# CUS 24

# Dengue fever

# Dengue fever, NSI antigen becomes available on the French health system.

Dengue fever, an infectious viral disease transmitted by mosquito bites in tropical and subtropical regions of the planet. This disease is most frequently encountered in urban and semi-urban areas and is endemic in French Overseas territories where there are regular epidemics of variable length. This disease is notifiable in France and other countries. The presence of the mosquito vector in the south-east of France is a real cause for concern regarding the implantation of the disease in main land France. Clinically, dengue fever causes severe flu like symptoms. Dengue haemorrhagic fever is a potentially fatal complication and is found in the majority of Asian counties. In several of these countries it has now become a major cause of hospitalization and infantile mortality. There are 4 serotypes of the Dengue virus. Recovery from this disease entails definitive immunity against the serotype that caused the infection but only provides a partial and indefinite immunity against the three other serotypes.

Secondary infection by a different serotype than that of the primary infection could evoke a greater risk of severe disease and haemorrhagic complications. Clinical diagnosis is performed by detection of the virus or its components in the blood in the first days of infection. Culturing of the virus is possible but the benchmark technique used is RT-PCR. Screening for circulating NS1 antigen is a simple and efficient alternative for early stage diagnosis regardless of whether it is a primary or secondary disease. IgM antibodies are detectable at approximately 8 days after the onset of the first symptoms, followed by IgG. During secondary Dengue fever IgG antibodies rapidly increase whereas the IgM level remains at a low level or even absent.

#### NSI antigen (Ag)

The detection of this antigen has recently been added to the French nomenclature of acts of medical pathology (Official Journal 27/08/2010).

NS1 antigen can be screened for in both serum and plasma by either classic ELISA via a microplate technique or by rapid immunochromatography (ICT) (30 minutes) which has proved to be advantageous for diagnosis. The specificity of these two similar tests is 100%. Although the NS1 antigen is, in theory, detectable up to 7 days after the start of symptoms, studies have shown up until now that the sensitivity of the test is optimal between day 0 and day 5. The sensitivity is slightly better that ELISA. The positive predictive value of NS1 antigen is excellent. However, a negative test does not exclude infection (sample taken too late or sensitivity default). It is necessary to complete the profile by a RT-PCR and/or an IgM-IgG serology.

### Antigen and antibody kinetics during a primary infection of Dengue fever



Source: Institut Pasteur de Paris, Centre national de référence des arbovirus

# IgGSymptoms $2^{nd} serum$ $\Delta Ac \ge 4$ $d-7 \quad d-2 \quad 0 \qquad d5 \qquad d15-21$ Culture/ IgM? $d-7 \quad d-2 \quad 0 \qquad d5 \qquad d15-21$ Culture/ IgM? Serology

## Antigen and antibody kinetics during a secondary infection of Dengue fever

Source: Institut Pasteur de Paris, Centre national de référence des arbovirus

| Test                      | Sample                               | Details   | Openlab |
|---------------------------|--------------------------------------|---|---------|
| Dengue                    | type                                 |   | code    |
| NS1<br>antigen            | Serum or<br>plasma<br>at 4°C         | From day 1 to day 5<br>Primary and secondary<br>Dengue fever  | 4734    |
| Viral RNA<br>by<br>RT-PCR | Serum or<br>EDTA<br>plasma at<br>4°C | From day 1 to day 10<br>Primary and secondary<br>Dengue fever | 8863    |
| lgM                       | Serum at                             | From day 8  |         |
| antibodies                | 4°C                                  | Primary Dengue fever  |         |
| lgG                       | Serum at                             | Immunity screen   | 4730 or |
| antibodies                | 4°C                                  | Secondary Dengue fever  | 4730M   |

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