

## Medical Policy Manual

**Topic:** Salivary Hormone Testing for Aging and Menopause

**Date of Origin:** May 6, 2003

**Section:** Laboratory

**Approved Date:** February 2013

**Policy No:** 36

**Effective Date:** April 1, 2013

### IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

### DESCRIPTION

For several decades, there has been interest in testing various hormone levels using saliva as the specimen rather than blood, plasma, or urine. Salivary testing has been viewed as potentially more advantageous due to its noninvasive nature and the relative ease and convenience of sample collection, which can be done in the home.

Consumers now have the ability to order home saliva tests over the Internet for some hormones such as estrogen, progesterone, testosterone, melatonin, cortisol, and dehydroepiandrosterone (DHEA). A physician's prescription is not required for these saliva tests, which are primarily promoted for the evaluation of menopause and aging.

### MEDICAL POLICY CRITERIA

Salivary hormone testing is considered **investigational** for the screening, diagnosis and/or monitoring of aging and menopause. Salivary hormone tests include, but are not limited to:

1. Cortisol
2. Dehydroepiandrosterone (DHEA)

3. Estrogen
4. Melatonin
5. Progesterone
6. Testosterone

## SCIENTIFIC EVIDENCE

Validation of any new diagnostic technique involves the following steps:

1. Technical feasibility of the test must be demonstrated, including assessment of its reproducibility and precision. For comparison among studies, a common standardized protocol is necessary.

Hormone concentrations in saliva are subject to a number of factors, which influence their correlation with the total plasma concentration, or the unbound ("free") fraction of hormone. Such factors include: binding affinity for specific protein carriers; saliva flow; use of pharmacologic agents, which may disturb the ratio of free to bound hormone by displacing the bound hormone; metabolism of the hormone by salivary gland epithelial cells or oral bacteria; circadian rhythms; and contamination of the saliva specimen with blood, food, gingival fluid, or tissue debris.<sup>[1,2]</sup> Despite these variables, the technical feasibility of measuring some salivary hormone levels has been demonstrated in some published studies. However, it is not clear that standardized protocols for measuring salivary hormone levels are used.<sup>[1,3]</sup> There also continues to be a need for a protocol for sample collection and handling. Whembolua and colleagues studied the saliva sample of 19 healthy adults who provided saliva samples upon rising in the morning, rinsed their mouths with water, and donated a second specimen 10 minutes later.<sup>[4]</sup> Samples were either left untreated or passed through a 0.22-micron filter and then frozen at -80°C or incubated at room temperature for 10 days. Aliquots of each sample were cultured on agar to determine baseline and post-incubation (or freezing) bacteria load. Bacteria counts were not significantly influenced by rinsing (with water), were substantially reduced by filtration, and increased by incubation at room temperature. Average levels of salivary testosterone and cortisol, but not DHEA, were significantly lower in samples stored at room temperature than samples frozen the day of collection. The change in bacteria count induced by storing samples at RT was associated with a change in testosterone but not cortisol or DHEA. When samples were passed through a 0.22-micron filter bacteria counts were reduced, and the association between bacteria and testosterone was reduced to nonsignificant. These findings contribute to a growing body of literature revealing that the process of sample collection, storage, and handling can dramatically influence the accuracy of information generated when salivary biomarkers are integrated into research and clinical diagnostics.

2. Normal and abnormal values as studied in different clinical situations must be established. For accurate interpretation of study results, sensitivities, specificities, and positive and negative predictive values compared to a gold standard must be known.

There are no published studies documenting sensitivity, specificity, or positive and negative predictive values for any salivary hormones when used to diagnose, treat, or monitor menopause or aging.

3. The clinical utility of both positive and negative tests must be established. The clinical utility of a diagnostic technique is related to how the results of that study can be used to benefit patient management. Relevant outcomes of a negative test (ie, suspected pathology is not present) may be avoidance of more invasive diagnostic tests or avoidance of ineffective therapy. Relevant outcomes of a positive test (ie, suspected outcome is present) may also include avoidance of a more invasive test plus the institution of specific, effective therapy.

There are no published clinical trials that demonstrate how the results of salivary hormone testing can be used clinically to direct patient treatment of menopause or aging. In addition, there are no published national practice guidelines that advocate the use of salivary hormone testing in the diagnosis, treatment or monitoring of menopause or aging.

## **Clinical Practice Guidelines**

The American College of Obstetricians and Gynecologists (ACOG) and the American Society of Reproductive Medicine Practice Committee (ASRM)<sup>[5]</sup>

In 2012, ACOG and ASRM published a joint committee opinion on the use of bioidentical hormone therapy as a therapy treatment for menopause. Bioidentical hormones are identical in molecular structure to women's endogenous hormones, but they are synthesized from plant products.<sup>[6]</sup> Advocates of therapy with bioidentical hormones recommend the use of salivary hormone testing as a means of offering individualized treatment for menopause. The ACOG/ASRM statement concluded the following:

The interest in a more natural approach to hormone therapy has focused attention on bioidentical hormones — hormones that are identical in molecular structure to the hormones women make in their bodies. They're not found in this form in nature but are made, or synthesized, from a plant chemical extracted from yams and soy. Bioidentical estrogens are 17 beta-estradiol, estrone, and estriol. (Estradiol is the form of estrogen that decreases at menopause.) Bioidentical progesterone is simply progesterone. It's micronized (finely ground) in the laboratory for better absorption in the body.

- “There is no evidence that hormonal levels in saliva are biologically meaningful.
- First, salivary levels do not consistently provide a reasonable representation of endogenous, circulating serum hormones. There is large within-patient variability in salivary hormone concentrations, especially when exogenously administered hormones are given. Salivary hormone levels vary depending on diet, time of testing, and specific hormone being testing.
- Second, because the pharmacokinetics of exogenously administered compounded hormones cannot be known, it is not possible to estimate with reliability how and when to test saliva to obtain a representative result.
- Third, saliva contains far lower concentrations of hormone than serum and is prone to contamination with blood, infectious agents, and epithelial cells—all of which may affect the level of hormone to be measured.”

American Association of Clinical Endocrinologists (AACE)<sup>[7]</sup>

In 2011, AACE published medical guidelines for the clinical practice of diagnosing and treating menopause. The group specifically addressed the use of saliva testing as part of bioidentical hormone therapy, stating:

- “Salivary hormone level testing is recommended by many bioidentical hormone proponents as a means of providing patients with “individualized” therapy. Yet these methods are not approved by either the FDA or the Clinical Laboratory Improvement Amendments (the US Health and Human Services agency regulating laboratory standards). Accurate studies have revealed large intrasubject variability in salivary sex hormone concentrations, which fluctuate depending on numerous variables, including diet, hydration, and circadian rhythm.”

#### North American Menopause Society (NAMS)<sup>[8]</sup>

In 2012, NAMS published a position statement regarding hormone therapy and directly addressed the increased use of custom-made hormone therapy formulas along with salivary hormone testing. NAMS warns that the use of these types of therapy and saliva testing have proven to be inaccurate and unreliable. Specifically, NAMS states:

- “Custom-compounded formulations, including BHT [bioidentical hormone therapy], have not been tested for efficacy or safety; product information is not consistently provided to women along with their prescription, as is required with commercially available HT; and batch standardization and purity may be uncertain. The dosing of compounded progesterone is particularly difficult to assess because the levels in serum, saliva, and tissue are markedly different.”

#### **Summary**

There is insufficient evidence in the published scientific literature to permit conclusions concerning the impact of salivary hormone testing on health outcomes. Specifically, it is not known how such testing alters the diagnosis, treatment or monitoring of menopause and aging; therefore salivary hormone testing is considered investigational for these indications.

#### **REFERENCES**

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## CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	None	
HCPCS	S3650	Saliva test, hormone level; during menopause