

Planning for the Future: A Review of Cancer in Pregnancy and Fertility

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Cancer and Fertility in Adults¹⁻⁴

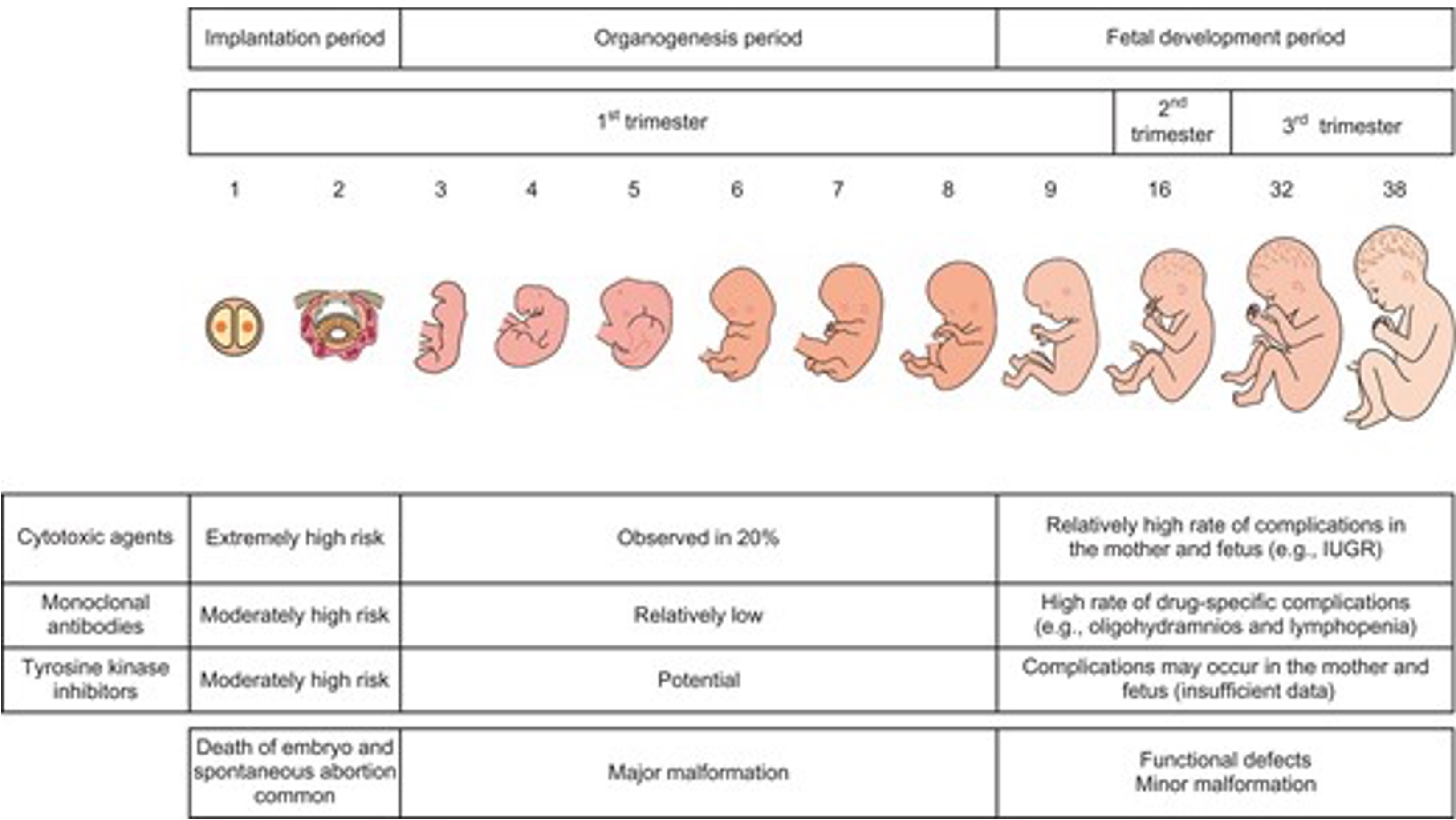
- Surgery
 - Surgery to reproductive organs, endocrine glands, abdomen, or pelvis may affect a patient’s ability to have children
 - Men: surgery may injure nerves in prostate or testicles
 - Women: depending on stage and location of cancer, extensive surgery may be required, resulting in loss of reproductive organs
- Radiation
 - Radiation to the brain may affect pituitary gland, due to proximity, which can affect testosterone, follicle-stimulating hormone, luteinizing hormone, and gonadotropin-releasing hormone
 - Radiation to pelvis or reproductive organs may affect sperm or ovaries
 - Mechanisms exist to protect reproductive organs during radiation treatment
- Antineoplastic agents
 - Alkylating agents and anthracyclines, which are the backbone for many regimens, pose the biggest risk to reproductive organs
 - These agents are especially worrisome as they are utilized frequently in many pediatric regimens as well

Antineoplastic and the Effects on Fetuses⁵⁻⁸

- Administration during pregnancy
 - Administration of chemotherapy during the first trimester increases the risk of congenital abnormalities
 - If chemotherapy needs to be administered during the first trimester, monotherapy is associated with a lower risk of abnormalities
 - The risk of abnormalities when chemotherapy is administered during the second and third trimesters is comparable to women who do not received chemotherapy during pregnancy.
 - Treatment should be stopped when the mother is 33 weeks along to avoid the mother delivering during nadir
- Anti-metabolites: teratogenic; can cause significant abnormalities, miscarriage, or stillbirth
- Rituximab: B-cells may be decreased in child
- Tamoxifen: increases risk of fetal abnormalities
 - However, later stages of pregnancy has higher levels of estrogen, which can worsen hormone related cancers

Safe Antineoplastic Agents During Pregnancy^{5-6,8-9}

- Frequency
 - Administering treatment weekly is more favorable compared to less frequent administration due to the smaller chance of myelosuppression and shorter nadirs
- Chemotherapy
 - Generally, lower rates of placental transfer during second and third trimesters are considered safer
 - Some preferred agents: doxorubicin, cyclophosphamide, vincristine
- Tyrosine kinase inhibitors
 - Safe to give in the second and third trimesters
 - Can cross into the placenta during the first trimester
 - Example: imatinib administered during the first trimester places the fetus at greater risk of anomalies or miscarriage
- Monoclonal antibodies
 - Do not cross into the placenta until after week 15 because they are large and hydrophilic molecules
 - Example: 75% of women who received trastuzumab in the first trimester only gave birth to healthy babies compared to 41.7% of women who received trastuzumab in the second or third trimester
 - Most common side effect: anhydramnios or oligohyramnios



Methods of Fertility Preservation¹⁰

Women	Men
Oocyte cryopreservation	Semen cryopreservation
Ovarian shielding	Testicular shielding
Embryo cryopreservation	Testicular sperm extraction
Ovarian tissue cryopreservation (experimental)	Testicular tissue freezing (experimental)
Oophoropexy	
Radical trachelectomy	
Gonadotropin-releasing hormone agonist	

- Oophoropexy: a procedure to move the ovaries away from the field of radiation temporarily
- Radical trachelectomy: extraction of the cervix, lymph nodes, and the upper vagina
 - The remaining vaginal area and the uterus are then connected via a band that acts the cervix
 - Used for patients with cervical cancer
- Ovarian tissue cryopreservation: surgery that involves the removal of ovarian tissue, freezing the tissue, thawing at a later date, and surgically reattachment
 - Only an option for people who have not gone through puberty
 - Few pregnancies have been reported via this method and more research is needed
- Testicular tissue cryopreservation: surgery that involves the removal of testicular tissue, freezing the tissue, thawing at a later date, and surgically reattachment
 - Only considered an option for people who have not gone through puberty
 - Currently only recommended as part of a clinical trial

References

1. Fertility Issues in Girls and Women with Cancer. Reviewed February 24, 2020. Accessed February 1, 2023. <https://www.cancer.gov/about-cancer/treatment/side-effects/fertility-women>.
2. Fertility Issues in Boys and Men with Cancer. Reviewed February 24, 2020. Accessed February 1, 2023. <https://www.cancer.gov/about-cancer/treatment/side-effects/fertility-men>.
3. Fertility Concerns and Preservation for Men. ASCO. Published September 2019. Accessed February 1, 2023. <https://www.cancer.net/navigating-cancer-care/dating-sex-and-reproduction/fertility-concerns-and-preservation-men>.
4. Fertility Concerns and Preservation for Women. ASCO. Published September 2019. Accessed February 1, 2023. <https://www.cancer.net/navigating-cancer-care/dating-sex-and-reproduction/fertility-concerns-and-preservation-women>.
5. Peccatori FA, Azim Jr HA, Orecchia R, et al. Cancer, pregnancy, and fertility: ESMO clinical practice guidelines for diagnosis, treatment, and follow up. *Ann Oncol*. 2013; 24 Suppl 6: vi160-170. DOI: 10.1093/annonc/mdt199.
6. Esposito S, Tenconi R, Preti V, Gropali E, Principi N. Chemotherapy against cancer during pregnancy: A systematic review on neonatal outcomes. *Medicine* 2015; 95(38): e4899. DOI: 10.1097/MD.0000000000004899.
7. Doll DC, Ringenberg QS, Yarbro JW. Antineoplastic agents and pregnancy. *Semin Oncol*. 1989;16(5):337-46.
8. Miyamoto S, Yamada M, Kasai Y, Miyauchi A, Andoh K. Anticancer drugs during pregnancy. *Jpn J Clin Oncol*. 2016;46(9):795-804. DOI: 10.1093/jco/hyw073.
9. Bader AA, Schlembach D, Tamussino KF, Pristauz G, Petru E. Anhydramnios associated with administration of trastuzumab and paclitaxel for metastatic breast cancer during pregnancy. *Lancet Oncol*. 2007;8(1):79-81. DOI: 10.1016/S1470-2045(06)71014-2.
10. Oktay K, Harvey BE, Partridge AH, et al. Fertility preservation in patients with cancer: ASCO clinical practice guideline update. *J Clin Oncol*. 2018;36(19):1994-2001. DOI: 10.1200/JCO.2018.78.1914.