In an ideal case the serological diagnosis of a fresh infection is not difficult: with a serum pair it is possible to identify a significant increase in specific IgG antibodies, whereas the IgM is positive in the first sample and weaker or even negative in the second sample. However, laboratories are usually required to provide a reliable diagnosis from a single serum in the shortest time possible, because therapy cannot wait for 14 days until a second blood sample is taken. Moreover, IgM antibodies often cannot be reliably detected in fresh infections or, in other cases, the IgM persists for months or years. IgM analysis is further complicated by well-known interference factors.

Of increasing interest therefore is a test to supplement IgM diagnostics, with which fresh infections can be serologically identified using a single sample, i.e. the determination of the avidity of specific IgG. A previously unknown infectious pathogen cannot at first induce matching antibodies in an organism. But, by (controlled) chance, a very small part of the immunocompetent cells already has a weak affinity for the new infectious antigens. These cells are stimulated to settle in the lymph nodes in the area of the infection source and to proliferate. During the course of infection, the B-lymphocytes whose specific determinants (coded by hypervariable gene sequences) best match the antigens of the agent are continuously stimulated to divide. As a result of this maturation process antibodies that match the agent better and better develop from the B-lymphocyte differentiating plasma cells. The initially low avidity of the specific IgG increases by several powers (from the beginning, the pentavalent IgM has a higher avidity than IgG).

Nowadays, avidity determination is an indispensable component of the diagnostic repertoire in modern infectious serology. By analysing avidity with indirect immunofluorescence (IIF) or ELISA we are able to decide if an IgG positive reaction originates from a recent or a past infection. In our reference laboratory it is commonplace to receive several hundred samples daily, mainly difficult cases where therapy decisions rest solely on the avidity result.

EUROIMMUN offers a variety of test systems for the determination of antibody avidity based on ELISA and immunofluorescence. These tests allow clarification of many difficult serological constellations and significantly facilitate the diagnosis of fresh infectious diseases such as toxoplasmosis, rubella, infectious mononucleosis, cytomegaly, varicella and WNV infection (in development: measles, mumps, borreliosis). The test systems are CE labelled.

### Pathogenic agent | Test system
---|---
Toxoplasma gondii | ELISA, IIF
Rubella virus | ELISA, IIF
Epstein-Barr virus (EBV) | ELISA, IIF
West Nile virus (WNV) | ELISA, IIF
Cytomegalovirus (CMV) | ELISA, IIF
Varicella zoster virus (VZV) | ELISA, IIF
Measles virus | ELISA
TBE virus | ELISA

### Relative Avidity Index (RAI) in %

<table>
<thead>
<tr>
<th>RAI</th>
<th>Number of Patients</th>
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</thead>
<tbody>
<tr>
<td>0</td>
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</tr>
<tr>
<td>2</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

Primary Infection | Previous Infection

**Figure:**

- **Principle of the avidity test:**
  - Low-avidity IgG: destroyed bond with urea
  - High-avidity IgG: stable bond with urea

- **Antibodies against EBV capsid antigen (IIF):**
  - Without urea: low-avidity IgG
  - With urea: high-avidity IgG

- **Antibodies against EBV capsid antigen (ELISA):**
  - Without urea: low-avidity IgG
  - With urea: high-avidity IgG