**Clinical significance:** Dengue viruses (types 1, 2, 3 and 4) are enveloped ssRNA viruses of the family Flaviviridae. They are transmitted from human to human via the mosquito Aedes aegypti. This mosquito bites in the daytime, is adapted to human habitats and has a strong preference for human blood. It breeds in relatively clean water stored for drinking or washing purposes, and in rainwater that collects in manmade containers.

The population explosion in the last 60 years and subsequent migration from rural to urban areas, often with poor living conditions, has resulted in the spread of A. aegypti to almost all tropical countries. Of the 2.5 billion inhabitants of these areas, it is estimated that about 50-100 million individuals become infected with dengue viruses each year. Since the early 1950s, a syndrome first recognized in South East Asia – dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS) – has spread globally, resulting in hundreds of thousands of hospitalizations and thousands of death each year. Travellers to most tropical areas are at risk of infection with dengue virus. In 2001, Hawaii experienced a 6-month epidemic of dengue type 1 transmitted by Aedes albopictus.

Most primary dengue virus infections in children and many in adults are silent. Dengue infection presents clinically as three overlapping syndromes: undifferentiated fever, dengue fever syndrome and DHF/DSS. The symptoms of overt dengue infections are common to many acute viral, bacterial and parasitic infections. The pathophysiologic presentation of classic DSS (history of recent high fever, thrombocytopenia, elevated hematocrit and hypotension or narrow pulse pressure) is unique in infectious diseases. Presumptive diagnosis of dengue fever or DHF requires a careful travel history to establish possible exposure to dengue virus infection.

Antibodies against dengue viruses can be detected early after onset of symptoms. Antibodies of class IgM are detectable from the fifth day of illness and for 2-3 months following initial infection. IgG antibodies are often not detectable after a second infection with another serotype. Antibodies of class IgG arise several days later than IgM and reach their maximum concentration 2-3 weeks after infection. They probably persist for life. After a second infection with another serotype an increase in IgG concentration of over 10-fold is often found.

**Relevance of serological diagnostics:** Dengue fever should always be differentially diagnosed by Aedes aegypti. This mosquito bites in the daytime, is adapted to human habitats and has a strong preference for human blood. It breeds in relatively clean water stored for drinking or washing purposes, and in rainwater that collects in manmade containers.

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**Relevance of serological diagnostics:** Dengue fever should always be differentially diagnosed from other tropical diseases such as malaria, yellow fever, typhus, and dengue shock syndrome. The infectious agent can only be detected within the first five days of the disease during a viraemic phase using RT-PCR or performing an in vitro cultivation of the virus. Antibodies can be detected after approximately the fifth day of illness. Since the virus itself can only be detected for approximately ten days and the symptoms occur with a delay, resulting in a delayed medical examination, the serological detection of antibodies against Dengue virus plays a significant role in the diagnosis of the disease. Cross reactions with other Flaviviruses must be taken into account.
**EUROIMMUN**

**ImmunobLOTS**

**Autoantibody determination: EUROASSAY:**

- Flexible profiles of up to 7 antigens from: HIV, HBsAg, HCV, HAV, CMV, EBV, HSV, varicella-zoster virus, influenza, respiratory syncytial virus, H. pylori, aprotinin, streptococcus, staphylococcus, neisseria, salmonella, schistosoma, aspergillus, candida, dermatophytes, toxoplasma, cryptosporidium, trypansom, leishmania, leprosy, malarial parasites, and many more.

- Reproducibility: Coefficients of variation (CVs) were determined using 3 sera in different areas of the standard curve. The intra-assay CVs are based on 20 measurements for each serum and the inter-assay CVs on four measurements repeated on six different days.

- Reference range: The titer of antibodies against dengue virus (IgG) was determined in a panel of 500 apparently healthy blood donors using the EUROIMMUN ELISA. 0.8% of the blood donors were anti-dengue virus positive (IgG) at a cut-off of 20 RU/ml. This can also be due to cross reactivity (e.g. antibodies against TBE from immunisation).

- Sensitivity and specificity: 70 clinically characterised patient samples (Bernhard-Nocht Institute, Hamburg, Germany; University of Luebeck, Germany) were investigated with the EUROIMMUN Anti-Dengue Virus ELISA (IgG). The test demonstrated a sensitivity and specificity each of 100%.

**Correlation with Panbio ELISA:** Antibody concentrations were determined in 82 sera from patients with suspected dengue virus infection using Anti-Dengue Virus ELISA from EUROIMMUN and Panbio. The qualitative results of the two ELISA were 99% in agreement.

**Technical Data:**

- **Antigen:** The antigen source is dengue virus type 2 cultivated in vero cells. Microplate wells are coated with high-purified virus particles. Due to the high structural similarity between dengue virus types 1 to 4, the use of one virus type is sufficient to detect antibodies against all four virus types.

- **Calibration:** Quantitative, in relative units per milliliter (RU/ml).
  - Calibration serum 1: 200 RU/ml
  - Calibration serum 2: 200 RU/ml; cut-off
  - Calibration serum 3: 200 RU/ml

- **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.

- **Test procedure:** 30 min / 30 min / 15 min. Room temperature. Fully automatable.

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

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

- **Order no.:** EA 266b-9601-G

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