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Title Diagnosis of congenital cytomegalovirus infection through serology testing and/or viral genome detection

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Reference Link to full report in French: http://www.has-sante.fr/portail/jcms/c_2572929/fr/diagnostic-par-serologie-et/ou-par-recherche-du-genome-viral-de-l-infection-congenitale-a-cytomegalovirus

Aim

The Association of Health Insurance Funds (UNCAM) is applying for the inclusion on the list of procedures and services (LPS) reimbursed by the French National Health Insurance system, of several diagnostic tests relating to mother-to-child transmission of cytomegalovirus (CMV) infection *in utero*. These are the anti-CMV IgG avidity test and CMV viral load testing by gene amplification (PCR) in several types of sample: amniotic fluid from the mother, and urine and saliva from the neonate. UNCAM also suggests removing immunoenzymatic testing for anti-CMV IgG alone in pregnancy, and cell culture for CMV, from the LPS.
The aim of this report is to establish whether data from a critical analysis of the synthetic literature (good practice guidelines, systematic reviews and technology assessment reports) are consistent with the content of UNCAM's application and whether they therefore support this application for the inclusion or removal of the above tests on/from the LPS.

Conclusions and results

Noting that there is consistency between the conclusions of the synthetic literature analysis and almost all the content of UNCAM's application, HAS agrees with the applicant as regards:

- the proposal to include the anti-CMV IgG avidity test, as long as it is specified that after the first trimester of pregnancy, the results should be interpreted by clinicians and laboratory specialists with good knowledge of the use of this test;
- continuing to include anti-CMV IgM + IgG testing in pregnant women where recent CMV infection is suspected;
- the proposal to include CMV viral load testing in amniotic fluid, as long as it is specified that amniocentesis should be performed at least 7 weeks after the presumed time of maternal infection and after 21 weeks of pregnancy;
- the proposal to include CMV viral load testing in neonatal urine and saliva, as long as it is specified that samples should be taken in the first 3 weeks of life; UNCAM's proposal of a 10-day time window is considered too restrictive;
- the proposal to remove isolated testing for anti-CMV IgG in pregnancy from the LPS, as long as it is still included for late (retrospective) diagnosis of congenital CMV infection;
- the proposal to remove cell culture for CMV in pregnancy from the LPS.

In view of the critical analysis of the synthetic literature selected, the current strategy for laboratory diagnosis of congenital CMV infection can be summarised as follows. First-line diagnostic testing for primary maternal CMV infection is based on anti-CMV IgG and IgM tests. If anti-CMV IgM is positive, unless an IgG seroconversion is identified (proving the primary infection), then anti-CMV IgG avidity testing is recommended to date the primary infection. If there is a diagnosis (or suspicion) of recent maternal CMV infection, antenatal diagnostic testing may be requested to determine whether vertical transmission has occurred and whether the foetus is infected. This diagnosis involves amniocentesis, performed at least seven weeks after the primary infection and after the 21st week of pregnancy, which allows PCR testing for the virus in the amniotic fluid. An antenatal diagnosis must always be confirmed (or disproved) within 3 weeks of birth by PCR testing for the virus in neonatal urine or saliva.

Methods

The method selected was a short procedure involving the following steps:

1. identifying synthetic literature through an exhaustive literature search;
2. selecting publications with an adequately developed methodological quality;
3. analysis of consistency and writing a short rationale;
4. submitting the rationale directly to the HAS Board for approval.

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