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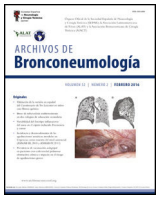

Editorial

The Name of COPD: Semiotics and Precision☆

El nombre de la EPOC: semiótica y precisión

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Stat rosa prístina nomine, nomina nuda tenemus. And what is left of the rose is only its name.

Umberto Eco, in The Name of the Rose.[1]

Is it asthma or COPD? Solving this commonly encountered dilemma can lead us through a maze no less complex than the labyrinthine medieval library of the famous novel of the late author and semiotician, Umberto Eco. Perhaps Professor Eco could have helped us define what we understand as disease, syndrome, overlap, comorbidity, phenotype or endotype. Our intention here is to review these concepts in an attempt to avoid confusion and indiscriminate use.

Pathos, Nosos and Aegritudo

The concept of disease or "morbid species" emerged from a taxonomic tradition that aimed to classify knowledge in all scientific disciplines. Classifications were based on *pathos* and *nosos*, terms referring to the underlying condition of the disease and its manifestation in signs and symptoms,[2] and on etiology, although this was rarely determined. Underlying these attempts is not only the need for "getting as genuine and natural a description, or history of all diseases as can be procured", as Sydenham wrote, but also a "fix'd and complete method of cure thereof".[3] This therapeutic differentiation still leads us in practice to subclassify diseases such as COPD or asthma according to different therapeutic approaches, or to highlight when these diseases overlap, whether with each other or with conditions such as sleep apneas or bronchiectasis, all of which might impact on a patient's clinical management.

The term *aegritudo* complements *pathos* and *nosos*, as a synonym of disease[2] in the sense of the episode as experienced by the patient. The intention of modern medicine, namely, to determine disease from the signs and symptoms observed at the patient's bedside, known as the Oslerian paradigm, appears to give little importance to the impact of personal experience on the disease. Osler said "the good physician treats the disease; the great physician treats the patient who has the disease", thus acknowledging a concept of disease as independent from the patient. Until very recently, personalized medicine was considered an empirical "art".[4]

Subcategories of Disease: From Syndrome to Phenotypes and Endotypes

A syndrome is commonly understood as a set of interrelated signs and symptoms. Since the times of Avicenna, Aristotelian inductive logic has been used to build on this method of grouping postulates to arrive at a diagnosis. At times, the relationship is so clear that the syndrome is identified as the disease, as occurs with genetic disorders, such as Down syndrome or Klinefelter syndrome.

Equally related with *nosos* is the concept of "phenotype", which describes all observable characteristics in an individual, such as morphology, markers or biochemical or physiological behavior. The conventional use of the term "phenotype" derives from Mendelian genetics, understood as the expression of the genotype. More recently, it has been used to describe a distinctive disease profile in a wider "clinical phenotype" sense that, in the case of COPD, represents "those attributes of the disease alone or in combination that describe the differences between individuals with COPD in relation to parameters that have clinical significance".[5,6]

It is interesting to note that selective therapeutic approaches are more focused on the modification of biological processes (*pathos*) than on phenotype. This observation is more apparent in the case of asthma, in which phenotypes are complemented by so-called "pathophenotypes" or "endotypes". A more personalized molecular therapeutic intervention should be possible if the various biological mechanisms that cause a disease are defined.[7] To achieve this, these disease pathways or endotypes must be identified and characterized by "biological markers" that can be either pathognomonic, such as alpha-1 antitrypsin deficit in affected patients, or simply orientative, as is the case for polymorphonuclear neutrophils in the sputum of asthma patients.

Of course, these mechanisms are not exclusive for any single disease, but rather generate associations of entities that in patients are called comorbidity. The "comorbidome" is a graphical representation of all the relationships occurring in a disease.[8] For a disease to be considered comorbid, the association must occur more

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often than by pure chance, and we call this coinciding or overlapping. If defining an entity is difficult, it is even harder to define asthma-COPD overlap syndrome (ACOS), a term used both as a syndrome, due to lack of diagnostic definition, and as a catch-all for all phenotype–endotype intersections of both entities.[9] Only its future use will clarify its meaning.

Personalized, 4P and Precision Medicine

The interaction of genetic, environmental, biological, clinical and even psychological aspects of the pathogenic mechanism affects how diseases present and evolve. Phenotypes and endotypes are simplified terms that allow us to build a concept of personal variability within a disease. The aim of personalized medicine is to convert an empirical approach, understood as an art, into knowledge. The observation that this exhaustive knowledge can be used as a tool for measuring and modifying health risks gave rise to the idea of "4P medicine": predictive, preventive, personalized and participatory. "Precision medicine" should represent the ultimate definition of disease mechanisms, allowing us to intervene with the confidence of an assured outcome.

It may be that this vision of medical science based on ever larger registries of genetic, epigenetic, molecular, experience-based, or therapeutic data predicts a future in which only specific cases are treated, a future in which the concept of disease becomes outdated. Until then, we must depend on the rational tradition represented by Brother William of Baskerville,[1] replica of Conan Doyle's Sherlock Holmes created in turn inspired by his clinical teacher, Joseph Bell. We will continue to use our deductive skills to hunt out the name of the disease as a mainstay for our reasoning and actions. New cohort studies, such as those which expanded the concepts of COPD and asthma, must be undertaken to further investigate the significance of those names. Much research and discussion will be needed if we are to clearly define subtypes worthy of attention, as well as biomarkers and parameters[10] that will be of practical use in opening the door to even more personalized and precise treatments.

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