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Titanium and Iron in Lung of a Soldier With Nonspecific Interstitial Pneumonitis and Bronchiolitis After Returning From Iraq

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To the Editor:

The abnormal respiratory illnesses of soldiers after Iraq deployment reported by King et al[1] are corroborated by our studies. Their discovery of crystalline material in lung tissue is enhanced by our identification of copper and hotspots of titanium and iron in lung tissue of an affected soldier. Supervisor of laundry staff in Iraq and Kuwait, he denied exposure to grinding apparati and industrial paint. His exposure sources include the following: airborne dust in the laundry facility, improvised explosive device blasts, sandstorms, burn pits, and the occasional cigar. Postdeployment, he noted coughing and wheezing, despite taking prednisone 20 mg/d for 6 months. A lung biopsy showed nonspecific interstitial pneumonitis with peribronchiolar inflammation. A lung section analyzed at Brookhaven National Laboratory's National Synchrotron Light Source contained the aforementioned metals (Fig. 1; Please see online supplemental digital content for methodology, http://links.lww.com/JOM/A79). The calculated high iron:titanium ratio, rare in nature, is most consistent with anthropogenic particulate sources.[2] Iron, a known reactive oxygen species generator, offers an explanation for the inflammation.[3] Furthermore, both titanium and iron are associated with pulmonary fibrosis and pulmonary hypertension in humans.[4,5]

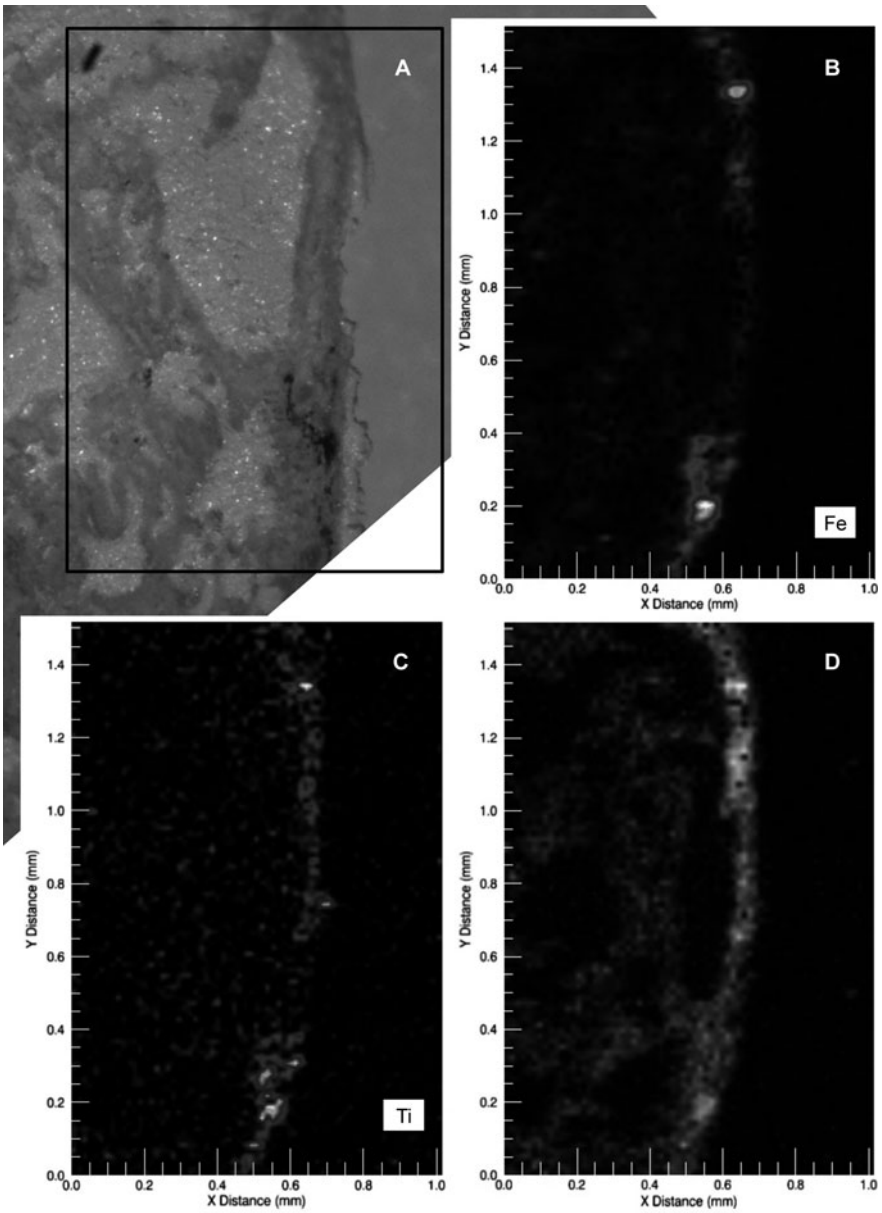

FIGURE 1. A, Lung tissue studied; B, iron hot-spot (Fe); C, titanium (Ti); D, superimposed Fe and Ti in the same location.

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Sarcoidosis and World Trade Center Disaster

To the Editor:

Several findings weaken the authors' conclusion that a causal relationship exists between World Trade Center Disaster (WTC) exposure and the development of sarcoidosis.[1]

1. Dose-response: Assuming causation, one would expect inhalation of airborne, pulverized material from the disaster explosions, the highest systemic dose, to generate the greatest likelihood of developing sarcoidosis. The authors reported a sarcoidosis odds ratio of 1 between those exposed and unexposed to the dust cloud (Table 4).
2. Exposure-disease interval: The interval between immunogenic exposure and inception of granulomatous diseases, for example, tuberculosis and histoplasmosis, is measured in weeks to a few months. A similar interval is occasionally identified in persons in whom inception is definable (acute onset sarcoidosis), who, fortuitously, have had a recent, normal, presymptomatic chest radiograph. Evolution of a positive Kveim response requires 6 to 8 weeks. Ascribing the evolution of sarcoidosis up to 5-year postexposure (Table 2) implies a latency of immunological response inconsistent with the natural history of infectious granulomatous disorders and our circumscribed knowledge of the time course of sarcoidosis. In addition, were WTC exposure a cause of sarcoidosis, one would expect a secular incidence decline over time-since-exposure. Constant incidence for years following the exposure (Table 2) renders a causal connection less plausible. Might it not represent the background incidence of radiographically detectable sarcoidosis (the majority of screen-identified cases are clinically inevident) in the surveilled, working-age cohort?

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Authors' Response

To the Editor:

Our nested case–control study found a strong relationship between performing rescue/recovery work on the 9/11 dust and debris pile and post-9/11 sarcoidosis but did not detect such a relationship between dust cloud exposure and post-9/11 sarcoidosis. We may have lacked sufficient statistical power to detect the latter relationship. It is also possible that the more intense 9/11-related exposures experienced by rescue and recovery workers as compared with others in our study enabled us to detect a relationship in the former group but not in the latter.

We found a relationship between 9/11-related exposures and sarcoidosis diagnosed several years after 9/11. Nevertheless, we could not determine when the disease process was initiated for the individuals in our study, only the year when the illness came to medical attention and was definitively diagnosed. It is plausible that some of the cases, particularly those that were diagnosed incidentally, had begun years before. As we did not have access to pre-9/11 chest radiographs or other medical records, and because the exposure–disease interval for sarcoidosis is unknown, it is not possible to confirm this. It is not clear how the exposure–disease interval for post-9/11 sarcoidosis, which is likely of an environmental etiology, compares with the exposure–disease interval for infectious granulomatous diseases.

Table 2 of our report[1] shows the year of diagnosis for the cases in our study. These data cannot be used to compute incidence rates, which we could not calculate because we did not have a systematic way of identifying all cases in our study population. We do not believe that any conclusions about trends in incidence over time can be drawn from our data.

The World Trade Center Health Registry conducts periodic health surveys but is not a clinical surveillance program. It is true that many of our enrollees may participate in such surveillance programs at other institutions, and, therefore, that our population may receive, on average, more screening chest radiographs compared with the general public. Nevertheless, both cases and controls in our study are likely to have received this heightened degree of medical attention, so detection bias is unlikely to explain the strong exposure–disease relationship we reported.

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The Use of Alcohol-Based Hand Sanitizers by Pregnant Health Care Workers

To the Editor:

The use of alcohol-based hand sanitizers is the currently recommended procedure for the control of infection in health care settings. The American College of Obstetricians advises that "women should avoid alcohol entirely while pregnant or trying to conceive." Is the use of alcohol-based hand sanitizers by pregnant health care workers a risk to their unborn fetuses?

A review of the literature revealed that few studies have been done to measure blood alcohol concentrations after the use of these alcohol-based hand sanitizers. Miller et al[1] had 5 volunteers (all men) apply hand sanitizer (62% ethanol) 50 times over a 4-hour period, and found all blood alcohol concentrations to be below 5 mg/dL.

Kramer et al[2] had 12 volunteers (six men and six women) use three different hand sanitizers (95%, 85%, and 55% ethanol) for a Basic Hand Hygiene application regimen. The volunteers applied 4 mL of hand sanitizer for 30 seconds each time, 20 times over the course of 30 minutes, with 1-minute breaks between applications. They then measured blood alcohol levels immediately after the last applications, and at intervals up to and including 90 minutes after the last application. This group reports peak blood alcohol levels to occur 30 minutes after the last application. They report levels from 0.69 to 2.1 mg/dL for the different strengths of alcohol-based hand sanitizers.

Although the Centers for Disease Control and Prevention reports averages of five to 30 hand rubs/health care worker/shift,[3] Dr Michele Walsh (MD, Director, Division of Neonatology, Case Western Reserve University, Rainbow Babies' and Children's Hospital, personal communication, August 2011) estimates that a health care worker in the neonatal intensive care unit at Case Western Reserve's Rainbow Babies' and Children's Hospital often uses a hand sanitizer as many as 100 times over an 8-hour shift. Using Kramer et al's[2] data and Walsh's maximum-use information, a predicted blood alcohol level for a real-life intensive care unit health care worker using alcohol rubs even at the 95% ethanol composition to sanitize hands would be 0.65 mg/dL.

Bessonneau et al[4] published a mathematical model to predict inhalation exposure to ethanol from an alcohol-based hand sanitizer. They postulated a health care worker uses an alcohol-based sanitizer 30 times in an 8-hour shift. Assuming no room air exchanges, they calculated an inhalation exposure of 5500 mg/m^3/8-hour shift, which is above the Occupational Safety and Health Administration permissible exposure limit and National Institute for Occupational Safety and Health recommended exposure limit of 1900 mg/m^3.[5] This would translate to an exposure of 687.5 mg/m^3/h, and with a standard ventilation factor of six exchanges per hour, the projected worker exposure would be 114.58 mg/m^3/h.

The excessive use of alcohol during pregnancy is well documented to cause fetal alcohol syndrome, and more recent studies are showing that lower levels of alcohol during pregnancy may also result in adverse effects on the developing neurologic system of the fetus.

Bearer et al[6] studied the effect of ethanol on normal neurological development using animal models, and have found adverse effects at a concentration as low as 4.6 mg/dL, although a no observed adverse effect level was not identified.

Sood et al,[7] in a study at an urban university-based maternity clinic, screened women at their first prenatal visit for alcohol use. They stratified these women into none; <0.3 oz; and >0.3 fl oz absolute alcohol a day. Six years later, they contacted and tested the children's behavior using the Achenbach Child Behavior Checklist. They found that the odds ratio of scoring in the range for delinquent behavior was 3.2 in children with any exposure to alcohol. Further statistical tests suggested that "adverse effects of prenatal alcohol exposure on child behavior at age 6 to 7 years are evident even at low levels of exposure."

As to available alternatives, Larsen et al[8] compared the effect of two hand hygiene regimens, a traditional antiseptic hand wash and an alcohol-based hand sanitizer in two neonatal intensive care units. They found that infection rates and microbial counts on nurses' hands were equivalent, although they acknowledge that "other practices such as frequency and quality of hand hygiene are likely to be as important as product in reducing risk of cross-transmission."

In conclusion, the blood alcohol levels found in Kramer et al's[2] study for all strengths of alcohol-based hand sanitizers are all well below the 4.6 mg/dL level found to cause adverse neurologic developmental effects in laboratory animals, and Bessonneau et al's[4] study does not suggest a significant inhalation exposure to health care workers. These data are reassuring that exposure to alcohol-based hand sanitizers would, at most, lead to very low blood alcohol levels; yet, no, NOAEL (no observed adverse effect level) of fetal alcohol has been identified. We suggest therefore that if an additional risk reduction is desired by pregnant health care workers, work practices should be modified to allow the use of soap and water as a substitute for the alcohol-based hand sanitizer.

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