Anti-Rubella Virus Glycoprotein ELISA (IgM)

**Indication:** Test system for the in vitro determination of antibodies against rubella virus glycoproteins in human serum or plasma for the diagnosis of the following disease: rubella.

**Clinical significance:** The pathogenic agent of rubella is the rubella virus, which is present worldwide. It is a positive single-stranded, enveloped RNA virus and the only species belonging to the genus Rubivirus of the Togaviridae family. The rubella virus was first isolated in 1962 by Parkman, Weller and Neva. There are 2 genotypes, which are divided into further subgenotypes. The rubella genotype I (RGI) occurs in the western hemisphere, whereas the rubella genotype II (RGII) is mainly found in Asia.

A rubella infection is transmitted by aerosols. It is considered contagious already during the incubation period of two to three weeks. Typical symptoms are headache, lymph node swellings, particularly in the neck area, and a blotchy exanthema, which generally persists for 3 days. This generalised, macular, not confluent, light red exanthema spreads from the face to the trunk and the extremities in a postauricular manner. A known complication is arthritis in the finger, hand, elbow and ankle joints, which may last for up to three weeks in adults. Further complications are myocarditis, neuritis, otitis, bronchitis and, very rarely, rubella encephalitis with a good prognosis. The majority of infections occur between the ages of 5 to 14 years and lead to lifelong immunity. An infection spread of 80 to 90% is assumed for adults in central Europe. This means that 10 to 20% of women of child-bearing age are not immune.

Rubella virus transmitted diaplacentally during the first trimester of pregnancy causes the highest rate of embryonic deformities. Severe forms of rubella embryopathy are found in around 80% of cases. In the foreground are Gregg’s Triad consisting of heart deformations, eye defects and hearing damage such as congenital vitium cordis in around 48%, retinopathy in around 39%, cataract/myopia in around 29%, glaucoma in around 3% and deafness in around 67% of cases. Ideomuscular retardation (partly in combination with microcephalus) in around 45%, neonatal purpura with hepatosplenomegaly and diabetes mellitus in around 23% and death (incl. spontaneous abortion) in around 16% of cases are also known to occur. In many countries, an acute rubella infection is considered to be a medical indication for termination of pregnancy. Various inoculation strategies have been employed worldwide to prevent rubella infections. Since active immunization is well tolerated, vaccination programs aim to protect all young persons before puberty using a two-stage rubella vaccination.

**Application of the Anti-Rubella Virus Glycoprotein ELISA:** Laboratory investigations using serological methods such as haemagglutination inhibition test (HIT) or ELISA play a key role in the diagnosis of rubella infections. An increase in the IgG antibody titer within 10 days or the presence of IgM antibodies indicates an acute infection. It must, however, be taken into consideration that anti-rubella IgM antibodies may be present months after an infection. Due to the fact that the HIT does not allow differentiation of the immunoglobulin classes, ELISA is clearly superior to HIT. In contrast to conventional ELISAs, which are generally based on lysates from rubella virus infected cells, the new EUROIMMUN Anti-Rubella Virus Glycoprotein ELISA (IgM) uses only highly purified, native rubella virus glycoproteins as antigens. These are the main target of the immune response.

Sera from healthy pregnant women, which were positive in the Anti-Rubella Virus Lysate ELISA, were collected in a diagnostic laboratory over a period of four years. For these patients acute infection could be excluded due to the presence of high-avidity IgG antibodies and the lack of symptoms. In the 64 serum samples no IgM antibodies were found using the Anti-Rubella Virus Glycoprotein ELISA. This leads to the assumption that the results obtained with the lysate ELISA were false-positive. Unspecific reactions, such as cross reactions, which are known to occur in ELISAs using virus lysate or in indirect immunofluorescence, are minimised using the Anti-Rubella Virus Glycoprotein ELISA.
Reproducibility: The reproducibility of the test was investigated by determining the intra- and inter-assay coefficients of variation using 3 sera. The intra-assay CVs are based on 20 determinations and the inter-assay CVs on 4 determinations performed in 6 different test runs.

Reference range: Levels of anti-rubella virus glycoprotein antibodies were analysed in a panel of 500 healthy blood donors (origin: Germany) using the EUROIMMUN ELISA. With a cut-off of ratio 1.0 RU/ml, 1.6% of the blood donors were anti-rubella virus glycoprotein positive (IgM).

Sensitivity and specificity: A panel of 81 clinically characterised patient samples (INSTAND, Labquality, UK NEQAS) was investigated using the EUROIMMUN Anti-Rubella Virus Glycoprotein ELISA (IgM). Both the specificity and sensitivity were 100%.

Cross reactivity: Sera from patients exhibiting IgM antibodies against various infectious agents were analysed using the Anti-Rubella Virus Glycoprotein ELISA (IgM). Only two of 55 patients with an acute CMV infection showed antibodies against rubella virus. It is assumed that these reactions can be attributed to polyclonal B-cell stimulation, which is well described in literature. No signs of cross reactivity were found.

Technical data:

Antigen: Highly purified native glycoproteins from rubella virus (strain HPV-77, cultivated in vero cells) are used as the antigen.

Calibration: Semiquantitative. Calculation of a ratio from the extinction of a sample and the extinction of the calibrator.

Interpretation of results: Ratio < 0.8: negative
Ratio ≥ 0.8 to < 1.1: borderline
Ratio ≥ 1.1: positive

Sample dilution: Serum or plasma; 1:101 in sample buffer.

Reagents: Ready for use, with the exception of the wash buffer (10x). Colour-coded solutions, in most cases exchangeable with those in other EUROIMMUN ELISA kits.

Test procedure: 60 min (37°C) / 30 min / 15 min. Room temperature. Fully automatable.

Measurement: 450 nm. Reference wavelength between 620 nm and 650 nm.

Test kit format: 96 break-off wells. Kit includes all necessary reagents.

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