

## The Determination of Risk Factors for Acute Exposure to Powdered Aerosols

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With every breath we take, we inhale aerosols of many kinds, some may be liquids such as condensed oil droplets, some nondescript, amorphous dusts and some like asbestos, microcrystalline solids. They may be large particles, bordering on the upper limits of respirability, like road dust, or they may be submicron size such as fumes and diesel exhaust.

For today, we will focus on short-term exposures to high levels of amorphous dusts. Because we are constantly breathing air containing aerosols, our lungs have many mechanisms to clear foreign bodies. However, a concern when considering high level, short-term exposures is that these clearance mechanisms function well when challenged by low levels of dust, but can be overwhelmed by very high levels. This can actually impede the clearance process resulting in retention of the particles for much greater periods of time than would have been predicted.

In trying to understand the potential risk associated from this form of exposure, several factors should be considered. First, one should determine if the particles are going to be respirable. Generally, particles larger than 10 micrometers are not considered respirable. That is, they will not be entrained in the inspired air. A marked exception to this are the needle-like, fibrous particles. Due to their aerodynamic geometry, even long fibers, up to 100 micrometers, can penetrate into the lung. Particles that are heavily charged, on the other hand, may rapidly coalesce forming nonrespirable agglomerates or they may be rapidly collected in the upper respiratory tract. In addition to these considerations, properties such as solubility, density and shape will influence the aerodynamic character of a particle and may either enhance or inhibit its potential to penetrate deep into the respiratory system.

**As** you can see from the graph of particle deposition versus particle size, deposition (or retention) is dramatically influenced by the particle size. Larger particles will be preferentially collected in the upper respiratory tract by impaction. Smaller particles will be removed from the air mostly by sedimentation and diffusion. Charged particles may also undergo electrostatic deposition and fibers may be removed by interception. These last **two** mechanisms are dependent on other properties of the particles in addition to size.

The particle size and aerodynamic diameter will determine whether a particle gets into the body, how much is retained and where deposition occurs. This is just one criterion for the potential for an adverse effect. Other considerations include the toxicity of the substance or substances making up the particle, its biological half-life, and various physical properties. The longer a particle is retained in the lung, the greater its potential to cause harm. Long-term retention may result in fibrosis, emphysema, tumors or cancer.

While many physical properties will affect the overall toxicity of a particle, some of the most prominent are durability, solubility and reactivity. Particles that are readily broken down physically can more easily be transported out of the lung by both mucociliary clearance and macrophage transport. Large particles, especially fibers or toxic substances, are cleared less efficiently by these mechanisms. Solubility is also important. If a particle is soluble, such as a sodium chloride or sulfate aerosol, it is rapidly cleared. However, if the particle contains a toxic, soluble substance, inhalation of a large amount in a short period of time may result in very severe consequences that might not have been anticipated from longer term, low level exposures. The chemical/biological reactivity is also of primary importance when considering overall toxicity. A chemical may, itself be relatively non-toxic, but if it can be converted in the respiratory system to a more toxic substance, both the reaction rate and product will determine its toxicity. Additionally, surface area and surface properties can be

important **considerations**. Particles with large surface areas, that is rough surfaces, will be more soluble and more reactive than the same size particle with a smoother surface. This is because the reactivity of a particle occurs on the surface. **A** particle with a potential *to* absorb gases may pose a unique hazard through its potential *to* transport other materials deep into the lung. This is a concern especially in a fire where many toxic pyrolysis products will be present in the air.

The site of deposition will be primarily controlled by the respiration rate, that is, the velocity with which the air moves through the respiratory passages, the geometry of the passages and the aerodynamic shape of the particle. Under conditions of stress or hard work, two things will happen. We will breath heavier and we will breath through our mouth as well as our nose. Breathing heavier increases the velocity of the air as it goes through the respiratory system. This will increase the rate of deposition by impaction and interception, but decrease the rate of deposition by sedimentation. **A** confounding factor is that by breathing heavier, the amount of air we inhale goes up and, therefore, the dose (quantity of particles inhaled) goes up. Generally, if we are breathing through our nose, the more rapidly we breath, the more aerosol we retain. The picture changes if we breath through our mouth. This by-passes all of the protective mechanisms of the nasal passages and delivers the toxicant directly *to* the trachea and lung. **As** such, lung deposition increases dramatically, especially for larger particles that would ordinarily be deposited in the upper airways.

Overall, larger particles tend to be removed in the nasal passages, smaller particles, from **4** micrometers to 0.5 micrometers are removed in both upper and lower respiratory tract. Fibers will tend to be intercepted, and removed in the bronchi, although some are trapped in the upper respiratory tract. Small particles, less than 1 micrometer, will reach the alveoli, deep in the lung. Retention of these particles is by diffusion and is favored in these small areas with a high surface to volume ratio. Highly charged particles will tend to be removed in the upper respiratory system. Naturally, acute inhalation of very high levels of aerosol will lead to a marked increase in

deposition near the portal of entry, that is, the nose or mouth, but the higher concentration will also deliver more material throughout the respiratory system.

Once deposited in the respiratory system, there are five mechanisms for removal. These include dissolution, physical removal by lung macrophages (phagocytosis), entrapment in the mucous layer lining the respiratory tract and clearance via ciliary action into the digestive tract, direct transport into the lymphatic system, and transport to the blood, most often of dissolved material.

In summary, acute exposure to high levels of aerosols raises a few unique concerns. These high levels of exposure can actually retard clearance from the respiratory tract so that it will occur at a slower pace than with a lower level exposure. This is the result of a slowing down of the mucociliary clearance rate. It will also lead to more widespread distribution of the aerosol in the respiratory tract. If choices are available in particle size or physical characteristics, a few factors should be taken into consideration. Soluble particles can be easily cleared from the lungs by dissolution. Large particles will not penetrate as deeply into the lung as small ones, but if they do, they may be more difficult to clear. Fibrous particles may represent a unique hazard due to their ability to penetrate deep into the lung and their resistance to clearance. Particles with a lower surface area to volume ratio are less likely to adsorb other materials and transport them to the lung. If a particle can degrade in the lung, the toxicity of the parent material as well as the breakdown products must be considered.

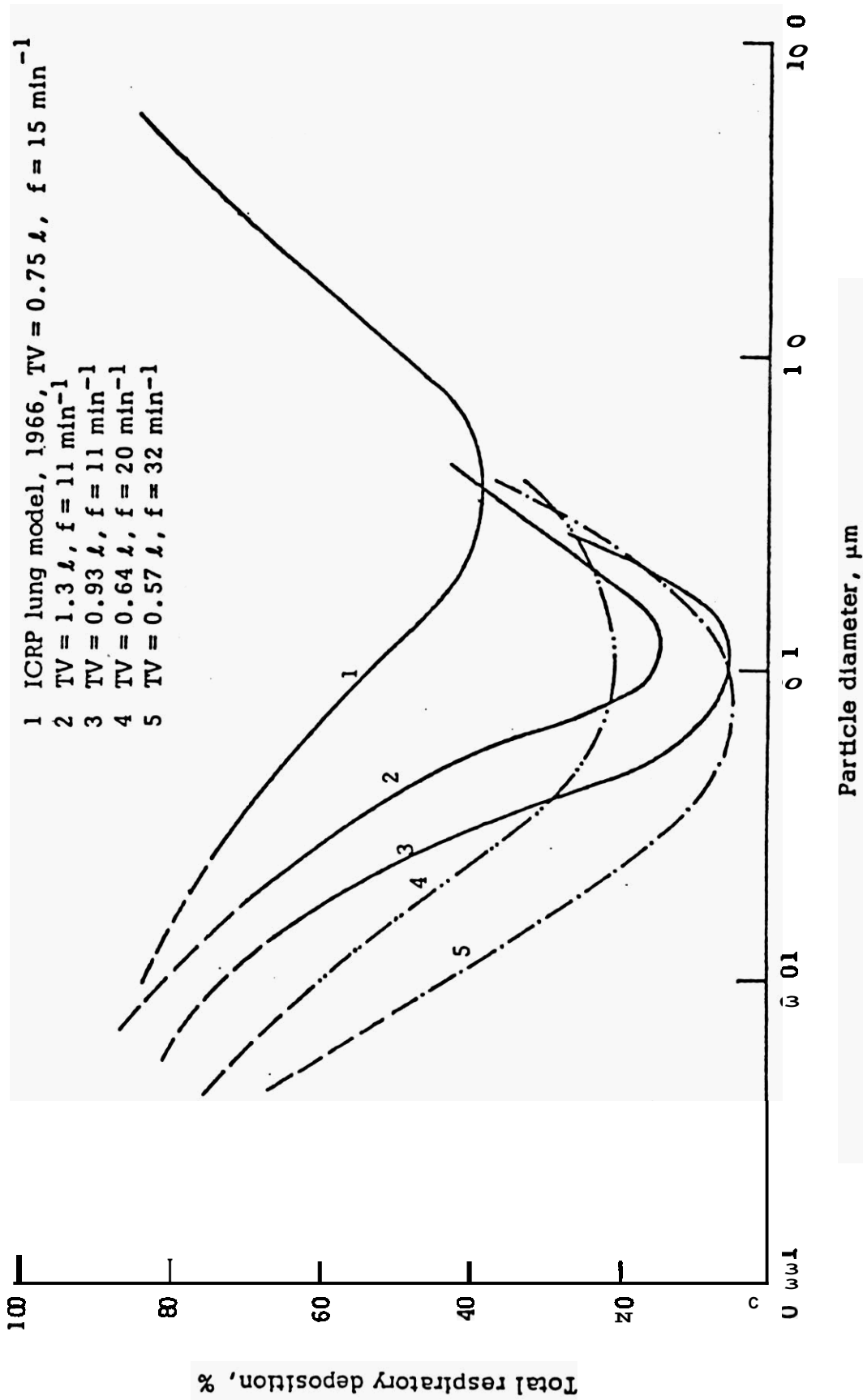
Our ideal particle is one that is amorphous, smooth, nonreactive but soluble in biological fluid, and has an aerodynamic mass media diameter greater than 1 micrometer.

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## Sources for Additional Information

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THE DETERMINATION OF RISK FACTORS FOR ACUTE EXPOSURES TO POWDERED AEROSOLS



Respiratory deposition as a function of particle size, tidal volume (TV) and respiratory frequency (f)

## THE DETERMINATION OF RISK FACTORS FOR ACUTE EXPOSURE TO POWDERED AEROSOLS

### Short Term vs Chronic Exposure

- High Level Short Term (Bolus)
  - Long Term Low Level
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## THE DETERMINATION OF RISK FACTORS FOR ACUTE EXPOSURE TO POWDERED AEROSOLS

### What is a Respirable Particle

- Size
  - Geometry
  - Charge
  - Other Physical Properties
- 

## THE DETERMINATION OF RISK FACTORS FOR ACUTE EXPOSURE TO POWDERED AEROSOLS

### Mechanisms of Deposition

- Sedimentation
  - Impaction
  - Diffusion (Brownian Movement)
  - Electrostatic Deposition
  - Interception
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## THE DETERMINATION OF RISK FACTORS FOR ACUTE EXPOSURE TO POWDERED AEROSOLS

### Toxicity Considerations

- Toxicity
- Biological Half-Life
- Physical Properties

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**Physical Properties of Particles**

- Durability
  - Solubility
  - Reactivity
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**Site of Deposition**

- Nasal Passages
  - Lower Respiratory Tract
  - Deep Lung
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**Mechanisms of Clearance**

- Solubilization
  - Uptake by Macrophage
  - Mucociliary Transport
  - Transport to Lymphatic System
  - Transport to Blood
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