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From the authors:

We read with interest the correspondence by H. Kanamori and co-workers, who reported a “beyond extensively drug-resistant tuberculosis” (XDR-TB) case described in Japan, which makes reference to our recent *European Respiratory Journal* (ERJ) article on the subject [1].

The correspondence is, in our opinion, extremely informative on the “real-life” problems surrounding prevention and clinical management of those dramatic cases we tried to summarise below:

1) Epidemiology and transmission. Although the absolute number of XDR-TB cases is low, their appearance and clustering call for further investigation on how transmission occurs in Japan. This is in line with the recommended policies to reach elimination [2].

2) Clinical history. It was really complicated. The patient underwent previous anti-TB treatment for 13 years, having comorbidities (hypertension, diabetes and chronic pancreatitis) and risk factors (alcohol addiction). During treatment the patient developed intolerance to pyrazinamide and mental instability [3].

3) Clinical management and development of “super-resistance”. The case was initially treated with three drugs (isoniazid, rifampicin and ethambutol), during which the time the clinician in charge was “blind” on drug-susceptibility testing (DST) results. When it was evident that the strain was poly-resistant, a fluoroquinolone was added (levofloxacin), opening the way to the XDR-TB status. Then, other second-line drugs were used, including cycloserine, ethionamide and sultamicillin. When managed at the reference centre, the authors immediately used the new rapid molecular diagnostics to orient their clinical decisions [2].

4) Need for new drugs. DST demonstrated that the strain of *Mycobacterium tuberculosis* was resistant to all the drugs tested (including linezolid) except cycloserine, which, incidentally, was administered previously [4]. The difficulty to interpret DST for cycloserine was correctly discussed by the H. Kanamori and co-workers. Interestingly, capreomycin is not available in Japan. The patient was treated with three drugs (cycloserine, ethionamid and sultamicillin). The importance of having more alternatives available to design a regimen likely to be effective (delamanid and bedaquiline among others), in such complicated cases, is obvious [3, 4].

5) Surgery. The patient, having monolateral cavitations in the left, upper lobe, was proposed for a lobectomy, after careful evaluation of pros and cons, also taking into account the possible post-intervention complications related to diabetes (bronchopleural fistula); however the patient refused.

6) Infection control. The patient remained sputum-smear positive until the new regimen was prescribed and was correctly admitted in a room that was equipped with negative-pressure ventilation.

7) Need for adequate long-term facilities providing palliative care. As is for several of these cases, admission is long, and not necessarily successful, a new vision for long-term care is being advocated by many organisations. The core services to be provided, on top of quality diagnosis and care, are adequate infection control measures, palliative care and comprehensive support of the patient and their families.

We are grateful to the ERJ for hosting such an important debate and for pro-actively promoting quality care for XDR-TB and other difficult-to-treat cases of TB with different initiatives, including the electronic ERS/WHO Consilium [3].



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Prevention and clinical management of real-life problems with beyond-XDR-TB

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Admissions and patterns of mechanical ventilation of critical COPD: an old and common friend, are we still prepared?

To the Editor:

Patients with chronic obstructive pulmonary disease (COPD) admitted to an intensive care unit (ICU) due to an acute exacerbation are still confronted with a substantial hospital mortality rate of 24% and worse clinical outcomes, respectively [1]. About 10% of COPD patients are at high risk for prolonged mechanical ventilation and mortality ranges 55–78% [2]. However, there is a paucity of long-term survival data regarding admissions and patterns of mechanical ventilation of critical COPD patients.

In their study, FUNK *et al.* [3] describe the impact of mechanical ventilation strategies in patients with COPD exacerbations by means of a large epidemiological survey [3]. We consider that this is an important contribution to the knowledge of mechanical ventilation patterns, especially the subdivision into non-invasive ventilation (NIV) and invasive ventilation.

However, some characteristics of this study remained untested that could further consolidate their observations. We believe that some points investigated in this study are of interest that will allow a better understanding in future, especially if the following issues are taken into consideration.

First, the impact of alternatives other than that of NIV and decannulation on shortened and improved weaning from mechanical ventilation has yet to be verified [4, 5]. Additionally, they did not consider common strategies that are based on tracheotomy.

Secondly, poor details on the aetiology of COPD exacerbations and comorbidities are given by the authors as follows: a) the presence of number of comorbidities may be of interest especially in reference to future epidemiology studies; b) physiological abnormalities at admission to ICU and development of non-respiratory organ failure are important predictors of hospital outcome of critically ill patients with acute exacerbation of COPD (AE-COPD); and c) history of previous mechanical ventilation and ICU admissions should have been mentioned [5]. Additionally, the impact of increased age is discussed controversially. It is a known fact that the mortality rate of patients aged ≥ 65 years doubles in 1 year, from 30% to 59% [6, 7]. Unfortunately, the current study lacks a strategy of how to manage this growing demand of elderly patients that need mechanical ventilation in the ICU. Normally, these patients suffer from poor nutritional status and low activities of daily living scores, which may both be further factors relevant to prolonged mechanical ventilation [8].

Thirdly, indications of NIV and IMV have not been clearly analysed. Especially the aspect of a so-called “learning curve” of NIV seems missing [9, 10]. To be specific, the following aspects should be taken into account. a) Predictors of NIV failure: it would be interesting to know the risk for AE-COPD patients of having a second episode of acute respiratory failure after an initial (first 48 h) successful response to NIV. This event is more likely to occur in patients with more severe functional and clinical disease, who are likely to have more complications at time of admission to ICU apart from a very poor in-hospital prognosis [9, 10]. b) Admission source and NIV indications are not well specified in this survey that are commonly of