AEROSOL DRUG DELIVERY TO THE LUNGS

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1 INTRODUCTION

The delivery of therapeutic agents locally to the lungs through the inspiratory route is, in the majority of cases, the preferred course of treatment of respiratory diseases. Indeed, inhaled aerosols have long been employed in the management of asthma, cystic fibrosis, and chronic obstructive pulmonary disease (COPD). Gas-borne suspensions of fine liquid droplets or solid particles are introduced into the patient's inspiratory airflow to carry drugs into the lungs. Over recent years, it has become apparent that systemic drug delivery through the lungs to the bloodstream is an attractive alternative to more traditional methods of delivery, such as oral or intravenous administration. Targeting of inhaled aerosols to the lungs' alveolar regions allows for transport of deposited drug across the alveolar epithelium into the capillaries. Accordingly, aerosol drug delivery has emerged as a viable option for systemic administration of a large variety of drugs and will likely play an important role in the development of new therapies over the next decade.

The development and evaluation of aerosol drug delivery systems requires a level of comfort with fields such as aerosol mechanics, fluid mechanics, and transport phenomena that may be unfamiliar to newcomers whose training backgrounds lie outside of the physical sciences. The intent of the first section of this chapter is to provide a very brief introduction to aerosol mechanics as related to the transport and deposition of inhaled drug particles throughout the respiratory tract. This familiarization will serve as requisite background for the discussion of aerosol particle sizing instruments in use for research and development, regulatory, and quality assurance purposes, as well as for descriptions of the different types of aerosol delivery systems currently available and in development.

2 RESPIRATORY TRACT DEPOSITION OF INHALED PARTICLES

The human respiratory tract is made up of a complicated series of branching, or bifurcating, airways. Phillips et al. [1] have described in detail much of the influential work done in measuring and modeling respiratory tract geometry. Despite its limitations, the most widely adopted model remains the highly idealized, symmetric model given by Weibel [2], and referred to as the Weibel A model. Under the Weibel A model, airways are classified by a generation number (beginning with zero at the trachea), which indicates the number of bifurcations separating the airway from the trachea. Airway diameters and lengths become progressively smaller as the generation number increases. Generations 0–16 make up the tracheobronchial region, through which air is conducted upon inhalation and exhalation, while generations 17–23 comprise the alveolar region, wherein gas exchange with the capillaries occurs. In addition, the extrathoracic region, consisting of the oral and

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