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 immunogenum.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 pseudocaligenes) than by mycobacteria (M immunogenum).7 In the same work environment, M immunogenum 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 immunogenum is related to MWF-HP is more than an attractive hypothesis. M immunogenum 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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References

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
patients). Similarly, determining the incidence of HIT in patients exposed to therapeutic treatment with heparin was supported by a paper reporting a retrospective study assessing the incidence of secondary thrombocytopenia recorded in the discharge boards of patients who were referred for a short stay in nonfederal US hospitals with a diagnostic code for thromboembolism and related outcomes. Beside the fact that the meta-analysis reported in this paper did not focus on HIT, it lacked most quality parameters.\(^3,\)\(^4\)

Although high-quality evidence from randomized controlled trials regarding the incidence of HIT in postoperative patients has, to date, been sparse,\(^5\) I believe the previous examples indicate that there is a need to explore this issue more carefully in the ACCP Guideline to prevent this dangerous, adverse drug reaction.

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Response
To the Editor:

Dr Junqueira has brought to our attention that some of the studies referenced in Table 2 (regarding the incidence of heparin-induced thrombocytopenia [HIT]) in the “Treatment and Prevention of Heparin-Induced Thrombocytopenia” chapter in the most recent edition of the antithrombotic therapy and prevention of thrombosis clinical practice guidelines\(^1\) are of poor methodologic quality. Many of the studies in the HIT literature, including those that reported the incidence of HIT, are of similar poor quality. In preparing this topic, we did not conduct a formal meta-analysis of HIT incidence studies primarily because evaluating the incidence of HIT was not one of our objectives. The references provided in the table were only intended to be examples of the incidence in various patient populations and heparin exposure groups. It is noteworthy, however, that had we conducted a formal meta-analysis as Dr Junqueira did in a recently published review,\(^6\) the result would not have been significantly different from that we provided in the table.

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REFERENCES


Significance of Lymphadenopathy in IgG4-Related Sclerosing Disease and Sarcoidosis

To the Editor:

We read with interest the recent article in CHEST (November 2012) by Rho et al.\(^1\) The authors presented an interesting case of IgG4-related sclerosing disease; we were wondering whether there was any significant lymphadenopathy. Asymptomatic IgG4-related lymphadenopathy is