**Indication:** Test system for the in vitro determination of antibodies against Hantavirus (strains Hantaan, Dobrava and Puuma) in human serum or plasma for the diagnosis of the following diseases: haemorrhagic fever with renal syndrome (HFRS), kidney failure, acute respiratory syndrome, Hantavirus pulmonary syndrome (HPS), Hantavirus cardiopulmonary syndrome (HCPS).

**Clinical Significance:**

Hantaviruses belong to the Bunyaviridae family (other members are Sandfly fever virus, Crimean Congo fever virus) and they are transmitted by rat and mouse species. They cause persistent infections in their hosts and are excreted via saliva, faeces and urine. Transmission to humans occurs through the respiratory tract by inhalation of dust and aerosols containing virus-contaminated excrements of apparently infected rodents. Hantaviruses are found worldwide. The Hanta species Hantaan, Seoul, Puuma and Dobrava are the causative agents of the haemorrhagic, nephropathic syndrome (HFRS), whose degree of manifestation depends on the virus type involved. HFRS can be treated with chemotherapy.

The incubation period is 5 to 35 days. The disease generally starts with abrupt high fever, which lasts for 3 to 4 days, and unspecific flu-like symptoms, e.g. headache, myalgia, shivering and conjunctivitis. This phase continues for 4 to 10 days. In approximately 30% of cases this is followed by haemorrhagic symptoms, which manifest themselves as petechiae of the eye and the mucous membranes and which are often accompanied by thrombocytopenia, haematuria and proteinuria. Kidney function may be impaired to the extent that dialysis is required. The lethality rate of nephropathia epidemic is approximately 1%. In approx. 16% of cases, acute kidney failure is associated with an involvement of the lungs showing peribronchial infiltrates and pleural effusion. The first week of infection is characterised by a decrease in blood pressure which leads to a state of shock in 1 to 15% of patients and is fatal in one in three cases. In reconvalescent patients the remission of symptoms and the return to normal electrolyte levels take up to 3 months.

**Anti-Hanta Virus Pool ELISA (IgG):** Diagnosis of Hantavirus infections is generally based on the clinical picture and serological test results. Cultivation of the virus is difficult and hardly ever succeeds. Detection of viral RNA in the blood using PCR can only be carried out during the first few weeks after infection since the viraemic phase is very brief and ends shortly after the occurrence of the first symptoms. IgM antibodies against Hantavirus can be found at an early stage and often occur with the onset of first symptoms. IgG antibodies can be detected shortly after. Whereas IgM antibodies generally disappear within 2 to 3 months (in individual cases weak IgM results can still be found 1 to 3 years after infection), IgG antibodies persist for many years, sometimes even lifelong. The Anti-Hanta Virus Pool ELISA contains a mixture of recombinant nucleocapsid antigens from the Hantavirus strains Hantaan, Dobrava and Puuma, which are found in Asia and Europe. With this mixture, it provides a sensitive and specific test system for the detection of Hantavirus infections in these regions.
Test Characteristics

Anti-Hanta Virus Pool ELISA (IgG)

Linearity: The linearity of the Anti-Hanta Virus Pool ELISA (IgG) was determined by performing 4 serial dilutions of 6 serum samples. The linear regression $R^2$ was >0.95 for all samples. The Anti-Hanta Virus Pool ELISA (IgG) is linear in at least the tested concentration range of 14 RU/ml to 142 RU/ml.

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: The levels of anti-Hantavirus antibodies (IgG) were analysed with the EUROMMUN Anti-Hanta Virus Pool ELISA (IgG) in a panel of 500 healthy blood donors. With a cut-off value of 20 RU/ml, 4.4% of blood donors were anti-Hantavirus positive (IgG), in agreement with the known infection level in adults.

Correlation with the PROGEN ELISA: A panel of 40 patient samples was investigated using the EUROMMUN Anti-Hanta Virus Pool ELISA (IgG) and the PROGEN Hantavirus ELISA (IgG). The agreement between the qualitative results of the two ELISAS was 86% (excluding borderline sera). Four of the five discrepant samples achieved a negative result in the EUROMMUN Anti-Hantavirus IIFT (IgG).

Sensitivity and specificity (IgG): 8 characteristics of patient samples (INSTAND quality assessment, Germany) were tested using the EUROMMUN Anti-Hanta Virus Pool ELISA (IgG). Both the sensitivity and specificity were 100%, excluding the borderline serum.

Cross reactions: 228 sera from patients with different infectious diseases (positive IgG results) were investigated with the EUROMMUN Anti-Hanta Virus Pool ELISA (IgG). No cross reactions (CR) were found.

Technical data:

Antigen: A mixture of recombinant antigens from the Hantavirus strains Hantaan, Dobrava and Puumula.

Calibration: Quantitative, in relative units per millilitre (RU/ml).

Calibration sera: 1: 200 RU/ml; calibration sera 3: 20 RU/ml; cut-off calibration sera 2: 2 RU/ml

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

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

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

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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