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Reply to Hallifax *et al.*: From Recommendations to Implementation: Also a Multidisciplinary Matter

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From the Authors:

Randomized controlled studies provide the highest level of evidence. The results of these studies, when available, help feed, qualify, and determine the strength of the proposed recommendations of the clinical practice guidelines.

We designed the EXPRED (exsufflation of primary spontaneous pneumothorax versus chest tube drainage) study with this aim, and to date, this study represents the largest randomized study comparing simple aspiration versus standard thoracic drainage in first-line treatment of patients with first episodes of complete, primary pneumothorax (1). These results help inform and guide good practice recommendations for primary spontaneous pneumothorax. The study was performed in 31 emergency departments in France. During study conception, and during the course of the management and follow-up of the patients, we had to make a trade-off between rigor and flexibility: rigor because the study was randomized and controlled, and its inclusion criteria were strictly defined, and flexibility because the inclusion of patients in emergency departments remains a challenge, the overcrowded conditions making it difficult to conduct randomized controlled trials, sometimes contrary to the habits of care. Thus, the decision to keep patients for a longer or shorter time in the hospital after their inclusion in the EXPRED study was left to the discretion of the team at each center. This may explain the relatively high length of hospitalization in the aspiration arm. Moreover, a study of practice in France by Kepka and colleagues revealed that even in the absence of any procedure to evacuate intrapleural air, almost all patients remain under hospital surveillance (2).

One of the current and future difficulties is the application of the recommendations at the patient's bedside. Many obstacles exist; the most frequently identified are awareness, familiarity, agreement, self-efficacy, outcome expectancy, ability to overcome the inertia of previous practice, and absence of external barriers to enacting

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suggest manual aspiration via a three-way tap, as undertaken by the majority of studies included in Cochrane analyses (5), and there is no recommendation for early initiation of suction.

Recent studies suggest a conservative approach for minimally symptomatic patients regardless of size, and there are advocates of nonintervention as standard (2). Although we agree that minimally symptomatic patients can be treated conservatively regardless of the size of the pneumothorax (as was advocated in the BTS 2010 guidelines [3]), we believe that symptomatic patients who opt for treatment should still be offered aspiration or insertion of a device containing a Heimlich valve to allow ambulatory management (6), if suitable care pathways are established in that institution. This will be the premise of the upcoming BTS 2023 guidelines. Two upcoming trials in the United Kingdom will answer the questions of: 1) whether conservative management of symptomatic patients with PSP is effective in terms of reducing the number of subsequent procedures (NIHR133653); and 2) whether early suction can reduce hospital stay for patients with PSP in the hospital with chest drains (NIHR133787).

We are delighted that the management of pneumothorax is being debated and encourage further research to optimize care. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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What the Placebo Tells Us about Chronic Cough



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To the Editor:

Chronic cough can be a terrible experience, often continuing for months and years. It can prevent school attendance for children and interfere with occupational and social functioning in adults. More than 40% of chronic cough cases seen at specialty cough clinics are refractory to treatment trials or have no identified cause (1). Gefapixant, a P2X4 receptor antagonist, has been the subject of several placebo-controlled trials, including a research letter by Birring and colleagues in this issue of the *Journal* (pp. 1539–1542) (2). The data in that study and a previously published report have shown that the clinical effect of the 45-mg dose of gefapixant was significantly greater in decreasing cough than the placebo (3). However, it is the placebo effect in those studies that may be of greater clinical relevance. Figure 1 in the study by Birring and colleagues illustrates the rapid decrease of cough frequency and severity and improved quality of life with the placebo that closely parallels the results of the gefapixant. Although the effect of gefapixant is statistically significantly greater than placebo, the difference between them may be of less clinical importance than the substantial improvement in cough from placebo seen also in Figure 2 of a previous publication (3).

A substantial decrease in frequency and severity of cough occurs from the placebo, only somewhat less than that seen with the gefapixant. The impressive clinical effect of the placebo appears analogous to the effect of suggestion therapy that, without a pharmacologic agent, results in the cessation of cough in children (4) and adults (5). The placebo appears to provide the patient with the suggestion that the cough will decrease from the medication, just as it does with various modes of suggestion therapy that enable patients to control their habit cough.

The power of the placebo effect has been studied by Professor Ted Kaptchuk of Harvard (6). He writes that intervention without an active drug can stimulate a real physiological response. The placebo effect apparent in the studies of gefapixant (2, 3) should stimulate greater interest in nonpharmacologic approaches to treatment of chronic cough. Suggestion therapy has been shown to have a great effect in hundreds of children with habit cough and in some adults (4). How many adults with unexplained chronic cough have habit cough and could respond to suggestion therapy requires investigation. ■

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recommendations (3). In the design and conduct of the EXPRED study, pulmonologists, surgeons, and emergency physicians were associated and involved. We visited the eligible centers before formal inclusion to identify the preferential management pathway that existed after the emergency visit, either pneumological or surgical. These pathways were respected in the follow-up of the patients in the EXPRED study.

The first French recommendations concerning spontaneous pneumothorax are in press (4). These recommendations are based on consensus among French societies of pneumologists, surgeons, intensivists, and emergency physicians. They define a common reference that will probably contribute to the harmonization of the management of this benign pathology and will lead to privileging ambulatory management by means of minimally invasive suction devices, allowing quick return to patients' homes.

If standard chest drainage continues to be used at many centers, it is also because the patient's point of view is not always the top priority. Indeed, it may seem simpler and less risky at 3 A.M. to set up a chest tube drainage and hospitalize a patient than to use an ambulatory management pathway, especially if the procedure is not well formalized.

The production of national and international recommendations is essential. They must be adopted (and probably partially adapted) at each center by all the specialists involved—pulmonologists, emergency physicians, and surgeons—to guarantee 24/7 compliance with the management algorithms inspired by the recommendations. Setting up this kind of ambulatory management is therefore a multidisciplinary affair and is the *sine qua non* for their effective implementation at the bedside. ■

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