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From the authors:

It is widely recognised that cases of hypersensitivity pneumonitis (HP) occurring in metalworking fluids (MWFs) workers in the literature tend to be more often described in Europe [1, 2]. In certain cases, difficulty in gaining access to the samples of some companies (related to the reluctance of employers) and the lack of knowledge of MWF-HP can also lead to underdiagnosis. We agree with C.M. Barber and colleagues that this is an important subject that deserves evaluation at the European level and a large-scale prevention policy covering workshop design and the composition of MWF. In France, we are continuing with microbiological evaluation of MWF-HP and have investigated two further large car engine factories and 14 micromechanics companies (STEFI study (*Santé au Travail et Exposition aux Fluides de coupe Industriels*)) since our article was published [3].

C.M. Barber and colleagues evoke the elusive nature of the exact aetiology of MWF-HP whilst noting that, in the UK investigation at the Powertrain UK metalworking site (Birmingham, UK), it was not possible to culture any opportunistic mycobacteria or find any evidence of mycobacterial DNA by PCR of 125 MWF samples [2, 4]. In our series, similarly to a number of US outbreaks, *Mycobacterium immunogenum* has been implicated as the cause of the MWF-HP. Evidence of the causative role of *M. immunogenum* was further strengthened by two animal-model studies published in 2006. These demonstrated that the disease was induced in the mouse by repeated nasal instillation of lysates of *M. immunogenum* or MWF contaminated by *M. immunogenum* [5, 6]. Finally, there are few studies like ours [3] that simultaneously identify both a possible antigen in the MWF and the precipitins. Indeed, it has been emphasised that the demonstration of the presence of precipitin is a major factor in facilitating the diagnosis of HP, even if such precipitins are sometimes also present in exposed asymptomatic people [7].

Regarding the differences in culture efficacy and microbiological identification, for the two new car factories investigated in France, we have again cultured *M. immunogenum* on Müller–Hinton and on Middlebrook 7H10 agars. It should be noted that, in case of intense growth, samples were either serially diluted or decontaminated. Rods morphologically consistent with the genus *Mycobacterium* were identified by amplification of partial *hsp 65* gene and sequenced using the previously described primers Tb11 and Tb12. Our current work (unpublished data; G. Reboux, personal communication) compares three car factories and 14 micromechanics companies. ~30% of samples in the first (n=83 aqueous samples) and second car factory (n=44 aqueous samples) were positive for *M. immunogenum*. In the third factory (n=38 aqueous samples), which had undergone intensive treatment with biocides, only two samples were positive when cultured and none were positive from the micromechanics factories [8]. This shows that the isolation of *M. immunogenum* also depends on the treatment of MWF carried out at the factory.

Our study [3] discussed the threshold value of five arcs to differentiate MWF-HP patients from healthy exposed subjects. For *M. immunogenum* the threshold of discrimination between ill and asymptomatic exposed subjects was fairly high (five arcs). Nevertheless, we agree that a threshold can always be questioned, even if it shows good sensitivity and specificity. Thus, one of the healthy exposed subjects in our series had a value of 12 arcs, which was one of the highest levels in our series. The existence of exposed subjects with precipitins has been known for some time. The level of evaluation that differentiates ill from healthy subjects depends on the immunological techniques used and the use of the antigen to which the subjects have actually been exposed. Our laboratories routinely use a panel of between three and 12 antigens for each profession and set the thresholds per antigen with respect to groups of asymptomatic and ill subjects [9]. Electrosyneresis

on cellulose acetate is very sensitive and enables a variable threshold to be set according to the nature of the antigens [10].

Finally, we agree with the authors that exposure to MWF can induce varied symptoms and respiratory pathologies, such as chronic cough, chronic obstructive pulmonary disease, asthma and bronchial hyperresponsiveness. In our study, we preferred to compare subjects whose phenotype has been precisely described: on the one hand, exposed subjects who had no respiratory symptoms and, on the other hand, exposed ill subjects meeting the criteria of HP. Moreover, it is true that certain patients with asthma or symptoms of bronchitis or COPD can produce precipitins or immunoglobulin G, but at low levels, rarely reaching the thresholds we advocate.

In conclusion, it is true that standardisation of antigens is needed. For this reason, we are currently developing recombinant antigens for farmer's lung and mechanical operators' lung [11]. MWFs are complex microbial environments whose composition changes radically with the vast use of biocides and according to environmental circumstances, and the nature of the oils and the metals that are being treated.

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