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EDITORIAL

Velcro crackles: the key for early diagnosis of idiopathic pulmonary fibrosis?

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Idiopathic pulmonary fibrosis (IPF), affecting individuals mostly aged 60–70 yrs, is the most common and the most severe of idiopathic interstitial pneumonias, with a median survival of only 3 yrs. The incidence and mortality of IPF has risen dramatically in the last decade [1]. Furthermore, IPF is one of the most challenging diseases for therapy developments, due to its complex and unresolved pathogenic processes, the possible inadequate drug diffusion in fibrotic lungs, and difficulties in designing clinical trials [2]. Up until now, no treatment could prevent the relentless progression of IPF to end-stage lung and ensuing death. However, drug therapy in IPF has recently regained hope with the publication of clinical trials using pirfenidone or the triple tyrosine kinase inhibitor BIBF 1120 that demonstrated an effect in limiting the decline in lung function [3–5].

Given these therapeutic advances, diagnosing IPF at an earlier stage becomes a relevant healthcare issue. Indeed, pirfenidone has been approved in Japan and in the European Union, and is indicated in mild-to-moderate IPF, which in the absence of a consensus definition may correspond to patients with forced vital capacity (FVC) >50% predicted and diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$) >35% pred (*i.e.* pulmonary function inclusion criteria for the recent phase III pirfenidone trials) [3]. Similarly, in a phase II study, BIBF 1120 has demonstrated a trend toward a reduction in lung function decline in patients with FVC >50% pred and $D_{L,CO}$ >30% pred [4], and is currently evaluated in a phase III study (clinical trial identifier number NCT01335464). The criteria chosen for these trials [3–5] are consistent with the postulate that therapy may more likely demonstrate efficacy in patients with the least advanced disease.

However, the diagnosis of IPF at an early stage remains a challenge by itself. In a recent study [6], the delay between first symptoms and referral to an IPF centre was 2.2 yrs, similar to other rare (orphan) lung diseases [7]. Reasons for such delay may include patient-dependent factors (*e.g.* reluctance to acknowledge symptoms that may herald health problems and a sedentary lifestyle masking dyspnoea at exercise), disease-dependent factors (*e.g.* progressive onset and slow progression of IPF allows the disease to go undetected unless exacerbations occur), and physician-dependent factors (*e.g.* lack of awareness of rare diseases by general practitioners and even by lung specialists). It cannot be ignored anymore that a longer delay in accessing a tertiary care centre is associated with a higher risk of death independent of the severity of IPF [6].

How, then, can the diagnosis of IPF be made earlier? The present authors suggest that the assessment of velcro crackles by lung auscultation is currently the only realistic means for the earlier diagnosis of IPF.

Patients with chronic cough or dyspnoea expect their doctors to proceed to lung and heart auscultation, which has been routine practice since the invention of the stethoscope by René Théophile Hyacinthe Laennec in 1816. In his treatise De l'Auscultation Médiate ou Traité du Diagnostic des Maladies des Poumons et du Cœur [8], Laennec defined and characterised different sounds, especially ''crepitant rales'' (crepitations). The variety of normal and adventitious (*e.g.* not normally occurring) breath sounds has been standardised. Crackles (often referred to as crepitations in the UK and as rales in the USA), best detected during slow, deep breaths [9], are discontinuous, short explosive non-musical sounds predominating during inspiration and best heard over dependent lung regions [10, 11] and sometimes associated with expiratory crackles [12]. They are considered to be produced by the sudden opening of abnormally closed small airways [12, 13]. According to the American Thoracic Society nomenclature, fine crackles are softer, shorter in duration and higher in pitch than coarse crackles [11]. Similar to the sound heard when gently separating the joined strip of velcro on the blood pressure cuff (or jogging shoes), fine crackles have been coined ''velcro'' rales by DINES and DEREMEE [14] from the French words velours (velvet) and crochet (hook) [15].

Fine crackles at auscultation are easily recognised by clinicians and are characteristic of IPF [16]. In a study of 272 cases with diffuse parenchymal lung disease documented by lung biopsy, bilateral fine crackles were heard in 60% of those with interstitial pneumonia including those with a pathological diagnosis of usual interstitial pneumonia (the pathological hallmark of IPF), and in only 20% of those with sarcoidosis and other granulomatoses [17]. Crackles are present early in the course of IPF, appearing first in the basal areas of the lung where the disease process initiates, with further progression to the upper zones. Although not specifically studied according to the stage of IPF, crackles may be present in virtually any patient with IPF according to current diagnostic criteria [18]. They are an early sign of pulmonary impairment in asbestosis [17, 19], a condition that shares close similarities with IPF

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(including the first appearance of crackles in the lung basal areas [19]). In asbestosis, crackles are present before abnormalities are detected by chest radiograph [20], and are thus useful for screening populations exposed to asbestos [21]. The agreement between observers regarding crackles is sufficiently good to monitor asbestos-exposed workers for crackles [22]. The presence of crackles, together with dyspnoea or gas exchange abnormalities, may indicate interstitial lung disease even if the chest radiograph is normal [17, 23]. Crackles are also present in the majority of patients with idiopathic nonspecific interstitial pneumonia [24], a condition that affects individuals younger by about 10 yrs than those with IPF [25], and in pulmonary fibrosis associated with connective tissue disease.

As crackles are not specific for IPF, they must prompt a thorough diagnostic process. They may occasionally be heard in healthy individuals, especially elderly persons breathing at rest [26], over the anterior chest [27, 28], because of closure of small airways in dependent areas of the lungs; however these usually disappear after several deep breaths. Follow-up of asymptomatic subjects with crackles can also reveal occurrence of congestive heart failure [26]. Crackles may also be heard occasionally in patients with chronic obstructive pulmonary disease or bronchiectasis, probably due to greater traction forces being exerted on the small airways. However, crackles in IPF are heard throughout the entire inspiratory time [29, 30]. Adventitious sounds associated with heart failure and pneumonia are higher in frequency and quite distinct from fine crackles of IPF [15, 31], and rales are present in only one in four patients with left heart congestion due to systolic heart failure [32].

Until a prospective, modern study can re-appraise the genuine value of lung auscultation for the diagnosis of IPF according to current guidelines [18, 33], we consider that the identification of fine crackles has an excellent sensitivity and good specificity for the disease process of pulmonary fibrosis and thus advocate that lung auscultation is valuable in diagnosing earlier IPF. Pulmonologists should educate students and general physicians to recognise the characteristic sound of fine velcro crackles and be aware of their diagnostic relevance. If present throughout the inspiratory time and persisting after several deep breaths, and if remaining present on several occasions several weeks apart in a subject aged $\geqslant$60 yrs, bilateral fine crackles should raise the suspicion of IPF and should lead to consideration of a chest radiograph and/or high resolution computed tomography of the chest (more sensitive than the chest radiograph, which may falsely reassure the patient). It is time that the stethoscope draped around the neck of physicians, which tends to be used for identification purposes rather than for medical diagnosis, be also the (presently only) genuine tool for an earlier diagnosis of IPF, the prerequisite for earlier treatment, and maybe for improvement of the long-term clinical outcome of this dreadful disease.

STATEMENT OF INTEREST

Statements of interest for both authors can be found at www.erj.ersjournals.com/site/misc/statements.xhtml

REFERENCES

1 Olson AL, Swigris JJ, Lezotte DC, *et al.* Mortality from pulmonary fibrosis increased in the United States from 1992 to 2003. *Am J Respir Crit Care Med* 2007; 176: 277–284.
2 Nathan SD, du Bois RM. Idiopathic pulmonary fibrosis trials: recommendations for the jury. *Eur Respir J* 2011; 38: 1002–1004.
3 Noble PW, Albera C, Bradford WZ, *et al.* Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomised trials. *Lancet* 2011; 377: 1760–1769.
4 Richeldi L, Costabel U, Selman M, *et al.* Efficacy of a tyrosine kinase inhibitor in idiopathic pulmonary fibrosis. *N Engl J Med* 2011; 365: 1079–1087.
5 Taniguchi H, Ebina M, Kondoh Y, *et al.* Pirfenidone in idiopathic pulmonary fibrosis. *Eur Respir J* 2010; 35: 821–829.
6 Lamas DJ, Kawut SM, Bagiella E, *et al.* Delayed access and survival in idiopathic pulmonary fibrosis: a cohort study. *Am J Respir Crit Care Med* 2011; 184: 842–847.
7 Brown LM, Chen H, Halpern S, *et al.* Delay in recognition of pulmonary arterial hypertension: factors identified from the REVEAL Registry. *Chest* 2011; 140: 19–26.
8 Laennec RTH. De l'Auscultation Médiate ou Traité du Diagnostic des Maladies des Poumons et du Cœur fondé principalement sur ce nouveau moyen d'exploration. [Of the Mediate Auscultation or a Treatise of the Diagnosis of Diseases of the Lungs and Heart based mainly on this new means of exploration.] Paris, Brosson JA et Chaudé JS, 1819.
9 Kiyokawa H, Greenberg M, Shirota K, *et al.* Auditory detection of simulated crackles in breath sounds. *Chest* 2001; 119: 1886–1892.
10 Forgacs P. Crackles and wheezes. *Lancet 1967 22*, 2: 203–205.
11 Schraufnagel DE, Murray JF. History and physical examination. *In*: Mason RJ, Broaddus VC, Martin TR, *et al.*, eds. Murray and Nadel's Textbook of Respiratory Medicine. 5th Edn. Elsevier Saunders, 2010; pp. 349–367.
12 Vyshedskiy A, Alhashem RM, Paciej R, *et al.* Mechanism of inspiratory and expiratory crackles. *Chest* 2009; 135: 156–164.
13 Forgacs P. The functional basis of pulmonary sounds. *Chest* 1978; 73: 399–405.
14 Dines DE, DeRemee RA. Meaningful clues and physical signs in chest disease. *Mod Treat* 1970; 7: 821–839.
15 DeRemee RA. Clinical Profiles of Diffuse Interstitial Pulmonary Disease. New York, Futura Publishing Company, Inc, 1990.
16 Baughman RP, Shipley RT, Loudon RG, *et al.* Crackles in interstitial lung disease. Comparison of sarcoidosis and fibrosing alveolitis. *Chest* 1991; 100: 96–101.
17 Epler GR, Carrington CB, Gaensler EA. Crackles (rales) in the interstitial pulmonary diseases. *Chest* 1978; 73: 333–339.
18 Raghu G, Collard HR, Egan JJ, *et al.* An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011; 183: 788–824.
19 al Jarad N, Strickland B, Bothamley G, *et al.* Diagnosis of asbestosis by a time expanded wave form analysis, auscultation and high resolution computed tomography: a comparative study. *Thorax* 1993; 48: 347–353.
20 Shirai F, Kudoh S, Shibuya A, *et al.* Crackles in asbestos workers: auscultation and lung sound analysis. *Br J Dis Chest* 1981; 75: 386–396.
21 Murphy RL Jr, Gaensler EA, Holford SK, *et al.* Crackles in the early detection of asbestosis. *Am Rev Respir Dis* 1984; 129: 375–379.
22 Workum P, DelBono EA, Holford SK, *et al.* Observer agreement, chest auscultation, and crackles in asbestos-exposed workers. *Chest* 1986; 89: 27–29.
23 Epler GR, McCoud TC, Gaensler EA, *et al.* Normal chest roentgenograms in chronic diffuse infiltrative lung disease. *N Engl J Med* 1978; 298: 934–939.
24 Flaherty KR, Martinez FJ. Nonspecific interstitial pneumonia. *Semin Respir Crit Care Med* 2006; 27: 652–658.
25 Fell CD, Martinez FJ, Liu LX, *et al.* Clinical predictors of a diagnosis of idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2010; 181: 832–837.

26 Kataoka H, Matsuno O. Age-related pulmonary crackles (rales) in asymptomatic cardiovascular patients. *Ann Fam Med* 2008; 6: 239–245.

27 Thacker RE, Kraman SS. The prevalence of auscultatory crackles in subjects without lung disease. *Chest* 1982; 81: 672–674.

28 Workum P, Holford SK, Delbono EA, *et al.* The prevalence and character of crackles (rales) in young women without significant lung disease. *Am Rev Respir Dis* 1982; 126: 921–923.

29 Piirila P, Sovijarvi AR, Kaisla T, *et al.* Crackles in patients with fibrosing alveolitis, bronchiectasis, COPD, and heart failure. *Chest* 1991; 99: 1076–1083.

30 Dalmasso F, Guarene MM, Spagnolo R, *et al.* A computer system for timing and acoustical analysis of crackles: a study in cryptogenic fibrosing alveolitis. *Bull Eur Physiopathol Respir* 1984; 20: 139–144.

31 Vyshedskiy A, Bezares F, Paciej R, *et al.* Transmission of crackles in patients with interstitial pulmonary fibrosis, congestive heart failure, and pneumonia. *Chest* 2005; 128: 1468–1474.

32 Damy T, Kallvikbacka-Bennett A, Zhang J, *et al.* Does the physical examination still have a role in patients with suspected heart failure? *Eur J Heart Fail* 2011; 13: 1340–1348.

33 Raghu G. Idiopathic pulmonary fibrosis: guidelines for diagnosis and clinical management have advanced from consensus-based in 2000 to evidence-based in 2011. *Eur Respir J* 2011; 37: 743–746.