Select Health Medical Policies

Women's Health Policies

Table of Contents

Select Health

MEDICAL POLICY

EVE BREAST SYSTEMS

Policy # 508

Implementation Date:9/3/12

Review Dates: 10/24/13, 10/18/14, 10/15/15, 10/20/16, 10/19/17, 10/25/18, 10/15/19, 10/15/20, 11/28/21, 9/15/22, 10/22/23, 10/10/24

Revision Dates: 12/6/21

Related Medical Policies:

#507 Autologous Fat Transfer (AFT) in Breast Reconstruction

Disclaimer:
1. Policies are subject to change without notice.
2. Policies outline coverage determinations for Select Health Commercial, Select Health Medicare (CMS), and Select Health Community Care (Medicaid) plans. Refer to the "Policy" section for more information.

Description

There are many reasons why a woman may undergo breast reconstruction surgery. Common reasons include breast cancer treatment that has disfigured the breast, trauma to the breast, burns, Poland syndrome (i.e., non-development of a breast), or amastia.

Various methods may be chosen to perform the breast reconstruction. There are two general types of reconstructive options, prosthetic devices (e.g., saline implants, silicone implants, tissue expanders), or autologous tissue reconstructions with tissue flaps that are transferred from adjoining or distant donor sites to the anterior chest wall.

An alternative method more recently being employed in select women is the use of autologous fat transfer to create a reconstructed breast from a person's own fat transferred from another location in the body. In most cases, AFT is accomplished by lipoinjection of autologous adipose tissue directly into breast tissue. Lipoinjection is performed in 1−3 stages, as needed.

For some of these women, they may be considered suboptimal candidates for use of internal breast expanders, which create the space in which the autologous fat is placed. For these women, a new device is offered which creates external traction on the skin.

EVE (also known as Breast Enhancement and Shaping System or BRAVA) + AFT (autologous fat transfer), (Bio-mecanica, Inc. Miami, FL), consists of 2 semi-rigid domes, with specially engineered silicone gel rims and a sophisticated minicomputer, called a SmartBox, that creates and regulates tension within the domes. A sports bra is also included, to hold the domes and the SmartBox in place. A small pump gently takes the air out of the domes to create a vacuum and a computer chip that records the amount of time the system is worn, as well as the pressure inside the domes. The system is to be worn for ≤ 8 hours a day for the first 2 days. On day 3, the patient may begin wearing the system for 10 hours a day. After 2 weeks, the patient begins wearing the system > 10 hours a day.

COMMERCIAL PLAN POLICY AND CHIP (CHILDREN'S HEALTH INSURANCE PROGRAM)

Select Health does NOT cover the EVE system (also known as Breast Enhancement and Shaping System or BRAVA) + AFT for any indication. Current evidence is inadequate to draw conclusions regarding the efficacy, effectiveness, and clinical profile of candidates for use. This meets the plan's definition of experimental/investigational.

SELECT HEALTH ADVANTAGE (CMS)

Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS, and InterQual criteria are not available, the Select Health Commercial policy applies. For the most up-to-date Medicare policies and coverage, please visit their search website http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?from2=search1.asp& or the manual website

SELECT HEALTH COMMUNITY CARE (MEDICAID)

Select Health Community Care policies typically align with State of Utah Medicaid policy, including use of InterQual. There may be situations where NCD/LCD criteria or Select Health commercial policies are used. For the most up-to-date Medicaid policies and coverage, please visit their website http://health.utah.gov/medicaid/manuals/directory.php or the Utah Medicaid code Look-Up tool

Summary of Medical Information

A Medical Technology Assessment performed by Select Health in August 2012 did not identify any systematic reviews and only 3 published peer-reviewed studies were identified. It is important to note that 1 of the 3 papers was authored by the inventor of the EVE Breast Systems. The 3 studies evaluated 146 women for between 5 and 18.5 weeks.

The effectiveness, durability, and safety of the EVE therapy are the most significant points of concern. As there are only 3 published articles concerning the use of EVE, it is difficult to determine, to a statistically significant degree, just how effective, durable, and safe the technology is.

Effectiveness: All participants reported breast growth, though, results varied between patients. It is difficult to ascertain how well EVE works on its own without the added benefit of concurrent autologous fat transplantation (AFT) as only 1 of the 3 papers used EVE exclusively. Schlenz et al. reported the use of EVE without surgical intervention in 50 women who used the device for 18.5 weeks. The median volume increase was 155 cc and the participants were 85% compliant in their use of the technology. In a head-to-head trial comparing autologous fat transfer to EVE plus autologous fat transfer, Khouri et al. found 58% greater breast growth (233 mL vs. 134 mL) in women who used EVE in conjunction with AFT, and 27% greater graft survival at 1-year, compared to women who underwent AFT alone.

Durability: Little data is available concerning the durability of outcomes in women who used EVE alone. Schlenz et al. noted that long-term (7−20 months) breast enlargement without surgery is possible with the use of an external tissue expander.

Safety: Where 2 of the 3 studies combined the use of EVE with AFT, the standalone safety of EVE is not demonstrated. This said, none of the 3 authors reported any significant complications with the use of EVE itself.

Current published literature on the EVE system is scarce. Additionally, several articles have methodological flaws which reduce the impact of their conclusions due to biases induced by the study design. Given the scarcity of information regarding the use of EVE, as either adjunct to autologous fat transfer or as a standalone technology, it is difficult to determine in which patient populations EVE would be most beneficial, appropriate treatment protocols, or how compliance will affect outcomes.

Billing/Coding Information

Not covered: Investigational/Experimental/Unproven for this indication

CPT CODES

19499	Unlisted procedure, breast

Select Health

HCPCS CODES

No specific codes identified

Key References

1. Alderman, AK, McMahon, L, Jr., Wilkins, EG. (2003). The national utilization of immediate and early delayed breast reconstruction and the effect of sociodemographic factors. Plast Reconstr Surg. 111. 2:695-703; discussion 704-5.
2. Alderman, AK, Wei, Y, Birkmeyer, JD. (2006). Use of breast reconstruction after mastectomy following the Women's Health and Cancer Rights Act. JAMA. 295. 4:387-8.
3. Brandberg, Y, Malm, M, Blomqvist, L. (2000). A prospective and randomized study, "SVEA," comparing effects of three methods for delayed breast reconstruction on quality of life, patient-defined problem areas of life, and cosmetic result. Plast Reconstr Surg. 105. 1:66-74; discussion 75-6.
4. BRAVA. (2012). Is BRAVA Right For Me? Bio-medica. Last Update: May 4, 2012. Available: http://www.mybrava.com/is-brava-right-for-me.asp. Date Accessed: June 29. 2012.
5. BRAVA. (2012). The BRAVA AFT Systen. Bio-mecanica, Inc. Last Update: May 4, 2012. Available: http://www.mybrava.com/brava-aft-system.asp. Date Accessed: August 10. 2012.
6. BRAVA. (2012). What Does it Look Like? Bio-mecanica, Inc. Last Update: May 4, 2012. Available: http://www.mybrava.com/what-does-it-look-like.asp. Date Accessed: June 29. 2012.
7. Breastcancer.org. (2012). What is Lumpectomy. Breastcancer.org. Last Update: March 15, 2012. Available: http://www.breastcancer.org/treatment/surgery/lumpectomy/what_is.jsp. Date Accessed: June 28. 2012.
8. Burvin, R, Robinpour, M, Milo, Y, et al. (1996). Female breast burns: conservative treatment with a reconstructive aim. Isr J Med Sci. 32. 12:1297-301.
9. Christian, CK, Niland, J, Edge, SB, et al. (2006). A multi-institutional analysis of the socioeconomic determinants of breast reconstruction: a study of the National Comprehensive Cancer Network. Ann Surg. 243. 2:241-9.
10. Cuzick, J, Stewart, H, Peto, R, et al. (1987). Overview of randomized trials of postoperative adjuvant radiotherapy in breast cancer. Cancer Treat Rep. 71. 1:15-29.
11. Del Vecchio, DA, Bucky, LP. (2011). Breast augmentation using preexpansion and autologous fat transplantation: a clinical radiographic study. Plast Reconstr Surg. 127. 6:2441-50.
12. Food and Drug Administration. (2012). MAUDE Adverse Event Report: BRAVA INT'L LLCBRAVABREAST ENHANCEMENT DEVICE. FDA. Last Update: June 29, 2012. Available: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/detail.cfm?mdrfoi__id=421640. Date Accessed: July 16. 2012.
13. Groen, J.W., Piatkowski, A. A., Sawor, J. H., Wilschut, J. A., Khouri, R. K., van der Hulst, R. R.., & Ritt, M. J. Autologous Fat Transfer After Augmentation and Reconstruction of the Female Breast: An International, Cross-Sectional Photo-Comparison Study Among Different Physician and Laymen Study Groups. (2018). *Surg Innov*. 25(6): 594−601.
14. Guerra, AB, Metzinger, SE, Bidros, RS, et al. (2004). Breast reconstruction with gluteal artery perforator (GAP) flaps: a critical analysis of 142 cases. Ann Plast Surg. 52. 2:118-25.
15. Gutowski, KA, Force, AFGT. (2009). Current applications and safety of autologous fat grafts: a report of the ASPS fat graft task force. Plast Reconstr Surg. 124. 1:272-80.
16. Joslyn, SA. (2005). Patterns of care for immediate and early delayed breast reconstruction following mastectomy. Plast Reconstr Surg. 115. 5:1289-96.
17. Khouri, RK, Eisenmann-Klein, M, Cardoso, E, et al. (2012). Brava and autologous fat transfer is a safe and effective breast augmentation alternative: results of a 6-year, 81-patient, prospective multicenter study. Plast Reconstr Surg. 129. 5:1173-87.
18. Meretoja, T, Suominen, E. (2005). Demand for plastic surgical operations after primary breast cancer surgery. Scand J Surg. 94. 3:211-5.
19. Morrow, M, Mujahid, M, Lantz, PM, et al. (2005). Correlates of breast reconstruction: results from a population-based study. Cancer. 104. 11:2340-6.
20. Nahabedian, M. (2012). Breast reconstruction in women with breast cancer. Up to Date. Last Update: June 4, 2012. Available: http://www.uptodate.com/contents/breast-reconstruction-in-women-with-breast-cancer?source=search_result&search=breast+reconstruction&selectedTitle=1~79. Date Accessed: June 28. 2012.
21. Plus, M. (2012). Breast Reconstruction. National Institutes of Health. Last Update: Available: http://www.nlm.nih.gov/medlineplus/breastreconstruction.html. Date Accessed: June 27. 2012.
22. Schlenz, I, Kaider, A. (2007). The Brava external tissue expander: is breast enlargement without surgery a reality? Plast Reconstr Surg. 120. 6:1680-9; discussion 1690-1.
23. Spear, SL, Majidian, A. (1998). Immediate breast reconstruction in two stages using textured, integrated-valve tissue expanders and breast implants: a retrospective review of 171 consecutive breast reconstructions from 1989 to 1996. Plast Reconstr Surg. 101. 1:53-63.
24. Tseng, JF, Kronowitz, SJ, Sun, CC, et al. (2004). The effect of ethnicity on immediate reconstruction rates after mastectomy for breast cancer. Cancer. 101. 7:1514-23.

Disclaimer

This document is for informational purposes only and should not be relied on in the diagnosis and care of individual patients. Medical and Coding/Reimbursement policies do not constitute medical advice, plan preauthorization, certification, an explanation of benefits, or a contract. Members should consult with appropriate healthcare providers to obtain needed medical advice, care, and treatment. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the member's individual benefit plan that is in effect at the time services are rendered.

The codes for treatments and procedures applicable to this policy are included for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Select Health

Select Health

MEDICAL POLICY

INFERTILITY EVALUATION AND TREATMENT

Policy # 500

Implementation Date: 12/22/11

Review Dates: 12/18/14, 12/10/15, 2/16/17, 2/15/18, 2/4/19, 2/17/20, 2/18/21, 1/20/22, 2/16/23, 2/20/24, 2/14/25

Revision Dates: 3/18/16, 2/16/17, 1/29/20, 6/7/22, 6/30/23, 9/20/23, 1/1/24, 1/15/24, 2/25/25

Disclaimer:
1. Policies are subject to change without notice.
2. Policies outline coverage determinations for Select Health Commercial, Select Health Medicare (CMS), and Select Health Community Care (Medicaid) plans. Refer to the "Policy" section for more information.

Description

Infertility affects approximately 7.3 million women and their partners in the United States, which is an estimated 12% of the reproductive-age population. Infertility is a condition of the reproductive system that impairs the ability of a couple to conceive children. Infertility is not always just a woman's problem. The Practice Committee of the American Society for Reproductive Medicine (ASRM) defines infertility as the result of a disease (an interruption, cessation, or disorder of body functions, systems, or organs) of the male or female reproductive tract which prevents the conception of a child or the ability to carry a pregnancy to delivery. The duration of unprotected intercourse with failure to conceive should be about 12 months before an infertility evaluation is undertaken, unless medical history, age, or physical findings dictate earlier evaluation and treatment. Both men and women can have problems that cause infertility.

Conception is a complicated process and depends on many factors: the production of healthy sperm by the man and healthy eggs by the woman; unblocked fallopian tubes that allow the sperm to reach the egg; the sperm's ability to fertilize the egg when they meet; the ability of the fertilized egg (embryo) to become implanted in the uterus; and sufficient embryo quality. For the pregnancy to continue to full-term, the embryo must be healthy and the woman's hormonal environment adequate for its development. When just one of these factors is impaired, infertility can result. Infertility evaluation and treatment is recommended for a couple when they are unable to achieve or sustain pregnancy after one year of unprotected intercourse.

COMMERCIAL PLAN POLICY AND CHIP (CHILDREN'S HEALTH INSURANCE PROGRAM)

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request.

Select Health covers *certain* diagnostic testing to determine the etiology of infertility.

Laboratory tests covered as part of the infertility benefit in the evaluation of infertility:

Female:

- Anti-Muellerian hormone (AMH)
- Clomiphene citrate challenge test (CCCT)
- Dehydroepiandrosterone sulfate (DHEAS)
- 17-hydroxyprogesterone
- Estradiol
- Fasting glucose

Select Health

- Follicle stimulating hormone (FSH)
- Free and/or total testosterone
- Human chorionic gonadotropin (HCG)
- Luteinizing hormone (LH)
- Progesterone challenge test

Male:

- Semen analysis
  - volume
  - concentration
  - motility
  - pH
  - fructose
  - leukocyte count
  - microbiology
  - morphology
- Follicle stimulating hormone (FSH)
- Luteinizing hormone (LH)
- Post-ejaculatory urinalysis
- Semen culture
- Sperm antibodies

Procedural tests covered under the infertility benefit in the evaluation of infertility:

Female:

- Karyotyping for chromosomal abnormalities
- Diagnostic laparoscopy with or without chromotubation
- Endometrial biopsy
- Hysterosalpingography
- Hysteroscopy
- Salpingoscopy
- Sonohysterography
- Ultrasound (i.e., serial transvaginal, pelvic, ovarian)

Male:

- Karyotyping for chromosomal abnormalities
- Scrotal exploration
- Scrotal ultrasound
- Sperm evaluation (cervical mucus penetration test)
- Testicular biopsy
- Transrectal ultrasound (TRUS)
- Vasography
- Y-chromosome microdeletion testing in males with nonobstructive azoospermia or severe oligospermia

The following section is intended ONLY for employer groups who have elected infertility treatment coverage

Select Health covers *certain* treatments for infertility as outlined below:

Treatments covered under the infertility MPS (member payment services) include:

Female:

- Artificial insemination (intrauterine)
- Assisted embryo hatching
- Cryopreservation of embryos
- Fimbrioplasty
- Fluoroscopic/hysteroscopic selective tube cannulation
- Gamete intrafallopian transfer (GIFT) or pronuclear stage transfer (PROST), or natural cycle IVF
- In vitro fertilization with embryo transfer (IVF-ET)
- Intracytoplasmic sperm injection (ICSI)
- Low tubal ovum transfer (LTOT)
- Lysis of adhesions
- Myomectomy
- Ovarian drilling and wedge resection
- Ovulation induction medications
- Ovulation monitoring studies
- Removal of tumors and cysts
- Salpingectomy
- Salpingostomy
- Septate uterus repair
- Sperm isolation
- Sperm washing
- Surgical laparoscopy
- Therapeutic hysteroscopy
- Zygote intrafallopian transfer (ZIFT)

Male:

- Electroejaculation
- Excision of tumors (e.g., epididymal)
- Microsurgical epididymal sperm aspiration (MESA)
- Orchiopexy
- Percutaneous epididymal sperm aspiration (PESA)
- Pharmacologic treatment of endocrinopathies
  - androgens
  - corticosteroids
  - human chorionic gonadotropins
  - human menopausal gonadotropin
  - pulsatile gonadotropin-releasing hormone
- Repair of varicocele
- Seminal vesicle sperm aspiration

- Sperm isolation
- Sperm washing
- Spermatic vein ligation
- Testicular fine needle aspiration (TEFNA)
- Testicular sperm aspiration (TESA)
- Testicular sperm extraction (TESE)
- Transurethral resection of the ejaculatory ducts (TURED)
- Vasal sperm aspiration

Select Health does NOT cover the following tests, treatments, or procedures for infertility; they are considered experimental/investigational.

Not-covered tests, treatments, or procedures (this list is not all-inclusive):

- Antiphopholipid antibodies
- Antiprothrombin antibodies
- Circulating natural killer cell measurement
- Co-culturing of embryos/oocytes
- Computer-assisted sperm motion analysis
- Cryopreservation, storage, and thawing:
  - oocytes
  - ovaries
  - semen
  - testicular tissue
- Cryopreservation and storage of embryos when not undergoing covered active infertility treatment
- Direct intraperitoneal insemination
- Donor charges
- Embryotoxicity assay
- Endometrial receptivity testing
- Fallopian tube sperm transfusion
- Fine needle aspiration mapping
- Hemizona test
- Hyaluronan binding assay (HBA)
- Intrafollicular insemination
- IV immunoglobulins
- Laser-assisted necrotic blastomere removal from cryopreserved embryos
- Leukocyte immunization
- Over-the-counter (OTC) prediction/pregnancy tests
- Post-coital test
- Reactive oxygen species testing (ROS)
- Serum inhibin-B for detecting ovarian reserve
- Sperm evaluation (hamster penetration test)
- Sperm DNA integrity testing
- Sperm precursors
- Sperm viability test (diagnostic)
- Surrogacy

- Vasectomy reversal

The following plan-specific terms also apply:

Colorado Based Plans [Effective January 1, 2024]

The following services are covered:

a. Services to diagnose infertility, including fulguration of ova ducts, hysteroscopy, hysterosalpingogram, certain laboratory tests, diagnostic laparascopy, and some imaging studies; and

b. Artificial insemination, except for donor semen, donor eggs, and services related to their procurement and storage.

Nevada Based Plans

The following services are not covered:

a. Reversal of surgically performed sterilization or subsequent resterilization

SELECT HEALTH MEDICARE (CMS)

Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS, and InterQual criteria are not available, the Select Health Commercial policy applies. For this policy, specifically, there are no CMS criteria available; therefore, the Select Health Commercial policy or InterQual criteria apply. Select Health applies these requirements after careful review of the evidence that supports the clinical benefits outweigh the clinical risks.. For the most up-to-date Medicare policies and coverage, please visit their search website http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?from2=search1.asp& or the manual website

SELECT HEALTH COMMUNITY CARE (MEDICAID)

Select Health Community Care policies typically align with State of Utah Medicaid policy, including use of InterQual. There may be situations where NCD/LCD criteria or Select Health commercial policies are used. For the most up-to-date Medicaid policies and coverage, please visit their website http://health.utah.gov/medicaid/manuals/directory.php or the Utah Medicaid code Look-Up tool

Summary of Medical Information

An infertility evaluation is usually initiated after one year of regular unprotected intercourse in women under age 35 and after 6 months of unprotected intercourse in women age 35 and older. However, the evaluation may be initiated sooner in women with irregular menstrual cycles or known risk factors for infertility, such as endometriosis, a history of pelvic inflammatory disease, or reproductive tract malformations.

Laboratory Tests for Females

For women over 35 years of age and younger women with risk factors for premature ovarian failure, testing for ovarian reserve with a day 3 FSH level is recommended. Other tests such as the clomiphene citrate challenge test (CCCT), antral follicle count, and anti-müllerium hormone (AMH) level are utilized by specialists and in special circumstances.

Follicle Stimulating Hormone (FSH) and Clomiphene Citrate Challenge Test (CCCT)

Both the day 3 FSH level (where day 1 is the first day of full menstrual flow) and the CCCT, which is a provocative test for measurement of FSH, are widely used for screening ovarian reserve. The CCCT involves oral administration of 100 mg clomiphene citrate on cycle days 5−9 with measurement of day 3 and day 10 FSH levels and day 3 estradiol levels.

The basis of these tests is that women with good ovarian reserve have sufficient production of ovarian hormones from small follicles early in the menstrual cycle to maintain FSH at a low level. In contrast, women with a reduced pool of follicles and oocytes have insufficient production of ovarian hormones to provide normal inhibition of pituitary secretion of FSH, so FSH rises early in the cycle.

Meta-analyses of nonrandomized studies concluded that basal cycle day 3 FSH and the CCCT testing perform similarly for predicting ability to achieve a clinical pregnancy in women undergoing infertility treatment. With either test, a normal result is not useful in predicting fertility, but a highly abnormal result (FSH > 20 mIU/mL) suggests that pregnancy will not occur with treatment involving the woman's own oocytes.

Elevated basal estradiol levels are due to advanced premature follicle recruitment that occurs in women with poor ovarian reserve. High estradiol levels can inhibit pituitary FSH production, and thus, mask one of the signs of decreased ovarian reserve in perimenopausal women. Thus, measurement of both FSH and estradiol levels helps to avoid false-negative FSH testing.

If CCCT is performed, FSH less than 15 mIU/mL on both day 3 and day 10 are suggestive of adequate ovarian reserve; an elevated FSH level on either day 3 or day 10 suggests decreased ovarian reserve. Estradiol can be measured on day 3, but a cycle day 10 estradiol is not part of the standard CCCT as it reflects the magnitude of the ovarian follicular response to clomiphene 100 mg daily for 5 days, not ovarian reserve.

Dehydroepiandrosterone Sulfate (DHEAS)
Women with signs of androgen excess or menstrual irregularity should be tested with levels of total and calculated free testosterone, as well as 17-hydroxyprogesterone and dehydroepiandrosterone sulfate levels to rule out CAH or androgen-secreting tumors.

Luteinizing Hormone (LH).
The luteinizing hormone (LH) is produced by the pituitary gland. In women, LH stimulates estrogen and progesterone production from the ovary. A surge of LH in the midmenstrual cycle is responsible for ovulation, and continued LH secretion subsequently stimulates the corpus luteum to produce progesterone. Development of the ovarian follicle is largely under FSH control, and the secretion of estrogen from this follicle is dependent on FSH and LH. The granulosa cells of the ovary secrete inhibin, which plays a role in cellular differentiation.

Progesterone Challenge Test
This is given to see if a woman is still secreting estrogen. It consists of doses of progesterone given over a 10-day period. When the reproductive anatomy of a woman is normal, the absence or the loss of ovulation is usually caused by a hormonal condition. If estrogen is present, the progestin challenge test will then trigger a menstrual period in the woman. This situation is called ovulation, in which case estrogen levels are typically normal.

Laboratory Tests for Males
Semen Analysis
The semen analysis is the cornerstone of the assessment of the male partner of an infertile couple. In addition to the standard analysis, specialized analyses can be performed in some laboratories. The semen sample should be collected after 2−7 days of abstinence and should be submitted to the laboratory within 1 hour of collection.

The semen analysis is the cornerstone of the assessment of the male partner of an infertile couple. In addition to the standard analysis, specialized analyses can be performed in some laboratories. The standard semen analysis consists of the following:

- Measurement of semen volume and pH
- Microscopy for debris and agglutination
- Assessment of sperm concentration, motility, and morphology
- Sperm leukocyte count
- Search for immature germ cells

Because of the marked inherent variability of semen analyses, at least 2 samples should be collected 1−2 weeks apart. The semen analysis should be performed using standardized methods. In addition, the

laboratory should employ internal quality control measures and participate in external quality control programs.

Sperm Autoantibodies
Sperm autoantibodies are present in about 4%−8% of subfertile men. The presence of agglutination in the initial semen analysis suggests sperm autoimmunity; this should be confirmed by the mixed antiglobulin reaction or the immunobead test, both of which detect sperm surface antibodies. Antibodies are considered clinically important when over 50% of the spermatozoa are coated with them and when the spermatozoa fail to penetrate preovulatory human cervical mucus or demonstrate impaired fertilizing capacity. Studies suggest use of new proteomic analyses to assess such antibodies may provide a greater understanding of this disorder.

Follicle Stimulating Hormone (FSH) and Lutenizing Horrmone (LF)
In men, LH stimulates testosterone production from the interstitial cells of the testes (Leydig cells). FSH stimulates testicular growth and enhances the production of an androgen-binding protein by the Sertoli cells, which are a component of the testicular tubule necessary for sustaining the maturing sperm cell. This androgen-binding protein causes high local concentrations of testosterone near the sperm, an essential factor in the development of normal spermatogenesis. Sertoli cells, under the influence of androgens, also secrete inhibin, a polypeptide, which may help to locally regulate spermatogenesis. Hence, maturation of spermatozoa requires FSH and LH.

Post-Ejaculatory Urinalysis (PEU)
This test is done to see whether some or all the sperm is ejaculated backward into the bladder, a condition known as retrograde ejaculation. To perform this test, it is necessary for a man to provide a semen sample, and immediately afterwards, a urine sample. This post-ejaculatory urine is then examined for the presence of sperm.

Semen Culture
Semen culture is frequently performed in men whose semen samples contain inflammatory cells to diagnose bacterial contamination of the semen.

Procedural Tests for Females
Diagnostic Laparoscopy with or without Chromotubation
The diagnosis and severity of endometriosis are established by laparoscopy and biopsy using the revised American Fertility Society system, which classifies the severity of endometriosis into 4 stages: stage I (minimal), stage II (mild), stage III (moderate); and stage IV (severe). This classification system is widely used and includes visual assessment, which is subject to inter- and intra-observer error. However, disease severity has not been shown to predict the chance of pregnancy.

Laparoscopy is indicated in women with a suspicion of endometriosis (dysmenorrhea, pelvic pain, deep dyspareunia) or pelvic adhesions/tubal disease (history of pelvic pain, complicated appendicitis, pelvic infection, pelvic surgery, or ectopic pregnancy) based on history, physical examination, or HSG. When laparoscopy is performed, chromotubation is also performed simultaneously to assess tubal patency and hysteroscopy to evaluate the uterine cavity. For this reason, if laparoscopy is planned, then HSG can be omitted.

The advantage of performing laparoscopy early in the evaluation of women suspected of having endometriosis or pelvic adhesions is that surgical therapy can be initiated, while avoiding potentially ineffective or unnecessary empiric medical treatment for ovulation induction. Endometriosis, if identified, can be excised or ablated at the time of the diagnostic procedure and pelvic adhesions can be lysed.

Endometrial Biopsy
This test is designed to evaluate the endometrial lining of the uterus and historically to obtain an objective assessment of ovulation or to rule out luteal phase defect (LPD). LPD is defined as either a short luteal phase (less than 12 days) which is the second part of the menstrual cycle after ovulation and until menstruation or inadequate progesterone production. Currently, LPD diagnosis is questionable and the practice of doing an endometrial biopsy solely to document ovulation is no longer acceptable. The most common reason for an endometrial biopsy is to rule out precancerous growth in the uterine cells called endometrial hyperplasia or endometrial cancer.

The test can be done anytime but preferably before ovulation (first part of the cycle) to avoid interference with a possible pregnancy in the uterus. Historically, it has been done in the second part of the cycle to document ovulation and changes in the endometrial cells. This approach was used to document any discrepancy in the morphological appearance of the cells compared to the days post-ovulation in the luteal phase and to diagnose LPD. Microscopic evaluation of the endometrial cells provides information regarding the luteal phase of the cycle, documentation of ovulation and secretory changes in the endometrium, and also, regarding endometrial hyperplasia (precancerous endometrial cells) and endometrial cancer. In certain cases, it may be combined with hysteroscopy (camera to visualize the inside of the uterus) to allow a directed biopsy of a suspected lesion in the endometrial cavity.

Hysterosalpingography

Hysterosalpingogram (HSG) is usually done in all patients to look for tubal occlusions, unless laparoscopy is planned. Either water or lipid soluble contrast media can be used. HSG also provides information about the uterine cavity. Women with abnormalities on HSG should be referred to a reproductive endocrinologist to discuss treatment options. HSG is not useful for detecting peritubal adhesions or endometriosis.

A meta-analysis of 20 studies involving 4,179 patients compared HSG and laparoscopy with chromotubation (the gold standard); the calculated sensitivity and specificity for diagnosis of tubal patency were only 65% and 83%, respectively. However, when subgroups of women undergoing HSG were analyzed, HSG appeared to have very high specificity and sensitivity for diagnosing distal tubal occlusion or major distal tubal adhesions, but much lower specificity for diagnosing proximal tubal occlusion.

Proximal tubal occlusion on HSG often represents testing artifact due to tubal spasm or poor catheter positioning leading to unilateral tubal perfusion. Given these deficiencies, findings of proximal tubal occlusion on HSG could be confirmed by a secondary test such as a repeat HSG, fluoroscopic or hysteroscopic selective tubal perfusion, or laparoscopic chromotubation, if definitive diagnosis will influence further management.

Diagnostic HSG also appears to have therapeutic effects. A systematic review of 12 randomized trials found that pregnancy rates were significantly higher in subfertile women who underwent tubal flushing with oil soluble media than in those who did not undergo HSG (OR 3.30, 95% CI 2.00−5.43), and that pregnancy rates were similar whether oil or water-soluble media were used (OR 1.21, 95%CI 0.95−1.54).

Hysteroscopy

Uterine abnormalities such as adhesions, polyps, submucous leiomyomas and septae have been found in 10%−15% of women seeking treatment for fertility problems. Compared with HSG, hysteroscopy is recognized as the 'gold standard' test for identifying uterine abnormalities as it allows direct visualization of the uterine cavity.

Opinions differ as to whether hysteroscopy should be considered as a routine investigation in addition to HSG and laparoscopy and dye in the infertile couple. A causal relationship between leiomyoma and infertility has not been established. In women undergoing assisted reproduction, the presence of uterine leiomyoma is associated with a reduced chance of clinical pregnancy or delivery. However, the effectiveness of surgical treatment of uterine abnormalities to enhance pregnancy rates is not established.

Salpingoscopy

Salpingoscopy is an endoscopic technique that allows direct evaluation of the ampullary tubal mucosa at the time of laparoscopy. It has been reported that the presence of ampullary mucosal adhesions can negatively affect reproductive outcome and increase the risk of ectopic tubal pregnancy. Various studies have suggested that the extent of intra-luminal adhesions may not correlate with the nature and extent of periadnexal adhesions. Further studies on salpingoscopic and laparoscopic correlations with regards to fertility outcome have been reported in the literature. Recently, microsalpingoscopy has been introduced, with the number of nuclei stained by methylene blue dye employed as a prognostic factor of conception in women with infertility. As an alternative to salpingoscopy performed during laparoscopy, which requires hospitalization and general anesthesia, 2 groups have described salpingoscopy as an office procedure performed during transvaginal hydrolaparoscopy or in conjunction with fertiloscopy.

The prognostic value of salpingoscopy during operative laparoscopy for tubal factor infertility in terms of reproductive outcome has been confirmed. The prognostic significance of microsalpingoscopy needs

further validation in large-scale clinical trials. Transvaginal hydrolaparoscopy and fertiloscopy appear to be an alternative to hysterosalpingography as a first-line procedure to investigate female infertility.

Sonohysterography
Saline infusion sonohysterography refers to a procedure in which fluid is instilled into the uterine cavity transcervically to provide enhanced endometrial visualization during transvaginal ultrasound examination. The technique improves sonographic detection of endometrial pathology, such as polyps, hyperplasia, cancer, leiomyomas, and adhesions. In addition, it can help avoid invasive diagnostic procedures in some patients as well as optimize the preoperative triage process for those women who require therapeutic intervention. It is easily and rapidly performed at minimal cost, well-tolerated by patients, and is virtually devoid of complications. Saline infusion sonohysterography is useful for detecting potential anatomic causes of reduced fertility, such as submucous myomas, endometrial polyps, anomalies, and intrauterine adhesions, and appears comparable to or better than hysterosalpingography (HSG) or hysteroscopy. However, an outline of the fallopian tubes (as seen with HSG) is not observed with sonohysterography. Accretion of instilled fluid in the posterior cul-de-sac is a sign of patency of at least 1 tube.

Ultrasound (i.e., serial transvaginal, pelvic, ovarian)
Compared with bimanual pelvic examination, transvaginal ultrasound enables pelvic anatomy to be identified with more accuracy and reliability. Ultrasound can be used in the evaluation of pelvic pathology, such as endometriosis, endometrioma, cysts, polyp, leiomyoma, adnexal, and ovarian abnormality, where such abnormalities are present. The diagnostic criteria for polycystic ovaries and PCOS, in which ultrasonic parameters have an important role, have been evolving over many years, and have recently been clarified in an international consensus statement.

Procedural Tests for Males
Karyotyping for Chromosomal Abnormalities
There is a consensus to counsel and offer to karyotype the male partner if there is severe oligospermia, as these men are at higher risk of karyotypic abnormalities. Separate testing for Y chromosome microdeletions may also be offered. Physicians suggest karyotyping women with very early premature menopause (prior to age 40) and both partners if there have been recurrent pregnancy losses. In most other circumstances, karyotyping is not indicated as part of the initial evaluation because of the low incidence of abnormalities in women with unexplained infertility, endometriosis, or tubal factor infertility. Karyotype may be useful in patients with these conditions who have failed initial treatment approaches and plan to undergo IVF, although the cost-effectiveness of universal karyotype screening prior to IVF has not been established.

Scrotal Exploration
Scrotal evaluations may reveal testicular defects, obstruction, or congenital defects of vas deferens to determine the location of the obstruction and attempt to correct it. This is major surgery, with all its risks. It is an outpatient surgery procedure usually performed under general anesthesia. The variation in cost will generally reflect the complexity of the repair and the time required to perform the operation, from 1 ½–5 hours. Before the scrotal exploration, the urologist may recommend a biopsy of the testicle as a separate procedure to determine if enough sperm are present before proceeding on to the more serious scrotal exploration. The biopsy is also an outpatient procedure that can be performed under either local or general anesthesia.

Scrotal Ultrasound
Ultrasound (US) is a readily available and relatively inexpensive imaging modality that can be performed on patients at any age without the need for sedation or any other pretest preparation. US examinations are safe and there is no significant biologic risk from radiation exposure. Gray-scale US provides high-resolution depiction of scrotal anatomy and Doppler technique demonstrates perfusion.

Different pathologies of the scrotum may have similar clinical presentation, such as acute scrotal pain or scrotal mass. US of the scrotum can better guide treatment by improving the definition of the scrotal pathology. For these reasons, US became the imaging modality of choice for evaluation of scrotal pathology, and, in most cases, US is the first and only imaging needed for evaluation of scrotal pathology. This test uses high-frequency sound waves to produce images inside the body. A scrotal ultrasound can help find evidence of a varicocele or obstruction of the part of the testicle that stores sperm (epididymis). A small wand is moved over the surface of the scrotum to produce images on a video screen.

Sperm Penetration Assay (SPA)
Originally, the SPA, also known as the Zona-free hamster oocyte penetration test, was used primarily as a diagnostic technique for male infertility. More recently, the advent of sperm micromanipulation techniques, specifically ICSI, has changed the role of IVF and changed the role of SPA. IVF was originally developed as a treatment option for women with irreversible tubal damage, but the development of sperm micromanipulation techniques as an adjunct to IVF has now expanded the indications for IVF to those with severe male factor infertility. Thus, SPA can be used to identify those normospermic patients who would benefit from ICSI or other adjuncts to IVF. In 2001, Freeman et al. reported on the diagnostic accuracy of sperm penetration assay in predicting success of in vitro fertilization. Among 216 couples, the sperm penetration assay predicted IVF with high negative (84%) and positive (98%) predictive value, with correct prediction in 88% of cycles. While there is still concern regarding standardization of the procedure, these results suggest that the results of the SPA can be used to select patients for ICSI.

Testicular Biopsy
Diagnostic testicular biopsy is 1 parameter for determining the testicular histopathology pattern and apparently it is the strongest indicator to foresee the possibility of finding sperms in the testis. Identification of the border line between normal and disturbed spermatogenesis substantiate the diagnosis of impaired male fertility. In the past, testicular biopsy was reserved for azospermia patients with a normal-sized testis and normal findings on hormonal studies to evaluate for ductal obstruction. Azospermic men with testicular failure (non-obstructive azospermia) have either sertoli cell only pattern, maturation arrest or hypospermatogenesis on testis biopsy. Until recently, it was assumed that men with non-obstructive azospermia were untreatable. The discovery that azospermic men with germinal failure often have minute foci of spermatogenesis was observed in the early studies of quantitative analysis of spermatogenesis. However, testicular biopsy is now also an invaluable procedure for further workup of the infertile male and for therapeutic sperm retrieval in assisted reproductive techniques. One study confirms that testicular biopsy is an important tool in the investigation and the assessment of male infertility as it provides some light on the etiology as well as providing essential prognostic information of azospermic men in Egypt. The most common finding in this series was that of normal testis denoting obstruction (24%), while among cases of functional azospermia, Sertoli cell only (34%) and spermatogenic arrest (28%) was the most frequent.

Transrectal Ultrasound (TRUS)
TRUS has replaced incisional vasography as diagnostic technique of choice in the evaluation of male pelvic reproductive anatomy. This is due in part to a urologist's overall familiarity with TRUS for prostate anatomy and biopsies, along with the superb visual resolution of seminal vesicle and ejaculatory duct anatomy that TRUS provides.

TRUS is commonly performed with a high resolution 6.5−7.5 MHz probe with the patient's bladder partially filled to maximize bladder, perivesical, and seminal vesicle anatomy. TRUS is most commonly obtained if the diagnosis of ejaculatory duct obstruction is being considered. As such, TRUS is indicated in infertile patients with low volume azoospermia and low volume oligoasthenospermia as well in men with painful ejaculation or recurrent hematospermia. As outlined in, several characteristic TRUS findings are highly suggestive of ejaculatory duct obstruction. These findings are derived from the normal anatomical findings described in fertile men, cadavers, and prostatectomy patients. It is important to remember that these findings can be unilateral or bilateral.

Vasography
A vasogram involves the injection of dye or contrast media into the vas deferens to determine whether a physical obstruction exists in the vas deferens, seminal vesicles, or ejaculatory ducts. Although bowing to TRUS as the first line diagnostic procedure in the setting of ejaculatory duct obstruction, it remains the "gold standard" procedure for diagnosis of pelvic, inguinal, or scrotal vasal obstruction. Vasography can be performed in either an antegrade (testis to prostate) or retrograde (prostate to testis) fashion, by transrectal, transperineal, transurethral, or transscrotal routes. The most reliable approach is transscrotal, but this procedure is also the most invasive as it involves a vasotomy, either microsurgical or by puncture. The risk of vasal scarring that attends this approach has led investigators to consider other, less invasive measures such as TRUS guided procedures to garner similar information.

Y-chromosome Microdeletion Testing in Males with Nonobstructive Azoospermia or Severe Oligospermia
Males with nonobstructive azoospermia should have genetic testing before proceeding to assisted reproductive technologies. Genetic disorders may be characterized as karyotype abnormalities. In some

men, microdeletions of the Y chromosome contribute to azoospermia. Male offspring born to fathers of Y-chromosome microdeletion are expected to inherit these deletions. Counseling regarding genetic issues should be a critical part of the male evaluation.

Fertility Treatments for Females.
Daily vaginal progesterone suppositories 24 to 34 weeks gestation may be considered medically necessary in pregnant women with a prior history of preterm delivery before 37 weeks gestation, a prior cervical cerclage, or a uterine anomaly. Us of these suppositories is also indicated in women with short cervix on ultrasound between 16 weeks and 24 weeks gestation.

Artificial Insemination (intrauterine) [IUI]
Intrauterine insemination (IUI) is a procedure in which processed and concentrated motile sperm are placed directly into the uterine cavity. IUI is useful in couples with severe sexual dysfunction since coitus can be avoided. Its advantages in cervical factor and male factor infertility are that sperm bypass potentially hostile cervical factors, and the number of sperm that gain access to the uterine cavity is enhanced. In women undergoing ovulation induction, randomized trials have reported higher pregnancy rates with ovulation induction combined with IUI compared with ovulation induction alone, or with timed intercourse.

IUI is contraindicated in women with an active cervical, intrauterine, or pelvic infection. This would be in the setting of a recently documented or diagnosed infection, or if there were concern at time of IUI, such as purulent discharge from the cervix or recent exposure to a sexually transmitted disease.

The cumulative pregnancy rate after IUI generally ranges from 5%−20%; the reported range varies widely and depends upon multiple factors. Lower pregnancy rates may occur when there has been a longer duration of infertility, female age is over 40 years, or in the presence of severe male factor infertility. Higher pregnancy rates have been documented when ovulation induction was combined with IUI. This increase in pregnancy rates appears to be due to an increase in the number of mature oocytes available for fertilization, but multiple gestation rates were also increased to 10%−40%.

Assisted Embryo Hatching
Assisted hatching is a technique performed to enhance the likelihood that the transferred embryo will implant in the uterus and establish a viable pregnancy. The technique involves in vitro disruption of the zona pellucida surrounding the embryo so that the embryo can "escape" and implant into the uterine wall. Assisted hatching has also been referred to as zona drilling and partial zonal dissolution. Assisted hatching is commonly performed as part of an IVF procedure in women over 40, who have a decreased incidence of implantation after embryo transfer, and in women with prior failed IVF cycles due to failed implantation.

Cryopreservation of Embryos
If there are embryos that are not needed for transfer in the current cycle, cryopreservation may be used. This is a process in which the embryos are frozen in liquid nitrogen and may be thawed for future use. A significant percentage of embryos do not survive the process of freezing and thawing; however, cryopreservation may result in hardening of the zona pellucida which may affect hatching and implantation of blastocyst. Some embryos lose 1 or more blastomeres after thawing and are referred to as "partially damaged" embryos. While partially damaged embryos can give rise to term pregnancy, authors agree that the developmental potential of these embryos is inferior to those that are fully intact. Some authors have reported that laser-assisted removal of necrotic blastomeres from partially damaged cryopreserved embryos before embryo transfer increases embryo development potential.

Available data on the effects of cryopreservation of embryos did not indicate any apparent negative impact on perinatal outcome, early infant development, or congenital malformation rate. A retrospective study compared babies (n = 283) from births from cryopreserved embryos with babies (n = 961) after conventional IVF. There was no difference in the incidence of twins, triplets, their mean gestational age, birth weight, and perinatal mortality rates between the 2 groups. The incidence of major congenital malformations was significantly lower in the cryopreserved group (1%) than in the IVF group (3%). One study matched 255 children from cryopreserved embryos for maternal age, parity, single, or twin pregnancy and date of delivery with 255 children born after standard IVF with fresh embryos and 252 children from spontaneous pregnancies. Growth, the incidence of major malformations and the prevalence of chronic diseases at 18 months were similar in all 3 groups.

Fimbrioplasty

Fimbrioplasty is performed for treatment of partial obstruction of the distal end of the fallopian tube. The tube is patent, but there are adhesive bands that surround the terminal end. The longitudinal folds of the tube are usually preserved. Fimbrioplasty involves dividing the peritoneal adhesive bands that surround the fimbria. Gentle introduction of an alligator laparoscopic forceps into the tubal ostium followed by opening and withdrawal of the forceps helps to stretch the tube and release minor degrees of fimbrial agglutination.

In one series of 35 infertile women with severe fimbrial occlusions treated with laparoscopic fimbrioplasty, the intrauterine pregnancy rate was 51%, the live birth rate was 37%, and the ectopic pregnancy rate was 23% after 2 years follow-up. Another study found similar outcomes after fimbrioplasty or salpingostomy: the pregnancy and fecundity rates after laparoscopic fimbrioplasty were 40% and 4%, respectively, compared to 56% and 16% following salpingostomy. The overall ectopic pregnancy rate was about 5%. It appears that the results of salpingostomy are equivalent to that of fimbrioplasty. The latter procedure results in more normal tubal anatomy.

Fluoroscopic/Hysteroscopic Selective Tube Cannulation

Obstruction of the fallopian tube close to its insertion into the uterus, which is conventionally termed "proximal," is the most treatable because if often occurs because of the accumulation of mucus or debris, which forms an impacted plug in the interstitial or proximal isthmic portion of the tube. Fallopian tube catheterization has developed as an extension of hysterosalpingography. Tubal cannulation results in improved visualization of the fallopian tube anatomy. It is also a treatment for infertility caused by proximal tubal obstruction (10%−20% of patients with tubal disease).

Tubal cannulation has almost eliminated the real and false diagnosis of unilateral tubal occlusion, identified patients with proximal and distal occlusion ("bipolar tubal occlusion"), and eliminated or postponed the need for a costly hysteroscopy or laparoscopy. Distal obstruction in the tube is caused by fibrosis and peritubal disease, which are not amenable to catheter recanalization techniques.

The procedure should not be performed if catheterization is unlikely to be successful, such as patients with Mullerian anomaly, cornual fibroids, or severe salpingitis isthmica nodosa (SIN). Both wire recanalization and balloon tuboplasty yield 80%−90% tubal patency, and 40%−50% 6-month pregnancy rates in selected patients. In summary, the tubal cannulation and easy to perform coaxial system allows versatile diagnosis and treatment of cornual tubal occlusion, as well as isthmic tubal obstruction.

Occlusion that develops more distally in the isthmus, or in the ampullary or fimbriated portions of the tube is commonly due to previous pelvic infection or endometriosis. It is more difficult to recanalize and patients are less likely to have a successful intrauterine pregnancy. To estimate the potential impact of fallopian tube recanalization (FTR) depends on the percentage of cases in which the occlusion is proximal. Early figures ranged between 20%−25%, meaning that the number of potentially treatable patients in the U.S. may be as high as 230,000. However, since the overall incidence of tubal disease in the 2 populations is similar (219 patients or 44%), the implication is that the number of treatable patients in the U.S. may be only 140,000 or less.

There is no agreement between gynecologists and radiologists regarding the proper sequence for diagnosing and treating obstructed fallopian tubes, nor is there a consensus within either of those 2 disciplines. There are also no established reporting standards, so it is difficult to make accurate comparisons between techniques, success rates, and treatment strategies. Pregnancy rates vary widely among authors, not so much because of differences in technique, but because of how the results are reported.

Gamete Intrafallopian Transfer (GIFT), Pronuclear Stage transfer (PROST), or Natural Cycle IVF

The GIFT procedure is also called pronuclear stage transfer (PROST), or natural cycle IVF. In GIFT, the egg cells are retrieved laparoscopically and transferred to the fallopian tubes using a catheter containing 2−3 egg cells and approximately 100,000 sperm. Unfertilized oocytes are mixed with sperm and transferred back into the tubes. Fertilization occurs in the body as in unassisted reproduction, as compared to IVF in which fertilization occurs outside the body. Indications for GIFT are the same as for IVF, except that the woman must have 1 patent fallopian tube. Reported pregnancy rates are comparable to those associated with IVF.

In vitro fertilization (IVF) refers to a procedure designed to overcome infertility and produce a pregnancy as a direct result of the intervention. In general, the ovaries are stimulated by a combination of fertility medications and then 1 or more oocyte(s) are aspirated from ovarian follicles. These are fertilized in the laboratory ("in vitro"), after which, 1 or more embryo(s) are transferred into the uterine cavity. These steps occur over about a 2-week interval of time, which is called an IVF cycle.

The first pregnancy after the fertilization of a human egg in vitro and the first birth from an in vitro-fertilized embryo were reported more than 2 decades ago. Since then, a few million pregnancies have been achieved worldwide by IVF and its modifications known generically as assisted reproductive technologies (ARTs). As experience has accumulated, success rates have increased, and the indications for these procedures have expanded, ART now accounts for 1%−3% of live births in the United States and Europe.

A complete infertility evaluation should be performed on both partners prior to embarking on IVF.

The initial experience with IVF involved women with tubal disease that could not be surgically corrected. With its efficacy established, IVF has been made available to women with other causes of infertility.

Indications for IVF include:

- Tubal factor
- Ovulatory dysfunction (after failing treatment with less invasive therapies) Diminished ovarian reserve
- Endometriosis (after failing treatment with less invasive therapies)
- Severe male factor infertility
- Ovarian failure
- Unexplained infertility (after failing treatment with less invasive therapies)

The use of IVF in these subgroups of patients is discussed in detail in the individual topic reviews listed above. The relationship between reported IVF success rates and specific infertility diagnoses is shown in the figure.

Disadvantages of IVF include the high cost, the need for procedures and drugs associated with some risk to the woman, an increased rate of multiple gestations (which accounts for much of the direct cost of pregnancies conceived via IVF, and possibly a slight increase in fetal complications. Therefore, alternative treatment options, including observation, should be considered when counseling women with open fallopian tubes and without severe male factor infertility. Although such women may have some indications for IVF (e.g., pelvic disease, endometriosis, unexplained fertility, failed gonadotropin/intrauterine insemination therapy), they also have substantial treatment-independent pregnancy rates. In young women, treatable causes of subfertility should be treated prior to initiating IVF because treatment may enhance the likelihood of natural conception. In general, in the absence of absolute impediments for conception (blocked fallopian tubes, severe male factor), couples may be offered 3−6 cycles of superovulation and intrauterine insemination (IUI) before proceeding to IVF. A reasonable course when counseling young couples with no clear block to conception is to complete a total of 1 year of unprotected intercourse and 1 year of conventional treatment, since conception is quite likely during this time (about 85% conceive during the first year and a further 50% during the second year). A shorter period is generally used in older couples, as conventional treatment is less successful, and time plays a much greater role in the probability of conception. It is not unreasonable to offer IVF as a primary treatment option to couples with the female partner over 40 years of age.

<u>In Vitro Fertilization with Embryo Transfer (IVF-ET)</u>

The technique of IVF-ET is now being widely used to treat infertility. Although the method was originally restricted to women who had no functioning oviducts as a result of severe tubal disease, it is now being used for women with severe endometriosis and couples with male factor or unexplained infertility. Because the rate of pregnancy after IVF is directly related to the number of embryos placed in the uterine cavity, nearly all IVF clinics currently utilize some form of ovarian hyperstimulation to increase the number of oocytes obtained at the time of follicle aspiration. Stimulation protocols utilizing clomiphene citrate, HMG or FSH, or a combination of agents are being used. These agents are usually given after a period of suppression with a GnRH agonist. GnRH antagonists are increasing being used only at midcycle, particularly in older women with poor responses. Monitoring of follicle growth is usually performed by both daily ultrasonography and estrogen measurement.

A few hours after egg retrieval, sperm that has been separated from semen are added to the culture medium. About 18 hours later, the oocytes are observed to determine if fertilization has occurred. The oocytes that are fertilized are then cultured for an additional 48−96 hours, and from 1−4 normally cleaving embryos are then placed into the uterus of the patient in a sterile environment without the use of general anesthesia. Embryo placement is performed through a small catheter placed through the cervical canal. With the development of sequential culture media, it has become possible to allow embryos to develop in vitro to the blastocyst stage, 5 days after fertilization, prior to transfer into the endometrial cavity. Several centers report per cycle pregnancy rates of 40%−60% with blastocyst culture and transfer. Most centers are freezing the embryos not utilized and transferring them in subsequent spontaneous ovulatory cycles, if pregnancy does not occur in the initial treatment cycle.

Intracytoplasmic Sperm Injection (ICSI)
ICSI is a laboratory procedure developed to assist couples who are undergoing IVF for severe male factor infertility. The ICSI procedure is used in conjunction with IVF, GIFT, and ZIFT. This procedure has replaced 2 previously developed micromanipulation techniques, partial zona dissection (PZD), and subzonal insertion (SUZI) because it achieves higher fertilization rates. ICSI involves the injection of a single sperm directly into the cytoplasm of an oocyte. Several studies have demonstrated efficacy and short-term safety of ICSI.

It should be noted that in the United States, the reported risk of multiple gestations after ICSI is 30%−35% for twin gestations and 5%−10% for triplet or higher-order gestations. Some conditions may carry an increased risk for transmission of genetic abnormalities to offspring via ICSI. Whether the increased prevalence is related to the procedure or to the characteristics of couples who require ICSI is unclear. Genetic counseling may be appropriate in selected cases.

Low Tubal Ovum Transfer (LTOT)
A partial alternative to IVF, the ovum is aspirated from the dominant follicle during laparoscopy immediately preceding the expected time of ovulation and injected back into the lumen of the fallopian tube above the utero-tubal junction (for upper tubal obstruction). After being mated, high number of pregnancies prevailed, thereby preserving the efficiency and safety inherent to in vivo fertilization.

Lysis of Adhesions
Pregnancy can occur in women with periadnexal adhesions, but the pregnancy rate appears to be higher in those who undergo adhesiolysis. In the only controlled study examining this issue, salpingo-ovariolysis was performed in 69 infertile women with pelvic adhesions, while 78 women with a similar degree of adhesions were not treated. The cumulative pregnancy rate at 24 months follow-up was significantly higher in treated women, 45% vs.16% in the untreated group. Although adhesiolysis was done at laparotomy, equivalent results can be expected with laparoscopic adhesiolysis.

Myomectomy
Myomectomy is the surgical removal of fibroids from the uterus. It allows the uterus to be left in place and, for some women, makes pregnancy more likely than before. Myomectomy is the preferred fibroid treatment for women who want to become pregnant. After myomectomy, chances of pregnancy may be improved but are not guaranteed.

Before myomectomy, shrinking fibroids with gonadotropin-releasing hormone analogue (GnRH-a) therapy may reduce blood loss from the surgery. GnRH-a therapy lowers the amount of estrogen the body makes. If patients have bleeding from a fibroid, GnRH-a therapy can also improve anemia before surgery by stopping uterine bleeding for several months.

Ovarian Drilling and Wedge Resection
The traditional surgical treatment for PCOS was ovarian wedge resection. The procedure was performed by excising approximately one third of the ovary via laparotomy. In an initial series of 108 patients undergoing bilateral ovarian wedge resection, regular menstrual cyclicity was restored in 95% of patients, with a pregnancy rate of 85%. Subsequent reports confirmed the benefits of the procedure, with varying rates of success. However, it became clear that wedge resection was often associated with development of periadnexal adhesions, thus, obviating the beneficial effects of surgery. Ovarian wedge resection can also be performed laparoscopically. One small series of 25 patients reported a pregnancy rate of 60%; however, 36% of patients developed postoperative adhesions, again negating some of the benefits of the surgery. In addition, ovarian resection, whether performed laparoscopically or by laparotomy, is

associated with substantial tissue loss. Instances of premature ovarian failure have been described, rendering the procedure obsolete by any approach.

Laparoscopic ovarian drilling is a modification of the ovarian wedge resection. Multiple holes are made on the surface of the ovary using either laser or electrocautery. This results in a decrease in circulating androgen levels, with resumption of cyclic ovulation.

Ovulation Induction Medications

Ovulatory disorders can be identified in the woman in 18%−25% of couples presenting with infertility. Most of these women have oligomenorrhea, arbitrarily defined as menstruation that occurs at intervals of 35 days to 6 months. While ovulation may occasionally occur, spontaneous conception is unlikely.

Induction of ovulation in these women is aimed at inducing monofollicular development, subsequent ovulation and ultimately pregnancy and birth of a healthy newborn. Induction of ovulation should be differentiated from stimulation of multiple follicle development in ovulatory women, as is done with assisted conception techniques.

The mechanism of action of antiestrogens is unclear. These agents are thought to occupy estrogen receptors in the hypothalamus and pituitary, thereby blocking the negative feedback action of estradiol. Thus, the main mechanism appears to be a rise in serum FSH concentrations by around 50%, resulting in stimulation of follicle growth and follicular estradiol production. However, other mechanisms, such as induced changes in the insulin-like growth factor system and SHBG levels, may also contribute.

Antiestrogen Therapy

Clomiphene citrate (CC) is the most widely used antiestrogen for ovulation induction and is most effective in normogonadotropic anovulatory women.

Tamoxifen, like clomiphene, is a nonsteroidal antiestrogen capable of inducing ovulation. However, it has less of an antiestrogenic effect at the uterine level. The usual starting dosage is 20 mg daily given for 5 days starting on day 3−5 of the cycle. In a randomized comparison between tamoxifen and clomiphene, no significant difference between ovulation and pregnancy rates were observed.

Correction of hyperinsulinemia with metformin has been shown to have a beneficial effect in anovulatory women with PCOS by increasing menstrual cyclicity and improving spontaneous ovulation. However, it does not appear to improve live birth rates.

Aromatase inhibitors are a class of drugs that block the conversion of testosterone and androstenedione to estradiol and estrone, respectively (unlike clomiphene which blocks estrogen action), thereby reducing negative estrogenic feedback at the pituitary. In contrast to CC, they appear to be free of the adverse effects on endometrial and cervical mucus attributed to clomiphene citrate.

Gonadotropin Therapy

Since their introduction into clinical practice in 1961, gonadotropins extracted from the urine of postmenopausal women (human menopausal gonadotropins [hMG]), in which the ratio of LH to FSH bioactivity is 1:1, have assumed a central role in ovulation induction. Refinement of the initially crude preparation resulted in the availability of purified and highly purified urinary FSH. Since 1996, recombinant human FSH (rFSH, > 99% purity) has been available. Recombinant preparations are appealing due to their ease of administration (subcutaneous rather than intramuscular).

The aim of ovulation induction with gonadotropins, as with clomiphene, is the formation of a single dominant follicle. In spontaneous cycles, this is achieved at the beginning of the cycle by a transient increase in serum FSH concentrations above the threshold value. The concentrations then decrease, preventing more than 1 follicle from undergoing preovulatory development. Because ovarian sensitivity to FSH stimulation varies among individual women, specific treatment and monitoring protocols are needed to achieve development of a single follicle when exogenous gonadotropin is administered.

In the conventional gonadotropin protocol, the starting dose of FSH is 150 int.units/day. However, this regimen is associated with a multiple pregnancy rate of up to 36% and ovarian hyperstimulation occurs in up to 14% of treatment cycles.

In patients with PCOS, who are at particular risk for complications, this approach has been largely abandoned in favor of a low-dose, step-up protocol designed to allow the FSH threshold to be reached gradually, minimizing excessive stimulation, and therefore, the risk of development of multiple follicles. In this protocol, the initial subcutaneous or intramuscular dose of FSH is 37.5−75 int. units/day; the dose is increased only if, after 14 days, no response is documented on ultrasonography and serum estradiol monitoring. Increments of 37.5 int. units then are given at weekly intervals up to a maximum of 225 int. units/day. Other clinicians choose to increase the FSH dose if there is no ovarian response after 5−7 days. The optimal interval for increasing the dose has not been well-studied in PCOS patients.

The detection of an ovarian response is an indication to continue the current dose until human chorionic gonadotropin (hCG) can be given to trigger ovulation.

The low-dose step-down protocol of ovulation induction mimics more closely the physiology of normal cycles. Therapy with 150 int. units FSH/day is started shortly after spontaneous or progesterone-induced bleeding and continued until a dominant follicle (> 10 mm) is seen on transvaginal ultrasonography. The dose is then decreased to 112.5 int. units/day followed by a further decrease to 75 int. units/day 3 days later, which is continued until hCG is administered to induce ovulation. The appropriate starting dose can be determined by using the low-dose step-up regimen for the first treatment cycle.

The degree to which the type of FSH compound employed may influence outcome of ovulation induction remains the subject of controversy. Two meta-analyses comparing the effectiveness of daily urinary FSH (uFSH) to daily human menopausal gonadotropin (HMG) for inducing ovulation in women with PCOS who had not responded to clomiphene citrate demonstrated no difference in pregnancy rate per treatment cycle. However, the women given FSH were less likely to have ovarian hyperstimulation syndrome.

In a meta-analysis of randomized controlled trials comparing recombinant human FSH (rhFSH) with uFSH for ovulation induction in women with clomiphene citrate-resistant PCOS, no significant differences were demonstrated for the ovulation rate (OR 1.19; 95% CI 0.78−1.80). Furthermore, the odds ratios for pregnancy rate (0.95; 95% CI 0.64−1.41), miscarriage rate (1.26; 95% CI 0.59−2.70), multiple pregnancy rate (0.44; 95% CI 0.16−1.21) and for ovarian hyperstimulation syndrome (1.55; 95% CI 0.50−4.84) showed no significant difference between rhFSH and uFSH.

Purified urinary FSH has some LH activity, but rFSH does not. The experience with rFSH in hypogonadotropic hypogonadal women indicates that those women who have very low serum LH concentrations (< 0.5 int. units/L) need exogenous hCG (or 75 int. units/day sc recombinant LH) to maintain adequate estradiol biosynthesis and follicle development.

Long-acting recombinant FSH preparations are currently being studied but are not yet commercially available.

Human chorionic gonadotropin (hCG) is used to trigger ovulation when the ovarian follicles are mature. Both urinary and recombinant hCG preparations are available. A dose of 250 mcg of recombinant hCG appears to be equivalent to the standard doses of urinary hCG (5,000−10,000 units).

Dopamine agonist drugs enhance the tonic suppression of prolactin synthesis and release from the pituitary, substituting for or supplementing endogenous dopamine. Bromocriptine, the first dopamine agonist drug to prove effective in the treatment of hyperprolactinemia, remains in widespread use. Drugs that bind more specifically to dopamine D2 receptors on the lactotroph cells, such as cabergoline are associated with fewer side effects. The safety of bromocriptine with regards to teratogenesis is much better established than that of cabergoline, so many physicians and patients prefer bromocriptine to attempt pregnancy, but patients who have severe side effects from bromocriptine prefer cabergoline.

However, cabergoline has been associated with a dose-dependent increase in valvular heart disease. Although most cases have occurred in patients taking high dose cabergoline for Parkinson's disease, long-term use of relatively low doses for hyperprolactinemia may also be associated with excess risk.

Ovulation Monitoring Studies

For couples pursuing pregnancy, the highest probability of conception appears to be with intercourse 1−2 days prior to ovulation. Therefore, attempting to identify the fertile period and timing intercourse during this interval maximizes the probability of conception. This can be inferred by comparing the results of the following studies: the first series consisted of 100 fertile couples who conceived without timed intercourse and reported pregnancy rates of 50% at 3 months, 75% at 6 months, and over 90% at 12 months.

Whereas a second series of similar couples who used a method of fertility awareness with timed calendar and basal body temperature (BBT) methods, are not very reliable for identifying the fertile period because of normal variation in cycle length, and because the temperature rise associated with ovulation occurs too late to be useful. Better alternatives are methods that have the woman examine her vaginal discharge for changes suggestive of a preovulatory estrogen effect, such as an increased volume of clear, stretchy, slippery mucus. Measurement of urinary luteinizing hormone is more expensive, but also effective.

The LH surge can be detected in either urine or serum samples. The LH surge appears in the urine within 12 hours after it appears in the serum; as a result, it can accurately predict ovulation, and therefore, the optimal time for intercourse. The rise in serum LH typically occurs approximately 36 hours before the oocyte is released from the follicle into the fallopian tube. Women typically begin testing their urine 1 or 2 days before the expected surge, so that the increase over baseline levels can be clearly observed. Electronic monitors have been developed, which monitor both the estradiol and LH rise in urine to predict ovulation more precisely.

Any condition associated with elevated LH levels, such as polycystic ovary syndrome, premature ovarian failure, and menopause, can yield false positive results despite the absence of ovulation. Patients should be instructed in correct use of the kit as false positive interpretation of the LH surge occurs in 7% of cycles.

Salpingectomy

There are several methods for total laparoscopic salpingectomy. One approach is to bring the fallopian tube through a pre-tied surgical loop using grasping forceps and 2−3 laparoscopy ports. The knot is tightened, and a second loop is then similarly placed. The tube can then be resected and removed.

Alternatively, electrosurgery can be used to fulgurate vessels in the mesosalpinx followed by resection of the specimen with scissors. The cornual portion of the tube is desiccated close to the uterus. It is important to elevate the tube when applying electrocautery to avoid inadvertently damaging the ovarian vessels. A partial or segmental salpingectomy can also be done.

Laparotomy is rarely performed due to the widespread acceptability of laparoscopy. Total salpingectomy is accomplished by placing a clamp across the mesosalpinx and then placing a second clamp across the proximal portion of the fallopian tube as close as possible to the cornua. The tips of the clamps should touch to completely occlude the vessels in the mesosalpinx. The tube is then excised, and the pedicles ligated using a 2-0 or 3-0 synthetic absorbable suture.

If the tubal damage is confined to the tubal segment containing the ectopic gestation, a partial salpingectomy can be performed. The clamps are placed proximal and distal to the ectopic gestation.

The decision for partial vs. total salpingectomy depends on the patient's age and desire to conceive. In general, we perform partial salpingectomy to allow the option for tubal anastomosis at a future date. However, in women who will undergo IVF treatment, we prefer total salpingectomy to decrease the possibility of tubal stump pregnancy.

Salpingostomy

Linear salpingostomy is the standard approach for management of ectopic pregnancy in women who wish to preserve their fertility. The ectopic pregnancy is identified, and the tube is immobilized with laparoscopic forceps. A 22-gauge needle is inserted through a 5 mm portal and used to inject a solution of vasopressin (0.2 IU/mL of physiologic saline) into the wall of the tube at the area of maximal distention; this helps to minimize bleeding at the salpingostomy site. Using laser, unipolar needle electrocautery, ultrasonic cutting and coagulation device, or scissors, a 10−15 mm longitudinal incision is then made along the antimesenteric border overlying the ectopic. The products of conception are released from the tube using a combination of hydrodissection with irrigating solution under high pressure and gentle blunt dissection with a suction irrigator. The specimen can then be grasped with 10 mm claw forceps to remove it from the abdominal cavity; a laparoscopic pouch is useful for removal of large fragments of placental tissue.

The tube is carefully irrigated and inspected under water for hemostasis. Bleeding points can be controlled by pressure or coagulated with light application of bipolar coagulation. In order to avoid excessive coagulation to the tube, microbipolar forceps are used. If bleeding persists, vessels in the mesosalpinx can be ligated with a 6-0 polyglactin suture.

The placental bed inside the tube should not be coagulated because this will seriously damage the tube. The incision is left open to heal by secondary intention; the subsequent rates of fertility and adhesion formation are similar after secondary intention or primary closure.

Septate Uterus Repair
Hysteroscopic metroplasty has become the method of choice for repair of most uterine septa. Benefits to the transcervical approach include less morbidity, no abdominal or transmyometrial incisions, and faster return to normal activity. As there is no abdominal incision, possible infections and intra-abdominal adhesions that may cause future infertility problems or pain are avoided. Women may attempt pregnancy sooner after a vaginal/transcervical approach than after abdominal procedures; vaginal delivery is not contraindicated.

Zygote Intrafallopian Transfer (ZIFT)
A technique in which a woman's egg is fertilized outside the body, then implanted in 1 of her fallopian tubes. First, the egg and the male sperm needed to fertilize it are harvested. Then the egg and the sperm are united in a petri dish, a multi-purpose glass or plastic container with a lid. If all goes well, the sperm fertilizes the egg, and the physicians then implant it in a fallopian tube. From there, nature takes its course, and the egg eventually is deposited by the fallopian tube into the uterus (womb) for development.

A zygote is the combined cell resulting from the union of sperm and egg. A zygote develops into an embryo. An embryo, a mass of cells with no recognizable human features, begins formation of a human body.

Fertility Treatments for Males
Electroejaculation
This technique is used in patients with complete absence of antegrade ejaculation as well as a fructose-negative, sperm-negative, nonviscous postorgasmic urinalysis, usually in patients with spinal cord injuries.

This procedure involves use of a rectal probe to stimulate the perirectal, periprostatic sympathetic nerves electrically. Patients without a spinal cord injury or those with low or incomplete spinal cord lesions will require general anesthesia.

Excision of Tumors (e.g., epididymal, spermatocele, etc.)
Obstructions that inhibit the delivery of sperm may be caused by benign tumors and cysts. A spermatocele is a benign cystic accumulation of sperm that arises from the head of the epididymis. Although often disconcerting to the patient when noticed, these lesions are benign. Spermatoceles can develop in varying locations, ranging from the testicle itself to locations along the course of the vas deferens. Nevertheless, in common usage, spermatoceles are intrascrotal, paratesticular cystic collections of sperm that arise from the epididymis.

Most surgeries to excise tumors or cysts are aimed at testis-sparing surgeries through laparoscopic and microscopic techniques.

Microsurgical Epididymal Sperm Aspiration (MESA)
This technique is appropriate for men who have an epididymal or vasal obstruction. Microsurgical epididymal sperm aspiration enables the surgeon to collect large numbers of motile sperm for cryopreservation. The disadvantage of this method is that it involves a surgical procedure requiring an operating microscope, and consequently, increases the cost for a couple who also require IVF-ICSI.

Orchiopexy
An undescended testis sometimes escapes detection until adulthood. If the contralateral testis is normal, these men are likely to be fertile. If both testes are truly undescended, infertility is very likely, with most of the patients being azoospermic. Bilateral orchiopexy in adults can result in induction of spermatogenesis, and pregnancy, and preserves testicular hormonal function.

Percutaneous Epididymal Sperm Aspiration (PESA)

Sperm are aspirated through a butterfly needle that is placed into the caudal portion of the epididymis. This method of obtaining sperm for cryopreservation or fresh IVF-ICSI is relatively quick and inexpensive compared with microsurgical open aspiration.

Pharmacologic Treatment of Endocrinopathies

- Androgens
  Exogenous androgen treatment for male infertility is not indicated. Historically, androgens were among the first empiric treatments for idiopathic male infertility, based on the premise that raising serum testosterone levels would improve epididymal maturation and boost spermatogenesis. Another rationale for the use of androgens is the so-called "rebound phenomenon." Exogenous testosterone inhibits the HPG axis and results in azoospermia; a transient increase in gonadotropins upon stopping testosterone administration has been observed. A third hypothetical potential benefit of testosterone administration has been in the treatment of men who have androgen insensitivity. The resistance of these patients could be overcome with higher circulating testosterone levels. No data suggest this treatment approach is effective. More than 11 randomized, controlled trials have evaluated whether androgen therapy improves pregnancy rates. Testosterone enanthate, testosterone undecanoate or mesterolone (orally active dihydrotestosterone derivative) were used in these trials. Liu and Handelsman performed a meta-analysis pooling data from 10 of these studies involving more than 1,000 men and found no improvement in pregnancy rate with androgen therapy (OR, 1.09; 95% CI, 0.73–1.62). Two prior meta-analyses also did not demonstrate efficacy of androgens for idiopathic infertility. Available evidence strongly argues against any role of androgen monotherapy for idiopathic male infertility.
- Corticosteroids
  Corticosteroids have been the most commonly employed medications used to attempt to suppress antisperm antibody formation. In some patients, corticosteroid treatment may result in improved fertility; however, this does not occur in the majority of patients.
- Human Chorionic Gonadotropins (hCG)
  Sperm production cannot be stimulated in men who are infertile as a result of primary hypogonadism (due to damage to the seminiferous tubules). However, sperm production can usually be stimulated to a level sufficient enough to restore fertility in men who are infertile as a result of secondary hypogonadism, i.e., due to damage to the pituitary or hypothalamus. Men who have pituitary disease can be treated with gonadotropins, while those with hypothalamic disease can be treated with gonadotropins or gonadotropin-releasing hormone (GnRH). Secondary hypogonadism is associated with decreased secretion of the gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), resulting in reductions in testosterone secretion and sperm production.

  Gonadotropin treatment of men with hypogonadotropic hypogonadism results in the appearance of sperm in the ejaculate in up to 90% of these men, but often not to normal. Even if pregnancy does not occur spontaneously, the number of sperm is often sufficient that pregnancy can be achieved with the help of an assisted reproductive technique.
- Human Menopausal Gonadotropin (hMG)
  Human menopausal gonadotropin (hMG) contains FSH and is the pharmaceutical preparation used to replace FSH in stimulating spermatogenesis in men who are infertile due to secondary hypogonadism. FSH appears to be necessary for the initiation of spermatogenesis, but not for its maintenance or reinitiation.
- Pulsatile Gonadotropin-releasing Hormone
  Gonadotropin-releasing hormone (GnRH) is administered in a pulsatile fashion by a pump and syringe that is programmed to deliver a bolus of GnRH every 2 hours and is connected to a subcutaneous needle. The apparatus is worn continuously until pregnancy occurs. The rationale for this treatment is that replacement of GnRH in a physiologic manner, in pulses every 2 hours, will stimulate the gonadotroph cells of the pituitary to secrete LH and FSH, which in turn will stimulate the testes to produce testosterone and sperm. Sperm may appear in the ejaculate as soon as 12 months after the initiation of treatment but more often 3 years or more are required.

Repair of Varicocele

A varicocele is a dilation of a vein (like a varicose vein) in the scrotum. Many men with varicocele have a low sperm count or abnormal sperm morphology (shape). The reason a varicocele affects the sperm may

be related to a higher than normal temperature in the testicles, poor oxygen supply, and poor blood flow in the testes.

Varicocele can be treated surgically by cutting the veins connected to the varicocele. However, surgery does not always improve fertility and is not recommended for most men unless there is a large varicocele. A varicocele that has been present for a long time can cause irreversible damage that cannot be surgically treated.

Seminal Tract Washout

Seminal tract washout (STW) is a technique involving the cannulation of the vas deferens and subsequent antegrade washing of the vas with collection of sperm from the bladder. STW may be used in situations where male infertility is due to incomplete voiding of the distal seminal tract, and spermatozoa can be retained downstream of the epididymis. Common conditions include diabetes, spinal cord injury, and extended retroperitoneal lymph node dissection.

Testicular Fine Needle Aspiration (TFNA)

The technique of testicular fine-needle aspiration (TFNA) of the testis was initially described as a diagnostic procedure in azoospermic men. Subsequently, testicular fine needle aspiration or biopsy for the recovery of spermatozoa has been described. Percutaneous puncture and aspiration of the testis can be performed using a 21−23-gauge needle connected to a 20cc syringe in a Menghini syringe holder. Percutaneous testicular needle biopsy can be performed with an automatic biopsy gun. The limited published experience to date with TFNA makes critical evaluation of this technique difficult, although it is evident from experience that: 1) sperm retrieval is routinely possible with TFNA for men with obstructive azoospermia, and 2) occasional hematoceles and hematomas are possible with this technique. The advantages of percutaneous aspiration techniques are that they can be performed with local anesthesia, without open scrotal exploration and its attendant postoperative discomfort, and without microsurgical expertise.

Testicular Sperm Aspiration (TESA)

Testicular sperm aspiration (TESA is a needle biopsy of the testicle. It is an office procedure performed under local anesthesia. A small incision is made in the scrotal skin and a spring-loaded needle is fired through the testicle. While it is possible to retrieve sperm using this technique, the amount is often low because the needle cuts a thin sliver of tissue. Many embryologists find this small amount of tissue difficult to work with and do not get enough sperm to freeze for future use.

Testicular Sperm Extraction (TESE)

Testicular sperm extraction (TESE) is an open procedure performed under direct vision and therefore minimizes potential complications. A small piece of testicular tissue is removed through a ½ inch skin incision. The tissue is placed in culture media and morsalized into tiny pieces. Sperm are liberated from within the seminiferous tubules (picture to the right) where they are produced and are then extracted from the surrounding testicular tissue. This can be an exhaustive process depending on the degree of sperm production.

Transurethral Resection of the Ejaculatory Ducts (TURED)

Transurethral resection of the ejaculatory ducts (TURED) is the primary treatment of ejaculatory duct obstruction. A 24 French resectoscope is placed into the urethra, and resection is carried out at the level of the verumontanum. An O'Connor drape is used with a finger in the rectum to allow better depth perception and visualization of the posterior prostate. If an ejaculatory duct cyst is present, it is usually deep and just posterior to the verumontanum. Therefore, the verumontanum is deeply resected with care not to injure the rectum. Real-time ultrasonography can be used concurrently to visualize the resection of the ejaculatory cyst. Once efflux from the ejaculatory ducts of copious cloudy material or indigo carmine, if present, is identified, the resection is complete. If the cyst still is not unroofed, a Collings knife is used to make bilateral incisions just lateral to the base of the resected verumontanum. These incisions make it possible to open obstructed ejaculatory ducts that may have been missed during the initial midline incision. Electrocautery is used judiciously to avoid occlusion of the newly opened ejaculatory ducts.

Vasal Sperm Aspiration

Vasal aspiration is an easy procedure requiring only local anesthetic. Those with an obstructed vas deferens or who have had a vasectomy within 5 years are candidates for this procedure. A syringe is inserted into the vas deferens and the liquid inside is removed. The vas deferens is massaged in order to

produce more liquid; recovery time is generally 1 day. This is the only surgical sperm retrieval procedure that retrieves mature sperm.

Billing/Coding Information

Covered for the conditions outlined above

CPT CODES

10004 Fine needle aspiration biopsy, without imaging guidance; each additional lesion (List separately in addition to code for primary procedure)
10005 Fine needle aspiration biopsy, including ultrasound guidance; first lesion
10006 Fine needle aspiration biopsy, including ultrasound guidance; each additional lesion (List separately in addition to code for primary procedure)
10007 Fine needle aspiration biopsy, including fluoroscopic guidance; first lesion
10008 Fine needle aspiration biopsy, including fluoroscopic guidance; each additional lesion (List separately in addition to code for primary procedure)
10021 Fine needle aspiration biopsy, without imaging guidance; first lesion
49322 Laparoscopy, surgical; with aspiration of cavity or cyst (eg, ovarian cyst) (single or multiple)
54640 Orchiopexy, inguinal or scrotal approach
54650 Orchiopexy, abdominal approach, for intra-abdominal testis (eg, Fowler-Stephens)
54692 Laparoscopy, surgical; orchiopexy for intra-abdominal testis
54830 Excision of local lesion of epididymis
54840 Excision of spermatocele, with or without epididymectomy
55530 Excision of varicocele or ligation of spermatic veins for varicocele; (separate procedure)
55535 Excision of varicocele or ligation of spermatic veins for varicocele; abdominal approach
55540 Excision of varicocele or ligation of spermatic veins for varicocele; with hernia repair
55550 Laparoscopy, surgical, with ligation of spermatic veins for varicocele
55870 Electroejaculation
55899 Unlisted procedure, male genital system (TESA, TESE, PESA)
57135 Excision of vaginal cyst or tumor
58140 Myomectomy, excision of fibroid tumor(s) of uterus, 1 to 4 intramural myoma(s) with total weight of 250 g or less and/or removal of surface myomas; abdominal approach
58145 Myomectomy, excision of fibroid tumor(s) of uterus, 1 to 4 intramural myoma(s) with total weight of 250 g or less and/or removal of surface myomas; vaginal approach
58146 Myomectomy, excision of fibroid tumor(s) of uterus, 5 or more intramural myomas and/or intramural myomas with total weight greater than 250 g, abdominal approach
58321 Artificial insemination; intra-cervical
58322 Artificial insemination; intra-uterine
58323 Sperm washing for artificial insemination
58340 Catheterization and introduction of saline or contrast material for saline infusion sonohysterography (SIS) or hysterosalpingography
58540 Hysteroplasty, repair of uterine anomaly (Strassman type)
58545 Laparoscopy, surgical, myomectomy, excision; 1 to 4 intramural myomas with total weight of 250 g or less and/or removal of surface myomas
58546 Laparoscopy, surgical, myomectomy, excision; 5 or more intramural myomas and/or intramural myomas with total weight greater than 250 g
58555 Hysteroscopy, diagnostic (separate procedure)
58559 Hysteroscopy, surgical; with lysis of intrauterine adhesions (any method)
58565 Hysteroscopy, surgical; with bilateral fallopian tube cannulation to induce occlusion by placement of permanent implants
58660 Laparoscopy, surgical; with lysis of adhesions (salpingolysis, ovariolysis) (separate procedure)
58672 Laparoscopy, surgical; with fimbrioplasty
58673 Laparoscopy, surgical; with salpingostomy (salpingoneostomy)
58700 Salpingectomy, complete or partial, unilateral or bilateral (separate procedure)
58740 Lysis of adhesions (salpingolysis, ovariolysis)
58760 Fimbrioplasty
58770 Salpingostomy (salpingoneostomy)

58800 Drainage of ovarian cyst(s), unilateral or bilateral (separate procedure); vaginal approach
58805 Drainage of ovarian cyst(s), unilateral or bilateral (separate procedure); abdominal approach
58920 Wedge resection or bisection of ovary, unilateral or bilateral
58925 Ovarian cystectomy, unilateral or bilateral
58970 Follicle puncture for oocyte retrieval, any method
58974 Embryo transfer, intrauterine
58976 Gamete, zygote, or embryo intrafallopian transfer, any method (GIFT, ZIFT)
76948 Ultrasonic guidance for aspiration of ova, imaging and supervision
83498 Hydroxyprogesterone, 17-d
89250 Culture of oocyte(s)/embryo(s), less than 4 days;
89251 Culture of oocyte(s)/embryo(s), less than 4 days; with co-culture of oocyte(s)/embryos
89253 Assisted embryo hatching, microtechniques (any method)
89254 Oocyte identification from follicular fluid
89255 Preparation of embryo for transfer (any method)
89257 Sperm identification from aspiration (other than seminal fluid)
89258 Cryopreservation; embryo(s)
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
89268 Insemination of oocytes
89272 Extended culture of oocyte(s)/embryo(s), 4-7 days
89280 Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes
89281 Assisted oocyte fertilization, microtechnique; greater than 10 oocytes
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
89342 Storage (per year); embryo(s)
89352 Thawing of cryopreserved; embryo(s)

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

HCPCS CODES

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
S4013 Complete cycle, gamete intrafallopian transfer (gift), case rate
S4014 Complete cycle, zygote intrafallopian transfer (zift), case rate
S4015 Complete in vitro fertilization cycle, not otherwise specified, case rate
S4016 Frozen in vitro fertilization cycle, case rate
S4017 Incomplete cycle, treatment cancelled prior to stimulation, case rate
S4018 Frozen embryo transfer procedure cancelled before transfer, 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
S4028 Microsurgical epididymal sperm aspiration (MESA)
S4035 Stimulated intrauterine insemination (iui), case rate
S4037 Cryopreserved embryo transfer, case rate
S4042 Management of ovulation induction (interpretation of diagnostic tests and studies, non-face-to-face medical management of the patient), per cycle

Select Health

Key References

1. Barratt, CL, Osborn, JC, Harrison, PE, et al. (1989). The hypo-osmotic swelling test and the sperm mucus penetration test in determining fertilization of the human oocyte. Hum Reprod 4.4: 430-4.
2. Basso, O, Olsen, J, Bisanti, L, et al. (1997). Repeating episodes of low fecundability. A multicentre European study. The European Study Group on Infertility and Subfecundity. Hum Reprod 12.7: 1448-53.
3. Berberoglugil, P, Englert, Y, Van den Bergh, M, et al. (1993). Abnormal sperm-mucus penetration test predicts low in vitro fertilization ability of apparently normal semen. Fertil Steril 59.6: 1228-32.
4. Bolumar, F, Olsen, J, Boldsen, J. (1996). Smoking reduces fecundity: a European multicenter study on infertility and subfecundity. The European Study Group on Infertility and Subfecundity. Am J Epidemiol 143.6: 578-87.
5. Brassard, M, AinMelk, Y, Baillargeon, JP. (2008). Basic infertility including polycystic ovary syndrome. Med Clin North Am 92.5: 1163-92, xi.
6. Brugh, VM, 3rd, Lipshultz, LI. (2004). Male factor infertility: evaluation and management. Med Clin North Am 88.2: 367-85.
7. Brugh, VM, 3rd, Matschke, HM, Lipshultz, LI. (2003). Male factor infertility. Endocrinol Metab Clin North Am 32.3: 689-707.
8. Campbell, MF, Wein, AJ, Kavoussi, LR. (2007). Campbell-Walsh urology / editor-in-chief, Alan J. Wein; editors, Louis R. Kavoussi ... [et al.]. 9th ed. 4 vols. Philadelphia: W.B. Saunders.
9. Center for Reproductive Health. (2010) Treatments for men: Percutaneous Epididymal Sperm Aspiration (PESA). Last Update: 2010. The Center for Reproductive Health. Available: http://www.reproductivehealthctr.com/treatments_for_men_pesa.htm. Date Accessed: October 4, 2010.
10. Fitzpatrick, C. (1988). Prolactin measurement in the investigation of infertility in women with a normal menstrual cycle. Br J Obstet Gynaecol 95.1: 104.
11. Glazener, CM, Kelly, NJ, Hull, MG. (1987). Prolactin measurement in the investigation of infertility in women with a normal menstrual cycle. Br J Obstet Gynaecol 94.6: 535-8.
12. Goldstein, SR. (2009) Saline infusion sonohysterography. 18.2. Last Update: May 2010. UpToDate. Available: http://www.uptodate.com/online/content/topic.do?topicKey=gyn_proc/2539&source=related_link. Date Accessed: September 26, 2010.
13. Hadziselimovic, F. (2002). Cryptorchidism, its impact on male fertility. Eur Urol 41.2: 121-3.
14. Hatch, EE, Bracken, MB. (1993). Association of delayed conception with caffeine consumption. Am J Epidemiol 138.12: 1082-92.
15. Hendriks, DJ, Mol, BW, Bancsi, LF, et al. (2006). The clomiphene citrate challenge test for the prediction of poor ovarian response and nonpregnancy in patients undergoing in vitro fertilization: a systematic review. Fertil Steril 86.4: 807-18.
16. Inoue, M, Kobayashi, Y, Honda, I, et al. (1992). The impact of endometriosis on the reproductive outcome of infertile patients. Am J Obstet Gynecol 167.1: 278-82.
17. Jabbour, SA. (2009) Follicle-Stimulating Hormone Abnormalities. Last Update: June 15, 2009. sMedicine. Available: http://emedicine.medscape.com/article/118810-overview. Date Accessed: September 27, 2010.
18. Jain, T, Soules, MR, Collins, JA. (2004). Comparison of basal follicle-stimulating hormone versus the clomiphene citrate challenge test for ovarian reserve screening. Fertil Steril 82.1: 180-5.
19. Karmazyn, B. (2010). Scrotal Ultrasound. Ultrasound Clin.5: 61-74.
20. Katz, VL, Lentz, GM, Lobo, RA, et al. (2007). Comprehensive Gynecology, Management of the Causes of Infertility. Chapter 41. 5 ed. Philadelphia Mosby.
21. Laboratory manual of the WHO for the examination of human semen and sperm-cervical mucus interaction. (2001). Ann Ist Super Sanita 37.1: I-XII, 1-123.
22. Lessey, BA. (1998). Endometrial integrins and the establishment of uterine receptivity. Hum Reprod 13 Suppl 3: 247-58; discussion 259-61.
23. Liu, WX, Luo, MJ, Huang, P, et al. (2007). Effects of removal of necrotic blastomeres from human cryopreserved embryos on pregnancy outcome. Cryo Letters 28.2: 129-36.
24. Macklin, NS, Fauser, BC. (2009) Overview of ovulation induction. 18.2. Last Update: May 27, 2009. UpToDate. Available: http://www.uptodate.com/online/content/topic.do?topicKey=r_endo_f/18204&selectedTitle=1%7E150&source=search_result. Date Accessed: September 27, 2010.
25. Marana, R, Catalano, GF, Muzii, L. (2003). Salpingoscopy. Curr Opin Obstet Gynecol 15.4: 333-6.
26. Meikle, SF, Zhang, X, Marine, WM, et al. (1994). Chlamydia trachomatis antibody titers and hysterosalpingography in predicting tubal disease in infertility patients. Fertil Steril 62.2: 305-12.
27. Nagy, ZP, Taylor, T, Elliott, T, et al. (2005). Removal of lysed blastomeres from frozen-thawed embryos improves implantation and pregnancy rates in frozen embryo transfer cycles. Fertil Steril 84.6: 1606-12.
28. Norwitz, ER. (2010) Prevention of spontaneous preterm birth. 18.2. Last Update: May 21, 2010. UpToDate. Available: http://www.uptodate.com/online/content/topic.do?topicKey=pregcomp/22936&selectedTitle=1%7E150&source=search_result. Date Accessed: September 24, 2010.
29. Papanikolaou, EG, Vernaeve, V, Kolibianakis, E, et al. (2005). Is chromosome analysis mandatory in the initial investigation of normovulatory women seeking infertility treatment? Hum Reprod 20.10: 2899-903.
30. Paulson, R. (2010) In vitro fertilization (IVF). 18.2. Last Update: October 16, 2008. UpToDate. Available: http://www.uptodate.com/online/content/topic.do?topicKey=wom_issu/11302&selectedTitle=2%7E132&source=search_result. Date Accessed: September 22, 2010.
31. Peters, AJ, Lloyd, RP, Coulam, CB. (1992). Prevalence of out-of-phase endometrial biopsy specimens. Am J Obstet Gynecol 166.6 Pt 1: 1738-45; discussion 1745-6.
32. Rashed, MM, Ragab, NM, Shalaby, AR, et al. (2008). Patterns Of Testicular Histopathology In Men With Primary Infertility The Internet Journal of Urology 5.2.
33. Revised American Fertility Society classification of endometriosis: 1985. Fertil Steril 43.3: 351-2.
34. Riccaboni, A, Lalatta, F, Caliari, I, et al. (2008). Genetic screening in 2,710 infertile candidate couples for assisted reproductive techniques: results of application of Italian guidelines for the appropriate use of genetic tests. Fertil Steril 89.4: 800-8.
35. Shin, D, Lemack, GE, Goldstein, M. (1997). Induction of spermatogenesis and pregnancy after adult orchiopexy. J Urol 158.6: 2242.
36. Shoupe, D, Mishell, DR, Jr., Lacarra, M, et al. (1989). Correlation of endometrial maturation with four methods of estimating day of ovulation. Obstet Gynecol 73.1: 88-92.

37. Sigman, M, Baazeem, A, Zini, A. (2009). Semen analysis and sperm function assays: what do they mean? Semin Reprod Med 27.2: 115-23.
38. Smarr, SC, Wing, R, Hammond, MG. (1988). Effect of therapy on infertile couples with antisperm antibodies. Am J Obstet Gynecol 158.4: 969-73.
39. Snyder, PJ. (2008) Induction of fertility in men with secondary hypogonadism. 18.2. Last Update: July 25, 2008. UpToDate. Available: http://www.uptodate.com/online/content/topic.do?topicKey=r_endo_m/5536&selectedTitle=1%7E150&source=search_result. Date Accessed: October 4, 2010.
40. Spira, A. (1998). The use of fecundability in epidemiological surveys. Hum Reprod 13.7: 1753-6.
41. Tulandi, T. (2009) Laparoscopic surgery for treatment of infertility in women. 18.2. Last Update: August 24, 2009. UpToDate. Available: http://www.uptodate.com/online/content/topic.do?topicKey=gyn_surg/14581&selectedTitle=2%7E6&source=search_result#H21. Date Accessed: September 27, 2010.
42. Tulandi, T. (2010) Surgical treatment of ectopic pregnancy and prognosis for subsequent fertility. 18.2. Last Update: January 12, 2010. UpToDate. Available: http://www.uptodate.com/online/content/topic.do?topicKey=gyn_surg/5788&selectedTitle=1%7E19&source=search_result#H7. Date Accessed: September 27, 2010.
43. Turek, P. (2002) Diagnostic Surgery: Vasography, Seminal Vesicle Aspiration and Testis Biopsy. Last Update: September 9, 2002. Available: http://reference.kfupm.edu.sa/content/t/u/turek_1_diagnostic_surgery__vasography___87787.pdf. Date Accessed: September 27, 2010.
44. van Noord-Zaadstra, BM, Looman, CW, Alsbach, H, et al. (1991). Delaying childbearing: effect of age on fecundity and outcome of pregnancy. BMJ 302.6789: 1361-5.
45. Wein, AJ. (2007). Campbell-Walsh urology ninth edition review. Philadelphia: Saunders/Elsevier.

Revision History

Revision Date	Summary of Changes
6/30/23	For Commercial Plan Policy, added procedure of thawing of cryopreserved semen as not covered.
9/20/23	For Commercial Plan Policy, added "Karyotyping for chromosomal abnormalities" as a covered procedural test to Female section to coincide with existing coverage in Male section.
1/1/24	For Commercial Plan Policy, added coverage criteria sections for Colorado Based Plans and Nevada Based Plans.
1/15/24	For Commercial Plan Policy, added vasectomy reversal to list of excluded treatments.
2/25/25	For Commercial Plan Policy, removed 17-hydroxyprogesterone caproate as a covered fertility treatment for females as this is no longer recommended according to clinical guidelines.

Select Health

Health, Inc. Also, the content of this Service is proprietary and is protected by copyright. You may access the copyrighted content of this Service only for purposes set forth in these Conditions of Use.

Select Health

Select Health

MEDICAL POLICY

MONALISA TOUCH

Policy # 656
Implementation Date:10/19/22
Review Dates: 10/19/23, 10/17/24
Revision Dates:

Disclaimer:
1. Policies are subject to change without notice.
2. Policies outline coverage determinations for Select Health Commercial, Select Health Medicare (CMS), and Select Health Community Care (Medicaid) plans. Refer to the "Policy" section for more information.

Description

The MonaLisa Touch system (Cynosure Inc.) is a fractional CO2 laser with a vaginal probe that was developed in Europe (SmartXide, DEKA M.E.L.A.). The CO2 laser beam is fractionated into nonablative beams of light that penetrate tissue to create small superficial wounds. Wounding immediately stimulates collagen remodeling and regeneration, a process that continues for several months. As a result, the treated vaginal tissue regains the moisture, tonicity, and elasticity that was lost due to estrogen depletion.

The procedure is performed in an office setting and takes approximately 10 minutes. A few minutes prior to treatment, the vaginal introitus and vulva are numbed with topical lidocaine and prilocaine cream. The MonaLisa Touch vaginal probe is inserted into the vagina and is rotated and withdrawn gradually during treatment to ensure complete coverage of the vaginal canal. Patients usually receive 3 treatment sessions at 6-week intervals.

COMMERCIAL PLAN POLICY AND CHIP (CHILDREN'S HEALTH INSURANCE PROGRAM)

Select Health does not cover the MonaLisa Touch procedure for any indication. There is a lack of any conclusive evidence which would demonstrate an improvement in health outcomes; this meets the plan's definition of investigational/experimental.

SELECT HEALTH MEDICARE (CMS)

Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS, and InterQual criteria are not available, the Select Health Commercial policy applies. For the most up-to-date Medicare policies and coverage, please visit their search website http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?from2=search1.asp& or the manual website

SELECT HEALTH COMMUNITY CARE (MEDICAID)

Select Health Community Care policies typically align with State of Utah Medicaid policy, including use of InterQual. There may be situations where NCD/LCD criteria or Select Health commercial policies are used. For the most up-to-date Medicaid policies and coverage, please visit their website http://health.utah.gov/medicaid/manuals/directory.php or the Utah Medicaid code Look-Up tool

Select Health

Billing/Coding Information

CPT CODES

58999 Unlisted procedure, female genital system (nonobstetrical)

Key References

1. Hayes, Inc. Health Technology Brief. Laser Therapy Using MonaLisa Touch (Cynosure, Inc.) for Vulvovaginal Atrophy. March 28, 2018.

Disclaimer

This document is for informational purposes only and should not be relied on in the diagnosis and care of individual patients. Medical and Coding/Reimbursement policies do not constitute medical advice, plan preauthorization, certification, an explanation of benefits, or a contract. Members should consult with appropriate healthcare providers to obtain needed medical advice, care, and treatment. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the member's individual benefit plan that is in effect at the time services are rendered.

The codes for treatments and procedures applicable to this policy are included for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Select Health® makes no representations and accepts no liability with respect to the content of any external information cited or relied upon in this policy. Select Health updates its Coverage Policies regularly, and reserves the right to amend these policies without notice to healthcare providers or Select Health members.

Members may contact Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Coverage Policy may call Select Health Provider Relations at (801) 442-3692.

Select Health

Select Health

MEDICAL POLICY

PROPHYLACTIC MASTECTOMY

Policy # 220
Implementation Date: 12/15/03
Review Dates: 2/21/08, 2/26/09, 2/18/10, 4/21/11, 7/18/13, 6/19/14, 6/11/15, 6/16/16, 6/15/17, 6/21/18, 6/20/19, 6/18/20, 6/17/21, 5/19/22, 8/22/23, 6/20/24
Revision Dates: 6/30/06, 4/13/07, 12/21/11, 9/24/20, 7/26/23, 11/7/23, 3/19/24

Related Medical Policies:
#172 Reduction Mammoplasty (Breast Reduction)
#189 Women's Health and Cancer Rights Act Clarification

Disclaimer:
1. Policies are subject to change without notice.
2. Policies outline coverage determinations for Select Health Commercial, Select Health Medicare (CMS), and Select Health Community Care (Medicaid) plans. Refer to the "Policy" section for more information.

Description

Prophylactic mastectomy is defined as the removal of the breast in the absence of malignant disease (simple mastectomy). Prophylactic mastectomies are performed to reduce the risk of future breast cancer. Individuals may be considered at high risk of developing breast cancer for a variety of reasons, including a strong family history of breast cancer, presence of a germline genetic mutation associated with a high risk of developing breast cancer, and prior receipt for thoracic radiation before the age of 30 years.

While a personal history of atypical hyperplasia or lobular carcinoma in situ (LCIS) confers increased risk of future breast cancer and was previously considered an indication for prophylactic mastectomy, current national guidelines, including from the National Comprehensive Cancer Network (NCCN) recommend risk-reducing endocrine therapy rather than surgical risk reduction through prophylactic mastectomy.

Prophylactic mastectomies are typically bilateral but can also describe a unilateral mastectomy in a patient who has previously undergone a mastectomy involving the opposite breast for an invasive cancer or in a patient simultaneously undergoing a mastectomy of the opposite breast for a primary malignancy. If the patient is considered high-risk in either breast, then a bilateral mastectomy is usually performed.

Contralateral mastectomy is also considered for symmetry purposes in individuals undergoing mastectomy for the contralateral breast for primary malignancy who have no plans for future breast reconstruction.

COMMERCIAL PLAN POLICY AND CHIP (CHILDREN'S HEALTH INSURANCE PROGRAM)

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request.

Select Health covers prophylactic mastectomy (simple mastectomy, skin sparing mastectomy, or nipple sparing mastectomy*) for individuals defined to be at high risk for developing breast cancer. Patients defined at high risk for developing breast cancer are as follows:

1. Personal diagnosis of breast cancer at 50 years of age or younger; or
2. Personal history of multiple primary or bilateral breast cancers; or
3. Triple-negative breast cancer at any age; or

4. Known to personally be a germline carrier of a pathogenic mutation in one of the following genes (for mutations in other genes with less well-established risk of breast cancer, management should be based on personal and family history of breast cancer):

   a) BRCA1 or BRCA2 (hereditary breast and ovarian cancer)

   b) TP53 (Li-Fraumeni syndrome)

   c) PTEN (Cowden and Bannayan-Riley-Ruvalcaba syndromes)

   d) PALB2

   e) CDH1

   f) CHEK2

   g) STK11 (Peutz-Jeghers); or

5. Personal history of receiving radiation treatment to the chest before age 30 years, such as for Hodgkin lymphoma; or

6. The individual's risk of breast cancer is greater than 40% on a validated assessment tool such as the Breast Cancer Risk Calculator, Gail Model, or Tyrer-Cuzick Risk Calculator; and the individual has undergone counseling from an appropriate provider, such as gynecologist, breast surgeon, or genetic counselor, to quantitate their risk.

Select Health covers contralateral mastectomy for symmetry purposes in individuals undergoing mastectomy for the contralateral breast for primary malignancy, and who have no plans for future breast reconstruction.

Select Health covers premastectomy mastopexy before nipple sparing prophylactic mastectomy for individuals with breast ptosis or macromastia (large breasts), as determined in Policy #172.

Select Health considers prophylactic mastectomy experimental and investigational for all other indications.

Select Health does NOT cover subcutaneous mastectomy as this has not been shown to be as effective as simple mastectomy in removing breast tissue, and therefore, is not as effective in reducing the risk of breast cancer.

*Definitions:

Simple mastectomy: A simple or total mastectomy is removal of the breast, nipple, and areola. No lymph nodes from the axillae are removed.

Skin sparing mastectomy: Removal of the breast, nipple and areola, keeping the outer skin of the breast intact. It is a special method of performing a mastectomy that allows for a good cosmetic outcome when combined with a reconstruction done at the same time. A tissue expander may also be placed as a space holder for later reconstruction. This method cannot be used if the cancer is near to the skin surface as total clean margin resection would not be possible.

Nipple sparing mastectomy: Removal of the breast tissue with preservation of the skin, nipple and areola. Incisions are often hidden underneath the breast or in the arm pit area. This method involves simultaneous reconstruction. Sometimes the completed reconstruction is done at the same time and in other cases, a tissue expander is inserted as a space holder for later reconstruction. This method cannot be used if the cancer is near to the skin surface or directly under the nipple as total clean margin resection would not be possible.

Radical mastectomy: A radical mastectomy (Halsted mastectomy) consists of en bloc removal of the breast, the overlying skin, the pectoralis major and minor muscles, and the entire axillary contents (level I, II, and III nodes).

Modified radical mastectomy: A modified radical mastectomy (MRM) is complete removal of the breast and the underlying fascia of the pectoralis major muscle along with the removal of the level I and II axillary lymph nodes.

Subcutaneous mastectomy: Removal of breast tissue, using a minimal incision. This type of mastectomy may be used to remove small areas of suspicious or cancerous tissue, but it can also be a cosmetic surgery procedure.

The table below is taken from NCCN Guidelines Version 1.2021/Genetic Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.

Gene	Breast Cancer Risk and Management for individuals assigned female at birth (AFAB)	Ovarian Cancer Risk and Management	Other Cancer Risks and Management
ATM	Increased risk of breast cancer – Screening: Annual mammogram with consideration of tomosynthesis and consider breast MRI with contrast starting at age 30-35 years[a,b] RRM (risk-reducing mastectomy): Evidence insufficient, manage based on family history	2%-3% lifetime risk; RRSO (risk-reducing salpingo-oophorectomy): Evidence insufficient, manage based on family history	Pancreatic; 5-10% lifetime risk, surveillance recommended for people with a family history of pancreatic cancer in FDR or SDR and ATM mutationData emerging for prostate cancer risk.
BARD1	Limited emerging evidence to suggest increased risk of breast cancer, particularly ER, PR, and HER-2 negative (triple negative disease); Screening: Annual mammogram with consideration of tomosynthesis and consider breast MRI with contrast starting at age 40 years[a,b]; RRM: Evidence insufficient, manage based on family history	Unknown or insufficient evidence for ovarian cancer risk	Unknown or insufficient evidence for other cancers
BRCA1	Increased risk of breast cancer (with predisposition to triple negative disease)	Increased risk of ovarian cancer	Pancreatic, Prostate
BRCA2	Increased risk of breast cancer (with predisposition to triple negative disease)	Increased risk of ovarian cancer	Pancreatic, Prostate, Melanoma
BRIP1	Potential increase in female breast cancer (including triple negative) risk with insufficient evidence for risk management	Increased risk of ovarian cancer (consider RRSO at 45 to 50 years)	Unknown or insufficient evidence for other cancers
CDH1	Increased risk of female lobular breast cancer[c]; Screening: Annual mammogram with consideration of tomosynthesis and consider breast MRI with contrast starting at age 30 years[a,b]	No increased risk of ovarian cancer	Diffuse gastric cancer

CHEK2	Increased risk of breast cancer (with predisposition to ER+ disease)[c]; Screening: Annual mammogram with consideration of tomosynthesis at age 40 and consider breast MRI with contrast age 30-35years[a,b]; RRM: Evidence insufficient, manage based on family history	No increased risk of ovarian cancer	Colon, emerging evidence for prostate
MSH2, MLH1, MSH6, PMS2, EPCAM	Unknown or insufficient evidence for breast cancer risk[b] (manage based on family history)	Increased risk of ovarian cancer	Colon, Uterine, Others; Pancreatic (insufficient evidence for PMS2)
NBN	Current data suggest that breast cancer risks are not increased pathogenic/likely pathogenic variants other than 657del5, for which there is mixed evidence for increased risk. Insufficient evidence for risk management	Mixed evidence for increased evidence of ovarian cancer; RRSO: Evidence insufficient, manage based on family history	Unknown or insufficient evidence for other cancers
NF1	Increased risk of female breast cancer[c]; Screening: Annual mammogram with consideration of tomosynthesis starting at age 30 years and consider breast MRI with contrast from ages 30 to 50[a,b]; RRM: Evidence insufficient, manage based on family history	No increased risk of ovarian cancer	Malignant peripheral nerve sheath tumors, GIST, others; Recommend referral to NF1 specialist for evaluation and management
PALB2	Increased risk of female breast cancer[c]; Screening: Annual mammogram with consideration of tomosynthesis and breast MRI with contrast at age 30[a,b]; RRM: Discuss option of risk-reducing mastectomy	Increased risk of ovarian cancer; RRSO: Evidence insufficient, manage based on family history	Pancreatic; Unknown or insufficient evidence for other cancers
PTEN	Increased risk of breast cancer	No increased risk of ovarian cancer	Thyroid, colon, endometrial
RAD51C	Potential increase in breast cancer risk (including triple negative disease) with insufficient evidence for risk management	Increased risk of ovarian cancer (consider RRSO at 45 to 50 years)	Unknown or insufficient evidence for other cancers
RAD51D	Potential increase in female breast cancer risk (including triple negative disease) with insufficient evidence for risk management	Increased risk of ovarian cancer (consider RRSO at 45 to 50 years)	Unknown or insufficient evidence for other cancers

STK11	Increased risk of female breast cancer; Annual mammogram and breast MRI with and without contrast starting at age 30 y. RRM: Discuss options	Increased risk of non-epithelial ovarian tumors	Pancreatic, colon, stomach, others.
TP53	Increased risk of female breast cancer	No increased risk of ovarian cancer	Pancreatic, Sarcomas, others.

a: May be modified based on family history (typically beginning screening 5 to 10 years earlier than the youngest diagnosis in the family but not later than stated in the table) or specific gene pathogenic/likely pathogenic variant.

b: For individuals assigned female at birth with pathogenic/likely pathogenic variants who are treated for breast cancer and have not had bilateral mastectomy, screening should continue as described.

c: Screening and risk-reduction management is extrapolated from BRCA 1 / 2 data based on levels of risk.

SELECT HEALTH MEDICARE (CMS)

Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS, and InterQual criteria are not available, the Select Health Commercial policy applies. For the most up-to-date Medicare policies and coverage, please visit their search website http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?from2=search1.asp& or the manual website

SELECT HEALTH COMMUNITY CARE (MEDICAID)

Select Health Community Care policies typically align with State of Utah Medicaid policy, including use of InterQual. There may be situations where NCD/LCD criteria or Select Health commercial policies are used. For the most up-to-date Medicaid policies and coverage, please visit their website http://health.utah.gov/medicaid/manuals/directory.php or the Utah Medicaid code Look-Up tool

Summary of Medical Information

The factors contributing to a person's risk of developing cancer of the breast are multiple and by no means simple. Much of the above policy can be traced to information and recommendations set forth by Hartmann et al., in the New England Journal of Medicine in 1999. This policy is also based on a compilation of factors which identify patients who are at high risk of breast cancer and who, therefore, are appropriate candidates for prophylactic mastectomy.

Hartmann's study was a retrospective cohort analysis of 639 women with a family history of breast cancer that underwent bilateral prophylactic mastectomy between 1960 and 1993 at the Mayo clinic. A total of 90% of the mastectomies were subcutaneous. The patients were divided into 2 groups: high-risk patients with a family history suggestive of hereditary breast cancer (n = 214), while the remaining 425 patients were arbitrarily considered to have a moderately increased risk. However, it should be emphasized that all women had some sort of family history of breast cancer. For each group, the reduction in the incidence of mortality due to breast cancer was estimated by comparison to a control group (sisters of high-risk patients) or predicted outcomes (using the GAIL model for moderate-risk patients).

For patients at moderate risk of breast cancer, 37.4 cancers were predicted by the GAIL model, and 4 were observed for an incidence reduction of 89.5%. Approximately 13 women would have to have prophylactic mastectomies to prevent 1 cancer. For those at high risk of breast cancer, reduction in breast cancer incidence ranged from 90%–94%. Four to eight women would need to undergo prophylactic mastectomy to prevent 1 occurrence of breast cancer.

While all patients in the Hartmann study had a family history of breast cancer, one should not conclude that all patients with a family history of breast cancer are candidates for a prophylactic mastectomy. Essentially, the decision is a complicated patient-driven risk-benefit analysis of the individual cancer risk. While the cancer risk is greatest for those considered at high risk, whether the cancer risk associated with moderate-risk patients warrants a prophylactic mastectomy, is a difficult question. While high-risk is more

objectively defined by either a family history alone, or the presence of a BRCA1 or BRCA2 mutation, moderate-risk may be conferred by a wide range of family histories in association with different breast pathologies.

The Hartmann study arbitrarily assigned all women not at high risk to be at moderate risk. It is not known what kind of risk assessment was performed, if any, prior to the mastectomy procedure. In the study, of the 425 women in the moderate-risk category, 268 had at least one affected first-degree relative, 46 had 2 aunts, cousins, or both with breast cancer and fewer second-degree or third-degree relatives. This group includes a wide variety of patients, with the spectrum potentially ranging from a patient with a first-degree relative with bilateral premenopausal breast cancer, to a patient whose elderly mother is diagnosed with breast cancer. While these facts underline the importance of adequate counseling, it also underlines the arbitrary nature of defining a risk level above which prophylactic mastectomy would be considered medically necessary.

The GAIL model has been used as patient selection criteria to identify women at increased risk of breast cancer who would be candidates for chemoprevention with tamoxifen. The Breast Cancer Chemoprevention Trial accepted patients between the ages of 35 and 59 years with a 5-year predicted risk of breast cancer of 1.66%, according to the GAIL model. Presumably, at the very least, the predicted cancer risk for candidates for prophylactic mastectomy should exceed that of candidates for chemoprevention.

Another tool for estimating breast cancer risk is the Breast Cancer Risk Assessment Tool, designed by the National Cancer Institute (NCI) in conjunction with the National Surgical Adjuvant Breast and Bowel Project (NSABP). The purpose of this tool is to determine a woman's estimated risk of developing invasive breast cancer over the 5 years up to age 90. This tool is available at http://www.cancer.gov/bcrisktool.

Billing/Coding Information

CPT CODES

Not covered: Investigational/Experimental for this indication

19304 Mastectomy, subcutaneous

Covered: For the conditions outlined above

19303 Mastectomy, simple, complete

HCPCS CODES

No specific codes identified

Key References

1. Adjuvant Breast and Bowel Project -1 Study. J Natl Cancer Inst 1998; 90:1371-1388. 1999 Tec Assessment; Tab 13.
2. American Cancer Society (ACS). (1998). What are the key statistics about breast cancer? American Cancer Society (ACS) website. Available at http://www.cancer.org/. Accessed June 1998.
3. BCBSA, Medical Policy Reference Manual, 12/01/99.
4. Bland KI; Menck HR; Scott-Conner CE et al. (1998). The National Cancer Data Base 10-year survey of breast carcinoma treatment at hospitals in the United States. Cancer, 83(6):1262-73.
5. Borgen PI, Hill AD, Tran KN et al. (1998). Patient regrets after bilateral prophylactic mastectomy. Ann Surg Oncol, 5(7):603-606.
6. Cummings SR, Eckert S, Krueger KA et al. (1999). The effect of raloxifene on risk of breast cancer in postmenopausal women. JAMA, 281:2189-2197.
7. Fisher B, Costantino JP, Wickerham DL et al. Tamoxifen for prevention of breast cancer; Report of the National Surgical.
8. Hartmann LC, Schaid DJ, Woods JE et al. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. N Eng J Med 1999; 340:77-84.
9. Hammond, D. C., & Little, A. K. The Role of Premastectomy Mastopexy and Breast Reduction in the Reconstruction of the Enlarged or Ptotic Breast. *Plast Reconstr Surg*. 2022 Aug 1; 150(2):270-280.
10. Hatcher MB, Fallowfield L, A'Hern R. The psychosocial impact of bilateral prophylactic mastectomy: prospective study using questionnaires and semistructured interviews. BMJ 2001 Jan 13;322(7278):76.
11. http://breastcancerprevention.org/breastcancerrisks.html. Accessed 1/29/07.
12. http://www.cancer.gov/bcrisktool/. Accessed 1/30/07.
13. NCCN Guidelines Version 2.2024. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.

Disclaimer
This document is for informational purposes only and should not be relied on in the diagnosis and care of individual patients. Medical and Coding/Reimbursement policies do not constitute medical advice, plan preauthorization, certification, an explanation of benefits, or a contract. Members should consult with appropriate healthcare providers to obtain needed medical advice, care, and treatment. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the member's individual benefit plan that is in effect at the time services are rendered.

The codes for treatments and procedures applicable to this policy are included for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Select Health® makes no representations and accepts no liability with respect to the content of any external information cited or relied upon in this policy. Select Health updates its Coverage Policies regularly, and reserves the right to amend these policies without notice to healthcare providers or Select Health members.

Members may contact Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Coverage Policy may call Select Health Provider Relations at (801) 442-3692.

Select Health

MEDICAL POLICY

SUBCUTANEOUS MASTECTOMY FOR FIBROCYSTIC BREAST DISEASE

Policy # 543
Implementation Date:11/8/13
Review Dates: 3/19/15, 2/11/16, 2/16/17, 2/15/18, 2/18/19, 2/17/20, 2/18/21, 1/10/22, 2/16/23, 2/14/25
Revision Dates: 1/6/14, 9/14/16, 1/14/22

Disclaimer:
1. Policies are subject to change without notice.
2. Policies outline coverage determinations for Select Health Commercial, Select Health Medicare (CMS), and Select Health Community Care (Medicaid) plans. Refer to the "Policy" section for more information.

Description

Fibrocystic breast 'disease' is a commonly used phrase to describe painful, lumpy breasts; the exact cause is not known. It is believed that hormones made in the ovaries result in a woman's breast feeling swollen, lumpy, or painful before or during menstruation each month. Up to half of women may have a fibrocystic breast disease (FBD) problem at some time during their life. It is most common between the ages of 20 and 45; it is rare in women after menopause, unless they are taking estrogen.

Symptoms usually improve after a woman experiences menopause as estrogen and progesterone production from the ovaries abates. Women taking birth control pills may have fewer symptoms whereas women on hormone therapy may have more symptoms. Symptoms are usually worse right before the menstrual period and improve after menses begins.

The goals of management are to exclude breast cancer by referral for further assessment, to explain symptoms and reassure patients who do not have cancer, to treat breast pain, to exclude treatable causes for nipple discharge, and to educate the patient in self-examination and breast care. Therapies may be medical or surgical in nature. Medical therapies can focus on treatment of the pain occurring in patients with FBD or to reduce the size of the lumps; often, the treatments overlap. Multiple therapies have been developed in an attempt to manage the pain associated with FBD. These therapies are variably effective depending upon the individual. Some current therapies being used/recommended include bromocriptine, Danazol, NSAIDs, and reducing methylxanthine intake (in coffee, tea, chocolate, cola, caffeinated medications, theophylline, and theobromine), tamoxifen, and oral contraceptives.

For patients with severe disease recalcitrant to medical therapy, subcutaneous mastectomy is sometimes considered to reduce pain related to the condition or reduce cancer risks for patients with large or frequent cysts. Though the concept of breast cancer reduction has been debunked in the literature, difficulty in identifying breast cancer and use of additional resources to diagnose breast cancer is often cited as the need prompting more aggressive interventions.

Two forms of subcutaneous mastectomy exist: skin-sparing mastectomy and nipple-sparing mastectomy. The "skin-sparing" mastectomy (SSM) is a surgical technique in which most of the natural breast skin envelope is not resected; in contrast, a conventional mastectomy incision removes a larger portion of the overlying skin. The breast parenchyma is excised, usually through a circular incision around the nipple areolar complex, with or without an extension if needed to access the superolateral breast. In some cases, existing biopsy scars and/or the skin overlying the tumor is also excised if present. A reconstructive procedure using autogenous tissue, or an implant-based method is typically performed in the same setting as an SSM. Preservation of the skin of the breast and the inframammary fold provides the reconstructed breast with a more natural shape and contour. The superior cosmetic result has resulted in the increasing popularity of this approach in both the United States and Europe. A nipple-sparing mastectomy (NSM) preserves the dermis and epidermis of the nipple and removes some of the

major ducts from within the nipple lumen. This approach is an option for carefully selected patients, particularly those who are having surgery for prophylactic purposes and are having immediate reconstruction. Subcutaneous mastectomy is a proposed surgical procedure for the treatment of fibrocystic breast disease.

COMMERCIAL PLAN POLICY/CHIP (CHILDREN'S HEALTH INSURANCE PROGRAM)

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request.

Select Health covers subcutaneous mastectomy for the treatment of recalcitrant fibrocystic breast disease when conservative therapy has failed.

Failure of conservative therapy is defined as documentation of failure of, or intolerance to, all the following:

1. At least a 3-month trial of at least 4 of the following medications:
    a. Bromocriptine 2.5 mg TID
    b. Danazol at a minimum dose of 200 mg twice a day
    c. Routine daily prescription nonsteroidal anti-inflammatory drugs (NSAIDs)
    d. Reducing methylxanthine intake (in coffee, tea, chocolate, cola, caffeinated medications, theophylline, theobromine)
    e. Tamoxifen 10 mg a day
    f. Oral contraceptives
2. Documentation of need for multiple cyst aspirations or breast biopsies
3. Symptoms present for greater than 1 year

SELECT HEALTH MEDICARE (CMS)

Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS, and InterQual criteria are not available, the Select Health Commercial policy applies. For the most up-to-date Medicare policies and coverage, please visit their search website http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?from2=search1.asp& or the manual website

SELECT HEALTH COMMUNITY CARE (MEDICAID)

Select Health Community Care policies typically align with State of Utah Medicaid policy, including use of InterQual. There may be situations where NCD/LCD criteria or Select Health commercial policies are used. For the most up-to-date Medicaid policies and coverage, please visit their website http://health.utah.gov/medicaid/manuals/directory.php or the Utah Medicaid code Look-Up tool

Summary of Medical Information

No systematic reviews and only one primary study met inclusion criteria for this report. It is notable that identified studies were all over 20 years old.

The single study meeting inclusion criteria was Pennisi et al.'s 1989 paper. This prospective clinical trial of 1,500 patients enrolled in the Subcutaneous Mastectomy Data Evaluation Center at Saint Francis Memorial Hospital in San Francisco. These patients had been operated on by 165 plastic surgeons and were followed-up on for nine years. Though the study was of reasonable quality it was not multi-centered, had no comparative arm, and its conclusions were based on the opinion that fibrocystic breast disease is a precursor for breast cancer, an assumption which current science has dismissed.

Given that there is very little peer-reviewed (and non-peer-reviewed) evidence regarding subcutaneous mastectomy for the treatment of fibrocystic breast disease and given that the evidence is more than 20 years old, it is difficult to derive reasonable conclusions from the literature concerning the safety and efficacy of this procedure (GRADE 2C).

Billing/Coding Information

CPT CODES

19304 Mastectomy, subcutaneous

19318 Breast reduction

Key References

1. Jones, R. (2011) Fibrocystic breast changes. Available: https://www.clinicalkey.com/#!/ContentPlayerCtrl/doPlayContent/21-s2.0-1014324/{"scope":"all","query":"Fibrocystic Disease of the Breast"}. Date Accessed: August 27, 2013.
2. Kwong, A. (2013) Mastectomy. February 14, 2013. Up to Date. Available: http://www.uptodate.com/contents/mastectomy?detectedLanguage=en&source=search_result&search=mastectomy&selectedTitle=1~128&provider=noProvider#H7005300. Date Accessed: August 28, 2013.
3. Medline. (2013) Fibrocystic Breast Changes. November 5, 2012. National Institutes of Health. Available: http://www.nlm.nih.gov/medlineplus/ency/article/000912.htm. Date Accessed: August 27, 2013.
4. Memon, A., Perveen, S., Sangrasi, A. (2007). "Response of Anti Prolactin (Bromocriptine) Treatment in ANDI (Aberration of Normal Development and Involution) Patients of Breast.
5. Pennisi, VR. (1976). Subcutaneous mastectomy and fibrocystic disease of the breast. Clin Plast Surg 3.2: 205-16.
6. Pennisi, VR, Capozzi, A. (1989). Subcutaneous mastectomy data: a final statistical analysis of 1500 patients. Aesthetic Plast Surg 13.1: 15-21.
7. Pizzorno, JE. (2013) Textbook of Natural Medicine. 4. Elsevier. Available: https://www.clinicalkey.com/#!/ContentPlayerCtrl/doPlayContent/3-s2.0-B9781437723335001656/{"scope":"all","query":"Fibrocystic Disease of the Breast"}. Date Accessed: August 27, 2013.

Select Health

Select Health

MEDICAL POLICY

UTERINE ARTERY EMBOLIZATION

Policy # 347

Implementation Date:4/23/07
Review Dates: 4/24/08, 4/23/08, 6/20/13, 4/17/14, 4/14/16, 4/27/17, 9/18/18, 4/13/19, 8/1/19, 8/20/20, 8/19/21, 7/21/22, 7/28/23, 7/26/24
Revision Dates: 5/2/17

Disclaimer:
1. Policies are subject to change without notice.
2. Policies outline coverage determinations for Select Health Commercial, Select Health Medicare (CMS), and Select Health Community Care (Medicaid) plans. Refer to the "Policy" section for more information.

Description

Uterine leiomyomata, or fibroids, are benign tumors of the uterus made up of smooth muscle and the extracellular matrix proteins, collagen, and elastin. They are exceptionally common; the cumulative incidence of a diagnosis of fibroids in women ages 25–45 is approximately 30%. Fibroids represent the most common indication for hysterectomy, accounting for 30% of hysterectomies in white women and over 50% of hysterectomies in black women. The cumulative risk of a hysterectomy for fibroids for all women between ages 25–45 is 7%; for black women, the risk is as high as 20%. Fibroids can cause abnormal uterine bleeding, dysmenorrhea, and non-cyclic pelvic pain. They also can contribute to symptoms related to an enlarging pelvic mass (e.g., urinary frequency or constipation).

Uterine artery embolization (whether surgically or embolically produced) appears to be a safe, effective, durable, and global fibroid treatment that is a compelling clinical alternative to drug therapy, myomectomy, or hysterectomy. Fibroids are supplied with blood from branches of the uterine arteries. In uterine artery embolization, the uterine arteries are acutely occluded bilaterally with embolic particles, which stop blood flow to the uterus both within the intrinsic arteries of the uterus and within fibroids. Being anatomically and genetically distinct from fibroid cells, myometrial cells can endure this period of transient uterine ischemia, while fibroid cells, in contrast, die because of the ischemia.

COMMERCIAL PLAN POLICY AND CHIP (CHILDREN'S HEALTH INSURANCE PROGRAM)

Select Health covers uterine artery embolization for the treatment of uterine fibroids.

SELECT HEALTH MEDICARE (CMS)

Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS, and InterQual criteria are not available, the Select Health Commercial policy applies. For the most up-to-date Medicare policies and coverage, please visit their search website http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?from2=search1.asp& or the manual website

SELECT HEALTH COMMUNITY CARE (MEDICAID)

Select Health Community Care policies typically align with State of Utah Medicaid policy, including use of InterQual. There may be situations where NCD/LCD criteria or Select Health commercial policies are used. For the most up-to-date Medicaid policies and coverage, please visit their website http://health.utah.gov/medicaid/manuals/directory.php or the Utah Medicaid code Look-Up tool

Select Health

Summary of Medical Information

A 2005 Hayes directory gave a 'B' rating to uterine artery embolization for women with symptomatic uterine fibroids who are candidates for surgical therapy but who wish to avoid hysterectomy or myectomy, while wishing to not preserve their childbearing potential. They offered the following conclusions regarding the procedure: "There is evidence from one randomized controlled trial (RCT) and from several large prospective uncontrolled studies that UAE can reduce menstrual bleeding, pelvic pain, and bulk-related symptoms, and may lead to a reduction in fibroid size and uterine volume in patients with symptomatic fibroids. Therefore, UAE may be a suitable alternative to hysterectomy and myomectomy for patients who have failed or are not candidates for medical therapy and who wish to avoid or have a contraindication to surgery. The lack of large-scale randomized trials comparing UAE with hysterectomy or myomectomy makes it difficult to arrive at definitive conclusions regarding the relative efficacy and safety of UAE, particularly with regards to long-term outcomes. The effects of UAE on ovarian and uterine function and on fertility are relatively unknown." UAE is not usually recommended in women who desire future pregnancy (myomectomy is still the standard in these patients).

Recent review of the medical literature identifies a few concerns related to the performance of UAE, such as increasing the risk for premature menopause. Also, a rare case of pyomyoma (suppurative leomyoma of the uterus) resulting from infarction and infection post-UAE has been reported. Rare cases of uterine rupture have also been reported in post-UAE patients who subsequently became pregnant. Cochrane Database Syst Rev. in 2014 concluded that "We found no clear evidence of a difference between UAE and surgery in the risk of major complications, but UAE was associated with a higher rate of minor complications and an increased likelihood of requiring surgical intervention within two to five years of the initial procedure." However, even though the gynecologic literature contains examples of some worrisome, although rare complications after UAE, the ACOG Opinion on UAE published in 2009 has still not been altered by the college to date. It states: "Based on long- and short-term outcomes, UAE is a safe and effective option for appropriately selected women who wish to retain their uterus. Women who wish to undergo UAE should have a thorough evaluation with an obstetrician-gynecologist to help facilitate optimal collaboration with the interventional radiologists and to ensure the appropriateness of therapy, taking into account the reproductive wishes of the patient."

Billing/Coding Information

Covered: For the conditions outlined above

CPT CODES

37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction

HCPCS CODES

No specific codes identified

Key References

1. AHRQ, 2001 – Evidence Report/Technology Assessment No. 34, *Management of Fibroids*. Publication No. 01-E052).
2. Goodwin SC, McLucas B, Lee M, Chen G, Perrella R, Vedantham S, Muir S, Lai A, Sayre JW, DeLeon M. Uterine artery embolization for the treatment of uterine leiomyomata midterm results. *J Vasc Interv Radiol*, 1999 Oct;10(9):1159-65. PMID: 10527191
3. Gupta JK, Sinha A, Lumsden MA, Hickey M. Uterine artery embolization for symptomatic uterine fibroids. Cochrane Database Syst Rev 2014; CD005073.
4. Hayes, Inc. May 2005. Uterine Artery Embolization for Treatment of Fibroids.
5. Hutchins FL Jr, Worthington-Kirsch R, Berkowitz RP. Selective uterine artery embolization as primary treatment for symptomatic leiomyomata uteri. *J Am Assoc Gynecol Laparosc*, 1999 Aug;6(3):279-84. PMID: 10459027
6. Machan L & M Martin. Uterine artery embolization to treat uterine fibroids. Can Assoc. *Radiol J*, 2001; 52(3):183-7.
7. Marshburn PB, Matthews ML, Hurst BS. (2009). Uterine Artery Embolization as a Treatment Option for Uterine Myomas.
8. Medscape article: Mark D. Levie, MD. Uterine Artery Embolization: Laparoscopic Myomectomy Assistant Professor of Obstetrics & Gynecology, Albert Einstein College of Medicine. Associate Director of Gynecology, Jack D. Weiler Hospital, Montefiore Medical Center, Bronx, New York.
9. Pelage JP, Le Dref O, Soyer P, Kardache M, Dahan H, Abitbol M, Merland JJ, Ravina JH, Rymer R. Fibroid-related menorrhagia: treatment with superselective embolization of the uterine arteries and midterm follow-up. *Radiology*, 2000. May; 215(2):428-31. PMID: 10796920
10. Rosen, M. L., et al. (2013). "Pyomyoma after uterine artery embolization." *Obstet Gynecol*, 121(2 Pt 2 Suppl 1): 431-433.

11. Silberzweig JE, Powell DK, Matsumoto AH, Spies JB. Management of Uterine Fibroids: A Focus on Uterine-sparing Interventional Techniques. Radiology 2016; 280:675.
12. Spies JB, Ascher SA, Roth AR, Kim J, Levy EB, Gomez-Jorge J. Uterine artery embolization for leiomyomata. *Obstet Gynecol*, 2001 Jul;98(1):29-34.
13. Subramanian S, Spies JB. Uterine artery embolization for leiomyomata: resource use and cost estimation. *J Vasc Interv Radiol*, 2001 May;12(5):571-4. PMID: 11340134.

Disclaimer
This document is for informational purposes only and should not be relied on in the diagnosis and care of individual patients. Medical and Coding/Reimbursement policies do not constitute medical advice, plan preauthorization, certification, an explanation of benefits, or a contract. Members should consult with appropriate healthcare providers to obtain needed medical advice, care, and treatment. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the member's individual benefit plan that is in effect at the time services are rendered.

The codes for treatments and procedures applicable to this policy are included for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Select Health® makes no representations and accepts no liability with respect to the content of any external information cited or relied upon in this policy. Select Health updates its Coverage Policies regularly, and reserves the right to amend these policies without notice to healthcare providers or Select Health members.

Members may contact Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Coverage Policy may call Select Health Provider Relations at (801) 442-3692.

Select Health

Select Health

MEDICAL POLICY

WOMEN'S HEALTH AND CANCER RIGHTS ACT CLARIFICATION

Policy # 189

Implementation Date:11/11/01

Review Dates: 4/21/03, 6/25/03, 6/24/04, 6/16/05, 6/22/06, 7/12/07, 6/19/08, 6/11/09, 6/17/10, 9/15/11, 7/18/13, 6/19/14, 6/11/15, 6/16/16, 6/15/17, 6/21/18, 6/16/19, 6/4/20, 6/11/21, 5/19/22, 6/15/23, 6/20/24

Revision Dates: 4/21/03, 3/19/24

Related Medical Policies:
#220 Prophylactic Mastectomy

Disclaimer:
1. Policies are subject to change without notice.
2. Policies outline coverage determinations for Select Health Commercial, Select Health Medicare (CMS), and Select Health Community Care (Medicaid) plans. Refer to the "Policy" section for more information.

Description

The Women's Health and Cancer Rights Act of 1998 (WHCRA) requires the following benefit:

A group health plan and health insurance issuer providing health insurance coverage in connection with a group health plan, which provides medical and surgical benefits with respect to mastectomy, shall also provide coverage for:

- Reconstruction of the breast on which the mastectomy has been performed;
- Surgery and reconstruction of the other breast to produce a symmetrical appearance; and
- Prostheses and treatment of physical complications of all stages of the mastectomy, including lymphedema; in a manner determined in consultation with the attending physician and the patient.

Note: The statute requires the WHCRA notification to be sent to participants no later than January 1, 1999. The act also requires plans to give notification to participants upon plan enrollment and annually thereafter.

COMMERCIAL PLAN POLICY AND CHIP (CHILDREN'S HEALTH INSURANCE PROGRAM)

1. Select Health covers breast reconstruction on all covered mastectomies consistent with the WHCRA of 1998 and the Department of Labor clarifications of August 2001.

2. Select Health will cover contralateral mastectomy for symmetry purposes in individuals undergoing mastectomy for the contralateral breast for primary malignancy, and who have no plans for future breast reconstruction.

SELECT HEALTH MEDICARE (CMS)

Coverage is determined by the Centers for Medicare and Medicaid Services (CMS); if a coverage determination has not been adopted by CMS, and InterQual criteria are not available, the Select Health Commercial policy applies. For the most up-to-date Medicare policies and coverage, please visit their search website http://www.cms.gov/medicare-coverage-database/overview-and-quick-search.aspx?from2=search1.asp& or the manual website

SELECT HEALTH COMMUNITY CARE (MEDICAID)

Select Health Community Care policies typically align with State of Utah Medicaid policy, including use of InterQual. There may be situations where NCD/LCD criteria or Select Health commercial policies are used. For the most up-to-date Medicaid policies and coverage, please visit their website http://health.utah.gov/medicaid/manuals/directory.php or the Utah Medicaid code Look-Up tool

Summary of Medical Information

Multiple questions have arisen since enactment of the Women's Health and Cancer Rights Act (WHCRA) of 1998 due to the somewhat ambiguous language used in crafting the legislation. Subsequently, attempts have been made to clarify the intent of the legislation and its implications on the healthcare delivered to affected individuals and the cost ramifications to Health Plans.

A conference call was held with the U.S. Dept. of Labor (DOL) representatives on August 29, 2001. At that time, it was made clear that in the absence of clarifying legislation or regulations the DOL was looking for "good faith compliance" with the principles of the WHCRA.

Additionally, specific questions involving common questions/scenarios were raised and discussed. These following questions and their associated answers represent an incomplete but improved picture outlining the expectations of SelectHealth in complying with the legislation:

1. How long is a health plan expected to provide coverage for "cosmetic" procedures on the unaffected breast to maintain an appearance of symmetry?

   Basically, use common sense and the guideline that symmetry only need be achieved once. Thus, if symmetry has been achieved at some point in the "treatment plan" then it is probably NOT necessary to cover a second effort. However, if no reconstructive procedure(s) were performed for this purpose since the mastectomy or lumpectomy (i.e., no attempt to achieve symmetry) then SelectHealth may be responsible for coverage of such efforts for "several" years beyond the initial mastectomy. If the asymmetry develops much beyond 10 years, it is probably legitimate to deny coverage if the surgery would not be approved for any other medical or legal reason. This is a value judgment guided by "good faith."

2. If a woman delays reconstructive surgery, how long after the initial mastectomy must a health plan cover the initial reconstructive surgery? 1 year? 2 years? 5 years? 10 years? 25 years? Can a health plan place time restrictions on seeking the initial reconstructive surgery?

   A "reasonable" time frame that shows "good faith" was recommended. Given that most cancers are not considered cured unless a patient is disease-free for 5 years, it is probably appropriate to allow at least 5 years after the time of the surgery to have reconstruction.

3. What degree of asymmetry is a health plan responsible to correct? If a woman has changes that are not perceptible to anyone other than her, with or without clothing, is the health plan responsible for providing coverage for continued reconstructive surgery/surgeries?

   Use common sense and a sense of what most laypeople without any medical education might expect with regards to symmetry. Symmetry does not mean perfectly equal. They did clarify that all that was required was achieving this once. If there was disagreement in the presence or absence of symmetry, it was recommended that multiple medical opinions be sought.

4. Is a health plan responsible for coverage of tattooing to create the sense that a person has a nipple where one does not exist?

   This is considered part of the reconstruction, this should be covered.

5. Is a health plan responsible for covering surgery on the nipple of the unaffected breast to reduce or enlarge it so that it more closely matches the appearance of the reconstructed nipple?

Again, a good faith effort should be done to provide a reasonable sense of symmetry as judged by the usual layperson.

6. Is the reconstruction requirement applicable to mastectomies only, or does it apply to lumpectomies as well?

   Lumpectomy itself does not mandate that the patient receive reconstruction benefits. Certainly, if the lumpectomy leaves the patient "deformed," reconstruction benefits should apply. For minimal lumpectomies, which leave minimal change in the breast, if the expectation of a layperson of reasonable intellect and with common sense would be that the lesion is deforming, reconstruction should probably be covered.

7. Does the statute apply to individuals who have undergone a mastectomy for a non-cancerous reason, such as fibrocystic disease of the breast? Does the statute apply to all types of mastectomies?

   The statute does not limit coverage to just cancer-related malignancies. However, if the plan covers a mastectomy or benefits in connection with such a mastectomy, regardless of the type of mastectomy, then the plan must also cover the reconstruction. If coverage of a mastectomy was denied, then the reconstruction can also be denied.

8. Is a health plan required to provide all modalities of treatment for lymphedema, such as pneumatic compression devices, decompressive physiotherapy, and/or compression garments? Or can a health plan restrict coverage to one type of therapy that is found to be superior to other methods?

   A health plan may restrict coverage to those types of therapies found to be safe and effective. It must offer some therapy but does not have to offer all therapies.

9. Does the statute require that a health plan cover any/all breast reconstructive methods (i.e., DIEP flap vs. TRAM flap) if the member requests a specific method?

   The health plan does not need to cover all methods of reconstruction, if those methods offered are safe and effective.

Billing/Coding Information

CPT CODES

No specific codes identified

HCPCS CODES

No specific codes identified

Key References

1. U.S. Dept. of Labor (DOL), Conference call, August 29, 2001.
2. Women's Health and Cancer Rights Act, 1998.

Revision History

Revision Date	Summary of Changes
3/19/24	For Commercial Plan Policy, added the following coverage consideration: "Select Health covers contralateral mastectomy for symmetry purposes in individuals undergoing mastectomy for the contralateral breast for primary malignancy, and who have no plans for future breast reconstruction."

Select Health

Disclaimer
This document is for informational purposes only and should not be relied on in the diagnosis and care of individual patients. Medical and Coding/Reimbursement policies do not constitute medical advice, plan preauthorization, certification, an explanation of benefits, or a contract. Members should consult with appropriate healthcare providers to obtain needed medical advice, care, and treatment. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the member's individual benefit plan that is in effect at the time services are rendered.

The codes for treatments and procedures applicable to this policy are included for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Select Health® makes no representations and accepts no liability with respect to the content of any external information cited or relied upon in this policy. Select Health updates its Coverage Policies regularly, and reserves the right to amend these policies without notice to healthcare providers or Select Health members.

Members may contact Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Coverage Policy may call Select Health Provider Relations at (801) 442-3692.