Asthma: What is in a Word?

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The words we apply to diseases of the airways of the lungs are well established and include asthma, COPD, bronchitis, chronic bronchitis, emphysema and bronchiectasis. However, while the meaning of some of these is clear, such as chronic bronchitis, emphysema and bronchiectasis (1,2), there is disagreement and confusion of others and especially of asthma. Asthma means different things to different people. To some it is a syndrome (3). To some it is a disease entity (4). To others it refers to a specific disorder of airway function (5,6). Some say asthma cannot be defined (7) and others that we should stop using the word (8-11). This disagreement is understandable but can it be resolved? We think it can.

Figure 1. Relation of symptoms to physiological and inflammatory components of asthma. Symptoms are non-specific and can also result from other respiratory and non-respiratory conditions.
Referring to asthma as a syndrome is a misunderstanding of the word “syndrome” and is easily discarded. A syndrome refers to “a group of concomitant symptoms of a disease” (12). It is the most primitive of defining characteristics of a disease (5,6). Symptoms are nonspecific (Figure 1). They can be due to different respiratory and non-respiratory conditions as well as different components of airway disease. They can also be insensitive. We can do better than to define asthma as a syndrome unless we live somewhere in the world where objective measurements are unavailable.

The primary reason for misunderstanding the meaning of asthma is that the condition is heterogeneous and there is no unifying cause (13). The heterogeneity is evident from different clinical, physiological, inflammatory and other pathological components, and genetic or environmental causes of these. The relation of the components to one another is known (Figure 1) but, with the exception of variable airflow limitation over short periods of time and airway hyper-responsiveness, they correlate poorly at best. Hence, reliance on symptoms without measurements frequently leads to misdiagnosis and mistreatment (14,15). Measurements of spirometry, airway responsiveness and airway inflammation are needed to understand what abnormalities are present and the appropriate treatment of these (8-10,13,16). Spirometry identifies the presence and severity of airflow limitation, and any reversibility after inhalation of a rapid acting beta-agonist. Measurement of airway responsiveness to methacholine is the most sensitive test to demonstrate abnormally variable airflow limitation and is especially required when this is suspected from symptoms but spirometry is normal. Hence, it is particularly required in mild disease which is more prevalent in primary patient care practice. The cellular inflammation in the airways is most comprehensively measured at present in spontaneous or induced sputum by quantitative non-squamous cell counts (13,17). These measurements are particularly useful in severe disease which is difficult to control, has frequent exacerbations, requires high dose corticosteroid treatment or is complicated by other non-airway respiratory or non-respiratory conditions. The cell counts, apart from identifying the presence and severity of inflammation, demonstrate different types, specifically eosinophilic, neutrophilic, or both of these which result from different causes (Table 1). These causes are common, can vary from one time to another and contribute to the heterogeneity of airway disease. The cell counts are not diagnostic of a specific airway disease but identify the inflammatory component associated with it. The causes of inflammation can also result in other pathological abnormalities such as bronchiectasis or emphysema.
Without a unifying cause for what we recognize as asthma, the main source of confusion with defining asthma arises from whether it is regarded as a disease entity (an essentialist definition) or whether it refers to the presence of a component within the disease by which the disease can be recognized (a nominalist definition) (5,6). At present, the former is most popular as illustrated by the GINA definition (4) which states “Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper-responsiveness which leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night and in the early morning. These episodes are usually associated with widespread but variable airflow obstruction within the lung, that is reversible spontaneously or with treatment”. This definition is a description of the components of the disease. It does not identify how the disease is recognized. It cannot be a disease entity without a unifying cause. The definition goes on to say that “Because there is no clear definition of the asthma phenotype…” Hence, it is no wonder that there is confusion about the meaning of asthma and why some say that asthma cannot be defined (7). The essentialist definition has no place in science (6). The components of disease could also be better stated. Specifically, while airway inflammation is common, evidence that it is always a chronic inflammatory disease needs validation. Also, sputum production may be present as an important symptom. While many cells play a part, eosinophils are worthy of emphasis because they are most often increased in patients with asthma and because, when they are increased, they predict clinical benefit from corticosteroid treatment.

The criticisms of the GINA definition are overcome with a nominalist definition which defines a disease as “the sum of the abnormal phenomena displayed by a group of living organisms in association with a specific common characteristic or set of characteristics by which they differ from the norm for their species in such a way as to place them at a biological disadvantage” (5). This definition takes into consideration the heterogeneity of components and causes of asthma and other airway diseases and highlights the deficiency of the essentialist definition, which is
that it provides no specific characteristic by which the disease is recognized. Such a characteristic, in ascending order, can be symptoms and physical signs (the worst), abnormal physiology, pathology or cause (the best). In the absence of a unifying cause or pathology, the best recognizing characteristic of asthma at present is a specific abnormality of airway function. As such the word asthma refers to “a disease characterized by wide variations over short periods of time in resistance to flow in intrapulmonary airways.” This type of variable airflow limitation can be demonstrated by significant improvement in spirometry after rapid-acting bronchodilator (for example, salbutamol reversibility of FEV1), or by significant spontaneous variation in airflow during the day (as with diurnal variation of peak expiratory flow), or by an increase in ease and magnitude of bronchoconstriction to stimuli acting directly on airway smooth muscle (like inhaled methacholine) or indirectly through release of chemical mediators which then act on the muscle (like exercise) which is known as airway hyper-responsiveness. This variability differs from the variability seen with corticosteroid treatment which can occur when airway hyper-responsiveness is absent (13). This nominalist definition falls in line with the definitions of COPD, which refers to a disease identified by another abnormality of airway function (18), and of emphysema and bronchiectasis which refer to pathology (1,2) (Figure 2). As improvements are made in recognition of disease, the specific characteristic can be improved. Hence bronchitis has been defined clinically by cough and sputum but, with measurement of inflammation, this can be improved to the cellular type of airway inflammation identified by sputum quantitative cell counts (13).

Figure 2. The words used to define airway diseases refer to their specific physiologic abnormalities or pathology (including airway inflammation).
While the word asthma refers to the presence of variable airflow limitation as described here, the disease includes other components with various causes (13). The inflammatory causes can vary from one time to another. Uncommonly, asthma does have a cause. In the individual patient, hypersensitivity to a common allergen or occupational sensitizer can cause an eosinophilic bronchitis with asthma which completely resolves when exposure is avoided (19). In the real world two or more inflammatory causes and components of disease are commonly present. For example, while there might be no other abnormality than variable airflow limitation, asthma is often associated with an eosinophilic bronchitis which is reversed by avoidance of sensitizing allergens or by corticosteroid treatment, and with episodes of infective neutrophilic bronchitis. In adults, and particularly the elderly, the disease might also be associated with COPD in a non-smoker (presumably as a result of uncontrolled eosinophilic bronchitis), or with cigarette smoking or fumes or dusts which can cause chronic bronchitis or COPD, or with bronchiectasis or emphysema, or with other complicating non-respiratory disease. It is also possible that a patient who had asthma in the past (demonstrable variable airflow obstruction) may progress to lose the variability either with the control of airway inflammation or with the development of COPD and therefore not have “current asthma”.

In conclusion if the word asthma refers to disease of the airways of the lungs in which there is a specific abnormality of airway function, we believe that the disagreement over definition can be overcome. Hence, in those with current asthma, variable airflow limitation is demonstrated by salbutamol reversibility, by an increase in diurnal variation or by airway hyperresponsiveness. Measurement of it is required for accurate diagnosis. This definition recognizes that the disease is heterogeneous and has other important components and no unifying cause. The disease presents with symptoms which can include chest tightness, wheeze, dyspnea, cough or sputum but these are not specific for asthma and can be a result of other diseases. In asthma they can be secondary to variable airflow limitation or to airway inflammation (bronchitis) or both. The inflammation can lead to airway hyperresponsiveness or to chronic airflow limitation (COPD). While the inflammation is common, evidence that asthma is always a chronic inflammatory disease is still not established. Of the various cells involved, eosinophils are especially important as a marker of benefit from corticosteroid treatment.

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