



SIEMENS



Enabling Fast and Accurate
Detection of CSF Leakage

N Latex BTP Assay

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Confident Detection of Cerebrospinal Fluid Leakage for Confident Clinical Decisions

Cerebrospinal fluid (CSF) leakage or fistula occurs when the barrier separating the spinal fluid space from the nose, sinuses, or ear breaks down. CSF leakage can occur after trauma or surgery or be spontaneous or idiopathic in origin.¹ Regardless of the cause, CSF fistulas present a direct gateway for free passage of pathogens, bacteria, and viruses that can cause a number of life-threatening conditions.

Untreated, patients with longer-duration or delayed diagnosis of CSF leakage are at risk of meningitis or meningoencephalitis.² The risk of bacterial meningitis associated with persistent CSF rhinorrhea is 19%,³ and the mortality rate of meningitis associated with CSF leakage is 8.9%.⁴

Symptoms or predictors for CSF leakage in trauma or head-surgery patients include a clear, nonsticky fluid draining from the nose or ear, or a halo sign—a clear ring pattern surrounding a bloody spot on a filter paper or tissue.

Thorough and timely detection of CSF leakage is critical for treatment. Because treatment might involve a range of measures, from relatively conservative options to invasive CSF diversion (e.g., by lumbar punctation and drainage) or even surgical management (transcranial, transnasal, endoscopic), a sensitive, fast, and practical screening approach is necessary to assist clinicians in determining next steps for patients.





The determination of beta-2-transferrin (B2Trf) via immunofixation electrophoresis (IEF) on agarose gels is a widely accepted qualitative technique for detecting CSF leakage. B2Trf is produced through cerebral neurominidase and is almost exclusively found in CSF, perilymph, and vitreous humor. It is highly sensitive and specific and can be tested with electrophoretic technique. However, disadvantages of this method include the need for lengthy and expert interpretation of the results. Also, carbohydrate-deficient transferrin (CDT) present in samples obtained from heavy drinkers might interfere with B2Trf.⁵ The localization of a CSF leak is mostly performed by imaging measures (e.g., MRI scanning). However, this method might not be ideal for screening.

Beta-trace protein (BTP)—also known as prostaglandin D2 synthase—is mainly synthesized in the central nervous system and forms one of the principal constituents of CSF. It is the second-most-abundant protein in CSF (after albumin) and has the highest CSF/serum ratio (34:1) of all CSF proteins, making BTP a very specific marker for CSF.^{6,7,8} Due to the significantly higher concentration of BTP in CSF, a leakage—even when masked with blood—will show a concentration above the highest normal serum concentration.

BTP provides a quick, easy, and accurate alternative to B2Trf for screening and detection of CSF leakage, enabling rapid clinical decision making.

The First Fully Automated Marker to Accurately Determine CSF Leakage with a Simple, Nephelometric Lab Test

The N Latex BTP assay from Siemens is the first fully automated assay to provide faster, accurate results to detect CSF in samples containing nasal or ear secretions.⁶ A random-access assay designed for the Siemens BN™ II and BN ProSpec® Systems, N Latex BTP employs a latex-enhanced, polyclonal reagent that provides high sensitivity (98.3%), and specificity for CSF leakage and lot-to-lot reproducibility.

BTP testing has been included in the European Federation of Neurological Societies (EFNS) guidelines on disease-specific CSF investigation for detection of CSF admixture in rhino- and otorrhea.⁹

Faster clinical decisions

With sample collection to result within one hour—including an assay time of 12 minutes compared to approximately 2 hours for electrophoresis—BTP is faster, easier, and less expensive, with no need for an electrophoresis expert.

Significant cost savings

A negative BTP result rules out CSF leakage, while a positive result requires additional studies to localize and treat the disruption of the brain membrane (Figure 1).^{10,11} A negative BTP result provides a cost savings compared to imaging for patients who are scanned but negative for CSF leakage.

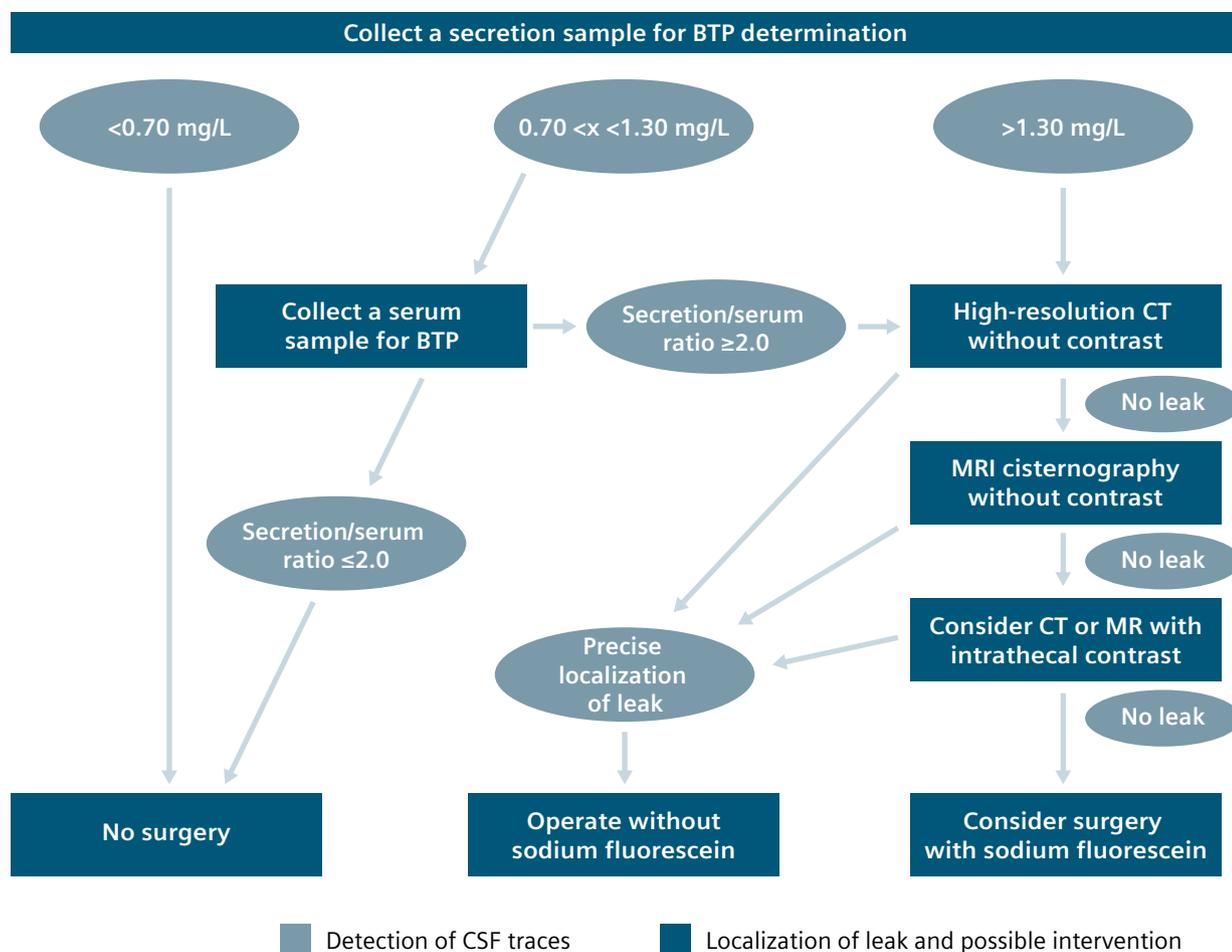


Figure 1. Diagnostic approach to CSF fistula using BTP (modified from Bachmann et al., 2008 with data from Bernasconi et al., 2016). The diagnostic approach consists of two parts: the detection of CSF traces (gray fields) and the localization of the CSF fistula (blue fields).



The BTP test allows a quantitative detection of CSF fistulas with a high sensitivity and specificity (level A recommendation) in combination with computed tomography and clinical investigations. Due to procedural advantages, BTP should be used as a first method depending on the frequency of requests.⁹

Results in less than half the time for less than half the cost

- Results are comparable to B2Trf, but BTP is faster, easier, and less expensive.¹⁰
- Results are accurate: high sensitivity of 98.3% and specificity of 96.0% with a negative predictive value (NPV) of 99.4% using the algorithm recommended by Bernasconi et al. (figure 1).¹¹
- BTP assay shortens time to result, so faster surgical intervention is possible.¹²
- Low incidence of false-positive results helps reduce costly imaging testing and possible loss of life due to misdiagnosis.
- Expensive MRI is required only to confirm positive results; use of the BTP assay promotes more efficient use of MRI.

N Latex BTP assay vs. B2Trf

Assay	Assay Time	Fully Automated	No Electrophoresis Expert Required	Economic Single-sample Determination
BTP	12 min	✓	✓	✓
B2Trf	Approximately 2 hours	no	no	no

Rapid Detection for Rapid Clinical Decisions

The Siemens N Latex BTP assay quickly and easily delivers the results clinicians need to diagnose CSF leakage and determine appropriate treatment. With the broadest menu on reliable, dedicated plasma-protein analyzers, Siemens enables confident clinical decisions.



Fast and accurate detection of CSF leakage

- Suitable for human serum, heparinized and EDTA plasma, urine, CSF, and nasal or ear secretions containing CSF
- Fully automated, random-access assay
- Low imprecision (total CV <5%)
- Latex-enhanced, polyclonal reagent providing high sensitivity (98.3%), specificity (98.0%) and an NPV of 99.4% for CSF leakage with the recommended algorithm (figure 1).¹¹ and lot-to-lot reproducibility

Expected values:⁵

	95th Percentile (Median)
BTP in serum	0.70 (0.50) mg/L
	2.5th–97.5th Percentile
BTP in CSF	8.89–25.9 mg/L

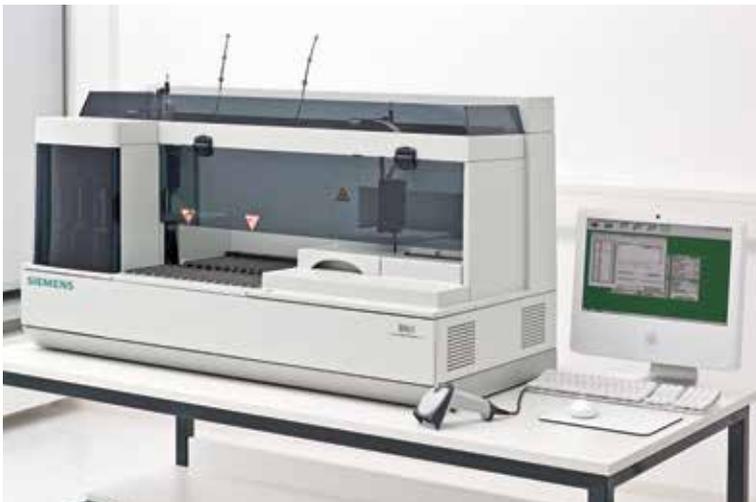
The new N Latex BTP assay is the first fully automated method to accurately determine CSF leakage with a simple, nephelometric lab test. Testing can be performed on minimal sample volumes of human serum, heparinized and EDTA plasma, CSF, and nasal or ear secretions containing CSF. Results are comparable to the β 2-transferrin immunofixation electrophoresis method, but faster, easier, and less expensive. You can confidently and accurately determine CSF leakage with the N Latex BTP assay for use on BN II and BN ProSpec Systems.

Take advantage of a powerful combination:

The N Latex BTP assay is available on the BN II and BN ProSpec Systems.



BN ProSpec System: Dedicated, compact system offering a consolidated menu of specialty and routine plasma-protein testing.



BN II System: Fully automated analyzer providing confidence in results for mid- to high-volume plasma-protein testing.

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Two applications—one accurate, convenient, fully automated assay.

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