

Translating New Understanding Into Better Care for the Patient With Chronic Obstructive Pulmonary Disease

David J Pierson MD FAARC

Introduction

Definition and Epidemiology of COPD

Making the Diagnosis: Screening Versus Case-Finding

New Understanding and Approaches for Exacerbations

Current Status of Alpha-1 Antitrypsin Deficiency

Comprehensive Disease Management and Its Importance in COPD

Smoking Cessation

The Role of Practice Guidelines in COPD Management

Pulmonary Rehabilitation: Proven Potential, Persistent Problems

COPD and Sleep

Surgical Treatments for COPD

Emerging and Future Drugs for COPD

The Role of Noninvasive Ventilation in COPD

Palliative Care for COPD Patients

Some Editorial Comments and Concluding Remarks

Despite an enormous amount of research and many official statements, the definition, diagnosis, and staging of chronic obstructive pulmonary disease (COPD) remain inconsistent, and we have yet to agree on who should be tested with spirometry or on where and how to do it. We know that inflammation, not just airflow limitation, is important in determining the course of COPD, especially with respect to exacerbations. We can detect and treat alpha-1 antitrypsin deficiency, an under-recognized condition, but whether alpha-1 antitrypsin augmentation therapy affects the disease's clinical course remains unclear. Smoking cessation is the most important of all interventions for COPD, with proven techniques and adjuncts, but implementation remains difficult and success rates are disappointingly low. Similarly, pulmonary rehabilitation has well-documented benefits but is grossly underutilized because it is difficult to pay for and is not made available to most patients. Symptoms, costs, and other outcomes can be improved through comprehensive disease management, including the use of practice guidelines, yet multiple barriers prevent the potential benefits of these interventions to patients from being realized. Many patients who do not meet threshold oxygenation criteria for oxygen therapy during the daytime desaturate during sleep, but evidence that nocturnal oxygen administration benefits these patients is lacking. However, other sleep-related breathing disorders are common in COPD patients. Lung volume reduction surgery has recently been shown to improve function and survival for certain COPD patients, but lung transplantation has generally been disappointing. New pharmaceutical agents are being developed for treating COPD, and at least one of them (tiotropium) should soon be available in the United States. Noninvasive ventilation is effective in treating acute decompensations of COPD and should be the standard of care in that setting; evidence supporting its use in stable patients with end-stage disease is scant. Appropriate palliative care can greatly benefit patients and their families in the terminal phase of COPD and needs to be more widely applied. *Key words: chronic obstructive pulmonary disease, COPD, emphysema, diagnosis, management, respiratory care, exacerbations, al-*

pha-1 antitrypsin deficiency, smoking cessation, pulmonary rehabilitation, outcomes, lung-volume-reduction surgery, noninvasive ventilation, palliative care, evidence. [Respir Care 2004;49(1):99–109. © 2004 Daedalus Enterprises]

Introduction

Being asked to summarize a RESPIRATORY CARE Journal Conference is an honor and a challenge.¹ Having done it twice before, I can testify to the adrenalin rush that comes with attempting to synthesize 2 days and more than 12 hours of high-powered lectures and discussions into a coherent presentation of 30–45 minutes that both captures the essence of the conference and is also original and instructive. In this instance the topic has been near and dear to my heart for more than 30 years, since my fellowship years in Denver, and I am pleased to offer this synthesis of the proceedings along with a few personal observations and editorial remarks.

Gordon Snider was originally to have been the conference summarizer, and although he was, unfortunately, unable to attend, these proceedings have been profoundly influenced by his contributions to the field, and his presence has been felt during nearly every presentation. Dr Snider mentored many of today's leaders in chronic obstructive pulmonary disease (COPD), including Jamie Stoller, Barry Make, Nick Hill, and Josh Benditt at this conference, and it is fitting that its proceedings be dedicated to him. I would also like to acknowledge the contributions of Tom Petty, a previous Journal Conference participant and another COPD pioneer, whose influence has also been much in evidence here. John Heffner, Paul Enright, and I were trained by Tom, and his research and teaching have also had a profound impact on several others in this group. Both Gordon Snider and Tom Petty have been working actively for more than 4 decades to increase understanding and improve management of COPD, and both continue to make important contributions to this field.

The title of this conference is not just “COPD,” but “Translating New Understanding Into Improved Patient Care,” and in the planning there was discussion about how

to make sure this didn't turn into just a “me too” conference, rehashing what has been presented many times before. There is certainly a lot out there on COPD—several comprehensive textbooks, dozens of review articles, the proceedings of other conferences, and, as John Heffner told us, some 40 clinical practice guidelines. The planners of this conference wanted to make sure that it had value over and above an up-to-date summary of the material. I think it has emerged during the last 3 days that there is much that is new in COPD, including new ways of thinking about the disease and its management. But there is also a crying need to improve the care of the millions of people who suffer from COPD. In this summary I will not only present what I took to be the key messages of the conference but also indicate some of the ways we need to change our thinking and do a better job for our patients, translating this new understanding into improved patient care.

Definition and Epidemiology of COPD

In David Mannino's presentation on the definition and epidemiology of COPD² he pointed out that this is the only major fatal disease the death rate of which is *increasing*—a disparity all the more striking amid the dramatic decline in deaths from coronary artery disease, stroke, and other cardiovascular disorders. Moreover, there are various definitions of and diagnostic criteria for COPD, not only in everyday practice but also in official statements and practice guidelines. Gordon Snider's recent article on nosology—the discipline of classification and terminology of diseases—takes COPD as an example and discusses the importance to research, epidemiology, and clinical practice of how this condition is described and defined.³ Differences in definition and diagnostic criteria remain barriers to both research and clinical practice. David talked about the use of clinical staging systems for COPD, which is something relatively new to this disease but long in wide use for many other chronic diseases. He discussed the current demographics and national impact of COPD, including its effect on 10 million Americans and its being either the direct or a contributing cause of 9% of all hospital admissions and a staggering \$14.7 billion in annual direct health care costs. This is no longer a disease mainly of men, women having for the first time overtaken their male counterparts in number of deaths from COPD per year in the United States.

Having COPD—not just smoking—is a separate risk factor for lung cancer, although not, apparently, for heart

David J Pierson MD FAARC is affiliated with the Division of Pulmonary and Critical Care Medicine, Harborview Medical Center and University of Washington, Seattle, Washington.

David J Pierson MD FAARC presented a version of this report at the 32nd RESPIRATORY CARE Journal Conference, Chronic Obstructive Pulmonary Disease: Translating New Understanding Into Improved Patient Care, held July 11–13, 2003, in Los Cabos, Mexico.

Correspondence: David J Pierson MD, Harborview Medical Center, 325 Ninth Avenue, Box 359762, Seattle WA 98104. E-mail: djp@u.washington.edu.

disease. On the other hand, asthma, even when life-long and incompletely reversible, does not eventually turn into COPD, at least from the standpoint of mortality and other adverse clinical outcomes. David reminded us that exposure to agents other than direct cigarette smoke may be important in the development of COPD, citing the example of long-term exposure to cow-dung smoke incurred in cooking in India, and also recalling Gordon Snider's work on cadmium exposure as an important factor in pathogenesis.

One of the features of the proceedings of the RESPIRATORY CARE Journal Conferences that sets them apart from other published resources in their subjects is the discussion sessions, which we go to great pains to capture on tape. In this summary I am going to point out the salient points from the discussions, in addition to what the speakers said in their formal presentations. After David's presentation there was some discussion of the difficulty in knowing when a smoker first develops disease, bringing up the concept of the so-called "healthy" smoker, and whether that really is a valid concept any more. Bronchoalveolar lavage and other sophisticated tools for detecting abnormalities in people who smoke cigarettes, even in the absence of airway obstruction, indicate that there may be no such thing as a healthy smoker. This is not something that the government or third-party payers want to hear, but it illustrates the difficulties we have in identifying when COPD starts. Sam Giordano offered the concept of the "leather people," meaning those individuals who are apparently able to withstand many years of heavy smoking without overt, or at least life-limiting, ill effects.

Making the Diagnosis: Screening Versus Case-Finding

Paul Enright next took the stage for his presentation, the title of which, as given by the conference organizers, was "Strategies for Screening for COPD".⁴ Paul reported that undetected airflow obstruction is very prevalent in our society and that it causes increased morbidity and other problems for the people who have it. We also know that smoking cessation slows the progression of the disease, so if we could detect more undiagnosed COPD cases, it would have an enormous impact on the health of the nation—millions of quality-adjusted life years—assuming that smoking cessation could be accomplished. However, Paul pointed out that "screening" is a bad word these days, in that it implies taking ordinary people on the street and trying to find some disease in them, which is anathema to health care payers and legislators trying to control health care expenditures. Therefore, Paul contends that we should be talking about *case-finding* rather than screening. Case-finding involves a patient who is already accessing the health care system, who has come to the doctor for some-

thing and could be identified as being at high risk for COPD by virtue of age and smoking history, and who has some kind of respiratory symptom. This is very different in concept from screening, an example of which would be going to a shopping mall or convention to try to find people who have airway disease. Pertinent to my comment above about the continuum of smoking-induced lung abnormalities, Paul made a plea for "not taking the *O* out of COPD," meaning that we should retain the presence of airflow limitation as the *sine qua non* for making this diagnosis. This point turns out to be important as we go through what evolved at the conference, with comments about inflammation and perhaps other ways that we have of detecting the process that eventually shows itself as COPD. Certainly, the National Lung Health Education Program recommendations for COPD screening by primary care practitioners in their offices⁵ are consistent with the notion that obstruction is the primary "bottom line."

Paul pointed out that very inexpensive devices—even in the range of \$50 each—are currently being introduced for the purpose of measuring forced expiratory volume in the first second (FEV₁) and the National Lung Health Education Program's proposed surrogate for vital capacity, the forced expiratory volume in the first 6 seconds (FEV₆) in identifying airflow limitation. He indicated that a lot of problems could potentially be introduced with the widespread adoption of such devices. He made the point that case-finding in COPD is really only worthwhile if (1) applied to current smokers who are seen in the health care setting and who have respiratory symptoms, (2) good quality spirometers can be obtained and interpreted correctly, and (3) the patient can be referred to a smoking cessation program that is nearby and functions properly. Those are a lot of "ifs," and they markedly constrict the topic implied by the title of Paul's presentation. However, the scheme as outlined is perhaps more realistic and practically attainable than the original notion of screening more broadly for COPD.

During the discussion period following Paul's presentation it was pointed out that there is a substantial gap between the American Thoracic Society's standards for acceptable spirometry and the desire to test as many people as possible, not in certified pulmonary function laboratories but in primary care providers' offices. Somehow we need to reconcile the hopeful optimism of the National Lung Health Education Program with the grim realities of the stringent American Thoracic Society standards for performance and interpretation of spirometry, and also with the cost implications if the millions of people who theoretically could be helped by case-finding are to benefit.

An issue not raised in the discussion but that often surfaces is that the bottom line with case-finding, with respect to altering the course of COPD, is that you tell the identified individual that he or she needs to quit smoking. But

we already know that *everyone* should stop smoking, so why go to all the trouble? Why not just dispense with the specific targeting and just try to get everyone to stop smoking? The logistic implications of such a strategy are horrendous, and it was pointed out that during the course of a person's experience with illness, there are "teachable moments" at which the likelihood of the clinician impacting the patient's behavior is markedly increased. A teachable moment with respect to respiratory disease is probably when the person is having some symptom or at least has been demonstrated to have something wrong with his respiratory system.

New Understanding and Approaches for Exacerbations

Jadwiga "Wisla" Wedzicha then talked about the pathogenesis of COPD and exacerbations.⁶ She told us about the East London COPD study that she and her colleagues have been carrying out for a number of years—a very ambitious project that has yielded a great deal of insight and information that may be very valuable clinically and that may change our thinking a lot. She focused her discussion on the epidemiology and clinical characteristics of exacerbations and emphasized something that came up repeatedly throughout the conference—the importance of inflammation, and not just airflow obstruction, in COPD. She summarized what we know about treatment in this context.

However, before going into that, here's a bulletin from the Department of Redundancy Department: what we are talking about here is not an "acute exacerbation," it's an "exacerbation." I hadn't thought about this before but an exacerbation, by definition, *is* acute. So, just as we should not say "chronic COPD" or "PCP pneumonia" (for *Pneumocystis carinii* pneumonia) or the other curious redundancies we tend to use in our daily practice, we need to get away from talking about "acute exacerbations" of COPD. That's going to be tough, as most of us are used to saying "acute exacerbation," and the acronym AECB (for acute exacerbation of chronic bronchitis) seems firmly ensconced in the lexicon of medical terminology. However, I'm convinced that Wisla is right.

The conclusions that Wisla drew included the following. First, decreasing the frequency of exacerbations may slow the progression of the disease, making this a very important goal of management. Second, patients with more severe disease may respond better to therapy to prevent exacerbations than do patients with less severe disease. Third, patients who produce a lot of sputum may be different somehow from patients who do not, again getting back to inflammation as an important determinant of the illness, and these patients may need different kinds of therapies for the prevention and treatment of exacerbations. Finally, reducing the severity of exacerbations is

also very important, and prompt and optimal therapy at these times is important not only for the patient's lifestyle but also in terms of progression of the disease.

The discussion after Wisla's presentation again emphasized the importance of inflammation as a separate category to pay attention to in COPD. Amidst an exchange about pathophysiology and biological markers of inflammation, Bonnie Fahy interjected a question that became an important theme throughout the rest of the conference: "What's the take-home message for the patient in all this?" This was a clarion call not to lose track of the underlying purpose (and title) of our conference—to make sure that in all of our discussions we did not lose track of the patient's perspective and experience, or of how our conclusions and discussion of the topic related to perception of benefit for the patient. Wisla's response was that the patient needs to get better at detecting an exacerbation and at getting it treated. She emphasized that, ideally, this should be done without the patient's having to be hospitalized or go to the emergency room.

Current Status of Alpha-1 Antitrypsin Deficiency

Jamie Stoller then talked about the diagnosis and management of emphysema caused by alpha-1 antitrypsin (AAT) deficiency.⁷ He reviewed the epidemiology and the strategies for treatment, discussing 3 main points and drawing 3 main conclusions: (1) AAT deficiency is a common disorder, (2) it is under-recognized by physicians, and (3) AAT augmentation therapy is efficacious.

Regarding the assertion that it is a common disorder, the true prevalence has been hard to determine because of differences in genetic characteristics and ethnic backgrounds of the populations, the highest prevalence being in Scandinavia; it is estimated that in Sweden 1 in 1,600 people has homozygous AAT deficiency. In contrast, in the United States the best estimates are that it may be about one-third that prevalent, and in some other parts of the world the condition is extremely rare. On the basis of available data, Jamie estimated there are 50,000–70,000 cases of AAT-deficiency-associated COPD in the United States.

With respect to its being under-recognized, that seems clearly to be the case, although the data on which this conclusion rests are not the kind of evidence that one would ideally like to have. The evidence comes primarily from a register of primarily self-identified alpha-1 patients—a very vocal and involved group. Most of these patients reported having had symptoms for a number of years and having seen several physicians for the symptoms before the diagnosis was made. Based on information provided by these patient groups one can estimate that perhaps only about 4% of the cases in the United States have been diagnosed.

With respect to the contention that AAT augmentation therapy is efficacious, Jamie pointed out that this is a therapy that has now been available in the United States for more than 15 years. There are 3 commercial preparations presently available. It came out in the discussion that the drug costs about \$30,000–35,000 per year, but that because of vigorous patient advocacy and other factors, it is fully reimbursed and readily available for us to give to patients. We know that augmentation therapy can raise both serum and alveolar AAT levels into the normal range and can keep them there with weekly or biweekly infusions. However, the database on clinical effectiveness is not the database we wish we had. It was decided a long time ago not to do a randomized, controlled trial in this country. There has been one randomized, controlled trial, in Denmark,⁸ which showed a trend toward a favorable effect from augmentation therapy, based on lung tissue density measured via computed tomography, although not according to other clinical variables studied. On this matter I have to say I wish we had better data, but that it does not appear to be firmly established whether AAT augmentation therapy has a clinically relevant effect on lung function decline, exacerbation frequency, or mortality from COPD associated with AAT deficiency.

The discussion after Jamie's presentation got pretty animated, and this was the first of several times during the course of the conference that we "beat up on him." Discussion focused on the clinical relevance and cost-effectiveness of AAT augmentation therapy. It was pointed out that a calculated cost of about \$600,000 per quality-adjusted life year has been determined, which is higher than for other screening and therapeutic techniques that were mentioned. Neil MacIntyre tossed out a figure of \$25,000 per mL of FEV₁ decline ameliorated; I'm not sure where he got that figure, but it was dramatic and created a stir.

The importance of inflammation was once again raised with regard to AAT deficiency, and in the future it may be that patient selection for AAT augmentation therapy may have something to do with our ability to detect which patients have more ongoing inflammation in their lungs. The issue of who should be tested for the presence of AAT deficiency was raised, and Jamie felt that all COPD patients merited testing. The question of whether or how to discontinue AAT augmentation was also raised, and the group had no satisfactory answer.

Comprehensive Disease Management and its Importance in COPD

The next presentation, by Barry Make, was on developing comprehensive disease management for COPD patients.⁹ He discussed the overall goals of what we should be attempting to achieve in COPD management. He mentioned the new and pretty good evidence base for the ef-

ficacy of drug combinations, particularly the bronchodilators. He discussed the concept of "compliance" versus "adherence" and the things that improve patient adherence with management. This led to introduction of the concept of disease management and its importance in COPD. The overall goals of COPD management are (1) to diagnose the disease correctly and assess it appropriately, (2) to reduce the patient's risk, (3) to reduce symptoms, and (4) to reduce complications. Ameliorating the downhill course of the disease was not included on the list, although I think Barry probably meant to include that in the goal of reducing risk.

With respect to efficacy of drug combinations there are now good data supporting the combined effect of inhaled long-acting β -agonists and short-acting anticholinergic bronchodilators as being more than just the sum of their parts with respect to several measures—not just airflow but also quality-of-life. Along the same line, theophylline and an anticholinergic given in combination have been shown to be better than either agent by itself. Now there is also evidence that long-acting β -agonists plus high-dose inhaled corticosteroids decrease the frequency of exacerbations and have other clinical benefits.

The issue of "compliance" versus "adherence" has to do with terminology, but is also important conceptually when we think about Bonnie's admonition to keep the patient in the middle of this discussion. The word "compliance" has an implication of a hierarchical relationship, with the physician on top, and that has not been considered appropriate in recent years. The term "adherence" is more palatable, and is consistent with the concept of an equal partnership between patient and clinician, with both being thoroughly involved in the management. With respect to improving adherence, Barry showed us a photograph of 5 different inhalers that a COPD patient might have prescribed to him, each of the devices of different design and with different instructions for use—different preparations, different rates of inhalation, different everything. It was a nice illustration of the barriers patients can face in doing what we ask them to do, that may keep them from actually accomplishing what we intend for them or what they may think they are doing—particularly when they're elderly and/or have co-morbidities or impaired ability to handle a complex regimen. To improve adherence Barry recommended education, better communication with the patient, emphasis on negotiation with patients (which I think physicians have traditionally not done very much), and streamlining of care, which leads into case management, to individualize care for each patient and make adherence more attainable.

Finally, Barry introduced the concept of disease management as a way to care for patients with complex illnesses closer to the way we believe their management should be. He also pointed out some of the down sides to

the way disease management has tended to be done so far—by a third party, usually outside the physician-patient relationship, and with the perspective of those paying for it appearing to be primary rather than the perspective of a better outcome for the patient. Certainly, this concept is something that needs to be applied in COPD and is something about which we are sure to hear a great deal more in the coming years.

The discussion after Barry's presentation initially focused on why COPD patients seem to have such poor adherence. It was pointed out again that the co-morbidities, various demographic characteristics, and educational and socioeconomic status of many COPD patients are stacked against them. There was a call for baby boomers to get on board with preventive care and the assertion that there is going to have to be a mandate from patients themselves, and not just from the medical profession, in order for better outcomes to be achieved. Patient support groups were identified as important facilitators of adherence, and Bonnie reminded us that pulmonary rehabilitation is the best of all patient support groups. Someone urged a greater role for respiratory therapists (RTs) in promoting patient adherence, and this became one of the themes of the conference, being brought up repeatedly and, I believe, appropriately.

Smoking Cessation

Next came Scott Marlow's presentation on smoking cessation.¹⁰ Certainly no conference on how to do the best thing for COPD patients could be held without a serious and in-depth discussion of smoking cessation, because that is the one intervention that we know of that can change not only the manifestations of the disease but also its prognosis. Scott told us that each pack of cigarettes sold costs society \$7.18. He also reviewed for us some important recent publications that greatly augment the available resources on smoking cessation. These include the United States Public Health Service clinical practice guideline, *Treating Tobacco Use and Dependence*,¹¹ which was released in 2000 and reprinted in *RESPIRATORY CARE*.¹²

Scott reviewed recent data on the efficacy of available treatments. He pointed out that physician advice, individual and group counseling, telephone counseling, and self-help materials all have very high evidence levels in terms of efficacy but relatively low magnitudes in terms of getting people to stop smoking or improving abstinence from smoking. There is a dose-response relationship for these behavioral interventions; that is, the more of these interventions you do simultaneously, the better the results. There are also 5 drug formulations currently with level A evidence of efficacy in getting people to stop smoking: nicotine gum, nicotine patch, nicotine nasal spray, nicotine inhaler, and bupropion. This level A evidence is a little

misleading in that some of the study conditions under which it was obtained differ a lot from real-world conditions. I certainly would not want to have to put something up my nose every 2 hours all day long in order to keep from smoking cigarettes, especially in the long-term. But at least we have solid evidence of the efficacy of these therapies.

Combining drug therapy and counseling techniques also improves the smoking cessation rate, although it was pointed out that the 11-year abstinence rate in the Lung Health Study, the largest study of this to date, was 22%—admittedly very much better than the 6% without these therapies, but still only 22% at 11 years.¹³ Existing studies on the role of the RT in smoking cessation—which we all agreed is a key role that should be expanded—are scant and not of very good quality.

After Scott's presentation we discussed interventions that work in reducing smoking. Increasing the price of cigarettes works, and limiting where people can smoke works. Anti-smoking advertising, as by the American Lung Association and other voluntary organizations, works. However, interventions that don't work include all the things the tobacco companies have been mandated to do by the courts. Money and politics also reared their ugly heads as we discussed the reality of how to attack the smoking problem, both globally and with our patients. Neil MacIntyre pointed out that although an absolute decrease in smoking of about 4 percent can be achieved for every 10 percent increase in the cost of cigarettes, that price increase is not happening, for reasons that weren't explicitly stated but could be imagined by everyone in the room.

The issue of smoking among health professionals came up, and someone suggested that it was particularly troublesome to see RTs smoking, in view of the desire that RTs be role models. Good data are lacking on relative rates of smoking in various health professions, but all of them have more smokers than they should. It was brought up that outside the United States the prevalence of smoking among physicians and other health care workers seems to be much higher than it is here. Members of the faculty gave anecdotal accounts of attending pulmonary meetings with breaks built into their schedules so that the attendees could leave the conference hall to go outside and smoke.

Everyone agreed about the important role of RTs in smoking cessation. It is a natural role, one for which RTs are trained and apparently motivated. On the down side, however, Kevin Shrake pointed out from the perspective of a former hospital administrator that there are a number of reasons beyond the control of respiratory care departments and individual RTs why their more active involvement in smoking cessation has not yet happened.

The Role of Practice Guidelines in COPD Management

Clinical practice guidelines have achieved prominence in many fields of health care during the last decade, including COPD management. In his presentation, "The Guideline Approach to COPD: How Effective?", John Heffner reviewed the reasons for the practice guideline explosion and the role of such guidelines in an era of evidence-based medicine.¹⁴ He then discussed some of the barriers that must be overcome "in the trenches" in order for the potential benefits of practice guidelines to be realized in actual patient care.

Citing one of the figures that stuck most in my mind during this conference, John pointed out that a million years of life are lost each year worldwide because of COPD. He made a strong case for guidelines in the era of evidence-based medicine, pointing out that one of the drivers for this is the enormous practice variation that occurs when clinicians are left on their own to do things the way they like. Such *laissez-faire* practice results in over-use and under-use, as well as misuse, of therapies, irrespective of their proven efficacy. The greatest practice variation in many health care interventions has been on the low-tech end, such as prescribing aspirin or a β blocker after an acute myocardial infarction—interventions that tend to make the biggest difference in patient outcomes, as opposed to the high-tech (and "high-billable"), more expensive interventions.

John reviewed the recent explosion in practice guidelines—including forty in COPD alone—and discussed the process by which they are developed. In many cases the evidence base for published guidelines is not as strong as we might like it to be. Guidelines do tend to reduce practice variation, but there are problems with the process of care, with physician knowledge of guidelines and their contents, and with the desired outcomes. These problems are owed in part to a number of barriers that John enumerated for us in the development, dissemination, and implementation of guidelines.

In the discussion after his presentation John pointed out the need to reconcile guidelines with local conditions, resources, and capabilities. John Hansen-Flaschen remarked that in a developing country the presence of a practice guideline is all well and good, but if the system and its clinicians lack access to the treatments the guideline recommends, the guideline will not help patients. As John Heffner pointed out, paraphrasing the late House speaker Tip O'Neil, "All guidelines are local." That important concept needs to be emphasized. Nick Hill emphasized the need for humility rather than arrogance in the people and groups that develop guidelines, and that guideline makers should not be "sitting on top of the mountain casting down their glowing guidelines on the great unwashed below."

Instead, guidelines need to be "transparent," and there needs to be an ongoing, equal relationship with the practitioners and the recipients of the care promoted by the guidelines.

Pulmonary Rehabilitation: Proven Potential, Persistent Problems

Bonnie Fahy's presentation, "Pulmonary Rehabilitation for COPD: A Scientific and Political Agenda,"¹⁵ addressed another topic that no conference about helping COPD patients could possibly omit. She emphasized that patients need "rehab" on the basis of their symptoms and the interference with their lives that COPD causes, not just because of some threshold FEV₁ or other physiologic measure of severity. She pointed out that the goal is independence and improved functioning on the part of the patient, as determined individually according to that patient's lifestyle. Pulmonary rehabilitation is an area in which effectiveness has been documented for a multiplicity of its components and at the highest level of evidence. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD classification was recently modified¹⁶ in order to make it a little more user-friendly and applicable for rehabilitation programs.

Bonnie pointed out that the location of the program (in-patient vs out-patient) is not terribly important so long as the program is done right. And, she reminded us, we do know how to do it right. Excellent, evidence-based guidelines have been promulgated and are available, with outcomes as important components in all of them. Here again, the role of the RT was agreed upon and emphasized. RTs have a great deal of training in pulmonary rehabilitation but, as Bonnie noted, they are substantially under-represented in current programs.

As would subsequently be presented by Josh Benditt, it was pointed out during the discussion after Bonnie's talk that 15% of the patients in the National Emphysema Treatment Trial (NETT)¹⁷ withdrew from the study after the mandatory pulmonary rehabilitation phase because they felt so much better that they no longer wanted to contemplate surgery. Reimbursement woes and future prospects for reimbursement were prominent in our discussion, as they had been in Bonnie's presentation, per her instructions from the conference organizers. Reimbursement differs among the states. Neil MacIntyre stated that the Centers for Medicare and Medicaid Services (formerly the Health Care Finance Administration) has an important problem in that the law they deal with specifically prohibits reimbursement for rehabilitation services. Someone lamented that if only we could get those tobacco industry funds diverted to rehabilitation, think of all the good that could be done. However, we all realized that we have to deal with practical reality. We talked about the relative

costs of rehabilitation versus some other COPD therapies. We beat up on Jamie a little bit more and moved on.

COPD and Sleep

Peter Gay then talked about COPD and sleep.¹⁸ He made the point that sleep in COPD patients is fundamentally normal, in that the basic architecture of sleep and ventilatory drive are still there. However, although those things are not altered very much by COPD itself, COPD patients have a very high prevalence of other sleep-related disorders. We talked about the “overlap syndrome,” which David Flenley described back in the mid-1980s,¹⁹ in which COPD patients also have a primary disorder of breathing and sleep. Because COPD and obstructive sleep apnea are both common diseases affecting middle-aged and elderly individuals, it is not surprising that the overlap syndrome is also common. Peter stressed the importance of evaluating COPD patients for the presence of other diseases.

Peter went over the evidence supporting nocturnal oxygen therapy for COPD patients who are hypoxemic during the day and also for patients who are normoxemic while awake during the day. He admitted that the database to support nocturnal oxygen therapy for people who only desaturate at night is not very good. This is one of those things that was declared reimbursable from the very beginning, but in fact some reasonably good studies have failed to support it by demonstrating any effect on survival or other outcomes. Peter recommended that a patient be selected for nocturnal oxygen therapy for hypoxia during sleep if he or she desaturates substantially, for example to less than 90% for at least 5 minutes, assuming that a saturation of more than 90% is actually sustainable with supplemental oxygen throughout the night.

In the discussion after Peter’s presentation Paul Enright made one of several curmudgeonly comments that served to keep us all honest during the conference; he asked whether nocturnal oxygen therapy is something that really benefits patients or just makes us feel better as clinicians because we’ve identified a physiologic abnormality and done something about it. I have to say that that is a pretty reasonable question in light of the available evidence. Peter acknowledged that the evidence supporting nocturnal oxygen therapy for people who desaturate only at night is not so great, but, he reminded us, it is important to consider the possibility of other conditions in our patients—not just their COPD.

Surgical Treatments for COPD

Next Josh Benditt talked about lung volume reduction surgery (LVRS) and lung transplantation for emphysema.²⁰ He began by going through the substantial list of surgical interventions that have been attempted during the

last hundred years in attempts to help patients with emphysema. Recently, the focus has been on two of these procedures: LVRS and lung transplantation.

Josh spent most of his presentation talking about the NETT study on LVRS, the main findings of which were recently published.¹⁷ This was a unique trial in a number of respects. It was the first ever collaborative venture between the National Heart Lung and Blood Institute, the Centers for Medicare and Medicaid Services, and the Agency for Healthcare Research and Quality. The NETT was funded by Medicare, with the federal government paying directly for research procedures for the first time. It was also an interesting collaboration between investigators from both pulmonary medicine and cardiothoracic surgery.

The study was also unique in that it required all patients to go through a comprehensive pulmonary rehabilitation program, representing the first time many of the collaborating centers had ever been involved in rehabilitation. It has turned out to be a model for other studies, which in hematology-oncology and other fields are now getting underway. Outcomes in the NETT study were better in patients with upper-lobe disease and low exercise performance. They were distinctly worse in the most severely obstructed patients who had homogeneous disease on computed tomography scan or a very low diffusing capacity, and in fact this group was the one spotlighted in the national press when enrollment of these patients was stopped early. Outcome also was distinctly worse in patients with non-upper-lobe predominance and high exercise performance. For those with upper-lobe predominance and high baseline exercise performance, and for patients with non-upper-lobe predominance and low exercise performance after rehabilitation, the procedure appeared beneficial but the results were not dramatic. How this is going to sort itself out in terms of what the Centers for Medicare and Medicaid Services are going to let us do remains to be seen.

Josh also talked about the possibility of non-surgical lung volume reduction via bronchoscopic volume reduction. This appears to be an effective intervention, at least in sheep, and raises the concept of a future turf war between thoracic surgeons and pulmonologists about who will be doing the lung volume reduction. It certainly would be an advance if patients did not have to undergo a big surgical procedure that, as Josh told us, has a mortality rate of nearly 8 percent right up front in the patients randomized to get the surgery.

Briefly, Josh talked about lung transplantation for COPD. This is the most expensive form of organ transplantation, and it has the worst survival. He presented us with a scheme for at least reasoning out which patients might be the most appropriate ones to consider for transplantation. I think it

is apparent, though, that lung transplantation is not going to be the answer for very many patients.

The discussion after Josh's presentation considered how bold a venture the NETT was for the investigators, for the government, and as John Hansen-Flaschen pointed out, for the patients who participated. It is still undecided, and very important, which patients are going to get funded for LVRS and which centers are going to do the procedure. If nothing else, the NETT study was very good press for pulmonary rehabilitation. I think rehabilitation programs everywhere will ultimately benefit from it.

Emerging and Future Drugs for COPD

Neil MacIntyre addressed the broad and fast-moving topic of emerging and future drugs for treating COPD.²¹ He devoted considerable attention to tiotropium, the long-acting, once-a-day anticholinergic agent that is administered as an aerosol and that 2 large randomized, controlled trials have now shown to be highly effective. Tiotropium may also hold promise for combination use, either with another bronchodilator or with an anti-inflammatory agent. It is unclear why it is taking so long to get this drug approved by the United States Food and Drug Administration, since its safety profile seems highly favorable and it is widely available elsewhere in the world.

The R,R isomer of the long-acting β_2 agonist formoterol was discussed. This agent is of interest but is not as far along as tiotropium in terms of potential clinical use. Neil mentioned some new phosphodiesterase inhibitors that might have future application in COPD, and also vasodilators, including nitric oxide. Anti-inflammation agents such as retinoic acid are also receiving attention as possible therapeutic agents for COPD. At this point, retinoic acid appears to be good if you're a rat and a lab technician has given you emphysema; it is unclear whether the drug could be helpful in humans, but the Feasibility of Retinoic Acid Treatment in Emphysema (FORTE) trial, currently ongoing, may begin to answer that question.

In Neil's discussion the importance of inflammation once again came up with respect to its importance to the development of new drugs. Our resident curmudgeon asked whether treatment should be denied to patients who will not, cannot, or at least *do* not, stop smoking. Responses were mixed.

The Role of Noninvasive Ventilation in COPD

Nick Hill addressed the topic of noninvasive positive-pressure ventilation (NPPV) for COPD.²² This increasingly important therapy can be considered in 2 contexts: in the management of acute respiratory failure, and as a long-term, elective treatment for clinically stable patients with severe disease. By far the best evidence is available for the

acute applications, and most of Nick's discussion was directed there. He explained the compelling rationale for NPPV in COPD exacerbations and emphasized that we now have a very large, very consistent, very strong database supporting NPPV, which should now be the standard of care for severe exacerbations. However, he pointed out that clinicians also have to know which patients are most likely to benefit from it, and especially which patients are inappropriate candidates because of the probability of therapeutic failure and serious complications.

Though the benefit of NPPV in acute-on-chronic ventilatory failure caused by a COPD exacerbation is established, its value in other clinical settings has been less clear. It appears that it can be efficacious in COPD patients with pneumonia. It appears to be helpful in patients with acute respiratory failure following lung resection. For NPPV as a bridge to weaning—that is, extubation to full- or part-time support via mask before the patient is able to be liberated from ventilatory support—the data are a little less compelling, but use in that context has promise. In patients who have failed extubation it seems a little less promising, in that extubation failure frequently happens because the patient is still too sick for weaning and has reasons why invasive ventilatory support should be continued. Data are also accumulating on what happens to patients who decline intubation for life-threatening respiratory failure but agree to noninvasive ventilatory support. A surprisingly large proportion of such patients do well and survive to hospital discharge.

The role of the RT was emphasized as crucial to the success or failure of NPPV in the acutely ill patient. Nick also talked about barriers to effective utilization, of which, unfortunately, the most prominent appears to be lack of motivation and knowledge on the part of physicians about this therapeutic modality.

In stable COPD patients it remains unclear whether we should be resting the respiratory muscles part of the time with NPPV. Studies to date have limitations and their findings are contradictory. Ventilatory support during sleep, especially for patients with very severe disease and nighttime hypoxemia, seems logical, but the evidence is lacking. Here we are reminded of the overlap syndrome and the high prevalence of other sleep disorders among COPD patients.

In the discussion after Nick's presentation, John Hansen-Flaschen reminded us of something he discussed in a previous Journal Conference, on palliative respiratory care.²³ This is what John has called patient-centered mechanical ventilation, which recognizes the importance of including the patient's experience on the ventilator as a constant, ongoing variable for us to follow during mechanical ventilation. John made a plea for including the question, "Are you short of breath right now?" in protocols and regimens for managing patients on ventilators.

There was discussion about where patients receiving NPPV for COPD exacerbations should be managed, whether in the intensive care unit, on a regular ward, or in a special respiratory ward. This will depend on the practice setting and local health care culture, but it is an important issue. We talked about NPPV as a potential way to relieve suffering in terminal care. The discussants had mixed opinions, and we concluded that it could qualify as palliative care but not necessarily so.

Palliative Care for COPD Patients

The final presentation of the conference, by John Hansen-Flaschen, was on palliative and terminal care for COPD patients.²⁴ This subject needs more emphasis in managing a disease that, after all, will eventually result in or contribute to the patient's death. John defined palliative care as *symptom relief and counseling in the shadow of death*. He discussed the components of a good death, which have been better described in recent literature than in the past. He talked about how important it is for us to anticipate death, and to help our patients and their families to do so as well. He stressed how important it is to give the patient and family an honest prognosis, and also how hard this is to do, illustrating the different patterns of functional decline before death in various diseases and the difficulties in knowing exactly how much longer a patient will live. He emphasized the importance of developing a plan for what to do when death finally comes to the COPD patient, and he discussed the primacy of the relief of dyspnea, pointing out how poorly we do with drug therapy for this. Whether this is a limitation of the drugs we have or a problem with our use of the drugs is not entirely clear. John made a plea that we use hospice more; our patients are eligible for hospice but it is grossly underused.

This whole discussion about death and dying is uncomfortable for most people. It's uncomfortable for many caregivers, and it's certainly uncomfortable for patients and families, although also usually gratefully received by them as well as by practitioners. John did a splendid job of emphasizing these things.

In the discussion after John's presentation Paul Enright suggested that we encourage our patients who have severe COPD to go out and get married, because it has been shown that people who are married have better long-term survival than unmarried people. John Hansen-Flaschen brought us back to reality by saying that that finding is an indicator of what an enormous burden the care and management of end-stage COPD is and how people who live by themselves without a spouse or other person to help are just unable to cope as well.

The role of the RT in palliative care was mentioned. We have had an entire previous Journal Conference relating to palliative care,²⁵ and the therapist's role in palliative care

is important in the acute care hospital, the intensive care unit, and in hospice care, although it is incompletely recognized or fulfilled at the present time. This is not through any fault of RTs, but rather a fault of the system.

Some Editorial Comments and Concluding Remarks

I would like to add some observations and opinions in concluding this conference summary. As I reviewed the notes I scribbled during the conference, several unifying themes emerged. We have learned a great deal about COPD and its management, and we have heard about a number of new treatments that may substantially expand our capabilities for helping people with this disease. However, we have also identified important barriers that keep us from realizing the full benefit of present knowledge and could prevent future therapies from being of real value to patients. Increased understanding and new approaches are good, but there is a big gap between knowing what should be done and actually getting it done. Getting it done better and for more patients is the big challenge, not only to those of us at the conference, but also to everyone with a stake in COPD—from governments and health care systems to professional organizations, to individual clinicians, to the patients themselves.

The gap between what we are capable of and actual patient benefit is related to a dichotomy in COPD management—something I call “the easy stuff versus the hard stuff.” The “easy stuff” is readily available within our health care system (though typically expensive): easy for physicians to prescribe and relatively easy for patients to do. Prescription drugs are the most obvious example, illustrated by the fact that most patients with severe COPD are on at least 4 or 5 medications. This “easy stuff” may or may not actually benefit patients in ways they can appreciate. The “hard stuff” typically requires more work on the part of the physician and others in the system, and also a lot of patient commitment and effort. Examples of this are smoking cessation, pulmonary rehabilitation, and collaborative patient self-management.²⁶ Unfortunately, in general the most important interventions we have in terms of improvements in quality of life and other outcomes fall in this latter category. It is a fact of human nature that we gravitate to what is convenient and that behavioral change is very difficult. I believe this goes a long way toward explaining the gaps between what we know and what we do, between what could potentially be done to benefit patients and what actually happens.

I do not want to end on a discouraging note. We have made enormous progress in understanding COPD and developing promising therapies. Recognition of the barriers we face in managing COPD more effectively helps to direct our efforts and should stimulate us as we face the challenges they pose. Bonnie Fahy's repeated challenge

during the conference that we keep the patient squarely in the middle of our discussions helps to point the way. We have better tools than ever before. Increasingly, research in COPD is being conducted in the context of evidence-based medicine.²⁷ A recent article by Deborah Cook emphasizes this and admonishes us to remember that the bottom line is not the evidence but the improved patient care that can be achieved through its use.²⁸

This conference has brought together a diverse and stimulating group of investigators and clinicians with broad expertise and a dedication to improving the care of COPD patients. I believe it has succeeded in its goals, and that the documents developed from it will prove valuable to clinicians who deal with COPD and their patients who suffer from this disease. The conference co-chairs and the American Respiratory Care Foundation have done a superb job in facilitating the process, and it has been an honor and a privilege for me—as well as a challenge—to bring it to a conclusion.

REFERENCES

- Pierson DJ. The RESPIRATORY CARE journal conferences: 20 years of excellence and innovation. *Respir Care* 2002;47(3):238–246.
- Mannino DM. Chronic obstructive pulmonary disease: definition and epidemiology. *Respir Care* 2003;48(12):1185–1191.
- Snider GL. Nosology for our day: its application to chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2003;167(5):678–683.
- Enright PL, Kaminsky D. Strategies for screening for chronic obstructive pulmonary disease. *Respir Care* 2003;48(12):1194–1201.
- Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. *Respir Care* 2000;45(5):513–530.
- Wedzicha JA, Donaldson GC. Exacerbations of chronic obstructive pulmonary disease. *Respir Care* 2003;48(12):1204–1213.
- Stoller JK. Key current clinical issues in alpha-1 antitrypsin deficiency. *Respir Care* 2003;48(12):1216–1221.
- Dirksen A, Dijkman JH, Madsen F, Stoel B, Hutchison DCS, Ulrik CS, et al. A randomized clinical trial of alpha(1)-antitrypsin augmentation therapy. *Am J Respir Crit Care Med* 1999;160(5 Pt 2):1468–1472.
- Make BJ. Chronic obstructive pulmonary disease: developing comprehensive management. *Respir Care* 2003;48(12):1225–1234.
- Marlow S, Stoller JK. Smoking cessation. *Respir Care* 2003;48(12):1238–1254.
- Fiore MC, Bailey WC, Cohen SJ, et al. Treating tobacco use and dependence. Clinical Practice Guideline. Rockville, MD: U. S. Department of Health and Human Services. Public Health Service. Jun 2000.
- Fiore MC. US public health service clinical practice guideline: treating tobacco use and dependence. *Respir Care* 2000;45(10):1200–1262.
- Anthonisen NR, Connett JE, Murray RP. Smoking and lung function of Lung Health Study participants after 11 years. *Am J Respir Crit Care Med* 2002;166(5):675–679.
- Heffner JE, Ellis R. The guideline approach to chronic obstructive pulmonary disease: how effective? *Respir Care* 2003;48(12):1257–1266.
- Fahy BF. Pulmonary rehabilitation for chronic obstructive pulmonary disease: a scientific and political agenda. *Respir Care* 2004;49(1):28–36.
- Fabbri LM, Hurd SS, for the GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of COPD: 2003 update (editorial). *Eur Respir J* 2003;22(1):1–2.
- Fishman A, Martinez F, Naunheim K, Piantadosi S, Wise R, Ries A, et al; National Emphysema Treatment Trial Research Group. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. *N Engl J Med* 2003;348(21):2059–2073.
- Gay PC. chronic obstructive pulmonary disease and sleep. *Respir Care* 2004;49(1):39–51.
- Flenley DC. Sleep in chronic obstructive lung disease. *Clin Chest Medicine* 1985;6(4):651–661
- Benditt JO. Surgical therapies for chronic obstructive pulmonary disease. *Respir Care* 2004;49(1):53–61.
- MacIntyre NR. Chronic obstructive pulmonary disease: emerging medical therapies. *Respir Care* 2004;49(1):64–69.
- Hill NS. Noninvasive positive pressure ventilation for chronic obstructive pulmonary disease. *Respir Care* 2004;49(1):72–87.
- Hansen-Flaschen JH. Dyspnea in the ventilated patient: a call for patient-centered mechanical ventilation. *Respir Care* 2000;45(12):1460–1464.
- Hansen-Flaschen J. Chronic obstructive pulmonary disease: the last year of life. *Respir Care* 2004;49(1):90–97.
- Palliative respiratory care. *Respir Care* 2000;45(11):1318–1410, and 2000;45(12):1460–1540.
- Make BJ. Collaborative self-management strategies for patients with respiratory disease. *Respir Care* 1994;39(5):566–579.
- Evidence-based medicine in respiratory care. *Respir Care* 2001;46(11):1200–1303, and 2001;46(12):1368–1449.
- Cook DJ. Moving toward evidence-based practice. *Respir Care* 2003;49(9):859–868.