COMMENTARY

Laboratory Testing of the Patient with Multiple Chemical Sensitivity

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Multiple diagnostic laboratory tests are frequently used in the clinical evaluation of persons with multiple chemical sensitivity without a clear a priori hypothesis. In addition, many of these tests are performed despite a lack of understanding of the test technical performance characteristics or the clinical significance (test sensitivity and specificity). The result is a plethora of laboratory data that have little clinical relevance and that can be both misleading and misused. — Environ Health Perspect 105(Suppl 2):443–444 (1997)

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As medical knowledge and technical capabilities have expanded, so have our abilities and tendencies to use laboratory tests to evaluate the function and/or dysfunction of human biological systems. In the practice of medicine, the outcome of these changes is an increasing reliance upon laboratory tests to reduce the uncertainties in making clinical decisions. Clinical medicine laboratory tests are most often used for evaluating and discriminating among alternative diagnostic considerations. Whether an electrocardiogram, biopsy, radiologic evaluation, or blood test, diagnostic tests are frequently employed by physicians to confirm or support the clinical diagnosis formed after the medical history and physical examination. Laboratory tests are also utilized for providing more definitive prognostic information, monitoring response to therapy, and for the screening for occult disease in otherwise healthy patients. However, unless the clinician selects the appropriate tests, understands the limitations of the information provided by a test, and is knowledgeable about the limitations of the test, the results can be misleading and potentially more harmful than beneficial. The proper interpretation of laboratory test results requires that the physician have a working understanding of how well the test discriminates between patients with and without the disease and what impact a negative, positive, or even borderline test result will have on decision-making. This stems from the realization that the predictive value of a test depends not only on its sensitivity and specificity but also on the prevalence of the illness in the population being tested and on the technical performance of the test. A technically good test is both reliable (consistantly reproduceable) and valid (accurately measures what it purports to measure without bias).

These considerations provide a basis for discussing certain aspects of the role of laboratory testing of the multiple chemical sensitivity (MCS) patient as put forth in the papers of Ross (1) and Ziem (2) about their perceptions of the clinical profile of the MCS patient. It is clear from their presentations that their view is one of MCS advocacy. Although Ross utilized a case presentation and Ziem reported upon a case series of MCS patients in her clinical practice, both researchers were effective in highlighting many of the controversies surrounding the clinical condition known as multiple chemical sensitivity. These controversies provide much of the basis for this workshop. Ross and Ziem touched on case definition, presumed etiology, diagnosis, and treatment, as well as invoked a number of the hypothetical constructs that have been devised to explain the MCS phenomenology. Both authors presented results from clinical laboratory testing that can also be considered controversial. Ross described a case study of a patient who developed asthma and the symptoms of MCS shortly after moving into a new home that was still in the process of being completed. Concomitantly with moving into the new home the patient underwent thoracic surgery that was complicated by a postoperative mediastinal hematoma. She was described as subsequently having repeated episodes of stridor and bronchospasm as well as other symptoms in response to multiple chemical exposures and medications. Her medical history and the report of stridor certainly raises the question of either mechanical or functional upper airway obstruction that should be further evaluated with appropriate pulmonary function testing and endoscopic examination of her upper airway. These tests either were not considered or not presented, yet measures of blood volatile organic compounds (VOCs) were included in her evaluation as indicators of xenobiotic contamination. However, measures of blood VOC levels in ambient exposure situations do not have any known relationship to disease. Furthermore, accurately measuring blood VOC levels is technically very difficult and requires special care both in obtaining and handling the specimen to prevent contamination with nonbody sources. In addition, the pharmacokinetics of VOCs makes blood levels a biomarker of acute exposure and would not, even if accurately measured, reflect xenobiotic contamination. Such measures of VOC levels in patients who report to a physician months to years after the exposure have minimal prognostic or diagnostic value for MCS patients.

In the report of her case series of MCS patients, Ziem presented the results of immune panels from two different clinical laboratories as evidence of the potential involvement of the immune system in the pathobiology of MCS; these assays included lymphocyte markers, autoantibodies, chemical antibodies, and various other markers of immune function. There are both technical and clinical problems with these sets of data. For many of these assays, the technical aspects are not well standardized and their clinical significance is either very specialized or undefined. Indeed, the change to the second laboratory was prompted because of documented concerns about the test reproducibility of the first

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Abbreviations used: MCS, multiple chemical sensitivity; VOCs, volatile organic compounds.

laboratory. In addition, the large number of parameters tested increases the likelihood of a spurious or false positive result; chances are that for every 20 tests, 1 will be positive. The observation that many of the tests reported as positive were borderline supports the contention that many were falsely positive. Further complicating the interpretation of these test results is the realization that the assays were performed on an exploratory basis without an a priori hypothesis other than the suspicion that the immune system might be involved. Similarly, there was no clear attempt to relate a particular set of symptoms and/or exposures to any specific alteration in function. For this type of testing to be of value requires that the test be shown to have some degree of sensitivity and specificity in identifying the parameter of interest. This would require carefully designed clinical epidemiology studies with a well defined patient population and appropriate control group.

Probably of more significance and controversy is the contention that the biologic plausibility of immune system involvement in the pathogenesis of MCS is suspect. The lack of consistent physical findings or laboratory evidence of systemic inflammation argues against an autoimmune basis for MCS. Moreover, a principal characteristic of the immune system is its specificity, and therefore immune system dysfunction is unlikely to account for the spreading phenomenon described by MCS patients. There also is little evidence of immune system dysfunction in terms of an MCS association with autoimmune disease, increase in opportunistic infections, increase in cancer risk, or even relationship to atopy. At best, some of these immune markers may be identified as biomarkers of exposure and this would also require carefully designed studies with rigorous attention to laboratory methods and exposure assessment. Unfortunately, by focusing interest on the immune system, this and similar reports have overlooked other components of host defense such as direct irritant responses and neurogenic inflammation even though they provide a potential biologic basis for components of the MCS symptomatology.

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