

HHV-6A & Implantation

Clinician Brief – coVee™ HHV-6A Uterine Environment Test

1. Overview

coVee™ is an at-home menstrual fluid collection kit that screens for HHV-6A DNA in material from the uterine environment. It is intended as an adjunct to standard infertility evaluation, particularly in patients with unexplained infertility, recurrent implantation failure, or recurrent pregnancy loss.

2. What the test measures

- Target: HHV-6A DNA in endometrial tissue shed into menstrual fluid.
- Sample: ~1–2 mL of menstrual fluid collected at home during normal flow days.
- Method: quantitative PCR (qPCR) with typing to distinguish HHV-6A from HHV-6B.
- Output: qualitative (positive/negative) with quantitative viral load for follow-up after treatment.

3. Clinical rationale (high level)

- HHV-6A has been detected in endometrial biopsies from a subset of women with recurrent implantation failure or primary unexplained infertility, and not in endometrium from fertile controls.
- Infection may alter local immune signalling and endometrial receptivity in some patients.
- Small clinical series suggest that HHV-6A–positive women who receive targeted antiviral management can experience higher implantation and pregnancy rates compared with HHV-6A–positive women who are not treated.
- HHV-6A screening has been proposed as part of a broader evaluation in difficult "unexplained" or recurrent failure cases.

4. Interpreting results

Positive result

- HHV-6A DNA detected in the uterine environment sample.
- In appropriate clinical context (e.g., unexplained infertility, recurrent implantation failure, or recurrent loss), may support considering antiviral or related management as part of a broader plan.
- Quantitative results can be used to follow change in viral load after treatment if repeat testing is performed.

Negative result

- HHV-6A DNA not detected in the sample tested.
- Makes HHV-6A infection less likely to be a major contributor to implantation failure at the time of sampling.

5. Sampling and analytical performance (summary)

- Menstrual fluid provides a broad sample of endometrial cells and secretions from the uterine lining, which may reduce sampling error compared with a focal biopsy.
- The qPCR assay is designed to detect low levels of HHV-6A DNA and to differentiate HHV-6A from HHV-6B.
- Internal validation has shown high analytical sensitivity and specificity; false positives and negatives are expected to be uncommon, though all PCR testing remains subject to pre-analytical variables.

6. When to consider testing or retesting

- Consider screening in patients with unexplained infertility, recurrent implantation failure, or recurrent pregnancy loss, particularly when standard work-up is unrevealing.
- For HHV-6A–negative patients, retesting can be considered if new, unexplained difficulty conceiving emerges later (for example, secondary infertility), given the possibility of latency and reactivation.
- For HHV-6A–positive patients who undergo antiviral or related treatment, a follow-up coVee™ test can be used to assess change in viral load over time.

7. Advantages of coVee™ vs endometrial biopsy for HHV-6A

- Non-invasive: at-home menstrual fluid collection; no procedure room, anesthesia, or recovery required.
- Broader sampling: menstrual fluid contains cells and secretions from across the uterine lining, not just a focal biopsy site.
- Typing: distinguishes HHV-6A from HHV-6B, reducing the risk of misattributing HHV-6B detection to uterine HHV-6A pathology.
- Quantitative: provides viral load data that can be followed over time to assess response to treatment.
- Cost and acceptability: typically less costly to the patient and easier to repeat when needed.

8. Important caveats

- coVee™ is a focused HHV-6A screen. It does not replace endometrial biopsy when broader histologic information is needed.
- Clinical decisions should integrate this result with the full clinical picture and your established protocols.

9. Selected references

- Marci R et al. Detection of HHV-6A in endometrial biopsies from women with primary unexplained infertility and not in fertile controls. PLoS One. 2016.
- Coulam CB et al. HHV-6 DNA in endometrial samples from women with recurrent implantation failure. Am J Reprod Immunol. 2018.
- Bortolotti D et al. HHV-6A infection of endometrial epithelial cells alters local immune factors and trophoblast invasion. Am J Reprod Immunol. 2019.
- HHV-6 Foundation clinical summaries on HHV-6A and infertility (hhv-6foundation.org).

For more information, visit: FERTILITYPHOENIX.COM/CLINICIANS or contact Fertility Phoenix to request a clinician-to-clinician call.