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The first edition of Respiratory SCOPE has touched more than 1300 readers since launch. Field Sales’ thirst for scientific knowledge is clear; and Commercial Learning shares your passion for developing our scientific acumen. In this edition, we take a deeper look at devices and fixed-dose combination therapies. Also in this edition, Mike DiPietro, Medical Director for Respiratory with US Medical Affairs shares a hypothetical case study that underscores the difficulty associated with diagnosis and management of COPD.

Here at AstraZeneca, we follow the science. We seek partners and collaborators who share our passion for science. Commercial Learning will continue to partner with you, the readers, to bring articles that pique your curiosity and stimulate your desire for deepened scientific knowledge.

Download this edition of Respiratory SCOPE and let us know what you think in this 2-minute survey. Please email SCOPEmagazine@astrazeneca.com to reach out to the SCOPE eMagazine team!

Sincerely,

Dave Ilconich
Senior Director, Sales Learning
US Commercial Operations

Clare Miller
Respiratory Sales Training Manager
US Commercial Operations
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CONTRIBUTORS

Donna Maier  Greg Irons  Amy Cohen  Liz Bodin
Clare Miller  Aaron Gates  Katie Peterson  Diane DiTomasso
Gina Padula  Jackie Freeman  Cathleen McQueeney  Jessica Phaup
Rick Honecker  Linda Price  Mike DePietro

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Clinician’s Corner

Are Jim’s symptoms due to COPD or could there be something else?

In this issue of the Clinician’s Corner, Dr. Mike DePietro will be discussing the complexity of diagnosing and managing a patient with COPD. You will meet Jim, a patient with shortness of breath and many complicating conditions and risk factors. Is his shortness of breath due to COPD or is there another issue as well? Keep reading to find out more...

Hi team. My name is Mike DePietro and I am a pulmonary-critical care physician. After many years in practice locally at the Christiana Care Health System in Delaware, I recently joined AZ as a medical director for respiratory with US medical affairs.

As you know, AstraZeneca has made a major commitment to the care of patients with respiratory disease and in particular those with chronic obstructive pulmonary disease (COPD).

COPD is a major health burden in the United States; it afflicts millions of Americans and is one of the leading causes of death in the United States. This is well known. What I would like to focus on here is something that may be less appreciated, but is also important in understanding the experience of patients with COPD—that is, the complexity of this disease and the challenges this complexity presents to patients and the health care team.

**COPD is complex in many ways.** Severity can vary among patients and over time within the same patient, impacting the approach to treatment. Much about the disease is still unknown. Why some patients have a faster decline in lung function than others and how to alter this loss of function remain questions. These are challenges, but I want to focus on another aspect of the complexity of COPD that we need to understand. COPD is typically associated with other diseases for which it shares risk factors and that complicate its management. To understand this let’s consider a hypothetical patient we will call “Jim.”

Jim is not a real person, but he is very similar to many of the patients I saw in practice. Let me tell you about “Jim”

Jim was a 58-year-old man who was still working as an auto mechanic. He smoked since high school. He had two grown children and he is recently divorced. He is overweight, and is tired most of the day. His father died of a heart attack when he was 56. He has high blood pressure and is on a medicine for this. Jim has a chronic cough, and has been a little bit short of breath for a couple of years, so his family doctor told him he had COPD and gave him an inhaled SABA (short-acting bronchodilating agent) to use. Jim was referred to me because his family doctor noticed
a “spot” on a chest x-ray, and Jim has been getting more short of breath at work, such that he can no longer carry tools or auto parts and must stop for frequent rests.

As a pulmonologist this kind of case was fairly routine. It is also deceptively complex.

Let’s look a little bit further to understand how a physician might think about this case.

Jim has two big problems his primary care doctor wants help with. He is progressively more short of breath, and he has an abnormal chest x-ray. Both are important, but let’s address the shortness of breath first, since Jim notices this more.

While one potential cause of worsening shortness of breath could be that Jim’s COPD might be getting worse with time, this is not the only potential cause. Like most patients with a diagnosis of COPD Jim is a smoker. That means he is at risk for many other diseases, which also cause shortness of breath. One example is heart disease. Smoking is a major risk factor for heart disease and many patients with COPD have both diseases. Smokers can develop coronary artery disease and be at risk for heart attacks. While most of us think of an impending heart attack as being associated with chest pain or “angina,” sometimes patients may only have shortness of breath. In addition Jim has high blood pressure. In some patients, high blood pressure, especially if poorly controlled, can cause the heart to work inefficiently, causing “congestive heart failure.” This in turn can cause fluid to build up in and around the lungs, also causing shortness of breath.

At this point it’s also important to remember that while Jim’s family doctor thought he had COPD, a pulmonologist would need to confirm this since there are many diseases besides heart disease that can be mistaken for COPD. For example Jim is an auto mechanic: he is exposed to brake linings in cars and maybe asbestos. Asbestos causes a disease of the lungs, promoting scar tissue formation and caused by asbestos exposure which can cause shortness of breath. So we see Jim presents lots of complicated questions:

DOES HE REALLY HAVE COPD OR SOME OTHER LUNG DISEASE?

If he has COPD, is it getting worse? Does he need additional medication for his COPD, or other treatments? Beyond just additional medicines such as the addition of a LAMA or an ICS-LABA, Jim could potentially need home oxygen, and could benefit from participation in a pulmonary rehabilitation exercise and teaching program. Oxygen provides selected patients with more advanced disease a significant relief of symptoms and even a lower risk of death, while participation in pulmonary rehabilitation benefits most patients with lung disease.

With that in mind, it is still necessary to answer the important question of whether there is another diagnosis causing or contributing to Jim’s shortness of breath, such as heart disease. Depending on the further details of his history and physical exam he may need testing for heart disease, such as a stress test or echocardiogram. If heart disease is found, this will require specific therapies including medicines or perhaps other interventions, even potentially heart surgery.

So even at this level, Jim is pretty complicated, but there is a lot more. As we mentioned Jim is overweight, has high blood pressure, and is tired all the time. Many patients with this combination have a condition called “obstructive sleep apnea” (OSA). Such patients have episodes during deep sleep in which they do not breathe well. The cause is excess tissue in the throat that blocks the airway when, during deep sleep, these muscles relax. Patients may have multiple episodes when they stop breathing during sleep. This leads to fractured sleep, fatigue, and if severe enough can place strain on the heart and increase risk for heart attack and stroke. When OSA is combined with COPD, stress on the heart may be even
worse, so sorting out whether Jim has OSA and treating him for it will be important. This problem is increasingly common in combination with COPD as obesity becomes a larger public health problem, so Jim is not alone. But we are not done yet!

Jim also was sent to us because he had a spot on his chest x-ray. As a smoker Jim is at risk for lung cancer, and patients with COPD are at particularly high risk for lung cancer. So it will be critically important to make sure the “spot on the chest x-ray” is not an early tumor. This may involve other tests such as a CT scan or a biopsy. It is possible that the spot represents some other lung disease; this too will need to be sorted out. Often, such spots or nodules are “scars” and cause no harm, but still need to be followed over time to make sure they do not change.

Finally, Jim has a couple of other problems, confronted with so many medical issues, being recently divorced, and having challenges performing his job because of his breathing issues it would not surprise us if Jim were depressed. Many patients with COPD are depressed, and this can itself cause physical symptoms and fatigue and affect his ability to adhere to treatment. This will need to be addressed.

Last but not least, none of these problems are helped by Jim’s tobacco addiction. Jim’s smoking will cause COPD to worsen more rapidly over time. It will increase the risk for heart disease and lung cancer. Smoking also worsens sleep apnea. It is a key feature of his treatment that the doctor helps Jim stop smoking.

So to recap we see the two problems Jim came into the office with really blossom into a dozen other questions:

Does Jim really have COPD? If so, is it getting worse?
How do I treat his COPD better?

Does he have some kind of heart disease? If he does, how do I help him with this?
What is the spot on Jim’s chest x-ray? Is it a scar? A cancer? Some other disease process?
Does Jim have sleep apnea? Is Jim depressed? How do I help him with these problems? How can I help Jim quit smoking?

It is easy to see how Jim could be overwhelmed. Certainly those of us whose goal is to help Jim can easily feel a little overwhelmed as well. But I am not describing this to make you feel frustrated or hopeless. I think we need to look at this typical situation as an opportunity.

The flip side of the complexity and many potential challenges presented is that this means there are a lot of potential options we can find to help patients like Jim. Every potential problem described above is really a potential target area to which we can look for a solution to help Jim breath and live better. We should all feel good about the fact that at AZ we are involved in developing medications that address many of Jim’s potential problems. We have medications and tools to help not just his COPD, but potentially heart disease if it is present, and even lung cancer if he ultimately should be faced with that frightening prospect.

That is the first place I would start the discussion with someone like Jim. For these patients, we could explain that their problem is complicated, but with time and their cooperation we could search for ways together to help them feel better. Very likely although not everything we consider will work, we can do much that would make a difference and improve things, working as a team.

As you engage with our customers, this is part of our message. We have much to offer and, working as a team with patients and their health care providers, we can make a positive impact on their health. Let us be very confident of the value that we provide even when faced with complex and difficult challenges such as Jim, and help support our customers by continuing to offer them the tools they are looking for to address the needs of patients.
It was a hot, dark evening. The night sky was illuminated by an orange glowing moon and piercing stars. Kyky was trying to go to sleep, but was restless. The calm of the night was shattered by her grandmother’s persistent cough. Finally, Mery entered the family’s stone home and patted Kyky’s head. “Help is coming,” she comforted her daughter. In a few moments, Mery helped her mother up and out into the night air. Before them was a fire heating bricks. Soon the physician pulled out a fiery red brick and slid it on the ground. He then threw black henbane weeds onto the hot brick and asked the old woman to inhale. The vapors began to surround her and she felt better.

None of them could imagine what respiratory treatments would exist 3500 years in the future. But for Mery’s mother in ancient Egypt, it was enough to get her through the night.

For the past 4000 years, respiratory diseases such as chronic obstructive pulmonary disease (COPD) have been treated with inhalation therapies. Modern-day treatments and devices are based on much older innovations. In fact, the first illustration of a “modern” inhaler dates to 1654. Physician Christopher Bennet drew a device very similar to a modern-day dry-powder inhaler (DPI).

Fast forward to 1778, when physician John Mudge created the Mudge inhaler, thereby introducing the term “inhaler” to the world. His inhaler was a modified pewter pot that heated opium in water for the treatment of cough.

In 1858, the first pressurized inhaler—the Pulverisateur—was invented in France by Sales-Giróns. Liquid medication was atomized by the pressure created in the device. The first manufactured DPI was invented in London in 1864. The design recognized modern principles of keeping the powder dry and finely pulverized.
**DO YOU KNOW?**

Asthma cigarettes were once sold! They burned combustible powders thought to alleviate symptoms of respiratory disease. These cigarettes often contained atropine or stramonium (nonselective M1-M5 muscarinic antagonists). They were common throughout the early decades of the 20th century.

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**PRESSURIZED METERED-DOSE INHALERS**

The modern era of inhalation therapy began in the 1950s, when a daughter of the vice president of Riker Laboratories (now 3M) wondered why her asthma medication couldn’t work like her mother’s hairspray. After 2 years of innovation, 2 pressurized metered dose inhalers (pMDIs), containing either isoprenaline or adrenalin, were developed and were launched in 1956.

Conventional pMDIs are still a popular device in use today. Some of the advantages of pMDIs are that they are portable, light, and compact, and offer multiple-dose convenience, short treatment time, and reproducible emitted doses. No drug preparation is required, and they are difficult to contaminate. Some of the disadvantages of pMDIs include the need for breath-hand coordination, patient activation, proper inhalation pattern, and breath-hold. Other shortcomings include fixed drug concentrations and doses, reaction to propellants by some patients, foreign-body aspiration from a debris-filled mouthpiece, oropharyngeal deposition, and difficulty determining the doses remaining in the canister without a dose counter. However, it is important to recognize that the respiratory field is working to overcome these shortcomings through the creation of novel inhalation device products.

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**INFOBITES**

A conventional pMDI contains many components. The metal canister holds the drug formulation inside the actuator. When the canister is depressed, the metering valve releases drug in propellant out the actuator nozzle, while the dose counter (if available) records each use.
Historically, pMDIs used chlorofluorocarbons (CFCs) as a propellant. However, because of environmental concerns, CFCs were phased out and replaced by the newer propellant, hydrofluoroalkane (HFA). Unfortunately, HFA devices have different properties from the CFC devices, which patients may notice. HFA devices have a softer spray, with smaller particles in each puff. They also have a different spray temperature and taste than CFC devices and need to be cleaned periodically to prevent clogging because of the small particle size. Like their CFC ancestors, HFA devices also require the coordination of inhalation and actuation.

**BREATH-ACTUATED INHALERS**

Breath-actuated inhalers (BAIs) were developed beginning in the late 1980s to address the difficulties in breath-hand coordination with the use of conventional pMDIs. When a patient breathes through the BAI, his or her breath triggers the device to release medication. Although BAIs are a good choice for patients with poor coordination, the disadvantages of this method of delivery include the need to keep the device clean and moisture-free.

**SMALL-VOLUME NEBULIZERS**

For children with respiratory disease and others who require an alternative to a hand-held inhaler, small-volume nebulizers (SVNs) are another treatment option. SVNs work by using compressed air or ultrasonic vibrations to convert liquid medications into aerosols for inhalation. The need for breath-hand coordination is eliminated with the use of SVNs; however, there are several disadvantages compared with hand-held inhalers, including less portability and more weight, noise, cost, and time of administration.

**CLINICAL GEMS**

A spacer or valved holding chamber can be used with a pMDI to optimize drug delivery. The spacer holds the medication, reducing the need to exactly time device actuation with inhalation. This can be especially useful for children or those adults who have difficulty using pMDIs.
What to Use When

Perhaps surprisingly, experts agree that all modern-day delivery devices provide similar outcomes in terms of efficacy. However, practitioners should consider some general principles when selecting the most appropriate device, as outlined in this table:

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pressurized Metered-Dose Inhaler</th>
<th>Breath-Actuated Inhaler</th>
<th>Small-Volume Nebulizer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Recommended for most patients. It is important for patients to have a short-acting beta-agonist inhaler (typically as a pMDI) for rescue therapy.</td>
<td>Recommended for patients unable to use conventional pMDI, especially those with difficulty maintaining breath-hand coordination.</td>
<td>Nebulizers may be a good option for patients with more severe disease or comorbidities, or those with considerable coordination difficulties, such as infants, children, and the elderly.</td>
</tr>
<tr>
<td>COPD</td>
<td>Recommended for patients as first-line treatment and may benefit from use of a spacer device.</td>
<td>Recommended for patients as first-line therapy and especially for those with difficulty using pMDIs because of poor breath-hand coordination.</td>
<td>pMDIs and BAIs are preferred over nebulizers. However, nebulizers may be a good option for patients with more severe disease or those with considerable coordination difficulties.</td>
</tr>
</tbody>
</table>

MARKET INSIGHTS

In order for a combination product (such as a device and drug) to be approved by the FDA, the manufacturer must first submit a request for designation (RFD) to the Office of Combination Products. The Office of Combination Products then determines which center is primary for the product—the Center for Devices and Radiological Health (CDRH), the Center for Biologics Evaluation and Research (CBER), or the Center for Drug Evaluation and Research (CDER).

However, inhalers are always approved by the CDER as a drug and device combination.
Devices of Tomorrow

Lori runs up to give her grandfather a big hug. His sweaty arms embrace her as he quickly jumps up. His pants are caked with mud, and dirt peeks out from under his nails—but his garden looks magnificent! Lori grabs a round ripe tomato and squishes it with her teeth. “Yummy!” Michael beams with pleasure, basking in the delight of seeing his only granddaughter. He thinks of how just 10 years earlier he never would have felt that he could have enough energy and stamina to tend to such a garden. Just then, he feels a small familiar buzz on his abdomen. “Just a second, honey,” he says. He snaps the familiar shiny black plastic off his belt loop, takes a quick puff of his controller medication, and snaps the device back into place. “The rest of the day is ours; what should we do next?”

Could a scene like this occur someday in the future? Only time will tell, but respiratory treatments will certainly continue to improve over time. The emphasis will remain on optimal drug delivery to avoid systemic side effects while maximizing efficacy.

Perhaps respiratory devices will become electronic with timers, microchips, and mobile applications integrated with patients’ electronic health records. Perhaps devices will become so small and portable as to become wearable. Only time will tell. How will this affect patient compliance and adherence? What do you imagine the respiratory device of the future will be?

A future issue of this magazine will look more closely at treatment differences between patients COPD vs asthma.

Where can you learn more?

- Inhalatorium. You can find images of historic inhalers and respiratory therapies here.
- Phisick. You can find additional images of respiratory-related medical antiques here.
- American Association for Respiratory Care (AARC). You can view resources about the science of aerosol delivery devices. Click here.
- FDA Guidance on Combination Products. You can view the guidance on how to write a request for designation here.
- American Thoracic Society. You can view the COPD guidelines here.
- American Academy of Allergy Asthma & Immunology. You can view the asthma practice parameters here.
Treatment guidelines for chronic obstructive pulmonary disease (COPD) recommend combining bronchodilators with different mechanisms of action for patients whose COPD is not controlled with a single bronchodilator. Treatment selection depends on the symptom severity and risk of exacerbations. Three types of fixed-dose combination medications are available for patients with COPD:

1. **Short-acting beta\(_2\)-agonist (SABA) and short-acting muscarinic antagonist (SAMA)**
   - Recommended as an alternative choice following SABA or SAMA monotherapy for patients with few symptoms and a low risk of exacerbations (Group A patients)

2. **Long-acting beta\(_2\)-agonist (LABA) and long-acting muscarinic antagonist (LAMA)**
   - Recommended as an alternative choice following LABA or LAMA monotherapy for patients with more significant symptoms but still a low risk of exacerbations (Group B patients)

3. **LABA and inhaled corticosteroid (ICS)**
   - Recommended for patients with few symptoms but a high risk of exacerbations (Group C patients) and for patients with many symptoms and a high risk of exacerbations (Group D patients)
### Initial Pharmacologic Management of COPD*

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Recommended First Choice</th>
<th>Alternative Choice</th>
<th>Other Possible Treatments**</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Short-acting anticholinergic prn or Short-acting beta₂-agonist prn</td>
<td>Long-acting anticholinergic or Long-acting beta₂-agonist or Short-acting anticholinergic and short-acting beta₂-agonist</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>Long-acting anticholinergic or Long-acting beta₂-agonist</td>
<td>Long-acting anticholinergic and long-acting beta₂-agonist antagonist</td>
<td>Short-acting beta₂-agonist and/or Short-acting anticholinergic Theophylline</td>
</tr>
<tr>
<td>C</td>
<td>Inhaled corticosteriod + long-acting beta₂-agonist or Long-acting anticholinergic</td>
<td>Long-acting anticholinergic and long-acting beta₂-agonist or Long-acting anticholinergic and phosphodiesterase-4 inhibitor or Long-acting beta₂-agonist and phosphodiesterase-4 inhibitor</td>
<td>Short-acting beta₂-agonist and/or Short-acting anticholinergic Theophylline</td>
</tr>
<tr>
<td>D</td>
<td>Inhaled corticosteriod + long-acting beta₂-agonist and/or Long-acting anticholinergic</td>
<td>Inhaled corticosteriod + long-acting beta₂-agonist and long-acting anticholinergic or Inhaled corticosteriod + long-acting beta₂-agonist and phosphodiesterase-4 inhibitor or Long-acting anticholinergic and long-acting beta₂-agonist or Long-acting anticholinergic and phosphodiesterase-4 inhibitor</td>
<td>Carbocysteine Short-acting beta₂-agonist and/or Short-acting anticholinergic Theophylline</td>
</tr>
</tbody>
</table>

*Medications in each box are mentioned in alphabetical order and therefore not necessarily in order of preference

**Medications in the column can be used alone or in combination with other options in the Recommended First Choice and Alternative Choice columns

### Is Combination Therapy Effective?

According to the GOLD guidelines, combining bronchodilators with different mechanisms of action may provide additional benefits for those living with COPD beyond what is provided by monotherapies alone. Combination therapy is recommended for patients whose symptoms are not controlled on bronchodilator monotherapy. The GOLD guidelines also recommend adding an ICS in conjunction with a bronchodilator in patients with more severe COPD prone to exacerbations. In fact, long-term treatment with ICS is recommended for patients with severe and very severe COPD and frequent exacerbations that are not adequately controlled by long-acting bronchodilators. However, ICS monotherapy is not recommended in COPD because it is less effective than combination treatment.
Combination of Mechanisms of Action May Improve Efficacy

Airway smooth muscle relaxation can be achieved by inhibition of acetylcholine signaling with a muscarinic antagonist, or by stimulation of \( \beta_2 \)-adrenoceptors with a \( \beta_2 \)-agonist. Therefore, the combination of a LAMA and a LABA has the potential to maximize the bronchodilator response without increasing the dosage of either component. LAMA/LABA combinations have been shown to improve lung function and reduce COPD exacerbations in several clinical trials, compared with each component used separately. Equally important, no unexpected safety issues have been observed to date with LAMA/LABA combination treatment. For example, the cardiovascular safety profile of several different LAMA/LABA combinations appears to be similar to that of placebo even though LAMAs and LABAs, when taken on their own, can both have a detrimental effect on the cardiovascular system.

It is important to remember that where a drug is deposited in the pulmonary airway is mainly decided by the size, shape, and density of the inhaled drug particles. Therefore, in a fixed-dose combination, each component medication may have a different particle size and thus have differing patterns of dispersion.

Recall from SCOPE eMagazine Issue 1: Particle size and lung deposition

- Depending on their size, inhaled drug particles will deposit in different regions of the lung
- Small particles penetrate more deeply into the lung and more effectively dilate the small airways than larger particles, which are deposited in the upper airways

Do Fixed-Dose Combinations Affect Patient Adherence?

Let's face it: it's not easy to cope with a chronic respiratory disease. In fact, patients with COPD take an average of 6 different medications. Patient adherence tends to decline over time and is inversely related to the number of medications a patient uses. In other words, the more medications you take, the harder it is!

When thinking about patient adherence in respiratory disease, it is important to consider the burden these patients face with using an inhaler or other respiratory device. Many patients have the additional burden of multiple devices with different dosing and cleaning instructions. In fact, patients with respiratory disease may be using 3 to 4 different types of inhalers. Mastering an inhaler is challenging. Patients with COPD are usually older and have multiple comorbidities. They may also have impaired physical and cognitive function. A treatment regimen that is simplified and tailored (such as a fixed-dose combination) may improve adherence.
Potential Benefits and Challenges of Fixed-Dose Combinations

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple mechanisms of action may improve drug activity and/or tolerability</td>
<td>Shifts in market and cost drivers</td>
</tr>
<tr>
<td>Potentially fewer devices for patient</td>
<td>Preclinical development and manufacturing to develop stable delivery under varying conditions</td>
</tr>
<tr>
<td>May increase patient adherence</td>
<td>Potential drug-drug interactions</td>
</tr>
</tbody>
</table>

**LOOKING FORWARD**

Triple fixed-dose combinations are on the horizon. In fact, technology being researched today will bring about the triple fixed-dose combinations of tomorrow.

Pearl Therapeutics received the 2013 Drug Delivery Partnerships™ (DDP) Innovation Award for their novel co-suspension formulation technology. The co-suspension technology has enabled highly uniform and efficient formulations of inhaled medicines, dual- and triple-drug combination products without drug-drug interactions, and stable delivery under varying conditions.

*A future issue of this magazine will look more closely at the obstacles in formulating a triple combination.*

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**Where can you learn more?**

- Global Initiative for Chronic Obstructive Lung Disease (GOLD). You can find the full Global Strategy for Diagnosis, Management, and Prevention of COPD consensus report [here](#).
- Pearl Therapeutics Press Release. You can find the full press release describing the award for innovative co-suspension technology [here](#).
Meeting the Need — Impact of Devices on Health Outcomes

Health care costs are substantial for patients with respiratory diseases, including chronic obstructive pulmonary disease (COPD). These costs include physician visits and medications (direct costs), as well as lost time at work and overall lost productivity (indirect costs). In 2010, the estimated health care costs associated with COPD in the United States totaled approximately $49.9 billion. Of this, $30 billion was due to direct health care expenses, and $20 billion represented indirect costs.

Even more startling are estimates that 28% to 68% of patients do not use their inhalers as prescribed and are consequently receiving suboptimal treatment for their respiratory disease. In fact, even the most appropriate and efficacious medication will not work optimally for a patient if he or she is unable to appropriately use the prescribed inhaler device. The solution is relatively simple: effective patient and clinician education on device usage. Unfortunately, clinicians often just don’t have enough time with patients to ensure proper education. If this is the case, collaborating with a nurse educator may allow time for successful patient education and improve patients’ inhaler technique.
As a nurse educator, I find that my patients often don’t understand how to properly use their inhalers. Sometimes they are frustrated with the lack of efficacy of their treatment, and this can sometimes lead to them giving up on their medications. It is so rewarding to be able to show them how their medication can be effective when properly administered and to give them hope that their disease is manageable.

The most common error in pressurized metered-dose inhaler (pMDI) use is hand-breath coordination, followed by patients not holding their breath long enough. Other common errors are breathing too rapidly and inadequately shaking the inhaler. Less common errors include putting the wrong end of the inhaler in the mouth and leaving the cap on while using the device.

<table>
<thead>
<tr>
<th>Error</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand-breath discoordination</td>
<td>27</td>
</tr>
<tr>
<td>Breath-hold too short</td>
<td>26</td>
</tr>
<tr>
<td>Inspiratory flow too rapid</td>
<td>19</td>
</tr>
<tr>
<td>Inadequate shaking of inhaler</td>
<td>13</td>
</tr>
<tr>
<td>Abrupt stop of inhalation (“cold-Freon effect”)</td>
<td>6</td>
</tr>
<tr>
<td>MDI actuation at total lung capacity</td>
<td>4</td>
</tr>
<tr>
<td>Multiple actuations with a single breath</td>
<td>3</td>
</tr>
<tr>
<td>Firing MDI in mouth, inhaling through nose</td>
<td>2</td>
</tr>
<tr>
<td>Exhaled during actuation</td>
<td>1</td>
</tr>
<tr>
<td>Wrong end of inhaler in mouth</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Cap left on MDI boot</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Inspiration without actuation</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Actuation without inspiration</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
What Are Some of The Misconceptions About Inhaler Use Held by Patients and Health Care Professionals?

INHALERS ARE SIMPLE AND PATIENTS NEED NO INSTRUCTION FOR THEIR USE.

Actually, inhalers can be pretty complicated for both patients and health care professionals. Without instruction, most patients and clinicians are unable to realize the maximum effect of the medication delivered through the device.

DRY-POWDER INHALERS (DPIS) ARE EASIER TO USE THAN PRESSURIZED METERED-DOSE INHALERS (PMDIS).

As it turns out, improper use of both devices is common. DPIs and pMDIs also require a similar number of steps per use.

NEBULIZERS ARE MORE EFFECTIVE AND EASIER TO USE THAN INHALERS.

Believe it or not, efficacy is similar across all devices. However, home nebulizers are more complex to set up, disassemble, clean, and maintain than inhalers.

PATIENTS WILL USE THEIR INHALED MEDICATIONS AS PRESCRIBED.

A large number of patients do not even fill prescriptions for inhalers. Clinicians should ask patients which medications they take and which medications they are not taking. They should also ask each patient what he or she does or does not like about each medication prescribed.

SOMEONE ELSE WILL TEACH THE PATIENT.

Inhaler misuse is an issue faced by patients every day, and it directly affects disease control. Each clinician prescribing inhaled medications must fully understand and explain how to use the device(s) or refer patients to an appropriate resource who can help provide education.

PATIENTS DO NOT USE INHALERS CORRECTLY, EVEN WHEN WELL INSTRUCTED.

Actually, it is more likely that health care providers are not effectively educating patients. Clinicians can help by demonstrating proper usage with placebo and having patients demonstrate proper use at each office visit. It is also important to have easy-to-understand explanations and written materials available for each patient to read and take home.

Clearly there is a cost to the improper use of inhaler devices. Device misuse and inadequate patient education negatively impact patient health, outcomes, and cost. Nonadherence to therapy among patients with chronic diseases is estimated to cost $300 billion in the United States annually, and COPD is among the conditions with the lowest levels of adherence. More than half of all COPD patients are considered to have poor adherence. If you were a physician, how might you “meet the need” for your patients with respiratory disease?

Where can you learn more?

• To learn more about asthma treatments, click here.
• To learn more about COPD treatments, click here.
• To learn more about respiratory devices, click here.
Test your respiratory vocabulary by matching the term at the top with the correct definition at the bottom. How much word power do you have? 

<10 = Red Zone; 11-16 = Yellow Zone; 17-20 = Green Zone. Answers at the bottom of the page.

1. Short-acting beta₂-agonists (SABAs)
   - A class of medications used for chronic management of asthma and COPD that acts as an agonist.

2. Long-acting beta₂-agonists (LABAs)
   - A drug that expands the bronchi by relaxing bronchial muscle. There are 3 classes: beta₂ adrenergic-receptor agonists, methylxanthines, and anticholinergic agents.

3. Short-acting muscarinic antagonists (SAMAs)
   - A slower-acting inhaled medication chronically used to prevent unexpected flare-ups from respiratory disease. Also called preventive or maintenance medication.

4. Long-acting muscarinic antagonists (LAMAs)
   - In pharmacology, a drug that binds to the receptor and stimulates the receptor’s function.

5. Corticosteroids
   - A type of phagocyte capable of engulfing and damaging microorganisms. They can also release an assortment of proteins that have antimicrobial properties. In COPD, they are rapidly recruited to areas of inflammation.

6. Phosphodiesterase inhibitors
   - A type of phagocyte responsible for engulfing and destroying damaging microorganisms or dead cell debris within the cells of the body. In the alveoli, they help fight bacterial infections, such as Haemophilus influenzae and Streptococcus pneumoniae.

7. Methylxanthines
   - A group of bronchodilators used to treat acute respiratory exacerbations.

8. Inhaled corticosteroids (ICSs)
   - A type of phagocyte capable of engulfing and damaging microorganisms. They can also release an assortment of proteins that have antimicrobial properties. In COPD, they are rapidly recruited to areas of inflammation.

9. Bronchodilator
   - A type of phagocyte responsible for engulfing and destroying damaging microorganisms or dead cell debris within the cells of the body. In the alveoli, they help fight bacterial infections, such as Haemophilus influenzae and Streptococcus pneumoniae.

10. Controller
    - A drug that expands the bronchi by relaxing bronchial muscle. There are 3 classes: beta₂ adrenergic-receptor agonists, methylxanthines, and anticholinergic agents.

11. Agonists
    - A drug that expands the bronchi by relaxing bronchial muscle. There are 3 classes: beta₂ adrenergic-receptor agonists, methylxanthines, and anticholinergic agents.

12. Antagonists
    - A type of phagocyte responsible for engulfing and destroying damaging microorganisms or dead cell debris within the cells of the body. In the alveoli, they help fight bacterial infections, such as Haemophilus influenzae and Streptococcus pneumoniae.

13. Drug-drug interaction
    - A group of bronchodilators used to treat acute exacerbations of asthma and COPD and acts as an agonist.

14. Exacerbation of COPD
    - A group of naturally occurring agents present in caffeine, theophylline, and theobromine. They act on the central nervous system, stimulate the myocardium, relax smooth muscle, and promote diuresis.

15. Triple therapy
    - A group of anticholinergic medications used for chronic management of respiratory disease.

16. Macrophages
    - A group of bronchodilators used to treat acute exacerbations of asthma and COPD and acts as an agonist.

17. Monocytes
    - A group of anticholinergic medications used for chronic management of respiratory disease.

18. Neutrophils
    - A group of anticholinergic medications used for chronic management of respiratory disease.

19. T cells
    - A group of anticholinergic medications used for chronic management of respiratory disease.

20. Reactive oxygen species
    - A group of anticholinergic medications used for chronic management of respiratory disease.


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Points to Ponder

Which article grabbed your attention the most? Why?

What is the one piece of information you found most striking?

Considering the range of topics in this disease state, what would you be interested in learning more about in future issues?

Looking at your level of scientific acumen, which article filled a gap-area and why?

What’s Next?
Resp: Next Edition

More about the treatment differences between COPD and Asthma