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NewsLetter

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EDITORIAL

CAN FERTILITY BE PRESERVED IN FEMALE CANCER SURVIVORS?

Fertility preservation in essence means preserving the ability of an individual or couple to start a family at a time of their choosing. **Oncofertility** is a term coined for fertility preservation in cancer patients. Improvement in cancer management and increasing survival rates has created a need for oncofertility. Unfortunately, fertility preservation services are rarely offered or even discussed with the patient before starting cancer therapy. Studies have shown that infertility is a significant survival concern. Patients who receive information regarding their sexual and reproductive health have lower levels of psychological distress than patients who do not receive this information. Informed decision reduces reproductive regret in these young men and women.

Chemotherapy and radiotherapy remain the mainstay of cancer treatments. Both can be damaging to the ovary depending on the agent used, dose given, and age of the patient. The prepubertal ovary is less susceptible to damage by chemotherapeutic agents while older women have a lower ovarian reserve and hence are more susceptible to premature ovarian failure. Alkylating agents have an extremely damaging effect and are responsible for high ovarian failure rates. Platinum-based compounds such as cisplatin cause DNA damage. They carry a medium risk of amenorrhea. Anthracycline antibiotics such as doxorubicin (DXR) induce oxidative stress. The amenorrhea and fertility risk is medium to low with this group of drugs.

Live birth rates from pregnancies in cancer survivors are similar to those of siblings. No significant increase in miscarriage, congenital malformations, genetic abnormalities, or malignant neoplasms have been found when conception has taken place long after completion of therapy. Risk of mutagenesis is maximum during the maturation phase of the oocyte, which is approximately 6 months and minimum during the dormant stage. It is, therefore, recommended that patients be asked to delay conception for 6 months after completing the treatment, and fertility preservation techniques such as oocyte and embryo cryopreservation are carried out 6 months after treatment and not between treatments.

Unlike chemotherapy, radiotherapy affects both the ovary and the uterus. Human oocyte is sensitive to radiation, with an estimated median lethal dose (LD50) of <2 Gy. Damage to the ovary by radiotherapy is dependent on the age of the patient and dose of the ovarian exposure. The effective sterilizing dose (ESD) is the dose of fractionated radiotherapy (Gy) at which POF occurs immediately after treatment in 97.5% of patients. ESD decreases with increasing age, being 18.4 Gy at 10 years, with only 6 Gy being required to cause permanent ovarian failure (POF) in women over 40. Ovarian failure has been reported in 90% of patients following total body irradiation (TBI) (10–15.75 Gy) and in 97% of females treated with total abdominal irradiation (20–30 Gy) during childhood. In adults, an exposure to TBI of 12 Gy is associated with significant uterine damage. Radiation doses of >25 Gy directly to the uterus in childhood appears to induce irreversible damage. Increased rates of infertility, miscarriage, preterm labor, intra-uterine growth retardation and low birth weight have been reported especially if conception occurs within a year of radiotherapy. It is suggested that patients receiving>45Gy during adulthood and >25 Gy in childhood should be counseled to avoid attempting pregnancy.

In colorectal cancers, radiation damage to the gonads and uterus is inevitable, hence fertility preservation techniques should be strongly advised. Ovarian transposition needs to be performed to get the ovary out of the radiation field. Standard management for cervical cancer is radical hysterectomy with lymph node dissection for early disease. Radical trachelectomycan be performed for women with early-stage cervical cancer (<2 cm in size) who have not yet completed their childbearing. No significant difference is noted between two surgical procedures in rates of recurrence, mortality, 5 years recurrence-free survival. Traditional management for ovarian cancer is total hysterectomy with bilateral salpingo-oophorectomy. Type of fertility-sparing surgery (FSS) depends upon the histology, stage of disease and preexisting ovarian reserve. Nonepithelial malignant ovarian tumors, particularly germ-cell tumors, do well with fertility-sparing surgery. Unilateral salpingo-oophorectomy or in some cases cystectomy is done with extensive staging and subsequent follow-up. Recurrence after cystectomy is high 25%. FSS has also been tried for early stage epithelial ovarian malignancy. Prerequisites for conservative surgery include well-differentiated unilateral disease, with no sign of extra-ovarian metastasis. Patients need to understand the risk of recurrence and give consent knowing this potential risk.

"Ferto-protective adjuvant therapy" is a term used for administration of adjuvant therapy during or prior to chemotherapy with an agent that can prevent loss of ovarian reserve. The list of drugs under investigation are sphingosine-1-phosphate (S1P) and imatinib that inhibit apoptosis, thalidomide and granulocyte colony-stimulating factor, mechanism of their action is unclear, tamoxifen which works as an antioxidant, and AS101 which causes modulation of follicle activation pathway.So far, the only drug used in clinical practice is the gonadotropin-releasing hormone (GnRH) agonist. Patients with leukemia may be good candidates for GnRH agonist co-administration in order to manage the ovulation and menstrual bleeding during chemotherapy.

Fertility preservation techniques in females include Embryo cryopreservation, Oocyte cryopreservation, Ovarian tissue cryopreservation (OTC) and In vitro maturation (IVM). Patients with breast cancer can undergo IVF while waiting for chemotherapy after surgery. The challenge here is the hyperestrogenemia. Aromatase inhibitors, mild stimulation protocols have been used to avoid high estradiol levels. IVM or ovarian tissue preservation can be offered to patients not willing for OS. They can have multiple OR's to preserve oocytes/embryos before BSO. OTC for transplantation is not advisable in patients carrying a BRCA mutation given the increased risk of ovarian cancer in this population. Parents have to be given full information of the process, associated risks and success rates. Thorough psychological counseling is required, and ethical considerations have to be kept in mind. Postpubertal girls under the age of 18 may be candidates for mature oocyte cryopreservation following OS. In prepubertal girls, OTC is currently the only way to cryopreserve gametes.

Careful counselling and informed consent is strongly recommended. Oocyte and embryo cryopreservation are now established techniques but have their limitations. OTC has a wider application and the advantage of keeping the fertility window

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STANDARDS OF SPECIMEN HANDLING IN OPERATION THEATRE: DOES IT AFFECT ADJUVANT TREATMENT DECISION ? From an oncosurgeon's perspective

Introduction: The purpose of the standards is to provide an outline that healthcare workers (HCWs) in the perioperative setting can use to develop and implement policies and procedures for the handling and care of surgical specimens. The standards are presented with the understanding that it is the responsibility of the healthcare facility to develop, approve, and establish policies and procedures for the handling and care of surgical specimens according to established healthcare facility protocols.

Rationale: The handling of specimens before they reach the pathology department is referred to as the preanalytic phase. Involving many HCWs and many steps including communication of information among the surgical team members, labeling, packaging and transport of the specimen that may contribute to increasing the risk of error.

1. **Mislabeling errors:** In one six-month study conducted at a university healthcare facility, the following was identified:

i. Of 10,354 surgery department specimens, 38 had errors.
ii. Of the 21,351 total number of specimens studied that originated from varioushospital departments, 54 of 91 mislabeled specimens originated from the surgerydepartment. Out of those 54, the surgical procedures in which specimens weremost commonly mislabeled are:
iii. Breast
iv. Skin
v. Colon
vi. Prostate

second and third category represents the greatest concern since an

i. incomplete diagnosis,
ii. misdiagnosis, or
iii. delayed treatment, and could result in wrong treatment, causing the patientto undergo additional treatment as a safety measure even though it may not be needed, orcause treatment of wrong area of the body.

* Additionally, for both categories, the healthcare facility is facing possible litigation.

As previously mentioned, delivering a specimen to the pathology department involves following steps including:

1. Correctly identify the patient.
2. Correctly identify and confirm the specimen by the surgical team.
3. Placing the specimen in an appropriate container and preservative.
4. Correctly label the specimen.
5. Complete the pathology requisition slip.
6. Transport the specimen to the pathology department.

Standard of Practice I: The proper handling and care of specimens begins during the preoperative phase of patient care and preparations including all communications should involve the surgical team.

Standard of PracticeII: Specimens to be transported to the pathology department should be placed in theproper container to preserve and protect the specimen.

Standard of Practice III: HCWs should practice appropriate precautions in the handling of specimens andthe containers to protect the specimen as well as to prevent self-contamination.

Standard of Practice IV: Specimen containers should be properly labeled.

1. **The following information should be written on the label in the operating room bythe circulator:**
a. Type of specimen
b. Site of specimen including left or right side
c. Two unique identifiers, eg patient name and hospital number13
d. Date and time specimen received from CST
e. Type of preservative, if used
f. Surgeon's name
g. Suture tag if present and placement, eg 12 o'clock position or lower leftQuadrant

Standard of Practice V: Preservative solutions should be handled, distributed and disposed of by HCWs in accordance with established healthcare facility policies and procedures.

Standard of Practice VI: Specimens designated for frozen section should be properly handled, transported and disposed of according to healthcare facility policies and procedures.

Standard of Practice VII: Aerobic and anaerobic culture specimens should be properly obtained, handled, transported and disposed of according to healthcare facility policies and procedures.

Standard of Practice VIII: Anaerobic culture specimens obtained with a syringe should be properly handled,transported and disposed of according to healthcare facility policies and procedures.

Standard of Practice IX: Radioactive specimens should be properly handled, transported and disposed of according to healthcare facility policies and procedures.

Standard of Practice X: The handling and reporting processes of defective medical device specimens should be established by the healthcare facility in accordance with federal regulations.

Standard of Practice XI: Foreign objects such as bullets are medical-legal evidence and should be properly managed in order to preserve the evidence as well as follow healthcare facility policies and procedures for documenting the chain of custody.

Standard of Practice XII: Healthcare facilities should establish policies addressing specimens that are identified as not having to be submitted to the pathology department, specimens that only require gross examination and specimens that should undergo routine microscopic examination.

Standard of Practice XIII: A systems approach should be utilized when developing the healthcare facility's procedures and policies for identification, handling, communication, documentation, transportation and disposition of specimens.

1. A systems approach places emphasis on viewing the process as a whole in the**handling and transport of specimens**. A systems approach focuses on the safeguards that can be established to reduce the risk of errors. Additionally, if an error occurs in the handling of a specimen, the system/policies and procedures can be reviewed and revised as necessary to avoid a future system error.

a. **Establishing consistent methods of verbal and written communication as well as** chain of custody is essential to decreasing the risk of errors. The development of a flowchart that can be periodically reviewed is a usefulaid.

b. **Immediately placing the specimen into the container and labeling the container** reduces the risk of losing the specimen during clean-up of the

c. **The use of pre-printed forms**, including checklists, laboratory requisition slips and daily specimen logs indicating information to be entered reduces the need for HCWs to rely on memory and ensure that all required information for processing specimens is obtained.

A **checklist** that is completed by the circulator prior to the specimen being transported out of the OR aids in reducing error.

The checklist can serve as a double check for accuracy; it can be prompted by the circulator asking **"has the specimen been verified"**and each member of the surgical team verifying.

d. **A requisition form should accompany all specimens delivered to the pathology or laboratory department**. The healthcare facility should have a pre-printed requisition form. Pertinent information may be stamped on the form using the patient's addressograph card. The following information should be completed on the form:

1. Patient's name
2. Patient's healthcare facility identification number
3. Patient's unit and/or room number
4. Clinical diagnosis
5. Surgeon's name
6. Source of specimen to include anatomical location where the specimen was removed, side, etc.
7. Type of tissue
8. Date and time of collection in the OR
9. Study requested, eg culture, Gram stain, frozen section, etc.
10. Other pertinent clinical information.
11. Name of circulator who completed documentation and preparation of the specimen for transport to the pathology or laboratory department

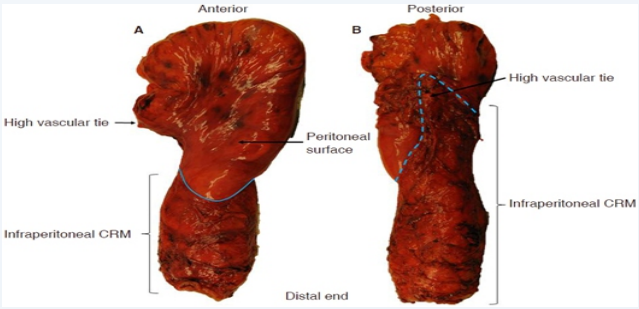
e. Chain of custody tracking should be established within the system for handling specimens. The chain of custody process should be simplified and the number of hand-offs kept at a minimum; each hand-off is represented as a potential source of error.

A surgery department specimen log book should be used to record each specimen to includename of specimen, two patient identifiers, date, time of log-in, and name of each HCW involved in the transport of the specimen.

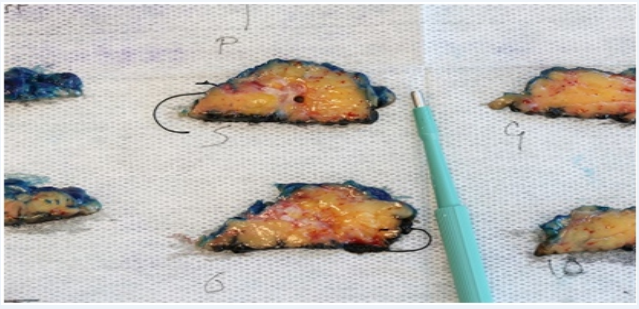
f. The pathology, laboratory and surgery departments should agree upon an established schedule for the pick-up/transport of permanent specimens.

g. To create ownership of the process of handling specimens, a healthcare facility department, such as the pathology department, should be designated as overseeing the system, including development and revision of policies.

2. Periodic training of HCWs involved in the handling of specimens should be completed. The training should involve review of policies and procedures, as well as receiving feedback from HCWs for improvement of the system.



CRM in surgery for Ca rectum



Breast cancer specimen

Dr. Seema Singh
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CME WITH INDIAN MEDICAL ASSOCIATION (IMA) LUDHIANA, PUNJAB

RGCIRC organized a CME in association with IMA Ludhiana on Friday, 12th November 2021 at Hotel Radisson Blu, Paschim Vihar, New Delhi. Dr. Vineet Talwar, Director – Medical Oncology delivered a lecture on **Environment and Cancer**. Dr. Narendra Agrawal, Sr. Consultant – Hemato-Oncology & Bone Marrow Transplant spoke on **Management of Hematological Malignancies**. The CME was very well appreciated by the gathering.

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EDITORIAL

open for a longer time. The need for fertility preservation has to be weighed against morbidity and mortality associated with cancer. There is thus a need for a multidisciplinary collaboration between oncologists and reproductive specialists to improve awareness and availability.

Dr. A. K. Dewan
Director - Surgical Oncology

12TH CHEMOPORT TRAINING PROGRAMME

After a long gap due to the COVID-19 pandemic, the Department of Surgical Oncology, RGCIRC successfully organized the 12th training course in Chemoport Insertion on 30th September - 01st October 2021 at RGCIRC, Rohini, Delhi. This 2 days course was held for doctors from various oncology centres who desired to learn this technique. It entailed interactive session by the faculty of RGCIRC as well as hands on training in the operating rooms. The topics covered were Chemoport Insertion, Hickman's Catheter Insertion, Pediatric Port, Arm Port, Peritoneal Port Insertion and snaring of fractured Port catheter. The course was highly gratifying and we received an excellent feedback.

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