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CORRESPONDENCE

Significance of sputum purulence to guide antibiotic therapy in exacerbations of COPD

To the Editor:

We read with interest the study by SOLER *et al.* [1] evaluating role of sputum purulence as a guide for antibiotic use in hospitalised patients with exacerbations of chronic obstructive pulmonary disease (COPD).

Besides bacteria, viruses and air pollution can also lead to exacerbations of COPD. These episodes are characterised by recruitment of leukocytes (neutrophils, eosinophils, *etc.*), which leads to sputum purulence. The sputum colour/purulence is strongly correlated with markers of bronchial inflammation, like myeloperoxidase (green coloured) and leukocyte elastase present within these inflammatory cells [2], and may not mandate the bacterial presence. Moreover, isolation of bacteria from sputum may represent bronchial colonisation, especially in conditions with co-existent architectural distortion like bronchiectasis.

In the study by SOLER *et al.* [1], sputum purulence was used as a criterion to initiate antibiotics. It would have been more representative if serial sputum examinations (for purulence) were used to decide the duration of antibiotics as well, thus correlating sputum purulence with total antibiotic exposure. In addition, excluding sick and recently treated patients from the study might have decreased the predictive value of sputum purulence as these patients are more likely to suffer from bacterial infections.

Absence of sputum purulence cannot rule out bacterial infection reliably [3]. In fact, comprehensive evaluation of presumptive signs and symptoms (fever, increased breathlessness and increase in sputum volume/purulence) along with relevant haematological investigations and supported by a physician's decision to treat are the major parameters guiding the use of antibiotics. Instead of conducting randomised control trials on sputum purulence, it may be useful if studies are conducted to evaluate new biomarkers of bacterial infectivity with better sensitivity and specificity and correlate them with crude indicators like sputum purulence.

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From the authors:

We thank D. Aggarwal and co-workers for their interest in our recently published paper regarding a sputum purulence-guided strategy of antibiotic treatment in patients with exacerbations of chronic obstructive pulmonary disease (COPD) requiring hospitalisation [1]. Their comments highlight important issues relating to the discrepancies reported in the literature about the relationship between sputum colour and the presence of pathogenic bacteria in the lower respiratory tract.

First, the question of whether isolation of bacteria from the sputum of patients with COPD is or is not directly related to exacerbations is still a subject of controversy. Classically, the Anthonisen criteria (*i.e.* increased dyspnoea, sputum production and sputum purulence) have been considered the most reliable predictors of bacterial infection as a cause of exacerbation [2]. Moreover, the most relevant advance in our ability to predict bacterial involvement in COPD exacerbations was the observation that not all three criteria have the same predictive value. STOCKLEY *et al.* [3], with the aid of colour chart, demonstrated that a change in sputum colour during exacerbations was a sensitive and specific marker for bacterial presence and, more importantly, proved the high accuracy of using mucoid sputum to rule out bacterial infection. These findings have been validated using more specific and sensitive sampling methods such as the protected specimen brush (PSB) in patients with severe COPD exacerbations. In a previously published bronchoscopic study, we found a high concordance between bacterial pathogens in samples retrieved by PSB and sputum sampling [4]. However, it is not feasible to use invasive diagnostic methods in clinical practice, and sputum sampling is still

irreplaceable in the diagnostic approach to lower respiratory tract infections.

By contrast, in our study, no information was collected about viral or mixed infection. Viruses may be isolated in up to 45% of severe COPD exacerbations, either alone or together with bacteria, and are likely to be present with fever, but their role in sputum purulence is unclear.

In addition, we agree with D. Aggarwal and co-workers about the interest of clarifying the association between sputum purulence and total exposure to antibiotics, but our study was not specifically designed for this purpose. Patients who had previously received antibiotics were excluded because this condition could skew the allocation of cases to each group.

Lastly, is known that purulence is strongly related to colour, although this sign can often be quite subjective. In prospective studies, mucoid sputum is usually described as colourless white, and purulence as ranging from pale yellow to dark green. A recently pooled analysis of clinical trials results in acute exacerbations of chronic bronchitis showed sputum colour to be a stronger predictor of pathogenic microorganism presence than other factors, including sputum purulence [5]. The authors found a significant and consistent relationship between purulence and the presence of a pathogenic bacteria in sputum, although it had less predictive value that the colour of the sample.

We previously evaluated the significant association between patient-reported sputum purulence as an exacerbation criterion and the presence of bacteria in the lower respiratory tract. Sputum was defined as ''purulent'' when patients reported a change in the colour of spontaneously expectorated samples within the 72 h prior to admission from uncoloured to yellow-green. Therefore, the findings of present pilot study support the efficacy and safety of the patient-reported purulence to guide antibiotic treatment.

The change in sputum colour in the course of a COPD exacerbation can be used in self-management plans, leading to early antimicrobial therapy that may reduce the reduction of the course of exacerbation and improve outcomes. In addition, avoiding the use of antimicrobials when the sputum is white will reduce inappropriate antibiotic prescribing and help slow down the appearance of bacterial resistance.

An additional finding increased the confidence in such guidance: nonpurulent sputum was significantly associated with a lower systemic inflammatory response as assessed by serum C-reactive protein concentration. Measurements of plasma biomarkers show the promise to increase the reliability of the assessment of the bacterial aetiology of exacerbation, identifying patients who require antimicrobial treatment.

The findings of our study cohort are the basis to perform a randomised placebo-controlled trial using sputum-guided treatment in nonpurulent COPD exacerbations.

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Who and what should we rely on in early diagnosis of idiopathic pulmonary fibrosis?

To the Editor:

In a recent *European Respiratory Journal* editorial, COTTIN and CORDIER [1] ranked velcro crackles among diagnostic clues in early idiopathic pulmonary fibrosis (IPF). We agree that auscultation is essential for early detection of IPF, but physical examinations should be integrated into a more comprehensive diagnostic strategy. This raises a question: who identifies IPF patients, and by what means?

IPF is a cryptogenic form of usual interstitial pneumonia (UIP), which is best confirmed pathologically or, to a lesser extent, by a radiographic UIP pattern [2]. However, the low incidence (two to 29 cases per 100, 000) makes it cost-ineffective to screen for IPF/UIP by computed tomography (CT) in general populations, let alone by lung biopsy [1, 2]. Alternatively, clinical features are more feasible and suggestive of IPF as well. The aggregate of three or more out of four characteristics (age >50 yrs, a gradual