3

RETENTION OF PARTICLES ABOVE THE RESPIRATORY BRONCHIOLES AS CALCULATED BY LANDAHL AND OTHERS

Respiration Frequency (R.) (per min.)	Tidal Air (T) (litres)	TR	Percentage Retention of Particles of Diameter (μ)*				
			0.25	0.6	2	6	20
15	0.45	6.75	2	2	5	42	99
7.5	0.9	6.75	2	2	9	49	97
5	1.35	6.75	3	1	9	50	93

* Particle diameters quoted as published.

Design of a Selective Sampling Apparatus

Having reviewed the best information available on the size-selecting properties of the human lung, it is appropriate to consider the retention curve to which a dust sampler ought to be designed in order that it should sample alveolar dust and be suitable for assessing long term health risks due to particles which dissolve in the lung fluids only slowly, if at all.

It is probably safer to neglect the ascent of particles to the bronchioles by phagocytosis since correction for this would be entirely speculative. To obtain strict correlation between dust samples and incidence of disease, the acceptance curve of the sampling instrument should be biased by a toxicity factor; existing knowledge, however, will only permit this to be done in exceptional cases so it will not be attempted in this paper.

Maximum alveolar retention occurs between 1.5μ and 2μ diameter and amounts to 50 to 60%. It is simplest to design selective sampling instruments to accept all dust particles of this size and to grade the cut-off of the larger sizes to about 50% at 5μ , at which size alveolar retention is equal to about half of its maximum value.

Although there is a pronounced falling off of alveolar retention from 1μ down to 0.3μ diameter, there is no doubt that still smaller particles are retained with increasing efficiency due to Brownian motion. There seems to be no advantage in trying to make the selector device match the alveolar retention curve for small particles, which would be very difficult, as the contribution of the smaller sizes to the mass of the sample is inconsiderable and little is known of the relative toxicity. We therefore aim at sampling all particles which are smaller than 1.5μ to 2μ diameter, together with a decreasing proportion of the larger sizes, so that 50% of the 5μ ones are collected.

It has been shown by Walton (1950) that if size separation is performed by elutriation of the air before sampling the residual fine portion, then, of the particles of diameter d originally present in the air, the fraction collected in the sample is equal to

$1 - (d/D)^2$, where D is the upper limit of size in the sample. If we decide on 50% acceptance at 5μ diameter for particles of unit density this formula gives $D = 7.1\mu$ and 92% acceptance at 2μ . The complete acceptance curve is plotted on Fig. 4 where it is compared with a curve computed from the mean alveolar retention function (Fig. 3) by adjusting the maximum to 100%. If anything, this

FIG. 4.—Acceptance curve of a selective dust sampling instrument with particles of unit density.

cut-off is rather too sharp, in comparison with alveolar retention, but it is unlikely that a practical instrument would exactly reproduce this theoretical formula and the appearance of a tail of coarser particles would be expected.

When the actual sampling instrument is preceded by a selector device operating to this specification, then the dust which it receives will be similar in size distribution to that reaching the alveoli of the human lungs. If the density of the particles is not equal to unity, which has been the basis of all our calculations, this conclusion is not modified in any way because segregation in the elutriator and deposition in the alveoli both depend on the same physical property of the dust particles, namely the rate of fall under gravity, and are altered in the same ratio. What does happen, of course, is that

the size of the particles accepted changes according to the law $\rho d^2 = \text{constant}$. Change in size with density is shown for various values of the acceptance in Table 4. Similarly, the shape of the particles does not affect the relationship between the dust in the sample and that in the alveoli, except, perhaps, that extreme shapes like asbestos fibres may lodge more readily against the walls of the bronchial tubes.

TABLE 4

PERCENTAGE ACCEPTANCE VALUES FOR A SELECTIVE SAMPLER OPERATING BY ELUTRIATION AS A FUNCTION OF PARTICLE DENSITY

Percentage Acceptance	Diameter of particles (μ) when Density (g./cc.) is			
	1	1.5	2	2.5
10	2.2	1.8	1.6	1.4
20	3.2	2.6	2.2	2.0
30	3.9	3.2	2.7	2.5
40	4.5	3.7	3.2	2.8
50	5.0	4.1	3.5	3.2
60	5.5	4.5	3.9	3.5
70	5.9	4.8	4.2	3.7
80	6.3	5.2	4.5	4.0
90	6.7	5.5	4.7	4.2

An important point in connexion with the precipitation system, or method of measuring employed to assess the selected sample, is its sensitivity to very small particles. It was pointed out earlier on in this paper that it would be more rational to correlate the weight of selected samples of dust with the incidence of pneumoconiosis than total weight or surface area. All the same, it must be remembered that alveolar retention is large for submicroscopic particles, and although the mass of these in dust clouds is usually small, the numbers of particles may be considerable, as has been shown by the analyses of Wynn and Dawes (1951) and the electron microscope studies of McCartney (1945) and of Sharpe and Hounam (1950). Hatch (1950) has pointed out that there are no grounds for assuming that these very small particles have no significance in certain lung disorders.

Summary

Selective dust sampling, in which only fine particles are collected, often offers better prospects of correlation with the incidence of disease than the assessment of total concentration by weight, because the coarser particles are deposited in the higher

bronchial tubes, from which they are excreted, while only small sizes reach the alveoli. The application of this principle is discussed in relation to the nature of the airborne dust.

With a view to defining a suitable acceptance curve for sampling apparatus, recent work on the retention of dust in the human alveoli is examined. For particles of unit density, the maximum alveolar retention is between 50% and 60% of the dust inhaled and occurs between 1.5 μ and 2 μ diameter; about 30% of the 5 μ particles are retained.

It is possible that when coal dust is inhaled the proportion which is retained in the alveoli is greater than in the case of quartz or rock dust.

Minimum alveolar retention occurs at 0.25–0.3 μ , smaller particles being more completely deposited.

Alveolar retention from 0.3 μ to 2 μ diameter depends on the ratio of tidal air to frequency of respiration and does not change rapidly with rate of working; upper lung retention varies with minute volume, however, and is therefore sensitive to muscular activity.

Selection of particles for sampling by an elutriator designed to accept 50% at 5 μ diameter (unit density) should give a good approach to an alveolar sample. Variation of the density or shape of the particles will affect alveolar retention and elutriation in the same way, since both depend on the sedimentation rate of the particles, so that a single selector will give a constant performance with all clouds.

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