Diagnosing the Tight Building Syndrome
by Sherry A. Rogers*

Formaldehyde is but one of many chemicals capable of causing the tight building syndrome or environmentally induced illness (EI). The spectrum of symptoms it may induce includes attacks of headache, flushing, laryngitis, dizziness, nausea, extreme weakness, arthralgia, unwarranted depression, dysphonia, exhaustion, inability to think clearly, arrhythmia or muscle spasms. The nonspecificity of such symptoms can baffle physicians from many specialties. Presented herein is a simple office method for demonstrating that formaldehyde is among the etiologic agents triggering these symptoms. The very symptoms that patients complain of can be provoked within minutes, and subsequently abolished, with an intradermal injection of the appropriate strength of formaldehyde. This injection aids in convincing the patient of the cause of the symptoms so he can initiate measures to bring his disease under control.

Introduction

A survey of the literature indicates homes with indoor chemical problems have higher concentrations of volatile organic compounds than houses without problems (1). The tight building syndrome is defined as a building in which worker complaints of ill health are more common than might be reasonably expected (2). Furthermore, it is assumed that nonoccupational explanations of symptoms have been ruled out. Some have called this illness in victims of the tight building the sick building syndrome (3), but medical specialists relate better to the treatment of people.

Over 25 years ago, Randolph (4) recognized that chemicals in the indoor air environment could provoke symptoms, but acceptance was delayed by lack of measurements and testing techniques which today abound. Because many of these indoor chemicals exist in outdoor air as well, a more accurate designation might be environmental illness, or EI.

Volatile organic hydrocarbons are but a part of the triggers of the tight building syndrome (TBS) or environmentally induced illness (EI). With the installation of urea foam formaldehyde insulation (UFFI), a concordant dramatic increase in symptomatology provided a vast number of victims for study. This provided us with a prototype from which we could observe the evolution and diversity of symptoms associated with an acute increase in one quantifiable indoor chemical, formaldehyde.

Over the last 6 years, increasing numbers of patients have presented with symptoms reminiscent of these UFFI victims (5), but they had no history of UFFI exposure (6, 7). Measurements of ambient levels of formaldehyde have shown that new mobile homes, newly constructed homes with particleboard subflooring, offices recently renovated with paneling or prefabricated walls, new clothing, or even new carpeting or new furnishings, and homes with new beds and cabinetry can accumulate as much formaldehyde, as a result of off-gassing, as a UFFI home (8–11). A variety of other commonly encountered volatile substances are capable of inducing the same symptoms (12–15). For example, the mean reported levels for formaldehyde in indoor air in residences was 0.08 ppm for houses without UFFI and 0.12 ppm for houses with UFFI (with and without complaints) (11). Some mobile homes had levels of 0.4 ppm, and the mean level for several hospitals was 0.55 ppm.

Guidelines are needed to facilitate diagnosis and identification of the triggering agents. Attacks of headache, nausea, inability to concentrate, mental obtundation, dizziness, lethargy, arrhythmia, flushing, laryngitis, dizziness, irritability, dysphonia, unwarranted depression, arthralgia, and extreme weakness, although nonspecific, are some of the most common symptoms of EI and frequently lead to a sequence of diagnostic evaluations which are ineffective; psychiatric evaluation is often suggested.

With proper questioning, the victim will often be able to associate the onset of disease with the purchase of new carpeting, furniture, beds, cabinets, renovation of

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he had been at home for the weekend, but felt well whenever he was out to town for a few days.

His blood serum level of formic acid (a metabolite of formaldehyde) was 10 \( \mu g/mL \) after a weekend at home, and 6 \( \mu g/mL \) after a day at work. A passive (badge) monitor showed an ambient 24-hr formaldehyde level of 0.06 ppm in his home. Note that current recommendations for maximum ambient air formaldehyde exposure levels range from 0.25 ppm (National Academy of Sciences) to 0.12 ppm (American Society of Heating, Refrigeration, and Air Conditioning Engineers), while concentrations below 0.06 ppm are considered of limited or no concern (13).

Single-blind testing with normal saline produced no symptoms. An injection of 0.01 cc of dilution 3 (0.15% formaldehyde) produced wheal growth and “a warm feeling”; 0.05 cc of dilution 4 (0.03%) produced “ringing in the ears and achy joints.” With a 0.05 cc of dilution 5 (0.006% formaldehyde), after 10 min all of his symptoms were clear, and there was no wheal growth. Another normal saline produced no wheal growth or symptoms.

M.B. was a 41-year-old teacher who had worked in the same school for 8 years. Over summer vacation, renovations were done in the school. When she re-entered the building in the fall, she started having symptoms that with each subsequent entry came on more quickly and more severely. She would eventually lose her voice as it gradually became more hoarse over the first few hours of work. She also experienced a sore throat and tender submandibular lymphadenopathy. She would have a feeling of achiness as though a flu were starting, and became exhausted. These symptoms persisted for a day or two after leaving the building and were proportional in duration and severity to the amount of time she spent there. At home she was without symptoms. Her serum level of formic acid was 10 \( \mu g/mL \) after a day at school and 6 \( \mu g/mL \) after a weekend at home. This measurement was repeated with the same results on subsequent days. The 24-hr level of formaldehyde in the school air, measured with a passive (badge) monitor, was 0.06 ppm. Single-blind testing to formaldehyde duplicated her symptoms in the office, with administration of 0.05 mL of dilution 5 (0.006% formaldehyde) producing visible facial flushing and weakening the patient’s voice. The next dose, 0.05 mL of dilution 6, cleared the symptoms.

All patients described were universally and unquestionably freer of symptoms after they had been through an intensive educational program to teach them how to lower their ambient levels of formaldehyde exposures.

Discussion

The last half decade has provided us with over 1000 patients with undiagnosed chronic symptoms, refractory to a wide variety of treatments. Single-blind testing to various chemicals generally identified a suspect chemical and provided convincing enough duplication of symptoms in patients to enable them to make incon-

Materials and Methods

In this study, U.S.P. 37% reagent grade formaldehyde was diluted 50% with Hollister-Stier diluent and was used as a concentrate. One milliliter of this concentrate was added to 4 mL of sterile water; this made dilution 1, a 3.7% formaldehyde solution. One milliliter of dilution 1 and 4 mL of diluent made dilution 2, which thus was a 0.7% solution. Fivefold serial dilutions as described by Miller and Morris (16,17) were thus prepared out to dilution 9, a solution containing just under 10\(^{-5}\) of 1% formaldehyde (0.000094%).

Testing of patients, who in all cases had failed to obtain relief with medical treatments elsewhere, was initiated with an intradermal injection of 0.01 cc of the dilution 3 (0.15% formaldehyde); this injection resulted in a 4 mm \( \times 4 \) mm wheal. After 10 min the symptoms and wheal size were determined. If no symptoms and no growth in wheal size were observed, 0.05 cc of dilution 3 was injected, resulting in a 7 mm \( \times 7 \) mm wheal. If after another 10 min both parameters were again negative, then the test was considered negative. If either parameter was positive, then 0.05 cc of dilution 4 (0.03% formaldehyde) was tested. If positive, then 0.05 cc of dilution 5 (0.006% formaldehyde) was used. Negative wheal growth and negative symptoms determined the point at which testing was terminated. If symptoms were produced with positive wheal growth and were subsequently eliminated by the dose that gave no wheal growth, the test was considered positive.

All tests were done in a single-blind fashion, and were preceded by at least one placebo injection of normal saline for baseline and placebo control. Patients were never aware of what they were being tested with until all tests had been completed.

In some cases, the blood serum level of formic acid, a metabolite of inhaled formaldehyde, was measured (SmithKline Laboratories, King of Prussia, PA). In others, a 24 hr level of formaldehyde in the ambient air of a suspect room was measured with a passive (badge) monitor.

Selected Case Examples

For brevity, only 2 of 24 cases are presented.

C.P. was a 39-year-old consulting engineer who traveled extensively. Two years ago he moved into a new home in the Syracuse, NY, area. There were new carpeting and particleboard subflooring throughout the house. Six months after moving he experienced an insidious onset of joint pain. He consulted an internist, a rheumatologist, and in spite of their treatments, he reported a year-and-a-half later that he had the same symptoms. He also indicated that he ached more after moving into a new dwelling, or insulating with UFFI. We now need a test that would substantiate that formaldehyde (or other chemicals) was among the triggers.
venient and costly environmental changes that appear to be a necessary part of a comprehensive program to bring about symptom relief for the first time. Obviously, we have extended these techniques to include other difficult-to-avoid chemicals such as toluene, benzene, xylene, ethanol, trichloroethylene, natural gas, and more, and in many instances have paired the intradermal skin tests with serum measurements before and after exposure to the suspected environmental xenobiotics (tests performed by Enviro-Health Laboratories, Richardson, TX).

In patients requiring legal proof of chemical exposure, serum levels of these chemicals are obtained after a day at work and another set after a day at home. When the levels at home are comparatively lower, we have been able to provoke and duplicate symptoms with the particular chemical, single blind or double blind, and then neutralize or terminate symptoms with the nonreacting intradermal dose in our office, which is exceptionally free of potential chemical pollutants.

To accomplish a pollutant-free environment in our office, carpets have been removed and replaced with hardwood or quarry tile floors. Wooden cabinets and synthetic chairs have been replaced with metal. As many extraneous materials as possible are kept out of the testing room. Metal lockers are provided in another area for purses, coats, and packages. No people are allowed into the office who do not pass the sniff test by nurses who are sensitive to chemicals. Nurses and all patients must be free of fragrances, fabric softeners, polyester clothes, dry-cleaning fluid, cosmetics, toiletries, tobacco smoke, home cooking odors, work odors, and, in fact, any detectable odors. Air depollution devices with charcoal and potassium permanganate filters to absorb chemicals are used extensively, and outdoor air is continually filtered and pumped inside.

It is evident that a supersensitive individual cannot be tested, for example, by a nurse wearing perfume. He can react to this trigger shortly after coming into contact with her, confusing the test results. The major problem is that the treatment dose for the chemical being tested will not stop his symptoms, because it is not the chemical that initiated them. This has been repeatedly demonstrated and has helped us attain a progressively less contaminated office and, in particular, testing area. Many people happily note the relative paucity of symptoms that they experience after they have been in our office for a period of time.

It seems that multiple changes in the immune system are triggered in part by the increasing environmental overload (19,20). The mechanism of this technique may involve in part the prostaglandin system (21). Many have pondered why only one specific dose of the same agent that causes the symptom can also abolish it, while all other doses trigger the actual symptom or are without effect. Many biological systems have dose-dependent diverse actions. Certainly, we know various biological responses have a dose that enhances and a dose of the same substance that suppresses (22). Likewise, many biological systems have a bell-shaped response curve where there is an optimum dose for response, and doses too high or too low will be ineffective. As well, nonimmunologic mediator release can even be triggered by a change in substrate concentration (23).

Two characteristics of environmentally induced illness are perhaps most worrisome; the phenomena of spreading and of heightened sensitivity. Illness in these patients was usually triggered by an over exposure to one chemical, such as formaldehyde; prolonged exposure to the initial stimulus will frequently result in the development of hypersensitivities to other chemicals, spreading to foods, or inhalants such as dusts and molds. Furthermore, once sensitized, the patient gradually reacts with heightened sensitivity to increasingly lower levels of the insulting agent.

The practitioner dealing with this select patient population is thus presented with a set of diagnostically baffling symptoms, which, despite accepted medical treatments, may become worse as weaker and less intense exposures to the initial chemical triggers symptoms. All the while, other chemicals and antigens may become triggers as well.

Formaldehyde exposure can be related to the level of fumaric acid measured in the blood. Formic acid is also a metabolite of endogenously produced formaldehyde. Formaldehyde oxidase normally rapidly converts aldehydes into acids, since aldehydes are harmful to the body in promoting cross-linking. But formaldehyde oxidase is limited in its production, and with ambient overload, production is unable to keep up with the increased demand. Once production is exceeded, the biochemistry switches from an oxidation reaction to a reduction reaction with alcohol dehydrogenase. This may explain the preponderance of cerebral or toxic brain symptoms as the aldehydes are reduced to alcohols (24–26).

Since these reactions require folic acid (27), often folic acid deficiency was observed, as well. Certainly, as deficiencies progressed with continual exposures, other biochemical systems would be adversely affected by a domino effect. This may explain the spreading phenomenon whereby other sensivities develop and other target organs became involved. It is an interesting observation that rats cannot get formaldehyde toxicity because formate does not accumulate in this species. Hence, the rat would appear to be an invalid animal in which to do formaldehyde toxicity studies (27).

The diversity of symptoms of E1 victims is more easily appreciated with the understanding of the extent of the damage that is rendered by inhaled xenobiotics or toxic chemicals. Toxic chemicals interfere with cellular energy metabolism by inhibiting glycolysis and mitochondrial respiration. They inhibit ATP synthesis and other enzymes, decrease the efficiency of the sodium pump, disrupt cell membranes, produce free radicals, overload the cytochrome P-450 detoxication system, and damage DNA (28). Each person's biochemical uniqueness serves to amplify the possibilities.

This paper presents a simple method for determining if a patient is sensitive to formaldehyde. We do not know the percentage of sensitivity or accuracy, nor do we
understand the mechanisms, but in testing over 1000 patients with these baffling symptoms, those reacting positively have all improved after being shown how to reduce their environmental chemical overload. Treatments were based on avoidance of chemicals that were shown to duplicate symptoms.

One important caution: The testing method will not work if the physician’s office has an ambient level of formaldehyde or any other triggering agent that provokes the patient’s symptoms. This may explain the major cause of failure of clinical investigators who have tried these techniques and been unable to reproduce these results. The need to lower the total load or total burden of chemicals presented to the patient (in his system and in the test area) is fundamental to the success of this technique and cannot be overstressed. The same subjects, tested double blind to the same chemicals in a normal office or hospital, do not respond in a predictable manner; whereas in an office such as ours, where special measures have been taken to omit many commonly occurring chemicals, the technique appears able to turn symptoms on and off like a switch.

Basic principles used to create a safe testing environment are decreasing the amount of synthetic materials used, markedly increasing the ventilation, and filtering the air. It is important to reiterate the variability in sensitivity and target organ of man and the need to focus attention on the importance of indoor air quality on health.

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