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Breathlessness despite optimal pathophysiological treatment: on the relevance or not of being chronic.

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Title

Breathlessness despite optimal pathophysiological treatment: on the relevance or not of being chronic.

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1 In the May 2017 issue of the *European Respiratory Journal* (ERJ), Johnson et al. [1]
2 propose the term "chronic breathlessness syndrome" to describe the clinical situation in
3 which "*breathlessness persists despite optimal treatment of the underlying pathophysiology*
4 *and results in disability of the patient*". The term "disability" in this definition corresponds to
5 "*physical limitations and/or a variety of adverse psychosocial, spiritual, or other*
6 *consequences*", which very closely matches the World Health Organisation definition of
7 "disability" [2]. Of note, the relationship between breathlessness and disability has been well
8 captured in the foreword of a document published in 2013 by the Forum of International
9 Respiratory Societies [3], of which the first sentence reads: "*When we are healthy, we take*
10 *our breathing for granted [...]. But when our lung health is impaired, nothing else but our*
11 *breathing really matters*". This sentence has become the "catch phrase" of the French lung
12 health foundation ("Fondation du Souffle", <http://www.lesouffle.org>). Of note also, the explicit
13 definition of "*chronic breathlessness*" as proposed by Johnson et al. is not very different from
14 the implicit definition of "refractory breathlessness", the term previously used in many
15 studies, and which has already been proposed as a distinct entity by some of the authors of
16 the ERJ May perspective article [4]. Johnson et al. [1] submit that defining and naming this
17 new syndrome will improve the visibility to a distressing and debilitating condition that is too
18 often overlooked and neglected [5]. They postulate that this enhanced visibility will result in
19 improved care and organisation of care, stronger research [6], and greater empowerment by
20 patients and their caregivers. The editorial by Prof. Meting Basoglu published in the same
21 issue of the ERJ [7] throws new light on this notion of empowerment. Making a daring but
22 fascinating parallel between untreated dyspnoea and torture, Prof. Basoglu reminds us how
23 and why addressing dyspnoea in general (and probably "chronic breathlessness" in
24 particular) is a fundamental issue not only from the point of view of medicine *per se*, but also
25 from the point of view of human rights [on this, see also 8]. He also makes a very convincing
26 case for the importance of empowerment in the management of dyspnoea. Still in the same
27 issue of the ERJ, Prof. Peter Calverley comments on the new syndrome [9] and, like all of us,
28 concurs with Johnson et al. [1] about the relevance of making breathlessness a foremost
29 concern of every clinician.
30

31 In order to contribute to the discussion called for in the article by Johnson et al. [1],
32 we (a French speaking group of physicians with a special interest in dyspnoea) would like to
33 make a few comments about this article and the accompanying editorial by Prof. Calverley
34 [9]. These comments mostly pertain to the choice of words that has been made to name the
35 new syndrome. In no way should they be interpreted as an expression of disagreement with
36 the proposed approach and its aims: some of the authors of the present letter participated in
37 the 2016 Dyspnea symposium during which the "chronic breathlessness" discussion was
38 finalised (CMP, DA, EA, CC, PL, LL, CP, TS), and one of the authors of the article by
39 Johnson et al. [1] is also a co-author of this letter (TS). Our letter should be taken as a mere
40 illustration of the fact that differences of opinions always exist within consensus, and also as
41 a substantiation of the dynamical nature of the syndrome naming process that is put forward
42 by Johnson et al. [1].
43
44

45 The first of our comments concerns the choice of "breathlessness" rather than
46 "dyspnoea" in the name of the syndrome. Since "dyspnoea" is widely used in the medical
47 literature and in medical practice, it would be useful to clarify whether or not "chronic
48 breathlessness syndrome" and "chronic dyspnoea syndrome" can be used interchangeably,
49 and if not, to explain why. This is an important issue particularly for non-native English
50 speakers. The answer to this question can have a significant impact on translations of the
51 name of the new syndrome in other languages.
52

53 The second comment pertains to the use of the term "optimal treatment" in the
54 definition of the syndrome, which can be ambiguous. We understand that, in this context,
55 "optimal" means "maximal", or "state-of-the art", but this may not be exactly the same thing:
56 in some conditions characterised by a marked irreversible component such as COPD or
57 pulmonary fibrosis, maximal therapy can fail to provide optimal results both physiologically
58 and, obviously, symptomatically. Beyond semantics, we feel that it is extremely important not
59 to label a patient as suffering from "chronic breathlessness" before being sure that everything
60

1 has been done to correct the underlying pathophysiological condition, as failure to do so
2 would be associated with a risk of depriving the patient of effective interventions in the
3 present or in the future. For example, if "optimal" treatment of an underlying condition exists
4 but is not available for a given patient at a given time, or if the patient refuses this treatment
5 for any reason, the use of nonspecific symptomatic treatment to alleviate dyspnoea would be
6 valid and in fact essential [as clearly reminded in the editorial of Prof. Basoglu, see 7]. Yet,
7 the definition of "chronic breathlessness" would not be met, and placing such patients under
8 the "chronic breathlessness" umbrella would carry the risk of "forgetting" that "optimal
9 treatment" has not been applied and should be undertaken as soon as it becomes possible.
10

11 The third comment pertains to the choice of the term "syndrome" itself. In his editorial
12 [9], Prof. Calverley challenges this choice and seems to suggest that "syndrome" should only
13 be used to identify a *"consistent group of patients"* with *"a likely primary condition"*. Another
14 reason to challenge the term "syndrome" is related to its very definition as *"a group of signs
15 and symptoms that occur together and characterize a particular abnormality or condition"*.
16 This definition is directly derived from the Greek etymology of the word, which means
17 "running together" and thereby implies a combination of items. Since "chronic breathlessness
18 syndrome" apparently comprises only one symptom, dyspnoea, use of the term "syndrome"
19 may be deemed inappropriate. However, the clinical situations covered by "chronic
20 breathlessness syndrome" actually share much more than dyspnoea, as they also have in
21 common the multiple deleterious consequences of this symptom (e.g. psychological, social,
22 etc.). The term "syndrome" may therefore be very appropriate, particularly to attribute a
23 consistency to otherwise inconsistent groups of patients. This seems to be exactly what has
24 been achieved with "chronic pain syndrome". "Chronic breathlessness syndrome" has the
25 advantage of defining a common basis for the care of patients with a variety of diseases and
26 disorders, but who are "unified" (as should their caregivers be) by breathlessness, or, more
27 generally, "respiratory suffering". It suggests that all respiratory physicians (and beyond that
28 all physicians caring for patients with dyspnoegenic diseases, and there are many of them...)
29 should be familiar with the principles of dyspnoea management in addition to the
30 management of the underlying disease (of note, this notion is explicitly stated in the 2017
31 edition of the GOLD statement, indicating that *"all clinicians managing patients with COPD
32 should be aware of the effectiveness of palliative approaches to symptom control and use
33 these in their practice"*)[10]. Using "symptom" instead of "syndrome" (or omitting
34 "syndrome"), as suggested by Prof. Calverley [9], would carry the risk of neglecting the
35 multidimensional and pervasive nature of dyspnoea [11-15]. The process initiated by
36 Johnson et al. [1] is designed to convince caregivers — and others — that the care of
37 dyspnoea cannot be limited to the treatment of the symptom, but should address its
38 behavioural and socio-psychological consequences. Consequently, we believe that
39 "syndrome" is an appropriate term, as it gives a holistic dimension to the management of
40 dyspnoea.
41

42 The fourth of our comments, and in fact the most important one, concerns the term
43 "chronic" in the name of the new syndrome. This choice emerged from a Delphi process,
44 which gives it validity. However, the study could have been biased by the composition of the
45 group of experts, which did not include many physicians involved in acute care [1]. If one of
46 the goals of creating the new syndrome is to "give consistency and visibility to inconsistent
47 and invisible groups of patients" (see above), we believe that the word "chronic" could well
48 be counterproductive in a number of cases, as it would deprive many patients of a significant
49 conceptual progress. Indeed, all of the words used to describe "chronic breathlessness" in
50 the article by Johnson et al. [1] can apply, word for word, to many clinical situations involving
51 acute rather than chronic dyspnoea. For example, all patients hospitalised with severe acute
52 exacerbations of COPD remain dyspnoeic at rest despite oxygen, bronchodilators and
53 corticosteroids, with the corresponding lack of control emphasized by Prof. Basoglu [7], and
54 shrunken lives. This description exactly fits the definition of the syndrome proposed by
55 Johnson et al. [1] except regarding the time frame. Although this is not standard practice at
56 the moment, these patients could, or more precisely should, be considered for dyspnoea-
57 oriented treatments in addition to pathophysiology-oriented treatments. Even more striking in
58 terms of the temporal dynamics of dyspnoea, critically ill patients receiving mechanical
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1 ventilation often complain of breathlessness [16]. After dealing with the various technical
2 aspects involved, including optimisation of inappropriate ventilator settings, many of these
3 patients remain breathless [16], a situation strongly suspected to contribute to the
4 development of post-traumatic stress syndrome [17]. It will be impossible to convince the
5 intensivists in charge of such patients that they suffer from "chronic breathlessness", even
6 though relief of dyspnoea in this setting is a fundamental clinical mission [18, 19]. We believe
7 that persistence of dyspnoea despite maximal pathophysiological treatment of an acute
8 condition is not a fatality and is not more acceptable than it is in the context of a chronic
9 condition. We therefore also believe that the principles governing the therapeutic approach to
10 acute breathlessness should be exactly the same as the those governing the therapeutic
11 approach to chronic breathlessness. Following are examples of clinical questions that can be
12 formulated to support this contention, such as "*should noninvasive ventilation be considered
13 in COPD patients during severe acute exacerbations despite complete normalisation of blood
14 gases in response to conventional treatment, in order to alleviate dyspnoea?*"; "*should we
15 design trials of short-term low-dose opioids in addition to pathophysiological treatment in
16 severe exacerbations of COPD?*"; "*should we re-think the management of opioids during
17 mechanical ventilation with a dyspnoea paradigm in mind?*"; "*should the concept of
18 "integrated breathlessness service", as developed in supportive care [20, 21], be transposed
19 to the ICU?*"; "*is there any reason to think that empathy, education, and cognitive therapies
20 would not be effective if "breathlessness that persists despite treatment" is acute rather than
21 chronic?*" and so on.... With this in mind, we are afraid that "chronic breathlessness
22 syndrome" could be a misnomer because it would "miss" many "non-chronic" but nonetheless
23 clinically relevant situations. Johnson et al. [1] and Prof. Calverley in his editorial [9] briefly
24 refer to this issue, but perhaps they do not attribute sufficient importance to what could
25 possibly be seen as a major gap by many practitioners. The name "persistent
26 breathlessness" would have avoided this problem, because it would have covered all acute
27 and chronic situations. "Persistent breathlessness" (or "resistant" breathlessness", or any
28 other "time neutral" term) would also have had the advantage of clarifying the discourse in
29 certain cases, possibly with some added teaching value. Let's take an example: "*Dear
30 Colleague, I am referring to you this patient with chronic obstructive pulmonary disease who
31 has been treated with dual bronchodilation and inhaled corticosteroids since last year, and
32 who presents with chronic breathlessness*". It could take quite a long time for this sentence to
33 be readily understood by a majority of practitioners. In contrast, "*Dear Colleague, I am
34 referring to you this patient with COPD who has been treated with dual bronchodilation and
35 inhaled corticosteroids since last year because she complains of persistent breathlessness?*"
36 is probably more readily understandable and "teachable" (without the negative connotation of
37 "refractory" that contributed to go from "refractory" to "chronic" during the Delphi process
38 elaborated by Johnson et al. [1]).

40 All physicians dealing with dyspnoeic patients must have the same objective, namely
41 to alleviate dyspnoea by all means, combining "pathophysiological" and "syndrome-based"
42 strategies, irrespective of the time-frame involved. We suggest that this general goal would
43 be more effectively promoted by the term "persistent breathlessness syndrome" than by
44 "chronic breathlessness syndrome" and we therefore advocate an evolution in this direction.
45 Polling the ERJ readership could perhaps provide useful information on this subject.
46

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