

N Latex Beta-trace Protein (BTP) assay

Enabling fast and precise detection of CSF leakage

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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, the most feared and severe complication, 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 of 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.



Brain imaging with cranial computed tomography (CT) or cranial magnetic resonance imaging (MRI) could localize the anatomic location of CSF leakage. However, these methods are not ideal for screening and may also not be available at each site.

Laboratory diagnostic tests can support screening and confirmation of possible CSF leakage events.

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 neuraminidase and is almost exclusively found in CSF, perilymph, and vitreous humor. It is highly sensitive and specific and can be identified by its unique electrophoretic migration. 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

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 actually 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} Due to the significantly higher concentration of BTP in CSF, a leakage—even when masked with blood—will result in a concentration above the highest normal serum concentration.

BTP provides a quick, easy, and sensitive alternative to b2Trf for screening and detection of CSF leakage, enabling rapid clinical decision making.

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 otorrhea⁸ as well as in national recommendations such as the German guideline for lumbar puncture and cerebrospinal fluid diagnostics.⁹



N Latex BTP assay: A simple, nephelometric lab test that supports improved testing outcomes

The N Latex BTP assay from Siemens Healthineers is the first fully automated immunoassay to provide faster, sensitive results to detect CSF in samples containing nasal or ear secretions.⁶ As a random-access assay designed for the nephelometric Atellica® NEPH 630, BN ProSpec®, and BN™ II Systems, N Latex BTP assay employs a latex-enhanced reagent that provides high sensitivity (98.3%), and specificity for CSF leakage and lot-to-lot reproducibility.

Faster clinical decisions

With sample collection to result within 1 hour—including an assay time of 12 minutes compared to approximately 2 hours for electrophoresis—turnaround of the N Latex BTP assay is faster, easier, and less expensive, with no need for interpretation by an electrophoresis expert.

Cost-effective diagnostic process

A negative BTP result rules out CSF leakage, while a positive result requires additional examinations to localize and treat the disruption of the brain membrane (Figure 1).^{10,11} Ruling out CSF leakage by BTP testing may lead to significant cost and time savings compared to imaging examinations for patients suspected for CSF leakage who are scanned and found negative.

In a recent case study, detection of rhinoliquorrhea using N Latex BTP assay supported treatment of a patient with proven bacterial meningitis. Skull base liquor leaks could then be localized with imaging technology and sufficiently closed.¹²

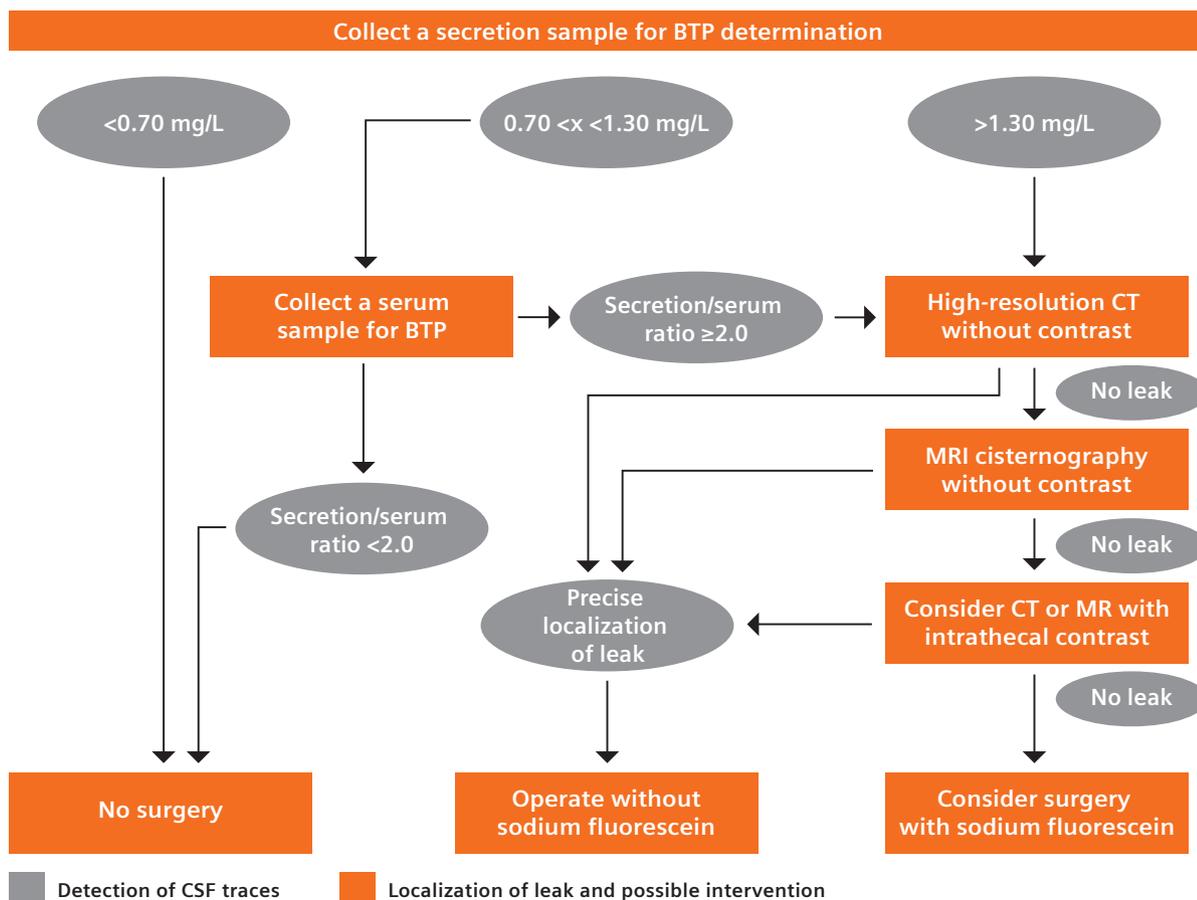


Figure 1. Diagnostic approach to CSF fistula using BTP (modified from Bachmann et al., 2008¹⁰ with data from Bernasconi et al., 2016¹¹). The diagnostic approach consists of two parts: the detection of CSF traces (gray fields) and the localization of the CSF fistula (orange fields).

Advanced testing process:

1. Obtain secretion sample, e.g., from nose or ear.
2. If needed, dilute sample with appropriate buffer.
3. Obtain serum sample.
4. Measure both samples on analyzer.
5. Evaluate results, e.g., by using the proposed pathway (Figure 1).

Clinical confidence in results

- Results are comparable to b2Trf, but BTP is faster, easier, and less expensive.¹⁰
- Good assay performance may reduce reruns, with high sensitivity of 98.3%, specificity of 96.0%, and a negative predictive value (NPV) of 99.4% using the algorithm recommended by Bernasconi et al. (Figure 1).¹¹
- The N Latex BTP assay shortens the time to result, so faster surgical intervention is possible.¹³

Improved financial and patient outcomes

- Screening for CSF leakage by quantification of BTP may reduce costs compared to screening with other methods and is available with a simple lab test.
- Expensive MRI or CT are required only to confirm positive results; use of the N Latex BTP assay promotes more efficient use of MRI and helps reduce the number of avoidable imaging examinations for patients.

N Latex BTP assay vs. b2Trf testing with electrophoresis

Assay	Assay time	Fully automated	No electrophoresis expert required	Economic sample determination
BTP	12 min	✓	✓	✓
b2Trf	Approximately 2 hours	no	no	no

The BTP test allows quantitative detection of CSF fistulas with high sensitivity and specificity (level A recommendation) when used 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.⁸

Rapid detection for rapid clinical decisions

The N Latex BTP assay from Siemens Healthineers rapidly and easily delivers the results clinicians need to diagnose CSF leakage and determine appropriate treatment.

Fast and precise 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 <6% for serum, plasma, and CSF sample pools)
- Latex-enhanced, polyclonal reagent providing high sensitivity (98.3%), specificity (96.0%), and an NPV of 99.4% for CSF leakage with the recommended algorithm (Figure 1),¹¹ plus lot-to-lot reproducibility.



Expected values

	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 N Latex BTP assay is the first fully automated method to 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 determine CSF leakage with the N Latex BTP assay for use on Atellica NEPH 630 and BN Systems.

The N Latex BTP assay also offers a fast and reliable method to determine the glomerular filtration rate and residual renal function in dialysis patients.

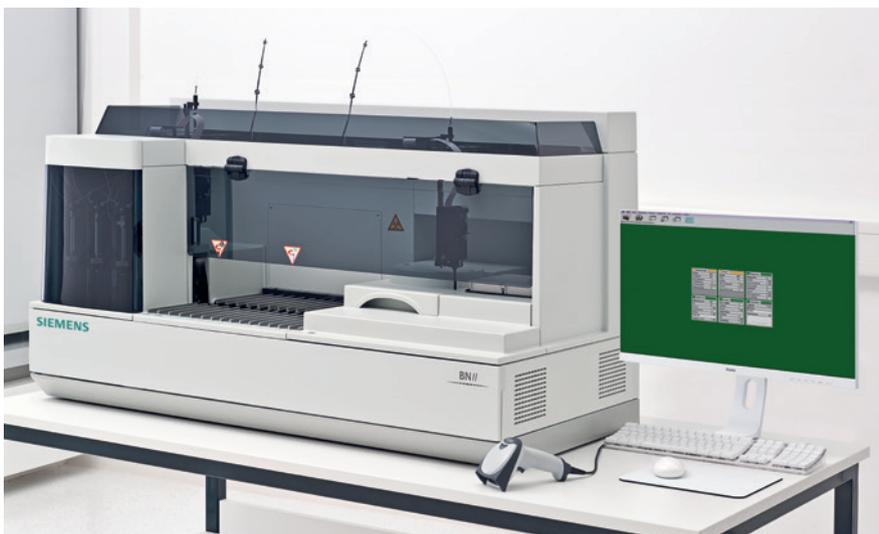
Take advantage of a powerful combination: The N Latex BTP assay is available on the Atellica NEPH 630 and BN Systems

N Latex BTP assay is designed to leverage proven nephelometric technology on the fully-automated Atellica NEPH 630 and BN Systems.



Atellica NEPH 630 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.

Two applications. One convenient, fully automated assay.

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