Policy Number	**MED207.161**
Policy Effective Date	**02/15/2025**
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Hydrogen or Methane Breath Testing

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Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

This medical policy has become inactive as of the end date above. There is no current active version and this policy is not to be used for current claims adjudication or business purposes.

Hydrogen or methane breath testing **is considered experimental, investigational and/or unproven** for all indications including but not limited to the following conditions:

- Irritable bowel syndrome (IBS);
- Lactose intolerance or deficiency;
- Small intestine bacterial overgrowth (SIBO);
- Small bowel transit time/gastroparesis.

Policy Guidelines

None.

Description

Background

Hydrogen or methane breath testing is considered a non-invasive diagnostic tool used for the diagnosis and management of various gastroenterological conditions including, but not limited to the following conditions:

- Small intestinal bacterial overgrowth (SIBO): A condition in which an excessive quantity of colonic bacteria is present in the small intestine.
- Lactose intolerance or deficiency: The process in which dietary sugars are not digested normally. The most common sugar that is poorly digested is lactose, the sugar in milk. Individuals who are incapable of properly digesting lactose are referred to as lactose intolerant. Testing may also be used to diagnose digestive issues of other sugars including sucrose, fructose, and sorbitol.
- Small bowel transit time/gastroparesis: A rapid or slow passage of food through the small intestine.

Gastroenterological conditions may cause symptoms which include abdominal pain, bloating, distention, flatulence, and altered bowel function (e.g., constipation and diarrhea). (1, 2)

In clinical practice, hydrogen or methane breath tests are performed with various substrates (e.g., glucose, lactulose, fructose, sorbitol, sucrose, and inulin). Current standardization is lacking regarding indications for testing, test methodology, and interpretation of results. (2) Testing is based on the theory that part of the gas produced by colonic bacteria fermentation diffuses into the blood and is excreted by breath, where it is quantified. (3) When hydrogen and methane breath tests are given, patients drink a solution, which is a mixture of water and a carbohydrate. After drinking the substrate solution, a series of exhaled breath samples are collected. In a healthy individual, one would not expect to see any hydrogen or methane in the breath samples for about 90-120 minutes, the approximate time it takes for the substrate to travel from the small intestine to the colon where the substrate would be fed upon by bacteria, releasing hydrogen and methane gas. (4) Multiple factors can impact the validity of hydrogen and methane breath tests. Factors include but are not limited to patients who have a lack of bacterial flora, recent history of oral antibiotics, or patients with high colonic enema use. In addition, false positive results may occur due to altered sleep, mouthwash, exercise, aspirin ingestion, or smoking. Furthermore, hydrogen and methane breath tests are not recommended in infants/young children as the large lactose load could cause diarrhea resulting in dehydration if lactose intolerance is identified. (5)

Regulatory Section

Hydrogen breath tests (HBTs) are regulated as class I devices that have been cleared by the U.S. Food and Drug Administration (FDA) through the 510(k) process under product code NRH (system, breath management). These devices are designed to measure constituents of exhaled breath as an aid in the diagnosis of sugar/nutrient malabsorption and other conditions. In 2004, the Micro H2 breath monitoring device with Hydra software utility was approved for use for

screening and diagnosis of lactose malabsorption. The device consists of a hand-held hydrogen breath monitor (K033688), a personal computer and software that acquires and logs successive breath measurement data from the hydrogen monitor and then provides data analysis of the measurements. (6)

Rationale

The current evidence on the validity of lactulose breath test for the diagnosis of small intestine bacterial overgrowth (SIBO) is conflicting. In 1990, Corazza and colleagues (7) performed a microbiological analysis of jejunal aspirates in 77 patients thought to have SIBO. Results were then compared to glucose and lactulose breath tests. Sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of glucose hydrogen breath test (HBT) to diagnose SIBO was 56%, 62%, 68% and specificities of 100%, 83%, and 44%. This study demonstrates the reliability of jejunal cultures and the inadequacy of HBT in the detection of SIBO.

Ghoshal et al. (2006) performed both glucose and lactulose breath tests on 83 patients on two separate days and reported that, when the breath test was compared to the culture of small bowel aspirate, both glucose and lactulose breath tests had lower sensitivities. (8) Using aspirate culture as the gold standard, sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy of glucose HBT to diagnose SIBO were 44%, 80%, 62%, 67% and 65%, respectively; the corresponding values for lactulose HBT was 31%, 86%, 62%, 54% and 55%. The authors suggest that glucose HBT and lactulose HBT are highly specific but insensitive for the diagnosis of SIBO in malabsorption syndrome patients. The authors suggest additional validation of this test as there is a lack of uniformity of methodology when performing the test.

Waud et al. (2008) recognized there was no gold standard for detecting patients with lactose sensitivity. (9) Biochemical investigation by HBT alone detects <50% cases and breath methane and symptoms are not recorded as standard practice. The clinical value of analyzing polymorphisms (C/T13910, G/A22018) that are strongly associated with lactose sensitivity has not been established. The study enrolled 210 patients with unexplained gut and systemic symptoms and controls were challenged with 50 g lactose. Breath hydrogen and methane were measured, and symptoms recorded. All patients were genotyped for 2 polymorphisms. CC(13910)/GG(22018) was noted in 14.5%, CT(13910)/GA(22018) was noted in 39% and TT(13910)/AA(22018) was noted in 46.5%. One hundred percent of CC(13910)/GG(22018) were lactose sensitive having a breath hydrogen >20 ppm and symptoms within 6 hours. The authors determined that the HBT lacked sensitivity and specificity in other groups. There was elevated breath hydrogen in 21% of T(13910)/GA(22018) and 15% of TT(13910)/AA(22018) within 6 hours, whereas 17 and 30.9% had elevated breath methane alone. Breath methane and breath hydrogen with clinical symptoms improved sensitivity and specificity, increasing detection of lactose sensitivity in genotypes CT/GA and TT/AA from <50 to >75%. The available data suggests that asymptomatic patients with high hydrogen should be investigated for causes other than lactose sensitivity.

Lee and colleagues (2013) sought to investigate the association between irritable bowel syndrome (IBS) and methane and hydrogen on lactulose breath tests. (10) Sixty-eight IBS patients meeting the Rome III criteria for IBS, and 55 healthy controls, underwent lactulose breath test. The IBS subjects recorded gastrointestinal symptoms on a questionnaire using visual analogue scales. Lactulose breath test positivity was defined to be above 20 ppm rise of hydrogen or 10 ppm rise of methane within 90 minutes. Gas amounts produced during lactulose breath test were determined by calculating area under the curve of hydrogen and methane excretion. Symptom severity scores were not different between the lactulose breath test (+) IBS and lactulose breath test (-) IBS subjects and between methane and non-methane producers. Gas produced during lactulose breath test was not associated with IBS symptoms, except a weak correlation between total gas volume and a few IBS symptoms such as bloating, flatulence, and abdominal pain only in lactulose breath test (+) IBS. The study determined that hydrogen and methane gas on lactulose breath test is not useful for predicting the customary symptoms and subtypes of IBS.

In 2014, Saad and Chey published guidance on diagnostic tests that are used to detect lactose intolerance and it states (11) “no perfect test exists for the diagnosis of SIBO and the current gold standard, small-bowel aspiration and quantitative culture, is limited by its high cost, invasive nature, lack of standardization, sampling error, and need for dedicated infrastructure”. There are clear advantages to the simplicity of breath testing, although it is important to realize this test can be subject to misinterpretation or over-interpretation. Generally, breath testing is unable to distinguish small bowel from colonic metabolism of the substrates. This is particularly problematic for the substrates glycocholic acid, d-xylose, sorbitol, and lactulose because they are not, or incompletely, absorbed in the small bowel. A variety of clinical conditions accelerating small-bowel transit can be equally challenging on the diagnostic accuracy of breath testing regardless of the substrate. Similar to jejunal culturing, a general lack of standardization for test preparation, test performance, and, most importantly, test interpretation has made it challenging to define the true diagnostic accuracy of breath testing.

In 2015, Kurada et al. (12) recognized the need for affordable, reproducible, easy to perform specific biomarkers for the diagnosis, differentiation and stratification of IBS. Investigators reviewed and discussed medical literature on volatile organic compounds found in exhaled human breath in gastrointestinal disorders, focusing on the diagnosis and differentiation of IBS. The researchers performed a systematic search in PubMed, Medline and Scopus. Breath pentane, ethane, propane, 1-octene, 3-methylhexane, 1-decene and nitrous oxide levels were elevated ($p < 0.05$ to $p < 10(7)$) and mean breath 1nonene, (E)-2-nonene, hydrogen sulphide and methane were decreased in IBS patients compared to healthy controls ($p = 0.003$ to $p < 0.001$). A combined panel of 3 volatile organic compounds (octene, (E)-2-nonene and decene) showed the best correlation between pediatric IBS and controls (AUC 0.96). Breath condensate cytokines were higher in IBS patients compared to healthy individuals ($p < 0.008$). Breath pentane, methane, propane, isoprene, and no levels correlated with disease activity in IBS patients. Breath condensate interleukin-1β showed an inverse relation with clinical disease activity. The authors concluded in this review article that breath analysis is a promising

approach that is not yet ready for routine clinical use in IBS. Additional well-designed trials, incorporating the latest breath detection techniques are needed to determine the exact breath metabolome pattern linked to the diagnosis and phenotype of IBS.

Dynamed evaluated available data for the diagnosis and management of IBS (13) and SIBO (14) in 2022, which include the following recommendations:

- For IBS, HBT (for lactose intolerance and bacterial overgrowth) is not needed to confirm the diagnosis of IBS. (13)
- Initial studies suggest high rates of SIBO in patients with IBS (the basis for the lactulose HBT), although subsequent studies have not confirmed it. (13)
- To confirm the diagnosis of SIBO, consider using non-invasive breath tests (such as HBT or methane breath test). It is unnecessary to perform hydrogen breath testing for asymptomatic patients taking proton pump inhibitors (PPIs). (14)
- The gold standard for SIBO diagnosis is gastrointestinal aspirate and culture but there is no universal consensus regarding specific number of bacteria required for diagnosis. The most commonly used thresholds are either $\geq 10^3$ colony-forming units (CFU)/ml or $\geq 10^5$ CFU/ml of intestinal aspirate. (14)

Summary of Evidence

Hydrogen and methane breath tests are being used for the diagnosis and management of multiple conditions including but not limited to lactose intolerance, small intestine bacterial overgrowth (SIBO), and to evaluate small bowel transit time/gastroparesis. Most available literature identifies breath tests as simple, safe to use products although none of the studies measure safety outcomes or adverse events. Standardization is lacking regarding indications for testing, test methodology, and interpretation of results. Furthermore, testing can be affected by multiple factors including smoking, exercise, chewing gum, breath mints, and antibiotic use. To date, there is insufficient evidence to determine the impact of hydrogen and methane breath tests on patient management and long-term outcomes, therefore hydrogen or methane breath test is considered experimental, investigational and/or unproven for all indications including but not limited to irritable bowel syndrome (IBS), lactose intolerance or deficiency, SIBO, and small bowel transit time/gastroparesis.

Professional Guidelines and Position Statements

The National Institute for Health and Care Excellence (NICE)

In 2016 (updated 2017), NICE issued guidance on the diagnosis and management of IBS (15) which maintains that HBT for lactose intolerance and bacterial overgrowth is not necessary in adult patients to confirm diagnosis. In addition, guidance also recommends food avoidance and exclusion diets only be given by a healthcare professional with expertise in dietary management to help manage IBS symptoms.

The North American Consensus (NAC) Group

In 2017, the NAC Consensus Group (2) published guidelines regarding hydrogen and methane breath testing due to the lack of standardization regarding the indications, preparation and

performance, and interpretation of results. Differences have led to considerable heterogeneity between different centers and practitioners and research gaps are widening due to interstudy variability in methodology. The NAC Group was supported by Commonwealth Labs and offers the following recommendations regarding hydrogen and methane breath tests:
"Indications:

- Breath testing is suggested in the diagnosis of SIBO syndrome (weak recommendation, moderate quality evidence);
- Breath testing suggested in assessing presence of antibiotic responsive microbial colonization of gastrointestinal tract until gold standard established (weak recommendation, moderate quality evidence);
- Evaluation for excessive methane excretion on breath test suggested in association with clinical constipation and slowing of gastrointestinal transit (weak recommendation, moderate quality evidence);
- Breath testing suggested in assessment of bloating symptoms (weak recommendation, moderate quality evidence).

Preparation before breath testing:

- Avoid antibiotics for 4 weeks prior to breath test (strong recommendation, high quality evidence);
- Uncertain if pro/prebiotics should be stopped or continued prior to breath testing (strong recommendation, very low-quality evidence);
- If tolerated by the patient, stop promotility drugs and laxatives > 1 week prior to breath testing (weak recommendation, very low-quality evidence);
- Avoid fermentable foods (such as complex carbohydrates) on day prior to breath testing (weak recommendation, moderate quality evidence);
- Fast for 8 hours-12 hours prior to breath testing (weak recommendation, low quality evidence);
- Avoid smoking on day of breath testing (strong recommendation, high quality evidence);
- Limit physical activity during breath testing (strong recommendation, high quality evidence);
- Stopping proton pump inhibitors may not be needed prior to breath testing (weak recommendation, low quality evidence).

Administration of breath tests (dosing):

- Glucose- 75 g mixed with or followed by 1 cup of water (weak recommendation, low quality evidence);
- Lactulose- 10 g mixed with or followed by 1 cup of water (weak recommendation, moderate quality evidence);
- Lactose- 25 g mixed with or followed by 1 cup of water (weak recommendation, low quality evidence);
- Measure hydrogen, methane, and carbon dioxide simultaneously during breath testing (Strong recommendation, High quality evidence).

Interpretation of breath tests:

- Consider rise of ≥ 20 ppm from baseline in hydrogen during test as positive for fructose and lactose breath testing (weak recommendation, low quality evidence);
- Consider rise of ≥ 20 ppm from baseline in hydrogen by 90 minutes as positive test to suggest presence of SIBO syndrome (weak recommendation, low quality evidence);
- Two peaks on breath test not required for diagnosis of SIBO syndrome (weak recommendation, low quality evidence);
- Consider methane level ≥ 10 ppm as positive for methane on breath test (weak recommendation, low quality evidence);
- Interpretation of methane level ≥ 3 ppm is uncertain (weak recommendation, low quality evidence)."

American Gastroenterological Association (AGA)

In 2020, the AGA published a clinical practice update on diagnosis and management of SIBO. (16) The purpose of the update was to provide a historical background to the concept of SIBO, critically review current concepts of SIBO (including symptomatology, pathophysiology, clinical consequences, diagnosis, and treatment), define unanswered questions and provide a road map toward their resolution. Best Practice Advice statements, based on a review of available literature, were developed following discussion. In conclusion, it was determined that, "there is much to do to determine the ideal approach to SIBO, recent work provides the foundation for standardizing definitions and outcomes to allow for better controlled studies in the future."

American College of Gastroenterology (ACG)

The ACG (2020) current clinical guidelines on SIBO state:

- "We suggest the use of breath testing (glucose hydrogen or lactulose hydrogen) for the diagnosis of SIBO in patients with IBS (conditional 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 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 recommendation, very low level of evidence).
- We suggest against the use of breath testing for the diagnosis of SIBO in asymptomatic patients on proton-pump inhibitors (PPIs) (conditional 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 recommendation, very low level of evidence).
- We suggest the use of antibiotics in symptomatic patients with SIBO to eradicate overgrowth and resolve symptoms (conditional recommendation, low level of evidence)." (17)

Ongoing and Unpublished Clinical Trials

Some currently ongoing and/or unpublished trials that might influence this policy are listed in Table 1.

Table 1. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04309396	Clinical Utility of Handheld Hydrogen Breathalyzer in Identification of Food Sensitivities (AIRE Study) (AIRE)	45	Oct 2024
Unpublished			
NCT03261856	Clinical Utility of Breath Tests in GI Tract	1080	Dec 2017
NCT02242175	Efficacy of Hydrogen Breath Test in the Patients with Irritable Bowel Syndrome	147	Aug 2020 (unknown status)
NCT04499742	Comparative Assessment of Radioisotope Glucose and Breath Test	25	Dec 2021 (unknown status)

Table Key: NCT: National Clinical Trial, GI: gastrointestinal

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	91065, 91299
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
12/31/2025	Document became inactive.
02/15/2025	Reviewed. No changes.
03/15/2024	Document updated with literature review. Coverage unchanged. References updated.
03/15/2023	Reviewed. No changes.
07/15/2022	Document updated with literature review. Coverage unchanged. Reference 5, 16 and 17 added; others updated.
03/01/2021	Document updated with literature review. Coverage unchanged. Several references updated.
10/15/2020	Review only. No changes.
11/15/2019	New medical document. Hydrogen or methane breath testing is considered experimental, investigational and/or unproven for all indications including but not limited to the following conditions: irritable bowel syndrome (IBS); lactose intolerance or deficiency; small intestine bacterial overgrowth (SIBO); and small bowel transit time/gastroparesis.