Aerosol therapy is a very important administration route in the treatment of lung diseases such as asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF) and bronchopulmonary dysplasia (BPD). Aerosols are also used to deliver systemic drugs such as vaccines, insulin, antibiotics and pain medications. To treat these diseases effectively with medical aerosols one needs to understand the basics of aerosol science and the operating principles of the devices available.
Inhaling medication is difficult for a significant amount of patients. This has been demonstrated in many of studies. Device instructions for use that come with the drug, does not lead to a perfect inhalation technique, not even immediately after reading the instructions and practicing with the device. Inappropriate device technique is due to the lack of formal patient training.
The purpose of this course is to increase your knowledge of the basic science of aerosol drug delivery. The course will cover the rationale, influencing factors and application of inhaled drug therapy. The focus will be on the concept of particle size as it relates to deposition in the respiratory tract and the detail of the three device platforms including pMDI, DPI & jet nebulizers.

<table>
<thead>
<tr>
<th>PHILIPS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td>Understand the justification, influencing factors and applications of inhaled drug therapy.</td>
</tr>
<tr>
<td>Become familiar with basic aerosol device principles: the importance of particle size and patient technique.</td>
</tr>
<tr>
<td>Understand the operating theories, advantages and disadvantages of the three respiratory drug delivery device platforms:</td>
</tr>
<tr>
<td>• Metered Dose Inhalers (MDIs)</td>
</tr>
<tr>
<td>• Dry Powder Inhalers (DPIs)</td>
</tr>
<tr>
<td>• Jet Nebulizers</td>
</tr>
</tbody>
</table>
Methods for generating aerosols, formulating drugs, and administering medications effectively to the desired site of action constitute the science of respiratory drug delivery.

Nebulization of substances for inhalation is among the oldest methods of delivery to the lung. The earliest reports can be traced back to the middle of the 19th century; European spas used systems to deliver thermal aerosolized water to treat lung afflictions. Smokers and drug abusers discovered that by inhaling substances into their lungs, the desired effect would be quicker, they would not need as much of the substances, and other elements of delivery could be eliminated, such as needles. ¹

The inhaled route has several advantages as demonstrated by the therapeutic window graph. Drug delivery via the lung allows direct delivery to the site of action, for small quantity of drug to be enough for an adequate response, an onset of action that is usually faster, and the systemic bioavailability has less variability in side effects and efficacy than other drug delivery methods. ²
Successful drug delivery to the lung is dependent on a variety of factors such as the physical characteristics of the aerosol, the device that is used to deliver the drug, the patient, the drug and the disease.  

Understanding the physical nature of aerosolized particles deposited within the human respiratory tract is a key part to understanding how respiratory drug delivery devices operate. Aerosols exist everywhere there is gas to breathe. From pollens and spores, to smoke, pollution and man-made chemicals, aerosols include any fine liquid or solid particles. Every day billions of particles are inhaled with ambient air by every human being. Our airways are constantly filtering and removing unwanted particles.
Aerosol therapy provides a fast, effective route for treating lung disorders because the drug is delivered to the site of action. Aerosol therapy is most commonly used to prevent or treat bronchospasm, prevent or treat inflammation, liquefy and mobilize secretions, and prevent or treat respiratory infections.

Aerosol therapy is also used to deliver systemic drugs such as vaccines, insulin and pain medications. 5 and 6
The primary reasons for utilizing respiratory drug delivery are; speed of action, less side potential effects and its comfort.

Respiratory drug delivery is in the management of chronic and acute respiratory disease. However, respiratory drug delivery is also used for systemic drug delivery. Examples include vaccines, pain medications, antibiotics and insulin.

The factors that influence drug delivery to the lung will be discussed in the next section.
The purpose of a respiratory drug delivery device is to create aerosolized particles or facilitate aerosol delivery to the lungs. The mechanisms of particle delivery to the lungs will be discussed in this section.
Understanding the physical properties of aerosolized particles is key to understanding how respiratory drug delivery devices operate.
Our respiratory system’s evolved filtration and elimination mechanism is an impediment to respiratory drug delivery. The nose removes particulate matter we breathe from the air before it deposits in the airways. Nasal hairs filter out large particles (greater than 15 μm in diameter). The respiratory tract has a variety of strategies for dealing with particles that bypass the nose. Coughing and sneezing reflexes triggered by airway irritation, accelerate the movement of particles up the conducting airways and out of the body. 7 and 8

Medicinal particles however, are sized and shaped to overcome our respiratory filtration system. Their deposition in the respiratory tract may be predicted.

Patients inhale drug particles for the treatment of respiratory diseases generated by formulations especially designed for this purpose. In contrast to ambient particles, medicinal particles are distributed over a limited size range: their shape and composition are known, and their deposition in the respiratory tract may be predicted rather precisely. 9 and 10
Respiratory drug delivery devices do not produce particles of just one size. They produce particles in a variety of sizes. The size of the particle produced by the device determines how deep the particle can penetrate into the respiratory tract. Smaller particles penetrate deeper into the lung and may allow the inhaled medication to work more effectively.\textsuperscript{11} and\textsuperscript{12}

\textbf{PHILIPS}

The Importance of Particle Size on Lung Deposition in Aerosol Therapy

- In order for the drug to reach the deep lungs, drug particles need to fall within a certain size range.
- Particles that are too big get stuck in the upper airways and particles that are too small are exhaled.
- The optimum particle size for asthma and COPD drugs is generally agreed to be between 1 micron and 5 microns.
Particle Size

Small particles are needed to distribute the drug throughout the lungs. Large particles carry significantly more drug.

Diameter 1
1 x 1 x 1 = 1

Diameter 2
2 x 2 x 2 = 8

Diameter 10
10 x 10 x 10 = 1000

Volume is a function of diameter cubed
Particle size is measured in microns. 1 micron is 1 millionth of a meter (1 thousandth of a millimeter). To understand how small that is, a human hair is between 40-60 microns. The eye cannot see discrete particles below 25-30 microns. Particles that are between 1-5 microns are considered to be respirable. 13
The factors affecting particle delivery to the lung are: Size - The physical property of the aerosol itself is the aerodynamic diameter. The ideal size for therapeutic aerosols is < 5 microns to penetrate the tracheobronchial tree. In order to evaluate and compare the efficiency of devices, the particle size must be measured and statistically described.

A descriptive term that is often used in the evaluation of particle size is Mass Median Aerodynamic Diameter (MMAD). MMAD is a multi-dimensional measurement used to evaluate particle size and its relationship to the mass (volume) of the aerosol produced. It is used to determine the depth of potential penetration of an aerosol particle into the respiratory tract.

The graph shows the diameter at which half of the aerosol particles are larger than the MMAD and half of the aerosol particles are smaller than the MMAD. In this graph, the MMAD is 10μm. MMAD is measured by cascade impaction. Cascade impaction is an invitro test that measures the size of particles based on their behavior in an air-stream. The mass of drug particles with a given aerodynamic diameter is analyzed.

Physical properties of the particle play an important role in the potential for delivery of particles to the lung. The shape, gravity and motion also impact the penetration of particles.
Aerosol testing is usually performed under simulated use conditions in a lab and it is assumed that patients will follow the instructions for use to optimize drug delivery. However, for many patients, aerosol devices are difficult to use without proper hands-on training. The age and disease state of the patient play major role in drug delivery to lungs. For example, a COPD patient’s airway is obstructed and resistant to air flow. That may lead to large airway particle deposition. Therefore, breathing techniques are needed to maximize drug delivery to their lungs.\textsuperscript{16 and17}

To understand the role the device plays in drug delivery, it is important to know how it operates and the factors that will optimize utilization such as; clinical setting, patient age and the ability to use the selected device correctly, device use with multiple medications, cost and reimbursement, drug administration time and convenience.\textsuperscript{18}

The next section will explain the operation of commonly used drug delivery devices.
As mentioned previously, successful drug delivery to the lung is dependent on a variety of factors such as the physical characteristics of the aerosol, the device used have the potential to deliver the drug, the patient, the drug and the disease. The first portion of the course focused on understanding the physical nature of aerosolized particles and where they are deposited within the human respiratory tract. This portion of the lecture will focus on understanding how aerosol delivery devices operate.
Despite the numerous methods that can be employed to generate aerosols in therapeutically useful particle size ranges and concentrations, only three basic aerosol delivery systems have found their way into commercially marketed drug products: metered dose inhalers (MDIs), Dry Powder inhalers (DPIs) and jet nebulizers.

None of these devices can be precisely dosed in a single breath, but are manufactured to achieve minimally acceptable dose. To be acceptable for clinical use the inhalation system must meet certain criteria: simple, convenient, inexpensive and portable.

Device and drug formulations undergo extensive clinical trials and regulatory approval before being released. However, there is no perfect, fail-safe, error-proof respiratory drug delivery device on the market today. For many patients, drug delivery devices are difficult to use without proper training.19
Since the 1950’s MDIs have been a mainstay of the respiratory drug delivery devices because they are compact, portable, provide multi-dosing and are perceived to be easy to use. Each MDI has a specific formulation and dose of drug depending upon the specific drug. Formulations include the drug as well as propellant and other things called excipients that help aerosolized the contents of the MDI. Each actuation of the inhaler is associated with a single inspiration of the patient. The MDI is typically a single patient use device that is dispensed from the pharmacy with a specific quantity of medication and disposed of when the medication has been depleted. 20, 21 and 22

The next few slides will examine the components and operation of the MDI; discuss advantages and disadvantages of the MDI.
Since its development by Dr George Maison in 1955, the pressurized metered-dose inhaler (pMDI) has been the most common aerosol generator prescribed for patients with asthma and COPD. This is because it is compact, portable, easy to use, and provides multi-dose convenience. 23, 24 and 25
Regardless of the manufacturer or active ingredient, the basic components of the pMDI include; an actuator nozzle, expansion chamber, metering valve, canister, gas phase or propellant vapor, formulation (liquid drug propellant mixture), metering chamber and actuator.

The metering valve is crimped onto the mouth of the canister, and the entire system is enclosed in the actuator through which inhaled ambient air is drawn in by the patient.

A typical canister may contain 150-300 doses of medication. A pre-measured amount of drug is delivered per actuation when the device is shaken inverted and the canister depressed.26, 27 and 28
When the device is actuated, the canister is exposed to atmospheric pressure, which leads to aerosolization (high velocity spray) of the drug. As it travels through the air, the aerosol warms, leading to evaporation of the propellant but the drug remains unchanged. Evaporation reduces the particle size to the desired range.

As the particles travel, they slow down as they collide with the surrounding air. The particle size emitted from the MDI is dependent on the vapor pressure of the propellant and diameter of the actuator opening. The size of particles emitted from these devices will be reduced as vapor pressure is increased and diameter of the actuator decreases. 29 and 30
A common end user problem that can prevent the metered amount of drug from reaching its target is not following the required steps for using a MDI.

Not shaking a pMDI canister that has been standing for a short time can decrease the respirable dose as much as 25% and 35%. This is because the drug in the canister is usually separated from the propellants when left standing. Therefore, MDIs must be shaken before the first actuation after standing in order to refill the metering valve with adequately mixed suspension from the canister.

Priming the MDI is also required after being unused for a period of time. Priming is releasing one or more sprays into the air. It is required because the drug may be separated from the propellant in the metering valve when the pMDI is new or has not been used for a while. Because shaking the pMDI will mix the suspension in the canister but not the metering chamber, priming of the pMDI is required.

Storage Temperature: Outdoor use of pMDIs in very cold weather may significantly decrease aerosol drug delivery. For example, dose delivery from HFA-MDIs decreased by 70% over the range of -20 to 20 ºC (44)

Cleaning: The amount of medication delivered to the patient is dependent upon the metering valve, cleanliness and the lack of moisture. The actuator nozzle is pMDI specific and the coordination of the nozzle with the medication will influence both inhaled dose and particle size. White and crusty residue due to lack of cleaning may crystallize the
medication and influence drug delivery. Therefore, the nozzle should be cleaned periodically based on the manufacturer’s recommendations 30, 31, 32 and 33
Only a small fraction of the drug may reach the lung if there is poor coordination between actuation and inhalation. 34

Some common hand/breath problems include firing into mouth while breathing through the nose, firing before start of inhalation and firing after inhalation and multiple actuations during a single inhalation.

It is also important to wait 60 seconds between each actuation. With each actuation there is a cooling of the contents and, if the contents are not allowed to re-warm, the predictability of the aerosol produced is poor when the contents are cool.

Inappropriate inhaled flow rate – to minimize impaction the patient must breathe in the medication slowly or less than 60 LPM. A breath hold after actuation is important to maximize particle deposition through sedimentation and diffusion. The longer a patient holds the drug in their lungs, the better the opportunity for the particle deposition and the fewer particles are exhaled. 35, 36 and 37

This radioscintigraphic picture demonstrates what can happen when a pMDI is not correctly used. Drug is deposited in the mouth, posterior pharyngeal and stomach region.
The steps required for MDI use make it difficult for the patient to properly inhale the drug. It is especially difficult to make a child or infant inhale the prescribed medical substances in the proper way. Children and infants have limited lung capacity and the force of a child's or infant's breath during inhalation (inhalation flow) is thus limited. This is even more so when the child or infant is suffering from asthma or other bronchial diseases. 38 and 39

For patients of limited or compromised inhalation capacity, inhalation through a MDI may be accomplished through the use of a spacer or valved holding chamber. 40, 41 and 42
Correct MDI Inhalation Technique

**Dosing**

- Actuate the pMDI as s/he begins to breathe in slowly
- Hold his/her breath for 10 seconds. If s/he cannot hold their breath for 10 seconds, then for as long as possible
- Wait 1 minute if another puff of medicine is needed.
- Repeat steps 2-10 until the dosage prescribed by the patient's doctor is reached
- If taking a corticosteroid, s/he should rinse the mouth after the last puff of medicine, spit the water out and not swallow it.
The picture shows the spray differences between HFA-pMDIs and CFC-pMDIs. HFA-pMDIs have a softer spray than do CFC-pMDIs. With a HFA propellant, the spray is propelled at a slower rate as shown in the picture. A slower velocity theoretically will improve drug deposition. However the HFA slower spray does not eliminate problems associated with coordination. This is especially true for small children who require a valved holding chamber (VHC). VHCs and spacers will be discussed in the next few slides. Additionaly, actuation with breath moisture may cause an HFA propelled metering valve to stick, therefore the canister should not be immersed in water. The float test that was used to determine canister load with CFC MDIs, is no longer recommended. Some newer HFA MDIs have dose counters but many do not and patients must keep track of actuations. The only method to determine the number of doses remaining in a HFA MDI without a dose counter is to count actuations manually. Manual methods include reading the label to determine the total number of doses available in the pMDI, and using a log to indicate every individual actuation given, including both priming and therapy doses. This tally is subtracted from the number of actuations on the label until all have been used.

Mouthpiece cleaning is recommended on a weekly basis. A moist cotton swab can be used to clean the circular opening by twisting the swab in circular motion to remove residue. More information is available on the device/drug insert or available on-line. Priming guidelines vary by product.
The design advantages of MDIs are listed above. Over the years a number of deficiencies have been identified and are listed under the disadvantages column. 50, 51 and 52

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portable</td>
<td>Steps required before actuation</td>
</tr>
<tr>
<td>Uncontaminated product</td>
<td>Hand-breath coordination is required</td>
</tr>
<tr>
<td>Tamper-proof</td>
<td>CFC to HFA propellant switch</td>
</tr>
<tr>
<td>Fast treatment times</td>
<td>Difficulty to determine the dose remaining in the canister without dose counter</td>
</tr>
<tr>
<td>Multiple dose</td>
<td></td>
</tr>
<tr>
<td>Accurate dose metering</td>
<td></td>
</tr>
<tr>
<td>High respirable fraction</td>
<td></td>
</tr>
</tbody>
</table>
Although the presence of a one-way valve prevents aerosol particles from exiting the chamber until inhalation begins, *optimal aerosol dosing still depends on inhaling as close to or simultaneously with pMDI actuation.*

Time delays can reduce the available dose for inhalation from a valved holding chamber. The one-way valve should have a low resistance so that it opens easily with minimal inspiratory effort. Ideally, there should be a signal to provide feedback if inspiratory flow is too high. ⁵³
The animation shows how the VHC traps large droplets that are emitted from the MDI allowing smaller particles to be inhaled.
The use of a spacer or valved holding chamber (VHC) can improve the effectiveness of MDI drug delivery and reduces oropharyngeal deposition by adding volume and space between the metering valve and the patient’s mouth. \textsuperscript{54, 55 and 56}
A metered dose inhaler (MDI) is a handheld pressurized metal canister that contains a pharmacological agent in suspension or solution, a surfactant, a propellant, a metering valve, and a mouthpiece for drug delivery. On actuation (i.e., the canister being triggered to deliver a dose), a fine atomized spray occurs over 100-200 milliseconds to deliver the dose (the delivered dose is dependent on the product used.)

MDI disadvantages include; requires priming, cleaning and correct actuation and inhalation coordination. Incorrect use results in oropharyngeal drug deposition.

Valved Holding Chambers and spacers improve the effectiveness of MDI drug delivery and are recommended for patients who have difficulty with breath actuation/coordination i.e. small children.

### PHILIPS

#### MDI Summary

- **Most popular aerosol device, portable, tamper proof and contains multiple doses**
- **Contains a mix of propellant and drug. The device is actuated when the patient presses down on the canister and fine atomized spray is created and is metered through a valve**
- **HFA propellant is more environmentally friendly and produces a slower, wider aerosol plume as compared with CFC propellant**
- **MDIs must be primed, correctly stored and cleaned to ensure consistent drug delivery. MDIs also require a coordinated actuation/breathing technique**
- **VHCs and spacers eliminate coordination/breathing problems and are recommended for small children.**
Dry powder inhalers (DPIs) are portable, inspiratory flow-driven devices that are used to administer dry powder formulations to the lungs. They have been developed to overcome the difficulties of using metered-dose inhalers and are often prescribed with the hope of providing the patient with an overall more user-friendly and more predictable therapy.

Over the past two decades, the market for dry powder inhalers (DPIs) has significantly increased. Advair® is an example of a DPI that is used in the management of chronic respiratory diseases. DPIs are also the device of choice for systemic drug delivery. Systemic drugs like vaccines and insulin for the treatment of diabetes are available in dry powder formulations.57
The first DPI introduced to the market was cromolyn containing Spinhaler, in 1971. It was not widely accepted due to the amount of powder that the patient needed to inhale into their lungs and fear of inhaling capsule fragments.

DPIs were developed to overcome the MDI disadvantages that we discussed earlier, such as dose counters, propellants and breath actuation problems.\textsuperscript{58}

The next slide will detail the operational aspects of the DPI.
The DPI procedure begins with the loading of a factory filled hard gelatin capsule or aluminum laminate blister that contains a mix of powder (carrier) and fine micronized drug particles into an inhalation chamber. After loading the capsule into the inhalation chamber, it is rotated and pierced. Once pierced, the powder is pulled through the chamber by the patient’s own inspiratory flow via the DPI mouth piece. The airflow dilutes the powder and propels it into a mesh or screen where the small particles are sheered from the powder and is converted into an aerosol. The patient is instructed to hold their breath for 5-10 seconds to ensure adequate particle deposition. The dose that can be delivered is typically less than a few milligrams in a single breath since larger powder doses may lead to provocation of cough.\textsuperscript{59, 60}
DPIs can be divided into their dose carrying capacities: Single Dose DPIs, Multiple Unit-Dose DPIs and Multiple Dose DPIs. Single-dose DPIs use a single-dose capsule, multiple unit-dose DPIs use single doses that are loaded into individual blisters and multiple-dose DPIs use either a reservoir or blister strips, designed to deliver repeated doses. Regardless of the type of DPI, they all operate as described in the previous slides.
Advair Diskus® is the most popular DPI and is a multiple dose DPI system. The doses are factory loaded and individually sealed in foil packets that protect them from moisture and humidity. 61 and 62
Resistance & Inspiratory Flow: Each type of DPI has a different intrinsic resistance to airflow that determines how much inspiratory flow needs to be created in the device to release the correct amount of drug. To give an example, the Twisthaler has a higher resistance than does the Diskus® and therefore requires a greater inspiratory effort. As demonstrated by the graph, the Diskus and the Twisthaler have a higher resistance profile than the 3M HFA pMDI. 63 and 64

When the patient inhales through the DPI, she or he creates an airflow with a pressure drop between the intake and exit of the mouthpiece. Thus, the patient can lift the powder from the drug reservoir, blister or capsule depending on the model being used. The patient’s inspiratory effort is also important in deaggregating the powder into finer particles. 65
In addition to overcoming DPI flow resistance, patients often fail to follow the instructions for use. In 2004, Dr. Melani published common DPI technique problems. The study shows that 35% of the patients that were observed did not hold the device correctly. The study also revealed that the observed patients did not coordinate the breathing pattern required for optimal drug delivery.66

This again underlines the point, if a patient is using it incorrectly, he/she will have poor clinical results. When a medication delivery system such as a DPI is used incorrectly, a patient is likely to compensate by taking more puffs than actually needed and the potential for unwanted medication side effects. Appropriate education on medication delivery systems is essential.
The portability, built in dose counter, and breath-actuated features are advantages that a DPI has over a MDI and jet nebulizer. Additionally, there is no priming requirement, the dose carrying capacity is higher, and the drug is more stable than the propellant driven MDI. A good example of a popular DPI is the Advair Diskus.

However, the patient’s inspiratory flow may not be adequate enough to draw the drug from the device and problems can occur when the patient does not follow the instructions for use. For example, the patient should know how to correctly hold the device while inhaling and not exhale into the device. This will optimize drug delivery and prevent the introduction of ambient humidity into the mouthpiece resulting in a negative effect to the medication. 67

It is important to make sure that the patient understands how the DPI works and how it should be used. The following slides will review the resistance of DPI and common patient use errors.
DPIs were developed to overcome the difficulties of using metered-dose inhalers and are often prescribed with the hope of providing the patient with a more user-friendly and more predictable therapy.

DPIs have both advantages and disadvantages as seen in previous slides. Because they do not require hand-breath coordination, the patient’s inspiratory flow should be adequate enough to draw the drug from the device. It is important that the patient understands how the DPI works and how it should be used.
The third and last respiratory drug device nebulizers are commonly used in hospitals and by patients who are unable to operate and coordinate a pMDI or a DPI. The first few slides will discuss the basic operating principles of the pneumatic jet nebulizer and then discuss different types that are currently available and their advantages and disadvantages. Breath-actuated and ultrasonic vibrating mesh nebulizers will also be discussed towards the end of this chapter.
Jet nebulizers use inhaled drug solutions that may not be available in pMDIs or DPIs (e.g. antibiotic drug solutions). In terms of breath coordination and procedure, the jet nebulizer is probably the simplest inhaler type for a patient to use if we assume that assembly, proper cleaning and maintenance is not a problem.
Operation as follows:

Air is drawn into a compressor and is filtered before it reaches the inside of the compressor. Compressed air is delivered through a plastic tube which connects to the base of the nebulizer hand set cup that contains the liquid drug. The nebulizer aerosolizes the liquid drug and makes it available through a mouthpiece or an aerosol mask. The aerosol is delivered to the lungs. 68, 69 and 70
The liquid drug is drawn from the nebulizer cup into a jet by a combination of gas flow and pressure. Small droplets are aerosolized out while large droplets are re-circulated. The Bernoulli’s principle is the reason the liquid is drawn up into the jet. Bernoulli was a Swiss mathematician born in 1740 who studied the flow of liquids and came up with his principle while looking at the river. The principle states that when a flow enters a constriction, velocity is increased and lateral pressure is reduced. 71

The next step is refining the liquid to sheer it into small particles (cavitations). This is accomplished by impaction against baffle. The baffle is simply a piece of material placed in the stream of particles onto which they impact and break up into smaller particles. Smaller particles are able to flow into the mouthpiece and avoid impact. The large droplets are re-circulated. 72
Studies have shown that as the gas flow rate increases, the particle size produced by the nebulizer decreases. The graph shows particle size reduction of four different nebulizers at three different (4, 6 and 8 lpm) flow rates. Higher gas flow rate will decrease the amount of treatment time needed to deliver the set amount of drug. 74 and 75
A minimum amount of gas flow ranging from 2 – 8 lpm is needed to convert the liquid medication into an aerosol. In the hospital, compressed (piped-in 50 psig) air or oxygen is often used to power a pneumatic jet nebulizer.

Compressors are usually the only option available for jet nebulizer home use. Compressors are electronically powered, durable and portable. Room air is drawn in and compressed then immediately forced out again. Portable compressors offer a DC power source and can operate at lower flow rates.
Various types of pneumatic jet nebulizers are available on the market today. There are four different designs of the pneumatic jet nebulizer: Conventional jet with reservoir tube, flow-enhanced passive venturi, breath-enhanced active venturi and breath-activated or actuated nebulizer. The next few slides will detail the design and the advantages and disadvantages of each one. 76, 77, 78 and 79.
The components of the conventional jet nebulizer consist of a medication cup, a mouthpiece attached to a T-shaped piece, a plastic tube that connects the gas source to the nebulizer cup and a six inch length of corrugated tubing. The respirable particles produced by the conventional jet nebulizer are between 10-20%. The medication available for inhalation is restricted, because the patient’s inspiratory flow is much greater than the nebulizer’s output of aerosol.

In order to decrease drug loss and increase inhaled mass, a t-piece and large bore tubing are attached to the expiratory side of the nebulizer. Additionally because standard jet nebulizers are inexpensive to produce, there is a wide variation in aerosol characteristics from unit to unit, batch to batch. The plastic a conventional jet neb is made from is not durable. Because both air and liquid is forced through the jet at a high velocity this, combined with the relatively cheap plastic that the nebulizer is made from, results in erosion of the jet. This reduces the therapeutic benefit of the aerosol. The output is highly variable. 80 and 81
The plastic used to make these conventional jet nebulizers is not durable and does not withstand the air and liquid that is repeatedly forced through at a high velocity. Over time, the quality of the jet stream is eroded and therapeutic benefit of the aerosol is reduced. The output is highly variable and will not be able withstand repeated cleanings. \(^{82, 83, 84, 85, 86, 87, 88}\)
A passive venturi (also known as flow enhanced) nebulizer utilizes an open-vent design. This design has been evaluated in several studies, which have reported greater pulmonary deposition with this design than with a conventional nebulizer. The advantage of the venturi design is an improvement in nebulizer output with an increase in flow. This is a result of the air flow coming into the nebulizer cup from the top of the nebulizer via the venturi. The venturi airflow is combined to the flow coming from the source gas increasing the probability of matching the patient’s peak inspiratory flow with aerosolized medication. The SideStream is a flow enhanced nebulizer. 89, 90 and 91
The total chamber flow will vary with the patient's inspiratory effort. 92, 93 and 94
When the patient inhales, the flow from the gas source combines with additional flow from a venturi and increases total flow going through the nebulizer cup. The patient’s inspiratory flow rate pulls the venturi valve open and therefore, total chamber flow will vary with the patient’s inspiratory effort. When the patient exhales the venturi valve closes and the exhalation valve opens.
The breath-actuated jet nebulizer or as it is sometimes referred to the dosametric nebulizer is relatively new to the jet nebulizer market. It is primarily used in the hospital and as its name implies, it is activated by the patient’s breath or on inspiration.

While this nebulizer is unique in the way it is activated, it is like all other jet nebulizers in terms of a gas flowing through a supply tube to the jet. Nebulizer jets we have previously discussed need a minimal gas flow of six liters of gas flow to draw fluid in to the jet for nebulization. This nebulizer requires eight liters of flow to power its jet, making this nebulizer difficult to use without a high gas flow source.

Similar to the inspiratory valve action of the breath enhanced jet nebulizer, the breath actuated jet nebulizer has an active venturi that opens on inspiration and closes on exhalation, allowing the nebulizer to match the patient’s peak inspiratory flow. On exhalation, the breath actuated nebulizer uses a spring-valve to stop air flow to jet nozzle during exhalation.

The feature of a breath-actuated nebulizer serve to preserve medication for inspiration, however, because it is active on inspiration only, a standard dose of liquid medication could take twice as long to nebulize as a standard jet nebulizer. As a means to shorten treatment times, hospital based clinicians will use an undiluted liquid medication, reducing the volume of liquid in the nebulizer cup. This practice must be monitored closely for any signs of side effects that may result from using high dose medications. High cost compressor
flow requirements and longer treatment times, cause the breath activated nebulizer to be seldom used in the home. There are some limitations in the hospital as well, he nebulizer does not fit standard masks and can’t be used in-line with a ventilator. 95, 96, 97, 98, 99, 100, 101 and 102
Hospitals have used ultrasonic nebulizers since the 1970’s. These were generally used to induce sputum. High frequency sound waves are applied to a piezoelectric transducer to create vibrations. The vibrations pass through the solution that breaks the surface of the liquid into small particles. The ceramic piezo element bonds to a metal shim and this vibrates in response to alternating voltage (+/- 12V, 2 MHz). The higher the frequency the higher the aerosol output and more heat is generated. Droplets are produced by surface vibration and cavitation and as is the case with compressor driven jet nebulizers, large droplets are re-circulated. 103, 104 and 105
The newer generation of ultrasonic nebulizers is more portable, efficient and quiet than the pneumatic jet nebulizer compressor systems. The mesh technology used in these devices ensures precise and consistent drug delivery to the lung.

Aerosol is generated by vibrating plate apertures or a horn that employ a mesh to generate precise particle sizes. 107,108 and 109
Keys to Successful Nebulizer Drug Delivery

Maximize patient compliance and convenience: Easy to use and durable nebulizer.

Maximize delivery rate. The delivery rate is dependent upon the performance of the nebulizer system and the patient's breathing pattern.

Minimize the residual volume.
- The residual volume is the amount of medication left in a nebulizer after the treatment has ended.

Easy to use and durable

Too many parts, high residual volume and not durable
In conclusion, the ideal device must produce the highest possible respirable mass. It must work properly across a wide range of inspiratory flow rates to ensure optimal delivery and efficacy. To eliminate errors in use the device should be easy to use and to prevent loss of medication it should be portable and easy to use.
Summary continued

There are many factors to consider when determining which aerosol delivery device to prescribe.

Cost, efficacy, ease of use, efficiency... The purpose was not to convince you that one is better than another but provide you with information that you can use when an aerosol device is prescribed.
Thank You