PRACTICE TIPS:

Using cellular tests correctly & Assessing the immune response in a nuanced way

LTT, ELISpot, Multi-pathogen test

Targeted diagnostics or broad screening?

In cases of chronic infections, persistent symptoms, or unclear immunological profiles, antibody diagnostics alone are often insufficient. Antibodies indicate whether contact has taken place – but they reveal little about whether the immune system is responding functionally and adequately.

This is where cellular testing methods come into play. They examine the reaction of T-cells following targeted antigen stimulation, thereby enabling a functional assessment of the immune response. Depending on the clinical question, three different methods are available:

- **Lymphocyte transformation test (LTT)**
- **ELISpot**
- **Multi-pathogen test (multiparametric cytokine release assay)**

These tests measure different levels of the immune response and are complementary; in other words, they are not interchangeable but rather complementary.

The clinical question determines the test procedure
Which form of immune response is to be assessed?

Sensitisation / Type IV reaction

LTT
Detection of cellular sensitisation

Examples:
- metals
- implants
- drug reactions

Specific suspicion of a pathogen

ELISpot
Detection of specific T-cell activity

Examples:
- Borrelia
- EBV
- CMV

Unclear infectiology or systemic activation

Multi-pathogen test
Comprehensive functional immune screening for 21 relevant pathogens

Examples:
- unclear infectious disease
- accute infection
- IL-10 regulation

GOOD TO KNOW!

The three methods measure different aspects of the T-cell response:

LTT → Proliferation
ELISpot → single-cell interferon and interleukin-2 response
Multi-pathogen test → functional cytokine interaction

Differing results therefore do not represent a methodological contradiction, but reflect different levels of the immune response.

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Lymphocyte Transformation Test (LTT)

When it comes to sensitisation or Type IV reactions
The LTT measures the proliferative capacity of T cells following contact with a specific antigen.

Typical indications:
- metal or implant intolerance
- contact allergies (Type IV reactions)
- questions regarding cellular sensitisation (e.g. to drugs)

In these reactions, the proliferative response is the primary focus. The LTT indicates whether specific cellular sensitisation is present – regardless of which specific cytokines are produced.
The test answers the question: **Is there specific cellular sensitisation or immune memory?**

ELISpot

If a specific pathogen is suspected
The ELISpot detects individual T cells that produce interferon or interleukin-2 following antigen contact – a key cytokine in the defence against viral and intracellular pathogens.

Typical indications:
- suspected Borrelia infection
- viral reactivation (e.g. CMV or EBV)
- monitoring the course of known infections

As each reactive cell is detected individually, the ELISpot is particularly sensitive to specific, pathogen-specific TH1 responses – i.e. when there is already a concrete suspicion. By measuring IL-2 release, the cellular memory response to past infections can also be specifically assessed.
The test answers the question: **Do T cells actively react to this specific pathogen?**

Multi-pathogen test (multiparametric cytokine release assay)

If the cause is unclear – functional screening for 21 pathogens
The multiparametric cytokine release test distinguishes between several pathogens (acute/chronic), but combines two diagnostic levels to increase its diagnostic value:

1. Simultaneous testing for 21 relevant pathogens
2. Measurement of multiple cytokines and chemokines for the functional classification of the immune response

Typical indications:
- unclear infectious disease without a specific initial suspicion of a pathogen
- multiple possible pathogens
- functionally impaired T-cell axes against specific pathogens (primary or secondary immune defects)
- immunologically compromised reactivity in cases such as chronic fatigue, Long COVID, etc.

The focus here is not on a single pathogen, but on whether the immune system is functionally activated – and to which pathogens it is responding.
The test is suitable as a functional screening method when several potential pathogens or complex immunological relationships need to be investigated simultaneously. In addition to testing for 21 relevant pathogens, it enables a differentiated assessment of functional immune activation.
The test answers the question: **Is the immune system functionally activated – and against which pathogens?**

CONCLUSION
The choice of test procedure depends on the clinical question: targeted diagnosis or broad screening? We can help you select the most suitable procedure.

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