PLEASE, take a deep breath

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Combining history taking and a bedside ultrasound may be the best way to predict symptomatic relief after thoracentesis in patients with pleural effusions http://bit.ly/2xwTJ9z

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Dyspnoea, a subjective experience of breathing discomfort, is a debilitating symptom which impacts quality of life in patients with pleural effusions. It consists of a number of perceptions, including a sense of work/effort, tightness in the chest and air hunger. Dyspnoea affects up to 80% of patients with malignant pleurisy [1–3], and an even higher percentage of those with heart failure-associated effusions [4]. Pleural effusions can have a large impact, not only on breathing and quality of life [5], but also on sleep [6] and exercise capacity [7].

The general mechanisms of dyspnoea are complex, involving many parts of the respiratory system: central control (motor and sensory brain cortex, brain stem), afferent signals (carotid and aortic chemoreceptors; upper airways, lung, chest wall and diaphragmatic mechanoreceptors) and efferent pathways (nerves to respiratory muscles and respiratory muscles themselves). Factors contributing to dyspnoea in conditions such as COPD, asthma, interstitial lung disease, obesity, pulmonary arterial hypertension and heart failure, have been sufficiently addressed in the medical literature [8]. However, the pathophysiology of dyspnoea in the context of pleural effusions has attracted less attention and still remains insufficiently understood.

What has been traditionally taught is that the presence of dyspnoea usually depends on the size of the effusion, the patient's underlying cardiopulmonary reserve and, plausibly, the coexistence of anaemia (whether inflammatory or secondary to chemotherapy). Consequently, dyspnoea may be caused by a large effusion in a patient with normal lungs, a moderate effusion along with an underlying heart or lung disease, or a small effusion with accompanying severe cardiopulmonary disease. Likewise, many physicians deprive patients of the potential benefits of a therapeutic thoracentesis in the belief that just a small or moderate effusion detected by an imaging test (often an insensitive chest radiograph) cannot justify the patient's shortness of breath. Finally, the increase in the volume of the lung (which collapsed to compensate for the presence of pleural fluid) following a thoracentesis has been the most conventional explanation for post-procedural symptomatic improvement, thus attributing a key role to compressive atelectasis in dyspnoea pathogenesis.

In this issue of the *European Respiratory Journal*, Muruganandan *et al.* [9] challenge the preceding assumptions. Under the PLEASE (Pleural Effusion And Symptom Evaluation) study, for the first time, both a prospective and extensive evaluation of the factors contributing to effusion-related dyspnoea was carried out. The investigation was conducted in 145 patients with symptomatic pleural effusions who underwent pre- and post (24–36 h)-therapeutic thoracentesis evaluation of various parameters, including oxygenation, lung function, functional exercise capacity, diaphragmatic mechanics and measurement of

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breathlessness using a number of validated assessment tools. Several findings of clinical and pathophysiological interest were described. First, patients with moderate to large pleural effusions commonly have normal oxygen saturation levels by pulse oximetry (95% pre-drainage values in the current study), unless a severe underlying lung disease coincides. Accordingly, pulse oximetry should not drive drainage decisions in this population. Second, the intensity of dyspnoea (evaluated through a simple visual analogue scale (VAS)) rather than the radiological size of the effusion was the most powerful indicator of the convenience of draining fluid (likelihood ratio negative of 0.21). Patients whose breathing significantly improved after a therapeutic thoracentesis (defined as a change in VAS >14 mm) had mean pre-procedural baseline VAS scores of 38 mm in a scale of 0 to 100 mm, wherein 0 mm means the worst possible breathlessness and 100 mm no breathlessness at all. The small impact that the quantity of fluid removed had on dyspnoea improvement could be explained by the large-volume aspirations which were generally performed (median of 1.68 L, interquartile range 1.1–2.6 L). In this way, another study of 58 lower volume effusion removals (range 200 to 1500 mL) did find a correlation between VAS improvement and the amount of fluid drained [10]. Third, symptom relief after thoracentesis occurred regardless of the presence of an unexpandable lung, a condition which characterised 21% of the study population [9] and has been reported in about one-third of malignant effusions elsewhere [11]. Therefore, clinicians must reject the old vision that patients with unexpandable lungs will surely not derive symptom benefits from fluid aspiration. Lastly, the study of Muruganandan *et al.* [9] gives insight into the principal mechanisms by which pleural fluid accumulation produces breathlessness and thoracentesis alleviates it [9]. Diaphragmatic abnormalities, instead of mechanical lung compression, appear to be critical in causing dyspnoea in subjects with pleural effusions. The presence of fluid in the pleural cavity can profoundly affect the inspiratory function of the diaphragm and provoke a caudal displacement (flattening or inversion) which leads to a decrease in the force-generating capacity of this primary muscle. In addition, the diaphragmatic contraction is not able to efficiently expand the lung, since pleural fluid lies in between. Ultimately, diaphragmatic dysfunction may seriously impact on respiratory system mechanics. A reduced or abnormal diaphragmatic movement was noted in about 70% of patients [9], a feature which independently anticipated a symptomatic amelioration as a result of thoracentesis. However, even though diaphragmatic dysfunction contributes to dyspnoea pathogenesis in pleural effusions, there must be other factors as well [3], since 27% of all participants and 25% of those with abnormal diaphragmatic movements did not experience significant relief after thoracentesis [9]. In a recent prospective study, Skaarup *et al.* [12] measured dyspnoea, using a modified Borg scale, and the ultrasonographic movement of the hemidiaphragm before and immediately after a thoracentesis in 32 patients for whom a mean of 1283 mL of pleural fluid was removed. The modified Borg scale decreased from 5.6 to 2.6 ($p<0.0001$) after the thoracentesis. Simultaneously, the hemidiaphragmatic movement, quantified through the area method, increased from 7.4 cm^2 to 26 cm^2. Interestingly, like in the study of Murunagandan *et al.* [9], patients who did not experience improvement of dyspnoea following fluid removal (15.6%) were those with lower pre-thoracentesis modified Borg scores (*i.e.* the less symptomatic ones) [12].

In summary, based on this pivotal study by Murunagandan *et al.* [9], consideration should be given to performing a therapeutic thoracentesis, if technically feasible, in patients with pleural effusions who are symptomatic enough and have no other obvious extrapleural explanations for their shortness of breath, no matter what the radiological size of the effusion is. The ultrasonographic evaluation of the hemidiaphragm movement, preferably in a quantitative manner [13], may help to predict which patients will satisfactorily respond to fluid aspiration. Once again, coupling medical history (*i.e.* degree of dyspnoea) with physical examination (*i.e.* taking a deep breath while diaphragmatic movement is being assessed using point-of-care ultrasound) [14] may represent the simplest criteria for making a clinical decision.

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References

1 Valdés L, San-José E, Ferreiro L, *et al.* Combining clinical and analytical parameters improves prediction of malignant pleural effusion. *Lung* 2013; 191: 633–643.
2 Tanrikulu AC, Abakay A, Kaplan MA, *et al.* A clinical, radiographic and laboratory evaluation of prognostic factors in 363 patients with malignant pleural mesothelioma. *Respiration* 2010; 80: 480–487.
3 Nieder C, Kämpe TA, Engljähringer K. Does patient-reported dyspnea reflect thoracic disease characteristics in patients with incurable cancer? *Anticancer Res* 2018; 38: 901–904.
4 Nazemiyeh M, Dorraji A, Nouri-Vaskeh M, *et al.* Congestive heart failure is the leading cause of pleural effusion in the north-west of Iran. *J Cardiovasc Thorac Res* 2019; 11: 244–247.
5 Sivakumar P, Saigal A, Ahmed L. Quality of life after interventions for malignant pleural effusions: a systematic review. *BMJ Support Palliat Care* 2020; 10: 45–54.
6 Marcondes BF, Vargas F, Paschoal FH, *et al.* Sleep in patients with large pleural effusion: impact of thoracentesis. *Sleep Breath* 2012; 16: 483–489.

7 Cartaxo AM, Vargas FS, Salge JM, *et al.* Improvements in the 6-min walk test and spirometry following thoracentesis for symptomatic pleural effusions. *Chest* 2011; 139: 1424–1429.
8 Laveneziana P. Dyspnea. *In:* Palange P, Rohde G, eds. ERS Handbook of Respiratory Medicine. 3rd Edn. Sheffield, European Respiratory Society, 2019; pp. 97–107.
9 Muruganandan S, Azzopardi M, Thomas R, *et al.* The Pleural Effusion And Symptom Evaluation (PLEASE) study of breathlessness in patients with a symptomatic pleural effusion. *Eur Respir J* 2020; 55: 1900980.
10 Psallidas I, Yousuf A, Talwar A, *et al.* Assessment of patient-reported outcome measures in pleural interventions. *BMJ Open Respir Res* 2017; 4: e000171.
11 Porcel JM, Torres M, Pardina M, *et al.* Predictors of indwelling pleural catheter removal and infection: a single-center experience with 336 procedures. *J Bronchology Interv Pulmonol* 2020; 27: 86–94.
12 Skaarup SH, Lonni S, Quadri F, *et al.* Ultrasound evaluation of hemidiaphragm function following thoracentesis: a study on mechanisms of dyspnea related to pleural effusion. *J Bronchology Interv Pulmonol* 2019; in press
13 Aguilera Garcia Y, Palkar A, Koenig SJ, *et al.* Assessment of diaphragm function and pleural pressures during thoracentesis. *Chest* 2020; 157: 205–211.
14 Porcel JM. Time to embrace POCUS as part of the bedside diagnosis of respiratory diseases. *Respirology* 2019; in press [https://doi.org/10.1111/resp.13692].