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# Work-Related Respiratory Disease in the Presence of Normal Tests for Hyperreactivity

Some patients who are worked up for work-related asthma have a negative test for hyperreactive airways: the absence of a significant response to a bronchodilator and to methacholine. Table I lists the common differential diagnoses of other workrelated conditions to possibly explain this clinical presentation.

The first possibility is that the patient does have work-related asthma, but has been away from the substance causing their symptoms long enough that their breathing tests for hyperreactive airways became negative. After removal from exposure individuals may become less sensitive to

Table I. Differential Diagnosis for a Patient with Possible Work-Related Asthma Who has a Negative Test for Hyperreactive Airways

> Irritative Symptoms Emphysema Work-Related Asthma a) Away from Exposure for a Prolonged Period b) Isocyanate Related Eosinophilic Bronchitis Vocal Cord Dysfunction Allergic Rhinitis Hypersensitivity Pneumonitis

methacholine and revert to a negative test, although the majority continue to show a significant reaction to both specific agent and methacholine challenge testing (1-3). The likelihood of reverting to a negative test increases with duration away from the exposure and has been described as early as two days away from work although, more typically, it occurs after months to years away from work (1).

The biological plausibility for a methacholine test becoming negative after exposure ceases is supported by the longitudinal studies conducted by Chan-Yeung and colleagues, of workers who develop work-related asthma (4). On preplacement medical examinations at the time of hire, these workers had negative methacholine test results. However, after a period of time in the job, but before the development of clinical symptoms, the workers developed positive methacholine test results.

The medical literature also describes isocyanateinduced work-related asthma among patients with negative breathing tests for hyperreactive airways. Four reports of work-related asthma from exposure to isocyanates demonstrated specific antigen challenge testing to the isocyanate but negative methacholine challenge testing (5-8). In these reports, the patients have been away from work, sometimes for very short periods such as days to weeks, at the time of the negative methacholine challenge testing. The methacholine challenge test typically became positive when the test was repeated after a specific challenge test to the isocyanate.

It is unusual for patients with occupational asthma to have a negative methacholine challenge test. Prominent researchers in the field of occupational asthma have indicated that "the absence of bronchial hyperresponsiveness after a person has worked for two weeks under his or her usual working conditions virtually rules out the diagnosis of occupational asthma"(9).

A second explanation for breathing symptoms with negative testing results is that the patient has Eosinophilic Bronchitis (10,11). Shortness of breath, chest tightness, wheezing and a dry cough have been described in an auto worker applying weather stripping with cyanoacrylate and methacrylate glue. She had normal spirometry and normal methacholine but increased eosinophil counts in blood and sputum while working. Three months after her exposure ended, she had a specific inhalation challenge test with no significant change in FEV, but she did have reoccurrence of her symptoms and an increase in her sputum eosinophil count. With continuous exposure it is unknown whether she would eventually have developed airway variability.

A third possible explanation is that the patient has vocal cord dysfunction (12). Perkner et al reported on 11 patients with vocal cord dysfunction which developed after acute irritant exposure to substances such as ammonia, cleaning agents, building construction dust, cleaning chemicals, metalworking fluids and smoke from a fire. Spirometry results were either normal or the patient was unable to perform the test because of the severity of their symptoms and the variability in their flow volume loops. These researchers used the following diagnostic criteria: 1) absence of a preceding laryngeal dysfunction or disease, 2) onset of symptoms within 24 hours after a single specific exposure to an irritating substance; 3) symptoms of wheezing, stridor, dyspnea, cough or throat tightness; 4) abnormal direct laryngoscopy for vocal cord dysfunction (vocal cord adduction during inspiration or early expiration with a posterior chink) and 5) exclusion of other types of significant vocal cord disease.

A fourth explanation is that the patient has irritative symptoms without sensitization. The typical clinical presentation would be onset of symptoms within the first week of exposure at work without time for the development of sensitization. A patient with underlying lung disease such as emphysema would presumably be at greater risk of developing this presentation of symptoms.

A fifth possibility is allergic rhinitis with post nasal drip from exposure to a substance at work. In a series of 49 adult patients with chronic persistent cough, the etiology of the cough for 29% of these individuals was post nasal drip without evidence of having asthma (13). Many patients who develop work-related asthma will first develop allergic rhinitis and, with continued exposure, eventually develop asthma.

Finally, in a number of recent outbreaks of hypersensitivity pneumonitis from exposure to metal working fluids in automotive parts manufacturing facilities, there were other workers who developed work-related asthma from exposure to the metal working fluids (14). The patients with work-related asthma were often indistinguishable from the patients with hypersensitivity pneumonitis, based on symptoms alone. The hypersensitivity patients had findings consistent with the diagnosis of interstitial disease and the absence of hyperreactive airways.

If a patient does not have evidence of hyperreactive airways, then serious consideration needs to be given to alternate diagnoses to work-related asthma. Table I summarizes the other work-related diagnoses discussed in this newsletter. In addition, there are other non workrelated conditions such as bronchiectasis, congestive heart failure, and mitral stenosis whose presentation can include shortness of breath and wheezing. However, before excluding work-related asthma, consideration must also be given to the length of time a patient has been away from the exposure at work to rule out the possibility of false negative methacholine challenge test results.

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## Annual Reports Available this Spring

The Annual Reports on Work-Related Asthma, Silicosis, Occupational Noise-Induced Hearing Loss and Occupational Diseases in Michigan will be available late Spring 1999. Look in your mail soon for a notice that the reports are available-through request by mail or phone, or on our internet web site: www.chm.msu.edu/oem/index.htm.

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