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A M E R I C A N C O L L E G E O F
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Toward a Consensus Definition for COPD Exacerbations*

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In patients with COPD, an acute worsening of respiratory symptoms is often described as an exacerbation. Exacerbations are associated with a significant increase in mortality, hospitalization, and health-care utilization, but there is currently no widely accepted definition of what constitutes an exacerbation of COPD. This paper summarizes the discussions of the workshop, "COPD: Working Towards a Greater Understanding," in which the participants proposed the following working definition of an exacerbation of COPD: a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD.

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Key words: COPD; definition; exacerbation

Abbreviation: ATS = American Thoracic Society

Acute exacerbations occur commonly in patients with COPD.^{1,2} Exacerbations may cause specific signs and symptoms, such as increased dyspnea, productive cough with altered sputum, and fever. Alternatively, the symptoms may be more nonspecific, such as malaise, fatigue, insomnia or sleepiness, and depression. Although such exacerbations are associated with impaired lung function, it is estimated that only 50% of all exacerbations are reported to physicians.²

Owing to the associated morbidity and mortality, health-care utilization is usually significantly increased during an exacerbation. A prospective study performed in the United States in 1995, involving 1,016 adults admitted to hospital for an exacerbation of COPD with a $\text{PaCO}_2 \geq 50$ mm Hg,¹ found the median length of hospital stay was 9 days (range, 5 to 15 days). In this cohort, the median cost of stay was \$7,100 (interquartile range, \$4,100 to \$16,000), and within the following 6 months, there were 754 hospital readmissions (in 446 patients).

Despite the fact that exacerbations of COPD represent a significant burden on patient welfare and on health-care resources, no complete, clear, or standardized definition of an exacerbation currently exists. Following the 1999 Aspen Lung Conference dedicated to COPD, a working group of respiratory

physicians from the United States and Europe was convened to discuss a common operational definition that could be presented to international health-care providers and all groups involved in respiratory care. The aim of this first meeting was to provide a starting point—to provoke discussion and interest in this important health-care issue—that will lead ultimately to a consensus definition of a COPD exacerbation.

The group fully recognizes that, in time, as technology advances and the understanding of the pathophysiologic mechanisms involved in COPD improves, this proposed definition will evolve. If one looks to the field of cardiology in the mid-1960s, a myocardial infarction was arbitrarily diagnosed on the basis of two of three criteria (characteristic chest pain, ST-segment elevation, or increased lactate dehydrogenase levels). By the standards of today, this is a primitive definition for a myocardial infarction; at the time, however, it was considered a useful and important first step.

THE NEED FOR A STANDARDIZED DEFINITION OF COPD EXACERBATIONS

While there is currently no general agreement on the definition for a COPD exacerbation, a standardized definition could provide benefits to patients, researchers, physicians, and other health-care providers.

For example, a standard definition will help patients to determine when they should approach their

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primary-care physician or visit the emergency department, and it will guide physicians with respect to appropriate pharmacotherapy and/or other interventions. An agreed definition will help in the design of consistent clinical trials, and allow the results to be evaluated and standardized from a common viewpoint. A standard definition will also allow a more accurate determination of the cost of COPD, and provide a benchmark for determining the health economic benefit of therapeutic interventions.

Although the purpose of the definition will influence the terminology used, *ie*, depending on whether it is directed to patients or health-care providers, any agreed definition needs to be sufficiently general so that it does not limit those who need to use it. The definition also needs to be flexible in order to allow a more detailed subclassification system based on the severity of the exacerbation.

Difficulties in Achieving a Consensus Definition

The 1995 American Thoracic Society (ATS) statement recognized that an acute exacerbation of COPD is difficult to define and that its pathogenesis is poorly understood.³ It is not surprising, therefore, that various organizations, societies, and investigators have created their own individual definitions. The difficulties in obtaining a standard definition for an exacerbation stem from two main issues: fluctuation of symptoms and the role of comorbid conditions.

Each patient with COPD experiences a fluctuation in symptoms in lung function and a general feeling of well-being; these can change from one day to the next. When defining an exacerbation, it is necessary to pinpoint when the decline in any of the continuous measures is worse than expected, taking into account day-to-day variability (Fig 1). Furthermore, the etiology and pathophysiology of COPD exacerbations are heterogeneous, and can underlie a diversity of observed signs and symptoms.

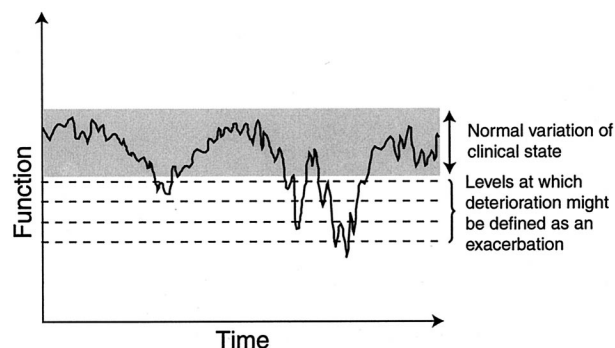


FIGURE 1. Day-to-day variability of a patient with COPD

Comorbid conditions can be a confusing factor when assessing exacerbations, as they can often cause respiratory symptoms in their own right, and influence the relationship between COPD and health-related quality of life.⁴ Among the list of potential common “causes” of acute exacerbations provided by the European Respiratory Society⁵ are pneumonia, heart failure, and pulmonary embolism. Such comorbid pathology can doubtless provoke COPD exacerbations, but might be better described as “triggers.” Physicians need to discriminate between the COPD exacerbation and any associated underlying diseases.

In 1987, Anthonisen and colleagues⁶ investigated whether antibiotic therapy could have a beneficial effect in the management of COPD exacerbations. They defined exacerbations specifically in terms of increased dyspnea, sputum production, and sputum purulence: signs indicative of an infectious etiology. However, exacerbations of COPD comprise a range of symptoms, and the presence or absence of increased sputum production or purulence provides only part of the picture. In such a study, certain patients showing other hallmark signs of an exacerbation would be excluded, which serves to demonstrate how an all-encompassing, standardized definition is essential to assessing the impact of clinical research.

WORKING GROUP DEFINITION

The objective of the workshop was to reach a common definition for COPD exacerbations that would initiate a dialogue between interested parties, and ultimately lead to a globally accepted consensus definition. The definition reached by the group was as follows: *a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD.* The rationale behind each component of this operational definition is provided below.

The *sustained* aspect of the definition provides some information on the time frame of the exacerbation. Usually, sustained implies a patient's condition to be worsened for at least 24 h. However, severe worsening of a patient's condition over a shorter period of time should not limit the definition. Indeed, some patients can present with acute shortness of breath, increased sputum production and purulence, and respiratory failure within a matter of hours. Such patients should also be considered to have an acute exacerbation of COPD.

The terminology, *worsening of the patient's condition*, is relatively imprecise because of the absence of established clinical markers, signs, or symptoms that can be used to predict confidently the presence or absence of an exacerbation. The British Thoracic Society⁷ noted that in a patient with an exacerbation of their underlying COPD, important symptoms that might be observed include increased sputum purulence and/or volume, increased dyspnea and/or wheeze, chest tightness, and fluid retention. Other, more general markers can be used to characterize an exacerbation, and Table 1 presents the clinical descriptors that should always be evaluated when an exacerbation is suspected. However, it can be beneficial to look for other signs and symptoms, such as the breathing pattern.

The definition acknowledges that a patient's *stable state* may fluctuate, and therefore includes the wording, *beyond normal day-to-day variations*. Furthermore, the definition demands that the worsening of the patient's condition should be *acute in onset*. This component recognizes the fact that COPD is a progressive disease and that, with time, a gradual decrease in a patient's overall status will occur.

Finally, the definition requires that the change in condition *necessitates a change in regular medication*. Implicit here is that the exacerbation does not respond to a short-acting β_2 -agonist bronchodilator. However, this has not been included in the definition in order to avoid the implication that bronchoconstriction has an important role to play in the underlying pathophysiology.

STAGING COPD EXACERBATIONS

Owing to the generalized nature of the definition presented above, some type of subclassification will be necessary to improve its practical utility. The most obvious staging system might relate to the severity of the exacerbation, and Table 2 shows a proposed system based on the utilization of health-care resources by patients with mild, moderate, or severe exacerbations. However, the ultimate purpose of the

Table 1—Clinical Descriptors Used To Characterize Acute COPD Exacerbations

Category	Descriptor
Respiratory	Increased shortness of breath
	Increased volume and purulence of sputum
	Increased cough
	Shallow/rapid breathing
Systemic	Increased body temperature
	Increased pulse/heart rate
	Impaired mental status

Table 2—Staging of a COPD Exacerbation Based on Health-Care Utilization*

Severity	Level of Health-Care Utilization
Mild	Patient has an increased need for medication, which he/she can manage in own normal environment
Moderate	Patient has an increased need for medication and feels the need to seek additional medical assistance
Severe	Patient/caregiver recognizes obvious and/or rapid deterioration in condition, requiring hospitalization

*It is also crucial to note the severity of the underlying COPD, any comorbid conditions, and the frequency of exacerbations.

definition will influence those parameters considered most appropriate on which to base the subclassification.

Classification of an exacerbation is strongly related to the underlying severity of the patient's condition. For example, in a patient with severe COPD, a small change in function may appear as a moderate-to-severe exacerbation because it necessitates physician intervention. On the other hand, in a patient with mild disease, a large change in function may only appear mild if the exacerbation does not impact sufficiently on the patient's functional capacity to seek medical attention. It is important, therefore, to note the severity of the underlying COPD alongside the severity of the exacerbation.

The physician should also be aware of the importance of recording the number of exacerbations experienced by the patient with COPD. If a patient experiences four or more exacerbations in a single year, his/her condition should be considered more serious than that of a patient who only experiences two or three.

Any underlying comorbid conditions should also be noted as these may often impact on the presentation of the patient. In patients with heart failure, for example, increased fluid retention can result in increased dyspnea, independent of the patient's COPD.

Working Group Recommendations

Recognizing the difficulties involved in reaching a universally agreed definition for COPD exacerbations, but also the important need for the medical community to have a standardized definition, the following statement is proposed as the first step in the process.

- COPD exacerbation: a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, necessitating a change in regular medication in a patient with underlying COPD.

Additionally, a generalized subclassification of exacerbations based on health-care utilization is proposed.

- Mild: patient has an increased need for medication, which he/she can manage in his/her own normal environment.
- Moderate: patient has an increased need for medication, and he/she feels the need to seek additional medical assistance.
- Severe: patient/caregiver recognizes obvious and/or rapid deterioration in condition, requiring hospitalization.

The current level of understanding relating to COPD exacerbations does not allow a more scientific staging system at this point in time. As more insight is gained into the pathophysiology and etiology of exacerbations, it may be possible to include further categorization, and thus provide more detail to the severity staging. However, further work cannot progress in the absence of a consensus definition for a COPD exacerbation itself. This operational definition is submitted for debate.

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