PARTICLE DEPOSITION IN THE LUNG

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Abstract
The deposition of aerosol in the lung is an important issue regardless of whether the aerosol results from airborne pollutants or aerosol therapy. The specific pattern of deposition of airborne pollutants is a determinant in the development of pulmonary diseases since this pattern determines the local doses in the airspaces and the subsequent redistribution and clearance of the deposited particles. Aerosol therapy allows drugs to be directly administered to injured lung tissues, where they can act more efficiently and rapidly than when administered by injection or ingestion. Deposition of inhaled aerosols can also be used as a diagnostic tool to noninvasively detect changes in the dimensions of airways and alveoli that are critically associated with the development of pulmonary pathologies such as emphysema, asthma, or bronchitis.

The deposition of inhaled particles in the lung is primarily determined by the mechanisms of inertial impaction, gravitational sedimentation, Brownian diffusion, and, to a lesser extent, the mechanisms of electrostatic precipitation and interception. Deposition is minimal for particles in the size range 0.4–0.7 μm that have minimal intrinsic mobility. Deposition of larger particles results from significant gravitational and inertial transport, whereas deposition of smaller particles is mainly due to diffusive transport. Apart from particle size, several factors affect particle deposition, including particle characteristics, physiological and environmental factors, and lung anatomy.

Description
The lung is a prime target for a wide variety of airborne particles. When inhaled, these particles are transported into the lung, where they can eventually deposit onto airway and/or alveolar walls. The specific pattern of particle deposition throughout the respiratory tract is an important factor in the development of pulmonary diseases since this pattern determines the local doses in the airspaces and the subsequent redistribution and clearance of the deposited particles. Airborne particles can accumulate in offices, industrial areas, and residential atmospheres in concentrations large enough to pose a potential health hazard to people.

Aerosols are also encountered in medical applications for therapeutic, diagnostic, and experimental purposes. Aerosol therapy allows drugs to be directly administered to injured lung tissues, where they can...
act more efficiently and rapidly than if they were administered by injection or ingestion. Deposition of inhaled aerosols can also be used as a diagnostic tool to noninvasively detect changes in the dimensions of airways and alveoli that are critically associated with the development of pulmonary pathologies such as emphysema, asthma, or bronchitis. These diagnostic techniques are based on the assumption that the rate of particle loss by gravitational sedimentation during breath-holding periods is directly related to the airspaces containing the particles. The aerosol bolus technique can be used to study regional deposition. It uses monodisperse particles confined to a small volume injected into an inspiration of pure air. Depending on the position of the bolus in the inspired air, particles may penetrate to different volumetric depths in the lung. Deposition is then determined by the difference between the number of inspired particles and that expired during the subsequent expiration. Finally, the deposition of radiolabeled or fluorescent aerosols can also be used as an alternative means to visualize ventilation distribution in different parts of the lung. This latter technique is based on the assumption that the aerosol deposited in different lung units is in direct proportion to the ventilation in these units.

**Deposition Mechanisms**

There are several mechanisms by which particles can be deposited in the respiratory tract (Figure 1). The three main mechanisms are inertial impaction, gravitational sedimentation, and Brownian diffusion. Deposition may also occur by other less important mechanisms, such as electrostatic precipitation and, in the case of elongated particles (fibers), interception.

**Inertial Impaction**

Inhaled particles follow a complex path through the respiratory tract. Each time the flow changes direction, the momentum of the particles tends to keep them on their existing trajectories, causing them to deviate from the air streamlines and to eventually impact on airway walls. The deviation of the particle from the air streamline is greater the larger the particle mass and the greater the flow rate.

Inertial impaction is the primary mechanism of deposition for particles larger than 5 μm in diameter and is an important deposition mechanism for particles as small as 2 μm. The most likely sites of deposition by inertial impaction are in the complex geometry of the upper respiratory tract (that extends from the nasal and mouth cavities to the entrance of the trachea) and at the conducting airway bifurcations.

**Gravitational Sedimentation**

The mechanism of gravitational sedimentation refers to the settling of particles under the action of gravity. Particles reach their terminal settling velocity when the gravitational force equals the opposing viscous resistive forces of the air. Particles in the respirable range (<10 μm) reach their terminal velocity in less than 1 ms, a negligible fraction of the typical airflow.
transit time in any generation of the respiratory tract. The terminal settling velocity for a spherical sphere is expressed by

\[ v_s = \frac{\rho_c d_p^2 \mu}{18 \rho g} \]

where \( g \) is gravitational acceleration. The probability that a particle will deposit by gravitational sedimentation is proportional to \( v_s \). Therefore, probability increases with increasing particle size and density. Such probability also increases with increasing residence time in the airways. Although deposition by gravitational sedimentation can also occur in the upper respiratory tract, it is most important in the small airways and alveoli.

Gravitational sedimentation is the dominant mechanism of deposition for particles with a diameter ranging between 0.5 and 5 \( \mu m \). Larger particles deposit mainly by inertial impaction, whereas smaller particles are predominantly affected by Brownian diffusion.

**Brownian Diffusion**

Deposition by Brownian diffusion results from the random motions of the particles caused by their collisions with gas molecules. The diffusion rate is proportional to the Brownian diffusion coefficient

\[ D_B = \left( \frac{c k T}{3 \pi \mu d_p} \right) \]

where \( k \) is Boltzmann’s constant, \( T \) is the absolute temperature, and \( c \) is the Cunningham correction factor that accounts for the decreased air resistance caused by slippage when the particle diameter comes close to the mean free path of the gas molecules so that the particle no longer moves as a continuum in the gas but as a particle among discrete gas molecules.

Unlike impaction and sedimentation, which increase with increasing particle size, deposition by Brownian diffusion increases with decreasing particle size and becomes the dominant mechanism of deposition for particles less than 0.5 \( \mu m \) in diameter. Deposition by Brownian diffusion occurs mainly in the acinar region of the lung, although for very small particles \( (d_p < 0.01 \mu m) \), deposition by diffusion is also significant in the nose, mouth, and pharyngeal airways.

**Electrostatic Precipitation**

Deposition by electrostatic precipitation results from charged particles inducing image charges of opposite sign onto the surfaces of the airways that are electrically conducting while normally uncharged. Charged particles then become electrostatically attracted to the airway walls, and as a consequence, deposition of charged particles may be greater than that of neutral particles. Deposition by electrostatic precipitation is small, however, contributing to less than 10% of overall deposition.

**Interception**

Interception refers to the situation in which, in the absence of the deposition mechanisms described previously, the center of gravity of an elongated particle is in the gas phase while one of its ends touches an airway or alveolar wall. Such a situation is more likely to occur when the dimensions of the particle are comparable to those of the airspaces. Deposition by interception is usually significant only for particles such as fibers for which the ratio between length and diameter is large. Interception is more likely to occur in small airways and alveoli.

**Particle Deposition in the Healthy Lung**

Most of the studies investigating total deposition in human lungs have been performed on healthy subjects with monodisperse, neutral, nonhygroscopic particles. All studies show the same trend in the extent of deposition as a function of particle size. A typical curve is shown in Figure 2. Particles of unit density in the size range 0.4–0.7 \( \mu m \) present minimum intrinsic mobility and none of the mechanisms of impaction, sedimentation, and diffusion are effective in particle transport. Consequently, these particles have minimum deposition in the respiratory tract because their intrapulmonary trajectories have the smallest deviations from the air streamlines. For

![Figure 2](image-url)
particles larger than 0.7 μm in diameter, total deposition increases with increasing particle size because of increased gravitational and inertial transport. For particles smaller than 0.4 μm in diameter, total deposition increases with decreasing particle size because of increased diffusive transport.

Although particle size is probably the major factor affecting particle deposition in the lung, several other factors influence not only the total deposition of particles but also their regional deposition. These factors can be classified into four main categories: particle characteristics, physiological factors, lung anatomy, and environmental factors. Apart from its size, a particle is characterized by its density, shape, electrostatic charge, and hygroscopic properties. Particle density affects deposition by both impaction and sedimentation but has no effect on diffusive transport. Shape can have a profound effect on the aerodynamic behavior of the particles and therefore on deposition efficiency. Because the relative humidity in most of the lung is close to 100%, hygroscopic growth may significantly alter total and also regional deposition compared to the patterns observed with nonhygroscopic stable particles.

Physiological factors affecting deposition include breathing patterns, breathing frequency, tidal volume, functional residual capacity, airflow dynamics, and breathing pathway (oral versus nasal). Increasing airflow rates increase the efficiency of the velocity-dependent deposition mechanism (impaction) and decrease that of time-dependent deposition mechanisms (sedimentation and diffusion). Increasing tidal volumes allow particles to reach more distal regions of the lung, where deposition by diffusion and sedimentation are likely to occur, therefore increasing their relative contribution to overall deposition compared to deposition by impaction. During exercise, both flow rates and tidal volumes are increased, leading to higher deposition by impaction in the large airways and by sedimentation and diffusion in the small airways and alveoli. Finally, the nasal route is more efficient at filtering particles than the oral route. Therefore, mouth breathers will tend to deposit more particles in their lungs than nose breathers.

Anatomical factors such as airway length, airway diameter, branching angles, and alveolar size also play a key role in particle deposition. Because of intersubject variability, there is a large coefficient of variation in deposition among normal healthy subjects breathing in the same manner. Even within the same individual, the dimensions of the respiratory tract change with lung volume, age, and pathological processes. Gender differences in lung structure also cause variations in deposition between men and women. For example, the average female thorax is smaller than in men and the volume of the conducting airways is only approximately 75% that in men. Deposition in the tracheobronchial tree is therefore higher in women than in men. However, when these volume differences are combined with smaller resting minute ventilation and flow rates observed in women, total deposition is lower in women than in men mainly because of a smaller penetration of the aerosol in the alveolar region of the female lung. Airway geometry and breathing conditions evolve from birth to adulthood. These changes affect particle deposition throughout childhood. Although there are few studies on particle deposition in children, they all show that deposition in children tends to be higher than in adults by an average factor of 1.5. More important, the number of particles deposited per surface area is increased by a factor of 4 or 5 in children because of their smaller lung surface area compared to that of adults.

Finally, environmental factors such as temperature and humidity are likely to affect particle deposition. However, there is little information on the effect of these factors on particle deposition, although ambient humidity can greatly affect hygroscopic particles and therefore their deposition efficiency. Another environmental factor is gravity. Studies performed in the absence of gravity during parabolic flights have shown that deposition in the size range 0.5–3 μm was greatly reduced compared to deposition in normal gravity. These studies also suggested that although reduced, particle deposition in the periphery of the lung is enhanced compared to that with normal gravity.

Particle Deposition in the Diseased Lung

There are many factors that alter the deposition pattern of inhaled particles in the diseased lung. These factors, which include airway obstruction, alteration in alveolar dimensions, and changes in breathing patterns, influence the distribution of inspired particles and therefore their potential site of deposition. Obstruction of airways observed in bronchitis, cystic fibrosis, lung cancer, and emphysema tends to divert most of the flow to nonobstructed healthy airways that are increasingly exposed to inspired particles, reducing aerosol exposure and therefore deposition in the alveolar spaces subtended by the obstructed airways. Narrowing of the airways by inflammation, mucus, or bronchial constriction increases the local velocities of the airflow, enhancing deposition by inertial impaction even for small particles. Most lung diseases seem to increase central deposition at the expense of alveolar deposition. Positive correlations have been found between the depth of deposition...
within the respiratory tract and the forced expiratory volume, suggesting decreased peripheral deposition in patients with airway obstruction.


Further Reading

Nomenclature
- \( c \): Cunningham correction factor (dimensionless)
- \( d \): airway diameter (cm)
- \( D_B \): coefficient of Brownian diffusion (cm² s⁻¹)
- \( d_p \): particle diameter (cm)
- \( g \): gravitational acceleration (≈ 981 cm s⁻²)
- \( k \): Boltzmann’s constant (≈ 1.38 × 10⁻¹⁶ g cm² s⁻² K⁻¹)
- \( S_{tk} \): Stokes’ number (dimensionless)
- \( T \): absolute temperature of air (K)
- \( u \): mean linear velocity in airway (cm s⁻¹)
- \( v_s \): terminal settling velocity (cm s⁻¹)
- \( \mu \): dynamic viscosity of air (g cm⁻¹ s⁻¹)
- \( \rho_p \): particle density (g cm⁻³)

PECTUS EXCAVATUM

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Abstract
Pectus excavatum (PE) is one of the most common major anomalies of childhood. Males are affected six times more often than females. PE is usually recognized in infancy, becomes more severe with adolescent growth, and remains constant throughout adult life. Symptoms are infrequent during early childhood, but become increasingly severe during adolescence causing fatigue, dyspnea, decreased endurance, chest pain, tachypnea, and tachycardia. The heart is variably deviated into the left chest causing reduction in stroke volume. Pulmonary expansion is confined, causing a restrictive defect. Repair is recommended for symptomatic patients who have an elevated pectus severity index. Open repair with minimal cartilage resection is usually performed after the age of 10 years, optimally between 12 and 19 years. Adults can be repaired with similarly good results. The open technique removes minimal cartilage routinely using a temporary internal support bar for 6 months. Pain is mild and complications are rare; 97% of patients experience a good to excellent result. A new minimally invasive Nuss repair avoids cartilage resection and takes less operating time, but is associated with severe pain, longer hospitalization, and more complications, with the bar remaining for 2 or more years. This technique is less applicable to older patients and those with asymmetric deformities.

Introduction
Pectus excavatum (PE) is the most common congenital malformation of the thorax and is characterized