Three Questions to Screen your Patients for Chemical, Food, and Drug Intolerances the Brief Environmental Exposure and Sensitivity Inventory (BREESI)

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Abstract

Background: The 50-item Quick Environmental Exposure and Sensitivity Inventory (QEESI) is a validated questionnaire used worldwide to assess intolerances to chemicals, foods, and/or drugs and has become the gold standard for assessing chemical intolerance (CI). Despite a reported prevalence of 8-33%, CI often goes undiagnosed in epidemiological studies and routine primary care. To enhance the QEESI's utility, we developed the Brief Environmental Exposure and Sensitivity Inventory (BREESI) as a 3-item CI screening instrument. We tested the BREESI's potential to predict whether an individual is likely to respond adversely to structurally unrelated chemicals, foods, and drugs.

Methods: We recruited 286 adult participants from a university-based primary care clinic and through online participation. The positive and negative predictive values of the BREESI items were calculated against the full QEESI scores.

Results: 90% of participants answering “yes” to all three items on the BREESI were classified as very suggestive of CI based upon the QEESI chemical intolerance and symptom scores both ≥ 40 (positive predictive value = 90%). For participants endorsing two items, 92% were classified as either very suggestive (39%) or Suggestive (53%) of CI (positive predictive value = 87%). Of those endorsing only one item, only 13% were found to be very suggestive of CI. However, 70% were classified as Suggestive. Of those answering “No” to all of the BREESI items, 99% were classified as not suggestive of CI (i.e., negative predictive value = 99%).

Conclusions: The BREESI is a versatile screening tool for rapidly determining potential CI, with clinical and epidemiological applications. Together, the validated BREESI and QEESI provide much needed diagnostic tools that will help inform treatment protocols and teach health care professionals about Toxicant Induced Loss of Tolerance – the mechanism driving CI.

Background

Chemical Intolerance (CI) is a common insidious health issue. Up to one-quarter of the U.S. population report being either “especially” or “unusually” intolerant to certain chemicals, with about 5% reporting physician-diagnosed CI.¹ The prevalence is reported to be between 8–33% in population-based surveys.^{1–3} In a prevalence study of a busy family practice medical clinic, Katerndahl et al.,⁴ reported a 20% CI prevalence rate.

CI-related symptoms may involve any and every organ system. Neurological symptoms such as memory problems, brain fog, and mood changes are common and often disabling. A particular initiating event (such as exposure to a sick building, Gulf War chemicals, or a pesticide) can result in intolerances that trigger multiple symptoms varying from person to person. Commonly-reported symptoms include: difficulties with attention, memory and mood; gastrointestinal problems; allergy-like symptoms; migraines and headaches; fatigue and muscle pain.

The specific mechanisms underlying CI remain elusive, however, there is evidence for a general disease process called Toxicant-Induced Loss of Tolerance (TILT) which parsimoniously captures the wide variety of symptoms and intolerances reported by researchers and individuals with this condition.⁵⁻⁷ TILT is a two-stage disease mechanism initiated by a major exposure event, or a series of exposures (Stage I, Initiation). Affected individuals experience symptoms triggered by everyday chemicals, foods, and medications that never bothered them before and do not bother most people (Stage II, Triggering). Initiating exposures include chemical spills, pesticides, cleaning agents, solvents, combustion products, medications and medical devices, and indoor air contaminants associated with materials used in construction or remodeling.⁵⁻⁸

Despite a relatively high population prevalence rate, CI often goes undiagnosed in routine primary care. Part of the challenge physician's face is that current diagnostic tools are too long and cumbersome to use routinely in primary care. A short screening instrument is needed. We developed and tested the Brief Environmental Exposure and Sensitivity Inventory (BREESI) as a 3-item screening instrument for CI (see Appendix). The items on the BREESI are hypothesized to forecast an individual's tendency to react adversely to diverse substances representing the major exposure categories (chemicals, foods, and drugs) on the Quick Environmental Exposure and Sensitivity Inventory (QEESI). The BREESI's three questions rapidly determine who should take the QEESI for a definitive classification for CI.

The QEESI is a validated 50-item, self-administrable questionnaire geared toward differentiating individuals with CI from the general population.⁸⁻¹⁰ The QEESI is now considered the standard for measuring CI and has been used in over a dozen countries around the world.¹¹⁻¹⁴ The BREESI would be useful for rapidly determining potential CI in primary care and other health care settings, as well as for epidemiologists and other researchers seeking a brief sensitive screening tool to assess CI.

This manuscript reports the positive and negative predictive value of the BREESI as a predictor of CI when compared to the QEESI.

Methods

Sample: Participants in this study were respondents of The Marilynn Brachman Hoffman TILT program (www.TILTresearch.org), an environmental health research project designed to improve health outcomes of individuals with CI by identifying environmental triggers in the home, and then providing best practices for reducing these triggers. Participants needed to be at least 18 years old.

Approached by a research nurse or project staff, 173 respondents completed the BREESI and QEESI in the waiting room of a busy family practice clinic. An additional 113 respondents completed the surveys online at our web site. IRB-approved informed consent was obtained in person for the clinic participants and collected digitally for the online participants.

QEESI Scores. The instrument has 4 scales: Symptom Severity, Chemical Intolerances, Other Intolerances, and Life Impact. Each scale contains 10 items (0 = "not a problem" to 10 = "severe or disabling problem."

Each scale ranges from 0–100. There is also a 10-item Masking Index which gauges ongoing exposures (such as caffeine or tobacco use) that may affect individuals’ awareness of their intolerances as well as the intensity of their responses to environmental exposures ^{9,10}.

Three classifications for CI are based on the QEESI Chemical Intolerance and Symptom Scales. Those scoring greater than or equal to 40 on each scale are very suggestive of CI. Scores less than 40 and greater than or equal to 20 are classified as suggestive of having CI, and scores less than 20 are not suggestive of CI ^{9,10}

Statistical analysis: To determine the predictive value of the BREESI, we calculated the positive and negative predictive values of the three BREESI items against the validated QEESI ranges. Sensitivity and Specificity of the BREESI were also calculated. Potential confounding variables were investigated using a multivariate logistic regression model. Odds-ratios, the c-statistic and 95% confidence intervals are reported for the BREESI as a predictor of CI. All analysis was conducted using SAS statistical Software¹⁵.

Results

No gender differences were found between online versus clinic participants. However online participants tended to be slightly older (53 versus 47 years old, $p < .002$). There was a slightly higher percentage of those categorized as very suggestive of CI among internet participants (47%) compared to in person participants (25.4%). Table 1 shows the age, gender, and internet comparisons by CI category. While there were statistically significant age, gender, and internet participant differences across CI categories ($P < .01$), female gender predominates all categories of CI. Also shown are the means of the QEESI chemical and symptom scores which were used to classify the CI categories.

Table 1
Characteristics of study sample by group.

	Very Suggestive of CI N = 98	Suggestive of CI N = 98	Not Suggestive of CI N = 90
	Mean (SD) or percentage	Mean (SD) or percentage	Mean (SD) or percentage
% Female within category	87.6%	73.6%	63.3%
% Internet participant	47.8%	10.6%	42%
Age	54.7 (10.6)	50.7 (13.1)	41.1 (15.3)
QEESI Scores	73.1 (16.2)	32.1(18.9)	5.1 (4.8)
Chemical Intolerances	68.4 (15.2)	30.0(15.8)	4.4 (5.1)
Symptom Severity			

Response rates for the total sample on the individual BREESI items were as follows: 25.9% (n = 74) of the 286 participants did not endorse any item; 27.3% (n = 78) endorsed one item; 23.4% (n = 64) endorsed two items; 24.5% (n = 70) endorsed all three items. Table 2 shows the percentage of the sample that endorsed specific BREESI Items by the number of items chosen. The Chemical item was endorsed by 88% of those choosing only one item. Of those choosing two items, 52% choose Chemical and Food, and 42% choose Chemical and Drug, with only 6% choosing Drug and Food items.

Table 2
Percentage of Sample Choosing Specific BREESI Items.

BREESI Items			
# Items Chosen (percent, N)	Chemical 70% (199/286)	Foods 40% (113/286)	Drugs 36% (104/286)
0 (26%, 74/286)	-	-	-
1 (27%, 78/286)	88% (69/78)	8% (6/78)	4% (3/78)
2 (23%, 64/286)	Chemical and food 52% (33/64)	Chemical and Drug 42% (27/64)	Drug and Food item 6% (4/64)
3 (24%, 70/286)	-	-	-

As shown in Fig. 1, 90% of participants answering “yes” to all three items on the BREESI were classified as very suggestive of CI based upon the QEESI chemical intolerance and symptom scores both ≥ 40 (positive predictive value = 90%). For participants endorsing two items, 92% were classified as either very suggestive (39%) or Suggestive (53%) of CI (positive predictive value = 87%). Of those endorsing only one item, only 13% were found to be very suggestive of CI. However, 70% were classified as Suggestive. Of those answering “No” to all of the BREESI items, 99% were classified as not suggestive of CI (i.e., negative predictive value = 99%).

A logistic regression model was used to assess the odds of being very suggestive of CI based on the responses of the BREESI. In an unadjusted model with only the BREESI as a predictor, there is a 12 fold increase in the probability of CI with each addition item chose on the BREESI (Odds Ratio = 11.97, 95% Confidence Interval = 6.6–21.6, $p < .0001$). The concordance statistic (c) indicates the ability of the BREESI to discriminate CI from non-CI respondents. The c statistic was .951 (95% CI = 90.3–96.9; calculated using the method of Delong et al.¹⁶, indicating that 95% of the time the model is able to correctly sort the respondents as very suggestive of CI as a function of BREESI scores.

The results of the logistic model adjusted for age, gender and online versus clinic participation) were Odds Ratio = 10.63, 95% Confidence Interval = 5.8–19.4, $p < .0001$. Of the covariates, only Age was statistically significant (OR = 1.04, 95% CI = 1.01–1.08, $p < .03$). The other covariates in the model were not significant, indicating that they are not independent predictors of CI given the responses on the BREESI. .

Discussion

This study is the first to evaluate a short screener for CI. Our analysis indicates that the BREESI possesses excellent positive and negative predictive validity with the QEESI and may be ideal for quickly determining potential CI in a range of health care settings and for epidemiological studies. While these findings appear robust, further replication of the BREESI's performance is needed in other population samples to further establish validity.

Notwithstanding, we highly recommend that anyone endorsing any one of the three items on the BREESI should take the full QEESI to specifically identify intolerances and confirm CI. From Table 2, it appears that endorsing the intolerance to chemical item is by far the most salient.

The BREESI is not a substitute for the QEESI but rather a time-saving tool to identify individuals with CI in medical clinics or epidemiological studies. Identifying those who are, or are not, likely to have CI with a highly sensitive screening tool greatly reduces clinical assessment time. In this regard, the BREESI may be particularly useful for researchers, clinicians, and workplace or community investigations.

In the past, there has not been a widely agreed-upon case definition for the diverse symptoms and conditions related to CI. For decades, this lack of consensus has thwarted research on CI, just as the lack of consensus regarding a case definition for "Gulf War Illness" has impeded research.¹⁷ Clinicians today have difficulty diagnosing TILT-related conditions because there has not been training regarding this disease mechanism in medical schools. Physicians who could benefit from using the BREESI include most primary care clinicians, allergists, occupational medicine doctors, psychologists, and psychiatrists. These clinicians commonly see patients with multi-system health complaints, cognitive confusion, fatigue, and depression. They could use the BREESI and QEESI to help them and their patients identify CI and avoid or minimize many illness triggers.

Exposures that may initiate TILT in susceptible individuals include oil spills, chemical releases, fracking, burn pits, as well as exposure events such as the EPA's sick building episode and the World Trade Center disaster. In addition to these major events, everyday exposures to pesticides, fragrances personal care or other fragranced products can initiate or trigger TILT. Clinicians and epidemiologists who work with exposed individuals or communities need to be conversant with the two-stage TILT disease mechanism if they hope to make sense of the seemingly unrelated health problems these individuals report. It is all too easy to dismiss TILT's physiological effects as being the result of stress or psychosomatic effects. "Too many symptoms in too many organ systems" frustrates clinicians and patients alike. Of course, TILT and stress can and do occur simultaneously. Stress can accompany any illness. However, it is important to recognize that usual medications prescribed for stress, such as antidepressants or anxiolytics, may exacerbate symptoms of TILT. When patients report myriad symptoms in multiple organ systems and complain of ineffective or adverse treatment outcomes, clinicians, patients, and families understandably may become frustrated and give up on one another.

How can clinicians differentiate TILT from “stress”? It is the new-onset (or marked worsening) of chemical, food and drug intolerances that are the hallmark symptoms of TILT— much as fever is a hallmark of infection whose presence always requires a careful work-up, including exposure histories and laboratory testing to rule out alternative explanations. Currently, there are no validated diagnostic tests for CI— except removing individuals from suspected exposures and a judicious reintroduction of triggers, optimally to occur within the confines of an Environmental Medical Unit (EMU).¹⁸ Indeed, most medical conditions recognized today initially suffered this same historical diagnostic dilemma, e.g., lupus, diabetes, HIV, stroke, and depression.

Although TILT and stress can occur simultaneously, the 3-item BREESI screener enables physicians and researchers to screen for chemical, food, and drug intolerances. Coupled with a detailed exposure history, the QEESI can assist in diagnosing TILT. Individuals answering “yes” to any one of the three BREESI screening questions, should undergo further evaluation using the 50-item QEESI. The QEESI’s four scales and masking index, provide a reasonably comprehensive overview of each person’s symptoms, intolerances, and the life impact of their illness (www.TILTresearch.org).

An especially useful feature of the QEESI is the “Symptom Star,” which is readily generated by graphing the 0–10 symptom severities from the QEESI on a 10-point ‘target’ diagram (see Fig. 2)¹⁸. When filled out in the patient’s presence, the Symptom Star enhances doctor-patient communication and helps assure patients that their concerns have been heard. The Symptom Star is similarly helpful for depicting changes in symptoms following an exposure event, as well as responses to interventions or treatments in individual patients, or in groups for research purposes¹⁹

The QEESI Symptom Star is shown in Fig. 2. This illustrates symptom severity in an individual before and after an exposure event (e.g., pesticide application, indoor air contaminants, chemical spills). Terms: HEAD = head-related symptoms; COG = cognitive symptoms; AFF = affective symptoms; NM = neuromuscular symptoms; MS = musculoskeletal symptoms; SKIN = skin-related symptoms; GU = genitourinary symptoms; GI = gastrointestinal symptoms; COR = heart/chest-related symptoms; AIR/MM = airway or mucous membrane symptoms; (•) before exposure event; (●) after exposure event. Two good examples of how the Symptom Star has been used in patient care are demonstrated in case reports by Yun et al.,²⁰ Imai and Imai²¹

Three potential uses for the QEESI include: (1) Research – to characterize and compare study populations, and to select subjects and controls; (2) Clinical Evaluations – to obtain a profile of patients’ self-reported symptoms and intolerances. The QEESI can be used at intervals to follow symptoms over time or to document responses to treatments or exposure avoidance; (3) Workplace, Community, or Epidemiological Investigations – to identify and assist those who may be more chemically susceptible or who report new intolerances. Affected individuals should have the option of discussing results with investigators or their personal physicians.

The BREESI can be administered in less than 1 minute and the QEESI can be completed in 10–15 minutes. Previously, tallying symptoms and symptom severities, as well as taking detailed exposure histories, could take hours—detering some clinicians from seeing patients with CI.

Our assessment tools can help identify susceptible individuals, even without knowing the specific disease mechanism and in the absence of any biomarker. TILT is observed worldwide following a broad spectrum of synthetic/petrochemical exposures since WWII (past 75 years). The increased recognition of TILT demands more research on the CI disease process and the taking down of silos between scientific domains and eliminating interdisciplinary barriers.

TILT is a viable disease mechanism initiated and triggered by environmental exposures (chemicals, foods, and drugs) involving prominent neurological symptoms, which are not necessarily psychogenic in nature. TILT provides a unifying explanation for the myriad symptoms clinicians see today.^{4, 6, 7, 22, 23}

Historically, new theories of disease arose when physicians observed patterns of illness that did not fit accepted explanations for disease at that time, for example, the germ or immune theory of disease. Similarly, CI does not conform to current accepted explanations for disease or toxicity because there is not yet a known physiological mechanism to explain chemical intolerance; no biomarker has been identified; and avoidance of chemical, food, and drug triggers is difficult and often impractical.

Conclusion

Chemical intolerance has been reported to be in 1 of 5 primary care patients, yet is often missed by busy practitioners⁴. The BREESI is a useful screening tool for rapidly determining potential CI, with clinical and epidemiological applications. Implementation of the BREESI screener in primary care and specialty clinics for patients with undifferentiated, multi-system complaints, coupled with the QEESI, can help identify and improve outcomes for those suffering from TILT. Symptoms may resolve or improve with the avoidance of salient chemical, dietary (including caffeine and alcohol), and drug triggers. Given greater medication intolerances in chemical intolerance, primary care clinicians could use the BREESI and QEESI to identify patients for potentially appropriate triage to comprehensive nonpharmacologic care.

Declarations

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Availability of data and materials

The raw data used to calculate the results are stored at the Department of Family & Community Medicine at the University of Texas Health Science Center San Antonio. The de-identified dataset analyzed in the current study can be available by contacting the corresponding author for permission.

Authors' contributions

RFP, CRJ, RBP, RR, JV and CSM designed the study. RFP carried out the data analysis. RFP and CSM wrote the first version of the article, which was then revised by all the authors. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the University of Texas Health Science Center San Antonio Internal Review Board (approval number HSC20150821H). Written informed consent was obtained from all participants in clinical setting and electronic consent was obtained for online participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no conflict of interest.

Abbreviations

Chemical Intolerance (CI)

Quick Environmental Exposure and Sensitivity Inventory (QEESI)

Toxicant-Induced Loss of Tolerance (TILT)

Brief Environmental Exposure and Sensitivity Inventory (BREESI)

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Figures

Number of Items Endorsed on the BREESI versus QEESI Chemical Intolerance Category (N = 286)

Figure 1

Number of Items endorsed on the BREESI Versus QEESI chemical intolerance category

Figure 2

QEEG Symptom Star.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [AppendixBREESI.docx](#)