



Human herpesvirus-6 (HHV-6) qRT-PCR test

The test is performed to detect the presence of Human Herpes Virus type 6 (HHV-6) transcripts in endometrial biopsy samples. HHV-6 is a widespread double-stranded DNA virus. Two different species of HHV-6 are recognized: HHV-6A and HHV-6B. The HHV-6B is the predominant cause of childhood infection, roseola infantum [Yamanishi K. et al, 1988]. Specific diseases associated with HHV-6A have yet to be identified. Majority of HHV-6 infections are asymptomatic. Clinical symptoms associated with HHV-6A infection might include febrile illness, hepatitis, pneumonitis, encephalitis, but they primarily are associated with immunosuppression either primary or acquired (HIV infection, posttransplantation) [Dockrell DH, Paya CV, 2001]. The host tissue tropism for HHV-6 is broad and includes salivary glands, lymph nodes, liver, tonsils [De Bolle L et al, 2005]. It was reported that HHV-6A presence in endometrium might be an important factor in female unexplained infertility development. HHV-6A DNA was found in 43% of endometrial biopsies from primary unexplained infertile women compared with 0% of fertile controls; in contrast, HHV-6B analysis did not reveal presence of this variant in endometrium [Marci et al, 2016].

Methodology: mRNA expression is evaluated by RT-qPCR.

Reference result: Negative

Interpretation: a positive result indicates the detection of specific mRNA transcripts representative for HHV-6A/B presence in tested sample. A negative result indicates that no HHV-6A/B specific transcripts were detected in the specimen, but it does not exclude the possibility of recent infection.

Specimen requirements: endometrial biopsy obtained during the mid-luteal phase, 7 to 9 days after ovulation. Biopsy should be performed according to a standard procedure with a Pipelle catheter or similar. About 30-50 milligrams of tissue is required for analysis (for illustration purposes, this equates to one or two cubes of approximately 3x3 millimeters). Specimen should be collected into a tube with 3ml of RNA stabilization solution (provided by the laboratory) and shipped to the laboratory at ambient temperature.

Specimen stability in RNA stabilization solution: room temperature - 1 week, refrigerated - one month.

Rejection criteria: absence of sizeable endometrial tissue fragments; inadequate sample consisting only of blood and/or mucous substance.

Turnaround time: 5 – 7 business days.

References:

1. Yamanishi K., Okuno T., Shiraki K., Takahashi M., Kondo T., Asano Y., Kurata T. Identification of human herpesvirus-6 as a causal agent for exanthem subitum. *Lancet*. 1988;1:1065–1067.
2. Dockrell DH, Paya CV. Human herpesvirus-6 and -7 in transplantation. *Rev Med Virol* 2001, 11(1):23-36
3. De Bolle L, Naesens L, De Clercq E. Update on human herpes-virus 6 biology, clinical features, and therapy. *Clin Microbiol Rev*, 2005, 18:217-245
4. Marci R, Gentili V, Boetolotti D, Lo Monte G, Casellu E, Bolzan S, Rotola A, Di Luca D, Rizzo R. Presence of HHV-6A in endometrial epithelia cells from women with primary unexplained infertility. *PLoS ONE* 2016;11(7)