Title Diagnosis of infections with the *herpes simplex* virus and the varicella-zoster virus by virus detection and/or serology in the mother/child setting

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Aim

National Health Insurance wishes to change the list of refundable procedures in laboratory medicine in respect of diagnostic tests for infections due to the *herpes simplex* virus (types 1 and 2, HSV-1/-2) and the varicella-zoster virus (VZV), viruses that belong to the family *Herpesviridae*, within the context of mother-to-child transmission (or the "mother/child setting"). The proposed changes, which have been specified by the national reference laboratory for these viruses, focus on the inclusion of testing for their DNA in various contexts and samples using PCR, the removal of other techniques for direct virus detection (direct immunological diagnosis and specific cultures), and the inclusion, the removal or the restriction of serological tests.
The aim 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 the application and whether they therefore support the proposals submitted by the applicant, so as to formulate an opinion relating to these proposals.

Conclusions

The conclusions of the critical analysis are consistent with almost all of the content of the application. HAS therefore favourably recommends these proposals. In some cases (shown below), the conclusions of the critical analysis do not support the application; in these cases, the opinion of HAS is based on the literature.

Overall, HAS agrees to the following:

For diagnostic tests for HSV-1/-2 infections in the mother/child setting:

- the proposal to include testing for the HSV genome by DNA amplification:
  - on maternal genital lesions during childbirth,
  - in neonates if there is a risk of neonatal herpes:
    - from the mucous membranes (conjunctiva, oropharynx, nasal cavities), but also from skin lesions, if present (item not included in the application),
    - in cerebrospinal fluid and blood, only in neonates presenting diagnostically suspicious signs of neonatal herpes of clinical (symptomatic baby) and/or laboratory (positive result for skin or mucous membrane samples) origin,
    - under the following conditions:
      - compliance with a delay of at least 24 h after birth before collection of the samples,
      - sampling from the various mucous membranes using a single swab to optimise the sensitivity of virus detection;
- the proposal to include testing for type-specific HSV-1 and -2 IgG antibodies, specifying (item not included in the application) that this test is carried out in the context of the first known episode of genital herpes in the course of the pregnancy or at childbirth, in order to establish whether it is a primary infection or a recurrence; the interpretation of the result of this test requires knowledge of the HSV serotype present in the lesions;
- the proposal to remove from the Nomenclature of Procedures in Laboratory Medicine:
  - the direct immunological diagnostic methods for the detection of HSV,
  - the specific cell culture and the non-specific culture (NSC) for virus identification (NSC remains a technique required for antiviral sensitivity testing, which is not a refundable test),
  - testing for non-type-specific HSV-1/-2 IgM antibodies for the diagnosis of primary HSV infection in the pregnant woman,
  - testing for non-type-specific HSV-1/-2 IgG antibodies in the pregnant woman,
  - testing for non-type-specific HSV-1/-2 IgM and IgG antibodies in neonates;

For diagnostic tests for VZV infections in the mother/child setting:

- the proposal to include testing for the VZV genome by DNA amplification:
  - in amniotic fluid, but on condition of mentioning (item not included in the application) the need to assess the risk/benefit relationship before performing the test, particularly as a function of the

stage of pregnancy, with the assistance of competent specialists,
    - in neonates, in samples from vesicles (vesicular fluid, vesicular lesions) and, if neurological involvement is suspected, in cerebrospinal fluid,
    - in the vesicles (vesicular fluid, vesicular lesions), only in the case of atypical eruptions in pregnant women;
- the proposal to remove from the Nomenclature of Procedures in Laboratory Medicine:
    - the direct immunological diagnostic methods for the detection of VZV,
    - the specific cell culture for VZV and the non-specific culture for virus identification (NSC remains a technique required for antiviral sensitivity testing, which is not a refundable test),
    - testing for VZV IgM + IgG antibodies for the diagnosis of recent VZV infection in the pregnant woman and neonates;
- the proposal to restrict the indication for the test for VZV antibodies included in the Nomenclature of Procedures in Laboratory Medicine to the following two contexts:
    - pregnant women who have had contact with a subject with chickenpox (item not included in the application) in whom the principal objective of the test is treatment with VZV immunoglobulin (Ig) antibodies, which should be carried out within 96 h and up to 10 days at a maximum following the risk contact (according to the SPCs of the immunoglobulins currently available),
    - women of reproductive age who are candidates for anti-VZV vaccination to comply with the current guidelines concerning the vaccination schedule that are in force in France.

Methods

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

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

Written by

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