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Idiopathic Environmental Intolerance

We aren't sure what it is, but we think we can help

By William Glenn

"Within minutes, Mrs. Smith was breathless, lightheaded, confused, and dissolving in panic; her condition deteriorated so dramatically that her daughter had to be asked to leave the room."

Scientists call it "idiopathic environmental intolerance" or IEI these days, a bundle of unpleasant symptoms without any accepted organic explanation. The word "idiopathic" just means "of unknown origin", but whether you prefer the older labels "environmental illness" or "multiple chemical sensitivity" or "universal allergy" or "20th Century disease", this debilitating and difficult-to-diagnose syndrome has been a hot-button issue both in the media and in the medical community since the early 1970s.

Alternative medical practitioners have insisted that exposures to low levels of synthetic chemicals -- levels usually considered safe or even undetectable -- were to blame for transforming healthy, productive employees into chemophobic shut-ins. Today, the accumulating evidence from the conventional medical community has all but settled on a psychological explanation. But just because a syndrome's "all in your head" doesn't mean you don't feel like hell. Psychological or physical, genetic or environmental -- whatever the root cause -- the key to relief is to seek out the most effective treatment for what ails you.

But that is not always as easy as it sounds. One of the more common manifestations of IEI is that sufferers believe intensely that the causes are environmental and furiously resist any treatment that suggests it is not.

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"Mrs. Smith", a diagnosed IEI patient who complained that the smell of second-hand tobacco smoke made her horribly ill, was brought into Dr. Arthur Leznoff's office for what's called a

“challenge” test. After taking a blood sample, the doctor would expose Mrs. Smith to cigarette smoke, observe her symptoms and take a second blood sample to note any change in carbon dioxide (CO_2) levels. A drop in CO_2 would confirm that the subject was hyperventilating, a condition most commonly associated with acute anxiety and emotional distress, but not with chemical exposure.

The patient’s daughter, a confirmed smoker, sat 10 feet away, pulled out a cigarette and lit it. Within minutes, Mrs. Smith was breathless, lightheaded, confused, and dissolving in panic; her condition deteriorated so dramatically that her daughter had to be asked to leave the room. Dr. Leznoff had the gasping woman breathe into a paper bag to replace some of the carbon dioxide blown off during hyperventilation. It took about five minutes, time enough to bring all her symptoms under control, before Mrs. Smith felt well enough to continue the interview -- in a room still filled with the second-hand smoke that was supposed to have triggered her reaction.

Mrs. Smith was one of 15 IEI patients who visited Dr. Leznoff in 1996 and 1997 to take part in a series of open inhalation challenges. One subject said he couldn’t stand the smell of bathtub sealants, another that "new carpet" smell, yet another the printing inks in the telephone directory. Many attributed their conditions to a workplace chemical exposure -- asphalt fumes, disinfectants, a hydrocarbon solvent or something similar -- that had eventually made them unemployed and unemployable. Each underwent the same procedure as Mrs. Smith.

A staff physician at St. Michael’s Hospital in downtown Toronto, Dr. Leznoff specializes in allergies, immunology and internal medicine. In conducting the challenge tests, he wanted to gather some of the first hard evidence on what exactly happens when an IEI patient is exposed to one of his or her triggering chemicals. Were the patients reacting to the presence of the chemicals themselves? Or, as Dr. Leznoff suspected, were their reactions a physical manifestation of their fear of what those chemicals might do to them?

One participant, a nurse, reported being exquisitely sensitive to Albuterol, a common antiasthmatic drug which, unlike most other chemicals that trigger a response in IEI patients, has no odour. Instead, Dr. Leznoff planned to spray salt water in the air as a trigger in a blinded experiment. Unfortunately, there was an opened package of Albuterol on the counter of the examining room. The nurse, who was very familiar with the product, could see that one cap had been removed and immediately suffered a violent attack, retching, gasping and hyperventilating so violently, the

doctor was unable to take the second blood sample. The symptoms were triggered not by the chemical itself -- there had been no Albuterol released into the room -- but simply by the fear that the chemical was present in the air.

Vast Array of Symptoms

Several of the most common symptoms reported by IEI patients are very similar to the physical effects extreme anxiety can produce. Following their challenge tests, 11 of the 15 subjects presented a very similar set of physical responses -- chest tightness, lightheadedness, confusion, weakness, loss of coordination, palpitations and, finally, hyperventilation -- the hallmarks of a classic anxiety or panic attack. In addition, each showed a precipitous drop in blood CO_2 following the appearance of symptoms; this was the physiological evidence Dr. Leznoff was looking for. Not surprisingly, the four patients who did not show a change in CO_2 levels also did not show any of their IEI symptoms.

It should be noted that IEI cannot be characterized by any uniform or simple set of symptoms. It's one of those fuzzy functional syndromes, like chronic fatigue or fibromyalgia or repetitive strain injury or irritable bowel syndrome. They are all physical illnesses, but largely without organic explanation or diagnostic standard. IEI patients don't display any identifying structural damage. There is no reproducible laboratory test that will pinpoint a characteristic abnormality. In most cases, a patient is diagnosed with IEI because he or she reacts violently to an environmental stimulus, usually some obtrusive chemical, and no other disease, condition or explanation seems to fit the symptoms.

Dr. Leznoff's subjects represent just one subset of IEI sufferers, but other patients have ascribed virtually every condition in the medical textbook to their environmental exposure to toxic chemicals. In alphabetical order, they may complain of asthma and breathing problems, autoimmune disorders, bloating or other intestinal problems, "brain fog", cardiovascular irregularities, chest pain, chronic exhaustion, constipation, diarrhea, depression, disorientation, dizziness, drowsiness, fatigue, flu-like symptoms, food allergies and intolerances, forgetfulness, frequency of urination, genitourinary problems, headache, inability to concentrate, irritability, itchiness of the eyes and nose, lightheadedness, mental exhaustion, mood swings, muscle and joint pain, muscle incoordination, nasal stuffiness, rashes, sneezing and wheezing, stomach upset, swelling of various parts of the body, and tingling of fingers and toes. Most of the major systems of

the body -- respiratory, central nervous, cardiovascular, digestive and immune -- may be impacted at one time or another.

"Is it the chemical that causes the reaction through some (as yet unknown) toxic mechanism?" asks Dr. Leznoff. "The answer is 'no'. There are no studies that demonstrate an organic basis for the condition in human beings." Unlike an employee who develops a sensitivity to a particular workplace chemical, IEI patients typically react to a wide variety of compounds -- simple aliphatic chains, compound polyaromatics, even inorganics. "I'll ask a patient if he or she also reacts to Javex with ammonia D -- that's an inorganic compound -- and they'll usually say that they do," says Dr. Leznoff. That means, "we are clearly not dealing with an immunological or allergic response here."

There are those, however, who still subscribe to a physical cause for the development of IEI in an individual. Generally, these theories fall into three categories. There are theories based on various allergy or auto-immune mechanisms. Then there are the theories of non-specific inflammation in which low-level irritants amplify the immune response. And finally, there are the neurotoxic theories, in which exposure to odours and respiratory irritants may cause various IEI symptoms. Much of this sensitization research revolves around "limbic kindling" in which repeated chemical stimuli can induce seizure activity in lab animals.

None of these approaches has won the broad support of the scientific community. The American Medical Association, the American Academy of Allergy, Asthma and Immunology, the American College of Occupational and Environmental Medicine and a number of other professional bodies have each issued reports or position statements decrying the deficiencies in the available IEI diagnostic tools, the dubious and unreliable treatments being offered, and the uncertain causes of the syndrome. In general, the conventional medical community feels there is not enough hard scientific evidence to support the toxic effects environmental chemicals are purported to be having on IEI patients.

Even the laboratory experiments that show test animals becoming more sensitive to chemical exposures only reveal a two, three or four-fold increase in sensitivity. However, IEI patients routinely show a chemical sensitivity five thousand to 10 thousand times higher than normal, and in some cases up to four million times higher. When examined quantitatively, the studies purporting to show a physical mechanism for IEI are "nonsense", says Dr. Leznoff.

Parallels to Panic

Dr. Karen Binkley, an assistant professor at the University of Toronto's Division of Clinical Immunology and Allergy, was also struck by the parallels between IEI and panic disorder. They share a similar set of physical symptoms that appear during episodic attacks. Their victims can suffer debilitating anxiety anticipating the arrival of the next attack. And both groups of patients are particularly phobic about avoiding the triggers or situations associated with previous attacks.

At the time Dr. Leznoff published his findings, Dr. Binkley was working with a group of IEI patients who showed no sign of an immunological or allergic condition, but did exhibit anxiety-like symptoms. "I thought, gee, maybe we should look into this more," she recalls. "Fortunately, there is a way to test for panic disorder. In fact, it's one of the only psychiatric disorders for which a reasonably reproducible clinical test exists."

In a pilot study, five patients with characteristic IEI symptoms (that they attributed to various chemical exposures) were alternatively administered a placebo and sodium lactate. The latter is a known panicogenic agent that will trigger panic attacks in those who have experienced them before, but is unlikely to in those who have not. When given the sodium lactate, all five of the IEI patients exhibited symptoms that met the criteria for a panic attack, according to a standardized psychiatric questionnaire. But none showed any panic symptoms when given the saline placebo. Although the sample size was small, Dr. Binkley concluded that the results "are those expected if IEI is in fact a variant of panic disorder in these patients." Follow-up research with another panicogenic agent, CO2, verified the results in larger study.

What may be the most convincing evidence was published earlier this year. In a paper that appeared in the May, 2001 issue of the *Journal of Allergy and Clinical Immunology*, Dr. Binkley postulates that IEI patients share an inherited gene that has been linked to many of the symptoms associated with panic disorder. With the permission of some of her IEI patients, the doctor submitted blood samples to the same laboratory that had earlier identified the variations on the CCK-B gene believed responsible for panic disorder. When the results came back, it was seen that some 40 per cent of the IEI patients shared the same CCK-B receptor; in comparison, only two of 11 members of the matched control group exhibited that particular genetic variation.

"It's only part of the picture," says Dr. Binkley. "There are probably other genes involved as well." Given that both IEI patients and those who experience panic disorder share the same specific

genetic variation, the two conditions may also share the same underlying genetic basis. If confirmed in larger scale studies, this link may provide a basis for more effective treatment.

While the experts are still debating the causes of the syndrome, other researchers are profiling the typical sufferer. The patient is probably female; on average, between 70 and 80 percent of the subjects in the various reported IEI studies are women. She’s intelligent, works in a white-collar job -- perhaps she’s a teacher or a civil servant -- and generally developed her chemical sensitivities slowly, beginning in her 20s or 30s. Perhaps most telling of all, she’s likely had some history of mental illness.

Most full-blown IEI patients seldom leave their homes for fear of chemical exposure. They won’t go the movies or the mall. They can’t ride on subways or buses. They can’t even drive their own cars because the vehicle stopped next to them at the traffic light is belching out pollution. This profile is very similar to the behaviour of agoraphobics, says Dr. Leznoff. And 50 percent of patients who suffer panic attacks are agoraphobic.

According to Dr. Donald Black, a psychiatric researcher with the University of Iowa College of Medicine, "the diagnosis of IEI is strongly associated with psychiatric co-morbidity." Dr. Black reviewed 12 different studies that assessed the psychological health of some 323 IEI patients. About three-quarters of the IEI patients -- between 42 and 100 per cent of the subjects in each study -- were diagnosed with some kind of mental illness or psychological disorder. Mood, anxiety, somatoform (formerly considered a kind of hysterical neurosis) and personality disorders were the most common. However, psychotic and substance abuse disorders were rare.

There have been complaints about the methodology employed in the individual studies. Some critics reject the findings completely. But the research does show a certain consistency in its findings. An IEI patient is three or four times as likely to suffer from some kind of psychological disorder as someone in the general population. And these are pre-existing conditions, based on lifetime diagnoses, not a side effect of their debilitating IEI symptoms. In Dr. Black’s view, many IEI patients are "genetically loaded for mental disorder". First-degree relatives of persons diagnosed with IEI were significantly more likely to have a mental disorder.

In Dr. Black’s own contribution to the body of research, he compared the mental health of 26 persons diagnosed as environmentally ill against 23 age- and gender-matched controls. Only three of the IEI patients failed to meet the criteria for psychological disorder; 87 per cent were diagnosed

with some kind of psychiatric problem compared with 28 per cent in the general population. In a paper published in *Occupational Medicine: State of the Art Reviews*, he concluded that chemically sensitive patients "frequently suffer from unrecognized psychological distress, which probably accounts for some or all of the symptoms attributed to environmental illness by their clinical ecologists."

Preoccupied with Symptoms

Compounding the problem, their psychological outlook makes many IEI patients poor subjects for counseling or treatment. According to the research compiled by Black and his associates, IEI patients tend to be preoccupied with symptoms, believing there is something seriously wrong with their bodies, and absolutely convinced that there's a physical link between their illness and some outside factor. Generally, they believe that physicians aren't taking their condition seriously and find it difficult to be reassured. They also have a tendency to reject responsibility for their condition, genetic or not, and to show a decided preference for medical -- not psychological -- treatment.

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Despite the weight of recent evidence pointing to a psychological explanation for many IEI symptoms, some 25 per cent of the patients in the studies Dr. Black reviewed had no history of mental illness. They were not depressed or phobic or suffering from panic disorder. Still, by any objective assessment, they were sick.

"Just because there is a psychological component, it doesn't mean there isn't a physical one as well," cautions Dr. Paul Lehrer. "The psychological symptoms may even be triggered by physical exposures." Dr. Lehrer, a professor of psychology at the Robert Wood Johnson Medical School at Rutgers University, is an expert in behavioural conditioning, with a special interest in respiratory psychophysiology.

Modern medicine has blurred the dichotomy between the psychological and the physical. "It's not an either/or proposition," cautions Dr. Lehrer. "The brain *is* part of the body." While conceding that conditioning is just one aspect in the development of IEI, Dr. Lehrer thinks behaviour modification is a very valid treatment for reducing or eliminating symptoms.

Desensitization through intentional exposure is one behavioural technique that holds some promise, says Dr. Lehrer, an approach that differs radically from the chemical avoidance strategies advocated by many clinical ecologists. Dr. Lehrer believes that at least some of an IEI patient's chemical triggers have been learned through classic Pavlovian conditioning -- a bad reaction to a noxious stimulus has evolved into a physical aversion to the slightest whiff of a wide array of pungent chemicals. The behavioural therapist attempts to have the patient "unlearn" or, more precisely, override those negative associations with new ones. The patient can also be taught relaxation responses and other desensitization techniques to counter the unpleasant effects produced by exposure to symptom-evoking stimuli.

Still, the psychological make-up of the average IEI patient presents a challenge to the behavioural therapist. Some IEI patients exhibit a desensitization personality structure, says Dr. Lehrer. "They don't recognize a psychological or emotional component in their own behaviour," he explains. "They don't admit to the psychological foibles or faults that we all have. These people tend to show more physical suffering."

Staying Open Minded

Dr. Patricia Sparks says that it's important to view the patient as a whole person. If someone presents himself or herself in your office complaining of an environmental illness, and the major symptoms are headache, short-term memory loss, muscle aches, and a lack of energy, then you have to consider depression as a possible diagnosis. In preparing the differential diagnosis, the physician must first rule out the other well defined toxic or allergic processes. Maybe it's not IEI, but asthma or solvent intoxication or sinusitis instead. "When hearing hoof beats, the physician should first look for horses rather than zebras," says Dr. Sparks.

That means that whoever sees the patient has to have a broad-based medical background, as well as being prepared to evaluate the clinical significance of a patient's exposure history. There's no gold standard for evaluating IEI, Sparks warns. A clinical ecologist preoccupied with possible low-dose exposures and chemical sensitivities may not consider the other, more likely, medical alternatives. "If you only work with hammers, all you see are nails," laughs Dr. Sparks.

Through her Seattle-based consulting practice, specializing in occupational and environmental medicine and clinical toxicology, Dr. Sparks has been involved with IEI for a decade or more. She recommends a nonjudgmental approach to evaluation and treatment that's based on the assumption

that the patient’s symptoms are "real", regardless of the outcome of the ongoing debate over their root cause.

"Psychological factors play a major role in, if not totally explain, the symptoms experienced by many IEI patients," says Dr. Sparks. So many are profoundly dysfunctional in their work and home lives, but they won’t seek psychological treatment. "It’s very important to them to project their distress onto the environment," Sparks says, “to blame their physical deterioration on an employer, or a chemical-maker, or a colleague that overindulges in perfume.”

But that distress can still be treated. "Some patients will permit me to put them on a low-dose antidepressant medication," says Dr. Sparks. "It’s not ideal, but you should remember that most patients suffering from depression are treated by primary care physicians," not psychologists. In any case, the IEI patient’s problems should never be dismissed with a cavalier “it’s all in your head attitude”; if it’s not possible to effect a cure, the physician is still in a position to help control the symptoms and, in turn, help IEI patients better manage their lives.

While therapy must be modified to meet the needs and limitations of the individual patient, a balanced regime of supportive therapy could include some or all of the following actions:

* Provide behavioural desensitization to low-level chemical exposures in order to increase tolerance levels and ultimately remove chemical triggers. In some cases, the use of double blind provocation tests could help the patient distinguish which environmental stressors, if any, contribute to his or her condition.

* Treat any co-existing psychiatric disorders, such as panic attacks or depression, in order to reduce symptoms and ease disability. Regardless of whether the cause is ultimately proven to be physical or psychological, such treatment would make the life of an IEI patient more bearable.

* Enhance a patient’s sense of control over workplace or home stressors, including odours, noxious chemicals and other prominent environmental chemical exposures, to provide some (immediate) relief from symptoms. It should be noted, however, that the current research does not support the complete avoidance of chemical exposures. While impossible to execute, such action could also perpetuate the belief that the exposure is entirely responsible for the condition.

* Reduce psychosocial stress and encourage relaxation, through massage, physical therapy, meditation, regular exercise and so on, in order to further reduce stress and any stress-related symptoms.

* Increase the level of physical and social activity. The loss of social support and economic independence associated with a withdrawal from modern life can exacerbate depression and other psychological disorders and make a full recovery even more difficult. The benefits of friends, family, a rewarding job and outside interests raise the prognosis for success.

* Prescribe suitable pharmacological treatment to control symptoms, such as anxiety, depression, mood swings, chronic fatigue or difficulty sleeping, that typically accompany IEI. However, drugs should only be one component of an overall treatment strategy.

* Teach hyperventilation control techniques, such as rebreathing into a paper bag, to provide both temporary relief and offer the patient some valuable coping skills so that he or she need not become further isolated from society.

In some cases, it can useful for patients to maintain a diary of their possible exposures and resulting symptoms, but this may not be appropriate for everyone. As Dr. Sparks writes in a recent issue of *Occupational Medicine* (Vol. 15, #3, 2000), there is a fine line between urging patients to pay attention to the effect of various environmental exposures on their symptoms and promoting symptom attribution by suggestion.

The physician has to have a feel for the patient, says Dr. Sparks. If somebody walks into your office with five briefcases stuffed with hour-by-hour logs of their symptoms, it’s not too difficult to conclude you’re dealing with an obsessive-compulsive, she says, "and you don’t want to encourage that kind of maladjustive behaviour."

Anger Runs High

Dr. Sparks admits that her work in the IEI field has been "rife with controversy and a few unhappy relationships with patients ... But some [IEI sufferers] are receptive to treatment and I try to help them to the extent they will let me." Still, it’s hard to think of another health issue or scientific controversy that arouses more invective, outrage and character assassination than the never-ending debate over the cause and treatment of IEI.

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In one camp, there are IEI sufferers who feel marginalized and ignored by traditional medicine. Unable to continue working, sometimes cut off from compensation, isolated from family and friends, many spend their days in a fruitless cycle of allergists, occupational therapists, naturopaths, herbalists and dieticians. And it would appear that at least some of them spend their nights in front of a computer flooding the Internet with a blow-by-blow record of their disappointments.

Enter the term "environmental illness" into the powerful on-line search engine Google and you'll register more than 21,000 "hits" -- a litany of depressing case histories, bizarre cures and rants against the medical establishment, interspersed with the occasional research report or scientifically reputable study.

Then there are the scientists, digging for clues on the causes and development of the syndrome -- evidence that will stand up to the accepted standards of scientific scrutiny and that can be used to fashion effective treatment. But the situation can become very complicated and very political, says Dr. Leznoff, especially when patients become plaintiffs fighting for compensation and disability packages. "There are non-medical factors that make it important to support an IEI diagnosis," he notes.

So, do the experts wish they had chosen another line of research? "Absolutely, I regret it," says Dr. Leznoff. "Scientists in this field are subject to intimidation in a very broad sense." There can be harassing phone calls and e-mails at home, derogatory postings on the Internet, and demonstrations at lectures. Then there are the frivolous but aggravating complaints to employers or medical boards. Even when proven groundless, "every complaint takes a tremendous amount of time and energy to refute," says Dr. Leznoff.

Many physicians are saying "I don't need this" and avoiding the IEI debate entirely. The result, "alternative medicine triumphs by default," says Dr. Leznoff. And IEI patients remain isolated, out of work and in pain.

William Glenn is associate editor of hazardous materials for ohs canada.