

Chapter 12

Setting Up an Oncofertility Program

H. Irene Su, Lindsay Ray, and R. Jeffrey Chang

Introduction

Each year, over 150,000 reproductive age individuals face fertility-threatening cancer treatments. The overarching goal of a clinical oncofertility program is to help these young patients and their physicians consider the impact of treatment on future fertility and facilitate fertility preservation efforts in what is often a limited time period before treatment begins. This chapter will discuss our (University of California at San Diego and The Oncofertility Consortium) approach to building an oncofertility program [1].

A comprehensive fertility preservation program has several missions:

- Provide timely and comprehensive fertility preservation consultations for patients facing fertility-threatening treatments
- Offer or refer patients to a range of appropriate fertility preservation treatments
- Coordinate care for and safely navigate medically complicated patients through fertility preservation treatments
- Serve as a resource for patients and health-care providers who are seeking up-to-date fertility preservation information

To fulfill these missions, a successful fertility preservation program requires an interdisciplinary team; a clear patient flow plan; access to equipment, supplies, and expertise for banking gametes, embryos, and gonadal tissue, which often must occur

H.I. Su, M.D., M.S.C.E. • R.J. Chang, M.D. (✉)
Division of Reproductive Endocrinology, University of California,
9500 Gilman Drive #0633, La Jolla, CA 92093-0633, USA
e-mail: rjchang@ucsd.edu; hisu@ucsd.edu

L. Ray, B.S.N.
Reproductive Partners-UCSD Regional Fertility Center, 9850 Genesee Avenue,
Suite 800, La Jolla, San Diego, CA 92037, USA
e-mail: lindsay.ray@integamed.com

on short notice; and communication and marketing support. These represent the integral building blocks for any oncofertility program and are discussed in detail below.

The Oncofertility Team

Medical Team

Care of oncofertility patients requires an interdisciplinary medical team (Table 12.1). Most often, the team is initially assembled by a reproductive endocrinologist or an oncologist. Early identification of key medical contacts facilitates the navigation of patients across specialties and within the tight timelines necessary for fertility preservation in cancer patients.

The process begins with medical professionals addressing the possibility of infertility with patients who face exposure to fertility-threatening therapies before or during their reproductive years ([2]; see also Chaps. 1 and 2 in this volume). The role of the treating oncologists, hematologists, rheumatologists, and their clinical staff is not to perform full fertility preservation consultations but rather to address the issue of fertility and refer patients who would like a more in-depth discussion to a reproductive endocrinologist. It is important that fertility preservation services and practices are clearly identified in order to facilitate referrals of newly diagnosed cancer patients by the medical team members.

For any fertility preservation program, it can be extremely helpful to have a designated oncofertility patient navigator to whom medical providers could refer cancer patients to reproductive endocrinologists for consultation. Patient navigators are frequently nurses or other allied health-care professionals who can help by responding to fertility preservation requests, obtain key clinical data on patients, and provide basic information and resources to both patients and oncologists regarding fertility risk and fertility preservation options. In this role, the oncofertility patient navigator can also assist in triage of patients, direct patients to the right fertility preservation consultant, and facilitate fertility preservation appointments (see Chap. 13 in this volume for more information on this topic).

The reproductive endocrinologist and urologist provide fertility preservation consultations and perform fertility preservation procedures. At the initial consultation, they will review with the patient the standard of care and any experimental options for fertility preservation (see Chaps. 3 and 4 in this volume for a description). These physicians take into account the diagnosis, proposed treatment, and other medical and social circumstances to individualize options for fertility preservation. Consultations are also used to review the data on pregnancy outcomes after cancer diagnosis and/or treatment (see Chap. 10 for an in-depth discussion of these issues). For patients who contemplate undergoing fertility preservation treatments, the reproductive endocrinologist or urologist then communicates with the oncology

Table 12.1 The oncofertility team

Patient navigator	<ul style="list-style-type: none"> Responds to fertility preservation requests Collects key clinical information on patients seeking care Provides basic information and resources regarding fertility preservation options Triages patients Refers patients and providers to appropriate fertility preservation medical providers Facilitates fertility preservation appointments
Reproductive endocrinologist	<ul style="list-style-type: none"> Provides fertility preservation consultations Directs fertility preservation treatments with input from oncology or rheumatology, anesthesia, pathology, and other medical specialties
Reproductive urologist	<ul style="list-style-type: none"> Provides fertility preservation consultations in males Performs testicular tissue biopsies or orchiectomies for banking
Oncology, hematology, and rheumatology care teams	<ul style="list-style-type: none"> Address the possibility of infertility with patients treated before or during their reproductive years Refer patients who are interested in future fertility for fertility preservation consultations
Anesthesiologist	<ul style="list-style-type: none"> Provides anesthesia plan for fertility preservation surgeries
Pathology	<ul style="list-style-type: none"> Aids in shaping protocols for handling tissue for fertility preservation
Surgeon	<ul style="list-style-type: none"> Performs fertility preservation surgeries. This may be a reproductive endocrinologist, oncologist, urologist, or pediatric surgeon
Genetic counselor	<ul style="list-style-type: none"> Provides genetic counseling
Psychology and social work	<ul style="list-style-type: none"> Provide counseling and support services
Cell and tissue banking personnel	<ul style="list-style-type: none"> Performs clinical tissue banking
Financial counselor	<ul style="list-style-type: none"> Discusses out-of-pocket expenses for fertility preservation with patients Checks insurance benefits, file insurance appeals Facilitates application to aid programs such as Sharing Hope
Marketing personnel	<ul style="list-style-type: none"> Publicizes the oncofertility program

team, anesthesia, and other relevant medical personnel to discuss safety, timing, and coordination of fertility preservation procedures and cancer treatment.

An experienced anesthesia team plays a central role in evaluating patients for surgical fertility preservation procedures. While egg retrieval, the mainstay of female fertility preservation, is a common surgical procedure, oncofertility patients may pose complex medical scenarios that require advanced planning. Many egg retrievals and testicular biopsies are performed in ambulatory surgery centers, which benefit from adjacent embryology laboratories, surgical and embryology equipment, and surgical team expertise. While these surgicenters may facilitate gamete retrieval, they often have limited advanced cardiopulmonary monitoring and support. For challenging fertility preservation patients—for example, lymphoma patients with mediastinal or neck masses—the choice to undergo egg retrieval in the familiar

in vitro fertilization (IVF) surgicenter is weighed against moving the surgery to the hospital operating room, where more intensive monitoring and resuscitation are available. Therefore, it is key to have an experienced anesthesiologist as part of the oncofertility team to formulate a sound plan for surgical retrievals in these less straightforward cases.

The pathologist is a crucial contact for discussing disposition of ovarian and testicular tissue obtained for banking. Removal of ovarian or testicular tissue for fertility preservation requires maintaining sterility, keeping the tissue at 0–5°C during transport, and minimizing time from removal to processing for freezing. Pathology examination protocols vary by site. Ideally, the minimum amount of tissue required for pathology exam (if any) should be prespecified and removed after the tissue in its entirety has been transported to the lab for preservation procedures. The protocol for handling tissue for banking needs to be worked out in advance, ideally, with the input of a pathologist.

The surgeon is the part of the team that harvests ovarian or testicular tissue. This person may be a reproductive endocrinologist, oncologist, urologist, or, in the case of infants and children, a pediatric surgeon. It is absolutely imperative that the surgeon understand the guidelines that determine the suitability of tissue to be removed for fertility preservation.

Genetic counselors can help determine if there are heritable conditions that patients may transmit to their offspring. In embryo banking cases, the possibility of preimplantation genetic testing may be considered.

Psychologists and social workers can help young patients and their families with counseling needs.

Collective expertise in managing oncofertility cases is emerging (see Clinical Cases in Oncofertility within this book). With few exceptions, the number of medically complex fertility preservation cases is limited at any one center. Therefore, having a forum to discuss oncofertility cases with reproductive endocrinology or urology colleagues has proven to be invaluable. One source for peer-to-peer clinical care communication has been the Oncofertility Consortium FERTLINE, a national fertility preservation hotline.

Laboratory Team

Freezing of cells and tissues must be performed by laboratory personnel who are highly experienced in clinical tissue banking. In most centers, this will be embryologists, andrology lab personnel, or bone marrow lab personnel and not, generally speaking, research lab personnel or physicians. These personnel are familiar with:

- Sterile technique and good tissue banking procedures.
- Tissue dissection and preparation.
- Addition of cryoprotectant solutions.
- Loading of tissues into vials.
- Labeling and documentation.

- Programming and use of slow cooling freezing equipment.
- Manual seeding.
- Storage in liquid nitrogen.
- Preparation of cryopreserved tissue for shipping.
- In some practices, isolation of oocytes, in vitro maturation (IVM), and oocyte and embryo cryopreservation; if these services are not available locally, the practice will need to be able to refer patients out to other facilities, using resources such as FERTLINE.

Financial Counseling, Marketing, and Public Relations Team

The financial counselor can help check insurance benefits, prepare letters of medical necessity, file insurance appeals, act as advocate for patients, and facilitate application to financial assistance programs like Fertile Hope's Sharing Hope program. The counselor also conveys clearly the out-of-pocket costs for fertility preservation treatments to each patient.

Marketing and public relations personnel can help educate oncology practices, rheumatology practices, and primary care practices about oncofertility, as well as the local community about fertility preservation programs for cancer patients. This team helps to build websites, create informational materials, and leverage social media approaches to publicize the program.

Patient Flow

Patients who are facing chemotherapy, radiotherapy, hormonal therapy, or surgeries should be informed of the potential impact, if any, of these treatments on future reproductive options. Because this discussion must happen in the context of a recent cancer diagnosis, patients may not immediately process the information they receive about fertility preservation. For this reason, an oncofertility consultation is not as straightforward as an IVF consultation, and multiple methods of communication—oral, printed materials, and web-based resources—are essential for helping patients understand the risk their planned cancer treatment may have on their future reproduction and their options for fertility preservation in the often abbreviated period of time prior to starting cancer treatment. Interested patients and families should be referred to the oncofertility program (Fig. 12.1), and both patients and providers then contact and work closely with the fertility preservation program. Either the designated oncofertility patient navigator or trained appointment staff will expedite the referral of these patients to a full fertility preservation consultation. At the time of initial contact, patients or medical providers can be asked to provide basic pertinent medical information in advance of the fertility preservation consultation to help the oncofertility team prepare for the visit. Figure 12.2 is an example of a referral form

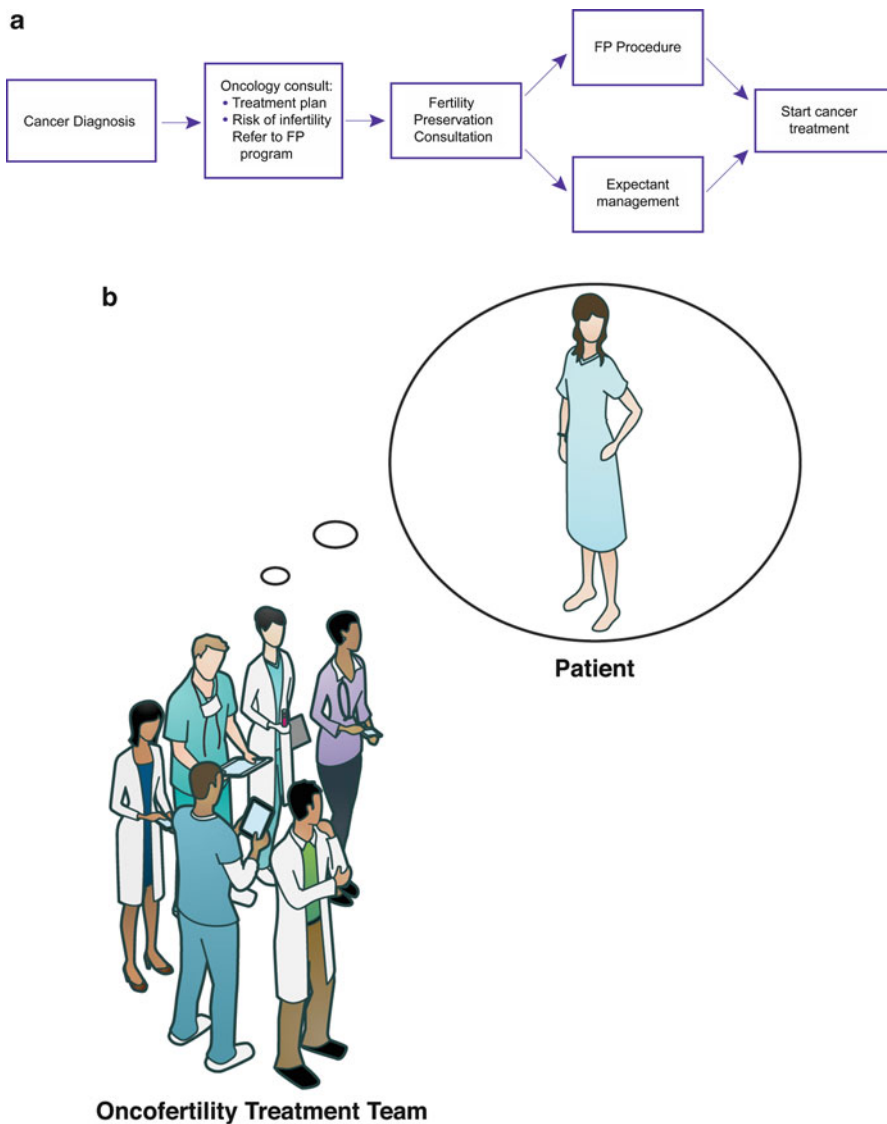


Fig. 12.1 Interdisciplinary team collaboration is integral to **a**) care for the oncofertility patient, and **b**) navigate the patient through the fertility preservation process

that is currently in use at our institution. For most programs, consultations occur within 24–72 h of referral.

The fertility preservation consultation entails a discussion of the risks posed by the proposed cancer treatment on future fertility; an evaluation of the patient's ability to undergo fertility preservation treatments; a discussion of the specific options for fertility preservation, referring patients to resources on fertility preservation; and a review of the costs associated with fertility preservation procedures. Application for

**XX Fertility Center
Fertility Preservation Program
Physician Referral Form**

Patient contact information

Last name		First name	
Street address		City	Zip code
Primary phone	Secondary phone	Email	
Date of Birth			

Patient diagnosis and treatment plan

Medical diagnosis	ICD-9 code for diagnosis
Anticipated surgical, radiation and medical treatment course (please be as specific as possible, i.e. AC x 4 for breast cancer)	
Anticipated treatment start date (please include timing of surgery, chemotherapy or radiation)	
Date of last menstrual period (MM/DD/YYYY)	
Additional pertinent information	

Physician contact information

Name		
Practice Name		
Practice Address		
Primary phone	Secondary phone	Email

Thank you for your referral!

Fig. 12.2 The fertility preservation physician referral form

financial assistance from programs such as Sharing Hope is initiated. Most decisions on whether to pursue treatment are made over the ensuing days and involve communication among the patient, their support system, the reproductive endocrinologist or urologist, and the treating oncologist or rheumatologist. Referrals to psychology and social work are generated as needed, and a bioethicist should be available for consultation when ethically challenging situations arise. For programs with research protocols, the research staff is contacted.

For patients who elect to undergo ovarian stimulation for egg or embryo banking, a protocol is selected to minimize treatment time, and tentative egg retrieval dates and chemotherapy start dates are given. Women who elect to use anonymous donor sperm are directed to sperm banks. Anesthesia consultations are initiated. During the time of ovarian stimulation, close communication between the fertility preservation team and the medical oncology or rheumatology team maintains a continuous

update on patient status. In addition, appropriate infectious disease testing of the patient or couple is undertaken. Of note, infectious disease testing should be performed at FDA-approved labs if the gametes or embryos are to be used in third-party reproduction in the future.

Surgical dates are set for patients who decide to preserve ovarian and testicular tissue or undergo other fertility preservation surgeries such as ovarian transposition. Pathology is contacted regarding disposition of the tissue to maximize future fertility potential.

After fertility preservation treatment is completed, a summary of the procedure is communicated to the patient and their oncology, hematology, or rheumatology team. Annual follow-up of the patient regarding banked tissues is conducted.

Laboratory and Storage Considerations

Handling reproductive tissues require appropriate laboratory expertise, equipment, and FDA registration. For storage facilities, there are also state-specific licensure requirements. Once licensed, there are regular monitoring updates and reporting schedules. As most tissues for fertility preservation are stored long term, banking at off-site storage facilities may be a consideration for the program.

Communication and Marketing

One barrier to fertility preservation referrals is the lack of awareness of fertility preservation programs [3]. It is crucial to inform both the medical and general communities to the presence of an oncofertility program. Good marketing staff help to facilitate these outreach efforts. For individual programs, experiences include:

- A dedicated telephone number (Oncofertility FERTLINE) to reach the fertility preservation program. This is publicized clearly in all of the outreach efforts on behalf of the program.
- Grand rounds to primary care physicians, hematologists and oncologists, rheumatologists, and other medical professionals who care for this population.
- Attendance at tumor boards.
- Distribution of fertility preservation educational materials and resources to medical practices. The Oncofertility Consortium brochures are available to the public and can be individualized to specific programs. They provide easy branding of a center (Fig. 12.3).
- Creation of the oncofertility program website. Presence on or links to local cancer program websites are important.
- Work with local advocacy groups such as Young Survivors Coalition (breast cancer) and I'm Too Young For This! Cancer Foundation (young adult cancer survivors).
- Holding continuing medical education programs on fertility preservation.

a Exploring Your Options

For information about fertility preservation or to get a referral to a fertility preservation center near you, please call the FERTLINE! This resource is available to patients, families and health care professionals.



Online Resources:

- Myoncofertility.org
- Oncofertility.northwestern.edu
- Fertilehope.org
- SaveMyFertility.org
- Stupidcancer.com
- Youngsurvival.org

- Facebook.com/pages/Oncofertility-Consortium/274654090671
- Twitter.com/oncofertility



The Oncofertility Consortium® is a comprehensive program that addresses the needs of young cancer patients who want to preserve their fertility. Our efforts are supported by funds from private philanthropy, government and institutional grants, and patient service revenue. We invite you to help us achieve our daily goals in patient care, research, and education. Your commitment would advance promising research; recruit talented physician-scientists; develop new educational programs; or expand our existing efforts.

For more information about giving options, please contact:

Courtney Weeks
Senior Associate Director,
Major Gifts

Phone: (312) 503-3080
Email: c-weeks@northwestern.edu
www.feinberg.northwestern.edu/giving



FERTILITY PRESERVATION PROGRAM



b Planning For Your Future Family

More than ever, cancer patients are surviving their disease and can look forward to the future. The ability to have children and build a family is important to cancer survivors. Many therapies that improve survival for cancer patients have side effects including loss of fertility and early menopause.

Oncofertility is a new, interdisciplinary field that bridges oncology (the study of cancer) and women's health to expand and provide good options for preserving fertility in patients facing fertility-threatening cancer treatments.

The National Physicians Cooperative (NPC) is a nationwide network of fertility preservation centers that participate in the NIH-funded Oncofertility Consortium. The Consortium aims to explore and preserve the reproductive future of patients facing fertility-threatening cancer treatments.

The NPC provides a framework for:

- Nationwide referral of patients for fertility preservation procedures in their area
- Multicenter clinical research studies in reproductive medicine
- Dissemination of best practices and clinical breakthroughs
- A national ovarian tissue repository to foster research to improve fertility preservation options for women and girls

National Physicians Cooperative
Fertility Preservation Programs



What are Options Before Cancer Therapy?

In vitro fertilization and embryo banking

Embryo banking is the most established form of fertility preservation and is an excellent option for women who have a male partner or are interested in using donor sperm. For breast cancer patients, there are specific ovarian stimulation protocols that may be considered to reduce exposure to estrogen. Embryos are frozen for future use.

Egg banking

In recent years, significant advances in freezing eggs for future use have occurred. Early clinical experiences suggest that egg banking may have similar success to embryo banking, but it is still too early to know that the success is as good as banking embryos.

Ovarian tissue banking

One ovary is removed through a minor surgical procedure called laparoscopy. The portion of ovary containing eggs is frozen for later use. This option is experimental but may be the best option for woman who must start their cancer treatments immediately.

Fertility sparing surgery

For patients who will receive abdominal or pelvic irradiation, it may be possible to move the ovaries surgically out of the field of radiation. For patients with early stage gynecologic cancers, it may be able to conserve reproductive organs at the time of cancer surgery.

Additional options

Preimplantation genetic diagnosis (PGD), ovarian suppression, ovarian shielding, psychological support and financial counseling are among other options discussed at a fertility preservation consultation.

Safety of pregnancy after cancer

Thus far, research on the safety of pregnancy after cancer is reassuring. Further research is necessary to confirm these findings.



What are options After Cancer Therapy?

After cancer therapy, survivors who desire to have children may wish to have a consultation with a reproductive endocrinologist about fertility potential.

Fertility treatment and assisted reproduction

For women who are subfertile after cancer therapy, traditional assisted reproductive technologies may be appropriate to help some cancer survivors achieve pregnancy.

Third party reproduction: egg donation

For cancer survivors who become menopausal with cancer treatment, egg donation is a highly effective option for becoming pregnant.

Third party reproduction: gestational surrogacy

A gestational surrogate is a woman who will carry a pregnancy for intended parents. Because some women are unable to carry a pregnancy after cancer therapy, having a gestational surrogate carry their pregnancy may be an option for these cancer survivors.

Adoption

Adoption is another option for cancer survivors to achieve a family.

Oncofertility Clinical Trials

The Oncofertility Consortium is actively engaged in research to address issues of reproductive health in cancer survivors.

- National Fertility Preservation Registry
- Oncofertility Consortium Ovarian Tissue Cryopreservation Study

In addition, there are a number of additional studies at individual NPC centers. For more information, please call our research team at: (866) 708-FERT (3378)

Fig. 12.3 The National Physicians Cooperative brochures **a**) Front of trifold brochure include contact information through the national FERTLINE, fertility preservation options, and the ability to individualize with branding for each center **b**) Back of trifold brochure

Table 12.2 Educational and financial resources for providers and patients

Resources	Contact information	Description
My Oncofertility	www.myoncofertility.org	Educates patients, parents, and partners on fertility and cancer
Oncofertility Consortium	www.oncofertility.northwestern.edu	A research consortium that educates patients, health professionals, and researchers on fertility and cancer
Save My Fertility	www.savemyfertility.org	Online fertility preservation toolkit and mobile application for patients and providers
FERTLINE	866-708-FERT (3378)	National hotline to connect providers and patients with fertility preservation programs
You Tube	http://www.youtube.com/user/oncofertility	Watch experts in the oncofertility field discuss the history of the field and research advances
Fertile Action	www.fertileaction.org	Negotiates financial discounts for women wishing to preserve fertility prior to cancer treatment
Sharing Hope	www.fertilehope.org	Provides fertility preservation discounts for men and women prior to cancer treatment

Financial Considerations

Most fertility preservation treatments are not covered by insurance. Currently, there are no state or national laws that mandate health insurance coverage of fertility preservation services [4]. Many oncofertility centers have a negotiated package price for patients undergoing fertility preservation treatments. Some programs have lowered global rates for all fertility preservation patients. Other centers participate in financial assistance programs such as the Sharing Hope program (Table 12.2). Finally, some oncofertility programs have undertaken fundraising to help patients defray the significant costs of fertility preservation services.

Summary

Establishing a clinical oncofertility program provides an invaluable resource to the local community. Diverse expertise is required to discuss and undertake fertility preservation options in young cancer patients facing fertility-threatening therapy. Outreach efforts to inform the community about fertility preservation and the oncofertility program are integral to the success of any program.

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References

1. Woodruff TK. The Oncofertility Consortium—addressing fertility in young people with cancer. *Nat Rev Clin Oncol*. 2010;7:466–75.
2. Lee SJ, et al. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *J Clin Oncol*. 2006;24:2917–31.
3. King L, et al. Oncology nurses' perceptions of barriers to discussion of fertility preservation with patients with cancer. *Clin J Oncol Nurs*. 2008;12:467–76.
4. Campo-Engelstein L. Consistency in insurance coverage for iatrogenic conditions resulting from cancer treatment including fertility preservation. *J Clin Oncol*. 2010;28:1284–6.