THERAPY DURING PREGNANCY

Kenneth Alonso, MD, FACP

- 1 case in every 1000 pregnancies
- The five most commonly diagnosed tumors during pregnancy:
- Breast cancer
- Cervical cancer
- Thyroid cancer
- Hodgkin's lymphoma
- Non-Hodgkin's lymphoma

- Molecules of <500 Daltons pass easily through the placenta
- It is rare that molecules >1000 Daltons pass through the placenta
- Lipids pass easily through the placenta
- Polarity, fetal and maternal pH, and the amount of protein bound drug affect placental passage
- Maternal metabolism affects the quantity of drug that reaches the placenta

- No drug should be employed between the time of conception until somites have been formed in the fetus (8-14 days).
- Gastrulation of the embryo begins the second week of conception and terminates the eighth week.
- It is a period of rapid organ development.
- The genitalia, the eyes, the brain, the palate, and the hematopoietic system are sensitive to a teratogenic insult until delivery.

- 5% of fetuses and 1% of neonates of mothers who have received chemotherapy die as a result of treatment.
- Others manifest organ maturation delay.
- As well, >7% of neonates of mothers treated with chemotherapy have birth weights below those from a normal pregnancy
- 5% of neonates from mothers treated with chemotherapy are born prematurely.
- 10-20% of neonates of mothers treated with chemotherapy present major malformations
- 6%, if methotrexate is excluded

- CAT scans, PET scans, or bone scans should not be used during pregnancy.
- Ultrasound examination and MRI without gadolinium do not place the fetus at risk.

- It is better to delay radiotherapy until after delivery.
- >100mGy is associated with a 1% risk of fetal damage.
- ¹³¹I use will damage the fetal thyroid gland.
- If it becomes necessary to radiate cerebral metastases, cervical column lesions, or those of the shoulders, it is possible to radiate those sites when the uterus is protected from radiation.

- Chemotherapy in the first semester should be avoided if at all possible.
- Gestational diabetes and premature rupture of amniotic membranes are found in greater numbers in women treated with chemotherapy in the second or third trimester of pregnancy than in those women who have not been treated.

- Patient weight should be calculated as if she were not pregnant.
- <u>Doxorubicin, epirubicin, vinblastine, vincristine,</u> <u>cyclophosphamide, dacarbazine, paclitaxel,</u> <u>docetaxel, cisplatin, carboplatin, bleomycin, and</u> <u>5FU do not pose a risk to the fetus if used after the</u> <u>first trimester of pregnancy.</u>
- The weekly use of paclitaxel does not require the use of high dose steroids as are required with a three weekly dose of paclitaxel.

- <u>Daunorubicin and idarubicin</u> are lipophilic and cross the placenta. They should not be used in pregnancy.
- <u>Etoposide</u> is associated with malformations. It should not be used in pregnancy.
- <u>Tamoxifen</u> is associated with malformations and ambiguous genitalia.

- The fetal kidney expresses HER2. The use of <u>trastuzumab</u> increases the likelihood of oligohydramnios.
- <u>Rituximab</u> is associated with depletion of fetal B cells and lowers the innate immunity of the neonate.
- <u>Bevacizumab</u> is associated with malformation. It should not be used in pregnancy.

- <u>Trentoin</u> is associated with malformations if used during the first trimester of pregnancy.
- Tyrosine kinase inhibitors such as <u>imanitib</u> should not be used during the first trimester of pregnancy.
- <u>Interferon-a</u> can be used in pregnancy.

- The use of prophylactic low molecular weight heparin (LMWH) for thrombosis prophylaxis is preferred.
- Vitamin K antagonists should be avoided.
- If possible, delivery of the fetus should be postponed until the fetus has completed >35 weeks of gestation
- In those patients treated every 21 days, chemotherapy is delayed from the 34th week onward to avoid chemotherapy induced immunosuppression.

- Chemotherapy should be delayed until after delivery by Cesarian section.
- The mother should not breast feed her infant during chemotherapy.

- Patients presenting with cervical cancer should receive a platinum based therapy instead of undergoing radiotherapy.
- Involved lymph nodes may be removed surgically if necessary.
- Patients presenting with ovarian cancer should receive paclitaxel and carboplatin until delivery.
- Radical surgery can be delayed until after delivery.

References

- I. Gideon Koren, Nathalie Carey, Robert Gagnon, Cynthia Maxwell, Irena Nulman, Vyta Senikas, "Chemotherapy During Pregnancy Working Group," J Obstet Gynaecol Can 2013;35(3):263–278
- Approved by the Society of Obstetricians and Gynecologists of Canada.
- II. HA Azim, FA Peccatori, "Cancer Treatment During Pregnancy," in Veronika Ballová, Mariano Palencio Pulla (eds)., <u>ESMO Handbook of Cancer Treatments</u> <u>in Special Situations</u>. ESMO press. Viganello-Lugano, Switzerland 2013.