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Fertility preservation in patients with medical indications: a committee opinion

Practice Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Washington, D.C.

Patients preparing to undergo therapies that pose a risk to their fertility or who are at risk of premature ovarian insufficiency should be provided prompt counseling regarding available options for fertility preservation. Fertility preservation can best be provided by comprehensive programs designed and equipped to confront the unique challenges facing these patients. This document replaces the document entitled "Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion," last published in 2019. (Fertil Steril® 2026;125:247–59. ©2025 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Fertility preservation, premature ovarian insufficiency, infertility, reproductive endocrinology

Systemic therapy, radiation therapy, and surgery for medical conditions in children, adolescents, and adults of reproductive age can harm future fertility. Moreover, some medical conditions increase the risk of premature gonadal failure. Fertility preservation strategies have been shown to be effective in decreasing infertility risks in these populations.

Utilization of fertility preservation services remains low and is related to social determinants of health, despite increasing health insurance coverage, awareness among clinicians and patients, and availability of fertility preservation programs (1). This document summarizes components of comprehensive fertility preservation care and provides specific clinical recommendations on the basis of currently available strategies.

COMPONENTS AND FUNCTIONS OF A FERTILITY PRESERVATION PROGRAM

Clinics offering fertility preservation should have the expertise and infrastructure to provide timely interventions. Table 1 lists the components of a comprehensive fertility preservation program. Timely initiation of reproductive risk counseling by the primary medical team and rapid referral to a reproductive specialist for fertility preservation consultation is central. When appropriate, safe, and efficient completion of fertility preservation treatment should take place, followed by post-treatment counseling and documentation (Fig. 1). Financial navigation is a key component. Programs unable to provide specific components of fertility preservation services should still counsel patients about all options and provide timely referrals to programs with needed resources.

REPRODUCTIVE RISK AND FERTILITY PRESERVATION OPTIONS COUNSELING

Patients should be counseled on known and unknown reproductive risks of planned medical treatments. The risk of future infertility and secondary hypogonadism varies on the basis of the disease and treatment regimen and may not be fully known at the time of counseling. The safety of future pregnancy in females should be addressed. Counseling of patients considering fertility preservation should include a discussion of relevant treatments and alternatives, including expectant management, potential use and efficacy of future fertility treatments, use of donor gametes or embryos, adoption, and living child-free. The patient's current state of health must be considered, as some may be too ill to safely undergo fertility preservation. A team approach to patient counseling is recommended. As time permits, patients may meet with physicians, nurses, and mental health professionals to discuss decisions. This allows for a more comprehensive evaluation to explore and understand the psychosocial and medical needs of each patient.

Consent and disposition

In patients who cryopreserve gametes, embryos, or tissues, disposition in the event of death should be discussed and documented, and minors should reconsent once they become adults. It is important for clinics to specify

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TABLE 1

Components and functions of a comprehensive fertility preservation program.

Component	Activities	Personnel
Fertility preservation team identification	Select feasible activities, personnel to support them, and generate standardized processes: • Expedite referral to fertility specialist • Counsel on known and unknown reproductive risks from medical treatment or condition • Counsel on (tailored) options for fertility preservation, storage, potential need for a gestational carrier, and disposition of reproductive materials/tissues • Counsel patients on heritable disease and potential for gametes to carry mutations/discuss preimplantation genetic testing • Determine who needs FDA testing • Perform fertility preservation procedures • Perform fertility preservation laboratory procedures: oocyte/sperm/embryo/gonadal tissue cryopreservation • Counsel on financial costs, insurance coverage, and philanthropic programs • Assist patients in accessing insurance and philanthropic programs • Coordinate care among primary medical and fertility preservation teams • Identify and refer to outside facilities for fertility preservation services that cannot be provided locally	Fertility program administrators Fertility specialist for females and males (reproductive endocrinology, urology, and reproductive surgeon) Fertility preservation navigator Fertility nursing Assisted reproductive technology and andrology laboratory Financial team Mental health clinicians Social workers Genetic counselors Maternal fetal medicine specialists Legal experts Ethics
Patient identification process	Collaborate with medical teams that have patients who need medically indicated fertility preservation Decide on strategies to identify patients consistently • Set criteria for eligible patients • Determine the best process for identification, e.g., EHR best practice alerts, new patient checklist Referring to clinician education sessions on patient identification	Fertility specialist Fertility preservation navigator Primary medical team champion
Patient referral process	Decide on strategies to refer patients consistently • Single point easy access • Fertility preservation team e-mail and consult phone number • EHR enabled urgent referrals to fertility preservation team Coverage of referrals on weekends and holidays Referring to clinician education sessions on patient identification	Fertility specialist Fertility preservation navigator Fertility preservation program administrators Primary medical team champion EHR team
Financial support for fertility preservation	Contract with health insurance plans to provide patients with in-network clinicians, laboratories, and facilities Train the financial team on medical and pharmacy benefit verification, preauthorization, escalation to insurance plan supervisors, and appeals Identify state-level appeal processes with insurance regulators Generate appeals letter templates Assess feasibility of decreasing upfront, out-of-pocket costs Identify loan and philanthropic programs Generate patient-facing materials for cost-sharing estimates, loan and philanthropic programs, and insurance navigation	Fertility preservation navigator Financial team Social worker
Educational materials for patients	Find/develop health literacy appropriate • Website • Handouts a. Reproductive risks b. Fertility preservation procedures c. Next steps	Fertility specialist Fertility preservation program administrators

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TABLE 1

Continued.

Component	Activities	Personnel
Quality improvement	Review the fidelity of fertility preservation program Provide feedback Adapt the program for improvement	Fertility preservation program administrators

FDA = Food and Drug Administration, EHR = electronic health record.

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where gametes/embryos will be stored and for how long (2). Patients benefit from anticipatory guidance on the potential limits and restrictions on stored materials, including state laws, regulations for transfer, and clinic policies restricting acceptance of outside tissues (3, 4). The possibility of using a gestational carrier should be addressed, particularly for patients who may not be able to carry an autologous pregnancy because of effects of therapy, ongoing treatments, or health (5).

EFFECTIVE FERTILITY PRESERVATION STRATEGIES FOR FEMALES

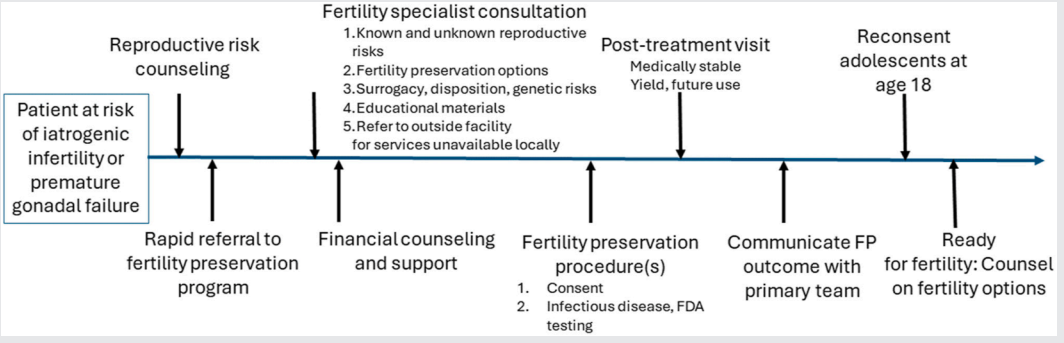
Mature oocyte cryopreservation

For postpubertal females, mature oocyte cryopreservation is an established fertility preservation technique. This process requires controlled ovarian stimulation (COS), that is, stimulating the ovaries with gonadotropins, and surgically retrieving oocytes, which are then cryopreserved. Oocyte cryopreservation allows for the future choice of sperm source and control of disposition. Cryopreservation of oocytes rather than embryos should be on the basis of patient choice. Patients should be advised that oocyte cryopreservation allows them to choose the sperm source in the future and allows them alone to control the disposition of the frozen eggs. Data on pregnancy and live birth rates from oocyte cryopreservation in medically indicated fertility preservation are scarce. Age at vitrification and the number of oocytes are predictors of future success (6, 7). One study found a 35% live birth rate in 80 oncofertility patients who returned to use their vitrified oocytes, a rate similar to patients who underwent planned oocyte cryopreservation (6). Patients should be thoroughly counseled about success rates given a patient's age and the number of oocytes cryopreserved, using clinic-specific success rates whenever possible. Although data on live birth rates from banked oocytes in specific, medically indicated fertilization preservation populations are limited, available data from patients who underwent oocyte cryopreservation for nonmedical indications may help guide counseling (8).

Embryo cryopreservation

Embryo cryopreservation using partner or donor sperm is an established fertility preservation technique that offers a more predictable likelihood of success on the basis of the number and quality of embryos stored. This process involves COS and surgically retrieving oocytes, which are then inseminated and cryopreserved. The stage at which to cryopreserve embryos depends on clinic-specific protocols and individualized patient counseling. Patients should be thoroughly counseled about success rates given a patient's age and the number and stage of embryos cryopreserved using clinic-specific rates whenever possible. Although data on live birth rates from banked embryos in specific, medically indicated fertility

FIGURE 1



Key processes in the patient journey for medically indicated fertility preservation and family building.

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preservation populations are limited, available data from infertile and donor populations can be used for counseling (9).

Role of genetic testing in embryo cryopreservation

Patients seeking embryo cryopreservation may be candidates for preimplantation genetic testing (PGT). Preimplantation genetic testing for monogenic disorders (PGT-M) may be offered to patients with known mutations that predispose them to cancer or other serious conditions (10). Patients diagnosed with hereditary cancers after urgent embryo cryopreservation may have embryos thawed and biopsied for testing (11, 12). Preimplantation genetic testing for aneuploidies (PGT-A) may be considered in select patients expected to have multiple embryos available for cryopreservation and who are of advanced reproductive age and/or plan to use a gestational carrier. Patients should be counseled that performing PGT will reduce the number of available embryos to transfer and that data do not support the routine use of PGT-A in in vitro fertilization (IVF). Clinicians should engage in shared decision-making with patients to tailor the fertility preservation strategy (13).

Ovarian stimulation for embryo or mature oocyte cryopreservation

Controlled ovarian stimulation for embryo or mature oocyte cryopreservation remains the most likely strategy to result in subsequent pregnancy. This procedure should be recommended as long as the patient's medical condition safely allows COS, there is adequate time, and there is a reasonable chance of response and oocyte retrieval.

Immediate start, random start, and duo-stimulation

To expedite fertility preservation, stimulation may be started immediately with antagonist-based protocols without regard to the phase of the menstrual cycle (immediate or random-start COS) (14). The trigger medication should be guided by the clinical scenario and may be human chorionic gonadotropin (hCG) only, dual trigger, or gonadotropin-releasing hormone agonist (GnRHa) only to minimize the risk of ovarian hyperstimulation syndrome (OHSS) (15). Compared with conventional stimulation, immediate-start stimulations result in negligible delays and have similar embryological and pregnancy outcomes (16, 17). Despite limited time, it is important to procure a sufficient number of oocytes to maximize the chance of a successful future pregnancy (18). Multiple ovarian stimulations may be possible and should be considered. Indications for multiple stimulations may include poor outcomes from the first cycle, advanced age, and/or intended PGT-M. If time allows, duo-stimulation may shorten the window from one stimulation to the next (19). Stimulation may occur before systemic therapy, before and after surgery, and in some scenarios while on adjuvant endocrine therapy. Financial and time constraints may preclude multiple cycles.

Posttreatment mature oocyte or embryo cryopreservation

Fertility preservation after treatment may be considered in some patients. Candidates include patients who have been exposed to medical treatments that increase the risk of premature ovarian insufficiency or infertility and who subsequently have a residual but narrower window of remaining ovarian function, as well as patients who completed fertility preservation but have insufficient cryopreserved materials for a reasonable chance at achieving their goals for family size.

In general, stimulation during or immediately after gonadotoxic treatments is not recommended. Animal data suggest that there may be an increased risk of miscarriage and birth defects (20). After gonadotoxic treatments, the probability of cycle cancellation is higher, and the number of oocytes retrieved, number of embryos, and successful pregnancies are lower when compared with individuals without prior gonadotoxic treatments (21). A case series reported stimulation between cycles of chemotherapy in four patients with hematologic malignancies yielded no follicular development (n = 2), no oocytes (n = 1), or low embryo development (n = 1) (22). Case reports of stimulation after and before hematopoietic stem cell transplant in patients with acute myeloid leukemia have reported successful ovarian stimulation with mature oocyte and embryo freezing (23, 24). There are no human studies that have specifically examined the quality of oocytes and embryos that result after a recent course of chemotherapy. It is known that chemotherapeutic agents can cause deoxyribonucleic acid (DNA) abnormalities, as well as oxidative damage, in somatic and germ cells (25, 26). In mice, conceptions that occurred within 3 months of exposure to cyclophosphamide resulted in a higher rate of pregnancy failures and fetal malformations (20). Although oocytes and embryos can be frozen and PGT-A performed, it is notable that transfer outcomes have not been reported, and PGT-A does not identify mutagenesis, so patients should be counseled accordingly. A safe interval for offspring health between completion of chemotherapy and oocyte or embryo cryopreservation has not been established.

The long-term optimal timing for ovarian stimulation for fertility preservation is unclear. Using antimüllerian hormone (AMH) as a measure of recruitable ovarian follicle pool, an overall postchemotherapy treatment trajectory shows increasing AMH levels for 2–3 years before plateau. These data suggest that for patients with residual ovarian reserve, peak oocyte yield would be highest when AMH plateaus after treatment (27). Prospective cohort studies are needed for validation. Studies examining pregnancy outcomes in cancer survivors remote from therapy have reported no significant increase in congenital malformations, genetic abnormalities, or malignant neoplasms in the resulting offspring (28–31).

SAFETY CONSIDERATIONS

Medically complex patients

Patients facing fertility-threatening treatments for malignancies or other systemic conditions often have underlying

comorbidities that increase the risk and complexity of fertility preservation (32). Fertility clinics differ in their ability to care for medically complex patients; thus, careful consideration must be taken when planning fertility preservation treatments. For example, patients with cardiovascular and airway risks (example: mediastinal masses) require anesthesia evaluation for potential modifications to anesthetics (example: local anesthesia without deep sedation), or procedures may need to be performed in a hospital setting rather than an ambulatory surgicenter. For pediatric patients, state and surgery center regulations may require pediatric advanced life support certification.

Depending on tumor location, patients may require nonvaginal oocyte retrieval approaches, including abdominal, transvesical, or laparoscopic. Patients with abnormal hematologic parameters at risk for hemorrhage or thrombosis may also need special care, including blood products, tranexamic acid, and anticoagulation. Multidisciplinary collaboration with the patient's medical providers is recommended.

Prevention of ovarian hyperstimulation syndrome

The impact of OHSS can be profound in medically complex patients, with the potential to delay planned therapy. Therefore, the use of appropriate strategies to reduce the risk of OHSS may be particularly valuable, including antagonist cycles, dosing gonadotropins to ovarian reserve, lowering the starting gonadotropin dose, using gonadotropin-releasing hormone (GnRH) agonist to trigger oocyte maturation, using a lower dose of hCG to trigger oocyte maturation (without definitive evidence of reducing OHSS), and starting a dopamine agonist on the day of hCG trigger. In letrozole ovarian stimulation cycles, follicle number should be used to choose strategies for reducing OHSS risk, because estradiol levels, masked by letrozole, remain low (15).

Cancer outcomes

The long-term safety of ovarian stimulation in the setting of cancer, notably in estrogen receptor-positive (ER+) cancer or breast cancer gene positive (BRCA+), is reassuring. Several observational studies in the setting of breast cancer show no differences in recurrence and/or disease-free survival (33–35). In addition, a limited dataset suggests ovarian stimulation has no impact on pathologic complete response in a neoadjuvant setting (36). In these studies, concomitant estrogen modulation was administered during ovarian stimulation with use of an aromatase inhibitor or tamoxifen, and therefore, its use is encouraged.

Ovarian tissue cryopreservation

Ovarian tissue cryopreservation is an acceptable technique and is no longer considered experimental. (37, 38). Cryopreservation of ovarian cortical tissue represents a way of preserving thousands of ovarian follicles at one time. This technique is recommended for patients facing highly gonadotoxic therapies who cannot delay cancer treatment to undergo ovarian stimulation and oocyte retrieval, and for prepubertal patients because there is limited experience with ovarian stimulation for mature oocyte cryopreservation before puberty (39, 40). In addition, it may be offered as an additional fertility preservation strategy for high-risk patients who have undergone other fertility preservation procedures.

Ovarian tissue cryopreservation involves obtaining ovarian cortical tissue before ovarian failure by laparoscopy or laparotomy, dissecting the tissue into small fragments, and cryopreserving it using either a slow-cool technique or vitrification. On the basis of current evidence, removal of both ovaries for cryopreservation is not justified at this time, unless the chemotherapy regimen has a high likelihood of inducing complete ovarian failure. After the treatment, patients with infertility or ovarian failure can undergo ovarian tissue transplantation orthotopically or heterotopically. Orthotopic transplantation has been the most successful method for using ovarian tissue, with only one live birth reported after heterotopic transplantation (41). Various surgical techniques have been utilized for transplantation, including transplantation into the existing ovary, under a peritoneal pocket in the pelvic side wall or abdominal wall. According to a 2022 systematic review, there have been at least 189 live births after autologous allogeneic ovarian tissue transplantation (42). Transplantation of previously cryopreserved ovarian tissue resulted in a 37% pregnancy rate and a 28% live birth rate. According to this study, 69% of pregnancies were conceived without assistance. Over 70% of patients had resumption of ovarian function at a mean time of 19 weeks posttransplant, lasting an average of 2.5 years (42–45). Thus, it is unlikely that ovarian tissue transplantation is effective for preservation of long-term endocrine function and should generally be performed to promote fertility when patients are ready to conceive.

Before undertaking ovarian tissue cryopreservation or transplantation, consultation with the patient's medical oncologist is appropriate to understand risks related to transplantation and potential options for tissue screening (46, 47). Where cancer cells may be present in ovarian tissue, it is unclear whether screening with histologic evaluation or with tumor markers is reliable and reduces the risk of reseeding tumor cells (48). One case of recurrent cancer has been reported posttransplant in a patient who had ovarian tissue frozen/transplanted in the setting of an ovarian granulosa cell tumor (42). Although there has been particular concern related to transplantation in patients with leukemia undergoing ovarian tissue cryopreservation, recent literature suggests that transplantation of ovarian tissue in leukemic patients may be safe in patients whose tissue was removed after receiving high-dose, preconditioning chemotherapy before stem cell transplantation (49). There have been 18 reported transplants in leukemic patients with nine resulting in live births, and there have been no cases of recurrence (49).

Cumulus oocyte complexes may be aspirated from small follicles or identified during ovarian tissue dissection and processing. These oocytes may be matured in vitro and cryopreserved before or after fertilization. This approach may be advantageous because it provides additional oocytes or embryos for cryopreservation, without additional delay.

Importantly, it offers patients the potential for pregnancy without ovarian tissue transplantation, which could pose a risk of reintroducing cancer cells in certain circumstances. A few live births have been reported in patients who underwent in vitro maturation of oocytes from ovarian tissue (37, 38, 50). Although in vitro maturation may be a reasonable approach to fertility preservation in some situations, outcome data are limited, and more established methods should be pursued whenever possible. Given the data on efficacy and safety, ovarian tissue cryopreservation should be considered an established fertility preservation technique with limited effectiveness and offered to carefully selected patients.

Ovarian suppression with GnRH analogues

A number of randomized controlled trials (RCTs) and meta-analyses have explored the benefits of GnRH analogs during chemotherapy (51–63). However, the use of GnRH analogues for ovarian protection during alkylating chemotherapy remains controversial. Several RCTs have demonstrated that menstrual function and ovulation are more likely to occur in patients with breast cancer after cotreatment with GnRH agonists during chemotherapy compared with those who did not receive this therapy (59). Benefits in terms of fertility outcomes in this population have been inconsistent, and studies have been limited by inadequate follow-up and few assessments of surrogate measures of fertility, rather than pregnancy rates (55, 57, 64). Although GnRH analogues are not currently approved by Food and Drug Administration (FDA) for fertility preservation, these medications may be used ''off-label.'' Given the evidence of efficacy, GnRH agonists may be offered to patients with breast cancer to reduce the risk of premature ovarian insufficiency and possibly increase the chance of future pregnancies. However, GnRH agonists should not be used in place of other fertility preservation procedures, such as egg or embryo cryopreservation. Further studies are required to establish the efficacy of this treatment and to determine which patients are the best candidates for its use. Nonetheless, this therapy may help to prevent heavy bleeding in patients with thrombocytopenia related to chemotherapy and stem cell transplantation, and it should be considered in such patients (65). Administration of depot GnRH agonists soon after trigger for oocyte retrieval has been associated with OHSS, and therefore, should be delayed for at least 7–14 days after retrieval, but chemotherapy should not be postponed (66).

Ovarian transposition

Patients requiring local pelvic radiation may benefit from transposition of the ovaries to sites away from maximal radiation exposure (67–70). Ovarian transposition may be accomplished at the time of initial oncologic surgery or at a later time. It is important to recognize that this procedure may preclude future transvaginal oocyte retrieval if IVF is required. Transabdominal retrieval may be accomplished in some patients (71). Outcomes on preservation of endocrine and reproductive function with ovarian transposition are age-dependent. A retrospective study of patients undergoing ovarian transposition found that 71.2% of patients aged 30 years or older underwent menopause, whereas only 26% of patients younger than 30 years became menopausal after treatment (72). The location of the transposed ovary is also important to consider; a distance of 4 cm from the field of radiation is recommended (73).

Conservative treatments for reproductive malignancies

Patients undergoing surgery for cervical, endometrial, ovarian cancer, or borderline tumors of the ovary may be candidates for conservative surgical approaches by way of fertility-sparing surgery, oophoropexy, or, in the case of endometrial disease, initial medical therapy. The success depends on the diagnosis and treatment (74–77). If a hysterectomy is performed, these patients should be counseled regarding a gestational carrier.

OTHER/EMERGING FERTILITY PRESERVATION STRATEGIES

In vitro maturation

In vitro maturation (IVM) is an emerging strategy for medically indicated fertility preservation. It generally refers to the collection and maturation of immature oocytes retrieved from small follicles after minimal or no ovarian stimulation (78). After maturation in the laboratory, these oocytes may be cryopreserved or fertilized. Most of the studies evaluating the efficacy of IVM have been conducted in patients with polycystic ovary syndrome to minimize the risk of OHSS. Although randomized studies are limited, literature has demonstrated lower pregnancy and live birth rates with IVM compared with traditional IVF (79, 80). However, IVM has some potential advantages for fertility preservation over traditional ovarian stimulation in patients facing gonadotoxic therapy, because less time is required for stimulation, estrogen levels remain in the physiologic range, and there may be less risk of OHSS. Disadvantages include lower success rates and less access to this option because only a few clinics in the US offer IVM (81). A few live births have been reported (82–84). The IVM performed ex vivo in combination with ovarian tissue cryopreservation is described under the section on ovarian tissue cryopreservation.

Uterine fixation and transposition

Uterine transposition and uterine fixation, or suspension, are emerging methods of preserving fertility and ovarian function for patients undergoing pelvic radiation for nongynecological cancers. The objective is to decrease uterine radiation therapy side effects in the setting of pelvic cancers, such as colon or anal cancer. Uterine fixation may be performed by fixing the uterus to the fascia of the anterior abdominal wall as cranially as possible to remove the uterus from the radiation field or by suspending the bilateral round ligaments to the anterior abdominal wall. Uterine fixation or suspension should be performed in conjunction with ovarian

transposition. Alternatively, uterine transposition is a complex surgical technique where the uterus is detached from the vagina and transposed to the upper abdomen with tubes and ovaries. The cervix may then be sutured to the paracolic gutter in the setting of menstrual suppression with hormonal therapy or to the umbilicus with the creation of a stoma for menstrual bleeding (85).

The largest prospective, multicenter observational study included eight patients undergoing pelvic radiation as part of their cancer treatment and had uterine transposition to the upper abdomen performed before irradiation (86). The uterus was repositioned into the pelvis 2–4 weeks after radiation therapy or at the time of rectosigmoid resection, and there was resumption of normal menses and hormonal levels in six of the patients. Cervical ischemia occurred postoperatively in three patients. Three patients attempted natural conception, and two achieved live births with deliveries at 36 and 38 weeks by cesarean section, without complications.

Children and adolescents

Fertility preservation is possible in children and adolescents. Postpubertal females, including those who are premenarchal, are candidates for ovarian stimulation for mature oocyte cryopreservation. One live birth has been reported in an adolescent patient who cryopreserved oocytes at age 17 (87). Although reports of ovarian stimulation in premenarchal females are scarce, a 7-year-old prepubertal patient with mosaic Turner syndrome cryopreserved six mature oocytes after low-dose COS and hCG trigger (88, 89). Care should be taken to avoid OHSS in children and adolescents, while recognizing that hCG is recommended for triggering oocyte maturation in the setting of an immature hypothalamic-pituitary-ovarian axis.

Ovarian tissue cryopreservation with IVM of tissue-derived oocytes may also be offered to this population. Ovarian tissue cryopreservation is currently the principal method to cryopreserve gametes in prepubertal girls. A live birth has been reported in a female who cryopreserved tissue before menarche (live birth after autograft of ovarian tissue cryopreserved during childhood) (90). Working with these individuals and their parents/guardians requires an approach that is sensitive to various levels of physical and psychological development. Close collaboration among primary physicians, reproductive endocrinologists, mental health professionals, and ethicists is helpful (91).

FERTILITY PRESERVATION METHODS FOR MALES

Ejaculated sperm cryopreservation

For postpubertal males, ejaculated semen cryopreservation is an established technology. The process involves masturbation, which is feasible and successful in the majority of adult males and adolescents (92). Ideally, multiple samples should be obtained for cryopreservation to support options of future intrauterine insemination and/or IVF (93). Sperm collection should be performed before the administration of gonadotoxic therapies such as chemotherapy or radiation therapy, as well as before surgical treatment if possible. Males suspected of having testicular cancer should be offered sperm cryopreservation before orchiectomy (94). Some males with cancer may have underlying impairment in spermatogenesis even before cancer therapy, yielding a limited quantity of sperm per ejaculate (95, 96). Patients should be thoroughly counseled about the quality and quantity of their cryopreservation sample(s) and how they can be used in the future.

Medically-assisted ejaculated semen collection

Some males may have difficulty collecting a semen sample because of psychogenic or organic erectile or ejaculatory dysfunction. Pubertal status, anxiety, fatigue, hypogonadism, pain, and comorbidities, such as diabetes, neurologic problems, and side effects from a variety of medications, like opioids and antidepressants, as well as the underlying disease itself, are contributory factors. Counseling and a comfortable environment to collect may be helpful (97). Use of medical therapy can help. Phosphodiesterase type 5 (PDE-5) inhibitors are oral agents that are classically used to treat erectile dysfunction. These inhibitors have been used with success for men experiencing difficulty providing semen samples (98).

Intracavernosal injections with vasoactive agents (i.e., alprostadil, phentolamine, and/or prostaglandin E1), penile vibratory stimulation, or collection of sperm in men with retrograde ejaculation could still prove to be effective at helping the patient collect a semen sample with masturbation, although these techniques are very rarely implemented in the population of males undergoing fertility preservation.

Surgical sperm retrieval

Surgical sperm retrieval is an alternative strategy for males who cannot ejaculate via the aforementioned techniques, or who have azoospermia or insufficient sperm in the ejaculate to freeze (99). Oncologic testicular sperm extraction (Onco-TESE) is a widely available and effective procedure (100). The testicular tissue containing sperm is processed and cryopreserved shortly after the procedure. The sample can be subsequently thawed, and sperm can be isolated and used for IVF/intracytoplasmic sperm injection at a later time. The Onco-TESE is typically performed in the operating room as an outpatient procedure, and consideration may be given to performing it concurrently with other procedures, such as placement of a central venous access device.

When a patient with a suspected testicular cancer is found to be azoospermic before radical orchiectomy, sperm extraction from the affected testis immediately after orchiectomy on a sterile "back bench" has been successfully utilized; this testicular tissue may represent the only source of viable sperm for cryopreservation in some patients (100, 101).

The Onco-TESE procedure can be performed with the assistance of operating microscope magnification (micro-TESE). This approach can, in some instances, facilitate the identification of more favorable appearing seminiferous tubules (i.e., full, opaque) that are more likely to contain sperm (102, 103).

Electroejaculation

For adults and peripubertal males with psychogenic anejaculation or other severe sexual dysfunction, electroejaculation may be offered as an alternative to Onco-TESE (104, 105). The nonspecific stimulation of pelvic tissues, including the prostate and seminal vesicles via a transrectal probe, may lead to seminal emission (106). Electroejaculation must be conducted under anesthesia, unless the patient also has a complete loss of sensation below the umbilicus (for example, a spinal cord injury).

Posttreatment sperm cryopreservation

Sperm cryopreservation for fertility preservation should be performed before the initiation of cancer therapy (107). The request for cryopreservation of semen samples after cancer treatment has been initiated presents a common dilemma faced by patients and fertility specialists. Chemotherapeutic agents and radiation therapy can cause deleterious genetic changes in sperm that may adversely affect reproductive outcomes and the health of the offspring. For this reason, many centers do not offer sperm cryopreservation after initiation of such cancer therapies. For those centers that do offer this option, patients should be counseled that the cancer therapy could introduce mutations into the sperm that may not be detectable with current or future preimplantation testing techniques (107). Many centers caution that patients use such samples only as a "last resort," in case no other sources of sperm are available.

Prepubertal males

Testicular tissue cryopreservation is an experimental technique performed under institutional review board (IRB)-approved protocols. This approach is offered to prepubertal males who are not yet producing sperm and/or have not yet had seminal emission/ejaculation. If sperm are observed on intraoperative analysis of testis biopsies, those samples can be processed and cryopreserved in the standard fashion used for TESE samples (108, 109). For prepubertal males, testicular tissue cryopreservation is performed with the hope that clinical techniques will emerge that will facilitate the use of immature, prepubertal testicular tissue to facilitate future fertility in affected patients. Current methods under study include in vitro spermatogenesis and germ cell transplantation techniques (110, 111).

Disposition and posthumous assisted reproduction

Clinics should have policies on the disposition of gametes, embryos, and gonadal tissue. They should also have written policies for perimortem and posthumous gamete and gonadal tissue retrieval, including whether the clinic participates in these requests and what documents are required by the individual making requests for tissue cryopreservation (112). Decisions surrounding posthumous reproduction are ethically complex and are addressed in the Ethics Committee opinion (112).

TABLE 2

Potential medical indications for fertility preservation.

Population	Specific conditions, including but not limited to:
Populations at risk because of exposures (treated with surgery, chemotherapy, radiation therapy, hormonal therapies, and other systemic therapies with unknown reproductive effects)	• Cancer patients facing imminent treatment • Survivors of cancer or medical treatments at risk for POI • Hematologic conditions (sickle cell disease, thalassemia) • Rheumatologic conditions • Autoimmune conditions • Gender affirming care (113)
Populations with whom the future risk of pregnancy is too high and will need to use a gestational carrier	• Medically complex conditions • Absence of the uterus related to cancer treatment
Populations with genetic mutations known to impact the health of offspring	• BRCA + for future fertility
Populations with genetic conditions that increase the risk of POI	• Fragile X premutation, other X chromosome abnormalities, including mosaic Turner syndrome • Galactosemia, autoimmune polyendocrinopathy, deficiencies of 17-hydroxylase, aromatase • BPES, Perrault, Fanconi anemia, Werner syndrome, Bloom syndrome, Hutchinson-Gilford progeria, GAPO syndrome • DSD, intersex

BRCA + = BReast CAncer gene positive, BPES = Blepharophimosis, Ptosis, Epicanthus inversus Syndrome, DSD = disorders (or differences) of sex development, GAPO = growth retardation, alopecia, pseudoanodontia, optic atrophy syndrome, POI = primary ovarian insufficiency.

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Health insurance coverage of medically indicated fertility preservation

Fertility preservation services are medically necessary to decrease iatrogenic infertility (Table 2) (113). Affordability is a key barrier to patients accessing fertility preservation services. All health insurance should cover established fertility preservation services inclusive of long-term storage and subsequent use of cryopreserved materials/tissues as standard of care. Although there is increasing health insurance coverage of medically indicated fertility preservation services, including through laws and employer choice, accessing these benefits through insurance plans may require appeals and independent medical review (114). Health insurance should not use prior authorization to allow for timely delivery of care and set patients' cost-sharing to be at parity

(e.g., copayments, coinsurance, maximum out-of-pocket costs) with other medical services for affordability (115).

SUMMARY

- Systemic therapy, radiation therapy, and surgery for medical conditions in children, adolescents, and adults of reproductive age can harm future fertility.
- Fertility preservation is medically effective in decreasing infertility.
- Established strategies for females include embryo cryopreservation, mature oocyte cryopreservation, ovarian tissue cryopreservation, and conservative management of reproductive malignancies.
- The GnRH agonist suppression (in breast cancer), ovarian transposition, and conservative gynecologic surgery have been shown to preserve ovarian function and may improve fertility.
- Emerging strategies include IVM and uterine fixation/transposition.
- Established strategy for males is sperm cryopreservation, which may require medical or surgical assistance.
- Postpubertal females, including those who are premenarchal, are candidates for ovarian stimulation for mature oocyte or embryo cryopreservation.
- Ovarian tissue cryopreservation is currently the principal method to cryopreserve gametes in prepubertal girls.
- Testicular tissue cryopreservation is currently considered investigational in prepubertal boys.

CONCLUSIONS

- All patients facing treatments that may impair reproductive function and who are at risk of premature gonadal failure deserve prompt counseling regarding their options for fertility preservation and rapid referral to an appropriate program.
- All patients should be counseled on known and unknown reproductive risks of planned medical treatments.
- Clinics offering fertility preservation should have the expertise and infrastructure to provide timely interventions. Programs unable to provide a specific component of fertility preservation services should still counsel patients about available options and/or provide expeditious referrals to programs with the available resources.
- Patients should be offered appropriate fertility preservation options. For patients undergoing COS or sperm banking, multiple collections may be considered to procure sufficient materials to maximize the chance of future pregnancy. After treatment fertility preservation may be considered in females who have been exposed to medical treatments that increase risks of premature ovarian insufficiency or infertility and subsequently have a residual but narrower window of remaining ovarian function, as well as females who underwent fertility preservation but have insufficient cryopreserved materials for a reasonable chance at achieving their goal family size.
- Medical complexity of patients should be considered to minimize risks of fertility preservation procedures.
- Fertility preservation should be offered to children with future fertility potential.
- Fertility preservation services are medically necessary to decrease iatrogenic infertility. All health insurance should cover established fertility preservation services inclusive of long-term storage and subsequent use of cryopreserved materials/tissues as standard of care. Health insurance should not use prior authorization to allow for timely delivery of care and set patients' cost-sharing to be at parity with other medical services for affordability.

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Preservación de Fertilidad en pacientes con indicaciones médicas: opinión del comité.

Preservación de la fertilidad en pacientes con indicaciones médicas: opinión del comité Comité de Práctica de la Sociedad Americana de Medicina Reproductiva, Sociedad Americana de Medicina Reproductiva, Washington, D.C., EE. UU. Los pacientes que van a someterse a terapias que implican un riesgo para su fertilidad o que presentan riesgo de insuficiencia ovárica prematura deben recibir asesoramiento oportuno sobre las opciones disponibles para la preservación de la fertilidad. La preservación de la fertilidad puede ofrecerse mejor mediante programas integrales diseñados y dotados específicamente para afrontar los desafíos únicos que afrontan estos pacientes. Este documento reemplaza al titulado «Preservación de la fertilidad en pacientes sometidos a tratamiento gonadotóxico o gonadectomía: opinión del comité», publicado por última vez en 2019.