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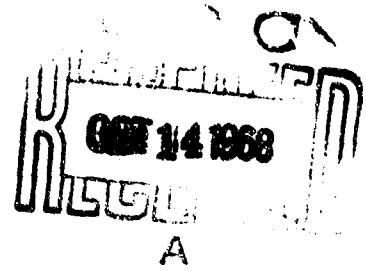

DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

ON THE INHALATION OF VERY FINE AEROSOLS -- A COMPARATIVE STUDY INVOLVING SMALL RODENTS

Fortschritte der biologischen aerosol Forschung
(Advances in biological aerosol research)
33:52-55

Dr. H. Oldiges

Increasing industrialization is accompanied by an enrichment of the atmosphere with suspended particles /aerosols/. Of course, a differentiated filter technology does make it possible to remove some of the coarser admixtures from industrial waste gases, for instance; but the very finest aerosol fractions continue to be fed into our environment in a by no means inconsiderable volume. In addition we have the contamination due to radioactive components released in atomic processes and nuclear explosions. Here it is again the very finest particles which constitute a long-range threat to vast areas because of their small speed of sedimentation. The physical and chemical affects of the very finest aerosols on biological processes in the organism however still require extensive clarification. It is therefore advisable to devote special attention to this portion of the suspended particles. From detailed animal experiments, using rats, mice, and golden hamsters, we tried to get an overall picture as to the quantitative sorption of very fine liquid aerosols in the watery phase.

Material and Method

The animal material used in these inhalation experiments was of homogeneous origin and nature. The average weight of the rats was 208 g, the golden hamsters weighed 62 g and the mice weighed 23 g, each. The fresh lung weights were around 1.5 g for the rats and the trachea weights were around 0.14 g. In the case of the golden hamster lung the figure was 0.6 g and for the trachea the figure was 0.07 g whereas we determined an average weight of 0.25 g for the mouse lungs and 0.03 g from the trachea.

All experiments were conducted at a room temperature of 21° C and a relative humidity of 63%. As aerosol generator we had available a well-known ultrasound atomiser which creates an aerosol along the surface of the liquid by means of a focused barium titanate oscillator. As sound frequency we selected 2.7 Mc. A continual O_2 current of 2 l/min conducted the relatively

homogeneous aerosol into a glass sphere by means of a hose system. On top of this glass sphere we had a Liebig cooler, such as it is customary in chemistry; this cooler was connected with a container by means of a hose; smaller plastic bottles, containing the experimental animals, were screwed to this container. The glass sphere, the Liebig cooler, and the entire conduit system were used for the extensive screening of the aerosols. By means of preliminary experiments and continual aerosol measurements we were able to prove that the droplet spectrum remained roughly constant on the level of the experimental animals and in the area of the experimental chamber [room] during the entire series of experiments. We had an aerosol whose largest particles had a diameter of no more than 1 mu. The most frequently found particle size was around 0.6 mu. The particle density was 10^8 particles per cm^3 and the spray density was 115 γ methylene blue per liter of aerosol. We atomized a 1.25% methylene blue solution with a pH value of 4.3. Each experimental series was repeated several times with ten animals, each time. The values shown are the average values from 4, respectively, 5 series of experiments.

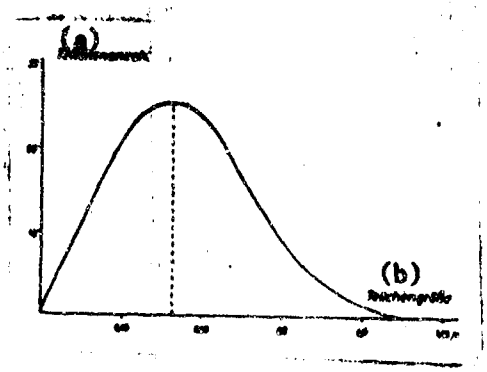

Figure 1. Legend: a--particle number; b--particle size.

Experimental Results

The investigations by Finnedisen, Stieve and others had shown that particles of the order of magnitude employed here can pass into the lungs and penetrate into the alveoli. According to data presented by Dirnagl, the main reason for the deposit in the air passage, in the case of the very finest aerosols, is the molecular movement of Brown. Accordingly, sedimentation plays only a subordinate role here. Furthermore, there is a close interrelationship between the breathing frequency [rate] and the retention, as Dirnagl and Pichlmaier were able to prove in human subjects.

We were trying to find out what quantities of the finest aerosol presented here were actually conducted into the lungs and what percentage is precipitated already in the trachea. A relatively high percentage will probably be precipitated already in the upper air passages because our experimental animals here were animals that normally breathe through the nose. Before

we go any further we might observe that the resorption of methylene blue through the respiratory tract can be overlooked when the experiment lasts 2 hours, followed by killing and immediate section. Methylene blue could not be established in any of the cases investigated here, not even as a leucobase in the urine.

The breathing rate of a rat is around 120 breaths per minute. Here the animals inhale 0.145 γ of methylene blue with every cm^3 of air inspired from the surrounding breathing air. Concentration measurements with the spectral photometer enabled us to establish only very small quantities of methylene blue in the respiratory tract. In the trachea, which was cut off all the way to the bifurcation, 11.2 γ of methylene blue had been precipitated whereas only 10.7 γ of methylene blue were precipitated in the lung itself.

Golden hamsters have a breathing rate of 160 breaths per minute. In this species of animal we were able to establish only 6.7 γ in the trachea and 3.6 γ of methylene blue in the lungs.

The breathing rate of mice is 210 breaths per minute. After 2 hours of experimentation we were able to establish 5.4 γ in the trachea and 2.4 γ of substance in the lung tissues. A comparison of the values for the various animals is quantitatively not informative here because the breathing rate and the breathing dynamics as well as the anatomic situation play a great role.

The series of experiments with rats, golden hamsters, and mice clearly show us that an increase in the breathing rate is accompanied by a noticeable decrease in the retention of methylene blue. In the rats, methylene blue was deposited in the lung tissues and in the trachea in still approximately equal weight proportions; in the golden hamsters, however, the lung reveals only slightly more than half of the volume of the tracheal precipitation. As the precipitation continues to increase -- something that happens when mice are the experimental animals -- the deposited portion in the lungs continues to drop and amounts to no more than half of the volume that can be established in the trachea.

The results presented here enable us to conclude that animals that breathe through the nose and that have a very high breathing frequency are not very suitable for investigations of very fine aerosols whose droplet spectrum extends up to 1 mu. A large portion of the substance volume offered is either retained in the area of the nose and the throat or it is removed from the lungs through expiration. Only half or 1/3 of the precipitating substance is separated in the lung tissues and here it will certainly penetrate all the way to the alveoli. But this very small portion can, under certain circumstances, become very significant when we are dealing with a pharmacological or toxic aerosol.

On the basis of these animal experiments, which we also expanded to other animal species, we must unfortunately state that comparative investigations on the effectiveness of aerosols with different animal species do

not make it possible to make any comparisons. We are dealing here, not only with a differentiation of aerosol sorption in the various animal species in terms of quantity but possibly also with a preferred sorption of certain aerosol fractions. This obvious difference is due not only to the physiological condition of the respiratory passages but also to the differing breathing mechanics.

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ON THE INHALATION OF VERY FINE AEROSOLS: A COMPARATIVE STUDY ON SMALL RODENTS

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pp 2-3

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The as yet almost unknown physical and chemical effects of very fine aerosols on the biological and physiological functioning of the organism make it seem advisable to devote special attention to these suspended particles. The attempt was made in animal experiments on rats, mice and golden hamsters to get a general view of the quantitative uptake of very fine aerosols of the aqueous phase. By means of familiar ultrasonic atomizers and by inserting the appropriate sifters a comparatively homogeneous aerosol was obtained for the inhalation experiments: the largest particles had a diameter of not more than 1 , and the most frequent particle size was 0.5 . The aerosol density could be varied correspondingly. Thus one is dealing with particle sizes which are designated as still capable of penetrating the lungs and which are perceptibly subject to Brownian molecular movement.

In choosing experimental animals preference was given to rodents since, as animals that breathe through the nose, in the event of a rather long duration of the experiment -- and the resultant aging of the aerosols, they possess in this organ a natural filter device which thoroughly prevents coarser particles from penetrating the respiratory tract. The inhalates detected in the trachea and lung, consequently, very probably consist only of precipitates of the original aerosol. Adopted as a tracer was Methylene Blue, a dye that is non-injurious to and easily tolerated by the organism. The amount taken up was quantitatively analyzed by means of spectral photometric measurements, separately for trachea and

lung. It was possible to relate the respiration rate and respiration volume of all three species of experimental animals, ascertained in parallel experiments, to the amount of the aerosol absorbed.