**Dosage forms: aerosols pulmonary & nasal**

**MDI**

- **Metered Dose Inhaler**
- Delivers a specific amount of drug to lungs
- Treats: asthma, COPD
- Drug: usually a bronchodilator or corticosteroid
- Most commonly used type of inhaler
- Spacers: an add-on device; a tube that acts as a reservoir to reduce the speed at which the aerosol enters the mouth; easier to inhale and ensures med gets into lungs and not the air
- Propellant: medium in which API is suspended/dissolved
- Propellants must pass strict criteria: bp, density, vapor pressure, nonflammable, good solvent, non-toxic
- Active ingredients should either be fully soluble or fully insoluble
- CFC
  - Chlorofluorocarbons
  - Phased out due to environmental safety concerns: kills the ozone layer
- HFA
  - Hydrofluoroalkanes
  - HFCs emerged as the only propellant suitable for pharmaceutical use. No other compound has been proven to meet the stringent criteria for a medical gas to be used for medicinal inhalation by patients
- Even though the inhaler may continue to work beyond that number of uses, the amount of medication delivered may not be correct
- Metering chamber: holds the liquid, which is expelled when the actuation is depressed and refilled when the actuator is released; the metering chamber allows an exact dose for each actuation
- How to use an inhaler: [http://www.youtube.com/watch?v=bq3E70xgSuY&NR=1](http://www.youtube.com/watch?v=bq3E70xgSuY&NR=1)
- Considerations for an ideal system: formulation, bioavailability, and compliance (along with their subcategories)

**DPI**

- **Dry Powder Inhaler**
- Non-pressurized device that delivers fine particle size drug transported to the lungs when the patient inhales
- Micronized powder packaged in single dose quantities in blisters or gel capsules containing the powdered medication to be drawn into the lungs by the user’s own breath
- Difficult formulation to compound
- Treats: asthma, bronchitis, COPD, emphysema, and even diabetes mellitus
- Medication is commonly held in a capsule for manual loading
- How to use: once loaded or actuated, the operator puts the mouthpiece of the inhaler into their mouth and takes a deep inhalation, holding their breath for 5-10 seconds
- How to use a diskus: [http://www.youtube.com/watch?v=HTbPfI0mlb4](http://www.youtube.com/watch?v=HTbPfI0mlb4)
- Inhalable insulin (Exubera): [http://www.youtube.com/watch?v=vU1gVsul0ME](http://www.youtube.com/watch?v=vU1gVsul0ME)
- Administration: need to initiate dose and activate particles before, and to rinse mouth after
- Benefits: rapid onset, avoid injection, avoid 1st pass metabolism, allows protein absorption (e.g. insulin)
- Problems: DPIs rely on the force of patient inhalation to entrain powder from the device and subsequently break-up the powder into aerosol particles that are small enough to reach the lungs
  - Insufficient patient inhalation flow rates may lead to reduced dose delivery and incomplete deaggregation of the powder
  - DPIs have a minimum inspiratory effort that is needed for proper use, therefore are normally used only in older children and adults
- Lactose: used as a bulking agent, to aid in powder uptake
- Storage: must be stored in a dry place or sealed packaging, since exposure of the powder to moisture degrades the ability of the device to disperse its medication as a fine powder upon inhalation
- Metering device: must be moisture-resistant so particles won’t stick together, and it may be necessary to use a spacer tube and/or motorized delivery device to ensure max inhalation of dose

### Inhalation Solutions (Nebulizers)

- Uses oxygen, compressed air or ultrasonic power, as means to break up medical solutions/suspensions into small aerosol droplets, for direct inhalation from the mouthpiece of the device
- Aerosol droplets need to be 1-5 microns in diameter
- Nebulizers accept their medicine in the form of a liquid solution, which is often loaded into the device upon use
- Venturi principle: the reduction in fluid pressure that results when a fluid flows through a constricted section of pipe
- It is a small compact air compressor. They are used for people having difficult breathing (e.g. asthma). It takes a liquid medication and puts it into the form of a fine mist, so that the mist can be distributed into the lungs. They are used for chronic therapy of respiratory disorders.
  - What is a nebulizer: [http://www.youtube.com/watch?v=2625nq6WF2M&feature=channel](http://www.youtube.com/watch?v=2625nq6WF2M&feature=channel)
  - How to use a nebulizer: [http://www.youtube.com/watch?v=KCALJSiGZNc](http://www.youtube.com/watch?v=KCALJSiGZNc)
  - How to load a nebulizer: [http://www.youtube.com/watch?v=XQAujJARy8U&feature=channel](http://www.youtube.com/watch?v=XQAujJARy8U&feature=channel)

### Nasal Sprays

- Non-pressurized device that delivers a fine mist containing active ingredients and transported by inhalation
- Either local or systemic use
- Method: instilling a fine mist into the nostril by action of a hand-operated pump mechanism
- Treats: antihistamines, corticosteroids, topical decongestants
- Uses: nasal decongestant, systemic corticosteroid, and more
  - How to use a nasal spray: [http://www.youtube.com/watch?v=wQbyC5cpEQI](http://www.youtube.com/watch?v=wQbyC5cpEQI)
- Why through the nasal route?
  - To alleviate nasal symptoms
  - Because some drugs are inactivated in the GI tract (e.g. proteins, peptides)
- Not an ideal route: affected by physiological conditions of the nose (vasculature, mucus flow rate), and changes in the surrounding (e.g. environment, temperature, humidity) which can change the nasal passage
- Formulation is either an aqueous solution or suspension, depending on the solubility of the API
  - The particle size needs to be 1-3 microns
  - No drip formula: cellulosic polymer is added to increase the viscosity
  - The formulation is buffered, isotonic, and preserved
- Two types of spray
  - Continuous spray: valve only
  - Metered dose spray: valve + dip tube
- Manufacturing is fairly easy since the liquid filling process is non-pressurized and non-sterile

### Aerosols

**OVERVIEW**
An aerosol dispenser contains a mixture consisting of the propellant and the pharmaceutical active substance dissolved or suspended in the liquefied propellant and sometimes with further excipients such as co-solvents and/or surfactants added in very small amounts.
THE PRINCIPLE
The principle behind this involves having the pressurized gas or the newly formed gas push the liquid out of the nozzle. In the can, there’s a tube running from the nozzle to the bottom of the can. When depressed, the tube opens, and the pressurized gas tries to escape the can by going out the tube. Because the liquid is in the way, the liquid is pushed out by the pressurized gas.

THE CONTAINER
Modern aerosol spray products have three major parts; the can, the valve and the actuator or button. The valve is crimped to the rig of the can, and the design of this component is important in determining the spray rate. The actuator is depressed by the user to open the valve; the shape and size of the nozzle in the actuator controls the spread of the aerosol spray.

THE PARTS OF AN AEROSOL
1. The product: in the form of a liquid, emulsion or suspension
2. The propellant: which can be a liquefied gas or a compressed gas

COMPRESSED GAS
An aerosol can contains one fluid that boils well below room temperature (the propellant) and one that boils at a much higher temperature (the product). There are two ways to configure this aerosol system. In the simpler design, you pour in the liquid product, seal the can, and then pump a gaseous propellant through the valve system. The gas is pumped in at high-pressure, so it pushes down on the liquid product with a good amount of force. When you push the head piece/actuator down, the high-pressure propellant gas drives the liquid product up the plastic tube and out through the nozzle. The narrow nozzle serves to atomize the flowing liquid -- break it up into tiny drops, which form a fine spray. The amount of gas in the headspace remains the same but it has more space, and as a result the pressure will drop during the life of the can. Spray performance is maintained however by careful choice of the aerosol valve and actuator.

LIQUEFIED GAS
This is the more popular (and slightly more elaborate) system. The propellant will take liquid form when it is highly compressed, even if it is kept well above its boiling point. Since the product is liquid at room temperature, it is simply poured in before the can is sealed. The propellant, on the other hand, must be pumped in under high pressure after the can is sealed. When the propellant is kept under high enough pressure, it doesn't have any room to expand into a gas. It stays in liquid form as long as the pressure is maintained. The actual can design in this liquefied gas system is exactly the same as in the compressed gas system, but things work a little bit differently when you press down the button. When the valve is open, the pressure on the liquid propellant is instantly reduced. With less pressure, it can begin to boil. Particles break free, forming a gas layer at the top of the can. This pressurized gas layer pushes the liquid product, as well as some of the liquid propellant, up the tube to the nozzle. When the liquid flows through the nozzle, the propellant rapidly expands into gas. The vapor can exist in equilibrium with its bulk liquid at a pressure that is higher than atmospheric pressure. As gas escapes, it is immediately replaced by evaporating liquid. Since the propellant exists in liquid form in the can, it should be miscible with the liquid or dissolved in the liquid. The consistency of the expelled product depends on several factors, including:

- The chemical makeup of the propellant and product
- The ratio of propellant to product
- The pressure of the propellant
- The size and shape of the valve system

As the product is used up as the valve is opened, some of the liquid propellant turns to gas and keeps the head space full of gas. In this way the pressure in the can remains essentially constant and the spray performance is maintained throughout the life of the aerosol.
The basic mechanism at work is the same: one fluid pushes another.