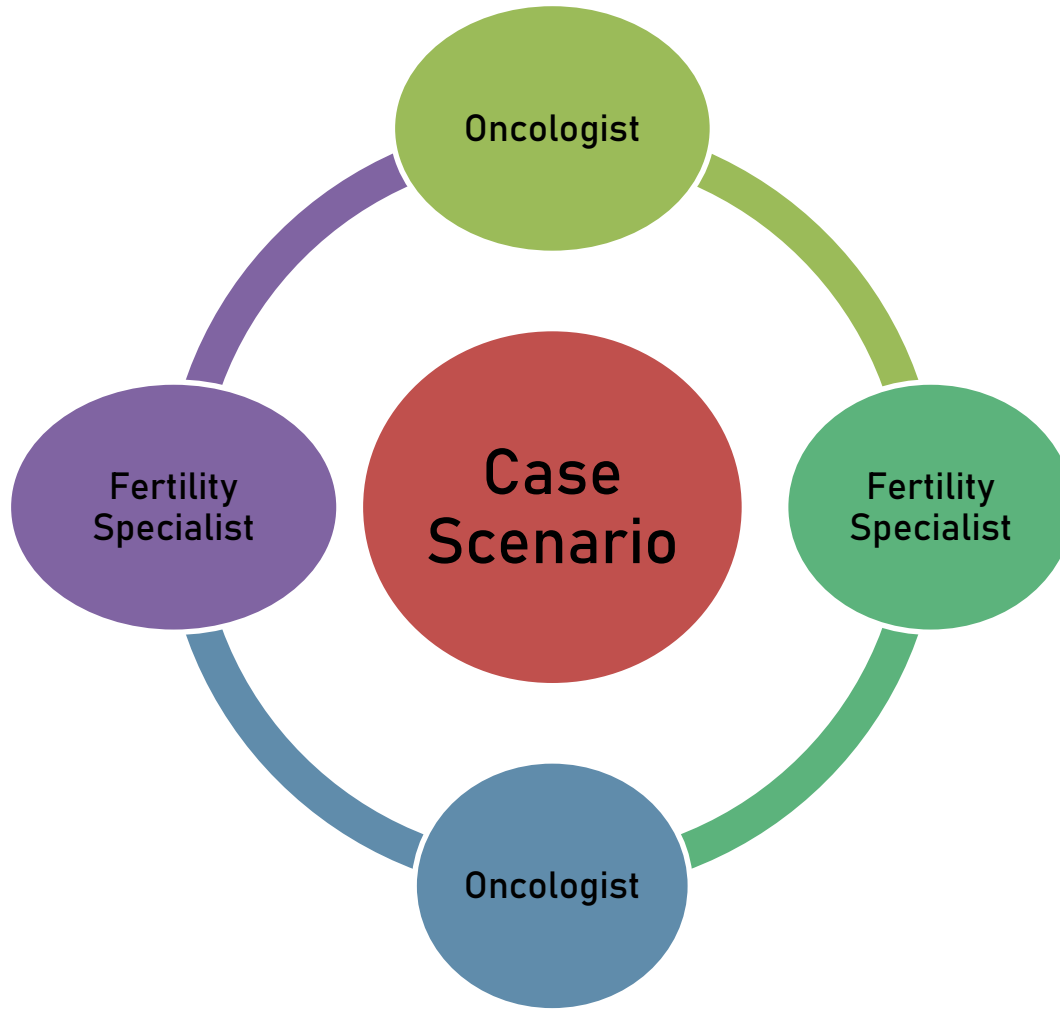




# Panel Discussion

## "Forming Oncofertility Team"

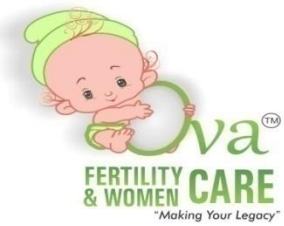




## Clinical Discussion Based On....

- **Case Scenarios**
- **Counselling**
- **Options for Fertility Preservation**
- **Referral Pathway**
- **Ethical Challenges**



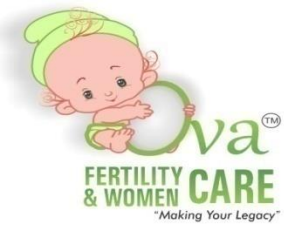


## Clinical Scenarios

**Patient Details** : 27 year old unmarried woman, asymptomatic diagnosed CIN III on routine PAP smear.

**Cancer Diagnosis** : Adenocarcinoma Stage IB1





## View Point....

In cervical cancer, what are the possible causes of fertility loss?



## View Point....

In large cervical tumors with low stage, is it possible to perform a fertility-sparing surgery?



## View Point....

What are the options for fertility preservation in cervical cancer patients ?



## Pearls of Wisdom....

- Cervical tumors larger than 2.0 cm are at increased risk of lymph node involvement.
- The cervical margins must be free of neoplasia to perform a fertility-sparing surgery with oncological safety.
- Until IB1 stage, it is possible to perform radical laparoscopy trachelectomy with pelvic lymphadenectomy. If the cancer has spread to the tissues next to the uterus, or to any lymph nodes, radiation with chemotherapy is recommended.

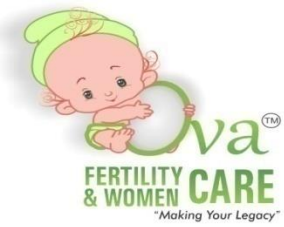




## Pearls of Wisdom....

- Chemotherapy and pelvic radiotherapy are strongly associated with ovarian failure and infertility.
- To patients with possibility of chemoradiation indication, it is recommended to discuss oocyte/ embryo/ovarian tissue cryopreservation and ovarian transposition; moreover, surrogacy and even uterus transplant should be addressed.



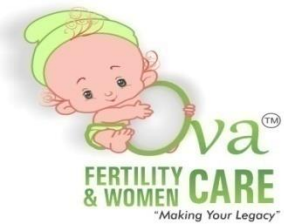


## Clinical Scenarios

**Patient Details** : 15-year-old post-menarchal girl

**Cancer Diagnosis** : Scleronodular Hodgkin's disease stage IIBb





## View Point....

How severe is the risk of damage to fertility potential in this case ?



## Pearls of Wisdom....

- Ovarian reserve markers may be low in hematologic malignancies before any chemotherapy.  
(Extreme catabolic state )
- Both ovarian tissue cryopreservation and oocyte vitrification are effective techniques and offer realistic chances of becoming a parent.
- Patient & Parents consent
- Discussion about transvaginal approach for OPU  
Other Options – Abdominal, Perurethral & transvesical pickup, Laproscopic



# What are the challenges in dealing with pediatric cancer population?



# Challenges

- Prepubertal patients only have experimental fertility preservation options available to them requiring Institutional Review Board (IRB) approval
- Children and adolescents may lack capacity to envision a future in which they want children but in adulthood regret a decision to not pursue fertility preservation when offered
- There are ethical concerns regarding parents making generational choices for their children





# Basic Ethical Requirements

## 1. Informed consent of parents

- Clear and accurate information about the storage of reproductive tissue including place costs of storage
- What will be done with the tissue if the child does not survive
- Who has the right to access the tissue and for what purposes
- FP does not mean a guarantee that the child will have fertility in adulthood
- FP does not imply that child's survival into adulthood is certain



# Basic Ethical Requirements

## 2. Assent of child (where child is old enough)

- The child should be given an developmentally appropriate explanation of the procedure that will be done and its purpose.
- Ideally, the child should be in agreement with the procedure.

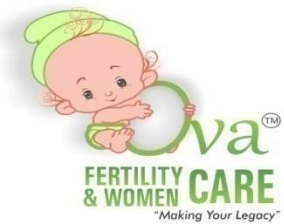




# Situations where Clinical Ethics Review is Required



- The procedure will delay or interfere with the cancer treatment
- The procedure is itself of greater than minimal risk (e.g. because of a co-morbidity which makes the procedure more risky than usual)
- The procedure has a significant risk of not leaving one gonad intact (e.g. if the child has only one gonad to begin with)
- The risk of loss of fertility due to chemotherapy is low
- The potential for retrieving tissue that might be useable in the future is lower than usual, for any reason



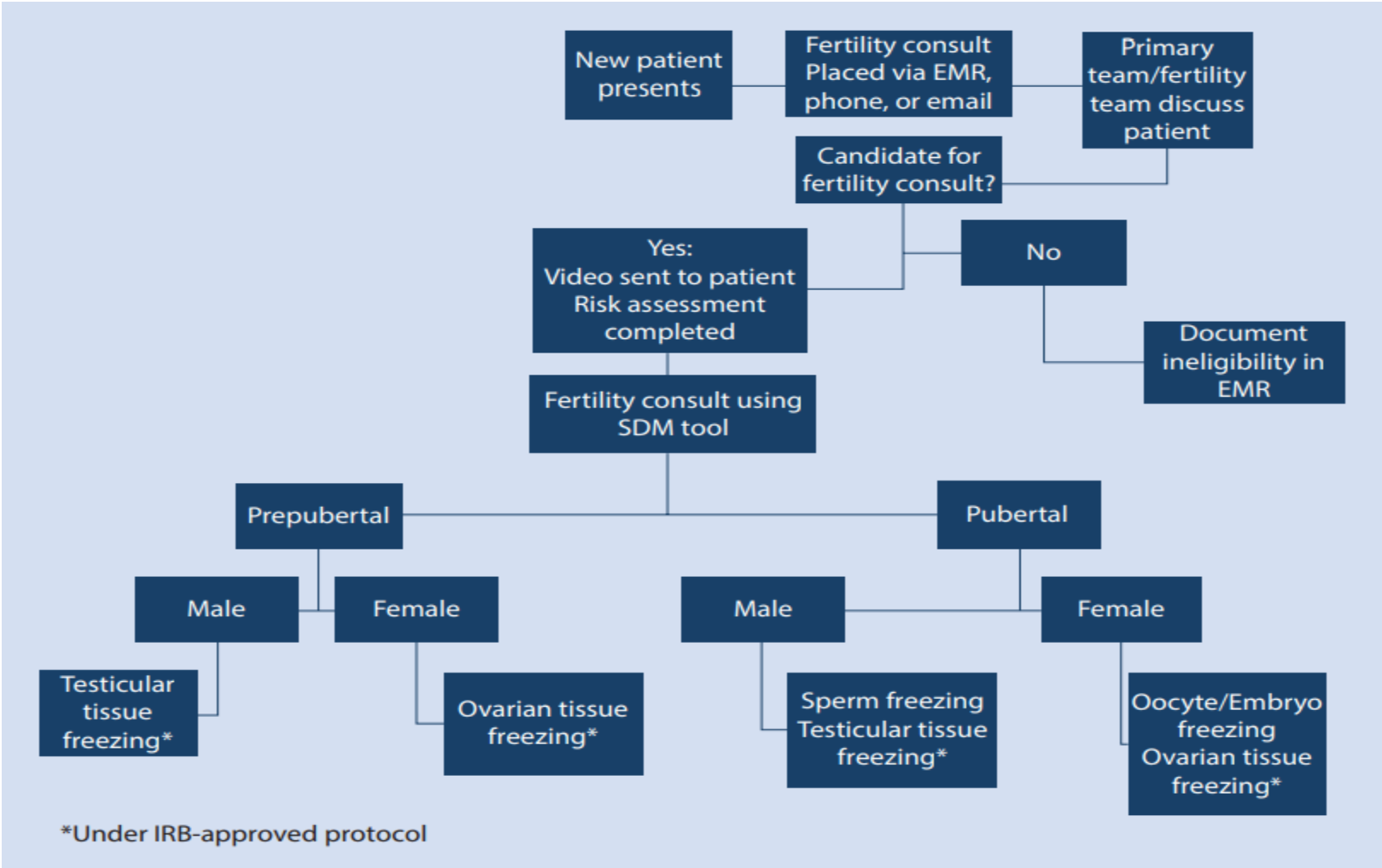
# Situations where Clinical Ethics Review is Required



- The child has an intellectual disability
- The child is pre-pubertal
- The child or young person objects to having a fertility preservation procedure, but parents still want to go ahead
- The parents are unwilling to inform the child about the procedure, when the child is at developmental stage where they would be able to understand at least the basic idea of the procedure
- Any treating clinician has an ethical question or concern about the procedure



# Program Workflow



## Clinical Scenarios

**Patient Details** : A 23-year-old man

**Cancer Diagnosis** : Flow cytometry confirmed an immunophenotype consistent with acute myeloid leukemia (AML)



## Pearls of wisdom....

- AML is considered an oncologic emergency and outcomes have been found to be dependent on the time from diagnosis to treatment initiation in younger patients, necessitating that this patient start therapy as soon as possible to maximize outcome.
- Optimal timing for sperm cryopreservation before any therapy is given to maximize the quality and DNA integrity of the semen specimen, which can be damaged by just one round of chemotherapy.
- Even though there is significant emotional stress and difficulty, it is important to discuss this at the time of diagnosis.



## Pearls of Wisdom.....

- Another option could have been testicular sperm extraction (TESE), which is called onco TESE
- Microdissection-TESE (micro-TESE) utilizes an operating microscope to identify small pockets or crypts of sperm production in comparison to tissue extraction done with TESE, which success depends on a higher level of spermatogenesis. It has been shown to increase yield in certain clinical settings with a similar clinical complication rate and decreased hematoma and testicular fibrosis.



## Clinical Scenarios

**Patient Details :** 32yrs, Nullipara, mass in the left breast (3cm irregular),  
Family history: Maternal grandmother-Pancreatic CA  
Maternal Aunt- postmenopausal breast CA  
Maternal uncle-melanoma

**Cancer Diagnosis :** Core needle biopsy-invasive ductal breast CA  
(ER+ve-95%, PR +ve 95%, HER2/neu +ve); No nodes



## View Point....

What special precautions to be taken during ovarian stimulation of these patients?





## View Point....

What are the ethical implications for cryopreservation of embryos compared to mature oocytes ?



## View Point....

What are the ethical implications preimplantation genetic diagnosis ?



# Stimulation Protocols

GnRH agonist based protocols	GnRH antagonist based protocols
Require of 3 weeks duration	Require 9-14 days of duration.
GnRH agonist has initial flare up effect on pituitary	GnRH antagonist immediately suppresses LH.
GnRH agonist has to be started in luteal phase of prior cycle.	GnRH antagonist has to be started on Day 5 or Day 6 of gonadotropins when dominant follicle is 13-14mm.

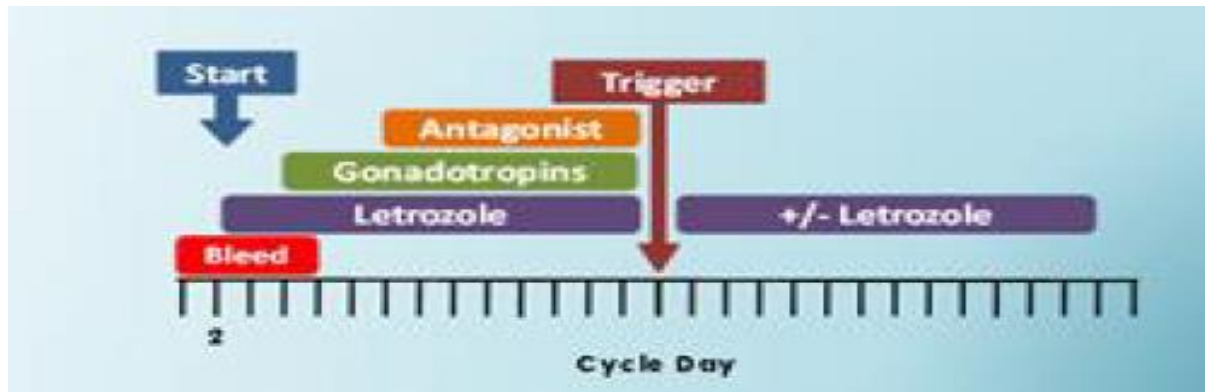


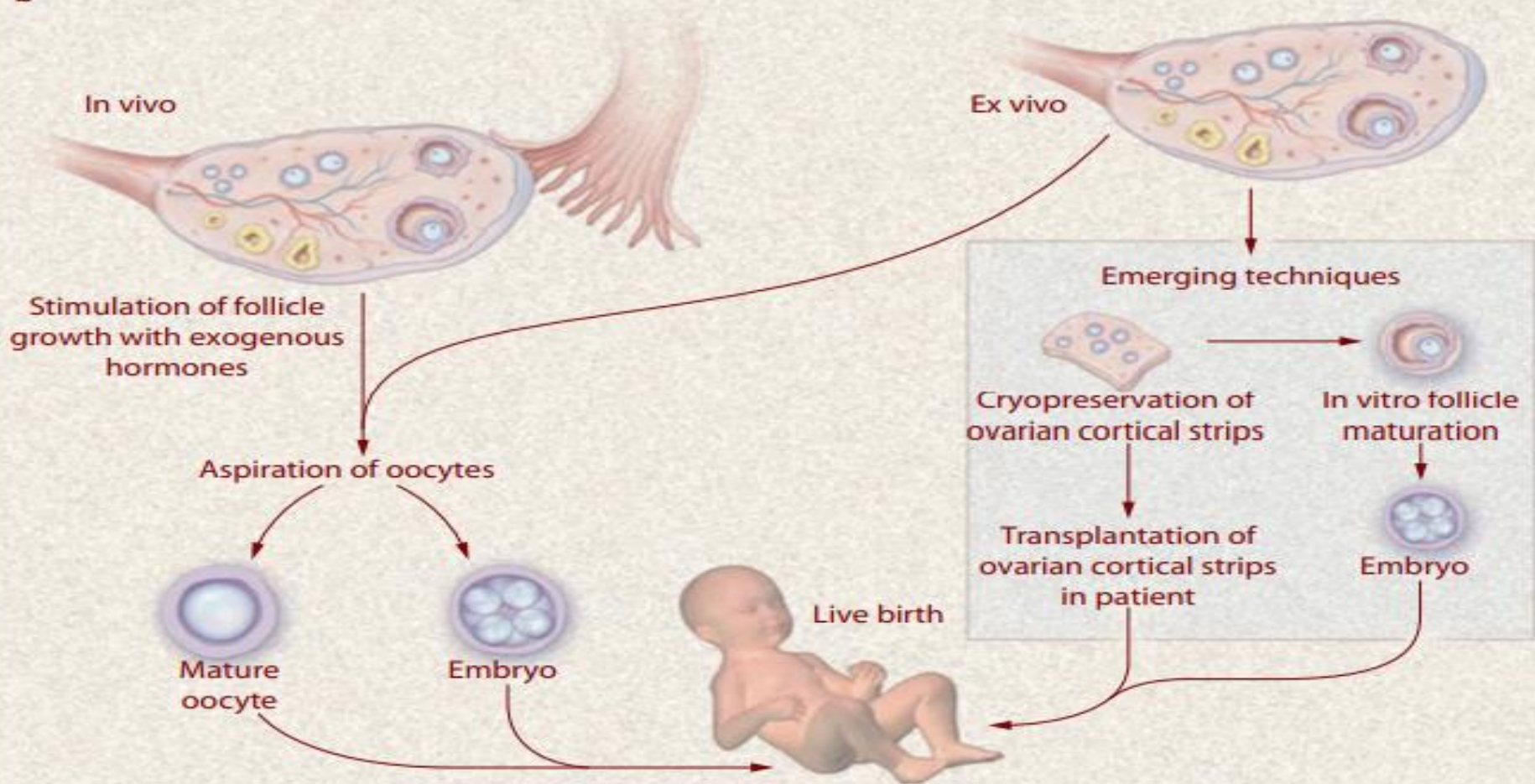
# What is different because of Cancer ??

- Affected function of HPO axis and decline in fertility due to malnutrition , catabolic state and raised stress hormones
- Might reduce response to stimulation
- BRCA mutations – oocytes prone to DNA damage
- Requirement of high gonadotropin dosages



# Letrozole based stimulation protocols



**a****b**



## Pearls of Wisdom....

- Genetic counseling & testing-BRCA 2 mutation
- PGD in HBOC (Hereditary breast and ovarian CA)- Mastectomy after breastfeeding completed and at 40 YRS-Risk reducing BSO
- Trastuzumab/Pertuzumab- contraindicated in pregnancy (direct fetal toxicity/Oligo/ pulmonary hypoplasia/skeletal dysplasia/fetal death)  
Contraception to be discussed while on these medications.



## Pearls of Wisdom.....

- Delay attempt of pregnancy for 7 months after completion of HER-2/neu-directed therapy  
3 months of washout period for antihormonal therapy : Tamoxifen (SERM)
- Depending on the size of the mass- breast conservation surgery – to retain the ability to breast feed in future





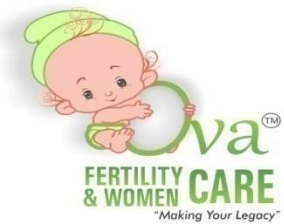
## Clinical Scenarios

**Patient Details** : 29 year old married female repeated episodes of chest pain and shortness of breath; HRCT s/o 6.6 x 5cm anterior mediastinal mass



**Cancer Diagnosis** : Primary Mediastinal B cell Lymphoma



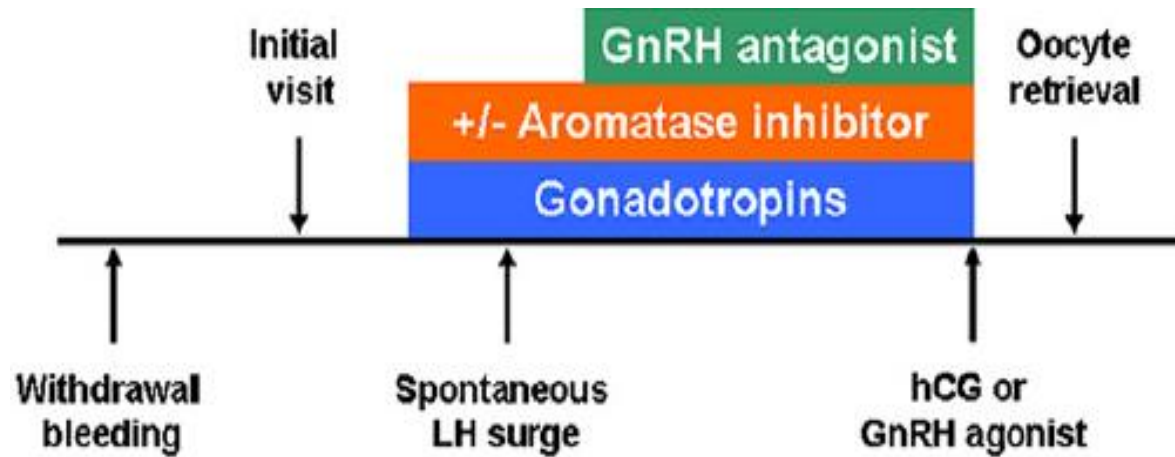


## View Point....

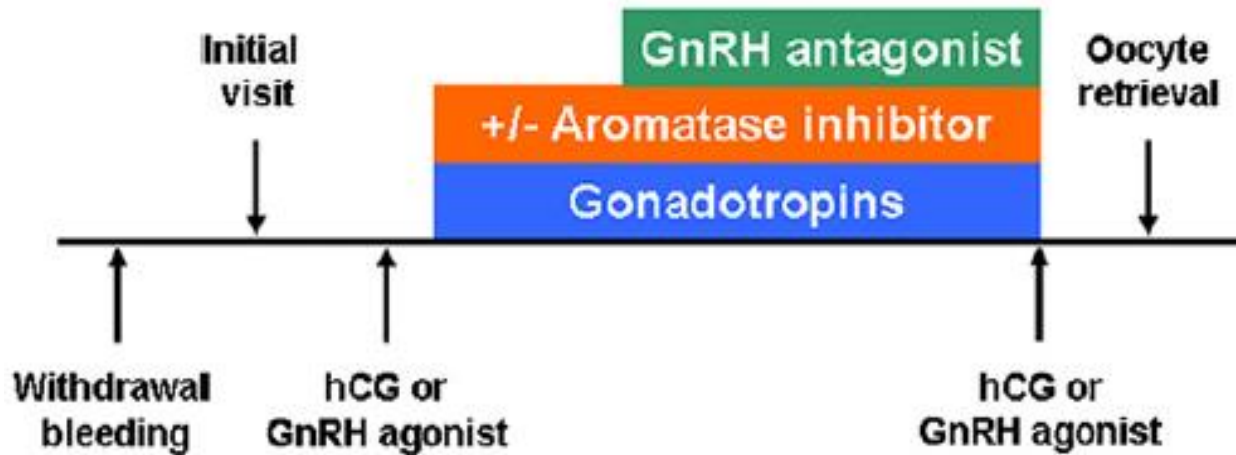
How much time can be offered in such case for fertility preservation ? In such scenario, how the urgency of cancer treatment decided?



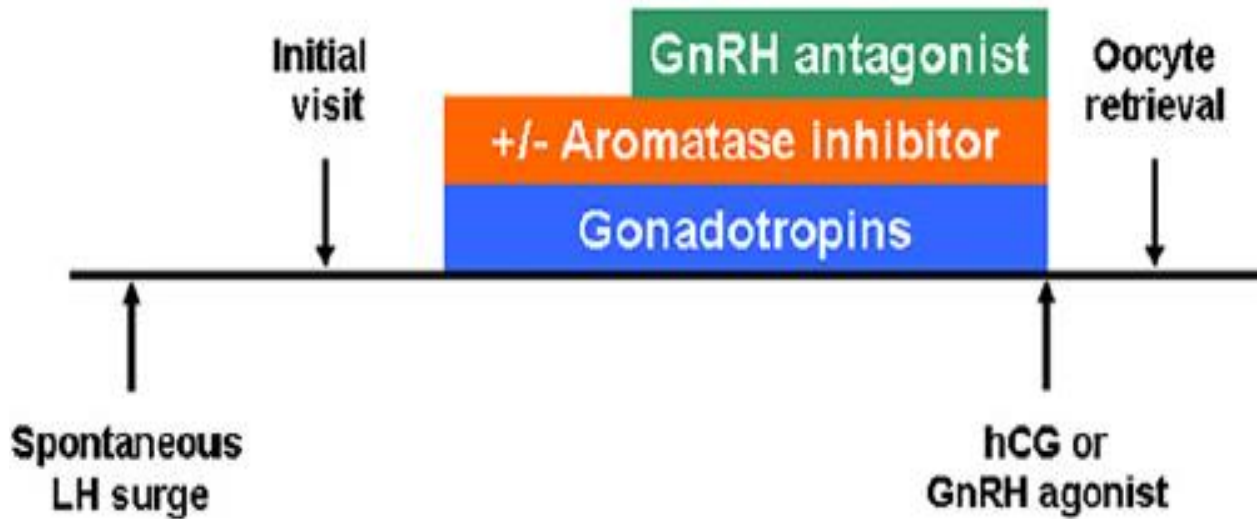
## Random Start Approach Late Follicular Phase Stimulation with GnRH Antagonist Protocol



## Random Start Approach Late Follicular Phase Stimulation with GnRH Antagonist Protocol



## Luteal Phase Stimulation with GnRH Antagonist Protocol



## Pearls of Wisdom...

- Urgency of treatment in symptomatic patients
- No delay in stimulation-Random start/Luteal phase stimulation
- Immature eggs-IVM
- Dealing with risks of bleeding, thromboembolism , infections and anaesthesia complications.



## Clinical Scenarios

**Patient Details** : 32 year old , P1L1 (5year old child) with history of right salpingo-oophorectomy for stage IA borderline ovarian tumor

**Current Diagnosis** : Left adnexal mass



## View Point.....

In this case, is it worthwhile to refer her for a fertility preservation consultation as she is already having one kid ?

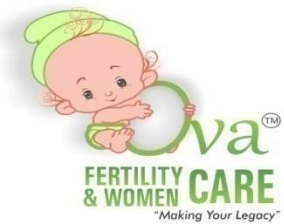




## Clinical Pearls

- Only 10% of ovarian cancers are diagnosed below the age of 40 years.
- Borderline ovarian tumors and malignant germ cell tumors have favorable prognosis than epithelial tumors. So fertility sparing surgeries like unilateral cystectomy or unilateral salpingo-oophorectomy can be possible in these cases.
- Around 46% spontaneous pregnancy rate has been seen in borderline ovarian tumors after fertility preserving surgery.





## Clinical Pearls

- Surgery is completed after pregnancy.
- In cases of ovarian cancers, there are safety concerns for controlled ovarian hyperstimulation and oocyte retrieval as well as ovarian tissue cryopreservation and auto transplantation.
- Use of donor eggs



## Clinical Scenarios

**Patient Details** : 22 year old woman, nulligravida

**Current Diagnosis** : Recurrent Hodgkin's lymphoma requiring Bone marrow transplant as early as possible



## View Point.....

What would be the challenges faced in this scenario ?



## Pearls of Wisdom....

- Treatment for hematological malignancies is highly gonadotoxic leading to premature ovarian failure due high dose combination chemotherapy and whole body irradiation before bone marrow transplant.
- Patients can be significantly ill at the time of diagnosis and abnormal hematological parameters increase the surgical risk.
- They may not afford time delay.
- Majority of the times ovarian tissue cryopreservation is offered but there are concerns regarding re-seedling of malignant cells after autologous transplantation. Histological and molecular evaluation of harvested tissue is recommended. Ovarian metastasis is detected by pre operative imaging like MRI or PET scan.



## Pearls of Wisdom....

- There is risk of thrombocytopenia due to high dose chemotherapy and bone marrow irradiation.
- GnRH agonist is used for ovarian protection as well as to prevent menorrhagia in high risk patients.
- If auto transplantation is not possible, ovarian tissue cryopreservation with in vitro maturation of immature oocytes can be offered.





**What are the challenges in survivorship when the fertility preservation options were not offered during cancer treatment?**



# Survivorship Issues

- Fertility Concerns
- Desire to have family

“ One of the Strongest predictors of emotional well being of cancer survivors is *Parenthood* representing return to normalcy and sense of fulfilment”







# Importance of Fertility Preservation

Receiving specialised counselling about reproductive loss and Fertility Preservation is associated with less regret and greater quality of life for survivors.



# What are the ethical and legal aspects of Oncofertility?

Common ethical concerns :

- A. Fertility preservation to be offered to whom?
- B. Financial consideration of fertility preservation- Insurance Cover ?
- C. Disputes over frozen gametes, embryos and gonadal tissue (reproductive material)
- D. Post Humous Assisted Reproduction



# Remarkable Cases at Ova..

## Post Humous Use of Gametes by Spouse

- Couple – 42 year old female and 48 year old male
- First IVF cycle – failed followed by death of husband
- Sperms frozen during that cycle with consent mentioning spouse can use the gametes in case of death
- Wife underwent another IVF cycle with Frozen sperms
- Currently – 32 weeks ongoing pregnancy



# Post Humous Reproduction....

*Reproduction as Joint Project of Couple*

*Need of Appropriate Documentation*



# Remarkable Cases at Ova..

## Live Birth in Breast Cancer Survivor

- 36 year old female, doctor by profession
- H/O Breast Carcinoma at the age of 26 years
- Unilateral mastectomy with chemotherapy received
- Completely cured but did not get any fertility preservation counseling prior to chemotherapy !!!



# Remarkable Cases at Ova..

- After 10 years when decided to plan pregnancy – AMH was very low (0.5ng/ml s/o low fertility potential)
- IVF cycle attempt with self egg - miscarriage
- Psychological challenge- feeling of regret / grief / difficulty in accepting donor eggs
- Multiple counselling session
- Second IVF cycle with Donor eggs – Now health baby of 6 months



# Happy Moments... *Our Bundle of Joy.....*



**Role of Counselling**

**Individualised Treatment Protocol & Emotional Support at each stage**



# Concluding Remarks.....





# Pregnancy, time to pregnancy and obstetric outcomes among female childhood cancer survivors: results of the DCOG LATER-VEVO study

[M. van Dijk](#) , [F. E. van Leeuwen](#), [A. Overbeek](#), [C. B. Lambalk](#), [M. M. van den Heuvel-Eibrink](#), [W. van Dorp](#), [W. J. Tissing](#), [L. C. Kremer](#), [J. J. Loonen](#), [B. Versluys](#), [D. Bresters](#), [C. M. Ronckers](#), [H. J. van der Pal](#), [C. C. M. Beerendonk](#), [G. J. L. Kaspers](#), [E. van Dulmen-den Broeder](#) & [M. H. van den Berg](#)

## Results

Among the subgroup of women who ever had the desire to become pregnant, the chance of becoming pregnant was significantly lower for CCSs than controls (OR 0.5, 95%CI 0.4–0.8). Moreover, TTP was 1.1 times longer for CCSs compared to controls ( $p = 0.09$ ) and was significantly longer in survivors of CNS and renal tumours. Overall, no differences were found between CCSs and controls regarding the probability of ever having had a miscarriage, still birth, or induced abortion. However, CCSs had a significantly increased risk of delivering preterm (OR 2.2, 95%CI 1.3–3.7) and delivering via caesarean section (OR 1.8, 95%CI 1.2–2.6). Treatment with lower abdominal/pelvic radiotherapy was strongly associated with several adverse obstetric outcomes.

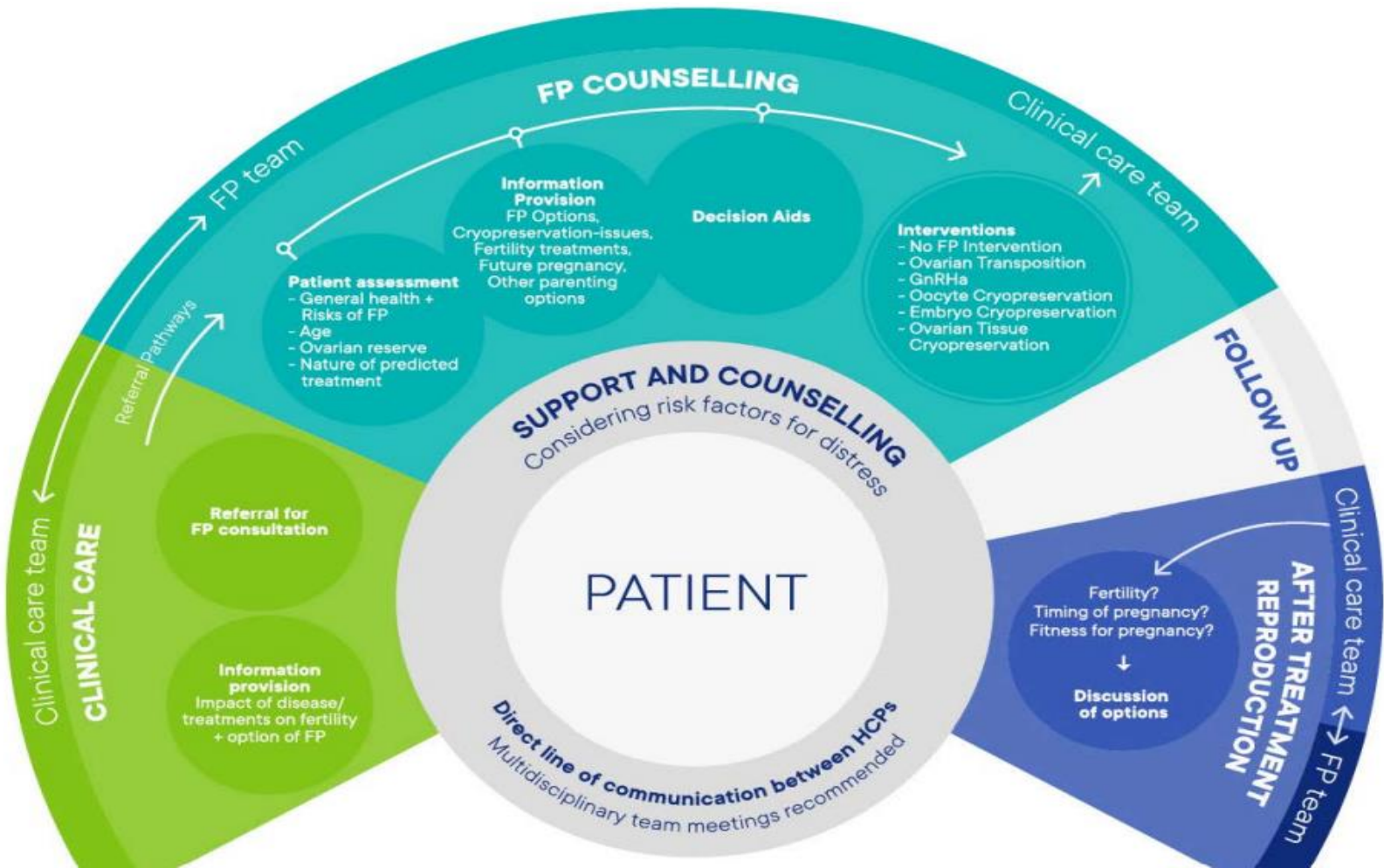
# Our Goal : Ideal Oncofertility Set Up

- No Delay in Appointments
- Time to time co-ordination with Fertility and Oncology team
- Customized Stimulation Protocols (Random Start / Low Estrogen Protocols)
- Advanced Cryopreservation Unit
- Basic to Advanced Fertility Treatment facilities under one roof
- Availability of dedicated super-specialty team 24/7
- Genetic Testing





# Model of Care for Fertility Preservation





I AM REALISTIC.

I EXPECT  
MIRACLES.

# THANK YOU

Department of Reproductive Medicine And Oncofertility  
Ova Fertility And Women Care

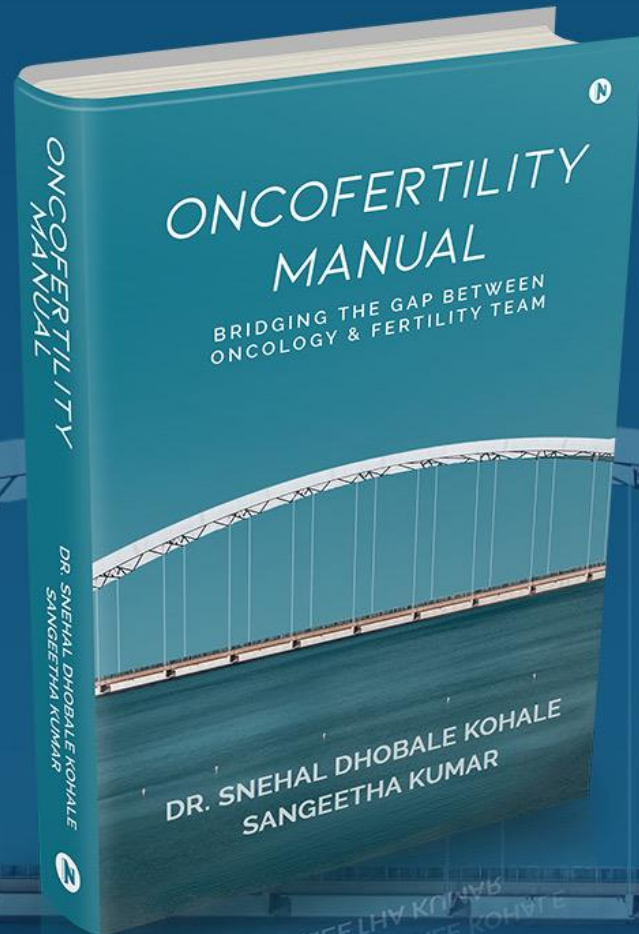
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Certified in Fertility Preservation  
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Senior Embryologist





**AVAILABLE NOW**

