INFERTILITY DIAGNOSIS TESTING

Policy Number: 2013M0041A  Effective Date: January 1, 2014

Table of Contents:

<table>
<thead>
<tr>
<th>Table of Contents</th>
<th>Page</th>
<th>Cross Reference Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>POLICY DESCRIPTION</td>
<td>2</td>
<td>Not Available</td>
</tr>
<tr>
<td>COVERAGE RATIONALE/CLINICAL CONSIDERATIONS</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>BACKGROUND</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>REGULATORY STATUS</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>CLINICAL EVIDENCE</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>APPLICABLE CODES</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>REFERENCES</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>POLICY HISTORY/REVISION INFORMATION</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

INSTRUCTIONS:

“Medical Policy assists in administering UCare benefits when making coverage determinations for members under our health benefit plans. When deciding coverage, all reviewers must first identify enrollee eligibility, federal and state legislation or regulatory guidance regarding benefit mandates, and the member specific Evidence of Coverage (EOC) document must be referenced prior to using the medical policies. In the event of a conflict, the enrollee’s specific benefit document and federal and state legislation and regulatory guidance supersede this Medical Policy. In the absence of benefit mandates or regulatory guidance that govern the service, procedure or treatment, or when the member’s EOC document is silent or not specific, medical policies help to clarify which healthcare services may or may not be covered. This Medical Policy is provided for informational purposes and does not constitute medical advice. In addition to medical policies, UCare also uses tools developed by third parties, such as the InterQual Guidelines®, to assist us in administering health benefits. The InterQual Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. Other Policies and Coverage Determination Guidelines may also apply. UCare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary and to provide benefits otherwise excluded by medical policies when necessitated by operational considerations.”
**POLICY DESCRIPTION:**

This policy provides information on the use of diagnostic procedures and tests to evaluate and determine the cause of infertility. Note that this policy does not address infertility treatment.

Infertility is a medical illness in which an otherwise healthy female member is unable to achieve pregnancy or produce conception after 12 months or more of regular, unprotected heterosexual coitus (sexual intercourse), or six months of frequent, unprotected heterosexual sexual intercourse if the female partner is over age 35.

**COVERAGE RATIONALE / CLINICAL CONSIDERATIONS:**

The first stage of infertility management is the accurate diagnosis of the condition. In order to be eligible for infertility benefit coverage, the female member must meet the **MEDICAL NECESSITY** criteria for infertility and age listed below:

- Failure to achieve pregnancy after 12 months or more of regular, unprotected heterosexual intercourse, OR
- Women aged 35 and older who are unable to achieve pregnancy after 6 months of regular, unprotected heterosexual intercourse.

Depending on the member of an infertile couples’ unique medical situation, the following diagnostic services may be considered **MEDICALLY NECESSARY**, when performed solely to establish the underlying etiology of infertility.

**FEMALE BASIC INFERTILITY DIAGNOSTIC SERVICES**

The following services are considered medically necessary for the diagnosis of infertility in women:

A. History and physical examination

B. Laboratory studies:
   1. Diagnostic tests for general medical evaluation, including complete blood count (CBC), liver function tests (LFT), lipid panel (total cholesterol, HDL cholesterol, triglycerides), fasting glucose challenge levels
   2. Rapid plasma reagin test (RPR), Human Immunodeficiency Virus (HIV), cultures for chlamydia and gonorrhea, Rubella serology
   3. Anti-sperm antibodies (e.g., immunobead or mixed antiglobulin method)
   4. Post-coital testing (PCT) (Simms-Huhner test) of cervical mucus
   5. Serum hormone levels:
      a. Androgens (testosterone, androstenedione, dehydroepiandrosterone sulfate (DHEA-S) if there is evidence of hyperandrogenism (e.g., hirsuitism, acne, signs of virilization) or ovulatory dysfunction
      b. Gonadotropins (serum follicle-stimulating hormone [FSH], luteinizing hormone [LH]) for women with irregular menstrual cycles or age-related ovulatory dysfunction.
      c. Human chorionic gonadotrophin (hCG)
      d. Prolactin for women with an ovulatory disorder, galactorrhea, or a pituitary tumor
      e. Progestins (progesterone, 17-hydroxyprogesterone)
      f. Estrogens (estradiol)
g. Thyroid stimulating hormone (TSH)

h. Adrenocorticotrophic hormone (ACTH) for ruling out Cushing's syndrome or Addison's disease in women who are amenorrheic

i. Clomiphene citrate challenge test

6. Karyotype testing for couples with recurrent pregnancy loss (3 or more consecutive spontaneous abortions)

C. Diagnostic procedures:

The following diagnostic procedures are considered medically necessary:

1. CT or MR imaging of sella turcica, if prolactin is elevated
2. Endometrial biopsy
3. Hysterosalpingography (hysterosalpingogram (HSG)) or hysterosalpingo-contrastultrasonography to screen for tubal occlusion.
4. Hysteroscopy, salpingoscopy (falloscopy), hydrotubation where clinically indicated
5. Laparoscopy and contrast dye to assess tubal and other pelvic pathology, and to follow-up on hysterosalpingography abnormalities
6. Sonohysterography to evaluate the uterus
7. Ultrasound (e.g., ovarian, transvaginal, pelvic)
8. Monitoring of ovarian response to ovulatory stimulants:
   a. Estradiol
   b. FSH
   c. hCG quantitative
   d. LH assay
   e. Progesterone
   f. Serial ovarian ultrasounds for cycle monitoring

**MALE BASIC INFERTILITY DIAGNOSTIC SERVICES**

The following services are considered medically necessary for the diagnosis of infertility in men:

A. History and physical examination

B. Laboratory studies:
   1. Anti-sperm antibodies (e.g., immunobead or mixed antiglobulin method)
   2. Cultures:
      a. Prostatic secretion
      b. Semen
      c. Urine
   3. Serum hormone levels:
      a. 17-hydroxyprogesterone
      b. Adrenal cortical stimulating hormone (ACTH)
      c. Androgens (testosterone, free testosterone)
      d. Estrogens (e.g., estradiol, estrone)
      e. Gonadotropins (FSH, LH)
      f. Growth hormone (GH)
      g. Prolactin for men with reduced sperm counts, galactorrhea, or pituitary tumors
      h. Sex hormone binding globulin (SHGB) for men with signs and symptoms of hypogonadism and
low normal testosterone levels. (SHGB is not indicated in the routine evaluation of male infertility)

i. Thyroid stimulating hormone (TSH) for men with symptoms of thyroid disease

4. Semen analysis (volume, pH, liquefaction time, sperm concentration, total sperm number, motility (forward progression), motile sperm per ejaculate, vitality, round cell differentiation (white cells versus germinal), morphology, viscosity, agglutination). Because of the marked inherent variability of semen analyses, an abnormal result should be confirmed by at least one additional sample collected one or more weeks after the first sample.

- For men with abnormal semen analysis exposed to gonadotoxins, up to 4 semen analyses are considered medically necessary.
- For men with a normal initial semen analysis, a repeat semen analysis is considered medically necessary, if there is no pregnancy 4 months after the initial normal semen analysis.
- If the result of the first semen analysis is abnormal and the man has not been exposed to gonadotoxins, up to 2 repeat confirmatory tests may be considered medically necessary.

5. Semen leukocyte analysis (e.g., Endtz test, immunohistochemical staining)

6. Seminal fructose

8. Blood test for cytogenetic analysis (karyotype and FISH) in men with severe deficits of semen quality or azoospermia (for consideration of ICSI)

9. Cystic fibrosis mutation testing in men with congenital absence of vas deferens

10. Y chromosome microdeletion analysis in men with severe deficits of semen quality or azoospermia (for consideration of ICSI). Note: Y chromosome microdeletion analysis is not routinely indicated before ICSI, and is subject to medical necessity review

11. Sperm function test (sperm penetration assay, zona-free hamster egg penetration test)

C. Diagnostic procedures:

1. CT or MR imaging of sella turcica if prolactin is elevated

2. Rectal ultrasound (indicated when ejaculatory duct obstruction is suspected)

3. Scrotal exploration

4. Scrotal (testicular) ultrasound

5. Testicular biopsy

6. Transrectal ultrasound

7. Vasography

8. Venography

For both female and male the following diagnostic tests or procedures are considered EXPERIMENTAL AND INVESTIGATIONAL for diagnosing infertility:

- Seminal alpha-glucosidase, zinc, citric acid, and acid phosphatase
- Computer-assisted sperm analysis (CASA)
- Hemizona assay
- Sperm hyaluronan binding assay (HBA)
- Hypoosmotic swelling test
- In vitro testing of sperm penetration such as postcoital cervical mucus penetration, sperm penetration assay (SPA), zona-free hamster egg assay or sperm acrosome reaction assay
- Sperm DNA integrity testing (e.g., Sperm Chromatin Structure Assay (SCSA), Comet assay, sperm DNA fragmentation assay, TUNEL assay, sperm nucleus maturation, sperm DNA Decondensation™ Test
Clinical Considerations:
Principles of care include providing information through couple-centered management, describing psychological effects of fertility problems, and providing specialist and generalist care.

- Couples who experience problems in conceiving should be seen together because both partners are affected by decisions surrounding investigation and treatment.
- Couples who experience fertility problems should be offered counseling because fertility problems themselves, and the investigation and treatment of fertility problems, can cause psychological stress.
- Couples who experience fertility problems should be informed that they may find it helpful to contact a fertility support group.
- Couples who are trying to become pregnant should be informed that alcohol intoxication is detrimental to semen quality and increases the risk of harming a developing fetus.
- Women who smoke should be informed that this is likely to reduce their fertility.
- Women who have a body mass index (BMI) of 30 or over should be informed that they are likely to take longer to conceive.
- Women who have a BMI of less than 19 and who have irregular menstruation, or are not menstruating, should be advised that increasing body weight is likely to improve their chance of conception.
- Men should be informed that there is an association between elevated scrotal temperature and reduced semen quality, but that it is uncertain whether wearing loose-fitting underwear improves

There is insufficient evidence to permit conclusions regarding the use of these tests. More studies are needed to support improved outcomes with use of these diagnostic tests.

Aging is not an illness and services to overcome the effects of natural aging are NOT MEDICALLY NECESSARY.

Infertility services for women with natural menopause, aged 40 years and older, are NOT MEDICALLY NECESSARY, as such services are not considered treatment of disease.
fertility.

- A number of prescription, over-the-counter, and recreational drugs interfere with male and female fertility, and therefore a specific enquiry about these should be made to people who are concerned about their fertility and appropriate advice should be offered.

**BACKGROUND:**

Infertility is defined as the failure to achieve pregnancy after twelve months of unprotected intercourse in women < 35, and after six months in women age 35 and over. U.S. prevalence is estimated at seven to eight percent of married women aged 18 to 44 years. The term primary infertility is applied to a couple who has never achieved a pregnancy, while secondary infertility indicates that at least one previous conception has taken place. (Agency for Healthcare Research and Quality [AHRQ], 2008; American Society of Reproductive Medicine [ASRM], 2008).

Infertility can affect one or both reproductive partners. Testing will determine if either partner has reduced fertility. A female factor is responsible for approximately 50% of cases, (e.g., pelvic adhesions, ovarian dysfunction, endometriosis, prior tubal ligation), while male factors account for up to 30% (e.g., abnormalities in sperm production, function, transport or prior vasectomy). Multiple causes are found in a number of cases. In up to 15% of cases, no obvious cause can be identified.

Some underlying factors are reversible through medical intervention. The major underlying causes of infertility include: ovulatory failure, fallopian tube damage or blockage, cervical, uterine/endometrial, and male partner factors. While infertility may be caused by disease, menopause and perimenopause are natural conditions. There are many known causes of infertility, and in some cases, no specific cause is found.

The preliminary approach to infertility involves physical examination, laboratory studies, diagnostic testing, and typically begins with the evaluation of ovulatory, tubal, and male factors. Other potential contributing causes that may be explored include genetic factors and immunological factors.

- The female infertility diagnostic workup to determine the underlying etiology includes a basic evaluation of ovulatory dysfunction, including basal body temperature recordings, laboratory studies and hormone levels. Additional studies are performed when the initial workup fails to provide definitive information. Tests may include:
  - Ultrasound
  - Hysteroscopy
  - Hysterosalpingography
  - Diagnostic laparoscopy with or without chromotubation
  - Sonohysterography

According to the ASRM, menopause is the natural cessation of ovarian function, when estrogen production decreases and menstruation ceases. Normally menopause occurs between 42 and 56 years of age. The society also notes that approximately 1% of women under the age of 40 develop early menopause, also called premature ovarian failure.

ASRM currently indicates that “Recurrent pregnancy loss is a disease distinct from infertility, defined by two or more failed pregnancies.” This distinct condition should be evaluated and treated in accordance
with the recommendations of the American College of Obstetrics and Gynecology (ACOG) and ASRM.

- The male infertility diagnostic workup to determine the underlying etiology begins with the physical examination and continues with the semen analysis, which is considered the primary screening test for male factor infertility. Semen analysis is generally done through the examination of two specimens at least one month apart, and generally precedes invasive testing of the female partner. The semen analysis provides detailed information on semen volume, sperm concentration, motility, pH, fructose, leukocytes, and morphology. Depending on the clinical situation, repeat semen analyses may be performed every one to three months, up to a total of five. Performing greater than five semen analyses provides little additional diagnostic value. Other laboratory studies include an endocrine evaluation, antisperm antibodies, post-ejaculatory urinalysis, urine culture and semen culture. Additional testing includes:
  - Transrectal ultrasound in individuals with azoospermia or oligospermia
  - Scrotal ultrasound for individuals in whom testicular mass is suspected or for whom physical exam is difficult or inconclusive
  - Vasography or testicular biopsy in individuals with azoospermia
  - Scrotal exploration

Genetic testing for cystic fibrosis is performed in males with congenital absence of vas deferens, for males with azoospermia, or severe oligospermia with palpable vas deferens (refer to the Genetic Testing medical policy). Karyotyping for chromosomal abnormalities and Y-chromosome deletion testing may be done in individuals with nonobstructive azoospermia or severe oligospermia.

Once the infertility has been diagnosed, basic treatments for infertility may begin.

**Smoking:** The prevalence of infertility is higher, and the time it takes to conceive is longer, in smokers compared to nonsmokers. Active smoking by either partner has adverse effects, and the impact of passive cigarette smoke exposure is only slightly smaller than for active smoking. Research indicates that cigarette smoking is harmful to a woman’s ovaries, and the degree of harm is dependent upon the amount and the period of time a woman smokes. Smoking appears to accelerate the loss of eggs and reproductive function and may advance the time of menopause by several years. Components in cigarette smoke have been shown to interfere with the ability of cells in the ovary to make estrogen and to cause a woman’s eggs (oocytes) to be more prone to genetic abnormalities. Smoking is strongly associated with an increased risk of spontaneous miscarriage and possibly ectopic pregnancy as well. Pregnant smokers are more likely to have low birth weight babies and premature birth. The incidence of sudden infant death syndrome (SIDS) also increases in households where someone smokes. Nearly twice as many in vitro fertilization (IVF) attempts are required to conceive in smokers than in nonsmokers. Studies of IVF have reported that female smokers require higher doses of gonadotropins to stimulate their ovaries, have lower peak estradiol levels, fewer oocytes obtained, more canceled cycles, lower implantation rates, and undergo more cycles with failed fertilization than nonsmokers. Miscarriage rates are also increased. The adverse effect of cigarette smoking is more noticeable in older women. Overall, the reduction in natural fertility associated with smoking may not be overcome by assisted reproductive technologies. Therefore, smokers should be strongly urged not to smoke for at least 2 months prior to infertility treatment.

**Obesity:** Obesity leads to an increase in spontaneous abortion after assisted reproductive treatment. Spontaneous abortion after assisted reproductive treatment occurs 18% for normal weight and 31% for Body Mass Index (BMI) ≥ 35. There is also increased surgical risk in oocyte retrieval. Obesity may be a sign of Polycystic Ovarian Syndrome (PCOS), which may require different treatment. It has been demonstrated
that weight loss can improve the fertility of obese women through the recovery of spontaneous ovulation and the response to ovarian stimulation. Live birth rate was 9% lower for women with BMI > 30 undergoing IVF. Therefore, women with BMI greater than 30 should be strongly encouraged to lose weight.

REGULATORY STATUS:

1. **U.S. FOOD AND DRUG ADMINISTRATION (FDA):**
   Sperm DNA integrity testing (Sperm Chromatin Structure Assay (SCSA)), Comet assay, sperm DNA fragmentation assay, TUNEL assay, Sperm DNA Decondensation Test and E-egrity uterine receptivity testing is regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988. Premarket approval from the FDA is therefore not required for this laboratory testing.

   In November 2003, the FDA approved the use of Sperm-Hyaluronan-Binding Assay for the following indications: 1) as a component of the standard analysis of semen in the diagnosis of suspected male infertility, and 2) as a component of analyses for determining the proper course of in vitro fertilization (IVF) treatment of infertility. Additional information is available at:

2. **CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS):**
   **Treatment for Infertility:** Reasonable and necessary services associated with treatment for infertility are covered under Medicare. Infertility is a condition sufficiently at variance with the usual state of health to make it appropriate for a person who normally is expected to be fertile to seek medical consultation and treatment. Medicare does not have a National Coverage Determination (NCD) for Infertility. See the Medicare Benefit Policy Manual, Chapter 15 – Covered Medical and Other Health Services §20.1 - Physician Expense for Surgery, Childbirth and Treatment for Infertility at [http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf](http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf).

   Non-covered services for infertility are addressed in the Non-covered Services Local Coverage Determinations (LCD) for non covered infertility services.

3. **MINNESOTA DEPARTMENT OF HUMAN SERVICES (DHS):**
   Minnesota DHS in its Provider Manual, Reproductive Health/OB-GYN Section (Revised: 01-07-2010), has the following coverage statement in regard to infertility:
   **Covered Services**
   - Infertility services, limited to diagnosis and treatment of medical problems causing infertility (e.g., pituitary or ovarian tumor, testicular mass).

   **Non-Covered Services**
   - Artificial insemination, including in vitro fertilization
   - Fertility drugs and all associated services
   - Reversal of voluntary sterilization
CLINICAL EVIDENCE:

**SUMMARY:**

Evidence evaluated in this report was obtained primarily from searches of the PubMed database spanning January 1990 through September 2013.

Formal evaluation of infertility is generally initiated in women attempting pregnancy who fail to conceive after one year or more of regular, unprotected intercourse. However, there are an increasing number of women over the age of 35 who are seeking infertility services. Since reproductive potential decreases in the early to mid thirties, for this age group formal evaluation typically begins earlier. For couples over age 35, it is generally recommended that infertility testing begins after 6 months of unsuccessful attempts at conception (ASRM, 2012d; Williams, Elam, 2007; Institute for Clinical Systems Improvement [ICSI], 2004). In some cases, an evaluation may be warranted prior to one year if there is a known male infertility risk factor such as bilateral cryptorchidism or known female risk factor (AUA, 2010a).

**Computer-Assisted Sperm Analysis (CASA)**

The evidence does not suggest that the predictive value of CASA is superior compared with conventional semen analysis. Only a very small proportion of the variance in fertility outcomes was explained by these variables, suggesting that other factors, not identified by semen analysis, are more important. Therefore, although CASA systems have the potential to reduce error in measurement and produce a larger array of semen variables, the literature to date does not demonstrate that these variables contribute clinically valuable information above and beyond the information already provided by conventional semen analysis (Hayes, 2011).

**Hemizona Assay (HZA) Test**

There is inadequate published scientific data to permit conclusions regarding the use of the hemizona assay test. A literature search identified one clinical trial that evaluated the value of HZA as a predictor of pregnancy in patients undergoing controlled ovarian hyperstimulation (COH) and intrauterine insemination (IUI). Results of the study indicated that HZA predicted pregnancy in the IUI setting with high sensitivity and negative predictive value in couples with male factor infertility (Arslan, 2006).

**Hyaluronan Binding Assay (HBA)**

There is inadequate published scientific data to permit conclusions regarding the use of HBA. A literature search identified one study that investigated the relationship between HBA and fertilization rate in conventional IVF in 175 IVF patients. The investigators concluded that the clinical predictive value of HBA for sperm-fertilizing ability in vitro is limited (Ye, 2006).

**Sperm DNA Integrity Testing (Sperm Chromatin Structure Assay [SCSA], Comet Assay, Sperm DNA Fragmentation Assay, TUNEL assay)**

A meta-analysis performed by Li et al. (2006) concluded that sperm DNA damage, as assessed by SCSA, had no significant effect on the chance of clinical pregnancy after in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) treatment. Another meta-analysis concluded that SCSA was significantly predictive for reduced pregnancy success using in-vivo, intrauterine insemination (IUI) and routine IVF (Evenson, 2006). A study conducted by Gandini et al. (2004) found no differences in SCSA parameter values between patients initiating pregnancies and not doing so in ICSI or IVF. Pregnancy was obtained even with high levels of DNA fragmentation index. A cross-sectional prospective study concluded that there is a moderate
correlation between sperm motility and SCSA parameters and supported the assumption that motility and SCSA can be relatively independent predictors of infertility (Giwercman, 2003).

**Sperm Penetration Tests**

Aoki et al. (2005) evaluated the relationship between SPA scores and polyspermy rates during conventional IVF cycles in 1350 consecutive IVF patients. A significant positive relationship was observed between SPA score and polyspermy rate. Clinical pregnancy and implantation rates improved slightly as SPA score increased and there was a decrease in the rate of spontaneous abortion as SPA score increased.

A prospective study by Freeman et al. (2001) evaluated the diagnostic accuracy of the sperm penetration assay (SPA) and standard semen parameters for subsequent fertilization in 216 couples undergoing IVF. The SPA predicted IVF fertilization with 84% negative predictive value and 98% positive predictive value, with overall correct prediction in 88% of cycles. In contrast, sperm concentration, motility, morphology, and complete sperm analysis showed poor predictive accuracy. Results suggest that SPA can predict which couples are likely to have success with normal fertilization in IVF and which might benefit from intracytoplasmic sperm injection.

A meta-analysis by Oehninger et al. (2000) used data from 2906 patients in 34 prospective, controlled studies to evaluate the predictive value of four categories of sperm functional assays, including SPA, for IVF outcome. In this analysis, the sperm-zona pellucida binding assay and the induced-acrosome reaction assay had a high predictive value for fertilization outcome. SPA had a relatively high positive predictive value (more than 70%), but the negative predictive value was variable, ranging from 11% to 100%, with most studies reporting NPV less than 75%. The authors noted that this assay was limited by the need for standardization.

**Uterine Receptivity Testing**

Results of available studies provide evidence that low levels of beta-3 integrin are correlated with infertility. Although the most thorough of the available studies found that the correlation between reduced beta-3 expression and infertility is reproducible, these studies fail to provide convincing evidence that assessment of beta-3 expression improves patient management or clinical outcomes. Since the E-tegrity Test has not been shown to provide definitive diagnostic information, its clinical role cannot be defined. Additional studies are needed to determine whether the test provides information that alters patient management or improves clinical outcomes, such as restoration of fertility (Hayes, 2010).

**Immunological factors Testing**

Immunological factors may adversely affect fertility. As a result, various testing and treatment modalities have been proposed including, but not limited to, natural killer cell testing, antiphospholipid antibodies, antiprothrombin antibodies, embryotoxicity assay, serum inhibin B testing, and immune treatments such as peril-implantation glucocorticoids, anti-tumor necrosis factor agents (infliximab, etanercept), leukocyte immunization and IV immunoglobulin therapy. Nonetheless, evidence in the published, scientific literature is insufficient to support improved individual outcomes (Royal College of Obstetricians and Gynaecologists [RCOG], 2003; RCOG, 2008).

Categories of other immunological tests such as immunophenotype measuring are also under investigation.

**Anti-mullerian hormone (AMH)**, produced by granulosa cells from preantral and early antral follicles, has also been evaluated as a predictor of ovarian reserve (Brodin, et al., 2013; Ankaert, et al., 2012; Kunt, et al., 2011; A La Marca, et al., 2011; Steiner, et al, 2011; Tremellen, et al., 2010; Kini, et al., 2010; Steiner, 2009; Kaya, et al., 2010; Guerif, et al., 2009). Authors generally agree the decline of ovarian reserve with aging is associated with a decrease in anti-mullerian hormone levels. Nonetheless, there appears to be little
consensus regarding a specific value of serum anti-mullerian hormone for defining those women who may respond poorly to assisted reproductive technologies such as in vitro fertilization. Evidence supporting improved clinical outcomes as a result of testing is mixed; some authors have reported strong predictive value, sensitivity and specificity, while others have not.

The endometrial receptivity array (ERA). Researchers have evaluated a series of markers that can potentially be used to assess the functional state of the endometrium. The endometrial receptivity array (ERA), a genomic diagnostic tool based on microarray technology, is under investigation as an endometrial receptivity marker (Diaz-Gimeno, et al., 2011). A test recently developed that can assess the expression of cyclin E and p27 is the Endometrial Function Test™ (EFT®) (Yale University School of Medicine, New Haven, CT). While some authors contend these tests may have a role in evaluating the endometrial receptivity, studies and data are limited, it is not conclusive, and the benefits of endometrial function testing in predicting pregnancy outcomes have not been established.

The clinical utility of the tests noted below has not been demonstrated in the medical literature. These studies have been proposed for a select subset of patients to identify a male factor contributing to unexplained infertility or in the treatment of infertility to select specific interventions. In general, they are reserved for those individuals for whom identification of the underlying cause of male infertility will direct specific treatment modalities.

- Sperm viability test (hypo-osmotic swelling test)
- Zona-free hamster oocyte test (sperm penetration assay)
- Hyaluronan binding assay (HBA)
- Reactive oxygen species

APPLICABLE CODES:

The Current Procedural Terminology (CPT®) codes and HCPCS codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered health service. The inclusion of a code does not imply any right to reimbursement or guarantee claims payment. Other medical policies and coverage determination guidelines may apply.

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<tr>
<td>55300</td>
<td>Vasotomy for vasograms, seminal vesiculograms, or epididymograms, unilateral or bilateral</td>
</tr>
<tr>
<td>58340</td>
<td>Catheterization and introduction of saline or contrast material for saline infusion sonohysterography (SIS) or hysterosalpingography</td>
</tr>
<tr>
<td>58345</td>
<td>Transcervical introduction of fallopian tube catheter for diagnosis and/or re-establishing patency (any method), with or without hysterosalpingography</td>
</tr>
<tr>
<td>58350</td>
<td>Chromotubation of oviduct, including materials</td>
</tr>
<tr>
<td>58355</td>
<td>Hysteroscopy, diagnostic (separate procedure)</td>
</tr>
<tr>
<td>74440</td>
<td>Vasography, vesiculography, or epididymography, radiological supervision and interpretation</td>
</tr>
<tr>
<td>74740</td>
<td>Hysterosalpingography, radiological supervision and interpretation</td>
</tr>
<tr>
<td>74742</td>
<td>Transcervical catheterization of fallopian tube, radiological supervision and interpretation</td>
</tr>
<tr>
<td>76856</td>
<td>Ultrasound, pelvic (nonobstetric), real time with image documentation; complete</td>
</tr>
<tr>
<td>76857</td>
<td>Ultrasound, pelvic (nonobstetric), real time with image documentation; limited or follow-up (e.g., for follicles)</td>
</tr>
<tr>
<td>76831</td>
<td>Saline infusion sonohysterography (SIS), including color flow Doppler, when performed</td>
</tr>
<tr>
<td>76870</td>
<td>Ultrasound, scrotum and contents</td>
</tr>
<tr>
<td>76872</td>
<td>Ultrasound, transrectal</td>
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<tr>
<td>80415</td>
<td>Chorionic gonadotropin stimulation panel; estradiol response This panel must include the following: Estradiol (82670 x 2 on three pooled blood samples)</td>
</tr>
<tr>
<td>82670</td>
<td>Estradiol</td>
</tr>
<tr>
<td>83001</td>
<td>Gonadotropin; follicle stimulating hormone (FSH)</td>
</tr>
<tr>
<td>83002</td>
<td>Gonadotropin; luteinizing hormone (LH)</td>
</tr>
<tr>
<td>83498</td>
<td>Hydroxyprogesterone, 17-d</td>
</tr>
<tr>
<td>83499</td>
<td>Hydroxyprogesterone, 20</td>
</tr>
<tr>
<td>84144</td>
<td>Progesterone</td>
</tr>
<tr>
<td>84146</td>
<td>Prolactin</td>
</tr>
<tr>
<td>84402</td>
<td>Testosterone; free</td>
</tr>
<tr>
<td>84403</td>
<td>Testosterone; total</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
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<td>----------------------------------------------------------------------------------------------------------------------------------------</td>
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<tr>
<td>84443</td>
<td>Thyroid stimulating hormone (TSH)</td>
</tr>
<tr>
<td>87070</td>
<td>Culture, bacterial; any other source except urine, blood or stool, aerobic, with isolation and presumptive identification of isolates</td>
</tr>
<tr>
<td>87071</td>
<td>Culture, bacterial; quantitative, aerobic with isolation and presumptive identification of isolates, any source except urine, blood or stool</td>
</tr>
<tr>
<td>89300</td>
<td>Semen analysis; presence and/or motility of sperm including Huhner test (post coital)</td>
</tr>
<tr>
<td>89310</td>
<td>Semen analysis; motility and count (not including Huhner test)</td>
</tr>
<tr>
<td>89320</td>
<td>Semen analysis; volume, count, motility, and differential</td>
</tr>
<tr>
<td>89321</td>
<td>Semen analysis; sperm presence and motility of sperm, if performed</td>
</tr>
<tr>
<td>89322</td>
<td>Semen analysis; volume, count, motility, and differential using strict morphologic criteria (e.g., Kruger)</td>
</tr>
<tr>
<td>89325</td>
<td>Sperm antibodies</td>
</tr>
<tr>
<td></td>
<td><strong>Diagnostic (Investigational)</strong></td>
</tr>
<tr>
<td>89329</td>
<td>Sperm evaluation; hamster penetration test</td>
</tr>
<tr>
<td>89330</td>
<td>Sperm evaluation; cervical mucus penetration test, with or without spinnbarkeit test</td>
</tr>
<tr>
<td>89398</td>
<td>Unlisted reproductive medicine laboratory procedure</td>
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</tbody>
</table>

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**REFERENCES:**


**POLICY HISTORY:**

<table>
<thead>
<tr>
<th>DATE</th>
<th>ACTION/DESCRIPTION</th>
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<tr>
<td>10/24/2013</td>
<td>Reviewed and approved by the Quality Improvement Advisory and Credentialing Council (QIACC).</td>
</tr>
<tr>
<td>11/25/2013</td>
<td>Published to UCare.org</td>
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