Interstitial lung disease: Does it matter what we call you, or what you look like, or how you behave?

Interstitial lung diseases (ILD) have over the past 80 years undergone a multitude of changes in naming conventions, clinical descriptions, pathological classifications, and therapeutic approaches.[1,2] Recent publications from the ATS/ERS and additionally, the Fleischner Society, have grouped the diffuse parenchymal lung diseases into various categories based on shared aetiology, histological and/or radiological pattern and associations with exposures or underlying rheumatological diseases.[3] Despite these consensus statements, there remain calls to abandon much of the nomenclature in terms of naming and focus on other aspects and ways of 'cohorting' patients with interstitial lung disease.[4,5]

The priorities for sorting/classifying/grouping ILDs have varied from: 'what to call it' such as CFA or IPF, 'what it looks like' such as UIP or NSIP, and more recently 'how it behaves' such as progressive pulmonary fibrosis. These priorities have been driven by the evolving understanding of pathophysiology, radiology, clinical course, and responses to newer therapies. For example, the big drive away from oral steroids for IPF arose from the Panther trial data,[6] and the focus on IPF treatment with antifibrotics after the INPULSIS, CAPACITY and ASCEND trials.[7-9] More recently the treatment focus has been on 'progressive pulmonary fibrosis'; regardless of original grouping/classification, focussing on 'behaviour' based on results from the INBUILD trial.[10]

Therefore, in answer to the question: "does it matter what we call you, or what you look like, or how you behave?" The answer is yes: The current focus on behaviour is predicated on an understanding of what the underlying disease is and how it generally behaves, or at least predicted to behave. Not all interstitial lung diseases progress at the same rate, even those classified as progressive pulmonary fibrosis. This has significant impact on planning for end-of-life care and planning for lung transplantation. Furthermore, the name we give something has implications[5] – not only for the patient (e.g., life expectancy with a label of IPF or RA-ILD), but also funders who will only pay for certain medications for certain conditions, as well as colleagues (rheumatology, dermatology) who may need to consult and care for the patient. And finally – what you are going to call the 'disease' in your manuscript or research grant proposal.

Athol Wells and colleagues[5] wrote a perspective paper in 2018 on thoughts around changing the name of IPF, and cited arguments from various quarters about why this should or should not happen. One of the key points made (quoting William James) which is relevant to the "name-appearance-or-behaviour" argument, is that 'classifications merely serve the purpose they serve'.[5] IPF or not, equals treatment with an antifibrotic or not; progressive fibrosis or not, equals treatment with nintedanib or not. This dichotomous approach currently runs the risk of distilling a vast array of varying complex clinical entities with varying complex manifestations into a single common pathway of fibrosis or not. This "reductionist" approach to management of respiratory disease is dual-edged. A single inhaler for both asthma and COPD, diseases divided into steroid responsive or not etc. belies the unique and complex nature of each of the conditions. The corollary is that this approach (for ILD) does simplify the treatment choices for clinicians who do not have ready access to surgical lung biopsies and more importantly, multi-disciplinary team (MDT) meetings to settle on diagnoses.

Fibrotic lung diseases have been the focus of several perspective articles in high impact journals given the dramatic responses to antifibrotics in recent trials of so called 'progressive pulmonary fibrosis', which still has no validated diagnostic criteria.[3,10] The temptation therefore, is for the clinician to ignore the 'name' and just focus on the 'behaviour'. Ultimately like the adage 'all bleeding eventually stops', 'most chronic respiratory conditions end with fibrosis' to a degree also holds true. The challenge however, is to differentiate the deterioration induced by active inflammation and that by active fibrosis, to correctly manage the underlying pathogenic process. The alternative is just to 'treat both' which in the era of precision medicine seems a step backwards, which Wuyts, George and colleagues elegantly contextualize in their recent opinion pieces.[11]

What has been given little attention in the current IPF 'name-appearance-or-behaviour' discussions, is the fact that when respiratory failure is imminent, name becomes important. The diagnosis/original label takes on a much greater significance when "slowing progression" has failed or is 'failing': IPF, is known to have a median survival of 3 - 5 years postdiagnosis, CTD-ILD is known to have a less dramatic progression but with systemic/joint complications, and Scleroderma associated-ILD is known to have significant obstacles to lung transplant, despite all potentially being lumped into a 'progressive fibrosis' bucket. Not only does 'What we call you' become of major importance but also 'how we treated you', and not only what are you receiving - an antifibrotic currently based on your recent 'behaviour'. This is particularly of importance in resource-limited settings: the differential cost of oral prednisone compared to an antifibrotic is enormous, HRCT scans are not freely available especially in follow up, and specialist resources such as MDT's are few and far between. Therefore, the temptation to default to oral prednisone, as there is little else to offer needs to be offset with the regulatory/funding fight to gain access to an antifibrotic for a specific patient.

Lung transplantation remains the final potential option in patients with end stage lung disease, is highly dependent on the underlying disease and any complications of treatment: scleroderma patients have specific risks associated with cardiac and oesophageal dysfunction that can impact on outcomes and may even preclude transplant;[12] steroid-induced obesity, diabetes and or osteoporosis from chronic steroids for sarcoidosis or COPD for example can complicate transplant patient care.[13,14] Connective tissue disease-associated ILD may complicate transplant by the nature of the underlying disease and the presence of antibodies increasing risk of rejection.[15,16]

It is therefore critical to 'label' our patients correctly, both for their acute management strategy, but also for their long-term management strategy. Thankfully the days of high dose steroids for IPF are over, but steroids are commonly used in many other interstitial lung diseases

such as sarcoid, NSIP, COP etc. – to very good effect, and only when intolerant or ineffective, are changes to other modalities of therapy considered. Not that any immunomodulatory /immunosuppressive therapy is without risk, managing the acute illness often rightly or wrongly takes precedence over managing the chronic. Steroid-induced diabetes/osteoporosis no matter how you look at it – has long term implications, especially for lung transplantation.

Our goal as clinicians must be to keep the 'name-appearance-behaviour' conundrum in balance as we care for patients with complex lung disease, varied underlying aetiologies and options for long term therapy. In low-resourced settings particularly, labelling takes on a different guise, as access to antifibrotics 'for all' is simply not an option and making difficult choices to not treat (with oral steroids), is challenging.

Focusing only on the behaviour belies the importance of the underlying condition both in the short and long term. Focusing only on the appearance may reassure us or blind us from a progressive behaviour. It may even cause us to persist with toxic and damaging therapy. Focusing only on label misses the point that there is a patient behind the FVC and that we at best slow down the progression, and when there is no FVC left, a person with a name remains.

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