Hormonal testing in menstrual blood enhances reproductive freedom

In the article "Concordance of hemoglobin A1c and reproductive hormone levels in menstrual and venous blood" by Nasseri et al. (1), the investigators demonstrate the option of using menstrual effluent with a dried blood spot (DBS) in a specially prepared pad, the Q-pad, to measure serum markers using standard laboratory techniques and noninvasive methods. The procedure was initially reported in 1989 (2), and since then, it has been a promising but little-used venue for obtaining valuable information on ovarian function. Menstrual effluent contains whole blood in addition to vaginal fluids and endometrial tissues (3), and the Q-pad can be used to measure both markers that require whole blood, such as hemoglobin A1c (HbA1c) levels, and those that require serum, such as follicle-stimulating hormone (FSH), luteinizing hormone, and antimüllerian hormone (AMH) levels, in addition to other steroid hormone levels. Previous studies have shown a good correlation between menstrual blood and peripheral blood measurements for HbA1c (4) levels, FSH levels, lipoprotein levels, and other marker levels (5). The correlation between menstrual DBS testing and serum in this study is excellent, and the investigators have evaluated the effect of various vaginal contaminants as to their effect on measurement, i.e., semen, vaginal medications, urine, and others, with only fecal contamination being an issue. Although the technique is not new and other studies have explored its applications, this represents a significant, controlled, prospective study.

The ability for the patient to collect a specimen at home is advantageous when transportation to a laboratory is not available and access to care is complicated. In addition, the stress-free collection would increase access and adherence for patients such as adolescents, those who fear needles, or all women in categories where venipuncture is not an option.

However, noninvasive laboratory testing remains a promise after >30 years of research. One of the reasons for this is that accuracy decreases with markers with a low concentration during the menses, such as estradiol concentrations.

This technology will need "real-world" testing in a clinical population. In this study, nearly 25% of consented individuals did not complete participation before sample acquisition, which is reported as a limitation. More importantly, 11%–20% of the samples tested did not result because of DBS sample issues, i.e., undersaturated strips, fecal contamination, or, in the case of serum sampling, the values fell below the test range. The investigators stated that 5%–10% of excluded samples resulted from patient error. They state that there is a need for adequate patient instruction to be paired with appropriate medical oversight. This "added burden" to medical practices will require evaluation.

Because for most women undergoing fertility testing, the initial evaluation includes a cycle-day 2–4 measurement of AMH, FSH, luteinizing hormone, and estradiol levels, measuring these markers in the menstrual effluent would be appealing and suitable. Adding AMH would complete the evaluation of ovarian reserve. This noninvasive testing tool is appreciated as it allows large volumes of women to assess their fertility potential when desired and endorses reproductive freedom. When further evaluations are needed, these can be quickly pursued to inform appropriate decisions.

It is essential to underscore the importance of having a trained reproductive endocrinologist interpret the results to avoid overreassurance, or alarmism, about women's reproductive potential.

In conclusion, this testing method would increase access to care for women in underserved and low-income areas, where it is not easy to obtain transportation, childcare, or the phlebotomy laboratory is out of reach, and it would be especially beneficial for the initial evaluation of ovarian reserve. In addition, it could alleviate at least the first of many venipunctures during in vitro fertilization treatment cycles.

We welcome and endorse the further development of this technology, which promises to significantly impact women's quality of life.

CRediT Authorship Contribution Statement

Laura Detti: Conceptualization, Writing – original draft, Writing – review & editing. **William E. Gibbons:** Conceptualization, Writing – original draft, Writing – review & editing.

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