Corporate Medical Policy
Infertility Services

Table of Contents

Description of Procedure or Service

Infertility is defined as the inability to conceive pregnancy within a 12-month period for individuals under age 35 (6 months for persons aged 35 or older) through unprotected intercourse or artificial insemination. Infertility may also be established through evidence of medical history and diagnostic testing. Infertility includes the need for medical intervention to conceive pregnancy either as an individual or with a partner, except following voluntary sterilization.

Iatrogenic Infertility is an impairment of fertility by surgery, radiation, chemotherapy, or other medical treatment affecting reproductive organs including gonadotoxic therapies, or ovary or testicle removal for treatment of disease; also includes infertility associated with medical and surgical gender affirmation.

In vitro fertilization (IVF) is a method of assisted reproduction that involves combining an egg with sperm in a laboratory dish. If the egg fertilizes and begins cell division, the resulting embryo may be transferred into the uterus where it may implant in the uterine lining and further develop or be cryopreserved for later transfer. A cycle of IVF is defined as stimulation of ovaries, oocyte retrieval, and embryo transfer or preservation.

Artificial Insemination is a surgical procedure for the introduction of sperm or semen into the vagina, cervix, or uterus to produce pregnancy.

Assisted reproductive technology (ART) includes all fertility treatments in which either eggs or embryos are handled. In general, ART procedures involve surgically removing eggs from the ovaries, combining them with sperm in the laboratory, and returning them to the birthing person's body or donating them to another person. They do NOT include treatments in which only sperm are handled (i.e., intrauterine - or artificial - insemination) or procedures in which a birthing person takes medicine only to stimulate egg production without the intention of having eggs retrieved.

Benefit Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Plan for availability of coverage.

* Benefits for treatment of infertility are different from benefits for iatrogenic infertility and will be discussed in individual segments below.

Infertility

Diagnosis and treatment of infertility is covered and is specific to procedures listed below except as shown in the Not covered section below.

- Artificial insemination is a surgical procedure for the introduction of sperm or semen into the vagina, cervix, or uterus to produce pregnancy. Artificial insemination procedures and related services and supplies may be covered when medically necessary, including:
  - Intravaginal insemination (IVI), except if performed outside of clinical setting
  - Intracervical insemination (ICI)
  - Intrauterine insemination (IUI)
- Fertility drugs

Iatrogenic Infertility

- Standard fertility preservation procedures (retrieval of and freezing of eggs or sperm) for members who have been diagnosed with iatrogenic infertility include:
  - the collection of sperm
  - cryopreservation of sperm
  - cryopreservation of embryo
  - collection of oocyte
  - cryopreservation of oocyte
  - benefits limited to up to 12 months of storage of sperm, oocytes and embryo
- Also includes infertility associated with medical and surgical gender affirmation.

In Vitro Fertilization (IVF) (High Option)

- Oocyte identification and retrieval
- Sperm preparation
- Insemination of oocytes
- Embryo culture
- Embryo biopsy and preimplantation genetic testing when determined to be medically necessary
- Intrauterine embryo transfer
- Cryopreservation of sperm and ova (gametes) and embryos for future transfer
- Storage of cryopreserved gametes and embryos for 1 year
- Fertility drugs

In Vitro Fertilization is limited to $25,000 annual benefit maximum. Dollar limits include procedures, supplies, and any related facility or anesthesia services. (High Option)

Policy Statement

GEHA will provide coverage for infertility treatment when it is determined to be medically necessary because the medical criteria and guidelines as documented below have been demonstrated.

Diagnosing Infertility

The following are proven and medically necessary for diagnosing and treating infertility:

A. Antisperm antibodies
B. Antral follicle count
C. Genetic screening tests:
    1. Cystic fibrosis gene mutations
    2. Karyotyping for chromosomal abnormalities
    3. Y-chromosome microdeletion testing
D. Hormone level tests:
    1. Anti mullerian hormone (AMH)
    2. Estradiol
    3. Follicle-stimulating hormone (FSH)
    4. Luteinizing hormone (LH)
    5. Progesterone
    6. Prolactin
    7. Testosterone (total and free)
    8. Thyroid-stimulating hormone (TSH)
E. Hysterosalpingogram (HSG)
F. Diagnostic hysteroscopy
G. Diagnostic laparoscopy with or without chromotubation
H. Leukocyte count in semen
I. Pelvic ultrasound (transabdominal or transvaginal)
J. Post ejaculatory urinalysis
K. Scrotal, testicular or transrectal ultrasound
L. Semen analysis
M. Sonohysterogram or saline infusion ultrasound
N. Testicular biopsy
O. Vasography

Note: Pre-Implantation Genetic Testing requires preauthorization.

General Indications

GEHA uses the following guidelines for determining medical necessity. The following are proven and considered medically necessary for IVF and after 3 unsuccessful attempts with IVI, IUI or ICI treatment:

A. No evidence of very poor or futile prognosis including but not limited to two or more of the following:
    1. FSH level ≥ 15 mIU/ml ; OR

2. AMH level < 0.2 ng/ml; OR
3. Antral follicle count < 3; OR
4. Risk for aneuploidy for all embryos is ≥85%; AND

B. Diminished ovarian reserve may be recognized by:
1. FSH level ≥ 10 mIU/ml; OR
2. AMH level < 1.0 ng/ml; OR
3. Antral follicle count < 7.

Artificial Insemination

Artificial insemination [Intravaginal insemination (IVI), Intracervical insemination (ICI), Intrauterine insemination (IUI)] is considered medically necessary for the treatment of infertility for any of the following:

A. Infertility with male-factor fertility problems (2 or more semen analyses, measured at least two weeks apart, have 1 or more variables below the 5th percentile); or
B. Unexplained infertility problems; or
C. Minimal to mild endometriosis; or
D. Medically refractory erectile dysfunction or vaginismus preventing intercourse; or
E. HIV positive and undergoing sperm washing; or
F. Clomiphene-citrate-stimulated artificial insemination (intra-cervical insemination or IUI) for infertile females with WHO Group II ovulation disorders such as polycystic ovarian syndrome who ovulate with clomiphene citrate but have not become pregnant after ovulation induction with clomiphene.

If a member meets appropriate clinical scenarios with supporting provider documentation, approval may be granted for IUI treatments with oral medications and triggers

Benefits for medications related to the treatment of fertility preservation are considered under the Outpatient Prescription Drug benefit or under the Pharmaceutical Products. Check the member specific benefit plan document for inclusion or exclusion. For medication related benefit questions, please contact GEHA at (800) 821-6136. Authorization of a fertility medication does not imply authorization of any related fertility procedures.

Assisted Reproductive Technologies (ART) (High Option)

Assisted Reproductive Technologies (ART) are considered medically necessary for the following conditions:

A. Unexplained infertility
B. Diminished ovarian reserve
C. Tubal factor infertility
D. Male factor infertility
E. Endometriosis
F. Ovulatory dysfunction
1. When ovulation induction has not resulted in conception

2. Poor response to ovulation induction
3. Hyper-response to ovulation induction where there is a risk for ovarian hyperstimulation or a multiple gestation

G. Failure to achieve conception with any other treatment modality

When Assisted Reproductive Technologies (ART) are not covered:

A. When using autologous oocytes in the setting of a very poor or futile prognosis
B. When there is a failure to respond to ovarian stimulation (e.g., as demonstrated by failure to achieve at least 1 follicle >12 mm in diameter); OR
C. ART cycle does not demonstrate the attainment of at least one (1) embryo suitable for transfer; OR
D. Lack of viable spermatozoa; OR
E. Ovarian failure where a couple is attempting conception with their own gametes; OR
F. Recurrent pregnancy loss except in the setting of recurrent aneuploidy or ≥5 unexplained losses OR
G. Greater than 2 consecutive ART cycles without adequate egg quality or production, fertilization and/or embryo quality or development.
H. When using autologous oocytes in the setting of very poor/futile prognosis.

Natural Cycle Assisted Reproductive Technologies (High Option)

Natural (unstimulated) Cycle Assisted Reproductive Technologies are indicated for the following:

A. Females under the age of 35 with normal ovarian reserve
B. Females ≥ 35 years of age with normal ovarian reserve.

When Natural Cycle Assisted Reproductive Technologies are not covered

Natural cycle IVF is not indicated if:

A. There have been not more than 2 natural ART cycle attempts with a failure to obtain an embryo suitable for transfer; OR
B. There has been a failure to attain a conception following two natural cycle intended retrieval cycle starts.

Intracytoplasmic Sperm Injection (ICSI) (High Option)

Intracytoplasmic Sperm Injection (ICSI) ICSI is considered medically necessary for the following:

A. Male factor infertility
    1. “Male factor” infertility is an alteration in sperm concentration and/or motility and/or morphology in at least two sperm analyses, collected 1 and 4 weeks apart.
B. After failed conventional insemination
C. Failed attempts at traditional IVF or conventional insemination when the quality of the ovarian stimulation was not the cause of failure.
D. Cases of IVF using pre-implantation genetic testing for monogenic disorders (when a covered benefit) or structural rearrangements.

E. When using previously cryopreserved oocytes.
F. When using TESE/PESE (surgically) derived sperm
G. Recurrent molar pregnancies

When ICSI is not covered:

A. Unexplained infertility
B. Advanced maternal age
C. Low oocyte yield
D. Repeat IVF attempts after documented poor ovarian stimulation
E. Routine IVF
F. When the diagnosis is limited exclusively to teratospermia unless <2% strict morphology has been demonstrated on at least two semen analyses.
G. In the setting of PGT-A
H. Cumulus cell removal is part of the ICSI process

Male Factor Infertility (High Option)

Varicocele Repair/Varicocelectomy

A. Surgical varicocelectomy is indicated in men attempting to conceive who have palpable varicocele(s), infertility, and abnormal semen parameters, except for azoospermic men.
B. Varicocelectomy is not indicated for men with non-palpable varicoceles detected solely by imaging.
C. Varicocelectomy is not indicated for men with clinical varicocele and non-obstructive azoospermia

Sperm Retrieval

A. Surgical sperm aspiration, (Microsurgical epididymal sperm aspiration (MESA), Percutaneous epididymal sperm aspiration (PESA), Open testicular biopsy (TESE), Percutaneous testicular sperm aspiration (TEFNA) or Percutaneous testicular needle biopsy) is indicated for obstructive azoospermia in the setting of:
    1. Congenital absence of the vas deferens (carrier of cystic fibrosis gene (Jaffe, 1994), OR
    2. Infection, OR
    3. Vasectomy, OR
    4. Trauma.
B. Surgical sperm aspiration by microdissection testicular sperm extraction (TESE) is indicated for non-obstructive azoospermia in the setting of:
    1. Maturation arrest, OR
    2. Sertoli-only syndrome
C. Men with retrograde ejaculation (RE) may be treated with:
    1. Sympathomimetics and alkalinization of urine with or without urethral catheterization, OR
    2. Induced ejaculation, OR

3. Surgical sperm retrieval.

D. Men with aspermia may be treated with:
    1. Surgical sperm extraction, OR
    2. Induced ejaculation (sympathomimetics, vibratory stimulation or electroejaculation).

Note: Surgical sperm aspiration is not indicated in the absence of azoospermia.

Cryopreservation (High Option, apart from Iatrogenic Infertility)

Embryo or mature oocyte cryopreservation is considered medically necessary for the following:

A. Prevention of ovarian hyperstimulation syndrome
B. Elective single embryo transfer to freeze and store supernumerary embryos or otherwise when there are supernumerary embryos
C. Pre-implantation genetic testing
D. Presence of poor endometrial development
E. When there is a failure to obtain sperm at the time of a fresh ART cycle at egg retrieval
F. Freeze only cycles:
    1. All embryos are cryopreserved with the intent for subsequent transfer within a 12 month time period
G. Iatrogenic Infertility (see criteria for Iatrogenic Infertility)

Sperm cryopreservation is considered medically necessary for the following:

A. Medically necessary surgically obtained (TESE, PESE, etc.) sperm
B. Iatrogenic infertility (see criteria for Iatrogenic Infertility)

When embryo or mature oocyte cryopreservation is not covered:

A. For the purpose of embryo or oocyte accumulation or banking
B. Fresh oocyte retrievals are not indicated when previously frozen oocytes (M2) or embryos of at least BB grading quality (or equivalent) are available for transfer and if tested, are genetically normal. A fresh cycle is indicated when there are <8 previously frozen oocytes (M2) as long as those oocytes are not being used in conjunction with a fresh cycle.

Elective Single Embryo Transfer (eSET) (High Option)

A. Elective single embryo transfer (eSET) is considered medically necessary for the following:
    1. All patients with a favorable prognosis as defined as:
        a. Expanded day 5 or 6 blastocysts with well-defined inner-cell mass and trophectoderm as defined by the individual embryology laboratory

When treatment for infertility is not covered:

A. Embryo transfer and gamete intrafallopian transfer (GIFT) and zygote intrafallopian transfer (ZIFT)
B. Charges for gestational carrier or surrogacy, including antenatal appointments and labor/delivery services

C. Charges for procedures to collect, analyze, manipulate, or otherwise treat gametes (sperm and ova) when the partner or donor who produces the gamete is not a covered member on the plan
D. Cost of donor egg
E. Cost of donor sperm
F. Elective preservation, such as egg freezing sought due to natural aging
G. Fertility drugs, provided by facilities or physicians, including ovulation induction cycles while on injectable medication to stimulate the ovaries. Fertility drugs must be obtained through the pharmacy benefits, see Prescription Drug Benefits and Specialty Drug Benefits within your plan brochure. Medications will not be covered when dispensed by other sources, including physician offices, home health agencies and outpatient hospitals.
H. Genetic counseling
I. Infertility services after voluntary sterilizations
J. Reversal of voluntary surgical sterilizations
K. Services and supplies related to non-covered ART procedures.
L. Treatments such as artificial insemination, assisted reproductive technology, and/or in vitro fertilization prior to establishing diagnosis of infertility.

The following are unproven and not medically necessary for diagnosing and/or treatment of infertility:

A. Co-culture of embryos
B. Computer assisted sperm analysis (CASA)
C. Cryopreservation of immature oocytes, ovarian tissue or testicular tissue
D. EmbryoGlue
E. Hyaluronon binding assay (HBA)
F. In vitro maturation (IVM) of oocytes
G. Inhibin B
H. Postcoital cervical mucus penetration test
I. Reactive oxygen species (ROS) testing
J. Sperm acrosome reaction test
K. Sperm capacitation test
L. Sperm DNA integrity/fragmentation tests
M. Sperm penetration assays
N. Uterine/endometrial receptivity testing
O. Treatments to improve uterine/endometrial receptivity.

Iatrogenic Infertility

Benefits are available for fertility preservation for medical reasons that cause irreversible infertility. Services include the following procedures, when provided by or under the care or supervision of a Physician:

A. Collection of sperm
B. Cryo-preservation of sperm

C. Ovarian stimulation, retrieval of eggs and fertilization
D. Oocyte cryo-preservation
E. Embryo cryo-preservation

Benefits for medications related to the treatment of fertility preservation are considered under the Outpatient Prescription Drug benefit or under the Pharmaceutical Products. Check the member specific benefit plan document for inclusion or exclusion. For medication related benefit questions, please contact GEHA at (800) 821-6136. Authorization of a fertility medication does not imply authorization of any related fertility procedures.

When treatment for Iatrogenic Infertility is not covered:

A. Cryopreservation of immature oocytes, ovarian tissue or testicular tissue
B. Embryo transfer
C. Long term storage costs (greater than 1 year)
D. Infertility treatment after voluntary sterilization (excluding gender affirmation)
E. Benefits are limited to one cycle of fertility preservation for Iatrogenic Infertility per covered person during the entire period of time enrolled for coverage under the healthcare plan.

Required Documentation

Medical notes documenting the following, when applicable:

- Initial history and physical
- All clinical notes including rationale for proposed treatment plan
- All ovarian stimulation sheets for timed intercourse, IUI, and/or IVF cycles
- All embryology reports
- All operative reports
- Laboratory report FSH, AMH, estradiol, and any other pertinent information
- Ultrasound report antral follicle count and any other pertinent information
- HSG report
- Semen analysis

Policy Guidelines

According to the American Society of Reproductive Medicine (ASRM) and American Society for Clinical Oncology (ASCO) medical practices and guidelines fertility preservation services are defined as those procedures indicated for an individual facing infertility due to chemotherapy, pelvic radiotherapy, or other surgical procedures expected to render one permanently infertile (e.g., hysterectomy, oophorectomy)

AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO): According to the ASCO guidelines on fertility preservation in patients with cancer, oocyte and embryo cryopreservation are considered standard practice (Oktay et al., 2018). ASCO purports that the field of OTC is advancing quickly and may evolve to become standard therapy in the future.

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM): An ASRM committee issued an opinion that OTC and reimplantation of tissue is experimental, although it may be an option for individuals in which gonadotoxic treatment is necessary immediately or among prepubertal girls (Hayes Report: Health Technology, 2021).

World Professional Association for Transgender Health (WPATH) Standards of Care 7th version recommends fertility preservation be available to patients under care for gender dysphoria. Health care professionals should discuss reproductive options with patients prior to initiation of medical treatments for gender dysphoria and encourage patients to consider reproductive preservations prior to initiation of hormone therapy or surgical treatments. Patients, especially those who have not already reproduced, should be informed about sperm preservation options, oocyte (egg,) or embryo freezing reproductive preservation options.

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM): The value of PGT-A as a routine screening test for all patients undergoing in vitro fertilization has not been demonstrated. Although some earlier single-center studies reported higher live-birth rates after PGT-A in favorable-prognosis patients, recent multicenter, randomized control trials in women with available blastocysts concluded that the overall pregnancy outcomes via frozen embryo transfer were similar between PGT-A and conventional in vitro fertilization. The value of PGT-A to lower the risk of clinical miscarriage is also unclear, although these studies have important limitations.

Background

Infertility affects approximately 186 million people worldwide and 8-12% of couples of reproductive age. Therefore, a comprehensive diagnostic evaluation of infertility is crucial to achieving improvements in targeted prevention and treatment outcomes (Wasilewksi, 2020).

Poor Prognosis and Futility

Examples where continued treatment may be futile: (ASRM, 2019)

FSH level ≥ 15mIU/ml; OR AMH level < 0.2 ng/ml (LaMarca, 2013); OR Antral follicle count < 3 (ASRM, 2021(a); LaMarca, 2013). Lack of viable spermatozoa. Ovarian failure where a couple is attempting conception with their own gametes. Numerous ART cycles without adequate egg production, fertilization and/or embryo development

National data from the SART registry 2019 demonstrates that the cumulative live birth per intended retrieval resulting in live births decreased progressively from: 55.0% in females younger than 35 years; 41.0% for females aged 35-37 years; 26.8% for females aged 38-40 years; 13.4% for females aged 41-42; and 4.14% for females over the age of 42. The age-related decline in fertility is accompanied by a significant increase in the rates of aneuploidy and spontaneous abortion. (SART, 2020)

Poor Prognosis: "Very poor prognosis'' refers to treatment for which the odds of achieving a live birth are very low but not nonexistent (>1% to <5% per cycle). (ASRM, 2019)

Aneuploidy

Female fecundity decreases with increasing age. aging, chromosome segregation errors during meiotic division are increasingly common lead to the production of oocytes an incorrect number chromosomes, referred aneuploidy. trophectoderm biopsies >15,000 blastocysts have shown that the rate of aneuploidy steadily increases after age 31 and reaches 85% at age 43 (Franasiak, 2014).

To determine an 85% risk for aneuploidy, a healthcare professional typically uses a prenatal screening test, like a combined first-trimester screening (cFTS), which combines maternal blood tests measuring specific markers (like PAPP-A and free β-hCG) with an ultrasound measurement of the fetal nuchal translucency (NT), and interprets the results based on the mother's age to calculate a risk score; a score indicating an 85% chance of aneuploidy would be considered "high risk" and usually warrants further diagnostic testing like chorionic villus sampling (CVS) or amniocentesis to confirm the diagnosis

The risk calculation takes into account maternal age, ultrasound findings (like NT thickness), and levels of specific biochemical markers in the blood (Russo, 2014) (Harris et.al., 2018).

Treatment in the Natural Cycle

Natural cycle treatment assumes: Normal ovulatory function with spontaneous (unstimulated) ovulation; At least one patent fallopian tube; Normal uterine cavity. Treatment options in the natural cycle encompass Timed coitus, Cervical insemination, Intrauterine insemination (IUI) and Assisted reproductive technologies (ART). Cervical insemination in the natural cycle may be beneficial in cases involving sexual dysfunction. Intrauterine insemination may be useful in cases involving cervical trauma (e.g., cervical ablation, following a wide cervical cone biopsy). There is no evidence that, absent sexual dysfunction or cervical trauma, natural cycle (i.e., no ovarian stimulation) IUI has any benefit over appropriately timed heterosexual intercourse. (Helmerhorst, 2005; ASRM, 2020). Natural cycle IUI may be considered in the setting of donor insemination when no other infertility factor is present.

Male Factor Infertility

World Health Organization Reference Limits for Human Semen Characteristics: Semen Parameter: One-Sided Lower Reference Limit (Fifth Centiles With 95% Confidence Intervals): Semen Volume 1.4 mL (1.3-1.5) Total Sperm Number 39 million per ejaculate (35-40) Sperm Concentration 16 million/mL (15-18 million/mL) Vitality 54% Live (50-56%) Progressive Motility 30% (29-31%) Total Motility (Progressive + Non-Progressive) 39% (40-43%) Morphologically Normal Forms 4.0% (3.9-4.0)

• Mild Male Factor: abnormalities in the semen analysis where the sperm concentration is ≥10 million/ml but <15 million/ml and/or progressive motility is ≥ 30% but <40% or ≥ 5 million total motile sperm

• Moderate Male Factor: abnormalities in the semen analysis where the sperm concentration is ≥5 million/ml but <10 million/ml and/or progressive motility is ≥ 25% but <30%

• Severe Male Factor: abnormalities in the semen analysis where the sperm concentration is <5 million/ml or sperm preparation techniques result in a sperm concentration of <1 million motile sperm/ml (Schlegel, 2020)

• Isolated teratospermia is considered a male factor when there is <2% normal morphology on at least two semen analyses 1-4 weeks apart.

Surgical Sperm Aspiration

Surgical sperm aspiration is the surgical removal of sperm to obtain high quality sperm in adequate numbers to be used in assisted reproductive technology cycles and/or cryopreservation. Approximately 5%-10% of males evaluated for infertility are azoospermic. (Schlegel,1997; Schlegel, 1999)

Elective Single Embryo Transfer (eSET)

Assisted reproductive technology (ART) poses a major risk of multiple pregnancy and birth that is associated with adverse maternal and infant outcomes. The principal reason behind the large number of multiple pregnancies after in-vitro fertilization (IVF) is the practice of transferring more than one embryo within the uterus in order to maximize pregnancy rates. (ASRM, 2012; Criniti, 2005;Pandian, 2009). Twin pregnancies and higher order gestations are associated with an increased risk of Preeclampsia, Hypertension, Preterm labor, Premature rupture of membranes, Low birth weight (<2,500 g), Operative delivery, Fetal death and/or Cerebral palsy. (Mullin, 2010)

Even though eSET requires subsequent frozen embryo transfer cycle(s) if the initial fresh cycle is unsuccessful, it is prudent to promote elective single blastocyst embryo transfer as a means of reducing the frequency of multiple gestations and the associated risks of poor maternal and birth outcomes. (Johnson, 2013; Sunderam, 2012). Numerous countries have adopted regulations that mandate eSET resulting in a twin gestation rate of <5%. Pregnancy rates for eSET are comparable to multiple embryo transfer. (Thurin, 2004). Although pregnancy outcome diminishes with increasing maternal age, allage groups should be considered for blastocyst stage eSET (Niinimaki, 2012; Kato, 2012) particularly in the context of preimplantation genetic testing or other technologies that enhance the embryo selection process.

Strategies to improve live birth have primarily focused on maximizing embryo selection and endometrial synchrony. These strategies include PGT-A, freezing only embryo transfer cycles, endometrial synchrony testing, and time lapse imaging and other noninvasive embryo testing strategies. There is currently a lack of robust and consistent evidence that these strategies improve the chances of achieving a live birth. In addition, while strategies to improve live birth are aimed at improving the livebirth success of each embryo transfer, they are not necessary to reduce multiple gestation. Performing SET without additional embryo or endometrial testing reduces the multiple gestation rate down to the background 1–2% risk of monozygotic twins in ART (Gardner 2004, Styer 2008, Crinit 2005). Single embryo transfer, regardless of additional testing, should be considered the gold standard to reduce multiple gestation. Given the lack of robust evidence or conflicting evidence for many of these tests to improve clinical outcomes, they are currently not routinely recommended as a strategy to increase SET (ASRM 2022)

Embryo Banking and Use of Frozen Embryos

There is no evidence in the medical literature to support the practice of repeated ART cycles for the purpose of accumulating (banking) embryos for later use (egg retrievals without a fresh or frozen embryo transfer) with the exception of freeze all cycles for medical necessity. It is clinically appropriate

and cost effective to utilize all frozen embryos for transfer prior to another fresh ART cycle. (Forman, 2013; Richter, 2006; Shapiro, 2011, 2013).

Cryopreservation

Cryopreservation is freezing at a very low temperature, such as in liquid nitrogen (-196C) to keep embryos, eggs, or sperm viable. Sub-zero temperature is not a physiological condition for cells and water ice crystals represent the main problem since they induce cell death, principally in large cells like oocytes, which have a meiotic spindle that degenerates during this process. Significantly, cryopreservation represents an option for fertility preservation in patients who develop gonadal failure for any condition and those who want to freeze their germ cells for later use (Estudillo, et. al., 2021).

Cryopreservation of gonadal tissue

Ovarian tissue cryopreservation (OTC) involves harvesting and freezing ovarian tissue, thus preserving oocytes in primordial follicles located in the ovarian cortex. The ovarian tissue can subsequently be auto transplanted after gonadotoxic treatment has ended.

A low-quality, limited body of evidence suggests that OTC and transplantation have the potential to restore ovarian function and may result in preserved fertility in patients who have undergone gonadotoxic cancer treatment. Limitations to the body of evidence include an evidence base composed of 2 poor-quality cohort studies, 6 poor-quality singe-arm studies, and 1 very-poor-quality cross-sectional study. Better quality prospective studies ensuring that all patients are followed after receiving transplantation would provide better assurance that the effects of OTC and subsequent transplantation on fertility and pregnancy outcomes reported herein are representative.

Cryopreservation, storage and thawing of testicular tissue is considered unproven in the treatment of infertility (ASRM, 2014).

Cryopreservation of testicular tissue in higher-risk prepubertal males is feasible, but still experimental. Female fertility preservation is more complex, requires more invasive procedures, and can delay initiation of treatment due to the requirement for hormone stimulation of follicles prior to harvesting (Romao & Lorenzo, 2017).

Co-culture of embryos

Studies describe different techniques of co-culture, but no standardized method of co-culturing has been defined. Further studies are necessary to support the effects of co-culture on clinical outcomes.

Coculture is a process by which embryos develop on culture containing cells grown from the patient's own endometrium (uterine lining). The endometrial cells collected by the physician are grown in the Embryology Laboratory. These cells are thawed prior to oocyte retrieval. Then, the embryos are placed with the cultured endometrial cells to support embryonic development (Weill Cornell Medicine, 2023).

Le Saint et. al. (2019) performed an interventional, randomized, double-blind study that took place at Clinique Ovo from March 2013 to October 2015 and included 207 healthy patients undergoing an IVF of which 71 were excluded before randomization. On the previous cycle, all participants underwent an

endometrial biopsy at D5 to D7 post-ovulation, following which the endometrial cells were prepared for AECC (autologous endometrial cell co-culture).

Results

The data demonstrated that AECC significantly increased the incidence of good-quality blastocysts compared with culture in conventional media (42.6% vs 28.4%, $P < 0.001$). No significant differences were found in pregnancy and live birth rates.

Conclusion

This study demonstrated the benefits of AECC on blastocyst quality compared with conventional embryo culture medium, in a broader category of patients referred to ART as opposed to other studies that concentrated on specific causes of infertility only. However, limitations of the study design should be taken into consideration; the analysis was performed using embryos rather than patients and a follow-up of children born following the treatments could not be conducted.

Computer Assisted Sperm Analysis (CASA)

There is insufficient evidence to permit conclusions regarding the use of this sperm function test. Study results to date have demonstrated low specificity, low sensitivity and a high rate of false positives.

The evaluation of sperm characteristics is part of the diagnostic process for infertile couples. Computer-aided semen analysis (CASA) uses a hardware- and software-based system to determine characteristics of sperm, including the kinematics/motility, concentration, and morphology.

In a recent systematic review conducted by Finelli et. al. (2021), The validity and reliability of computer-aided semen analyzers in performing semen analysis was examined. A total of 14 studies were included. Our results showed a high degree of correlation for sperm concentration and motility when analysis was performed either manually or by using a CASA system. However, CASA results showed increased variability in low (<15 million/mL) and high (>60 million/mL) concentration specimens, while sperm motility assessment was inaccurate in samples with higher concentration or in the presence of non-sperm cells and debris. Morphology results showed the highest level of difference, due to the high amount of heterogeneity seen between the shapes of the spermatozoa either in one sample or across multiple samples from the same subject. Overall, the study suggests CASA systems as a valid alternative for the evaluation of semen parameters in clinical practice, especially for sperm concentration and motility. However, further technological improvements are required before these devices can one day completely replace the human operator. Artificial intelligence-based CASA devices promise to offer higher efficiency of the analysis and improve the reliability of results.

EmbryoGlue

There is insufficient evidence supporting the clinical utility of EmbryoGlue. Further studies are needed to support improved clinical outcomes measures.

EmbryoGlue is a hyaluronan-enriched embryo transfer (ET) medium which aids in implantation of embryos, hence, improves pregnancy rates in in-vitro fertilization-ET cycles (IVF-ET).

Singh, et. al. (2015) conducted a prospective case-control study at an assisted reproductive center of a tertiary care hospital. Forty-two women undergoing IVF, embryos were transferred into 50 µL of EmbryoGlue for 10 min prior to transfer inside uterine cavity. In the control group (n = 42), embryos were transferred to conventional blastocyst culture medium. Clinical pregnancy rate in the study group was 7% higher than the control group. The difference, however, was not statistically significant. In addition, no improvement in implantation rates was observed in the study group. However, significant difference (P = 0.04) in clinical pregnancy rate was observed with the EmbryoGlue in patients with previous IVF failure. In the study group, 50% patients (6/12) with previous IVF failure had successful implantation, but in the control group none of the patients (0/11) with previous implantation failure could achieve pregnancy. It was concluded, It is difficult to conclude a favorable role of EmbryoGlue in IVF-ET cycles with a good prognosis. However, in patients with recurrent implantation failure, it may be considered as a useful transfer medium.

Hyaluronon binding assay (HBA)

There is insufficient evidence supporting the clinical utility of HBA testing as an advanced sperm selection technique. More studies are needed to support improved outcomes (i.e., increased successful pregnancies with delivery of liveborn children).

In a prospective study conducted by Lazarevic et. al. (2010), the question was examined: Hyaluronan binding assay (HBA) vs. sperm penetration assay (SPA): Can HBA replace the SPA test in male partner screening before in vitro fertilization?

Semen samples from 26 infertility couples were analyzed. Both, normal and male factor patients were included. The data obtained in this study showed no statistically significant relationship between the HBA and SPA results. The mean HBA scores 76.3%, 61.3% and 76.8% were statistically not significantly different as compared to patients with negative (<5), grey zone (5–8) and for positive (>8) sperm capacitation index values.

It was concluded that the HBA is not predictive of the results of the SPA. Therefore, HBA test does not reduce the need for and cannot replace the SPA test in male partner screening prior to infertility treatment.

In vitro maturation of oocytes

Although preliminary results with in vitro maturation are promising, studies to date show that implantation and pregnancy rates are significantly lower than those achieved with standard IVF. Further evidence from well-designed trials is needed to determine the long-term safety and efficacy of the procedure.

In vitro maturation (IVM) is a technique used to induce immature oocytes collected in different periods of embryonic growth.

A prospective study by Carles, et. al. (2023) evaluated the competence of our in vitro maturation autologous coculture method on the maturation and developmental potential of immature oocytes obtained from stimulated IVF-ICSI cycles, in order to obtain additional embryos for the couple as a

rescue system to increase the changes of cumulative pregnancy. Fourteen couples, managed in IVF-ICSI in our center, from January to March 2020. Thirty-eight oocytes, identified as immature after cumulus-oocyte complexes (COC) stripping for ICSI, were placed in our in vitro maturation medium with the addition of autologous cumulus cells. Oocytes that had reached the metaphase II stage after a maximum of 36 hours of maturation were microinjected. The fertilization and embryonic development potential of the in vitro matured oocytes were compared to those of 148 in vivo matured "siblings" oocytes from the same oocyte retrieval, and then also compared to those of 127 in vivo matured oocytes from different patients (control group). No significant difference was found in the main and secondary criteria of the study compared to the "siblings" in vivo matured oocytes from the same oocyte retrieval. However, a significant difference was obtained on the rate of early cleavage and useful blastulation when our cohort was compared to mature in vivo oocytes from different patients (control group).

Conclusion: This study has shown that after incubation in vitro maturation autologous cumulus cell co-culture with cumulus-oocyte cells, immature oocytes recovered during stimulated cycles can give rise to competent oocytes, i.e., capable of being fertilized, of cleaving, and of developing into embryos up to the blastocyst stage. Our study therefore seems to be in the direction of a favorable use of these immature oocytes obtained after stimulated IVF-ICSI cycles. The continuation of this study by including a larger number of oocytes is necessary in order to evaluate the real contribution of this technique in routine.

Inhibin B

There is insufficient evidence to permit conclusions regarding the use of inhibin B as a measure of ovarian reserve. More studies are needed to support improved outcomes (i.e., increased successful pregnancies with delivery of liveborn children) with the use this test.

The higher level of serum inhibin B of reproductive age women is one of the important factors to maintain a low level of serum FSH. However, with the increase of their age, both the quality and quantity of ovarian follicles decrease, the level of serum inhibin B decreases gradually, and the inhibitory effect on FSH will be weakened, which is also one of the important reasons for the progressive increase of their serum FSH levels. Inhibin B may have certain clinical application potential in assessing the progress of ovarian aging, diagnosing premature ovarian failure (POF) or premature ovarian insufficiency (POI), evaluating the ovarian function of cancer survivors, and predicting assisted reproductive technology (ART) outcomes (Wen, J. et. al. 2021).

Wen, J. et.al. (2021) conducted a study aimed to define the variation trend of inhibin B in healthy women with age and explore its value in the reflection of ovarian reserve. Although the results showed a slight advantage in predicting ovarian response, more studies are needed to provide clarity of the reference range and potential value of inhibin B.

Postcoital cervical mucus penetration test

There is insufficient evidence supporting the predictive value or clinical utility of this test. More studies are needed to support improved outcomes (i.e., increased successful pregnancies with delivery of liveborn children).

The postcoital test, also known as the cervical mucous penetration assay, is designed to evaluate impaired male factors such as hyperviscosity, abnormal penile anatomy, decreased semen volume despite good sperm density, and unexplained infertility. The postcoital test is performed by examining the cervical mucus several hours after intercourse, ideally around the periovulatory phase of the female. The cervical mucus is smeared on a slide and examined microscopically for the presence of ferning within the mucus and for the quantitative presence of sperm and forward sperm motility. The role of the postcoital test continues to be a point of debate (Mohit, K. 2006).

Reactive oxygen species (ROS) testing

There is insufficient evidence supporting the predictive value or clinical utility of this test. Additional studies are needed to support improved clinical outcomes.

Reactive oxygen species have a significant impact on spermatogenesis as well as on sperm function. Supraphysiologic levels of ROS can affect all aspects of the semen analysis. Multiple studies have demonstrated the detrimental effects of ROS on sperm concentration, motility, morphology and ROS are implicated in sperm DNA damage and apoptosis. Conversely, other studies have demonstrated no correlation between ROS and sperm motility. Recent studies have demonstrated that ROS values have a sensitivity of 68.8% and specificity of 93.8% in diagnosing male factor infertility (infertility due to abnormal semen parameters, not female-related factors) (Ko, E. et. al. 2014).

Sperm acrosome reaction test

There is insufficient evidence supporting the predictive value or clinical utility of this test. More studies are needed to support improved outcomes (i.e., increased successful pregnancies with delivery of liveborn children).

The acrosome reaction is induced by spermatozoa-ZP binding, right after the lytic acrosomal enzymes are released, and the spermatozoa proceed to the zonal matrix with increased flagellar motility. Sperm-ZP binding tests including sperm-zona binding test and hemizona test (HZA) and acrosome reaction tests have been shown to provide clinically significant information to predict IVF results. The highest specificity and sensitivity associated with sperm-ovum interaction are also provided by the sperm-ZP binding tests. Although there is a significant relation between the in vitro results of these tests and fertilization, there are problems about their utilization in routine clinical practice such as difficulties in terms of requirement for human material requirement, challenging occasionally time-consuming and expensive techniques (Fuat, K. & Baris, A. 2017).

Sperm capacitation test

There is insufficient evidence supporting the predictive value or clinical utility of this test. Additional quality studies are needed to support improved clinical outcomes.

Sperm capacitation is the set of natural physical changes that a spermatozoon undergoes in order to be able to fertilize the ovum. This occurs in vivo following ejaculation when the spermatozoa come into contact with the different fluids in the female genital tract.

The Cap-Score™ Sperm Function Test (Androvia LifeSciences, Mountainside, NJ), is an in vitro, laboratory-developed test designed to evaluate sperm function, particularly regarding capacitation. This assay identifies and analyzes the localization patterns of the ganglioside GM1 to evaluate the fertilizing ability of sperm. Conducting a Cap-Score test involves the incubation of sperm in medium containing capacitating stimuli (Cap) and non-capacitating (non-Cap) medium. The sperm that react to the capacitation stimuli are identified by specific GM1 localization patterns. The final data, called the "Cap-Score" reports the proportion of sperm within a sample that display the localization patterns that correspond with capacitation (Moody, 2017)

Sperm DNA integrity/fragmentation tests

There is insufficient evidence supporting the predictive value or clinical utility of this test. Prospective studies directly evaluating the impact of DNA fragmentation testing on the management of infertility are needed.

According to ASRM:

"For a diagnostic test to be clinically useful the results must be reproducible, applicable to a given patient, and change the management of the patient. For tests of DNA integrity to be clinically important there must be an association of sperm DNA damage with reproductive outcomes" (ASRM, 2013).

At the current time, there is a lack of studies demonstrating that sperm DNA fragmentation testing results in improved clinical outcomes (improves the likelihood of conception).

Sperm penetration assays

There is insufficient evidence supporting the clinical utility of this test in lieu of newer technologies for treating male infertility.

ASRM contributed the following recommendation to Choosing Wisely®:

Don't perform advanced sperm function testing, such as sperm penetration or hemizona assays, in the initial evaluation of the infertile couple. Studies document that extreme variability exists among these tests, with very little correlation between results and outcomes. They have also been shown not to be cost-effective and often lead to more expensive treatments (ASRM, 2019).

Uterine/endometrial receptivity testing

There is insufficient evidence supporting the safety and efficacy of uterine receptivity testing and/or treatment. More studies are needed to support improved outcomes such as successful pregnancies with delivery of liveborn children.

In a recent study by Hoogenhuijze et. al. (2021) the SCRaTCH trial was a non-blinded randomized controlled trial in women with one unsuccessful IVF/ICSI cycle and assessed whether a single endometrial scratch using an endometrial biopsy catheter would lead to a higher live birth rate after the subsequent IVF/ICSI treatment compared to no scratch. The study took place in 8 academic and 24 general hospitals. Participants were randomized between January 2016 and July 2018 by a web-based

randomization program. Secondary outcomes included cumulative 12-month ongoing pregnancy leading to live birth rate.

After the fresh transfer, 4.6% more live births were observed in the scratch compared to control group (110/465 versus 88/461, respectively, risk ratio (RR) 1.24 [95% CI 0.96-1.59]). These data are consistent with a true difference of between -0.7% and +9.9% (95% CI), indicating that while the largest proportion of the 95% CI is positive, scratching could have no or even a small negative effect. Biochemical pregnancy loss and miscarriage rate did not differ between the two groups: in the scratch group 27/153 biochemical pregnancy losses and 14/126 miscarriages occurred, while this was 19/130 and 17/111 for the control group (RR 1.21 (95% CI 0.71-2.07) and RR 0.73 (95% CI 0.38-1.40), respectively). After 12 months of follow-up, 5.1% more live births were observed in the scratch group (202/467 versus 178/466), of which the true difference most likely lies between -1.2% and +11.4% (95% CI).

This study was not blinded. Knowledge of allocation may have been an incentive for participants allocated to the scratch group to continue treatment in situations where they may otherwise have cancelled or stopped. In addition, this study was powered to detect a difference in live birth rate of 9%.

Regulatory Status

Infertility treatment is a procedure and, therefore, not subject to FDA regulation. However, any medical devices, drugs, biologics, or tests used as a part of this procedure may be subject to FDA regulation.

Applicable Codes

The following list of codes are intended for reference purposes only, is not an all-inclusive code listing. Applicable codes include but are not limited to:

Service Type	Code	Description
Diagnosis		
Antisperm Antibodies	89325	Antisperm antibody test
Antral Follicle Count	76830	Ultrasound, transvaginal
	76856	Ultrasound, pelvic (nonobstetric), real time with image documentation; complete
	76857	Ultrasound, pelvic (nonobstetric), real time with image documentation; limited or follow-up (eg, for follicles)
Genetic screening tests:		
Cystic fibrosis gene mutations		
	81220	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)

	81223	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence
	81224	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)
Karyotyping for chromosomal abnormalities	88230	Tissue culture for non-neoplastic disorders; lymphocyte
	88261	Chromosome analysis; count 5 cells, 1 karyotype, with banding
	88262	Chromosome analysis; count 15-20 cells, 2 karyotypes, with banding
	88280	Chromosome analysis; additional karyotypes, each study
	88291	Cytogenetics and molecular cytogenetics, interpretation and report
Y-chromosome microdeletion testing	81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
Pre-implantation-A (PGT-A)	81229	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis
	81479	Unlisted molecular pathology procedure
	89290	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); less than or equal to 5 embryos
	89291	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); greater than 5 embryos
Pre-implantation-M (PGT-M)	89290	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); less than or equal to 5 embryos
	89291	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); greater than 5 embryos
	81479	Unlisted molecular pathology procedure

Pre-implantation-SR (PGT-SR)	81228	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis
	81229	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants, comparative genomic hybridization (CGH) microarray analysis
	81479	Unlisted molecular pathology procedure
	89290	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); less than or equal to 5 embryos
	89291	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); greater than 5 embryos
Hormone level tests:		
Anti mullerian hormone (AMH)	82166	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified
	83516	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semiquantitative, multiple step method
Estradiol	82670	Estradiol; total
	82681	Estradiol; free, direct measurement (eg, equilibrium dialysis)
Follicle-stimulating hormone (FSH)	83001	Gonadotropin; follicle stimulating hormone (FSH)
Luteinizing hormone (LH)	83002	Gonadotropin; luteinizing hormone (LH)
Progesterone	84144	Progesterone
	83498	Hydroxyprogesterone, 17-d
Prolactin	84146	Prolactin
Testosterone (total and free)	84402	Testosterone; free
	84403	Testosterone; total
Thyroid-stimulating hormone (TSH)	84443	Thyroid stimulating hormone (TSH)
Laboratory panels	80418	Combined rapid anterior pituitary evaluation panel This panel must include the following: Adrenocorticotropic hormone (ACTH) (82024 x 4) Luteinizing hormone (LH) (83002 x 4) Follicle stimulating hormone (FSH) (83001 x

		4) Prolactin (84146 x 4) Human growth hormone (HGH) (83003 x 4) Cortisol (82533 x 4) Thyroid stimulating hormone (TSH) (84443 x 4)
	80426	Gonadotropin releasing hormone stimulation panel This panel must include the following: Follicle stimulating hormone (FSH) (83001 x 4) Luteinizing hormone (LH) (83002 x 4)
Hysterosalpingogram (HSG)	58340	Catheterization and introduction of saline or contrast material for saline infusion sonohysterography (SIS) or hysterosalpingography
	74740	Hysterosalpingography, radiological supervision and interpretation
	76831	Saline infusion sonohysterography (SIS), including color flow Doppler, when performed
Diagnostic hysteroscopy	58555	Hysteroscopy, diagnostic (separate procedure)
Diagnostic laparoscopy with or without chromotubation	58345	Transcervical introduction of fallopian tube catheter for diagnosis and/or re-establishing patency (any method), with or without hysterosalpingography
	58350	Chromotubation of oviduct, including materials
	74742	Transcervical catheterization of fallopian tube, radiological supervision and interpretation
Leukocyte count in semen	89325	Sperm antibodies
	S3655	Antisperm antibodies test (immunobead)
Pelvic ultrasound (transabdominal or transvaginal)	76830	Ultrasound, transvaginal
	76856	Ultrasound, pelvic (nonobstetric), real time with image documentation; complete
	76857	Ultrasound, pelvic (nonobstetric), real time with image documentation; limited or follow-up (eg, for follicles)
Post ejaculatory urinalysis	89331	Sperm evaluation, for retrograde ejaculation, urine (sperm concentration, motility, and morphology, as indicated)
Scrotal, testicular, or transrectal ultrasound	76870	Ultrasound, scrotum and contents
	76872	Ultrasound, transrectal;
Semen analysis	89260	Sperm isolation; simple prep (eg, sperm wash and swim-up) for insemination or diagnosis with semen analysis

	89261	Sperm isolation; complex prep (eg, Percoll gradient, albumin gradient) for insemination or diagnosis with semen analysis
	89310	Semen analysis; motility and count (not including Huhner test)
	89320	Semen analysis; volume, count, motility, and differential
	89321	Semen analysis; sperm presence and motility of sperm, if performed
	89322	Semen analysis; volume, count, motility, and differential using strict morphologic criteria (eg, Kruger)
	G0027	Semen analysis; presence and/or motility of sperm excluding Huhner
Sonohysterogram or saline infusion ultrasound	58340	Catheterization and introduction of saline or contrast material for saline infusion sonohysterography (SIS) or hysterosalpingography
	76831	Saline infusion sonohysterography (SIS), including color flow Doppler, when performed
Testicular biopsy	54500	Biopsy of testis, needle (separate procedure)
	54505	Biopsy of testis, incisional (separate procedure)
Vasography	74440	Vasography, vesiculography, or epididymography, radiological supervision and interpretation
Treatment		
Artificial Insemination:		
Intravaginal insemination	58999	Unlisted procedure, female genital system (nonobstetrical)
Intracervical insemination	58321	Artificial insemination; intra-cervical
Intrauterine insemination	58322	Artificial insemination; intra-uterine
Sperm washing	58323	Sperm washing for artificial insemination
Case Rates	S4035	Stimulated intrauterine insemination (IUI), case rate
	S4042	Management of ovulation induction (interpretation of diagnostic tests and studies, nonface-to-face medical management of the patient), per cycle
Iatrogenic Infertility (Fertility Preservation)		
Collection of sperm	S4030	Sperm procurement and cryopreservation services; initial visit
	S4031	Sperm procurement and cryopreservation services; subsequent visit

	89264	Sperm identification from testis tissue
	55899	Unlisted Procedure, Male Genital System
Cryo-preservation of sperm	S4030	Sperm procurement and cryopreservation services; initial visit
	S4031	Sperm procurement and cryopreservation services; subsequent visit
	89259	Cryopreservation; sperm
Ovarian stimulation,	S4042	Management of ovulation induction (interpretation of diagnostic tests and studies, nonface-to-face medical management of the patient), per cycle
Retrieval of eggs,	58970	Follicle puncture for oocyte retrieval, any method
	89254	Oocyte identification from follicular fluid
	76948	Echo guide ova aspiration
Fertilization	S4011	In vitro fertilization; including but not limited to identification and incubation of mature oocytes, fertilization with sperm, incubation of embryo(s), and subsequent visualization for determination of development
	89268	Insemination of oocytes
	89280	Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes
	89281	Assisted oocyte fertilization, microtechnique; greater than 10 oocytes
Oocyte cryo-preservation	89337	Cryopreservation, mature oocyte(s)
Embryo cryo-preservation	89258	Cryopreservation; embryo(s)
Storage	89342	Storage (per year); embryo(s)
	89343	Storage (per year); sperm/semen
	89346	Storage (per year); oocyte(s)
	S4027	Storage of previously frozen embryos
	S4040	Monitoring and storage of cryopreserved embryos, per 30 days
Embryo culture	89250	Culture of oocyte(s)/embryo(s), less than 4 days
	89272	Extended culture of oocyte(s)/embryo(s), 4-7 days
Assisted Reproductive Technology		
Embryo transfer	89255	Preparation of embryo for transfer (any method)
	58974	Embryo transfer, intrauterine

	58976	Gamete, zygote, or embryo intrafallopian transfer, any method
	S4037	Cryopreserved embryo transfer, case rate
Gamete intrafallopian transfer (GIFT)	S4013	Complete cycle, gamete intrafallopian transfer (GIFT), case rate
	58976	Gamete, zygote, or embryo intrafallopian transfer, any method
Zygote intrafallopian transfer (ZIFT)	S4014	Complete cycle, zygote intrafallopian transfer (ZIFT), case rate
	58976	Gamete, zygote, or embryo intrafallopian transfer, any method
In Vitro Fertilization (IVF)	S4011	In vitro fertilization; including but not limited to identification and incubation of mature oocytes, fertilization with sperm, incubation of embryo(s), and subsequent visualization for determination of development
	S4015	Complete in vitro fertilization cycle, not otherwise specified, case rate
	S4017	Incomplete cycle, treatment cancelled prior to stimulation, case rate
	S4020	In vitro fertilization procedure cancelled before aspiration, case rate
	S4021	In vitro fertilization procedure cancelled after aspiration, case rate
	S4022	Assisted oocyte fertilization, case rate
	89268	Insemination of oocytes
	89280	Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes
	89281	Assisted oocyte fertilization, microtechnique; greater than 10 oocytes
	S4016	Frozen in vitro fertilization cycle, case rate
	S4018	Frozen embryo transfer procedure cancelled before transfer, case rate
Cost of donor egg	S4023	Donor egg cycle, incomplete, case rate
	S4025	Donor services for in vitro fertilization (sperm or embryo), case rate
Cost of donor sperm	S4026	Procurement of donor sperm from sperm bank
Fertility drugs	S0126	Injection, follitropin alfa, 75 IU
	S0128	Injection, follitropin beta, 75 IU
	S0122	Injection, menotropins, 75 IU

	J9202	Goserelin acetate implant, per 3.6 mg
	S0132	Injection, ganirelix acetate, 250 mcg
	J3355	Injection, urofollitropin, 75 IU
	J0725	Injection, chorionic gonadotropin, per 1,000 USP units
	J9217	Leuprolide acetate (for depot suspension) 7.5 mg
	J9218	Leuprolide acetate, per 1 mg
	J1950	Injection, leuprolide acetate (for depot suspension), per 3.75 mg
	J1951	Injection, leuprolide acetate for depot suspension (Fensolvi), 0.25 mg
	J1952	Leuprolide injectable, camcevi, 1 mg
	J1954	Injection, leuprolide acetate for depot suspension (Cipla), 7.5 mg
	J1050	Injection, medroxyprogesterone acetate, 1 mg.
	J2675	Injection, progesterone, per 50 mg
	J1380	Injection, estradiol valerate, up to 10 mg
Genetic counseling	96040	Genetic counseling 30 min
	S0265	Genetic counseling, under physician supervision, each 15 minutes
Infertility services after voluntary sterilizations	Z98.51 Z98.52 Z31.0	Tubal ligation status Vasectomy status Encounter for reversal of previous sterilization
	S4028	Microsurgical epididymal sperm aspiration (mesa)
	89257	Sperm identification from epididymal or vasal fluid
Preimplantation diagnosis, testing, and/or screening of eggs, sperm, or embryos	89290	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); less than or equal to 5 embryos
	89291	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); greater than 5 embryos
	0254U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using embryonic DNA genomic sequence analysis for aneuploidy, and a mitochondrial DNA score in euploid embryos, results reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploidy, per embryo tested
Reversal of voluntary surgical sterilizations	55400	Vasovasostomy (unilateral or bilateral)

	58750	Tubotubal anastomosis
	58752	Tubouterine implantation
	58760	Fimbrioplasty
	58770	Salpingostomy (salpingoneostomy)
Services and supplies related to ART procedures	89253	Assisted hatching
	89255	Prepare embryo for transfer
	89352	Thawing of cryopreserved; embryo(s)
	89353	Thawing of cryopreserved; sperm/semen, each aliquot
	89356	Thawing of cryopreserved; oocytes, each aliquot
	89250	Culture of oocyte(s)/embryo(s), less than 4 days
	89272	Extended culture of oocyte(s)/embryo(s), 4-7 days
Unproven/ not medically necessary		
Co-culture of embryos	89251	Culture of oocyte(s)/embryo(s), less than 4 days; with co-culture of oocyte(s)/embryos
Cryopreservation of immature oocytes, ovarian tissue, or testicular tissue	89335	Cryopreservation, reproductive tissue, testicular
	89344	Storage (per year); reproductive tissue, testicular/ovarian
	89354	Thawing of cryopreserved; reproductive tissue, testicular/ovarian
	89398	Unlisted reproductive medicine laboratory procedure (includes cryopreservation immature oocytes; ovarian reproductive tissues)
	0357T	Cryopreservation; immature oocyte(s)
EmbryoGlue	89398	Unlisted reproductive medicine laboratory procedure
Hyaluronon binding assay (HBA)	89398	Unlisted reproductive medicine laboratory procedure; includes Hyaluronan binding assay (HBA)
	0087T	Sperm evaluation, Hyaluronan sperm binding test
In vitro maturation (IVM) of oocytes	89398	Unlisted reproductive medicine laboratory procedure
Inhibin B	83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified
Post-coital cervical mucus penetration test	89300	Semen analysis; presence and/or motility of sperm including Huhner test (post coital)
	Q0115	Postcoital direct, qualitative examinations of vaginal or cervical mucous

Reactive oxygen species (ROS) testing	82542	Column chromatography, includes mass spectrometry, if performed (eg, HPLC, LC, LC/MS, LC/MS-MS, GC, GC/MS-MS, GC/MS, HPLC/MS), non-drug analyte(s) not elsewhere specified, qualitative or quantitative, each specimen
	89240	Unlisted miscellaneous pathology test
Sperm acrosome reaction test	89398	Unlisted reproductive medicine laboratory procedure
	88346	Immunofluorescence, per specimen; initial single antibody stain procedure
Sperm capacitation test	89240	Unlisted miscellaneous pathology test
	0255U	Andrology (infertility), sperm-capacitation assessment of ganglioside GM1 distribution patterns, fluorescence microscopy, fresh or frozen specimen, reported as percentage of capacitated sperm and probability of generating a pregnancy score
Sperm DNA integrity/fragmentation test	89240	Unlisted miscellaneous pathology test
Sperm penetration assays	89329	Sperm evaluation; hamster penetration test
	89330	Sperm evaluation; cervical mucus penetration test, with or without spinnbarkeit test
Uterine/endometrial receptivity testing	0253U	Reproductive medicine (endometrial receptivity analysis), RNA gene expression profile, 238 genes by next-generation sequencing, endometrial tissue, predictive algorithm reported as endometrial window of implantation (eg, pre-receptive, receptive, post-receptive)
Treatments to improve uterine/endometrial receptivity		
	97810	Acupuncture, 1 or more needles; without electrical stimulation, initial 15 minutes of personal one-on-one contact with the patient
	97811	Acupuncture, 1 or more needles; without electrical stimulation, each additional 15 minutes of personal one-on-one contact with the patient, with re-insertion of needle(s) (List separately in addition to code for primary procedure)
	97813	Acupuncture, 1 or more needles; with electrical stimulation, initial 15 minutes of personal one-on-one contact with the patient

	97814	Acupuncture, 1 or more needles; with electrical stimulation, each additional 15 minutes of personal one-on-one contact with the patient, with re-insertion of needle(s) (List separately in addition to code for primary procedure)

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Policy implementation and updates

January 2024	Origination. Changed the code 83520 Anti-Mullerian Hormone to 82166.
March 2024	Updated definition of Infertility
April 2024	Added clarifying language to criteria: If a member meets appropriate clinical scenarios with supporting provider documentation, approval may be granted for IUI treatments with oral medications and triggers.
December 2024	Added coverage criteria for ART and IVF (implementation 1/1/25). Added background information. Added and updated references.
February 2025	Updates to policy: removal of criteria relating to multiple blastocyte transfer update to criteria for non-covered indications in Assisted Reproductive Technologies
May 2025	Added CPT 55899 Unlisted Procedure, Male Genital System