Updates In Pulmonary Medicine:
A ‘Hands On’ Approach with Novel Inhalers

Disclosures
The program chair and presenters for this continuing education activity have reported no relevant financial relationships, except:

- Dennis M. Williams - spouse is employee of GSK

Session Objectives
- Summarize primary literature of new inhaler devices in asthma/COPD and factors for patient selection
- Recommend strategies to help patients obtain inhalers at a lower cost
- Demonstrate how to use these new devices
- Counsel a patient on how to use these new devices

Novel Inhalers: The New Kids on the Block
Dennis Williams, PharmD, BCPS
Associate Professor
UNC Eshelman School of Pharmacy

Objective
- Summarize primary literature of new inhaler devices in asthma/COPD and factors for patient selection

Managing Lung Disease with Inhalational Therapies
- Preferred strategy for managing common lung diseases
- Delivery of medication directly to site of action
- Choices available for type of delivery device
- Incorrect use of all inhalational delivery systems is common, resulting in suboptimal outcomes
Future for Aerosol Delivery Devices

- Micro- and Macromolecules
  - Vaccines
  - DNA
  - Cytokines
  - Antibodies
  - Hormones
- Devices may require advanced designs in order to ensure stability of fragile molecules, but be affordable

Quick History pMDI

- 1959 – First pMDI patented in 1959
- A few cosmetic changes over the next 20 years
- 1975 – Study proved that most of dose was swallowed
- 1984 – Waxman-Hatch Act to develop strategies for bioequivalence
- 1986 – Signing of the Montreal Protocol to eliminate CFC propellants
- New 30 years – Significant advances in MDI technologies and exploration for alternative devices

Quick History of DPI

- Spinhaler and Rotahaler – early devices in 60s and 70s
- Relied on patient’s inspiratory force to disperse dose from capsule and carry to airways
- Progressed to a variety of single dose, multi-dose, blister, and reservoir systems
- Active, breath-assisted devices still in development (e.g., Spiros)

Multiple Factors Impact Delivery to Airways

- Optimal Delivery of Aerosol
- Drug molecule characteristics
- Patency of airways
- Fluid conditions
- Drug properties
- Aerosol properties

Desirable Features of Aerosol and Particles

- Particle sizes of 0.5 to 5 microns are generally considered respirable, depositing by sedimentation in the terminal bronchioles and alveoli
- GSDs of < 2 optimize the monodisperse characteristics

Considerations in Designing an Inhaler

- Aerosol Properties
  - MMAD
  - Geometric standard deviation (GSD)
  - Fine particle fraction (FPF)
  - Air/Particle velocity
- Physicochemical Properties
  - Solubility
  - Hygroscopicity
- Particle Properties
  - Volume diameter
  - Bulk density
  - Tap density
  - Shape
  - Charge
- Lung Properties
  - Geometry of respiratory tree
  - Influence of disease
  - Breathing pattern
Factors Influencing Effective Administration of Aerosolized Medications

- Patient's age
- Physical and cognitive ability
- Delivery system
- Patient-device interface

Problems with Inhalation Delivery Systems

- Hand-lung coordination with pMDI
- Electrostatic forces with VHC
- Poor inspiratory force with DPI
- Inefficient dose delivery with nebulizer
- Suboptimal technique with all devices
- Lack of knowledge and instruction among clinicians with all devices

Key Components of a pMDI

- Canister
- Metering valve
- Actuator
- Mouthpiece

pMDI Technical Performance

- When not in use, an inner valve is open and allows metering chamber to fill with propellant-drug mixture
- When actuated (pressed) by patient, outer valve opens, inner valve closes, and metered dose of medication is released
- Newer actuators include dose counter

pMDI Formulations

- Solutions or suspensions
- Can contain excipients such as ethanol or surfactants as solubilizers or to stabilize suspensions
- Propellants that are nontoxic, nonflammable, and compatible with drug formulation
- Propellant should maintain consistent vapor pressure for life of product

pMDIs 2nd Decade of 21st Century

- Significant advances in technology have occurred during last 20 years
- Dose counters becoming standard
- Auxiliary devices (e.g., spacers, VHC) important to allow evaporation, deceleration, and 'filtering' of large particles
- Spacers and VHC can modestly improve lung deposition and reduce risks
- VHCs may include features to facilitate teaching and improve technique
Dry Powder Inhalers

- Emerged as option during CFC transition
- Challenges include internal resistance (e.g., inspiratory force required to aerosolize powder)
- Risk of hygroscopicity

Current Dry Powder Inhaler Classification

- Single unit-dose
- Multi-unit dose
- Multi-dose reservoir

Dry Powder Inhalers (DPI)
Where We Are Today

- Significant advances in technology and ease of use
- Each device has specific instructions
- Efforts to simply use by open-inhale-close instructions
- Products include dose counter or indicator

Multi-dose liquid inhalers

- Example: Respimat
- Aerosolizes a propellant free drug solution as a soft mist
- Tension spring forces metered volume of drug through a capillary tube into a micropump
- When dose release button is pressed, the dose enters a ‘uniblock’ (e.g., a combination of filters and nozzles made of silicon and glass)
- Two converging jets of solution collide to produce an aerosol

Aerosol Product Recipe

Reproduced with permission from Allergy and Asthma Network
Respiratory Inhaler Poster. AllergyAsthmaNetwork.org
What a patient wants from a pulmonary delivery device

- No need for external power
- Convenient and unobtrusive to carry
- Quiet and unobtrusive to use in public
- Robust enough to survive routine transport, use, and cleaning
- No extraordinary respiratory maneuvers required for correct use
- Dose counter


What a clinician wants from a pulmonary delivery device

- Intuitive and easy to use
- Technique that can be easily taught
- Mastery of technique can be visually confirmed
- Familiar instructions for use


Case Scenario

Jessie Z. is a 68 year old male with longstanding diabetes and COPD who was recently hospitalized with a COPD exacerbation.

His COPD is attributed to a 60 pack-year smoking history, although he stopped smoking 2 years ago.

Prior to admission, he was treated with a tiotropium handihaler, 18 mcg daily, and used albuterol by nebulization as needed.

Upon discharge from the hospital, he is prescribed a budesonide/formoterol inhaler (160/4.5) 2 puffs twice daily, and an albuterol MDI for PRN use.

Case Scenario

He expresses a concern about using a MDI as he feels that he has developed some arthritis in his hands; however, he feels the spray works for him even when he is very short of breath.

He notes some difficulty in loading the capsule in his handihaler in the past.

He prefers to continue to have his nebulizer for use at home when symptoms are severe.

Considerations in Device Selection for this Patient?

Considerations When Counseling Patients Regarding Inhalation Devices

- Inhalation technique vary
  - pMDI – slow, deep inhalation
  - DPI – rapid, forceful inhalation
  - MDI is often 2 puffs, DPI is usually 1 puff
  - Mouth-rinsing recommended for ICS
  - Periodic cleaning of devices is required, but differs according to product
Key Takeaways

- Inhalation delivery systems have undergone significant technological advances during the last 50 years
- The device used to deliver the dose is as important as the medication itself
- Patient's ability to use inhalation device is an important and modifiable limitation

Right Drug, Wrong Price

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Internal Medicine Clinical Pharmacist
Chicago State University—College of Pharmacy

Objective

- Recommend strategies to help patients obtain inhalers at a lower cost

Meet MT

- 52 year old male reports to your free clinic for COPD management
- PMH: COPD X 3 yrs, DM X 10 yrs, OA, and HTN.
  - Last exacerbation was at diagnosis; none since that time
- Social History:
  - Former smoker, quit 3 yrs ago
  - Part-time construction worker; his employer does not offer health insurance
- Recent spirometry: FEV1/FVC of 0.66 and an FEV1 65%

MT: Medication List

- Current medications:
  - Benazapril 20 mg daily
  - Metformin 1000mg BID
  - Fluticasone 250 mg/salmeterol 50 mg 1 puff BID
  - Ipratropium/albuterol 1 puff q 6hrs prn
  - Tiotropium 18 mcg 1 puff daily
  - Acetaminophen 1000 mg PO q 8hr
  - Insulin glargine 35 units q HS
  - Insulin humalog 10 units with meals

MT: Patient Visit

- Demonstrates proper inhaler technique
  - States that using them sometimes is “hard on his arthritis.”
  - “Very” interested in only using one inhaler as opposed to three.
  - Additionally, he feels that all his money goes toward medications
  - Some meds are free from the clinic
  - Patient also has AARP prescription discount card
COPD and Inhalers: Factors to Consider

Financial Burden
- Part-time job, no insurance
- Medication burden: 8 prescriptions, 5 of which are “brand only”

Acceptability
- Patient prefers less inhalers
- Patient does not want to spend more money

Technique
- Patient has arthritis

Brief Group Discussion

- What factors presented within the case should be taken into account when deciding a course of action for managing MT’s COPD?

MT: Factors to Consider

- Financial Burden
  - Part-time job, no insurance
  - Medication burden: 8 prescriptions, 5 of which are “brand only”
- Acceptability
  - Patient prefers less inhalers
  - Patient does not want to spend more money
- Technique
  - Patient has arthritis

MT: Possible Plan of Action

- Discontinue:
  - Fluticasone/salmeterol
  - Ipratropium/albuterol
  - Tiotropium
- Initiate:
  - Umeclidinium 62.5 mcg/vilanterol 25 mcg, 1 inhalation daily
  - Albuterol HFA, 1 inhalation q 6 hrs prn SOB

Options for Uninsured Patients

- Cash prices
  - Pharmacy
  - Region of the country
  - Time of the year
- Discount drug programs
  - Drug
  - Specific program
  - Percentage of savings offered
  - Comparing programs can be difficult!

Methods to Assist MT

- Discount drug programs
- Seek patient assistance programs through the drug manufacturer
- Apply for governmental coverage

Discount Drug Programs

- GoodRX
- LowestMeds

Discount Drug Programs

- Other Programs
  - NeedyRx
  - 4Rx Card
  - America’s Drug Card
  - Easy Drug Card
  - Free RX Plus
  - True RX Savings
  - Many others...

Discount Drug Programs

- Advantages
  - Free
  - Personal information not required for enrolling
  - Some programs allow for "comparison shopping"
  - Coupons or discount cards are available for many drugs

- Disadvantages
  - Not all websites allow for true comparison shopping
  - Determining an exact price will not happen until the prescription is actually processed
  - Discounts likely will be minimal for brand name medications

Pharmaceutical Assistance Programs

<table>
<thead>
<tr>
<th>Pharmaceutical Assistance Programs for Newer Inhalers for COPD</th>
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<tbody>
<tr>
<td>Inhalar® Respimat® (Indacaterol)</td>
<td>GoodRx</td>
</tr>
<tr>
<td>BestRx® Respimat® (Indacaterol)</td>
<td>GoodRx</td>
</tr>
<tr>
<td>Spiriva® Respimat® (Ipratropium)</td>
<td>GoodRx</td>
</tr>
<tr>
<td>Sputnik® Respimat® (Indacaterol 2.5 mcg)</td>
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Discount card—Patients must register on website. Cash paying patients—program covers up to $100 per 30 day supply. Private insured patients—pay no more than $25/month. Card is valid for 1 year. No governmental insurance patients.
Governmental Assistance Programs

- Affordable Care Act
- Medicare (if MT was eligible)
  - Advantage plan (Part C)
  - Part D coverage
  - Extra Help
- State Pharmaceutical Assistance Programs
  - Only offered in 22 states

Key Takeaways

- Stay current with local, state, and national resources
- Collaborate with other team members who can help make medications as affordable as possible
- Remind patients they may have to “shop around” for the best deals

Objectives

1. Demonstrate how to use these new devices.
2. Counsel a patient on how to use these new devices.

General Counseling Points

- Preparing to use the Device
  - Controller versus rescue
  - Assembly, including timing of assembly
  - Documenting expiration date
  - Priming and if needed, re-priming
  - Activation

Step by Step: Hands on Approach to Patient Education

Nancy C. MacDonald, PharmD, BCPS
Transition of Care Coordinator
Henry Ford Hospital
Detroit, Michigan
**General Counseling Points**

- **Administration**
  - Best inhalation technique
  - Number of inhalations
  - Re-activate before subsequent dose
  - Audio or visual aids

- **Maintaining the Device**
  - Closure
  - Reading the counter
  - Calling for refill
  - Storage

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**Ellipta™**

**Pressair™**

**Respimat®**

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**Ellipta™ Device**

- **Cover**
- **Medication Devices**:
  - Tray opened ____
  - Discard_________

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**Ellipta™ Device**

- **Priming**
  - Not needed

- **Expiration**
  - When zero appears in counter or 6 weeks after tray is opened.

- **Call for refill**
  - When you have less than 10 doses left [RED appears in dose counter window].

- **Cleaning**
  - Not necessary

- **Storage**
  - Close mouthpiece.
  - Room temperature. Keep in a dry place away from heat and sunlight.

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### Ellipta™ Device

<table>
<thead>
<tr>
<th>Section</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Activation</strong></td>
<td>Slide cover down until you hear a click.</td>
</tr>
<tr>
<td><strong>Use of Device</strong></td>
<td>Slide cover down until you hear a click. Breathe out. Place mouth around mouthpiece and take one long, steady, deep breath in through mouth. Remove from mouth. Hold breath 3-4 seconds. Breathe out slowly/gently. Rinse mouth if needed with medication in device.</td>
</tr>
</tbody>
</table>

[Information source](https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Breo_Ellipta/pdf/BREO‐ELLIPTA‐PI‐MG.PDF#nameddest=MG Accessed 9/22/15)

### Interactive Scenario

Pick a partner and counsel them on how to prepare, use and store the device.  
When you are done, reverse roles.  
Do NOT place the device in your mouth during the demonstration.

### Pressair™ Device

<table>
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<tr>
<td>Pouch opened:</td>
<td>____</td>
</tr>
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<td>Use by:</td>
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<tr>
<td>** Priming/Re-priming**</td>
<td>Not needed</td>
</tr>
<tr>
<td><strong>Expiration</strong></td>
<td>When zero in RED appears or 45 days once removed from foil.</td>
</tr>
<tr>
<td><strong>Call for refill</strong></td>
<td>When RED ban appears in the dose indicator window (10 remaining doses).</td>
</tr>
<tr>
<td><strong>Cleaning</strong></td>
<td>Not necessary. Can clean outside of mouthpiece with dry cloth.</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>Place cap back on. Room temp away from heat/light. Keep in foil until ready to open.</td>
</tr>
</tbody>
</table>

[Information source](http://www.azpicentral.com/tudorza/pi_tudorza.pdf#page=1 Accessed 9/22/15)
Interactive Scenario

Pick a partner and counsel them on how to prepare, use and store the device.
When you are done, reverse roles.

ONE person can consider placing their mouth on the device to demonstrate how the proper inhalation of the demo inhaler will make the control window change color.

Respimat® Device

Discard By:
Cartridge
Clear Base

Respimat® Device

Priming/Re-priming
- Priming: Once spray is visible, perform "T.O.P" three more times.
- Re-priming: If not used for >3 days: release 1 puff. If not used for more than 21 days, full priming is required.

Expiration
- 3 months from the date the cartridge is inserted into inhaler.

Call for refill
- When the dose indicator is at 30 (RED zone).

Cleaning
- Mouthpiece, including metal part inside mouthpiece with damp cloth at least 1 time a week. Outside can be cleaned with damp cloth.

Storage
- Room temperature

https://www.respimat.com/functions_and_use/how_to_use.html
Accessed 9/22/15

Respimat® Device

Activation
- Hold upright & turn base until it clicks.

Use of Device
- Flip cap until open.
- Breathe out slowly & fully. Place device in mouth, pointing device to the back of throat.
- While taking slow, deep breath in, press the dose release button. Breathe in as long as you can. Hold breath for 30 seconds. Take device out of mouth and breathe out.

Turn
Open
Press

https://www.respimat.com/functions_and_use/how_to_use.html
Accessed 9/22/15

Interactive Scenario

Pick a partner and counsel them on how to prepare, use and store the device.
When you are done, reverse roles.

Do NOT place your mouth on the device during demonstration.
Key Takeaways

- Patients should be taught how to prepare, administer and maintain their inhaler device.
- The inhalation technique for each novel inhalation device is unique.

Active Learning

Reflection Questions:

- What patients might benefit from using each device?
- Share one counseling point that you found unique about each device.