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ROUTINE TEST MANAGEMENT POLICY – 15.01.036

Diagnosis of Idiopathic Environmental Intolerance

Ref. Policy:	G2056	
Effective Date:	Feb. 6, 2026	RELATED POLICIES:
Last Revised:	Oct. 14, 2025	15.01.041 Intracellular Micronutrient Analysis
Replaces:	N/A	

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Policy Description

Idiopathic environmental intolerance (IEI), formerly called multiple chemical sensitivity (MCS), is a subjective condition characterized by recurrent, nonspecific symptoms attributed to low levels of chemical, biologic, or physical agents in the absence of consistent objective diagnostic physical findings or laboratory tests that define an illness (AAAAI, 1999; ACOEM, 1999; Black & Temple, 2024).

Indications

The following is **not reimbursable** due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

1. In all circumstances, laboratory tests designed to confirm the diagnosis of idiopathic environmental intolerance is **not reimbursable**.
2. In all circumstances, the screening of blood, saliva, serum, plasma, urine, and/or stool samples for volatile solvents, organic acids, and organophosphates is **not reimbursable**.
3. In all circumstances, profiling of phthalates and parabens using a blood, serum, plasma, saliva, urine, and/or stool sample is **not reimbursable**.
4. For asymptomatic individuals, profiling of chlorinated pesticides, including DDE and DDT, using a blood, serum, plasma, saliva, urine, and/or stool sample is **not reimbursable**.

5. In asymptomatic individuals and/or during general encounters without abnormal findings, testing of blood, serum, plasma, saliva, urine, and/or stool samples for carnitine sufficiency, oxidative stress and antioxidant sufficiency, detoxification adequacy, methylation sufficiency status, lipoic acid and CoQ10 sufficiency, and/or intestinal hyperpermeability is **not reimbursable**.
6. In asymptomatic individuals and/or during general encounters without abnormal findings, testing of blood, serum, plasma, saliva, urine, and/or stool samples for vitamin sufficiency, mineral sufficiency, and/or nutritional analysis is **not reimbursable**.
7. The use of a breath hydrogen and/or breath methane test to assess or diagnose the following conditions is **not reimbursable**:

    a. Idiopathic environmental intolerance.
    b. Food allergies and sensitivities.
    c. Carbohydrate sensitivity or intolerance.
    d. Digestive disorders.
    e. Constipation, diarrhea, or flatulence.
    f. Neurological/neuromuscular disorders.
    g. Rosacea.
    h. Obesity.
    i. As part of a wellness visit and/or general encounter without abnormal findings.

8. In asymptomatic individuals and/or during general encounters without abnormal findings, testing of blood, serum, urine, cerebrospinal fluid, fingernails, hair, and/or stool sample for metals is **not reimbursable**.

Coding

Code	Description
CPT	
82108	Aluminum
82127	Amino acids; single, qualitative, each specimen
82136	Amino acids, 2 to 5 amino acids, quantitative, each specimen
82139	Amino acids, 6 or more amino acids, quantitative, each specimen
82300	Cadmium
82379	Carnitine (total and free), quantitative, each specimen
82380	Carotene

Code	Description
82441	Chlorinated hydrocarbons, screen
82495	Chromium
82507	Citrate
82525	Copper
82542	Column chromatography, includes mass spectrometry, if performed (eg, HPLC, LC, LC/MS, LC/MS-MS, GC, GC/MS-MS, GC/MS, HPLC/MS), non-drug analyte(s) not elsewhere specified, qualitative or quantitative, each specimen
82653	Elastase, pancreatic (EL-1), fecal; quantitative
82656	Elastase, pancreatic (EL-1), fecal, qualitative or semi-quantitative
82705	Fat or lipids, feces; qualitative
82710	Fat or lipids, feces; quantitative
82715	Fat differential, feces, quantitative
82726	Very long chain fatty acids
82978	Glutathione
83015	Heavy metal (eg, arsenic, barium, beryllium, bismuth, antimony, mercury); qualitative, any number of analytes
83018	Heavy metal (eg, arsenic, barium, beryllium, bismuth, antimony, mercury); quantitative, each, not elsewhere specified
83150	Homovanillic acid (HVA)
83497	Hydroxyindolacetic acid, 5-(HIAA)
83735	Magnesium
83785	Manganese
83885	Nickel
83918	Organic acids; total, quantitative, each specimen
83919	Organic acids; qualitative, each specimen
83921	Organic acid, single, quantitative
84134	Prealbumin
84255	Selenium
84446	Tocopherol alpha (Vitamin E)

Code	Description
84585	Vanillylmandelic acid (VMA), urine
84590	Vitamin A
84600	Volatiles (eg, acetic anhydride, diethylether)
84630	Zinc
86001	Allergen specific IgG quantitative or semiquantitative, each allergen
86353	Lymphocyte transformation, mitogen (phytomitogen) or antigen induced blastogenesis
89125	Fat stain, feces, urine, or respiratory secretions
91065	Breath hydrogen or methane test (eg, for detection of lactase deficiency, fructose intolerance, bacterial overgrowth, or oro-cecal gastrointestinal transit)
S3708	Gastrointestinal fat absorption study

Related Information

Table of Terminology

Term	Definition
5-HIAA	5-hydroxyindolacetic acid
AAAAI	American College of Physicians and the American Academy of Allergy and Immunology
ACOEM	American College of Occupational and Environmental Medicine
ACP	American College of Physicians
AMA	American Medical Association
ANA	Antinuclear antibodies
AND	The Academy of Nutrition and Dietetics
ANSES	French Agency for Food, Environmental and Occupational Health & Safety
BPA	Bisphenol A
BT	Breath test
CDSA	Comprehensive digestive stool analysis
CLIA '88	'88 Clinical Laboratory Improvement Amendments of 1988
CH4	Methane

Term	Definition
CMS	Centers for Medicare and Medicaid Services
CoQ10	Coenzyme Q10/ubiquinone-10
DAO	Enzyme diamine oxidase
DDE	Dichlorodiphenyldichloroethylene
DDT	Dichlorodiphenyltrichloroethane
DEDTP	Diethydithiophosphate
DETP	Diethylthiophosphate
DMDTP	Dimethyldithiophosphate
DMTP	Dimethylthiophosphate
DNMCC	Does not meet coverage criteria
EESI	Environmental exposure and sensitivity intolerance
EHS	Electromagnetic hypersensitivity
EL-1	Elastase (pancreatic)
ESPGHAN	European Society for Pediatric Gastroenterology, Hepatology, and Nutrition
FDA	Food and Drug Administration
FMV	First morning void
GC	Gas chromatography
GHBT	Glucose hydrogen breath tests
GI	Gastrointestinal
HPLC	High performance liquid chromatography
HVA	Homovanillic acid
H2	Hydrogen
IBS	Irritable bowel syndrome
IEI	Idiopathic environmental intolerance
IEI-EMF	Idiopathic environmental intolerance attributed to electromagnetic fields
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IQR	Interquartile ranges
LBT	Lactulose breath test
LC	Liquid chromatography

Term	Definition
LDTs	Laboratory-developed tests
LHBT	Lactulose hydrogen breath test
MCS	Multiple chemical sensitivity
MS	Mass spectrometry
NASPGHAN	North American Society for Pediatric Gastroenterology, Hepatology and Nutrition
ONE	Optimal nutritional evaluation
PCBs	Polychlorinated biphenyls
PHQ-9	Patient Health Questionnaire-9
SIBO	Small intestinal bacterial overgrowth
VMA	Vanillylmandelic acid
WHO	World Health Organization

Evidence Review

Scientific Background

Patients with idiopathic environmental intolerance (IEI) typically report sensitivity to multiple, chemically unrelated substances and become ill due to a wide range of nonspecific symptoms when exposed. Symptoms may include anxiety, shortness of breath, chest pain, and more. Psychiatric disorders may also be at the core of the IEI patient. The mean age of patients reporting IEI is between 30 and 40 years and individuals who are married are significantly more likely to be diagnosed with IEI than those who are not. IEI also occurs in 40% of people with chronic fatigue syndrome and in 16% of people with fibromyalgia (Black & Temple, 2024; Black et al., 2024).

The symptoms of IEI are nonspecific, ambiguous and common in the general population. There is no characteristic set of symptoms and ultimately no major differences between patients self-reporting IEI and those that do not. Virtually any symptom can be considered a symptom of IEI (Black & Temple, 2024). Within the definition of multiple chemical sensitivity (MCS), identified symptoms included “asthmatic-like, skin irritation, dermatitis, migraine, dysuria, dyspepsia, symptoms of supposed sensitization to food, persistent arthromial pain, vertigo, vestibular impairment”, with 80% of patients experiencing “asthenia, arthromial pain, dyspepsia, coriza, eructation, chest pain, insomnia” (Quarato et al., 2020). The classification of IEI as a distinct medical disorder is also in question, as a lack of reliable case reports, lack of consistent findings

or laboratory results, and reliance on surveys or self-reporting all cloud the condition and understanding of this disorder (Black & Temple, 2024).

Recently, many articles have been published suggesting a relationship between electromagnetic fields and IEI. Electromagnetic fields may include radiofrequencies from telecommunication devices (Eltiti et al., 2018; Huang et al., 2018), Wi-Fi and base stations (ANSES, 2018). For an unknown reason, these individuals claim to react to the exposure of certain electromagnetic triggers that most people can tolerate without issues; these triggers are below established toxicological and hazardous thresholds. ANSES (2018) researched the relationship between electric field exposure and IEI symptoms and stated that "either the symptoms experienced by EHS [electromagnetic hypersensitivity] individuals are not caused by exposure to electromagnetic fields and there are no quantifiable biological and/or physiological abnormalities when they are exposed to electromagnetic fields (assumption one) or the absence of results is due to the methodological limitations of the provocation studies (subject selection, sample size, exposure type, etc.) (assumption two)". These findings were corroborated by Schmiedchen et al. (2019), who, in their systematic review of articles pertaining to EHS, stated, "limitations in design, conduct and analysis could therefore have given rise to either false positive for false negative results," and that the "nocebo effect or medical/mental disorders may explain the complaints in many individuals". Characteristic symptoms of EHS include sleep and circadian rhythm disorders, migraines and headaches, hypersensitivity, and other related syndromes and disorders such as fibromyalgia, tinnitus and MCS (ANSES, 2018).

Tests such as elimination diets, food challenges, and provocation-neutralization tests have been used to test for food or chemical sensitivities. Immunological tests or tests measuring the amount of various chemicals in body tissues have also been performed (Black & Temple, 2024). In fact, testing for a wide range of autoantibodies is generally discouraged, as "pretest probability is low, and false-positive results are far more likely than true-positive results; a weakly positive ANA [antinuclear antibodies] is present in about 20% of the population" (Black & Temple, 2024). However, these assessments are typically not rigorous enough to provide strong evidence; for example, these tests are often not performed blinded or with placebo controls. No unusual laboratory findings have been reliably linked to IEI (Black & Temple, 2024). Due to the vast number of causes, symptoms, responses, and general heterogeneity of this condition, it may be very difficult to provide a scientifically valid or useful test. Worse, testing may even exacerbate or increase the number of symptoms of a patient. Physicians should use caution in testing for reassurance of patients as negative findings may increase anxiety instead (Barsky & Borus, 1999; Black & Temple, 2024).

Proprietary Testing

Due to the number of symptoms that may be considered part of IEI, there are a corresponding number of tests performed. These tests are generally unnecessary as the condition itself is far too ambiguous to reliably test for and any test can be ordered under the guise of IEI. For example, assessment of factors such as elastase, stool culturing, or fat differentiation may all be done for the sake of IEI treatment. These tests may have legitimate medical purposes (for instance a stool culture may be useful for numerous conditions) but their use for IEI is essentially none, as IEI itself carries no reliable characteristics to test for. Other tests that evaluate a tangentially relevant analyte, such as micronutrient panels or a lactose intolerance breath test (BT), may be done for IEI's sake as well. Since virtually any symptom or sign can be called IEI, these tests are sometimes ordered for nonspecific or subjective symptoms such as fatigue or pain. However, these tests cannot provide any useful results because of the dubious nature of IEI itself.

Another commonly used test for IEI are panels that test multiple factors in one. For example, the Triad Bloodspot Profile offered by Genova Diagnostics measures organic acid levels, "the level of IgG4 reactions for 30 common foods," and "essential amino acid imbalances" (Genova, 2021c). Genova offers several similar panels, such as the Organix Comprehensive Profile (which tests 46 analytes for subjective symptoms such as depression, weight issues and chemical sensitivities) (Genova, 2022a), the NutrEval FMV [first morning void] (which tests 118 analytes for symptoms such as fatigue, weight issues, and sports fitness optimization) (Genova, 2021a) and the Allergix IgG4 Food Antibodies (which tests 90 foods for sensitivity). Genova Diagnostics also offers the GI Effects Profile (advanced stool tests for the management of gastrointestinal [GI] health), a full line of allergy testing and assessment tests (measuring IgG and IgE food antibodies, inhalants, molds and spices), the Ion Profile (which evaluates various types of organic, amino and fatty acids as well as nutrient and toxic elements), the Comprehensive Digestive Stool Analysis (CDSA) 2.0 Profile with Parasitology (evaluates the microbiome, digestion and absorption), and SIBO Profile tests (breath tests which measure methane gases and exhaled hydrogen) (Genova, 2022b).

The hydrogen breath test is used to assess lactose malabsorption. After ingesting a lactose solution, serial breath samples are taken to determine hydrogen levels. Lactose should be used in amounts ranging from 25 to 50 g for those aged 18 and up. There is no current consensus on the lactose dosage in children, with estimates ranging from 0.5 to 2 g/kg lactose suspended in water to a maximum of 25 to 50 g. Proper test performance needs the following: Cigarette smoking or physical activity that causes hyperventilation should be avoided for two hours before testing, since it can reduce test accuracy. Complex carbs (i.e. bread, pasta, and fiber) and dairy should be avoided for 12 hours before testing. Antibiotics should be avoided four weeks before testing. Colonic cleaning for endoscopic or surgical procedures should be avoided for at least

two weeks before testing. The suggested test time is three to five hours; it may be completed sooner if a positive diagnosis of malabsorption is confirmed with the standard measuring interval for determining malabsorption being 30 minutes. However, longer intervals of up to 60 minutes might be appropriate (Hammer & Högenauer, 2024).

An evaluation of symptoms of IEI patients includes a history, physical examination, and laboratory tests (complete blood count, serum electrolytes and glucose, urine analysis) with further testing guided by reported symptoms. An occupational or environmental history is also useful as patients typically report problems from chemical exposure (Black & Temple, 2024). A questionnaire such as the "Environmental Exposure and Sensitivity Intolerance" (EESI) may be used for an initial screening (Rossi & Pitidis, 2018). A psychiatric history is also recommended as psychiatric disorders are often co-morbid with IEI. A screening questionnaire such as the Patient Health Questionnaire (PHQ-9) can be used to identify psychiatric conditions in an IEI patient (Black & Temple, 2024; Gilbody et al., 2007).

Micronutrients are the essential vitamins and minerals required by the body for proper functioning. Panels have been developed which evaluate intracellular levels of essential vitamins and minerals. These panels may also be used on IEI patients. This may help to identify nutritional deficiencies in otherwise healthy patients or in patients suffering from some type of disease. SpectraCell Laboratories have developed the Micronutrient Test Panel, which is able to measure 31 vitamins, minerals, metabolites, amino acids, fatty acids and antioxidants; this test also measures how these micronutrients affect cellular functioning in an individual (SpectaCell, 2024). SpectraCell Laboratories have also developed the SPECTROX, claiming it measures total antioxidant function in an individual, reporting on the repair mechanisms and net ability of each individual's cells (SpectraCell, 2008). As noted above, Genova Diagnostics has developed the NutrEval FMV that measures 118 markers, including amino acids, fatty acids and organic acids (Genova, 2021a). ONE (Optimal Nutritional Evaluation) FMV, also by Genova Diagnostics, is a urine-based nutritional test which assesses "the functional need for antioxidants, B-vitamins, minerals, digestive support and amino acids" (Genova, 2021b). The company notes that the ONE FMV test may be used for patients with mood disorders, fatigue, digestive issues, weight problems, general health, dietary guidance and fitness. Another nutrient panel blood test, developed by Life Extension, measures vitamin B12, folate, vitamin D 25-hydroxy, vitamin A, vitamin C, selenium, zinc, CoQ10 (coenzyme Q10) and magnesium (LifeExtension, 2024). Finally, Vibrant America provides a test which measures approximately 40 intracellular and extracellular vitamins, minerals, fatty acids, amino acids and antioxidants (Vibrant, 2017).

Clinical Utility and Validity

Very little information suggests that the intracellular micronutrient analysis assists with positive health outcomes. Houston (2013) published an article on the role of vitamins, minerals and

overall nutrition in the prevention and treatment of hypertension. This article reviewed hypertension-related clinical trials that include information on the "efficacy of nutrition, weight loss, exercise, and nutritional supplements, vitamins, minerals, and antioxidants" (Houston, 2013). Approximately 3338 individuals were treated with micronutrient testing over a five-year period, with 20% of these patients exhibiting abnormally high blood pressure. After six months, 62% of the hypertensive patients reached lower blood pressure goals. Hence, the author states that the diagnosis and treatment of various nutritional deficiencies can decrease the number of cardiac events as well as reduce blood pressure and improve vascular biology. However, data for the control group not treated with micronutrients was not provided for comparison.

Another technique that has been used to assess nutritional status is the measurement of the hepatic proteins prealbumin and albumin. However, it seems that a physical examination has evolved as the main technique to diagnose malnutrition in a clinical setting. "The current consensus is that laboratory markers are not reliable by themselves but could be used as a complement to a thorough physical examination" in a malnutrition diagnosis (Bharadwaj et al., 2016). The Academy of Nutrition and Dietetics (AND) also do not accept albumin and prealbumin as a diagnostic tool for malnutrition and state that "there is no laboratory test that is both sensitive to and specific for protein-calorie malnutrition" (AND, 2017).

Idiopathic environmental intolerance patients may also report bowel irritability. Small intestinal bacterial overgrowth (SIBO) occurs when excessive aerobic and anaerobic bacteria colonize the small intestine; these bacteria are not typically found in the colon and can cause chronic diarrhea and malabsorption (Pimentel, 2024). SIBO may be diagnosed by a breath test. However, a validated gold standard method for diagnosing SIBO has not been indicated (Rezaie et al., 2017).

The SIBO breath test uses carbohydrates in a simple, non-invasive and widely available testing method. A carbohydrate substrate (such as lactulose or glucose) is administered to the patient, which leads to the production of an analyte such as hydrogen or methane. "In individuals without SIBO, the administration of lactulose results in a single peak in breath hydrogen/methane within two to three hours due to the metabolism of lactulose by colonic flora. In patients with SIBO, administration of lactulose results in an early peak in breath hydrogen/methane levels due to metabolism by small bowel bacteria" (Pimentel, 2024). As noted above, Genova Diagnostics has developed the SIBO Profile test which is a two or three hour breath test that measures methane gases and exhaled hydrogen (Genova, 2022b). This test requires the patient to ingest a lactulose solution. "There are several limitations to breath tests as diagnostic test for SIBO. Rapid delivery of the test substrate to the colon (eg, in patients with short bowel syndrome) may lead to false-positive results, while gastrointestinal disorders where gastric emptying is delayed may cause a false-negative test. In general, the sensitivity and

specificity of the breath test are low, and there is a poor correlation between the breath test and the small bowel aspiration and culture method" (Pimentel, 2024).

De Geyter et al. (2021) investigated individuals below the age of 18 years that had symptoms suggesting lactose intolerance. The study's goal is to assess the value of measuring both H2 and CH4 in the diagnosis of lactose intolerance. The study comprised 209 individuals under the age of 18, with the average age being 8.3 years, who had symptoms of lactose intolerance and were tested with lactose H2 and CH4 breath test. Over 90% experienced gastrointestinal issues, namely cramping or stomach discomfort, flatulence, bloating, and diarrhea. Ninety-six individuals (46%) in this group tested positive for H2 in their breath. A positive H2 breath test revealed lactose malabsorption in 46% of people under the age of 18. Significantly more CH4 producers were present in the group of H2 producers (5.7 vs. 14.8%; CHI square < 0.001), supporting the idea that high levels of H2 are required for CH4 creation. Six of the ten patients who excreted large quantities of CH4 (>20 ppm over baseline) also tested positive for the H2 test. Almost 15% of those with a positive H2 breath test (>20 ppm above baseline) also tested positive for CH4. The study found considerable CH4 generation in 5.7% of patients with a negative H2 test (De Geyter et al., 2021; Geyter et al., 2021).

Bratten et al. (2008) completed a study with 224 individuals with irritable bowel syndrome (IBS) and 40 controls. A lactulose breath test (LBT) was used to measure methane and hydrogen production to identify patients with IBS. Results showed that "The majority of patients with IBS and healthy subjects meet criteria for an "abnormal" LBT using previously published test criteria, and groups are not discriminated using this diagnostic method" (Bratten et al., 2008). The authors then questioned the utility of an LBT to diagnose IBS as the testing did not discriminate between IBS patients and healthy controls. A more recent study by Ghoshal et al. (2014) evaluated 80 patients with IBS for SIBO. Culture had previously diagnosed 15/80 patients with SIBO. Both lactulose and glucose hydrogen breath tests (LHBT and GHBT, respectively) were used to measure SIBO. The authors conclude that "the specificity of GHBT was 100%, but the sensitivity of this test and the diagnostic performances of LHBT and breath methane were all very poor" (Ghoshal et al., 2014).

Speck and Witthöft (2022) included 410 patients in a cross-sectional study design to investigate the relationship between IEI symptoms associated with chemicals and schizotypy spectrum. They found that "schizotypal traits were found to be significantly positively associated with [modern health worries], [chemical odor sensitivity]…, and showed significant positive associations with hallucination proneness. Magical thinking was found to exhibit a significant positive relationship with both [modern health worries] and [chemical odor sensitivity]." This demonstrates how the principles surrounding IEI may need to consider associated psychiatric differential diagnoses to properly evaluate symptoms and testing. Finding that patients have symptoms of chemical odor

sensitivity and modern health worries can also conversely encourage further insight into the mental wellness of a patient.

Madigan et al. (2022) investigated the relationship between SIBO caused by Archaea and certain clinical symptoms. Archaea are anaerobic bacteria that produce methane specifically. Through a retrospective cross-sectional study, the researchers used glucose breath tests conducted for SIBO to correlate the bacteria to their phenotypic manifestations. From 1461 patients, they found that 33.1% were SIBO positive, with 38.8% producing only methane, 11.4% producing both methane and hydrogen, and 49.8% with hydrogen only producing organisms. Methane-producing SIBO patients had an increased odds of experiencing constipation and gassiness in comparison to SIBO(-) patients. On the other hand, hydrogen-producing SIBO patients had several "significant factors": "vitamin B12 deficiency (odds ratio, 1.44; CI, 1.01–2.06; P = .046), [Roux-en-Y Bypass] (odds ratio, 2.14; CI, 1.09–4.18; P = .027), cholecystectomy(odds ratio, 1.42; CI, 1.06–1.91; P = .020), , and diabetes (odds ratio, 1.59; CI, 1.13–2.24; P = .008)." However, when comparing methane-producing SIBO versus hydrogen-producing SIBO patients, "vitamin B12 deficiency was the only factor that reached significant (OR 0.57; CI, 0.34-0.97; P = 0.038), indicating that [methane-producing SIBO] patients were almost half as likely to report cobalamin deficiency." This study demonstrated the implications of varying gas producing organisms in SIBO and the clinical symptoms that can affect treatment and prognosis, solely by extrapolating data from breath tests (Madigan et al., 2022).

Rangan et al. (2022) conducted a review to investigate the clinical utility and drawbacks of SIBO breath testing. They identified that the "variability in oral-cecal transit time" was the biggest limitation in breath testing, and that it greatly contributed to common false-positive test results. This theoretically results from lactulose fermentation by normal colonic flora versus invasive microbial flora. In comparing the specificity and sensitivity for lactulose breath testing versus glucose breath testing, it was found that the former had a sensitivity of 42.0% and specificity of 70.6%, whereas the latter had a sensitivity of 54.5% and a specificity of 83.2%. However, those with a positive lactulose breath test result were more likely to respond to rifaximin therapy, thereby implying greater clinical utility. Despite the controversies in the substrates for testing, the researchers state that "notably, however, clinical symptoms have also been shown to be nonspecific for diagnosing SIBO, and thus breath testing remains a useful diagnostic tool in managing those patients with compatible symptoms and an absence of another diagnosis on endoscopy or imaging, particularly if there are other underlying conditions that could predispose to SIBO" (Rangan et al., 2022).

Bushyhead and Quigley (2022) corroborates the technical difficulties and clinical utility of SIBO breath testing discussed in the two studies mentioned above. In their review, they state that breath testing is less invasive and inexpensive relative to small bowel culture-based diagnoses. However, there is no solidified association between methanogenic overgrowth and

gastrointestinal symptoms like constipation, as the "positive breath test for methane may be due to methane production by resident anaerobic colonic methanogens rather than small bowel flora." They also concur on the idea that "an important factor that may confound the interpretation of lactulose breath tests… is orocecal transit time…It is also possible that glucose malabsorption, which may be more prevalent than previously considered, could lead to a positive glucose breath test. Prior upper GI surgery could also contribute to accelerated orocecal transit of glucose; conversely, those with constipation and preformed gas can confound more test results." The variability and contamination limit the diagnostic utility of breath testing in the setting of SIBO (Bushyhead & Quigley, 2022).

Usai-Satta et al. (2021) conducted a literature review to study the usefulness of breath tests (BTs) in the nutritional management of abdominal pain, bloating, and diarrhea. The authors note that while BTs are inexpensive and can be simple to preform, there is a lack of standardization in the indications, preparation, performance, and interpretation of testing which results in "considerable heterogeneity between different centers and practitioners." For the management of lactose malabsorption and intolerance, lactose BTs have "good sensitivity and optimal specificity," but are not accurate enough for a diagnosis. "An accurate diagnosis of lactose intolerance should require blind lactose challenge although this method is difficult to utilize in clinical practice." For the management of fructose malabsorption, there is "no gold standard available for fructose BT" and the authors found no significant validation studies to support the use of fructose BT. Similarly, for sorbitol malabsorption, there is no gold standard and no validation studies for the use of sorbitol BT. There are limited studies of BTs used for other carbohydrates including trehalose, maltitol, and sucrose, but there is "no sufficient evidence is available to recommend BTs related to these carbohydrates in clinical practice." The authors concluded that "blind sugar challenge remains the most valid technique to objectively demonstrate a clinical intolerance to carbohydrates" (Usai-Satta et al., 2021).

Guidelines and Recommendations

Due to the dubious nature of this condition, several prominent medical studies have regarded this condition with suspicion. In 1992, the American Medical Association (Anderson et al.) stated that multiple chemical sensitivity (now IEI) should not be recognized as a syndrome until accurate, reproducible, and well-controlled studies can be done (Coble et al., 1992). Other societies such as the American College of Physicians and the American Academy of Allergy and Immunology hold similar views (ACP, 1989; Anderson et al., 1986).

The American Academy of Allergy, Asthma, and Immunology (AAAAI)

In 2006, AAAAI referenced IEI in their position statement on the medical effects of mold stating that testing many nonvalidated immune based tests, as had been done to suggest an

immunologic basis for IEI (MCS), is expensive, not useful or valid, and should be discouraged (Bush et al., 2006).

American College of Occupational and Environmental Medicine (ACOEM)

In 1999, the ACOEM published a position statement that stated there have been no consistent physical findings or laboratory abnormalities in IEI (then called MCS) patients and recommended that a generalized clinical approach, such as establishing a therapeutic alliance and avoiding unnecessary tests, would be useful in the management of other nonspecific medical syndromes (ACOEM, 1999).

French Agency for Food, Environmental and Occupational Health & Safety (ANSES) Appraisal-Collective Expertise Report

An ANSES expert committee published an opinion piece regarding the expert appraisal on EHS or IEI due to electromagnetic fields. This committee IEI and therefore does not recommend any specific testing methods for this ailment, other than the psychological testing of patients (ANSES, 2018).

Consensus Document (1999)

An international document, created by 89 clinicians and researchers with broad experience in the field, aimed to establish consensus criteria for MCS. The recognition criteria of MCS set forth by this expert panel are as follows:

- Chronic condition
- Reproducible symptoms with repeated chemical exposure
- Low exposure levels cause syndrome to occur
- Removal of offending agents cause symptoms to subside
- There are responses to chemically unrelated substances ("Multiple chemical sensitivity: a 1999 consensus," 1999)

The 1999 Consensus Document is the most widely used criteria for recognition of MCS (Martini et al., 2013).

North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN)

The NASPGHAN and ESPGHAN have stated that “Clinicians should familiarize themselves with the limitations of nutritional biomarkers in the context of chronic liver disease” but do not give specific recommendations regarding nutritional laboratory testing (Mouzaki et al., 2019).

World Health Organization

The WHO published guidelines on the micronutrient intake in children with severe acute malnutrition. The guidelines recommend that the weight-for-height/weight-for-length status should be measured by clinicians to determine malnutrition. Micronutrient laboratory testing is not mentioned by the WHO (WHO, 2024).

The North American Expert Consensus Guidelines

A team of experts have published guidelines on breath tests including their use for a SIBO diagnosis. The authors have provided the following recommendations:

- "Current small bowel culture techniques are not satisfactory for the assessment of SIBO. [Quality of evidence: Low]
- If culture is considered for diagnosis of SIBO, based on the current evidence, we suggest the threshold of >10 3 c.f.u./ml for the definition of SIBO [Quality of evidence: Low]
- We suggest breath testing in the diagnosis of small intestinal bacterial overgrowth [Quality of evidence: Moderate]
- Until a true gold standard is established, we suggest breath testing in assessing the presence of antibiotic responsive microbial colonization of the gastrointestinal tract [Quality of evidence: Moderate]
- We suggest evaluating for excessive methane excretion on breath test in association with clinical constipation and slowing of gastrointestinal transit [Quality of evidence: Moderate]
- We suggest that breath testing should not be used for assessment of orocecal transit time [Quality of evidence: Moderate]
- We suggest breath testing for the diagnosis of carbohydrate maldigestion syndromes [Quality of evidence: Moderate]
- We suggest breath testing in the assessment of conditions with bloating [Quality of evidence: Low]
- We suggest that fructose and lactose breath test should be performed for at least 3 hours [Quality of evidence: Moderate]
- We suggest that the presence of bacterial overgrowth should be ruled out before performing lactose or fructose breath testing [Quality of evidence: Moderate]" (Rezaie et al., 2017).

It may be worth noting that the above recommendation of LHBT testing for SIBO was publicly criticized by Usai-Satta et al. (2018) due to high false positive rates and a low sensitivity. The authors state that "in our opinion, LHBT should be neither recommended nor suggested to detect SIBO in the clinical practice. Despite a low sensitivity, Glucose BT [breath test] remains the most accurate BT for non-invasive diagnosis of SIBO" (Usai-Satta et al., 2018). In contrast, an article published in Gastroenterology by Baker et al. (2021) did a retroactive study, examining

how these 2017 guidelines for glucose breath testing for SIBO compared to the older, modified Rome Consensus protocols. The authors found that the more recent North American Consensus protocol showed a higher percent of individuals with SIBO because of more prevalent positive methane excretion. Another article published by Pitcher et al. (2022) provide further support for the North American Consensus protocol for SIBO testing.

The Academy of Nutrition and Dietetics

The AND note that "serum proteins such as albumin and prealbumin are not included as defining characteristics of malnutrition because evidence analysis shows that serum levels of these proteins do not change in response to changes in nutrient intake. Hepatic proteins are not indicators of nutritional status, but are rather indicators of morbidity and mortality, and recovery from acute and chronic disease" (AND, 2017).

American College of Gastroenterology (ACG)

The ACG published an update on SIBO (Small Intestinal Bacterial Overgrowth). This guideline addresses diagnostic testing and treatment options for SIBO. Their recommendations include:

- "We suggest the use of breath testing (glucose hydrogen or lactulose hydrogen) for the diagnosis of SIBO in patients with IBS (conditional (weak) recommendation, very low level of evidence)."
- "We suggest using glucose hydrogen or lactulose hydrogen breath testing for the diagnosis of SIBO in symptomatic patients with suspected motility disorders (conditional (weak) recommendation, very low level of evidence)."
- "We suggest testing for SIBO using glucose hydrogen or lactulose hydrogen breath testing in symptomatic patients (abdominal pain, gas, bloating, and/or diarrhea) with previous luminal abdominal surgery (conditional (weak) recommendation, very low level of evidence)."
- "We suggest testing for methane using glucose or lactulose breath tests to diagnose the overgrowth of methane-producing organisms (IMO) in symptomatic patients with constipation (conditional (weak) recommendation, very low level of evidence)."

The ACG also notes that although "Small bowel aspirate and culture is often considered the gold standard for the diagnosis of SIBO," there have been some preliminary studies focusing on use of nucleic acid testing to diagnose SIBO. However, the ACG remarks that "Large-scale studies are currently underway to evaluate this further" (Pimentel et al., 2020).

US Food and Drug Administration (FDA)

No specific US Food and Drug Administration (FDA) approval or clearance of a test for idiopathic environmental intolerance was found. Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the

Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the US Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

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History

Date	Comments
11/01/25	New policy, approved October 14, 2025, effective for dates of service on or after February 6, 2026, following 90-day provider notification. Add to Routine Test Management Policy section. In all circumstances, any type of testing for idiopathic environmental intolerance (IEI) is not reimbursable.

Disclaimer: This policy for routine test management is a guide in evaluating the clinical appropriateness and reimbursement methodology for lab tests. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA).

Scope: Medical policies for routine test management are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices and reimbursement methodology. Coverage and reimbursement for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.