administered locally compared to delivery by the oral or parenteral routes, thereby reducing the potential incidence of adverse systemic effects and reducing drug costs. The pulmonary route is also useful where a drug is poorly absorbed orally, e.g. sodium cromoglicate, or where it is rapidly metabolized orally, e.g. isoprenaline. The avoidance of first-pass metabolism in the liver may also be advantageous, although the lung itself has some metabolic capability.

The lung may also be used as a route for delivering drugs having systemic activity, because of its large surface area, the abundance of capillaries and the thinness of the air–blood barrier. This has been exploited in the treatment of migraine with ergotamine, and the potential for delivering biopharmaceuticals, such as insulin, vaccines and growth hormone via the airways is now well established.

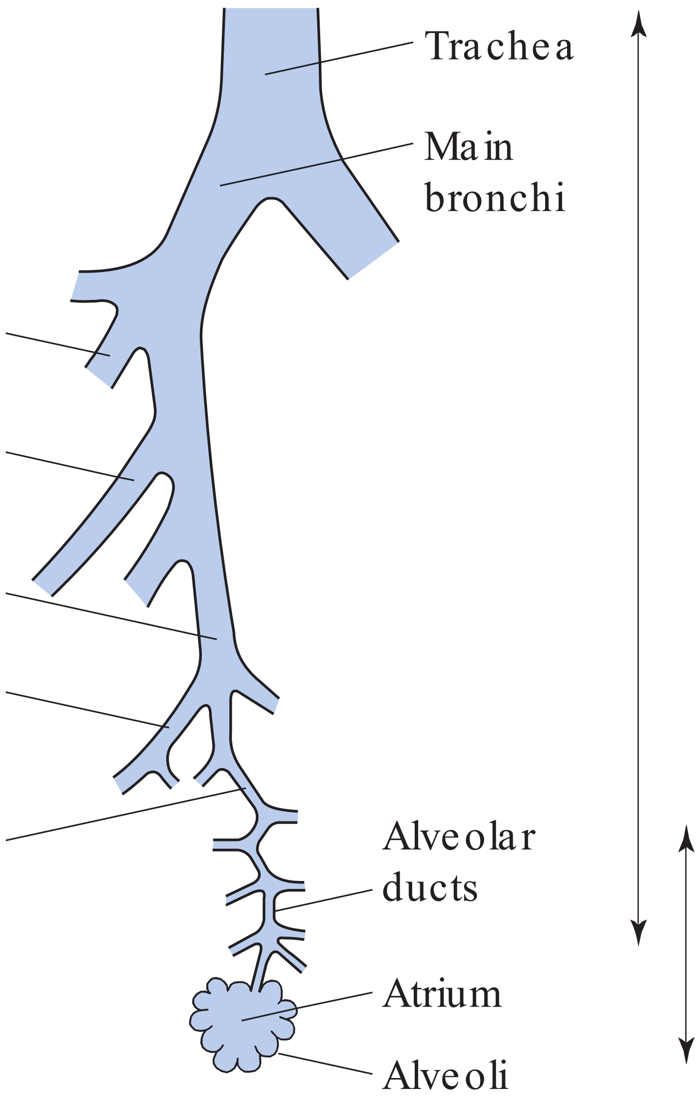

Fig. 37.1 • Schematic representation of the human airways.

Lung anatomy

The lung is the organ of external respiration, in which oxygen and carbon dioxide are exchanged between blood and inhaled air. The structure of the airways also efficiently prevents the entry, and promotes removal of airborne foreign particles, including microorganisms.

The respiratory tract can be considered as comprising conducting (central) regions (trachea, bronchi, bronchioles, terminal and respiratory bronchioles) and respiratory (peripheral) regions (respiratory bronchioles and alveolar regions), although there is no clear demarcation between them (Fig. 37.1). The upper respiratory tract comprises the nose, throat, pharynx and larynx; the lower tract comprises the trachea, bronchi, bronchioles and the alveolar regions. Simplistically, the airways can be described by a symmetrical model in which each airway divides into two equivalent branches or generations. In fact, the trachea (generation 0) branches into two main bronchi (generation 1), of which the right bronchus is wider and leaves the trachea at a smaller angle than the left, and hence is more likely to receive inhaled material. Further branching of the airways ultimately results in terminal bronchioles. These divide to produce respiratory bronchioles, which connect with alveolar ducts leading to the alveolar sacs (generation 23). These contain approximately 2–6 × 10^8 alveoli, producing a surface area of 100–140 m^2 in an adult male.

The conducting airways are lined with ciliated epithelial cells. Insoluble particles deposited on the airways walls in this region are trapped by the mucus, swept upwards from the lungs by the beating cilia to the throat, and are swallowed.

Inhalation aerosols and the importance of size distribution

To deliver a drug into the airways, it must be presented as an aerosol (with the exception of medical gases). In pharmacy, an aerosol is defined as a two-phase system of solid particles or liquid droplets dispersed in air or other gaseous phase, having sufficiently small size to display considerable stability as a suspension.

The deposition of a drug/aerosol in the airways is dependent on four factors: the physicochemical properties of the drug, the formulation, the delivery/liberating device, and the patient (breathing patterns and clinical status).

The most fundamentally important physical property of an aerosol for inhalation is its size. The particle size of an aerosol is usually standardized by calculation of its aerodynamic diameter, d_a, which is the physical diameter of a unit density sphere which settles through air with a velocity equal to the particle in question. Therapeutic aerosols are heterodispersed (polydispersed) and the distribution of sizes is generally represented by the geometric standard