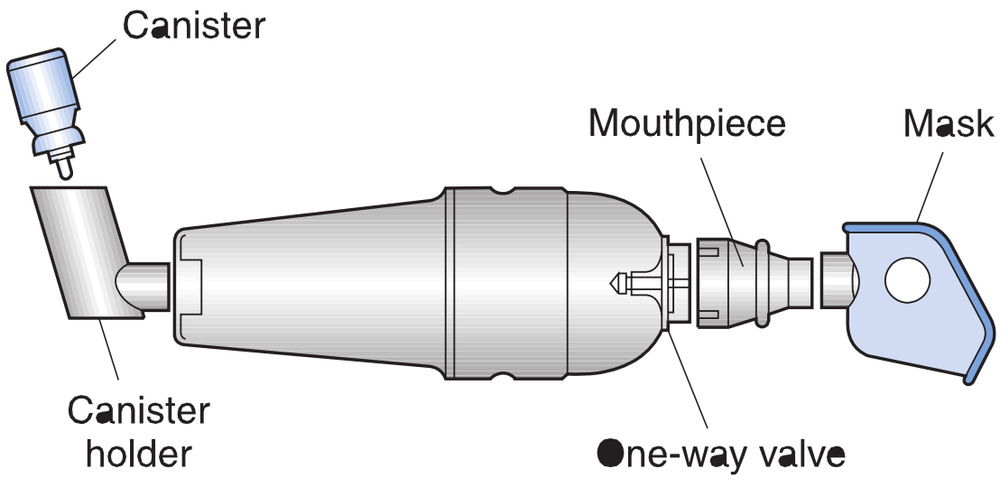

Fig. 37.4 • Spacer device, fitted with a facemask for use by a child.

evaporation occurs and the need for actuation/inhalation coordination is removed. The disadvantage of traditional spacers, though effective, is that they may be cumbersome because of their large volume, e.g. Volumatic® (GlaxoSmithKline), though smaller, medium-volume spacers are now available, e.g. AeroChamber Plus® (GlaxoSmithKline). Alternatively, extension tubes may be built into the design of the pMDI itself as an extended mouthpiece, e.g. Syncroner® (Sanofi-Aventis) and Spacer Inhalers® (AstraZeneca). Breath-actuated pMDIs do not release drug until inspiration occurs. In the Autohaler® (3M), an inspiratory demand valve triggers a spring mechanism to release drug, whilst in the Easibreathe® (Teva), a vacuum in the device is released on inspiration to trigger the actuation. Breath-actuated devices overcome the coordination problems of conventional pMDIs and are easy to use without adding bulk to the device.

Dry powder inhalers

In dry powder inhaler (DPI) systems, drug is inhaled as a cloud of fine particles. The drug is either preloaded in an inhalation device or filled into hard gelatin capsules or foil blister discs which are loaded into a device prior to use.

DPIs have several advantages over pMDIs. DPI formulations are propellant-free and usually do not contain any excipient, other than a carrier (see below), which is usually lactose. They are breath-actuated, avoiding the problems of inhalation/actuation coordination encountered with pMDIs. DPIs can also deliver larger drug doses than pMDIs, which are limited by the volume of the metering valve and the maximum suspension concentration that can be employed without causing valve clogging. However, DPIs have several disadvantages. Liberation of powders from the device and the deaggregation of particles are limited by the patient's ability to inhale, which in the case of respiratory disease may be impaired. An increase in turbulent air flow created by an increase in inhaled air velocity increases the deaggregation of the emerging particles but also increases the potential for inertial impaction in the upper airways and throat, and so a compromise has to be found. Further, DPIs are exposed to ambient atmospheric conditions, which may reduce formulation stability. For instance, elevated humidity may cause powders to aggregate. Finally, DPIs are generally less efficient at drug delivery than pMDIs, such that twice the dose is often required for delivery from a DPI compared to the equivalent pMDI.

Formulating dry powder inhalers

To produce particles of a suitable size (preferably less than 5 μm), drug powders for use in inhalation systems are usually micronized. Alternatives are spray drying, spray freeze drying and supercritical fluid technology. The high-energy powders produced by micronization have poor flow properties because of their static, cohesive and adhesive nature. The flowability of a powder is affected by physical properties, including particle size and shape, density, surface roughness, hardness, moisture content and bulk density.

To improve their flow properties, poorly flowing drug particles are generally mixed with larger 'carrier' particles (median size usually 30–150 μm) of an inert excipient, usually lactose (α-lactose monohydrate). Drug and carrier particles are mixed to produce an ordered mix in which the small drug particles attach to the surface of the larger carrier particles. This not only improves liberation of the drug from the inhalation device by improving powder flow, but also improves the uniformity of capsule or device filling. Once liberated from the device, the turbulent air flow generated within the inhalation device should be sufficient for the deaggregation of the drug/carrier aggregates. The larger carrier particles impact in the throat, whereas smaller drug particles are carried in the inhaled air deeper into the respiratory tract.

The success of DPI formulations depends on the adhesion of drug and carrier during mixing and filling of devices or hard gelatin capsules, followed by the ability of the drug to detach from the carrier during inhalation, such that free drug is available to