Hypersensitivity Pneumonitis Due to Metalworking Fluid Exposures

To the Editor:

We read with interest the recent article by Lacasse et al. (CHEST July 2012), which provided a comprehensive update on hypersensitivity pneumonitis (HP). We would like to comment, however, on the section relating to HP due to metalworking fluid (MWF) exposure and, in addition, highlight the experience in the United Kingdom in this area.1 Our group has recently published a review article summarizing the microbiologic and immunologic findings from all previously published MWF outbreaks.2 We have also investigated a number of MWF-HP outbreaks in the United Kingdom. In the most detailed of these, 17 workers met the case definition for MWF-HP,4 and in 14 of the 17 cases, the diagnosis was confirmed when reviewed by a panel of occupational respiratory disease experts.5 However, none of these workers (including one with a positive specific challenge to used MWFs from this workplace)4 or the other 112 workers tested had IgG precipitin responses to extracts of Mycobacterium immunogenenum, chelonae, or fortuitum. In addition, mycobacteria could not be cultured from any of the 125 MWF samples taken from the workplace, and there was no evidence of mycobacterial DNA identified by polymerase chain reaction. Multiple MWF samples taken from two other workplaces with unrelated outbreaks of MWF-HP (C. M. Barton, MD, unpublished data) similarly showed no evidence of mycobacterial contamination or DNA.

Although the findings in hot-tub lung and from animal studies indicate it may be biologically plausible that opportunistic mycobacteria are also causative in MWF-HP, the human cytokine stimulation studies referred to by Lacasse et al. have not been able to confirm a clear link.6 The presence of IgG to opportunistic mycobacteria is not sufficient to establish causation, because cases of MWF-HP also commonly demonstrate IgG to other bacteria and/or fungi.6 As an example, nine out of 13 of the French cases of MWF-HP also had measurable IgG arcs to Fusarium solani and/or Bacillus simplex, in addition to IgG arcs to M immunogenenum.7

Establishing the true cause is clearly relevant to preventing outbreaks, but it is also vital to inform the metalworking industry about how best to monitor, manage, and design their MWFs. Based on the experience in the United Kingdom, it is clear that outbreaks of HP can also occur in “mycobacteria-free” workplaces, and, therefore, designing MWF systems to resist mycobacterial contamination will not prevent all cases of disease. Given the difficulties in establishing causation, and given the presence of chemical asthmagens in MWF, engineering controls aimed at preventing exposures to mist remain just as important as managing microbial contamination.

In summary, we would like to clarify to the wider respiratory audience that the existing published evidence does not as yet support a simple causative link between HP and opportunistic mycobacteria and emphasize that further research in this area is required.

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REFERENCES


Response

To the Editor:

We thank Dr Barber and colleagues for their very specific comment on the role of nontuberculous mycobacteria in metalworking fluid (MWF) hypersensitivity pneumonitis (HP) that

Links:
- Mycobacterium immunogenenum
- Mycobacterium chelonae
- Mycobacterium fortuitum
followed our broad narrative review of HP in our recent article in CHEST.1 We also read with interest their systematic review of respiratory outbreaks associated with exposure to water-based MWF, to which they refer.2 We noted that eight of the 27 outbreaks included in their review involved patients with HP. Microbial contamination of MWF samples was variable. Mycobacteria were detected in MWF in 12 outbreaks; mycobacteria were also tested but not detected in three others. However, no detail was provided regarding the methods used to detect mycobacteria in MWF.

Although mycobacteria are ubiquitous in aqueous environments, identifying them is particularly difficult. Bacterial culture methods lack sensitivity. Establishing a link between mycobacteria and HP is further complicated by the fact that the immunogenic properties of HP agents do not seem to be linked to their viability, because animal models of HP use dead organisms or whole cell extracts.3,4

Our group developed a DNA extraction method and real-time polymerase chain reaction assay capable of quantifying mycobacterial load in environmental samples using a dual-labeled probe to specifically detect Mycobacterium immunogenenum.5 This method proved more sensitive than DNA extraction alone and standard culture.6 Our group also found that MWFs are more often contaminated by bacteria (mostly Pseudomonas pseudocaligines) than by mycobacteria (M immunogenenum).7 In the same work environment, M immunogenenum was not found in air samples.8 An explanation may be that high-level air contamination with mycobacteria in machining plants is intermittent only and depends on sporadic use of MWF-generating aerosols.

We would certainly agree that HP could occur in mycobacteria-free workplaces. However, that M immunogenenum is related to MWF-HP is more than an attractive hypothesis. M immunogenenum in MWF has been linked to HP outbreaks in several reports.9 Animal models clearly demonstrate that MWFs containing mycobacteria can induce granulomatous lung disease, peribronchiolar lymphocytosis, increased cell concentrations in lavage, and upregulation of several cytokines.4 These findings are consistent with HP. To our knowledge, such a model does not exist with Pseudomonas species or any other bacteria isolated from MWFs.

Contamination of MWFs with mycobacteria is often underestimated because of laboratory methods that lack sensitivity to detect them. We would be pleased to apply the methods we developed in our laboratory to MWF samples from the United Kingdom.

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American College of Chest Physicians Guidelines for Heparin-Induced Thrombocytopenia

A Need for Evidence-Based Assessment of the Baseline Risk of Heparin-induced Thrombocytopenia

To the Editor:

The ninth edition of the American College of Chest Physicians (ACCP) Antithrombotic Therapy and Prevention of Thrombosis Guidelines presented summary recommendations addressing a number of clinical problems in the form of evidence-based clinical practice guidelines. These guidelines advocate a rigorous methodology1 for collating and interpreting data obtained from a comprehensive and systematic literature review. The guidelines are respected worldwide and play an invaluable role in determining medical care and offering physician advice.

The most recent ACCP guidelines were published as a supplementary volume of CHEST (February 2012), which also included an article by Linkins et al2 focusing on the treatment and prevention of heparin-induced thrombocytopenia (HIT). I read with great interest the guideline regarding HIT, which based the key recommendations for its treatment and prevention on the risk (incidence) of this adverse drug reaction. The incidence of HIT can vary considerably, and Table 2 of the guidelines presents its incidence in various patient populations according to type of heparin. A careful analysis of the references presented in Table 2 reveals, however, that the incidence of HIT is not assessed according to standard methodology for grading the quality of evidence. For example, determining the incidence of HIT in postoperative patients who received standard heparin (prophylactic dose) vs low-molecular-weight heparin (prophylactic or treatment doses) was based on four papers (one, a letter to the editor [comparing two series of cases] and three, reports with overlapping cohorts of

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