

euroimmun 

From Revvity

CSF diagnostics.



CSF analyses in infection diagnostics.



The investigation of cerebrospinal fluid (CSF) is diagnostically decisive in acute or chronic inflammatory processes of the central nervous system (CNS). Acute CNS infections manifest as meningitis (inflammation of the meninges), meningoencephalitis (inflammation of the brain or meninges), or encephalitis (inflammation of the brain). These infections can be caused by bacteria (e.g. *Borrelia*, *Treponema pallidum*), viruses (e.g. HSV, VZV, measles virus, TBE virus, EBV) or parasites (e.g. *Toxoplasma gondii*). CSF analysis also plays a major role in the differential diagnosis of non-infectious diseases such as multiple sclerosis (MS). The detection of intrathecal synthesis of antibodies against measles, rubella and/or varicella zoster viruses (MRZ reaction) is a specific indicator of MS.

When determining an infection of the CNS, it is necessary to differentiate between intrathecally produced antibodies

and antibodies which have diffused from the blood into CSF. This is done by measuring the concentrations of pathogen-specific antibodies, total IgG and IgM and albumin in both the CSF and serum of the patient.

Determination of pathogen-specific antibodies

If there is an infection of the CNS, pathogen-specific antibodies are also formed in the CSF. Consequently, their proportion in CSF increases in contrast to that in serum. The intrathecal pathogen-specific antibody production is defined by the antibody specificity index (synonym: antibody index, AI). The quotient is calculated from the amount of specific IgG antibodies in total CSF IgG in proportion to the amount of specific IgG antibodies in total serum IgG (see figure below).

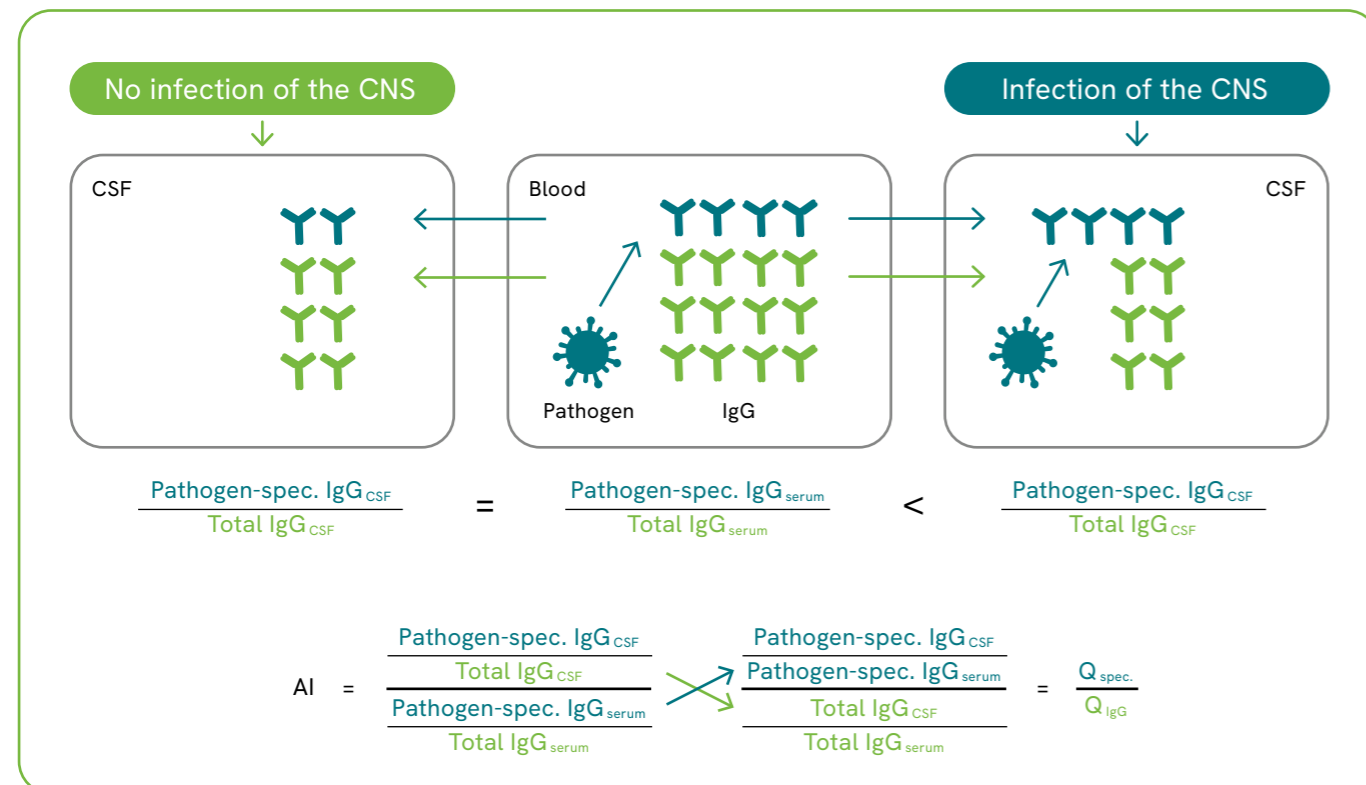
AI < 0.6: Implausible result;
Cause analysis recommended

AI 0.6 to < 1.3: Normal range

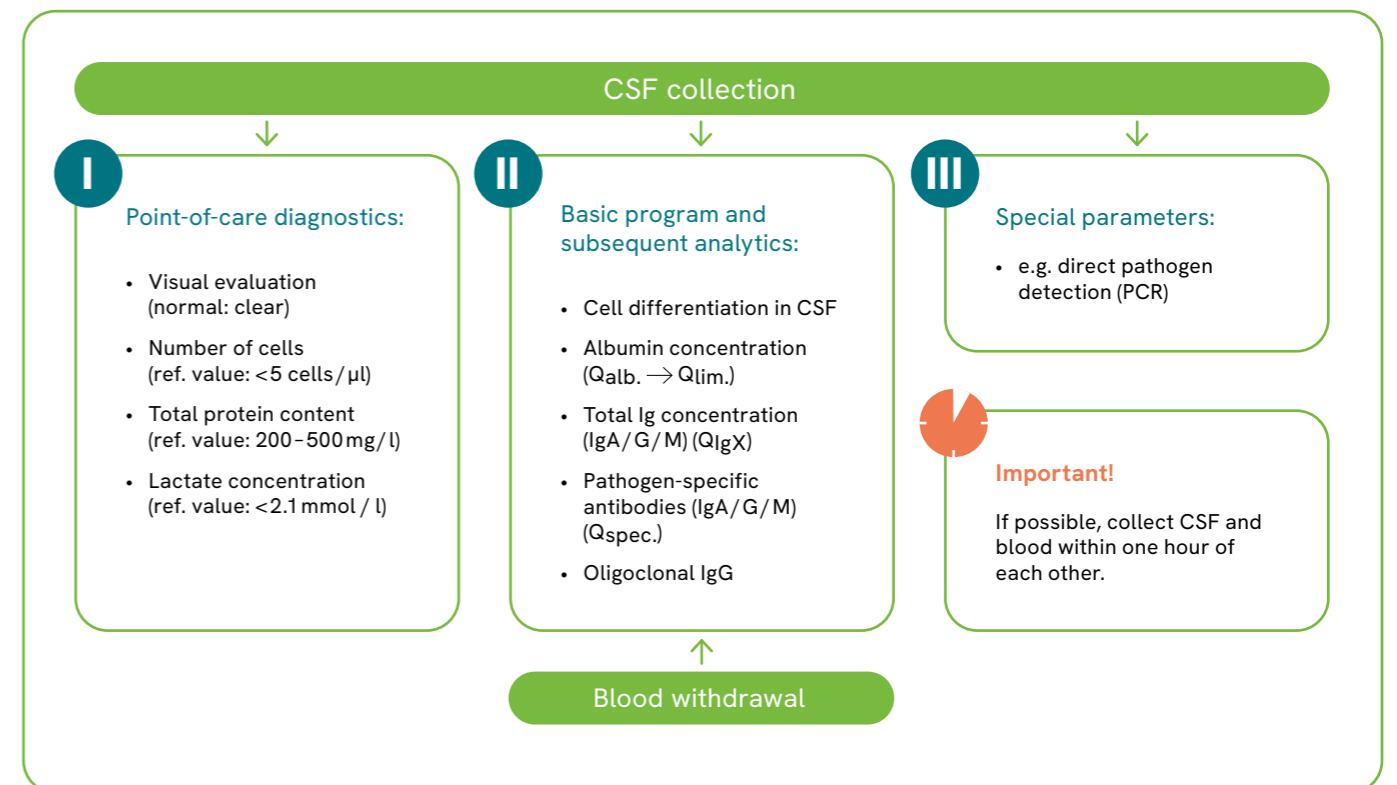
AI 1.3 to 1.5: Borderline area

AI > 1.5: Indication of pathogen-specific antibody production in the CNS

In some cases of inflammatory diseases of the CNS, a polyclonal stimulation of the intrathecal antibody synthesis can occur. Consequently, the CSF/serum quotient of the total immunoglobulin (Q_{IgX}) is correspondingly high and may not be used as a reference for the calculation of the AI. In this case, the CSF/serum quotient of the total albumin (Q_{alb}) is used as the basis for calculation, since albumin is never produced intrathecally and only reaches the CSF via diffusion from the blood. For each Q_{alb} , a maximal value of the total IgG quotient which can still be considered as normal is determined, which is referred to as limes quotient (Q_{lim}). If the calculated Q_{IgX} in a patient is higher than the Q_{lim} , the calculation of the AI is made based on the Q_{lim} , instead of the Q_{IgX} .



Schematic illustration of intrathecal pathogen-specific antibody production incl. calculation basis for the antibody index (AI) determination.



Steps of CSF diagnostics. Based on Wildemann B., Oschmann P., Reiber H. Neurologische Labordiagnostik. Georg Thieme Verlag, Stuttgart/New York, 2006.

ELISA test systems for the detection of specific antibodies in CSF.

Assay portfolio

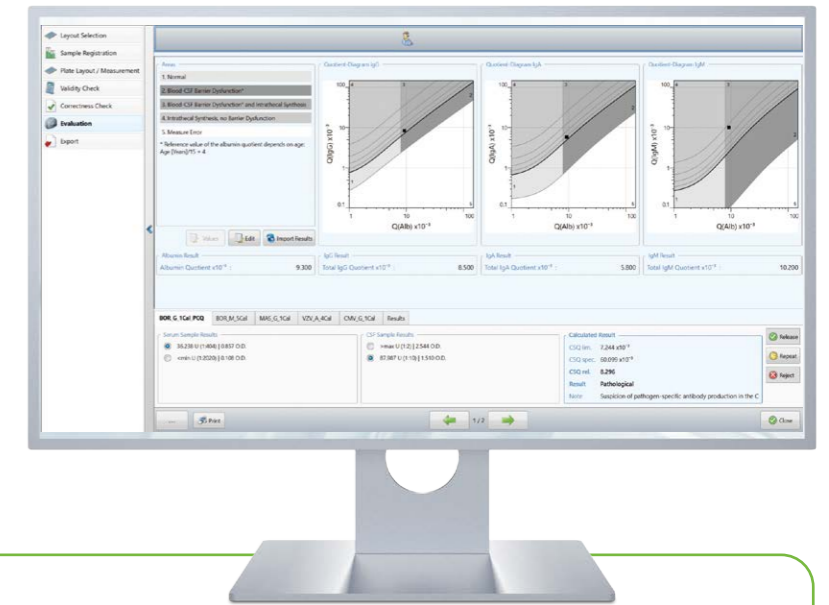
Euroimmun's product portfolio for CSF diagnostics comprises a large number of ELISAs for the determination of specific antibodies against *Borrelia*, *Toxoplasma gondii*, *Treponema pallidum*, CMV, EBV, HSV, VZV, measles, rubella, mumps and TBE viruses in CSF and serum.

- Proven quality - excellent pass rates in INSTAND quality assessment schemes
- Convenient evaluation with the EUROLabCSF software
- Quantitative results obtained by 4-6 point standard curve or reference of a single recalibrator to a stored master curve
- Lot-specific CSF/serum control pairs to check the validity of the incubation included in the kits of the product line "CSF ELISA 2.0"; additional CSF/serum control pairs available for all other CSF ELISAs
- Fully automatable, e.g. with the EUROIMMUN Analyzer I; EUROIMMUN Analyzer I-2P or EUROLabWorkstation ELISA

Automated processing

The ELISA test systems for CSF diagnostics can be processed fully automatically using the laboratory instruments from Euroimmun. Especially in combination with EUROLabCSF, this provides a convenient solution for laboratories with medium to large sample throughput.

- **EUROIMMUN Analyzer I:** Up to 70 tests per hour - up to 7 microplates and 180 samples in one run
- **EUROIMMUN Analyzer I-2P:** Up to 50 tests per hour - up to 3 microplates and 144 samples in one run
- **EUROLabWorkstation ELISA:** >200 tests per hour - up to 15 microplates and more than 700 samples in one worklist
- Tests can be combined owing to an identical incubation scheme, standard dilutions (1:2 CSF or 1:404 serum) and reagents that can be used across products.
- Saves consumables due to direct pipetting of buffer and CSF into the microplate
- Automated barcode identification of the patient samples and reagents increases safety and comfort



Innovative evaluation

EUROLabCSF is a software providing automatic calculation of the CSF/serum quotients (Q_{alb} , Q_{IgX} , Q_{spec} , Q_{lim} , and AI).

- Automated result calculation and digital transfer of data to the LIS (laboratory information system)
- No time-consuming manual data transfer and, consequently, avoidance of transmission and calculation errors
- Clear graphic display in quotient diagrams according to Reiber and Lange
- Simple data management: Search functions for patients or analyses, export of results



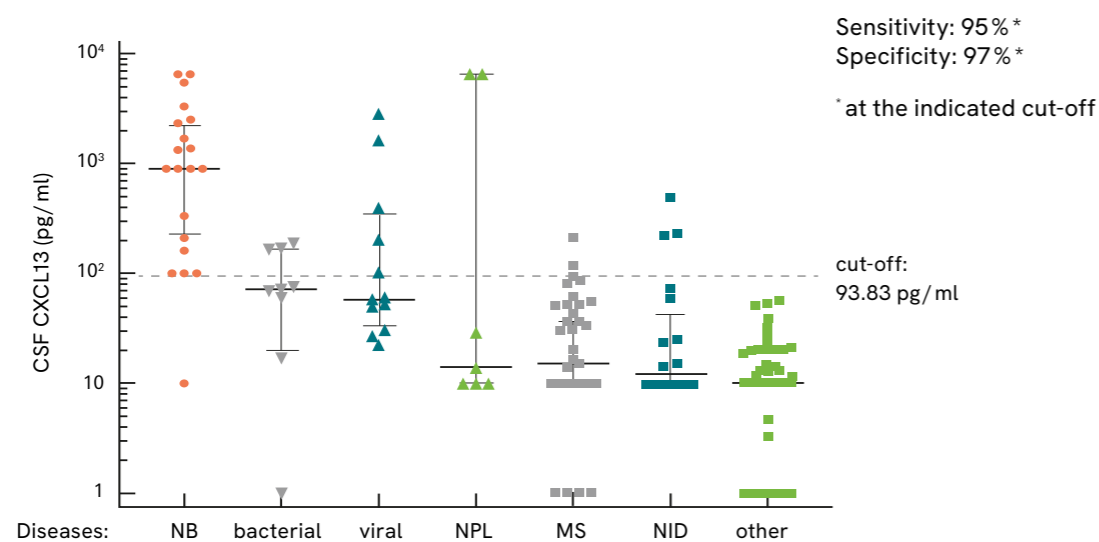
Exemplary workflow with the EUROLabWorkstation ELISA

Additional products for CSF diagnostics in neuroborreliosis.

CXCL13 ELISA

Alongside the determination of specific antibodies by means of the Anti-Borrelia ELISA, also the determination of the chemokine CXCL13 in the CSF is helpful for the detection of neuroborreliosis. Increased CXCL13 values in CSF may occur in different diseases of the CNS, but are especially high in cases of acute neuroborreliosis.

- High CXCL13 concentrations are often detectable before the specific antibodies against Borrelia
- Differentiation between acute and past neuroborreliosis with pathological Borrelia AI:
 - Low CXCL13 concentrations in CSF: acute neuroborreliosis rather unlikely
 - High CXCL13 concentrations in CSF: indication of acute neuroborreliosis
- Disease course marker: After successful therapy, the CXCL13 concentration in CSF decreases rapidly

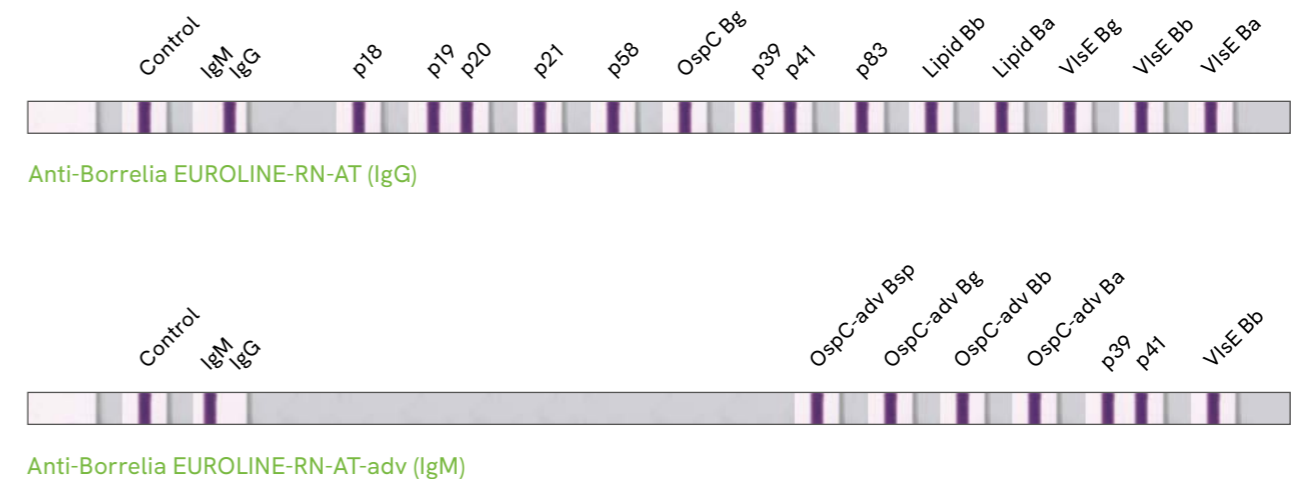


CXCL13 as a diagnostic marker for neuroborreliosis. Figure adapted according to Wagner et al., 2017. Medians with 95% confidence interval. NB: Neuroborreliosis, NPL: systemic neoplasia, MS: multiple sclerosis, NID: (other) neuro-inflammatory diseases

Immunoblots

The Anti-Borrelia EUROLINE-RN-AT comprise a large spectrum of diagnostically relevant Borrelia antigens for the detection of specific antibodies in serum and in serum/CSF pairs.

- Automated processing with the EUROBlotOne or EUROBlotMaster; special incubation programs for CSF
- Standardised evaluation using EUROLineScan software
- Fixed dilution factor for CSF (1:4) and simple calculation of the serum dilution by means of EUROLineScan
- Diagnostics based on the number and intensity of the specific bands



Bb: *Borrelia burgdorferi*, Ba: *Borrelia afzelii*, Bg: *Borrelia garinii*, Bsp: *Borrelia spielmanii*

Order informationen

| Product | Order number |
|--|--------------------|
| ELISA for CSF diagnostics | |
| Anti-Borrelia plus VlsE ELISA (IgG) | EI 2132-9601-L G |
| Anti-Borrelia CSF ELISA 2.0 (IgM) | EI 2132-9601-2L M |
| Anti-CMV ELISA (IgG) | EI 2570-9601-L G |
| Anti-EBV-CA ELISA (IgG) | EI 2791-9601-L G |
| Anti-TBE Virus CSF ELISA 2.0 (IgG) | EI 2661-9601-2L G |
| Anti-TBE Virus CSF ELISA 2.0 (IgM) | EI 2661-9601-2L M |
| Anti-HSV-1/2 Pool ELISA (IgG)* | EI 2531-9601-1 L G |
| Anti-Measles Virus ELISA (IgG)* | EI 2610-9601-L G |
| Anti-Mumps Virus ELISA (IgG) | EI 2630-9601-L G |
| Anti-Rubella Virus ELISA (IgG)* | EI 2590-9601-L G |
| Anti-Toxoplasma gondii ELISA (IgG) | EI 2410-9601-L G |
| Anti-Treponema pallidum ELISA (IgG) | EI 2111-9601-L G |
| Anti-VZV (IgG)* | EI 2650-9601-L G |
| Additional products for CSF diagnostics | |
| CXCL13 ELISA | EQ 6811-9601-L |
| Anti-Borrelia EUROLINE-RN-AT (IgG) | DN 2131-3201 G |
| Anti-Borrelia EUROLINE-RN-AT (IgM) | DN 2131-3201 M |
| Anti-Borrelia EUROLINE-RN-AT-adv (IgM) | DN 2131-3201-2 M |

* Test kit contains additional optional calibrators

Find more information about products for neurology at
www.neuro-company.com
 or contact us directly:
www.euroimmun.com/contact



EUROIMMUN Medizinische Labordiagnostika AG
 Seekamp 31 · 23560 Lübeck (Germany) · Phone: +49 451 2032-0
www.euroimmun.com

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