Cancer and Pregnancy

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Abstract: Cancer is the cells that grow out of control. Cancer cells can also invade other tissues. Growing out of control and invading other tissues are what makes a cell a cancer cell. Involved in more than 100 diseases, the cancer can cause serious illness and death. Normally, the cells become cancer cells because of DNA damage. This material is a literature collection of the researches on the cancer and pregnancy.
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1. Introduction

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Literatures

Agorastos, T., M. Zafrakas, et al. (2009). "Long-term follow-up after cervical cancer treatment and subsequent successful surrogate pregnancy." Reprod Biomed Online **19**(2): 250-1.

Preservation of fertility is a major concern for premenopausal women after diagnosis of cervical cancer. Successful surrogate pregnancy after treatment for cervical cancer has very rarely been reported. In the present report, a case of successful surrogate pregnancy after radical hysterectomy, lymphadenectomy and ovarian transposition for cervical cancer, followed by radiation therapy, is presented. After stimulation of the transposed ovaries using the short gonadotrophin-releasing hormone (GnRH) analogue protocol, four oocytes were retrieved transabdominally from the genetic mother. IVF followed and two embryos were transferred to the surrogate mother, leading to an uneventful singleton pregnancy, and ultimately normal vaginal delivery of a healthy female infant at term. The unique aspect in this case is the long-lasting favourable outcome for both genetic mother and child, observed during 8.5 years of follow-up, the longest follow-up period reported to date in such cases.

Battaglia, F., F. Plotti, et al. (2006). "Successful pregnancy after conservative surgery for stage IC ovarian cancer with serous borderline tumor on controlateral ovary: a case report." Gynecol Oncol **100**(3): 612-4.

BACKGROUND: In invasive ovarian cancer, fertility saving surgery is confined to early-stage and low-grade disease, and only few study reported sparing fertility up to FIGO stage IC ovarian cancer. CASE: We present a rare case of a 30-year-old woman affected by IC ovarian cancer with borderline tumor on controlateral ovary who underwent "conservative" debulking surgery followed by adjuvant chemotherapy. A spontaneous planned pregnancy occurred 5 years postsurgery. At 60-month follow-up, patients have no evidence of disease. CONCLUSIONS: Nowadays, preservation of ovarian function in women with tumors in early stage should be evaluated for conservative surgery. It is important to emphasize that patients selected for conservative surgery should have complete surgical staging. Careful follow-up is mandatory to ensure safety of this procedure.

Beadle, B. M., W. A. Woodward, et al. (2009). "The impact of pregnancy on breast cancer outcomes in women<or=35 years." Cancer **115**(6): 1174-84.

BACKGROUND: Some evidence suggests that women with pregnancy-associated breast cancers (PABC) have a worse outcome compared with historical controls. However, young age is a worse prognostic factor independently, and women with PABC tend to be young. The purpose of the current study was to compare locoregional recurrence (LRR), distant metastases (DM), and overall survival (OS) in young patients with PABC and non-PABC. METHODS: Data for 668 breast cancers in 652 patients aged<or=35 years were retrospectively reviewed. One hundred four breast cancers (15.6%) were pregnancy-associated; 51 cancers developed

during pregnancy and 53 within 1 year after pregnancy. RESULTS: The median follow-up for all living patients was 114 months. Patients who developed PABC had more advanced T classification, N classification, and stage group (all P<.04) compared with patients with non-PABC. Patients with PABC had no statistically significant differences in 10-year rates of LRR (23.4% vs 19.2%; P=.47), DM (45.1% vs 38.9%; P=.40), or OS (64.6% vs 64.8%; P=.60) compared with patients with non-PABC. For those patients who developed breast cancer during pregnancy, any treatment intervention during pregnancy provided a trend toward improved OS compared with delaying evaluation and treatment until after delivery (78.7% vs 44.7%; P=.068). CONCLUSIONS: Young patients with PABC had no statistically significant differences in LRR, DM, or OS compared with those with non-PABC; however, pregnancy contributed to a delay in breast cancer diagnosis, evaluation, and treatment. Primary care and reproductive physicians should be aggressive in the workup of breast symptoms in the pregnant population to expedite diagnosis and allow multidisciplinary treatment.

Bercovich, D. and G. Goodman (2009). "Pregnancy and lactation after breast cancer elevate plasma prolactin, do not shorten and may prolong survival." Med Hypotheses **73**(6): 942-7.

The affliction of breast cancer is doubled for young patients wishing to have a child. Because estrogens can cause breast cancer and its elevation during pregnancy, clinical advice historically restricted pregnancy to at least 5 years post-diagnosis. Opposing evidence gradually relaxed this. Furthermore, in the last decade it was clarified that overall, post-treatment pregnancy and breast-feeding do not shorten survival. Despite this evidence and patients such as S.B. (deceased) and remarkable L.H. (five children, starting immediately after treatment for node-positive breast cancer), much opposition and restrictive advice remain: additional therapy preferred over pregnancy. In healthy women, pregnancy reduces (cause unknown) the risk of breast cancer and lactation may reduce it. These are accompanied by highly elevated plasma prolactin (PRL) over many months (pregnancy, 15-25 x daily mean 10 ng/ml; lactation, up to 30 x daily mean). PRL concentration too increases in other natural and non-biological conditions, also apparently without increasing breast cancer incidence. Nevertheless, firm and implied support for early pregnancy (and lactation) post-diagnosis and treatment may face a new issue. Over a decade, some studies have claimed epidemiological evidence that a relatively minute PRL elevation (from zero to 0.6-0.8 ng/ml) over mean level increases the risk of breast cancer (i.e. it is a carcinogen) and that this supports (and is supported by) a similar view from some laboratory research. This two-pronged mutuality could create further anxiety and unjustified advice dashing the wish for a child. Is this justified? Epidemiology on PRL and breast cancer risk in the eighties/nineties was contradictory and inconclusive; in the last decade, it was also biologically implausible. 'Positive' laboratory results targeting a 'tamoxifen for PRL' have over-shadowed confounding, negative (often called 'inconsistent') laboratory evidence. Increasingly evident complexity of conflicting biochemical, hormonal, cellular and tissue interactions, confused further by failure of molecular genetics to confirm PRL as a carcinogen, make this target more a mirage than an oasis. While recognizing the value of laboratory research primarily for facts, future progress will be most sound and rapid from observation starting with the human entity, not with its parts. Molecular genetics makes this possible and will be the epicentre of breast cancer research. Meanwhile, young breast cancer patients after initial treatment and eager for a child can today reasonably benefit from advice based on phenomena evolved over eons: pregnancy, lactation and accompanying highly-elevated PRL will not increase risk of recurrence and will in some cases prolong survival.

Berg, G., L. Jacobsson, et al. (2008). "Consequences of inadvertent radioiodine treatment of Graves' disease and thyroid cancer in undiagnosed pregnancy. Can we rely on routine pregnancy testing?" Acta Oncol **47**(1): 145-9.

INTRODUCTION: Radioiodine and most cytostatic treatments are contraindicated in pregnancy. Still, inadvertent therapy does occur. Radioiodine was given to two pregnant women with Graves' disease and thyroid cancer respectively, both in their 20th gestational week. Routine pregnancy tests based on urinary beta-hCG had failed to indicate pregnancy in both cases. METHODS: Estimation of doses to the foetuses and foetal thyroids. Scrutiny of pregnancy testing. RESULTS AND CONCLUSIONS: Doses to foetal thyroids were ablative (250-600 Gy). Total foetal dose in the Graves' patient was 100 mGy and compatible with survival, whereas a foetal dose of approximately 700 mGy together with induced hypothyroidism was fatal for the foetus of the cancer patient. Routine pregnancy tests may fail early and late in pregnancy. The possibility of pregnancy should be considered in all fertile women before therapy with radionuclides or cytostatic regimens, and a clinical investigation undertaken on wide indications with determination of serum beta-hCG, preferably together with an ultrasound examination.

Berveiller, P., O. Mir, et al. (2008). "Ectopic pregnancy in a breast cancer patient receiving trastuzumab." Reprod Toxicol **25**(2): 286-8.

Cervico-isthmic pregnancy is a rare form of ectopic pregnancy with a poor obstetrical prognosis, whose mechanism remains unclear. Preclinical data indicate that HER-2 plays a major role in embryo implantation. We report a case of cervico-isthmic pregnancy occurring during treatment with trastuzumab (Herceptin, a monoclonal antibody to HER-2). A 43-year-old woman presented with abnormal vaginal bleeding, while she was receiving trastuzumab for the last 14 months as an adjuvant therapy for a node-positive, HER-2 positive breast cancer. The diagnosis of evolutive cervico-isthmic pregnancy was confirmed by iterative ultrasonographic examinations. Given the poor obstetrical prognosis, the patient underwent voluntary abortion. The use of trastuzumab during pregnancy is still poorly documented, and its safety is not yet established. Given the importance of HER-2 in embryo implantation and fetal development, its putative role in this abnormal embryo implantation should be discussed.

Bhat, R. A., A. K. Bhat, et al. (2008). "Pregnancy associated breast cancer--the obstetrician's role." J Indian Med Assoc **106**(4): 246, 248.

Breast cancer is the most common cancer in many geographic areas, the most frequent cause of cancer deaths in women, and is also the cancer most likely to be seen during pregnancy and lactation. Delay in diagnosis appears to be the primary reason for the generally worse prognosis overall for all patients with breast cancer diagnosed during pregnancy and lactation. In this context, the patient's family physician or obstetrician who performs the routine antenatal examinations can play an important role by performing a vital breast examination which might bring to light and prompt timely investigation of otherwise asymptomatic breast masses.

Bodner-Adler, B., K. Bodner, et al. (2007). "Breast cancer diagnosed during pregnancy." Anticancer Res **27**(3B): 1705-7.

Cancer is rare during pregnancy, but breast cancer is the second most common cancer in pregnant women. Pregnancy-associated breast cancer (PABC) is defined as breast cancer that occurs during pregnancy or within one year of delivery. Five cases of PABC occurring during the second and third trimester of pregnancy managed at the University Hospital of Vienna during the year 2005/2006 are reported. A review of the available literature is also presented. Five patients were diagnosed with PABC which was detected in completely different weeks of pregnancy. In two women, the diagnosis was made during the second trimester of pregnancy and in three during the third trimester. The treatment depended, among other things, on the gestational age at diagnosis. The patients diagnosed during the second trimester received six courses of neoadjuvant chemotherapy type FEC (5-fluorouracil, epirubicin, cyclophosphamide). Locoregional radiotherapy and surgery were postponed until after delivery. The three patients diagnosed during the third trimester received adequate therapy after delivery. The mean age of the patients at the time of diagnosis was 37 years (range: 33-40 years) and all patients were diagnosed at an advanced stage. All patients were alive and free of symptoms and signs at the time of writing. All infants are healthy and no congenital malformation or stillbirth was observed. In conclusion, late diagnosis and poor prognosis of PABC are common in literature. Treatment options seem to be reduced in pregnant women and mainly depend on the patient's condition as well as on the gestational age at presentation. In a multidisciplinary approach, an optimal therapy schedule should be assessed depending on these two conditions.

Boyd, A., V. Cowie, et al. (2009). "The use of cisplatin to treat advanced-stage cervical cancer during pregnancy allows fetal development and prevents cancer progression: report of a case and review of the literature." Int J Gynecol Cancer **19**(2): 273-6.

BACKGROUND: Cervical cancer is one of the most frequently encountered malignancies in pregnancy. For early-stage disease arising in late second/third trimester, treatment may be delayed until delivery. However, in advanced disease, data are lacking. CASE: A 26-year-old woman presented at 21 weeks gestation with a stage IIB high-grade clear cell cervical carcinoma. At 25 + 1 weeks gestation, cisplatin 100 mg/m(2) every 21 days was commenced. One month after cycle 3, a healthy infant was delivered. Thereafter, further cisplatin, intracavity cesium, and chemoradiation were administered. Findings from subsequent clinical examination and magnetic resonance imaging were normal. Fifteen months post treatment, both patient and baby remain well. CONCLUSION: Neoadjuvant cisplatin chemotherapy can be used in stage IIB cervical carcinoma during pregnancy to allow fetal development and prevent disease progression before delivery.

Calhoun, K. and N. Hansen (2005). "The effect of pregnancy on survival in women with a history of breast cancer." Breast Dis **23**: 81-6.

Nearly 25% of individuals diagnosed with breast cancer will be pre-menopausal women. As maternal age of first birth has risen in the United States, more females are being treated for breast cancer prior to child-bearing. Although surgery and radiation therapy appear to have no impact on future fertility, young women should be aware of the impact that systemic chemotherapy may have on ovarian function, as well as on future offspring. As regards survival, despite a link between female sex hormones and mammary carcinogenesis, the fear that pregnancy subsequent to breast cancer treatment would result in activation of dormant micrometastases has not been demonstrated in the literature. Published series have, in fact, shown either no impact on survival or a slightly protective effect when women deliver after breast cancer treatment. Although these studies are retrospective in nature and may be prone to selection bias and under-reporting of the true denominator, they can at a minimum be used to reassure women that a subsequent pregnancy is unlikely to have a negative impact on her survival.

Caluwaerts, S., V. A. N. C. K, et al. (2006). "Neoadjuvant chemotherapy followed by radical hysterectomy for invasive cervical cancer diagnosed during pregnancy: report of a case and review of the literature." Int J Gynecol Cancer **16**(2): 905-8.

Although cervical carcinoma is among the most frequently encountered malignancies during pregnancy, only four cases of neoadjuvant chemotherapy during pregnancy have been reported. A 28-year-old A0P1G2M0 was diagnosed at 15 weeks with stage Ib1 invasive squamous cervical cancer. Because she strongly desired the continuation of this pregnancy, after extensive counseling she was treated with 75 mg/m(2) cisplatin every 10 days starting at 17 weeks. After six cycles, clinically and radiologically stable disease with normalization of the squamous cell carcinoma tumor marker was obtained. An elective cesarean delivery followed by radical hysterectomy and lymphadenectomy was performed at 32 weeks gestation. The pathology report revealed a moderately differentiated squamous cell carcinoma of 3.5 cm, and all 33 lymph nodes were free of disease. Neonatal examination of the baby could not reveal any abnormalities, and this was confirmed at 6 months. The use of neoadjuvant chemotherapy enabled us to continue this pregnancy until the fetus was viable. Cisplatin did not influence the short-term outcome, but only a long-term follow-up will inform us on its safety during pregnancy.

Campagnoli, C., C. Abba, et al. (2005). "Pregnancy, progesterone and progestins in relation to breast cancer risk." J Steroid Biochem Mol Biol **97**(5): 441-50.

In the last two decades the prevailing opinion, supported by the "estrogen augmented by progesterone" hypothesis, has been that progesterone contributes to the development of breast cancer (BC). Support for this opinion was provided by the finding that some synthetic progestins, when added to estrogen in hormone replacement therapy (HRT) for menopausal complaints, increase the BC risk more than estrogen alone. However, recent findings suggest that both the production of progesterone during pregnancy and the progesterone endogenously produced or exogenously administered outside pregnancy, does not increase BC risk, and could even be protective. The increased BC risk found with the addition of synthetic progestins to estrogen in HRT seems in all likelihood due to the fact that these progestins (medroxyprogesterone acetate and 19-nortestosterone-derivatives) are endowed with some non-progesterone-like effects which can potentiate the proliferative action of estrogens. The use of progestational agents in pregnancy, for example to prevent preterm birth, does not cause concern in relation to BC risk.

Chen, J., R. J. Lee, et al. (2004). "Does radiotherapy around the time of pregnancy for Hodgkin's disease modify the risk of breast cancer?" Int J Radiat Oncol Biol Phys **58**(5): 1474-9.

PURPOSE: To determine whether the risk of secondary breast cancer after radiotherapy (RT) for Hodgkin's disease is greater among women who underwent RT around time of pregnancy. METHODS AND MATERIALS: The records of 382 women treated with RT for Hodgkin's disease were reviewed and divided into those who received RT around the time of pregnancy and those who were not pregnant. Comparisons of the overall incidence, actuarial rates, and latency to breast cancer between the two groups were made. Multivariate Cox regression modeling was performed to determine possible contributing factors. RESULTS: Of the 382 women, 14 developed breast cancer (3.7%). The increase in the overall incidence (16.0% vs. 2.3%, $p = 0.0001$) and the actuarial rate of breast cancer among the women in the pregnant group ($p = 0.011$) was statistically significant. The women treated around the time of pregnancy had a 10- and 15-year actuarial rate of breast cancer of 6.7% and 32.6%, respectively. The 10-year and 15-year actuarial rate for the nonpregnant women was 0.4% and 1.7%, respectively. The median latency from RT to the diagnosis of breast cancer was 13.1 and 18.9 years for women in the pregnant and nonpregnant groups, respectively. In the multivariate analysis, pregnancy around the time of RT was the only

variable associated with an increased risk of breast cancer. The risk was dependent on the length of time from pregnancy to RT, with women receiving RT during pregnancy and within 1 month of pregnancy having an increased risk of breast cancer compared with nonpregnant women and women irradiated later than 1 month after pregnancy (hazard ratio, 22.49; 95% confidence interval, 5.56-90.88; p <0.001). CONCLUSION: The results of this study indicate that the risk of breast cancer after RT is greater with irradiation around the time of pregnancy. This suggests that pregnancy is a time of increased sensitivity of breast tissue to the carcinogenic effects of radiation. Because of the small sample size and limited follow-up, additional studies are recommended to confirm these findings.

De Carolis, S., F. Grimolizzi, et al. (2006). "Cancer in pregnancy: results of a series of 32 patients." Anticancer Res **26**(3B): 2413-8.

BACKGROUND: Cancer complicates approximately 1 in 1000 pregnancies. In pregnancy management, whether the benefits outweigh the risks derived from therapy must be carefully considered. MATERIALS AND METHODS: Thirty-two pregnant patients with the diagnosis of malignancy were followed. The indications and timing for surgery, chemotherapy, radiotherapy or delayed treatment were decided according to the malignancy characteristics and gestational age. The patient's consent was obtained before every decision. RESULTS: The rate of live births, premature deliveries, foetal abnormalities and neonatal deaths was 97%, 82%, 9% and 3%, respectively. Three women (9%) died during puerperium because of disease progression. CONCLUSION: The cancer treatment took into full consideration the specific condition of each pregnant patient. A good rate of live births was observed, even if a high rate of preterm delivery occurred. The management of malignancy required a team of experts in order to optimise every available choice for maternal health and neonatal well-being.

de Wildt, S. N., N. Taguchi, et al. (2009). "Unintended pregnancy during radiotherapy for cancer." Nat Clin Pract Oncol **6**(3): 175-8.

BACKGROUND: A 27-year-old woman with upper mediastinum stage IIA Hodgkin lymphoma was treated with six cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine chemotherapy. Two months later she received a total of 4,250 cGy to the upper mediastinum and left clavicular region over a 1-month period. One week after completion of radiotherapy she was found to be 13-weeks pregnant. Her physician advised her to terminate pregnancy. She contacted a teratology information service for further information regarding the risks of radiation exposure for her fetus. INVESTIGATIONS: Estimation of fetal radiation exposure, literature review and synthesis of published cases and effects of fetal radiation exposure. DIAGNOSIS: Estimated fetal radiation dose between 5 and 18 cGy. MANAGEMENT: Counseling on the possible risks to the fetus as a result of radiation exposure.

Del Mastro, L., T. Catzeddu, et al. (2006). "Infertility and pregnancy after breast cancer: current knowledge and future perspectives." Cancer Treat Rev **32**(6): 417-22.

Fertility impairment induced by adjuvant treatments and potential risk associated with pregnancy, are major concerns of young pre-menopausal patients with early breast cancer. Although current evidences suggest that pregnancy does not negatively affect prognosis, a low rate (3-8%) of pregnancy after breast cancer has been reported. Among the potential causes of such a low rate there are a high chance of spontaneous abortions (25%) as well as the fertility impairment induced by adjuvant treatments. No standard strategy to preserve fertility in breast cancer patients is available so far. Experimental approaches include cryopreservation strategies, and use of gonadotropin-releasing hormone (GnRH) agonists to render germinal epithelium quiescent and less sensitive to the chemotherapy cytotoxicity. Here, we reviewed current knowledge about incidence and risks of pregnancy after breast cancer, risks of ovarian failure after adjuvant treatments and experimental strategies aiming to preserve ovarian function and fertility in young breast cancer patients.

Demirol, A., M. Bahce, et al. (2005). "Pregnancy following intracytoplasmic sperm injection and preimplantation genetic diagnosis after the conservative management of endometrial cancer." Reprod Biomed Online **10**(6): 770-3.

A rare case of a patient with conservatively treated endometrial carcinoma who conceived and delivered a healthy baby after the transfer of embryos with intracytoplasmic sperm injection (ICSI) and preimplantation genetic diagnosis (PGD) is presented. A 41-year-old woman had an office hysteroscopy in the infertility work-up and stage I endometrial adenocarcinoma was diagnosed. After conservative treatment, the patient underwent ICSI and PGD. She achieved pregnancy with two normal embryos. Two gestational sacs were observed but one of them was blighted. The patient subsequently delivered a healthy female infant. Repeated office hysteroscopy and endometrial sampling was performed after delivery. The appearance of the endometrium was normal on

hysteroscopy, and the histology report was normal. The principal concern with medical therapy is that the lesion cannot be fully evaluated until the hysterectomy is performed, the nodes palpated, and the uterus is sectioned. The patient was referred to a gynaecological oncologist for definitive surgery.

Diamond, J. R., C. A. Finlayson, et al. (2009). "Early-stage BRCA2-linked breast cancer diagnosed in the first trimester of pregnancy associated with a hypercoagulable state." Oncology (Williston Park) **23**(9): 784-91.

This patient was found to have a BRCA2 gene mutation. She underwent lumpectomy and axillary lymph node dissection without any evidence of lymph node metastasis. Systemic chemotherapy with doxorubicin and cyclophosphamide for four cycles was administered beginning in the second trimester. She was treated with prophylactic LMWH until delivery and then for 6 weeks postpartum. She delivered a healthy baby boy and, after a period of breast-feeding, underwent bilateral mastectomy with immediate reconstruction. She remains well and is expecting her second child. Prophylactic oophorectomy is planned after completion of this pregnancy.

Dunkelberg, J. C., J. Barakat, et al. (2005). "Gastrointestinal, pancreatic, and hepatic cancer during pregnancy." Obstet Gynecol Clin North Am **32**(4): 641-60.

Pregnancy affects the clinical presentation, evaluation, treatment, and prognosis of patients with gastrointestinal cancer. Pregnant patients may present with advanced gastrointestinal cancer as a result of delayed diagnosis, in part because of difficulty differentiating signs and symptoms of cancer from signs and symptoms of normal pregnancy. The approach to cancer surgery and chemotherapy must be modified in pregnant patients to minimize fetal and maternal risks. Because of these factors, women who develop gastrointestinal cancers during pregnancy seem to have a poor prognosis. This article focuses on cancers of the colon, stomach, pancreas, and liver that occur during pregnancy.

Edgar, A. B. and W. H. Wallace (2007). "Pregnancy in women who had cancer in childhood." Eur J Cancer **43**(13): 1890-4.

The majority of female cancer survivors will have normal reproductive function and would be expected to have a successful pregnancy. For the minority of young women who have received significant cytotoxic insult to the reproductive organs and yet still manage to conceive, pregnancy must be considered a high risk condition and these patients should be managed by a multidisciplinary specialist team. Female survivors of childhood cancer who are able to become pregnant carry an excess risk of preterm delivery and low birth weight baby. This restricted foetal growth and inability of the uterus to carry the foetus to term is associated with radiation-induced damage to the uterus. Chemotherapy does not appear to be associated with adverse pregnancy outcomes. However, prospective follow-up of cohorts of patients treated with contemporary therapies, frequently involving more intensive therapies are required to determine the risk. A number of large multi-centre studies, are underway and will provide new insights into pregnancy outcomes in survivors of childhood cancer.

Eedarapalli, P., N. Biswas, et al. (2007). "Epirubicin for breast cancer during pregnancy: a case report." J Reprod Med **52**(8): 730-2.

BACKGROUND: The rarity of breast cancer in pregnancy and conflict between the optimal maternal therapy and fetal risks make its management challenging. Chemotherapy is the standard treatment for advanced cases. Epirubicin as a combination agent has been reported for breast and other cancers in pregnancy but not as a single agent. We report a case of advanced breast cancer treated with epirubicin neoadjuvant chemotherapy in pregnancy. CASE: A 30-year-old primigravida with multifocal, grade 3 invasive ductal carcinoma, stage T2 N1M0, received 4 cycles of primary epirubicin chemotherapy in pregnancy from 23 weeks' gestation. The chemotherapy was well tolerated by the mother and fetus, and a good response was achieved prior to postnatal combination chemotherapy and definitive surgery. CONCLUSION: Epirubicin chemotherapy appears safe and effective in pregnancy.

Eedarapalli, P. and S. Jain (2006). "Breast cancer in pregnancy." J Obstet Gynaecol **26**(1): 1-4.

Breast cancer in pregnancy is rare with an incidence of 1:3,000 to 1:10,000 and is the second most common after cervical cancer. The outlook for such patients is less favourable than that of non-pregnant women probably because the stage of the disease is more advanced when it is discovered and also due to delay in therapy. The need for prompt treatment presents a clinical dilemma of considerable magnitude as there is always a conflict between optimal maternal therapy and the resultant risks imposed on fetal well-being. In the absence of a standardised protocol for management, this review focuses on the issues of diagnosis and treatment of breast cancer in pregnancy. Relevant current literature using Medline search strategy was examined.

Engels, E. A., J. Chen, et al. (2004). "Poliovirus vaccination during pregnancy, maternal seroconversion to simian virus 40, and risk of childhood cancer." Am J Epidemiol **160**(4): 306-16.

Before 1963, poliovirus vaccine produced in the United States was contaminated with simian virus 40 (SV40), which causes cancer in animals. To examine whether early-life SV40 infection can cause human cancer, the authors studied 54,796 children enrolled in the US-based Collaborative Perinatal Project (CPP) in 1959-1966, 52 of whom developed cancer by their eighth birthday. Those children whose mothers had received pre-1963 poliovirus vaccine during pregnancy (22.5% of the children) had an increased incidence of neural tumors (hazard ratio = 2.6, 95% confidence interval: 1.0, 6.7; 18 cases) and hematologic malignancies (hazard ratio = 2.8, 95% confidence interval: 1.2, 6.4; 22 cases). For 50 CPP children with cancer and 200 CPP control children, the authors tested paired maternal serum samples from pregnancy for SV40 antibodies using a virus-like particle enzyme immunoassay and a plaque neutralization assay. Overall, mothers exhibited infrequent, low-level SV40 antibody reactivity, and only six case mothers seroconverted by either assay. Using the two SV40 assays, maternal SV40 seroconversion during pregnancy was not consistently related to children's case/control status or mothers' receipt of pre-1963 vaccine. The authors conclude that an increased cancer risk in CPP children whose mothers received pre-1963 poliovirus vaccine was unlikely to have been due to SV40 infection transmitted from mothers to their children.

Epstein, R. J. (2007). "Adjuvant breast cancer chemotherapy during late-trimester pregnancy: not quite a standard of care." BMC Cancer **7**: 92.

BACKGROUND: Diagnosis of breast cancer during pregnancy was formerly considered an indication for abortion. The pendulum has since swung to the other extreme, with most reviews now rejecting termination while endorsing immediate anthracycline-based therapy for any pregnant patient beyond the first trimester. To assess the evidence for this radical change in thinking, a review of relevant studies in the fields of breast cancer chemotherapy, pregnancy, and drug safety was conducted. DISCUSSION: Accumulating evidence for the short-term safety of anthracycline-based chemotherapy during late-trimester pregnancy represents a clear advance over the traditional norm of therapeutic abortion. Nonetheless, the emerging orthodoxy favoring routine chemotherapy during gestation should continue to be questioned on several grounds: (1) the assumed difference in maternal survival accruing from chemotherapy administered earlier--i.e., during pregnancy, rather than after delivery--has not been quantified; (2) the added survival benefit of adjuvant cytotoxic therapy prescribed within the hormone-rich milieu of pregnancy remains presumptive, particularly for ER-positive disease; (3) the maternal survival benefit associated with modified adjuvant regimens (e.g., weekly schedules, omission of taxanes, etc.) has not been proven equivalent to standard (e.g., post-delivery) regimens; and (4) the long-term transplacental and transgenerational hazards of late-trimester chemotherapy are unknown. SUMMARY: Although an incrementally increased risk of cancer-specific mortality is impossible to exclude, mothers who place a high priority on the lifelong well-being of their progeny may be informed that deferring optimal chemotherapy until after delivery is still an option to consider, especially in ER-positive, node-negative and/or last-trimester disease.

Fanale, M. A., A. R. Uyei, et al. (2005). "Treatment of metastatic breast cancer with trastuzumab and vinorelbine during pregnancy." Clin Breast Cancer **6**(4): 354-6.

The management of breast cancer during pregnancy is a crucial clinical issue. It is important to evaluate the impact of chemotherapy on a woman and her fetus. Studies from our institution have demonstrated the safety and efficacy of treating women with adjuvant 5-fluorouracil/doxorubicin/cyclophosphamide during the second or third trimester of pregnancy. However, the literature regarding the treatment of metastatic breast cancer in a pregnant patient is scarce. In this article, we describe the successful treatment of a woman at 27 weeks of pregnancy with recurrent HER2/neu-overexpressing breast cancer who was symptomatic from multiple liver metastases. Per our review of the literature and to our knowledge, she is the first patient to be treated with weekly vinorelbine plus trastuzumab. Our patient had near complete resolution of her disease and delivered a healthy male infant at 34 weeks of gestation.

Fukushima, K., S. Ogawa, et al. (2009). "Can we diagnose invasive cervical cancer during pregnancy as precise as in nonpregnant women?: maternal and perinatal outcome in pregnancies complicated with cervical cancers." Int J Gynecol Cancer **19**(8): 1439-45.

Cervical cancer is the most common gynecologic malignancy associated with pregnancy. However, there are no consensus guidelines that define the indications for or the optimal length of expectant management. The subjects were women who had a preexisting invasive cervical cancer or

whose cancers were diagnosed during pregnancy or within 12 months after delivery. Thirty-nine consecutive women with cervical cancer, whose ages ranged from 20 to 40 years, were chosen as controls. We performed a retrospective chart review on the maternal profile and perinatal outcome and compared the clinical features between pregnancy- and non-pregnancy-associated cervical cancer in patients. The percentage of asymptomatic cases in which cancer was detected in a routine Papanicolaou test was significantly higher in the pregnant patients. The percentage of induced preterm labor or therapeutic abortions was 50%. Expectant management (mean length, 19.8 weeks) was chosen by 5 patients, and there were no cases of recurrence or death from disease. Seven subjects, including 5 patients whose diagnoses were changed from cervical intraepithelial neoplasm or condyloma to cancer, were managed as "unexpected expectant" because these subjects were not diagnosed as having stage IA/IB cancer during pregnancy. All of these subjects underwent vaginal delivery and included 2 patients with death from disease and lymph node recurrence. The percentage in which disease severity was underestimated was higher in pregnant patients. The option of therapeutic delay should be carefully discussed. Patient counseling should address the issue that risk may not be precisely estimated because of the possibility that disease severity may be underestimated during pregnancy.

Gadducci, A., S. Cosio, et al. (2003). "Chemotherapy with epirubicin and paclitaxel for breast cancer during pregnancy: case report and review of the literature." Anticancer Res **23**(6D): 5225-9.

BACKGROUND: Breast cancer diagnosed during pregnancy is a challenging clinical situation. Little data are currently available about chemotherapy in pregnant women with this malignancy. CASE REPORT: We report the case of a 36-year-old pregnant woman with a T2N1M0 breast cancer who received sequential chemotherapy including epirubicin (120 mg/m2 every three weeks for four cycles) and paclitaxel (175 mg/m2 every three weeks for three cycles) from the 14th to the 32nd week of gestation. The patient delivered a normal female baby by caesarean section at the 36th week. The immunohistochemical examination of the placenta showed a diffuse, strong P-glycoprotein expression. Thirty-six months after the delivery, the mother was disease-free and the infant showed normal development and growth. DISCUSSION: Sequential chemotherapy including epirubicin and paclitaxel should be taken into consideration as adjuvant treatment for pregnant women with high-risk breast cancer. The strong placental expression of P-glycoprotein may play a major role in limiting fetal exposure to anthracyclines and taxanes.

Garcia-Manero, M., M. P. Royo, et al. (2009). "Pregnancy associated breast cancer." Eur J Surg Oncol **35**(2): 215-8.

BACKGROUND: Breast carcinoma during pregnancy put the health of the mother in conflict with that of the foetus. The aim is to give optimal treatment to the mother to maximise the chances of survival, whilst minimising the risk of harm of the foetus. We report the epidemiology, pathology, clinical picture, therapeutic management and foetal outcome of pregnant women with breast cancer treated in our institution. PATIENTS AND METHODS: Twenty-two pregnant breast cancer patients were treated in our hospital from January 1996 to October 2006. Parents were surveyed by mail or telephone regarding outcomes of children exposed to chemotherapy in uterus. RESULTS: The treatment of breast cancer pregnancy should conform as closely as possible to standardised protocols for patients without concomitant pregnancy. Most of the patients underwent surgery during pregnancy In four cases diagnosed during the first trimester chemotherapy was initiated during the 10th week when organogenesis period was finished. None of the children exposed to chemotherapy during this trimester presented congenital malformations. All 11 cases diagnosed during second and third trimester were treated with Doxorrubicin, Fluoracil and Cyclophosphamide and four cases were treated with taxanes. No congenital malformations were detected. CONCLUSION: Breast cancer can be treated with FAC chemotherapy during the second and third trimesters without significant complications for the children exposed to chemotherapy in uterus. We report four cases treated with taxanes after the first trimester and no congenital anomalies were observed.

Garrido, M., J. Clavero, et al. (2008). "Prolonged survival of a woman with lung cancer diagnosed and treated with chemotherapy during pregnancy. Review of cases reported." Lung Cancer **60**(2): 285-90.

Lung cancer is the most common cause of cancer death in women in the US, diagnosis during pregnancy is rare and has been reported 34 times. We report a case of a 34-year-old woman with stage III locally advanced lung cancer diagnosed during the 27th week of pregnancy. Chest X-ray and thorax MRI revealed a 9cmx7cm mass in the upper right lung lobe. CT guided FNA biopsy indicated adenocarcinoma. Neoadjuvant chemotherapy was administered with vinorelvine (Navelbine) and cisplatin for three cycles with partial response. At 39 weeks, she delivered a healthy baby. Right upper lobectomy with complete

lymphadenectomy was performed 3 weeks later. Final pathology was reported as an adenocarcinoma of 7.5cmx6.2cm with involvement of 16/30 lymph nodes. She received three additional cycles of chemotherapy and radiotherapy. Follow-up with CT scan after 11 months did not show recurrence.

Goncalves, C. V., G. Duarte, et al. (2009). "Diagnosis and treatment of cervical cancer during pregnancy." Sao Paulo Med J **127**(6): 359-65.

CONTEXT AND OBJECTIVE: One third of all cervical carcinomas occur during the reproductive period. Cervical carcinoma is the second greatest cause of death due to cancer during this phase. The estimated frequency of cervical cancer during pregnancy is one case for every 1,000 to 5,000 pregnancies. The aim here was to provide information about the difficulties in diagnosing and managing cervical neoplasia during pregnancy. MATERIALS: A systematic review of the literature was undertaken through the PubMed, Cochrane, Excerpta Medica (Embase), Literatura Latino Americana e do Caribe em Ciencias da Saude (Lilacs) and Scientific Electronic Library Online (SciELO) databases, using the following words: pregnancy, cervical cancer, diagnosis and management. RESULTS: There was a consensus in the literature regarding diagnosis of cervical carcinoma and management of preneoplastic lesions during pregnancy. However, for management of invasive carcinoma, there was great divergence regarding the gestational age taken as the limit for observation rather than immediate treatment. CONCLUSION: All patients with cytological abnormalities should undergo colposcopy, which will indicate and guide biopsy. Conization is reserved for patients with suspected invasion. High-grade lesions should be monitored during pregnancy and reevaluated after delivery. In cases of invasive carcinoma detected up to the 12th week of pregnancy, patient treatment is prioritized. Regarding diagnoses made during the second trimester, fetal pulmonary maturity can be awaited, and the use of chemotherapy to stabilize the disease until the time of delivery appears to be viable.

Green, D. M., J. A. Whitton, et al. (2003). "Pregnancy outcome of partners of male survivors of childhood cancer: a report from the Childhood Cancer Survivor Study." J Clin Oncol **21**(4): 716-21.

PURPOSE: This study was undertaken to determine the effect, if any, on pregnancy loss, live births, and birthweight of treatment for cancer diagnosed during childhood or adolescence. PATIENTS AND METHODS: We reviewed pregnancy outcome among sexually active male Childhood Cancer Survivor Study (CCSS) participants who responded to a questionnaire before February 3, 2000. Medical records of all members of the cohort were abstracted to obtain chemotherapeutic agents administered, the cumulative dose of drug administered for several drugs of interest, and the doses, volumes, and dates of administration of all radiotherapy. RESULTS: There were 4,106 sexually active males; 1,227 reported they sired 2,323 pregnancies (69% live births, 1% stillbirths, 13% miscarriages, 13% abortions, 5% unknown or in gestation). The male-to-female ratio of the offspring of the partners of the male survivors was significantly different from that of the offspring of the partners of the male siblings of the survivors (1.0:1.03 v 1.24:1.0) (P =.016). The proportion of pregnancies of the partners of male survivors that ended with a liveborn infant was significantly lower than for the partners of the male siblings of the survivors who were the control group for comparison (relative risk = 0.77, P =.007). There were no significant differences in pregnancy outcome by treatment. CONCLUSION: This large study did not identify adverse pregnancy outcomes for the partners of male survivors treated with most chemotherapeutic agents. The reversal of the sex ratio and the association observed for procarbazine warrant further investigation.

Grupp, S., A. Einarson, et al. (2007). "Cancer in pregnancy: Motherisk on-line question and answer forum." Can Fam Physician **53**(11): 1891-2.

QUESTION: It seems to me that cancer is occurring or being diagnosed more frequently among young women who are or might become pregnant. In the past year, I have seen several such women in my practice and I have had difficulty finding appropriate information in order to counsel them. Is there somewhere I can go for information about cancer during pregnancy so that I can better educate and inform these patients? ANSWER: The Motherisk Program at the Hospital for Sick Children supports an on-line Cancer in Pregnancy Forum where physicians and other health care professionals can submit questions or details of experiences that they have had with patients who had cancer during pregnancy. Questions about the safety of chemotherapeutic drugs before and during pregnancy and about possible exacerbation of previous cancer by pregnancy are most common.

Gurgan, T., C. Salman, et al. (2008). "Pregnancy and assisted reproduction techniques in men and women after cancer treatment." Placenta **29 Suppl B**: 152-9.

There are many male and female patients of young age diagnosed with some form of invasive cancer. With current treatment regimens, including aggressive chemotherapy, radiotherapy, bone marrow

transplantation, and surgery, the cure rate for some malignancies now is very high. These treatments, however, can lead to gonadal failure and permanent infertility. Fertility preservation is a significant concern for such men and women faced with cancer treatment. Several alternatives have been attempted in an effort to preserve fertility in young women undergoing cancer treatment. Although ovarian tissue cryopreservation has recently been the focus of intense investigation, cryopreservation of embryos and mature oocytes has several advantages over ovarian tissue preservation. Also there are some strategies for minimizing female gonadal toxicity caused by cancer therapy including use of radiation shields, transposition of the ovaries out of the irradiation field, and suppression of ovaries by administration of gonadotropin releasing hormone agonists during adjuvant chemotherapy. In addition, fertility-saving surgical approaches are used in selected women with gynecologic cancers instead of more radical surgical procedures. Similarly, fertility preservation options such as conservative surgical approaches including partial orchiectomy with or without cryopreservation in testicular cancer patients and at least sperm cryopreservation in other male cancer patients should be offered before initiating therapy. Use of embryonic stem cells as a source of gametes also emerges as a hope in male and female cancer survivors.

Hahn, H. S., S. G. Yoon, et al. (2009). "Conservative treatment with progestin and pregnancy outcomes in endometrial cancer." Int J Gynecol Cancer **19**(6): 1068-73.

INTRODUCTION: The purpose of this study was to evaluate the efficacy of conservative treatment with progestin and pregnancy outcomes in women with early-stage endometrial cancer. METHODS: We retrospectively analyzed the medical records of 35 patients with endometrial adenocarcinoma, who were treated with progestin from January 1996 to December 2006. Women with early-stage grade 1 endometrioid endometrial adenocarcinoma, who wanted to receive conservative treatment or preserve fertility, were included. All women were treated with medroxyprogesterone acetate or megestrol acetate, with regular dilation and curettage performed. Complete remission (CR) was defined as no evidence of endometrial adenocarcinoma or hyperplasia. Partial remission was diagnosed when the patient developed endometrial hyperplasia, and persistent disease was defined as residual endometrial adenocarcinoma by pathologic confirmation. RESULTS: The median age was 31 years (range, 21-43 years), and the median follow-up period was 39 months (range, 5-108 months). Complete remission was achieved in 22 patients (62.9%), partial remission was achieved in 1 patient (2.9%), and 12 patients (34.3%) had persistent disease. The median time to CR was 9 months (range, 2-12 months). Of the 22 patients with CR, 9 (40.9%) had recurrent disease, and the median time to recurrence was 12 months (range, 8-48 months). Ten (83.3%) of the 12 patients with CR who tried to conceive were successful, and 8 of the 10 pregnancies resulted in live births. There were no congenital anomalies in babies associated with progestin treatment. CONCLUSIONS: Conservative treatment with progestin can be considered a good therapeutic option in patients with well-differentiated early-stage endometrioid endometrial adenocarcinoma who wish to preserve their uteri or become pregnant.

Halaska, M. J., G. Pentheroudakis, et al. (2009). "Presentation, management and outcome of 32 patients with pregnancy-associated breast cancer: a matched controlled study." Breast J **15**(5): 461-7.

Pregnancy-associated breast cancer (PABC) is a rare and challenging problem. We sought to describe epidemiology, management and outcome of women in whom breast cancer was diagnosed during pregnancy or within one year after delivery. Thirty-two women with PABC were referred to two European Union oncology centers between 1995 and 2007, 16 during pregnancy and 16 within 1 year after delivery. Data concerning diagnosis, management, delivery and fetal and maternal outcome were recorded. A group of 32 patients (matched controls) presenting with nonpregnancy-associated breast cancer (non-PABC) was matched for age at diagnosis, tumor size and stage to each PABC patient. Differences in outcome between the PABC and non-PABC groups were then assessed. Histological features were similar in both groups, except that estrogen receptor-negative tumors were more common in the PABC group. Three patients received chemotherapy and two others underwent surgery during pregnancy, with no excess toxicity or severe maternal/fetal adverse effects. All children in the PABC group were healthy, except for one exposed to epirubicin in utero and born with rectal atresia. Overall survival was similar in PABC and non-PABC patients ($p = 0.449$). The subgroup of patients with breast cancer diagnosed within one year after delivery showed a shorter time to relapse than controls or patients with gestational cancer ($p = 0.0178$). PABC is a special situation, necessitating individualized, multi-disciplinary management. Prognosis is similar for women with nongestational cancer matched for age and stage though poorer outcome postpartum should be further investigated.

Hemminki, K., A. Forsti, et al. (2008). "Risk of familial breast cancer is not increased after pregnancy." Breast Cancer Res Treat **108**(3): 417-20.

Risk of breast cancer is temporarily elevated shortly after pregnancy and the available limited data suggest that a family history of breast cancer may reinforce the risk. We used the nation-wide Swedish Family-Cancer Database to estimate the relative risk (RR) for invasive breast cancer following childbirth among women with or without a family history. The RRs were defined using Poisson regression model of person-years as offset, adjusted for age, period and age at first childbirth. For women without a family history, RRs for breast cancer showed a U-shaped pattern after last pregnancy. Among the 5,217 patients with a first-degree family history the familial risk was 1.77; there was no evidence of increased RRs immediately after last pregnancy. The present study is by far the largest one published on the theme. It shows that pregnancy is not an additional risk factor for women with a family history.

Holtan, S. G., D. J. Creedon, et al. (2009). "Cancer and pregnancy: parallels in growth, invasion, and immune modulation and implications for cancer therapeutic agents." Mayo Clin Proc **84**(11): 985-1000.

Many proliferative, invasive, and immune tolerance mechanisms that support normal human pregnancy are also exploited by malignancies to establish a nutrient supply and evade or edit the host immune response. In addition to the shared capacity for invading through normal tissues, both cancer cells and cells of the developing placenta create a microenvironment supportive of both immunologic privilege and angiogenesis. Systemic alterations in immunity are also detectable, particularly with respect to a helper T cell type 2 polarization evident in advanced cancers and midtrimester pregnancy. This review summarizes the similarities between growth and immune privilege in cancer and pregnancy and identifies areas for further investigation. Our PubMed search strategy included combinations of terms such as immune tolerance, pregnancy, cancer, cytokines, angiogenesis, and invasion. We did not place any restrictions on publication dates. The knowledge gained from analyzing similarities and differences between the physiologic state of pregnancy and the pathologic state of cancer could lead to identification of new potential targets for cancer therapeutic agents.

Ishioka, S., T. Endo, et al. (2007). "Pregnancy-related complications after vaginal radical trachelectomy for early-stage invasive uterine cervical cancer." Int J Clin Oncol **12**(5): 350-5.

BACKGROUND: Pregnancy-related complications after vaginal radical trachelectomy (RT) for early-stage invasive uterine cervical cancer were studied in comparison with those occurring after laser conization. The strategy to reduce vaginal RT-related complications during pregnancy is also discussed. METHODS: Pregnancy courses after vaginal RT in two patients and those after laser conization in five patients, whose operations were performed during the same period, were studied with respect to symptoms, cervical length, and infectious signs. RESULTS: The cervix shortened progressively both in patients with laser conization and in those with RT. However, throughout the pregnancy, the remaining cervix after the operation was longer in patients who had undergone conization than in those who had undergone vaginal RT. After laser conization, two of the five patients suffered from preterm rupture of the membrane (PROM) at 36 weeks of gestation, and both patients who had undergone vaginal RT had premature PROM (pPROM), at 32 and 24 weeks of gestation, respectively. CONCLUSION: Prevention of preterm labor and the following occurrence of pPROM is a significant task to be resolved in order to improve pregnancy outcome after vaginal RT for early-stage invasive uterine cervical cancer. Daily vaginal disinfection with povidone iodine and the administration of a ulinastatin vaginal suppository, bed rest, and the use of ritodrine would be the best approach, and a more conservative approach for stage Ia2 also might be taken into consideration.

Jacobs, I. A., C. K. Chang, et al. (2004). "Coexistence of pregnancy and cancer." Am Surg **70**(11): 1025-9.

The purpose of this study was to review patients with cancer during pregnancy, the effectiveness of the available methods of treatment, and their prognosis. A retrospective chart review was conducted of all women diagnosed with pregnancy-associated cancer between 1974 and 2002 at the University of Illinois at Chicago Medical Center. The demographics, clinical presentation, time and mode of diagnosis, treatment, pregnancy outcome, and maternal survival were noted. The incidence of carcinoma in pregnancy in the series was 0.32/1000 deliveries. The age ranged from 16 to 41 years (mean 30.5 years). No patient underwent a therapeutic abortion, and all patients delivered a healthy infant with no malformations. Metastases developed in three patients with median time of 44 months (range 13-96 months) to presentation of metastases from the time of initial diagnosis. Association of cancer with pregnancy is a rare occurrence. Rates of specific cancers in pregnant and nonpregnant women appear to be equivalent. Pregnant women with cancer are often

diagnosed at a later stage compared to their nonpregnant counterparts. Though the cancer may be diagnosed at a more advanced stage, pregnant patients with cancer do not appear to have a more aggressive clinical course.

Jacobson, H. I., N. Lemanski, et al. (2008). "Hormones of pregnancy, alpha-feto protein, and reduction of breast cancer risk." Adv Exp Med Biol **617**: 477-84.

Parity profoundly reduces breast cancer (BC) risk later in life. It has been reasoned that hormones (either estradiol E2 or estriol E3), progesterone (P) or human chorionic gonadotropin (hCG) in the serum of pregnant women might lead to that reduction in risk. These agents have been shown to reduce BC incidence in nonpregnant rats. We investigated the hypothesis that exogenously added E2, E3, P, or hCG are not the proximal effectors of risk reduction, but that they elicit alpha-fetoprotein (alphaFP) from the nonpregnant liver, and that cFP is the proximal agent by which reduction of BC risk is obtained. Methylnitrosourea (MNU)-exposed animals were treated with saline, E3, E2 + P, E3 + P, hCG, or were allowed to experience pregnancy, and AFP levels were measured in the serum and subsequent tumor incidence was recorded. Human HepG2 liver cells in culture were treated with E3, E2 + P, P, or hCG and elicited AFP was measured in the media. The HepG2 culture media containing elicited AFP was assessed for its ability to inhibit proliferation of T47D cells when applied to these human BC cells in culture, and to inhibit the estrogen-induced phosphorylation of the estrogen receptor in T47D cells. For each condition in the prevention studies, hormone treatment reduced the incidence of BC to an extent similar to that reported by the original studies. In each condition, alphaFP levels in serum were elevated over that in control animals. In culture, treatment of human liver cells with E3, E2 + P, or hCG, but not P alone, led to increased levels of AFP in the media. Media containing hCG-elicited AFP inhibited the estrogen-stimulated proliferation of T47D cells in culture, and inhibited phosphorylation of the estrogen receptor, whereas, estrogens and hCG did not inhibit the growth of these tumor cells in culture. In conclusion, since the hormones of pregnancy elicit alphaFP from the liver, and alphaFP but not the hormones of pregnancy has direct antitumor properties, it is concluded that alphaFP is the proximal agent through which reduction in BC incidence is realized from the experience of pregnancy.

Janni, W., P. Hepp, et al. (2009). "Treatment of pregnancy-associated breast cancer." Expert Opin Pharmacother **10**(14): 2259-67.

BACKGROUND: In primary breast cancer three therapeutic components-cytotoxic, endocrine and targeted antibody therapy-have led to a significant reduction in breast cancer mortality. In pregnancy associated breast cancer the right therapeutic choice is still under discussion while incidence is increasing. With an incidence of 1/3,000 to 1/10,000 pregnancies, pregnancy-associated breast cancer is the most common solid tumor in pregnancy after cervical carcinoma. OBJECTIVE: This article reviews the evidence base for the use of various treatment modalities in patients with pregnancy-associated breast cancer. METHODS: Medline review, searching for articles including years 2000 through 2008 was performed. Search was conducted for the terms "pregnancy" and "breast cancer". Cross references up to the second level were taken into account if of interest for this review. RESULTS: Loco-regional therapy of pregnancy-associated breast cancer follows the general guidelines for breast cancer therapy in principle. Radiation of the breast and/or chest wall is usually not performed during pregnancy. Chemotherapy is indicated for the majority of patients with pregnancy-associated breast cancer. After the first trimester, anthracycline-based chemotherapy is regarded as the treatment standard in pregnancy. Folate antagonists such as methotrexate are strictly contraindicated as they are the main cause of fetal malformations. Adjuvant endocrine therapy with anti-estrogens during pregnancy is contraindicated. Data on targeted biological treatment, particularly for HER2/neu positive tumors during pregnancy are scarce and this treatment should be postponed until after delivery. CONCLUSION: This article summarizes the special features of the diagnosis and primary therapy of pregnancy-associated breast cancer with particular emphasis on cytotoxic therapy.

Janni, W., B. Rack, et al. (2006). "Pregnancy-associated breast cancer -- special features in diagnosis and treatment." Onkologie **29**(3): 107-12.

For obvious psychological reasons it is difficult to associate pregnancy -- a life-giving period of our existence -- with life-threatening malignancies. Symptoms pointing to malignancy are often ignored by both patients and physicians, and this, together with the greater difficulty of diagnostic imaging, probably results in the proven delay in the detection of breast cancers during pregnancy. The diagnosis and treatment of breast cancer are becoming more and more important, as the fulfillment of the desire to have children is increasingly postponed until a later age associated with a higher risk of carcinoma, and improved cure rates of solid tumors no longer exclude subsequent pregnancies. The following article summarizes the special features of the diagnosis and

primary therapy of pregnancy-associated breast cancer with particular consideration of cytostatic therapy.

Jones, A. L. (2006). "Fertility and pregnancy after breast cancer." Breast **15 Suppl 2**: S41-6.

The mortality rate from breast cancer has decreased over the last two or three decades and issues of survivorship have become increasingly important. Approximately 1 in 200 women under the age of 40 develop breast cancer, and with the increasing age at first and subsequent pregnancies in the UK and Europe the issue of fertility for young women who may not have started their families may be a major consideration. The increasing use of adjuvant chemotherapy in breast cancer means that many women diagnosed with breast cancer will undergo temporary or permanent chemotherapy-induced amenorrhoea. This may be associated with physical, psychological and psychosocial implications, with women experiencing the acute toxicities associated with menopause as well as long-term health risks including loss of bone mineral density and possibly some increased cardiovascular risk. Following chemotherapy very few women become pregnant, and this may partly be due to concerns about the risks of pregnancy, both to themselves and in relation to their potential future offspring. Modern techniques used to preserve fertility in the general population may be applicable to some women with breast cancer. The use of such techniques needs to be considered on an individual basis for each woman in light of the recommended systemic adjuvant treatment, the woman's age and her own risk of recurrence with and without systemic treatment. Further clinical research is necessary to substantiate the safety of these approaches to fertility in women who have been diagnosed with breast cancer.

Karam, A., N. Feldman, et al. (2007). "Neoadjuvant cisplatin and radical cesarean hysterectomy for cervical cancer in pregnancy." Nat Clin Pract Oncol **4**(6): 375-80.

BACKGROUND: A 28-year-old Hispanic gravida 1 was found to have a 4-5 cm cervical mass when she presented at 23 weeks gestation. On pelvic examination, the tumor was shown to encompass the entire circumference of the cervix without parametrial or vaginal involvement. A biopsy of the mass revealed a poorly differentiated squamous-cell carcinoma of the cervix. An MRI study of the abdomen and pelvis showed a 4 cm cervical mass that was suspicious for left parametrial and rectovaginal septal involvement. No hydronephrosis or lymphadenopathy was noted. The patient elected to proceed with her pregnancy. INVESTIGATIONS: General physical and gynecological examinations, cervical biopsy, pelvic and obstetric ultrasound, histopathological examination, MRI of the abdomen and pelvis without and with gadolinium, neonatal hearing test and renal function studies. DIAGNOSIS: Poorly differentiated stage IB2 squamous-cell carcinoma of the cervix with MRI imaging suggestive of parametrial and rectovaginal septal involvement. MANAGEMENT: Neoadjuvant chemotherapy using weekly cisplatin from 24 to 30 weeks, bed rest and oral terbutaline at 31 weeks because of premature contractions, and a course of antenatal steroids to promote fetal lung maturity. At 33 weeks radical cesarean hysterectomy, bilateral pelvic and para-aortic lymphadenectomy and bilateral ovarian transposition were carried out, followed by adjuvant pelvic radiation therapy with cisplatin chemosensitization 4 weeks postpartum.

Kasum, M. (2006). "Breast cancer treatment--later pregnancy and survival." Eur J Gynaecol Oncol **27**(3): 225-9.

Although breast cancer (BC) affects patients at older age, it occurs more frequently in premenopausal women due to better diagnostic methods and an increasing trend towards delay in childbearing. The increasing population of women with BC delaying childbearing may be of concern regarding the effect of treatment on later pregnancy, as well as the influence of pregnancy on the prognosis of disease and survival. Radiotherapy has shown no adverse effects on the clinical outcome in the offspring except diminished lactation. The offspring of patients who became pregnant after chemotherapy have shown no congenital anomalies, although sometimes a high abortion rate (10-29%) has been demonstrated. Currently, several fertility-sparing options, including the use of endocrine therapy and assisted reproductive technologies, cryopreservation and ovarian tissue transplantation, are very promising. The survival of BC patients is not decreased by a subsequent pregnancy; compared with the non-pregnant group their survival rates are often the same or better, with favourable relative risks and lower recurrence of metastases.

Kelly, H. L., F. A. Collichio, et al. (2005). "Concomitant pregnancy and breast cancer: options for systemic therapy." Breast Dis **23**: 95-101.

Breast cancers diagnosed during pregnancy and lactation typically have an aggressive phenotype and an advanced stage at presentation. The timing of treatment modalities in pregnant women is complex and requires multidisciplinary input. Alternatives which are relatively safe for both mother and fetus are available, though unforeseen risks may exist. Chemotherapy is not thought to be safe for a fetus during the first trimester; however, in women with

high risk cancers, treatment should not be delayed. Thereafter, anthracycline based chemotherapy has a low incidence of fetal complications. Little evidence beyond case reports exists for taxanes or tamoxifen in pregnancy, and less is available regarding the safety of novel molecularly targeted therapeutics such as trastuzumab. The prognosis of breast cancer diagnosed during pregnancy and lactation is poor, largely because of advanced stage and aggressive phenotype; it is unclear whether pregnancy is an independent prognostic marker for poor outcome.

Kerr, J. R. (2005). "Neonatal effects of breast cancer chemotherapy administered during pregnancy." Pharmacotherapy **25**(3): 438-41.

A human fetus is most susceptible to teratogenic agents during the first trimester of pregnancy. Cyclophosphamide and doxorubicin are pregnancy category D agents; however, potential benefits may warrant treatment with these agents during pregnancy under special circumstances. During her first trimester of pregnancy, a 37-year-old Caucasian woman was diagnosed with stage IIB infiltrating ductal carcinoma in situ (breast cancer) that was estrogen and progesterone receptor negative and human epidermal growth factor receptor-2 positive. The patient was treated with doxorubicin and cyclophosphamide in the second and third trimesters and delivered a premature baby boy at 31 weeks' gestation. The neonate was intubated on delivery because of respiratory distress and failure; however, no physical anomalies were observed. He had neutropenia and anemia, quite possibly as a result of his mother's chemotherapy 1 week before delivery. He was prophylactically treated for sepsis, but all cultures were negative. The infant grew and developed normally during his first year of life and remained in good health. An objective causality assessment revealed that it was probable that the infant's adverse events (prematurity, neutropenia, and anemia) were related to his mother's doxorubicin and cyclophosphamide therapy; however, these were the only adverse events potentially linked to in utero exposure to chemotherapy during the second and third trimesters. Due to the special considerations of both mother and infant, optimal treatment for patients with pregnancy-associated breast cancer requires the expert opinion of a multidisciplinary care team.

Kim, J. H., H. S. Kim, et al. (2008). "Docetaxel, gemcitabine, and cisplatin administered for non-small cell lung cancer during the first and second trimester of an unrecognized pregnancy." Lung Cancer **59**(2): 270-3.

Although several chemotherapeutic agents have been proven to be safe for the fetus after the organogenesis period, there is limited information on their use during the first trimester of pregnancy. We here report the first case of a patient with lung cancer who was treated with platinum-based chemotherapy from the first trimester of an unrecognized pregnancy. A 35-year-old woman was diagnosed with stage IV non-small cell lung cancer with brain metastasis. Since she recalled the date of her last menstrual period at about 20 days prior to consult, we did not consider the possibility of conception at the time of diagnosis. With an object of controlling the increased intracranial pressure, we initially performed a craniotomy with tumor removal, followed by whole brain irradiation. Without our knowledge of her pregnancy, she received a palliative chemotherapy with docetaxel and cisplatin followed by gemcitabine and cisplatin as the second-line chemotherapeutic agents between weeks 9 and 22 of gestation. Follow-up computed tomographic scans performed 2 months after the last chemotherapy showed a fetus in the patient's abdomen. Cesarean section was performed at 33 weeks of gestation, delivering a 1490 g female newborn with no evidence of congenital malformations.

Kluetz, P. G. and M. J. Edelman (2008). "Successful treatment of small cell lung cancer during pregnancy." Lung Cancer **61**(1): 129-30.

The incidence of malignancy associated with pregnancy is rising. This issue is of increasing importance in lung cancer given the rising number of cases of lung cancer in women, many of childbearing age. Treatment with chemotherapy in patients who are pregnant is indicated in scenarios where the malignancy is aggressive and the risk of death of the mother outweighs the risk of fetal effects from chemotherapy. We report a case of a pregnant female with limited stage small cell lung carcinoma treated at 27 weeks gestation with cisplatin and etoposide and subsequent delivery of a healthy child.

Kobayashi, Y., F. Akiyama, et al. (2006). "A case of successful pregnancy after treatment of invasive cervical cancer with systemic chemotherapy and conization." Gynecol Oncol **100**(1): 213-5.

BACKGROUND: The standard therapy for invasive uterine cervical cancer causes loss of the woman's fertility. We report a successful pregnancy in a patient who desired fertility-sparing management of invasive cervical cancer and was treated with systemic chemotherapy and conization. CASE: A 28-year-old nulliparous woman was diagnosed with a large 30-mm-diameter stage IB1 squamous cell carcinoma of the uterine cervix. The patient received 4 courses of systemic chemotherapy with consecutive low-dose BOMP (cisplatin, bleomycin, vincristine and mitomycin C), which produced complete pathological

response assessed by examination of specimens from conization. Two years later, the patient became pregnant, resulting in the birth of a healthy infant. CONCLUSION: This procedure is one method of conservative management to preserve fertility in invasive cervical cancer.

Kolusari, A., G. Ugurluer, et al. (2009). "Rectal cancer and pregnancy: report of two cases." Eur J Gynaecol Oncol **30**(1): 100-2.

Colorectal cancers are rare during pregnancy and the management is controversial and challenging. Prognosis is usually unfavorable due to late diagnosis since the presenting symptoms of colorectal cancer are attributable to the usual manifestations of pregnancy. Management depends on the patient's age and desire for future pregnancy, gestational age, cancer stage and religious principles. Thus, the treatment should be individualized. We present two cases of rectal cancer during pregnancy.

Kontzoglou, K., M. Stamatakos, et al. (2009). "Successful pregnancy after breast cancer therapy: dream or reality?" Int Semin Surg Oncol **6**: 7.

BACKGROUND: Nowadays, more breast cancer patients want to have children after the diagnosis of cancer. The purpose of this study is to review the possibility and risks of giving birth among women with breast cancer previously treated by chemotherapy. CASE PRESENTATION: Two young women aged 28 and 34 respectively, were treated in our clinic for breast cancer, the first (negative hormonal receptors) by surgery, chemotherapy and radiotherapy and the second (positive hormonal receptors) by surgery, radiotherapy and tamoxifen. They both became pregnant, 1 and 8 years after completion of the therapy respectively. RESULTS: Laboratory testing during pregnancy was negative in both cases and after an uneventful course each woman gave birth to a perfectly healthy child. The first patient breastfed her baby for three months, while the second one did not breastfeed her baby at all. CONCLUSION: Women undergoing chemotherapy for breast cancer can maintain their fertility and get pregnant. Previous chemotherapy for breast cancer does not present any supplementary risks for the child's mental or physical health.

Koushik, A., M. E. Parent, et al. (2009). "Characteristics of menstruation and pregnancy and the risk of lung cancer in women." Int J Cancer **125**(10): 2428-33.

Lung tissue, both normal and cancerous, has been found to express estrogen receptors and patterns of expression have differed between men and women, suggesting a possible role for hormone-related factors in lung carcinogenesis in women. Few epidemiological studies have examined hormone-related variables and lung cancer risk and the findings have not been consistent. We investigated the association between characteristics of menstruation and pregnancy in relation to lung cancer risk in a population-based case-control study carried out in Montreal, Canada, including 422 women with lung cancer and 577 controls. For each variable, odds ratios (OR) and 95% confidence intervals (CI) were estimated using unconditional logistic regression modeling. Associations were also examined according to level of smoking and by lung cancer histology. All statistical tests were two-sided. Most characteristics of menstruation and pregnancy were not associated with lung cancer risk. However, an increased risk was observed for women who had had a non-natural menopause, which predominantly included women who had had a bilateral oophorectomy, compared with women who had had a natural menopause (OR = 1.92, 95% CI: 1.22-3.01). An inverse association with age at menopause was suggested. These results did not vary by level of smoking and they were similar for adenocarcinomas compared with other histological types. Our results suggest that hormonal factors, related to early menopause and/or ovary removal, may play a role in the risk of lung cancer. Further studies are needed to confirm these findings, and to assess the possible contribution of hormone replacement therapy.

Kroman, N., M. B. Jensen, et al. (2008). "Pregnancy after treatment of breast cancer--a population-based study on behalf of Danish Breast Cancer Cooperative Group." Acta Oncol **47**(4): 545-9.

BACKGROUND: Estrogen is an established growth factor in breast cancer and it has been hypothesized that pregnancy associated estrogens may increase the risk of recurrence of breast cancer. In 1997 we published a population-based Danish study indicating no negative prognostic effect of pregnancy after breast cancer treatment. The present study is a ten-year update. MATERIAL AND METHODS: Danish Breast Cancer Cooperative Group has since 1977 collected population-based data on tumour characteristics, treatment regimes, and follow-up status on Danish women with breast cancer. Pregnancy history was added from the Danish Civil Registration System, the National Birth Registry, and the National Induced Abortion registry. Cox regression was used to estimate the risk ratio of dying among women with a pregnancy after breast cancer treatment compared with women without such experience. RESULTS: In all, 10 236 women with primary breast cancer aged 45 years or less at the time of diagnosis were followed for 95 616 person years. Among these, 371 women experienced pregnancy

after treatment of breast cancer. In a multivariate analysis that included age at diagnosis, stage of disease, and pregnancy history prior to diagnosis, women who had a full-term pregnancy subsequent to breast cancer treatment were found to have a reduced risk of dying (relative risk: 0.73; 95% confidence interval: 0.54-0.99) compared with other women with breast cancer. The effect was not significantly modified by age at diagnosis, tumour size, nodal status, or pregnancy history before diagnosis of breast cancer. Neither spontaneous abortions nor induced abortions subsequent to breast cancer treatment had a negative impact on prognosis. CONCLUSION: In line with our previous study, but based on more than twice the patient material, we found no evidence that a pregnancy after treatment of breast cancer has a negative influence the prognosis.

Krychman, M. L. and T. King (2006). "Pregnancy after breast cancer: a case study resolving the reproductive challenge with a gestational surrogate." Breast J **12**(4): 363-5.

Pregnancy and fertility issues are substantial concerns for the young breast cancer survivor, yet the available literature is hampered by a lack of prospective clinical studies and meaningful long-term outcome data. A lack of reliable information often leads to physician discomfort and patients may be left to navigate the world of fertility preservation and reproductive technology on their own. This case exemplifies some of the many issues that breast cancer survivors may face and adds another dimension to the survivor's dilemma; once fertility options have been preserved, what is the best method to sustain the pregnancy--self or surrogate? For many, the goal of balancing optimal treatment and long-term survival with restoration of a complete quality of life, including childbearing, may be attainable. This discussion highlights the importance of offering young breast cancer patients an opportunity to discuss these issues with their health care providers prior to initiating therapy.

Kurabayashi, T., K. Isii, et al. (2004). "Advanced gastric cancer and a concomitant pregnancy associated with disseminated intravascular coagulation." Am J Perinatol **21**(5): 295-8.

Gastric cancer associated with pregnancy is extremely rare and the prognosis is generally grave. A 31-year-old Japanese women, 41 weeks pregnant, displayed disseminated intravascular coagulation (DIC), although clinical symptoms and diagnostic examinations did not indicate an obstetrical cause. She went into labor spontaneously and vaginally delivered a 3248-g normal female infant, after receiving a blood transfusion. On the day 5 postpartum, a gastroduodenal fiberscope examination indicated advanced gastric cancer. She was also diagnosed with bilateral chronic subdural hematoma and underwent an operation to allow drainage. It was not possible to treat her curatively, so she was treated conservatively for DIC. She died on day 13 postpartum. Necropsy of the iliac bone indicated bone marrow metastasis of adenocarcinoma. This is the first known case of a pregnant woman with DIC occurring as the first manifestation of advanced gastric cancer.

Lagiou, A., P. Lagiou, et al. (2003). "Comparison of age at first full-term pregnancy between women with breast cancer and women with benign breast diseases." Int J Cancer **107**(5): 817-21.

Benign breast diseases have a broadly similar risk profile to that of breast cancer, possibly reflecting a similar underlying endocrine milieu. We have hypothesized that a crucial distinction between breast cancer and benign breast diseases is that mammary gland terminal differentiation has not been successfully accomplished among women who tend to develop breast cancer. From October 2001 to December 2002, information concerning breast cancer risk factors and sociodemographic characteristics was collected from 174 women with breast cancer and 116 women with benign breast diseases, all 30 years old or older, who were histologically diagnosed at a major prevention center in Athens, Greece. Among the examined breast cancer risk factors, only age at first full-term pregnancy was significantly associated with the odds of having breast cancer rather than benign breast disease, and the association was evident among premenopausal [odds ratio (OR) per 5 years = 1.76, 95% confidence interval (CI) 1.10-2.93] and postmenopausal (OR = 2.10, 95% CI 1.16-3.71) women, as well as among all women (OR = 1.93, 95% CI 1.34-2.70). There was no evidence that any of the remaining breast cancer risk factors could discriminate between breast cancer and benign breast diseases. We conclude that early age at first pregnancy may convey substantial protection against breast cancer risk among women with benign breast diseases, probably operating through induction of terminal differentiation of mammary gland cells. The finding is accentuated by the fact that women with benign breast diseases are already at a relatively high risk for breast cancer.

Largillier, R., A. Savignoni, et al. (2009). "Prognostic role of pregnancy occurring before or after treatment of early breast cancer patients aged <35 years: a GET(N)A Working Group analysis." Cancer **115**(22): 5155-65.

BACKGROUND: Usual practices recommend waiting at least 2 years between diagnosis of early breast cancer (EBC) and pregnancy. Few data

highlighted a harmful effect of an early pregnancy for low-risk patients. The authors analyzed retrospectively data from women younger than 35 years who became pregnant before or after treatment of EBC. METHODS: Between 1990 and 1999, 908 consecutive EBC patients were analyzed. The primary endpoint was to compare overall survival (OS) between pregnant and nonpregnant patients. The secondary endpoint was to establish a score index laying down the risk of distant recurrence. RESULTS: Within the year before the diagnosis, 105 (11.6%) patients became pregnant and 118 (13%) were pregnant after treatment. In a multivariate model, a pregnancy before the diagnosis was not predictive of death but of local relapse. A pregnancy subsequent to breast cancer therapy resulted in a 77% decrease of death ($P < .001$). In good-prognosis score index patients, the annual risk of relapse remained low. In patients having the higher score, recurrences occurred mainly during the first years after the treatment. Beyond 80 months, the annual risk of relapse seemed to be similar to those of lower-risk subgroups. CONCLUSIONS: In women aged younger than 35 years, a pregnancy occurring before or after the diagnosis of breast cancer was not an independent prognostic factor of death. In the subset of patients having a high risk of relapse, it may be preferable to postpone a pregnancy beyond 5 years after the breast cancer therapy.

Leboeuf, R., L. E. Emerick, et al. (2007). "Impact of pregnancy on serum thyroglobulin and detection of recurrent disease shortly after delivery in thyroid cancer survivors." Thyroid **17**(6): 543-7.

OBJECTIVE: Since pregnancy can stimulate thyroid growth, we examined the effect of pregnancy on recurrence and serum thyroglobulin (Tg) shortly after delivery in thyroid cancer survivors. DESIGN: Retrospective analysis of thyroid cancer survivors who became pregnant after completing initial therapy. MAIN OUTCOME: 36 women (age 34 +/- 4 years) who became pregnant a median of 4.3 years after initial therapy for differentiated thyroid cancer were evaluated a median of 4 months after delivery. As part of their initial therapy, 23 women underwent total thyroidectomy with radioactive iodine remnant ablation (RRA), six had total thyroidectomy without RRA, and seven underwent lobectomy without RRA. Following total thyroidectomy with or without RRA, no evidence of recurrence was detected in the early postpartum period in women with negative prepregnancy ultrasound and either undetectable or low suppressed Tg levels. However, disease progression was documented as enlargement of a previously stable cervical lymph node in one of three patients and a marked rise in serum Tg without evidence of structural disease progression in a patient with previously stable distant metastases. When analyzed based on initial therapy, the mean suppressed Tg after delivery was not significantly different than the prepartum value. However, eight women had Tg values after delivery more than 20% higher than the baseline Tg before pregnancy (three with known disease, five with no clinical evidence of disease). CONCLUSION: In thyroid cancer survivors, pregnancy is unlikely to cause clinically significant disease recurrence in the early postpartum period when structural imaging studies confirm the absence of residual disease but can occasionally be associated with progression of known metastatic lesions. Even though the serum Tg did not differ significantly before and after pregnancy, the long-term implications of minor rise in serum Tg seen in some individual patients cannot be assessed without longer studies in larger cohorts.

Lee, H. J., I. K. Lee, et al. (2009). "Clinical characteristics of gastric cancer associated with pregnancy." Dig Surg **26**(1): 31-6.

BACKGROUND/AIMS: This study was conducted to evaluate the clinical features and treatment outcome of gastric cancer associated with pregnancy. METHODS: Clinicopathologic characteristics of 15 patients who were diagnosed as having gastric cancer during pregnancy or within 1 year after delivery (the P-related group) were compared with those of 53 age-matched pregnancy-unrelated gastric cancer patients (the control group). RESULTS: Significant differences were found in tumor stage and surgical curability; the numbers of stage IV disease were 12 (80%) and 21 (40%; $p = 0.006$), and those of curative resection were 4 (27%) and 20 (62%; $p = 0.02$) in the P-related and the control group, respectively. Three-year survival rate was significantly lower in the P-related group (23.3%) than in the control group (52.8%; $p = 0.007$). In the P-related group, only 3 patients, including one patient diagnosed using endoscopy, survived without recurrences. In the multivariate analysis, pregnancy was not identified as an independent risk factor associated with poor outcome. CONCLUSION: Gastric cancer associated with pregnancy is discovered at its advanced stage and consequently shows a dismal prognosis. Considering that the patients who underwent curative resection have a favorable prognosis, primary efforts should be focused on early diagnosis.

Lee, J. M., K. B. Lee, et al. (2008). "Cervical cancer associated with pregnancy: results of a multicenter retrospective Korean study (KGOG-1006)." Am J Obstet Gynecol **198**(1): 92 e1-6.

OBJECTIVE: The objective of the study was to analyze the characteristics of cervical cancer associated with pregnancy. STUDY DESIGN: Forty patients with cervical cancer associated with pregnancy were retrospectively identified between 1995-2003. Three controls for each case were matched on the basis of age, stage, histology, and date of treatment. RESULTS: Sampling of cervical cytology after the second trimester was the most common cause of delayed diagnosis. Among 12 patients who delayed treatment for fetal maturity, 2 died of disease. There was no difference in overall survival between pregnant and nonpregnant patients with stage Ib tumors. In contrast to nonpregnant patients, the depth of stromal invasion was not correlated with the incidence of lymph vascular space involvement and lymph node metastasis in pregnant patients. CONCLUSION: Thorough evaluation is warranted before deciding whether to delay treatment until fetal maturity. Pregnancy does not adversely affect the prognosis of early-stage cervical cancer significantly.

Lyons, T. R., P. J. Schedin, et al. (2009). "Pregnancy and breast cancer: when they collide." J Mammary Gland Biol Neoplasia **14**(2): 87-98.

Women of childbearing age experience an increased breast cancer risk associated with a completed pregnancy. For younger women, this increase in breast cancer risk is transient and within a decade after parturition a cross over effect results in an ultimate protective benefit. The post-partum peak of increased risk is greater in women with advanced maternal age. Further, their lifetime risk for developing breast cancer remains elevated for many years, with the cross over to protection occurring decades later or not at all. Breast cancers diagnosed during pregnancy and within a number of years post-partum are termed pregnancy-associated or PABC. Contrary to popular belief, PABC is not a rare disease and could affect up to 40,000 women in 2009. The collision between pregnancy and breast cancer puts women in a fear-invoking paradox of their own health, their pregnancy, and the outcomes for both. We propose two distinct subtypes of PABC: breast cancer diagnosed during pregnancy and breast cancer diagnosed post-partum. This distinction is important because emerging epidemiologic data highlights worsened outcomes specific to post-partum cases. We reported that post-partum breast involution may be responsible for the increased metastatic potential of post-partum PABC. Increased awareness and detection, rationally aggressive treatment, and enhanced understanding of the mechanisms are imperative steps toward improving the prognosis for PABC. If we determine the mechanisms by which involution promotes metastasis of PABC, the post-partum period can be a window of opportunity for intervention strategies.

Machado, F., C. Vegas, et al. (2007). "Ovarian cancer during pregnancy: analysis of 15 cases." Gynecol Oncol **105**(2): 446-50.

GOAL: Our goal was to analyze and describe cases of ovarian cancer in pregnant women treated at our hospital. METHOD: Retrospective study based on clinical histories from patients diagnosed and treated at our hospital for ovarian cancer and pregnancy from 1987 to 2005. RESULTS: Fifteen cases of ovarian cancer were diagnosed among pregnant women; the ratio is 0.11/1000 deliveries. Among them, 66.6% of patients were asymptomatic, and 86.6% had been diagnosed via ultrasound. Of the diagnosed tumors, 40% were malignant epithelial tumors, 26.6% of them were of low malignant potential. The 20% were germinal cell tumors. Of these primary ovarian malignancies, the 59.9% were stage I. The remaining 20% were metastatic tumors. Forty percent of the total were treated conservatively (salpingo-oophorectomy) and 60% with hysterectomy and bilateral salpingo-oophorectomy. Chemotherapy was administered to 66.6% of the patients, in two cases during pregnancy. Eighty percent of the newborns were healthy and presented no sequelae or malformations. Global survival at 5 years was 76%. CONCLUSIONS: Ovarian cancer is rare in pregnant women. Most malignant ovarian neoplasias in pregnant women are at early stages and are associated with good prognosis both for the mother and for the neonate.

Makgasa, M., R. S. Prichard, et al. (2009). "Pregnancy associated breast cancer." Ir Med J **102**(10): 314-7.

Treatment of pregnancy associated breast cancer (PABC) is usually compromised as both foetal and maternal health has to be taken into consideration. We have identified on our database twelve patients with PABC and twenty-four age-matched controls diagnosed in the same time-frame. The mean age was 36 and 38 years respectively. There was no difference in time to presentation between the two groups. The mean tumour size was 48.72 mm and 26.30 mm respectively ($p = 0.001$). Lymphovascular invasion and lymph node involvement were more common in the PABC group. In the PABC group, 5 patients (42%) were treated with neo-adjuvant chemotherapy including one patient in first trimester. All patients underwent surgery. Adjuvant chemotherapy was given to seven (58.3%) of the PABC patients. At median follow up of 36 months, there was a single mortality and two patients (17%) had developed recurrent disease. All children are healthy with no deformity or learning disability.

Mantovani, G., G. Gramignano, et al. (2007). "Use of chemotherapy for ovarian cancer during human pregnancy: case report and literature review." Eur J Obstet Gynecol Reprod Biol **131**(2): 238-9.

Marinoni, E., T. Di Netta, et al. (2006). "Metastatic pancreatic cancer in late pregnancy: a case report and review of the literature." J Matern Fetal Neonatal Med **19**(4): 247-9.

The occurrence of pancreatic carcinoma in a young patient is rare and even more so in pregnancy. In this case report, we discuss the presentation and management of pancreatic adenocarcinoma, with lung and liver metastases, diagnosed in a woman in her third trimester of pregnancy (28 weeks). Ultrasound and magnetic resonance imaging scans were carried out and pancreatic mass biopsy during endoscopic retrograde cholangiopancreatography was performed. Severe preeclampsia and fetal growth restriction occurred. A female infant was delivered by cesarean section at 30 weeks of gestation for worsening of maternal clinical conditions and hepatic and pancreatic tests. The patient died 50 days after delivery. Although pancreatic cancer is a very rare event in pregnancy, it should be suspected when epigastric abdominal pain and laboratory parameters suggestive of biliary tract obstruction occur in pregnancy to ensure, at the least, a better pregnancy outcome.

Marnitz, S., A. Schmittel, et al. (2009). "The therapeutic management of a twin pregnancy complicated by the presence of cervical cancer, following laparoscopic staging and chemotherapy, with an emphasis on cisplatin concentrations in the fetomaternal compartments amnion fluid, umbilical cord, and maternal serum." Fertil Steril **92**(5): 1748 e1-4.

OBJECTIVE: To evaluate the feasibility, toxicity, and pharmacokinetics in the maternal and fetal compartments during chemotherapy in a pregnant patient with cervical cancer. DESIGN: Case report. SETTING: University Hospital. PATIENT: A 35-year-old woman was diagnosed with an adenocarcinoma FIGO stage IB1 of the cervix uteri at 14 weeks' gestation with twin pregnancy. INTERVENTION(S): A laparoscopic transperitoneal pelvic lymphadenectomy was performed at 15 weeks' gestation There was no evidence of lymph node metastases (0/19). The patient decided to continue her pregnancy. Three cycles of neoadjuvant chemotherapy consisting of cisplatin during the second and third trimester were given and well tolerated. Amniocentesis was performed at the time of the second cisplatin cycle. MAIN OUTCOME MEASURE(S) AND RESULT(S): The concentration in the amniotic fluid samples reached 10% of the maternal blood levels at this time. At 32 weeks' gestation, a Caesarean section followed by radical hysterectomy was performed. The twins developed normally and displayed no chemotherapically related side effects. At the time of delivery, the corresponding concentration in the amniotic fluid was approximately one-third of the umbilical cord levels. CONCLUSION(S): To our knowledge, this is the first report quantifying the amount of transplacental transport of cisplatin during pregnancy in vivo. One-tenth of the maternal serum concentration was detected in the amniotic fluid; the concentration of cisplatin in the umbilical cord was three times higher than in the amniotic fluid.

Mendez, L. E., A. Mueller, et al. (2003). "Paclitaxel and carboplatin chemotherapy administered during pregnancy for advanced epithelial ovarian cancer." Obstet Gynecol **102**(5 Pt 2): 1200-2.

BACKGROUND: Ovarian cancer diagnosed during pregnancy is uncommon. Most chemotherapy use reported has been in combination with cisplatinum. Paclitaxel in combination with carboplatin during pregnancy has not yet been reported. CASE: A right adnexal mass was diagnosed during pregnancy at 5 weeks' gestational age in a 30-year-old woman. A laparotomy was performed 2 1/2 weeks later because of the worsening nature of her symptoms and the possibility of ovarian torsion. At surgery, the patient was diagnosed with stage IIIC ovarian papillary serous cystadenocarcinoma. She was treated with six cycles of paclitaxel and carboplatin beginning at 16-17 weeks' gestation. At 35.5 weeks' gestation, a cesarean hysterectomy, left salpingo-oophorectomy, and pelvic and paraaortic nodal sampling with multiple peritoneal biopsies was performed without incident. However, the patient had refractory disease present in the remaining ovary. She was treated with further chemotherapy and is currently doing well. The patient experienced no adverse reactions during her treatment, and the infant has normal growth and development at 15 months of age. CONCLUSION: Paclitaxel used in combination with carboplatin for the treatment of ovarian cancer during pregnancy caused no adverse effects in the infant.

Modares Gilani, M., M. Karimi Zarchi, et al. (2007). "Preservation of pregnancy in a patient with advanced ovarian cancer at 20 weeks of gestation: case report and literature review." Int J Gynecol Cancer **17**(5): 1140-3.

To report a case of FIGO stage III papillary serous carcinoma of ovary, diagnosed during pregnancy at 20 weeks of gestation and treated with unilateral salpingo-oophorectomy and surgical

staging, then initial combination chemotherapy while preserving the pregnancy. The patient underwent cesarean section at 35 weeks after four courses of taxol plus carboplatin. She delivered a healthy baby. After that total hysterectomy, omentectomy, pelvic and para-aortic lymphadenectomies were carried out. The surgical resection was complete and no macroscopic residual diseases were seen. During histologic examination, traces of resistant disease were found. The patient underwent three postoperative courses of chemotherapy (carboplatin plus paclitaxel regimen). After 6 months follow-up, the patient remained in complete remission and the child's development was normal. Combination chemotherapy during pregnancy with preservation of the fetus could be considered, and should be discussed with caution in case of epithelial ovarian cancer diagnosed during the second trimester of the pregnancy.

Molckovsky, A. and Y. Madarnas (2008). "Breast cancer in pregnancy: a literature review." Breast Cancer Res Treat **108**(3): 333-8.

PURPOSE: Breast cancer in pregnancy is a clinically challenging situation for patients and their physicians. A review of the literature was performed to help identify optimal treatment strategies. METHODS: A Medline search between 1966 to the present using the keywords "breast", "carcinoma", and "pregnancy" revealed numerous hits, from which English-language articles including epidemiologic studies, case series, and general summaries were reviewed. RESULTS: There is a paucity of prospective studies regarding diagnosis and treatment of breast cancer in pregnancy due to its rarity. However a general review of the literature database reveals that women diagnosed with breast cancer during pregnancy have similar disease characteristics to age-matched controls. Surgery remains the mainstay of treatment of breast cancer during pregnancy, and in some circumstances breast-conserving surgery is an acceptable option. Adjuvant treatment can proceed with some modifications that minimize harm to the fetus, namely limiting radiation exposure and timing chemotherapy properly. Post-partum decisions regarding lactation and future fertility should be addressed on a per-patient basis. CONCLUSION: Breast cancer in pregnancy is an uncommon phenomenon but one which poses dilemmas for patients and their physicians. A multi-disciplinary approach is recommended for optimal clinical-decision making.

Moran, B. J., H. Yano, et al. (2007). "Conflicting priorities in surgical intervention for cancer in pregnancy." Lancet Oncol **8**(6): 536-44.

Cancer in pregnancy is uncommon, with an incidence of about one to two cases in every 1000 pregnancies. There are no randomised trials on any aspect of the management of cancer in pregnancy. Stage for stage cancer outcomes are similar in women who are pregnant compared with those who are not. Misdiagnosis and delayed diagnosis are common where the index of suspicion by the mother and health carers is low. Surgical interventions pose some risk to the fetus, especially laparotomy for abdominal tumours and procedures undertaken during the first trimester. Chemotherapy is teratogenic in the early stages, but seems to be safe in later pregnancy, and radiotherapy can be used for localised tumours remote from the uterus, such as head and neck or limb neoplasms. Suspicious symptoms should be appropriately investigated during pregnancy, and recent advances in non-ionising-radiation staging techniques, such as MRI and ultrasound, are especially helpful. Surgical interventions can be safely undertaken with minimum risk, although there is almost always some element of maternal-fetal conflict.

Morice, P., F. Narducci, et al. (2009). "French recommendations on the management of invasive cervical cancer during pregnancy." Int J Gynecol Cancer **19**(9): 1638-41.

BACKGROUND: Cervical cancer is one of the most frequently diagnosed cancers during pregnancy, but the management of such cases remains unclear. A Working Group was set up in 2007 in France to propose national recommendations for the management of pregnant patients with invasive cervical carcinoma. METHODS: The recommendations are based on this literature review conducted by the members of the Working Group. RESULTS: Management of cervical cancer during pregnancy depends on 5 factors: stage of the disease (and the tumor size), nodal status, histological subtype of the tumor, term of the pregnancy, and whether the patient wishes to continue her pregnancy. In patients with early-stage disease diagnosed during the first 2 trimesters of pregnancy, there is an increasing tendency to preserve the pregnancy while awaiting fetal maturity in patients with absence of nodal involvement. The delivery (when the fetal maturity is attained) should be then performed using a cesarean section. CONCLUSIONS: This article proposes recommendations for the management of pregnant patients with invasive cervical cancer. These recommendations have been validated by the 3 main scientific societies of gynecologic oncology, pelvic surgery, and obstetrics and gynecology in France.

Morris, P. G., F. King, et al. (2009). "Cytotoxic chemotherapy for pregnancy-associated breast cancer: single institution case series." J Oncol Pharm Pract **15**(4): 241-7.

BACKGROUND: Pregnancy-associated (PA) breast cancer is a rare disease state that poses unique management challenges, specifically controlling the cancer and maximizing the survival of the expectant mother balanced with the health and safety of the developing fetus. As more women delay pregnancy into their 30s and 40s it is expected that this may become a more important clinical problem in the future. Existing data on PA-breast cancer comes from case series using older chemotherapy drugs. A review of practice was carried out to assess current experience with PA-breast cancer, particularly relating to current cytotoxic drugs and targeted agents. METHODS: The St James's Hospital breast cancer registry, a prospectively maintained database, was used to identify cases of PA-breast cancer over a 6.5-year period and a chart review carried out. Chemotherapy administered during pregnancy, breast cancer specific outcomes, and fetal outcomes were assessed. RESULTS: Five patients were identified with PA-breast cancer; median age 34 years (range 28-35). The median gestation at presentation was 18 weeks (range 14-29). Four women received chemotherapy during pregnancy; three received doxorubicin and cyclophosphamide (AC) and one paclitaxel. These agents were generally well tolerated. At median gestation of 36 weeks (range 35-40 weeks) four elective caesareans and one spontaneous delivery occurred. There were no fetal abnormalities. CONCLUSIONS: Common cytotoxics can safely be delivered in pregnancy. Further research on newer therapies such as trastuzumab is needed.

Nagarajan, R. and L. L. Robison (2005). "Pregnancy outcomes in survivors of childhood cancer." J Natl Cancer Inst Monogr(34): 72-6.

During the past several decades, survival rates of many childhood cancers have risen at a remarkable pace. The ever-growing population of cancer survivors is at potential risk for developing a broad spectrum of adverse outcomes relating to cancer diagnosis and treatment, including infertility, adverse pregnancy-related outcomes, and health problems of offspring. Unfortunately, these topics have not been extensively studied, particularly among pediatric cancer survivors receiving more recent therapies. Based on the current literature, therapy for childhood cancer, in general, does not appear to have a significant impact on pregnancy outcomes and on the health of offspring of childhood cancer survivors. Additional investigations, incorporating more rigorous designs, need to be conducted to further address potential long-term risks relating to birth outcomes, including birth weight. Studies currently underway to evaluate the incidence of and risk factors for birth defects, occurrence of cancer, and other serious health-related outcomes will provide valuable information to guide researchers, clinicians, and survivors and their families.

Navrozoglou, I., T. Vrekoussis, et al. (2008). "Breast cancer during pregnancy: a mini-review." Eur J Surg Oncol **34**(8): 837-43.

BACKGROUND: As modern women delay childbearing, pregnancy-associated breast cancer (PABC) becomes a more frequent problem faced by oncologists, gynecologists, and obstetricians alike. However, no evidence exists concerning the management of this condition. METHODS: We summarized the current literature regarding epidemiology, pathology, diagnosis, treatment and prognosis of PABC. Data were collected by searching PubMed and Medline for the period from 1950 to 2007. RESULTS: There are no randomized controlled trials regarding PABC management. Current evidence suggests that diagnosis may be carried out with limitations regarding staging; surgical treatment may be performed as for the non-pregnant women. Radiotherapy and endocrine therapy are contraindicated during pregnancy, while chemotherapy is allowed after the first trimester. Prognosis is considered poor. Subsequent pregnancy is allowed only 2 years after completing treatment. CONCLUSIONS: Due to lack of prospective randomized controlled clinical studies, both ongoing studies and future evidence are expected to solve problems related to breast cancer management during pregnancy.

Oduncu, F. S., R. Kimmig, et al. (2003). "Cancer in pregnancy: maternal-fetal conflict." J Cancer Res Clin Oncol **129**(3): 133-46.

The occurrence of malignancies during pregnancy has increased over the last decades. They complicate approximately 1 per 1000 pregnancies. The most common malignancies associated with pregnancy include malignant melanoma, malignant lymphomas and leukemia, and cancer of the cervix, breast, ovary, colon and thyroid. Since it is impossible for prospective randomized clinical trials to be conducted in this field, relevant data have been generated from case reports and matched historical cohort studies in order to evaluate the treatment outcomes and the issues complicating the management of malignancy in the pregnant patient. There is almost always a conflict between optimal maternal therapy and fetal well-being. The maternal interest is for an immediate treatment of the recently diagnosed tumor.

However, the optimal therapy, be it chemotherapy, radiotherapy or surgery, may impose great risks on the fetus. Consequently, either maternal or fetal health, or both, will be compromised. Therefore, both the pregnant patient and her physician are often in a dilemma as to the optimal course. On the basis of the medical facts, we discuss the issues raising potential ethical conflicts and present a practical ethical approach which may help to increase clarity in maternal-fetal conflicts. We review the available data informing the incidence and impact of the most common malignancies during pregnancy and their treatment on both the pregnant woman and her fetus. The optimal therapy for the tragic diagnosis of cancer in pregnancy requires a collaborative and interdisciplinary approach between gynecologists, oncologists, obstetricians, surgeons, neonatologists, psychologists, nursing staff and other disciplines. The purpose of this article is not to answer specific questions or to construct management schemes for specific tumors but to provide a framework for approaching some of these complex issues.

Ostrom, K., A. Ben-Arie, et al. (2003). "Uterine evacuation with misoprostol during radiotherapy for cervical cancer in pregnancy." Int J Gynecol Cancer **13**(3): 340-3.

Radiotherapy as definitive treatment for invasive cervical cancer during pregnancy causes spontaneous abortion in most cases. Surgical evacuation of the uterus is indicated when abortion does not occur, exposing patients to additional morbidity. Two Latin American women, diagnosed with FIGO stage IB2 cervical cancer at approximately 15 weeks gestation, underwent radiotherapy with radiosensitizing chemotherapy. After intrauterine fetal demise was detected, both women underwent induction with misoprostol. Results included one complete abortion and one incomplete abortion without complications or delays in treatment. These cases demonstrate that induction with misoprostol appears to be a safe and effective alternative to surgical evacuation of the uterus when spontaneous abortion fails to occur during radiotherapy for locally advanced cervical cancer.

Pereg, D., G. Koren, et al. (2008). "Cancer in pregnancy: gaps, challenges and solutions." Cancer Treat Rev **34**(4): 302-12.

Cancer is the second leading cause of death during the reproductive years complicating between 0.02% and 0.1% of pregnancies. This incidence is expected to rise with the increase in age of childbearing. The relatively rare occurrence of pregnancy-associated cancer precludes conducting large, prospective studies to examine diagnostic, management and outcome issues. This article reviews the available data regarding the different aspects of the diagnosis and treatment of cancer during pregnancy as well as the effect of pregnancy on cancer prognosis. In pregnant patients diagnosed with cancer during the first trimester, treatment with multi-drug anti-cancer chemotherapy or radiotherapy (with fetal exposure >0.1-0.2 Gy) is associated with an increased risk of congenital malformations and therefore should follow a strong recommendation for pregnancy termination. The risk for malformation diminishes as pregnancy advances and when cancer is diagnosed during the second or third trimesters there is usually no clear indication for abortion. Treatment postponement, until achieving fetal maturity, while closely monitoring tumor growth may be considered in selected cases. According to the available experience it seems that non-obstetrical surgery may be performed during pregnancy without an increased risk for adverse outcomes. In most types of cancer, pregnancy has no effect on maternal prognosis when compared to non-pregnant patients matched by age, cancer stage and treatment.

Potluri, V., D. Lewis, et al. (2006). "Chemotherapy with taxanes in breast cancer during pregnancy: case report and review of the literature." Clin Breast Cancer **7**(2): 167-70.

Two patients with breast cancer received docetaxel-containing chemotherapy as adjuvant or neoadjuvant therapy during pregnancy. The first pregnant patient began neoadjuvant therapy with doxorubicin/cyclophosphamide at 14 weeks of gestation. After 4 cycles of doxorubicin/cyclophosphamide and surgery, she received adjuvant docetaxel for 4 cycles. The second patient began neoadjuvant therapy with doxorubicin/docetaxel at 14 weeks of gestation and received 6 cycles. The fetus of the first patient had hydrocephalus on ultrasound at 17 weeks of gestation (before docetaxel therapy) that persisted on serial follow-up ultrasounds and spontaneously regressed over several months after delivery. No fetal malformations were detected in the second fetus. These 2 cases add to the existing data on the use of taxanes during pregnancy. Although the data are limited with case reports, pregnant patients with cancer can be treated with chemotherapy including taxanes during the second and third trimesters without significant risks to the fetus. Taxanes should not be excluded, if indicated, in pregnant patients with cancer.

Psyrri, A. and B. Burtness (2005). "Pregnancy-associated breast cancer." Cancer J **11**(2): 83-95.

PRECIS: Breast masses discovered during pregnancy should receive thorough evaluation. Delay in the diagnosis of breast cancer in pregnancy may cause increased mortality and should be avoided. As women delay childbearing, the incidence of breast cancer during pregnancy may increase. This article aims to review the pathophysiology, clinical presentation, and diagnostic and therapeutic approach to the pregnant breast cancer patient. In addition, the impact of pregnancy on subsequent breast cancer development in high-risk groups, such as BRCA1 and BRCA2 mutation carriers and patients with a prior history of breast cancer, is discussed. SOURCES AND STUDY SELECTION: We conducted a PubMed search using the words breast, cancer, carcinoma, and pregnancy. We also searched for abstracts presented at the American Society for Clinical Oncology meetings using the words breast cancer and pregnancy. Observational studies were not pooled because of the disparity of the data. We reviewed 117 articles and three abstracts referring to breast cancer in pregnancy. RESULT: A thorough breast examination at the first antenatal visit, before the physiologic changes in breast parenchyma obscure a possible mass, is essential. The work-up of masses detected during pregnancy should not be postponed until after delivery. Delays in diagnosis may contribute to the higher proportion of patients with advanced stage at presentation. The prognosis of the pregnant breast cancer patient is similar to her stage-matched nonpregnant counterparts in most series. Radiation therapy is contraindicated during pregnancy; this limits breast conservation to cases presenting during the third trimester. Some chemotherapies can be administered during the second and third trimesters. Therapeutic abortion is not necessary, although women with high-risk disease may find this preferable. Women with a history of breast cancer should be reassured that subsequent pregnancy is not known to increase the risk of recurrence. Women with a history of BRCA1/2 mutations should not be advised that early pregnancy decreases their breast cancer risk. CONCLUSIONS: Physicians should aggressively pursue work-up in women with a palpable breast mass because early diagnosis may improve the prognosis of breast cancer during pregnancy.

Puckridge, P. J., C. M. Saunders, et al. (2003). "Breast cancer and pregnancy: a diagnostic and management dilemma." ANZ J Surg **73**(7): 500-3.

BACKGROUND: The purpose of the present paper was to review the current knowledge of pregnancy concurrent with a diagnosis of breast cancer, and how best to manage this group of women and those breast cancer survivors who may subsequently conceive. RESULTS: Pregnancy-associated breast cancer or gestational breast cancer is defined as breast cancer diagnosed during pregnancy or in the 12 months post-partum. A review of the current literature on breast cancer-related pregnancy suggests an incidence of between 0.7 and 3.9%. The prognosis is thought not to be significantly different from non-pregnancy-associated breast cancer, except in cases where a delay in diagnosis is associated with more advanced disease. The treatment is similar to non-pregnant cases, with the exception of radiotherapy, which is contraindicated throughout pregnancy; and chemotherapy, which is contraindicated during the first trimester. Few breast cancer survivors go on to conceive, but those who do have no worse breast cancer or pregnancy outcomes. CONCLUSION: Most of the research in this field has come from small, specialized institutions and may not reflect what occurs in the wider community. Further population-based research in this area is needed, and is currently being undertaken in Western Australia.

Reulen, R. C., M. P. Zeegers, et al. (2009). "Pregnancy outcomes among adult survivors of childhood cancer in the British Childhood Cancer Survivor Study." Cancer Epidemiol Biomarkers Prev **18**(8): 2239-47.

PURPOSE: We used data from the first large-scale overwhelmingly population-based study (a) to quantify the risk of adverse pregnancy outcomes in survivors of childhood cancer in relation to cancer type and treatment and (b) to assess live birth rates relative to the general population. METHODS: A questionnaire, including questions inquiring about pregnancy outcomes, was completed by 10,483 survivors. A total of 7,300 pregnancies were reported. Odds ratios (OR) for live birth, miscarriage, termination, stillbirth, premature birth, and low birth weight were calculated for different types of childhood cancer and by whether initial treatment involved chemotherapy and abdominal or brain irradiation. For females, the observed number of live births was compared with that expected based on the general population of England and Wales. RESULTS: Female survivors exposed to abdominal irradiation had a significantly increased OR of delivering preterm [OR, 3.2; 95% confidence interval (95% CI), 2.1-4.7] and producing offspring with a low birth weight (OR, 1.9; 95% CI, 1.1-3.2). An increased OR of miscarriage was also associated with abdominal radiotherapy (OR, 1.4; 95% CI, 1.0-1.9). The number of live births observed from all female survivors was two thirds of that expected (O/E, 0.64; 95% CI, 0.62-0.66) and lowest among survivors treated with brain (O/E, 0.52; 95% CI, 0.48-0.56) and abdominal radiotherapy (O/E, 0.55; 95% CI, 0.50-0.61). CONCLUSION: Female

survivors of childhood cancer treated with abdominal radiotherapy are at 3-fold increased risk of delivering preterm, 2-fold increased risk of low birth weight, and a small increased risk of miscarriage. Overall, female survivors produce considerably fewer offspring than expected, particularly those treated with abdominal or brain radiotherapy.

Ring, A. (2007). "Breast cancer and pregnancy." Breast **16 Suppl 2**: S155-8.

The frequency with which breast cancer is diagnosed in pregnant women is low (in the region of 1 in 1000 pregnancies), but the management of these women presents a considerable challenge to those involved in their care. Women frequently present with tumours displaying adverse pathological prognostic features. Initial investigation may be carried out as for non-pregnant women, but with particular attention paid to the risks of exposure to the foetus of ionizing radiation. Surgery can be carried out with seemingly little increased risk to the mother or foetus, but radiotherapy is usually avoided. In terms of short-term complications chemotherapy may be given relatively safely when administered outside of the first trimester and not around the time of delivery. However, the principle concern with all of these interventions is what the long-term implications for the newborn might be.

Ring, A. E., I. E. Smith, et al. (2005). "Breast cancer and pregnancy." Ann Oncol **16**(12): 1855-60.

BACKGROUND: The management of women who have breast cancers diagnosed whilst they are pregnant is challenging. The aim is to give optimal treatment to the mother to maximise the chances of survival, whilst minimising the risks of harm to the fetus. However, few breast surgeons or oncologists develop expertise in this area owing to the rarity of the association. DESIGN: In this review we evaluate and summarise the current literature regarding the diagnosis, management and prognosis of pregnancy-associated breast cancer. Data were identified by searches of Medline, PubMed and references from relevant articles for the period from 1966 to 2004. Papers were selected based on their size and adequacy of design. RESULTS: There is a lack of controlled data concerning the management of pregnancy-associated breast cancer. The data available suggest that diagnosis and surgery may be carried out as for the non-pregnant patient, with some limitations on staging investigations. Radiotherapy is contraindicated during pregnancy although, in terms of immediate complications, chemotherapy can be used after the first trimester. CONCLUSIONS: Data from prospective databases that are currently recruiting will provide further important information concerning the management of this condition, and in particular the long-term sequelae for mother and fetus.

Ring, A. E., I. E. Smith, et al. (2005). "Chemotherapy for breast cancer during pregnancy: an 18-year experience from five London teaching hospitals." J Clin Oncol **23**(18): 4192-7.

PURPOSE: The rare association between breast cancer and pregnancy means that few oncologists gain an expertise in this area. In particular, there are few published data concerning the use of chemotherapy for breast cancer during pregnancy. In this retrospective case series, we describe the experiences of five hospitals in London, United Kingdom, and how they manage this condition. PATIENTS AND METHODS: Retrospective searches were performed at five London hospitals in order to identify women who received chemotherapy for breast cancer while pregnant. RESULTS: Twenty-eight women were identified who had received chemotherapy for breast cancer during pregnancy. Twenty-four women received adjuvant or neoadjuvant chemotherapy for early breast cancer, and four women received palliative chemotherapy for metastatic disease. A total of 116 cycles of chemotherapy were administered during pregnancy. Sixteen women were treated with anthracycline-based chemotherapy and 12 received cyclophosphamide, methotrexate, and fluorouracil. All but one of the women were treated after the first trimester. One spontaneous abortion occurred in the woman treated during her first trimester; otherwise, there were no serious adverse consequences for the mothers or neonates. CONCLUSION: These data provide evidence that in terms of peripartum complications and immediate fetal outcome, chemotherapy can be safely administered to women during the second and third trimesters of pregnancy.

Rippy, E. E., I. F. Karat, et al. (2009). "Pregnancy after breast cancer: the importance of active counselling and planning." Breast **18**(6): 345-50.

AIM: To investigate the effect of breast cancer, its treatment and counselling on future pregnancy and fertility. METHOD: Three hundred and four women 45 years and younger at the time of diagnosis of breast cancer were identified from one breast unit from 1997 to 2006. A questionnaire was sent to all patients asking about pregnancy, counselling and fertility issues. RESULTS: Of 304 women, 248 were still alive and not lost to follow up. The questionnaire response rate was 66% and the average follow up was 60 months. By questionnaire response, 39 women had wanted children before diagnosis, and 24 still wanted them post treatment, giving a successful pregnancy rate of 75%. Eighteen

patients have become pregnant, 4 with more than one pregnancy. 107 patients were specifically counselled about fertility prior to breast cancer treatment. The mortality due to breast cancer was 10% in non-pregnant patients and 6% in patients who became pregnant after breast cancer. CONCLUSION: Pregnancy after breast cancer does not confer a poor prognosis. A higher rate of pregnancy than expected was found after treatment, possibly due to newer treatments including fertility preservation and also possibly due to the active counselling programme in this unit. Patients should have active counselling about fertility when planning treatment and fertility conservation can then be incorporated into a treatment plan.

Rosenkranz, K. M. and A. Lucci (2005). "Surgical treatment of pregnancy associated breast cancer." Breast Dis **23**: 87-93.

As the average age of parity increases amongst American women, the incidence of pregnancy associated breast cancer is also rising. The physiologic changes of the breast in pregnancy must be appreciated and understood in order to accurately and expeditiously diagnose pregnancy associated breast cancer (PABC). Core biopsy provides the safest and most accurate diagnostic tool. Once a diagnosis is made, risks and benefits to both the mother and the fetus must be considered prior to accepting a definitive management strategy. Historically women with PABC were encouraged to undergo modified radical mastectomy and to terminate pregnancy in order to safely proceed with adequate adjuvant therapy. Current care, however, relies upon multimodality therapy directed by multidisciplinary teams. PABC diagnosed early in the first trimester is best managed surgically by modified radical mastectomy followed by adjuvant chemotherapy in the second trimester. Women diagnosed in the late first, or the second or third trimesters may be safely treated with the surgical techniques of their choosing. Neoadjuvant chemotherapy, sentinel node biopsy and breast conservation are now considered safe modalities in properly chosen pregnant patients.

Rouzi, A. A., N. N. Sahly, et al. (2009). "Cisplatinum and docetaxel for ovarian cancer in pregnancy." Arch Gynecol Obstet **280**(5): 823-5.

BACKGROUND: There is limited data on chemotherapy for advanced ovarian cancer during pregnancy. Most women received cisplatin-based chemotherapy. There are no published reports on the use of docetaxel for ovarian cancer in pregnancy. CASE: A 32-year-old pregnant lady underwent laparatomy at 18-week gestation for ruptured ovarian cyst. The pregnancy was the result of in vitro fertilization with intracytoplasmic sperm injection. Left salpingo-oophorectomy and omental biopsy were done. A diagnosis of stage IIIC, poorly differentiated papillary serous adenocarcinoma of the ovary was made. She was given four cycles of cisplatinum and docetaxel followed by cesarean hysterectomy, right salpingo-oophorectomy, and cytoreductive surgery. The mother is well and has completed six cycle of chemotherapy. CONCLUSION: This is the first report on the use of docetaxel during pregnancy for ovarian cancer.

Rugo, H. S. (2003). "Management of breast cancer diagnosed during pregnancy." Curr Treat Options Oncol **4**(2): 165-73.

Breast cancer during pregnancy is generally defined as cancer occurring during pregnancy or within 1 year of delivery, although treatment options are the most complicated when the disease is diagnosed during gestation. The challenges of treatment during gestation are discussed in this article. In general, a pregnant woman with breast cancer should be treated similarly to the nonpregnant patient, with specific recommendations tailored to gestational age at diagnosis, stage of the tumor, and the personal preferences of the patient. Despite the increasing literature focusing on treatment decisions, there are little prospective data regarding treatment or long-term outcome information to provide toxicity data that can be used to advise patients and guide decisions. Most of the retrospective and anecdotal data are based on the possibility of fetal loss or demise with specific treatment or treatment administered at specific times during pregnancy. Therefore, it is impossible to accurately quantify risks to the fetus or the mother, and decisions should be made after careful discussion between the patient, her family, and the medical team. The physician must have a clear understanding of the pharmacology and teratogenic potential of individual agents, thus limiting risks.

Russo, J., G. A. Balogh, et al. (2006). "Molecular basis of pregnancy-induced breast cancer protection." Eur J Cancer Prev **15**(4): 306-42.

We have postulated that the lifetime protective effect of an early pregnancy against breast cancer is due to the complete differentiation of the mammary gland characterized by a specific genomic signature imprinted by the physiological process of pregnancy. In the present work, we show evidence that the breast tissue of postmenopausal parous women has had a shifting of stem cell 1 to stem cell 2 with a genomic signature different from similar structures derived from postmenopausal nulliparous women that have stem cell 1. Those genes that are significantly different are grouped in major categories

on the basis of their putative functional significance. Among them are those gene transcripts related to immune surveillance, DNA repair, transcription, chromatin structure/activators/co-activators, growth factor and signal transduction pathway, transport and cell trafficking, cell proliferation, differentiation, cell adhesion, protein synthesis and cell metabolism. From these data, it was concluded that during pregnancy there are significant genomic changes that reflect profound alterations in the basic physiology of the mammary gland that explain the protective effect against carcinogenesis. The implication of this knowledge is that when the genomic signature of protection or refractoriness to carcinogenesis is acquired by the shifting of stem cell 1 to stem cell 2, the hormonal milieu induced by pregnancy or pregnancy-like conditions is no longer required. This is a novel concept that challenges the current knowledge that a chemopreventive agent needs to be given for a long period to suppress a metabolic pathway or abrogate the function of an organ.

Russo, J., R. Moral, et al. (2005). "The protective role of pregnancy in breast cancer." Breast Cancer Res **7**(3): 131-42.

Epidemiological, clinical, and experimental data indicate that the risk of developing breast cancer is strongly dependent on the ovary and on endocrine conditions modulated by ovarian function, such as early menarche, late menopause, and parity. Women who gave birth to a child when they were younger than 24 years of age exhibit a decrease in their lifetime risk of developing breast cancer, and additional pregnancies increase the protection. The breast tissue of normally cycling women contains three identifiable types of lobules, the undifferentiated Lobules type 1 (Lob 1) and the more developed Lobules type 2 and Lobules type 3. The breast attains its maximum development during pregnancy and lactation (Lobules type 4). After menopause the breast regresses in both nulliparous and parous women containing only Lob 1. Despite the similarity in the lobular composition of the breast at menopause, the fact that nulliparous women are at higher risk of developing breast cancer than parous women indicates that Lob 1 in these two groups of women might be biologically different, or might exhibit different susceptibility to carcinogenesis. Based on these observations it was postulated that Lob 1 found in the breast of nulliparous women and of parous women with breast cancer never went through the process of differentiation, retaining a high concentration of epithelial cells that are targets for carcinogens and are therefore susceptible to undergo neoplastic transformation. These epithelial cells are called Stem cells 1, whereas Lob 1 structures found in the breast of early parous postmenopausal women free of mammary pathology, on the contrary, are composed of an epithelial cell population that is refractory to transformation, called Stem cells 2. It was further postulated that the degree of differentiation acquired through early pregnancy has changed the 'genomic signature' that differentiates Lob 1 of the early parous women from that of the nulliparous women by shifting the Stem cells 1 to Stem cells 2 that are refractory to carcinogenesis, making this the postulated mechanism of protection conferred by early full-term pregnancy. The identification of a putative breast stem cell (Stem cells 1) has, in the past decade, reached a significant impulse, and several markers also reported for other tissues have been found in the mammary epithelial cells of both rodents and humans. Although further work needs to be carried out in order to better understand the role of the Stem cells 2 and their interaction with the genes that confer them a specific signature, collectively the data presently available provide evidence that pregnancy, through the process of cell differentiation, shifts Stem cells 1 to Stem cells 2 - cells that exhibit a specific genomic signature that could be responsible for the refractoriness of the mammary gland to carcinogenesis.

Saif, M. W. (2005). "Management of colorectal cancer in pregnancy: a multimodality approach." Clin Colorectal Cancer **5**(4): 247-56.

Colorectal cancer (CRC) is one of the 3 most common types of cancer in women, but CRC during pregnancy is rare, with a reported incidence of approximately 0.002%. Synchronous colon cancer during pregnancy presents a diagnostic and therapeutic challenge for clinicians because there are no generally accepted guidelines regarding diagnosis or treatment. The diagnosis is challenging because the presenting signs/symptoms of CRC are often attributed to the usual complications of pregnancy, which could delay the diagnosis and allow the cancer to progress to an advanced stage. Carcinogenesis of colon cancer in pregnancy is not clear, but a few studies suggest that the increased levels of estrogen and progesterone related to pregnancy stimulate the growth of CRC with their receptors. The aim of treatment is to start therapy for the mother as early as possible and to simultaneously deliver the baby at the earliest time allowable. The management mandates a multidisciplinary approach involving experts in obstetrics, neonatology, gastrointestinal surgery, and medical oncology. The medical community should be able to diagnose colon cancer earlier in pregnancy in order to improve prognosis. The primary care physician or obstetrician should refer the pregnant patient with significant gastrointestinal symptoms to the gastroenterologist for evaluation. Likewise, the

gastroenterologist should be prepared to perform sigmoidoscopy (preferably without endoscopic medications) for significant lower gastrointestinal symptoms such as persistent rectal bleeding. Herein, the author reviews the literature concerning the diagnosis and treatment of CRC in pregnancy and discusses the role of newer agents approved for the treatment of CRC.

Sakamoto, K., T. Kanda, et al. (2009). "Management of patients with pregnancy-associated gastric cancer in Japan: a mini-review." Int J Clin Oncol **14**(5): 392-6.

Gastric cancer associated with pregnancy is quite rare, and is most often diagnosed at an advanced stage. Furthermore, physicians are confronted with two conflicting issues in this condition: the need for early treatment of the maternal gastric cancer and the continuation of the pregnancy. To clarify the characteristics of pregnancy-associated gastric cancer and to obtain useful information that would help us choose the best treatment strategy for pregnancy-associated gastric cancer, we reviewed the existing literature, using the key words "pregnancy" and "gastric cancer". We were able to accumulate 136 cases, including 100 cases reported previously in Japan, and 1 case that we report here. We analyzed a total of 137 cases in the present study. With respect to the stage of gastric cancer, 92.5% of the patients studied had advanced gastric cancer, and only 45.3% of the patients underwent gastrectomy, including incomplete resection. Accordingly, the prognosis was very poor; the 1- and 2-year survival rates were 18.0% and 15.1%, respectively. However, the number of patients found to have early gastric cancer by endoscopic examination has been increasing recently. An endoscopic examination should be conducted immediately in pregnant patients presenting with persistent gastrointestinal symptoms for the differential diagnosis of hyperemesis gravidarum. When an endoscopic examination reveals that pregnant patients have gastric cancer, a therapeutic plan should be promptly formulated, in accordance with the number of weeks of gestation, by a medical team consisting of specialists in perinatal obstetrics and gastric cancer specialists.

Sakorafas, G. H., A. Ntavatzikos, et al. (2009). "Peritoneal tuberculosis in pregnancy mimicking advanced ovarian cancer: a plea to avoid hasty, radical and irreversible surgical decisions." Int J Infect Dis **13**(5): e270-2.

Tuberculous peritonitis is rare in most Western counties, and can cause significant diagnostic and therapeutic problems. A 28-year-old pregnant female presented with nausea and vomiting, right lower quadrant abdominal pain, fever and intra-abdominal fluid. During surgery for presumed complicated acute appendicitis, many small masses (considered to be 'implants') were found within the peritoneal cavity, with a larger mass in the pelvis, mainly on the right. The clinical intra-operative diagnosis was advanced ovarian cancer and multiple biopsies were taken. The histological diagnosis was peritoneal tuberculosis. The patient was successfully treated conservatively. Hasty decisions to undertake radical and irreversible surgery should be avoided; this type of surgery should be performed only after histological confirmation.

Sapir, T., M. Blank, et al. (2005). "Immunomodulatory effects of intravenous immunoglobulins as a treatment for autoimmune diseases, cancer, and recurrent pregnancy loss." Ann N Y Acad Sci **1051**: 743-78.

Intravenous immunoglobulin (IVIG) is a safe preparation, made of human plasma of thousands of healthy donors. The fascinating history of gamma globulin therapy begins in 1930 when Finland treated pneumococcal pneumonia patients with equine serum, which prolonged their survival from pneumonia. Since then, significant breakthroughs were achieved by Cohn, Bruton, Imbach, and others, whose clinical contribution to the world of medicine was of great importance. Originally IVIG was used to treat immunodeficiencies. Later on the use of IVIG extended to autoimmune diseases as well. The efficacy of IVIG has been established only in several autoimmune diseases; clinical reports of trials, series, and case reports indicate significant improvement in many more autoimmune diseases. IVIG have also showed antimetastatic effects in a variety of cancer cell lines, as well as in a few case reports. The efficiency of IVIG has also been observed in recurrent pregnancy loss (RPL), either as a result of an autoimmune disease or spontaneous. Several attempts were made to discover the immunomodulatory effects of IVIG, but it is still not fully understood. Clearly IVIG has multiple mechanisms of actions, which are thought to cooperate synergistically. One of the main mechanisms of actions of IVIG is its ability to neutralize pathogenic autoantibodies via anti-idiotypic antibodies within IVIG preparation. The ability of IVIG to neutralize pathogenic autoantibodies is of great importance in many autoimmune diseases, as well as in RPL. In cancer cell lines, IVIG modulates the immune system in a few ways, including the induction of IL-12 secretion, which consequently activates natural killer cells, and the induction of expression of proapoptotic genes only in cancer cells. Side effects from IVIG are rare and mostly mild and transient. More importantly adverse effects can be minimized by administration to a selective patient

population in a proper way: slow infusion rate of 0.4 g/Kg body weight IVIG for 5 consecutive days, given in monthly cycles. The only downside of IVIG therapy is its high price. Therefore, clinicians should balance efficiency versus cost in deciding whether or not to treat certain conditions with IVIG.

Saunders, C., M. Hickey, et al. (2004). "Breast cancer during pregnancy." Int J Fertil Womens Med **49**(5): 203-7.

The terms gestational breast cancer (GBC) and pregnancy-associated breast cancer are given to breast cancer that occurs during pregnancy and up to one year post-partum. It is an uncommon event, and for even the most experienced clinician, whether oncologist, obstetrician or primary health worker, the complex issues that surround a diagnosis of breast cancer during pregnancy make management difficult. The prognosis overall for women diagnosed with GBC is poor, possibly due to delays in diagnosis. Primary physicians and obstetricians can play an important role in the early detection of GBC by promoting breast awareness in premenopausal women, including women who are pregnant or lactating; and by undertaking prompt and appropriate referral of pregnant and lactating women with breast abnormalities. Even in pregnant or lactating women, clinicians should always investigate a breast abnormality using triple assessment--clinical assessment, imaging and tissue biopsy. Breast cancer during pregnancy requires a multidisciplinary approach to ensure optimal care for both the mother and the baby. Breast cancer management can be adapted to protect the fetus, but this will be dependent on the gestation and disease status at diagnosis. Pregnancy after breast cancer does not appear to affect either cancer prognosis or pregnancy outcome. Obstetricians have a vital role to play in the care of these women by supporting them through their pregnancy, providing reassurance of fetal health and maintaining good communication with their other health providers.

Sawka, A. M., D. C. Lakra, et al. (2008). "A systematic review examining the effects of therapeutic radioactive iodine on ovarian function and future pregnancy in female thyroid cancer survivors." Clin Endocrinol (Oxf) **69**(3): 479-90.

BACKGROUND: For women with differentiated thyroid carcinoma (DTC), the effect of radioactive iodine (RAI) therapy on gonadal and reproductive function is an important consideration. OBJECTIVE AND METHODS: We systematically reviewed controlled studies examining the gonadal and reproductive effects of RAI therapy in women and adolescents surviving DTC. We searched nine electronic databases. All abstracts and papers were independently reviewed by two reviewers. RESULTS: After reviewing 349 unique citations and 61 full-text papers, 16 papers including data from 3023 women or adolescents with DTC were included. All studies were observational, with no long-term randomized control trial data. The age at first RAI treatment varied from 8 to 50 years and the cumulative activities of RAI administered for treatment varied from 30 to 1099 mCi. Transient absence of menstrual periods occurred in 8-27% of women within the first year after RAI, particularly in older women. In addition, RAI-treated women experienced menopause at a slightly younger age than women not treated with RAI. In the first year after RAI therapy, several studies reported increased rates of spontaneous and induced abortions. However, RAI treatment for DTC was generally not associated with a significantly increased risk of long-term infertility, miscarriage, induced abortions, stillbirths, or offspring neonatal mortality or congenital defects. CONCLUSIONS: In female survivors of DTC, there is little observational evidence to suggest important adverse effects of RAI treatment on gonadal function, fertility or pregnancy outcomes beyond 12 months, with the exception of a possible slightly earlier age of menopause.

Sekar, R. and P. R. Stone (2007). "Trastuzumab use for metastatic breast cancer in pregnancy." Obstet Gynecol **110**(2 Pt 2): 507-10.

BACKGROUND: Trastuzumab is approved for first-line treatment for breast cancer in combination with docetaxel for stage 2 tumors positive for human epidermal growth factor receptor 2. The effects of trastuzumab on the fetus are mostly unknown. CASE: Our case report focuses on a woman who was treated for invasive ductal carcinoma 1 year before pregnancy. She presented at 20 weeks of gestation with metastases and was treated with docetaxel and trastuzumab. She underwent two cycles of chemotherapy, and an ultrasound scan at 30 weeks showed anhydramnios. There was no history of ruptured membranes. Reappearance of amniotic fluid was noted at 33 weeks of gestation, 7 weeks after cessation of treatment. CONCLUSION: Treatment with trastuzumab during midgestation may be associated with anhydramnios.

Shepherd, J. H., C. Spencer, et al. (2006). "Radical vaginal trachelectomy as a fertility-sparing procedure in women with early-stage cervical cancer-cumulative pregnancy rate in a series of 123 women." Bjog **113**(6): 719-24.

OBJECTIVE: To analyse the fertility rates, complications and recurrences in a group of women who have undergone radical vaginal trachelectomy

and pelvic lymphadenectomy for early-stage cervical cancer. DESIGN: An observational series. SETTING: A Gynaecological Oncology Centre. POPULATION: One hundred and twenty-three consecutive women who underwent radical vaginal trachelectomy and pelvic lymphadenectomy for early-stage cervical cancer. METHODS: Data were collected prospectively. MAIN OUTCOME MEASURES Complications, recurrences, pregnancies and live births are presented as percentages of the total population. Fertility is presented as a 5-year cumulative rate, with women attempting to conceive as the denominator. RESULTS: A total of 123 women were followed up for an average of 45 months. Eleven (8.9%) had completion treatment (two radical hysterectomies and nine chemoradiotherapy) at the time of initial treatment. There were three recurrences (2.7%) among the women who did not have completion treatment and two (18.2%) in those who did. There were 6 perioperative and 26 postoperative complications. Sixty-three women attempted pregnancy. There were 55 pregnancies in 26 women and 28 live births in 19. Three women had continuing pregnancies. The 5-year cumulative pregnancy rate among women trying to conceive was 52.8%. All but two women were delivered by classical caesarean section and seven (25.0%) babies were born at 31+6 weeks or less. CONCLUSIONS: For selected women with early-stage cervical cancer, radical vaginal trachelectomy and pelvic lymphadenectomy are fertility-sparing options, with a low incidence of recurrence and acceptable cumulative conception rates. Complications are few, although there is a high premature labour and miscarriage rate among pregnant women.

Shrim, A., F. Garcia-Bournissen, et al. (2008). "Trastuzumab treatment for breast cancer during pregnancy." Can Fam Physician **54**(1): 31-2.

QUESTION: One of my patients has been diagnosed with breast cancer and started treatment with trastuzumab. She has recently discovered that she is pregnant and wishes to continue the pregnancy. What are the consequences of trastuzumab treatment during pregnancy and can she continue her pregnancy? ANSWER: Human data regarding the safety of trastuzumab during pregnancy are scarce. Only 3 case reports could be located in the published literature. Anhydramnios was observed in a case where the exposure to trastuzumab occurred during the second trimester, which reversed after discontinuation of the drug without any apparent consequences to the baby. Evidence is insufficient to provide any recommendations, but in light of the case reports, pregnancies exposed to trastuzumab during the second trimester should be closely followed with particular attention to amniotic fluid volume.

Stark, A. H., G. Kossoy, et al. (2003). "Olive oil consumption during pregnancy and lactation in rats influences mammary cancer development in female offspring." Nutr Cancer **46**(1): 59-65.

This study examined the effects of variety and quantity of dietary fat consumed by rats during pregnancy and lactation on female offspring's response to chemically induced mammary cancer. Groups of six female rats were fed diets containing 7% corn oil (7-CO), 15% CO (15-CO), 7% olive oil (7-OO), or 15% OO (15-OO) for 5 wk prior to, and during, pregnancy and lactation. Female offspring (n = 15 per group) were fed a 7-CO diet, and mammary cancer was induced with 7,12-dimethylbenz[a]anthracene (DMBA). Three months following cancer induction tumor incidence and size were recorded, and markers of apoptosis, serum estrogen concentrations, and hepatic phase II enzymes were measured. Tumor incidence was 47% in offspring born to mothers fed the 7-OO diet, rose to 67% in 7-CO and 15-OO offspring, and reached 86% in 15-CO. A trend toward smaller tumors was observed in the 7-OO group, and offspring of mothers fed high-fat diets had significantly more tumors. Estradiol levels at the end of lactation were significantly lower in mothers fed 7-OO but were similar in all groups of offspring. In tumor tissue, Bcl-2 expression was highest in the 15-CO offspring, and Bak expression was significantly higher in rats exposed to OO. A distinct trend toward increased caspase-3 expression (20 kDa) was observed in the 7-OO offspring, and both low-fat diets significantly elevated caspase activity. In healthy mammary tissue, rats exposed to low-fat diets had significantly higher caspase-3 (32-kDa) levels, and caspase-3 activity was significantly higher in the healthy tissue from both OO groups. Hepatic quinone reductase activity was significantly lower in offspring of mothers fed the low-fat diets. These results indicate that perinatal exposure to OO may have a protective effect against future development of mammary cancer in female offspring, whereas high-fat diets fed to pregnant and lactating rats, in particular CO, may be deleterious.

Steinetz, B. G., T. Gordon, et al. (2006). "The parity-related protection against breast cancer is compromised by cigarette smoke during rat pregnancy: observations on tumorigenesis and immunological defenses of the neonate." Carcinogenesis **27**(6): 1146-52.

Early pregnancy is a powerful negative risk factor for breast cancer (BCa) in women. Pregnancy also protects rats against induction of BCa by

carcinogens such as N-methyl-N-nitrosourea (MNU), making the parous rat a useful model for studying this phenomenon. Smoking during early pregnancy may lead to an increased risk of BCa in later life, possibly attributable to carcinogens in cigarette smoke (CS), or to reversal of the parity-related protection against BCa. To investigate these possibilities, 50-day-old timed first-pregnancy rats were exposed to standardized mainstream CS (particle concentration = 50 mg/m3) or to filtered air (FA) 4 h/day, Day 2-20 of gestation. Age-matched virgin rats were similarly exposed to CS or FA. At age 100 days, the CS or FA-exposed, parous and virgin rats were injected s.c. with MNU (50 mg/kg body wt), or with MNU vehicle. Mammary tumors (MTs) first appeared in virgin rats 9 weeks post-MNU injection. While no MTs were detected in FA-exposed parous rats until 18 weeks post-MNU, MTs appeared in the CS-exposed parous rats as early as 10 wks ($P < 0.02$). As no MTs developed in CS-exposed rats not injected with MNU, CS did not act as a direct mammary carcinogen. Serum prolactin concentration on Day 19 of pregnancy in CS-exposed dams was reduced by 50% compared with FA-exposed dams ($P < 0.005$). CS exposure during a pregnancy may thus 'deprotect' rats, enhancing their vulnerability to MNU-induced BCa. Prenatal CS exposure had no detectable effect on the immune responses of the pups examined at 3, 8 or 19 weeks of age. However, prolactin concentration in stomach contents (milk) of 3-day-old pups suckled by CS-exposed dams was decreased when compared with that of FA-exposed dams ($P < 0.032$). As milk-borne prolactin modulates development of the central nervous and immune systems of neonatal rats, CS exposure of the dams could adversely affect later maturation of these systems by reducing milk prolactin.

Teran-Porcayo, M. A., A. C. Gomez-Del Castillo-Rangel, et al. (2007). "Cancer during pregnancy: 10-year experience at a regional cancer reference center in Mexico." Med Oncol **24**(3): 297-300.

INTRODUCTION: Cancer during pregnancy is uncommon. However, recent trends in the prolongation of the childbearing age have made cancer-associated pregnancies more frequent. The objective of our study was to describe the frequency, types of cancer, and treatment with this association in our institution. MATERIAL AND METHODS: The clinical records of 36 patients, who presented to a regional reference center in Mexico over 10 years were reviewed collecting demographics, pregnancy characteristics and outcomes, type of cancer, clinical stage, treatment, and oncological outcome. RESULTS: The following tumors were observed: Uterine cervix (20), breast (7), ovary (3), non-Hodgkin Lymphoma (2), and other malignancies (4). The mean age of the patients was 30 (range 20-39) years. Mean follow up was 17.8 (range 1-74) months. The pregnancies were synchronous in 23 cases and 13 were diagnosed in the following 12 months after birth. Mean gestational age of the product was of 37.4 weeks, resulting in 15 deliveries with healthy products, four abortions, and four deaths. The majority of patients had advanced clinical stages. Overall survival was 36.4%. DISCUSSION: Cancer during pregnancy appears to have a worse outcome when compared to the results reported in the literature of non-pregnant women with the same conditions. This may be related to the advanced clinical stages we found. Cancer during pregnancy requires specialized attention to improve both fetal and maternal outcomes.

Teran-Porcayo, M. A., A. C. Gomez-Del Castillo-Rangel, et al. (2008). "Cancer during pregnancy: 10-year experience at a regional cancer reference center in Mexico." Med Oncol **25**(1): 50-3.

INTRODUCTION: Cancer during pregnancy is uncommon. However, recent trends in the prolongation of the childbearing age have made cancer-associated pregnancies more frequent. The objective of our study was to describe the frequency, types of cancer, and treatment with this association in our institution. MATERIAL AND METHODS: The clinical records of 36 patients who presented to a regional reference center in Mexico over 10 years were reviewed collecting demographics, pregnancy characteristics and outcomes, type of cancer, clinical stage, treatment, and oncological outcome. RESULTS: The following tumors were observed: Uterine cervix (20), breast (7), ovary (3), non-Hodgkin Lymphoma (2), and other malignancies (4). The mean age of the patients was 30 (range 20-39) years. Mean follow up was 17.8 (range 1-74) months. The pregnancies were synchronous in 23 cases and 13 were diagnosed in the following 12 months after birth. Mean gestational age of the product was of 37.4 weeks, resulting in 15 deliveries with healthy products, four abortions and four deaths. The majority of patients had advanced clinical stages. Overall survival was 36.4%. DISCUSSION: Cancer during pregnancy appears to have a worse outcome when compared to the results reported in the literature of non-pregnant women with the same conditions. This may be related to the advanced clinical stages we found. Cancer during pregnancy requires specialized attention to improve both fetal and maternal outcomes.

Theodosopoulos, T., A. Marinis, et al. (2006). "Colorectal cancer emergencies during pregnancy case reports." Eur J Gynaecol Oncol **27**(4): 422-4.

Colorectal carcinoma emergencies during pregnancy are exceptionally rare. Three women 38, 31 and 36 years old, in the third trimester of gestation received treatment, respectively, for acute abdomen due to perforation of rectal carcinoma, ileus due to a sigmoid tumor, and deep venous thrombosis (DVT) from a cecal tumor compromising the right iliac vein. In the first two patients urgent cesarean sections were carried out with Hartmann's procedure and a loop colostomy was performed to resolve the ensuing intraabdominal sepsis and ileus, respectively. In the third patient, a cesarean section was carried out to treat the underlying DVT more aggressively, while right colectomy was postponed for three weeks. Restoration of the alimentary tract was achieved two months later in the first case, while in the second and third cases total colectomy due to familial polyposis and right colectomy were performed three weeks after the cesarean section. An overview of the clinical features, diagnostic pitfalls and therapeutic approaches to manage complications of colorectal cancer during pregnancy are discussed.

Theriault, R. and K. Hahn (2007). "Management of breast cancer in pregnancy." Curr Oncol Rep **9**(1): 17-21.

The concurrent diagnosis of breast cancer and pregnancy remains a challenging clinical situation. Ethical concerns regarding maternal and fetal well-being and potential risks and harms of treatment influence the clinical decision process. Ethical considerations of treatment initiation have emphasized the role of autonomy for the patient and the concept of beneficence and non-maleficence for patient and fetus. Limited prospective data are available to assist the physician and patient in making an informed decision. Recent data on diagnosis, evaluation, and management of pregnant patients with breast cancer have informed the development of international recommendations and guidelines for management of breast cancer during pregnancy. This article reviews the epidemiology, clinical presentation, diagnosis, therapy, and outcomes of breast cancer occurring concomitantly with pregnancy.

Thordarson, G., N. Slusher, et al. (2004). "Insulin-like growth factor (IGF)-I obliterates the pregnancy-associated protection against mammary carcinogenesis in rats: evidence that IGF-I enhances cancer progression through estrogen receptor-alpha activation via the mitogen-activated protein kinase pathway." Breast Cancer Res **6**(4): R423-36.

INTRODUCTION: Pregnancy protects against breast cancer development in humans and rats. Parous rats have persistently reduced circulating levels of growth hormone, which may affect the activity of the growth hormone/insulin-like growth factor (IGF)-I axis. We investigated the effects of IGF-I on parity-associated protection against mammary cancer. METHODS: Three groups of rats were evaluated in the present study: IGF-I-treated parous rats; parous rats that did not receive IGF-I treatment; and age-matched virgin animals, which also did not receive IGF-I treatment. Approximately 60 days after N-methyl-N-nitrosourea injection, IGF-I treatment was discontinued and all of the animal groups were implanted with a silastic capsule containing 17beta-estradiol and progesterone. The 17beta-estradiol plus progesterone treatment continued for 135 days, after which the animals were killed. RESULTS: IGF-I treatment of parous rats increased mammary tumor incidence to 83%, as compared with 16% in parous rats treated with 17beta-estradiol plus progesterone only. Tumor incidence and average number of tumors per animal did not differ between IGF-I-treated parous rats and age-matched virgin rats. At the time of N-methyl-N-nitrosourea exposure, DNA content was lowest but the alpha-lactalbumin concentration highest in the mammary glands of untreated parous rats in comparison with age-matched virgin and IGF-I-treated parous rats. The protein levels of estrogen receptor-alpha in the mammary gland was significantly higher in the age-matched virgin animals than in untreated parous and IGF-I-treated parous rats. Phosphorylation (activation) of the extracellular signal-regulated kinase-1/2 (ERK1/2) and expression of the progesterone receptor were both increased in IGF-I-treated parous rats, as compared with those in untreated parous and age-matched virgin rats. Expressions of cyclin D1 and transforming growth factor-beta3 in the mammary gland were lower in the age-matched virgin rats than in the untreated parous and IGF-I-treated parous rats. CONCLUSION: We argue that tumor initiation (transformation and fixation of mutations) may be similar in parous and age-matched virgin animals, suggesting that the main differences in tumor formation lie in differences in tumor progression caused by the altered hormonal environment associated with parity. Furthermore, we provide evidence supporting the notion that tumor growth promotion seen in IGF-I-treated parous rats is caused by activation of estrogen receptor-alpha via the Raf/Ras/mitogen-activated protein kinase cascade.

Tonetti, D. A. (2004). "Prevention of breast cancer by recapitulation of pregnancy hormone levels." Breast Cancer Res **6**(1): E8.

At the present time, the only approved method of breast cancer prevention is use of the selective estrogen receptor modulator (SERM) tamoxifen. Many breast cancers are driven to grow by estrogen, and tamoxifen exploits this by blocking

estrogen action at the estrogen receptor. A counter-intuitive and controversial approach to breast cancer prevention is administration of estrogen and progestin at an early age to achieve pregnancy levels. This approach is supported by the fact that breast cancer incidence is halved by early (< or = 20 years of age) full-term pregnancy. Moreover, it has been demonstrated in rodent models that mimicking the hormonal milieu can effectively prevent carcinogen-induced mammary cancer. In this issue of Breast Cancer Research Rajkumar and colleagues use the rodent model to further define the timing and type of hormonal therapy that is effective in preventing mammary carcinogenesis. Clearly, application of this approach in humans may be difficult, but the potential benefit is intriguing.

Traen, K., D. Svane, et al. (2006). "Stage Ib cervical cancer during pregnancy: planned delay in treatment--case report." Eur J Gynaecol Oncol **27**(6): 615-7.

Approximately 0.05% of pregnancies are complicated with cervical cancer. Treatment of this malignancy during pregnancy depends on the stage of disease and gestational age at the time of diagnosis. In women with Stage IB cervical cancer immediate treatment, without regard to the pregnancy, is traditionally advocated in the first and second trimester. A planned delay of treatment, to achieve foetal maturity, may be acceptable if there are no adverse maternal and foetal consequences. We present a case of a Stage IB1 cervical cancer, diagnosed during a twin pregnancy, and treated with a planned delay of 19 weeks. We have reviewed the literature and focused on what is known about planned delay in therapy of Stage IB cervical cancer, diagnosed before 30 weeks of gestational age.

Tsubura, A., N. Uehara, et al. (2008). "Estrogen and progesterone treatment mimicking pregnancy for protection from breast cancer." In Vivo **22**(2): 191-201.

Early age at full-term pregnancy lowers the risk of breast cancer in women; lactation seems to be of marginal importance and aborted pregnancy is not associated with reduced risk. Although early full-term pregnancy provides protection against breast cancer, first full-term pregnancy in older women appears to increase the risk. The protective effect of pregnancy has also been observed in rats and mice; in these animals, lactation has an additive effect and interrupted pregnancy provides partial but significant protection. Pregnancy at a young age (< or = 3 months) is highly effective, but pregnancy in older animals (> or = 4 months) is less effective. Parity-induced protection against mammary cancer in rodents can be reproduced by short-term treatment (approximately equivalent to gestational period of rodent or shorter) with the pregnancy hormones, estrogen and progesterone. Administration of pregnancy hormones to nulliparous women may be a useful strategy for protection against breast cancer. However, estrogen and progesterone are thought to play major roles in promotion of the proliferation of breast epithelial cells. Thus, the duration of such treatment and the age at which it is administered are essential factors that require further study. Experimental data suggest that short-term treatment of older rats (aged 6 months) with estrogen and progesterone accelerates mammary carcinogenesis and that long-term (>20 weeks) treatment abolishes the cancer-suppressing effect or even accelerates mammary carcinogenesis. Thus, the available evidence suggests that age and duration of estrogen and progesterone treatment are particularly important factors for protection from breast cancer.

Upponi, S. S., F. Ahmad, et al. (2003). "Pregnancy after breast cancer." Eur J Cancer **39**(6): 736-41.

The issue of pregnancy in patients previously treated for breast cancer is controversial. This paper reviews the literature using Medline and Embase databases over the last 50 years to address the issue. Overall survival in patients treated for breast cancer who subsequently become pregnant compares favourably with controls. This paper also addresses the effects of adjuvant therapy (loco-regional and systemic) on subsequent pregnancy. Introduction of a national registry of these patients may help inform such patients in the future.

van Dalen, E. C., H. J. van der Pal, et al. (2006). "Clinical heart failure during pregnancy and delivery in a cohort of female childhood cancer survivors treated with anthracyclines." Eur J Cancer **42**(15): 2549-53.

The cumulative incidence of peripartum anthracycline-induced clinical heart failure (A-CHF) was evaluated in a cohort of 53 childhood cancer survivors who had delivered one or more children. None of them developed peripartum A-CHF (cumulative incidence 0%; 95% confidence interval (CI) 0-5.7%). The mean follow-up time after the first administration of anthracycline therapy was 20.3 years. They received a mean cumulative anthracycline dose of 267 mg/m2. It is worth noticing that even 2 patients with A-CHF before pregnancy did not develop peripartum A-CHF. Since there were no cases of peripartum A-CHF in our cohort, it was not possible to evaluate associated risk factors. In conclusion, this study demonstrates a low risk of developing peripartum A-CHF in childhood cancer survivors. However, more cohort studies with

adequate power and long-term follow-up are needed to reliably evaluate the cumulative incidence of peripartum anthracycline-induced cardiotoxicity (both clinical and asymptomatic) and associated risk factors.

Vinatier, E., B. Merlot, et al. (2009). "Breast cancer during pregnancy." Eur J Obstet Gynecol Reprod Biol **147**(1): 9-14.

Breast cancer in pregnancy is an uncommon situation but poses dilemmas for patients and their physicians. There is a paucity of prospective studies regarding diagnosis and treatment of breast cancer during pregnancy. Women diagnosed with breast cancer during pregnancy have similar disease characteristics to age-matched controls. Current evidence suggests that diagnosis may be carried out with limitations regarding staging. Surgical treatment may be performed as for non-pregnant women. Radiotherapy and endocrine or antibody treatment should be postponed until after delivery. Chemotherapy is allowed after the first trimester. Physicians should be aggressive in the workup of breast symptoms in the pregnant population to expedite diagnosis and allow multidisciplinary treatment without delay.

Vitoratos, N., E. Salamalekis, et al. (2002). "Sigmoid colon cancer during pregnancy." Eur J Obstet Gynecol Reprod Biol **104**(1): 70-2.

Colorectal carcinoma during pregnancy is a rare event. We report a 23-year-old primigravida with advanced stage adenocarcinoma of the sigmoid colon diagnosed at 34 weeks of gestation. A healthy female infant was delivered by cesarean section. The treatment of choice was chemotherapy. The patient died 3 months after delivery.

Ward, R. M. and R. E. Bristow (2002). "Cancer and pregnancy: recent developments." Curr Opin Obstet Gynecol **14**(6): 613-7.

PURPOSE OF REVIEW: Breast carcinoma, cervical dysplasia and cervical carcinoma are some of the most common forms of precancerous and malignant changes seen in pregnancy due to their prevalence in reproductive age women. The impact of pregnancy on these diseases is complex and needs to be carefully considered for appropriate clinical management. RECENT FINDINGS: Recent studies indicate a relationship between hormone levels during pregnancy and subsequent breast cancer risk. For women who have already been diagnosed with breast cancer, retrospective studies show no adverse outcomes on maternal mortality with subsequent pregnancy. Prospective studies are needed to further elucidate these relationships. Recent research evaluating human papilloma virus in pregnant women indicates a similar prevalence of disease among pregnant and nonpregnant patients. Increased rates of human papilloma virus clearance postpartum may be related to an increased immune response within the cervix secondary to the trauma of labor. For women with early stage cervical cancer desiring to preserve future fertility, new trends in treatment allow for preservation of reproductive function. Few recent studies have been conducted regarding the use of chemotherapy during pregnancy, but one study reports increased rates of prematurity after the use of chemotherapy. SUMMARY: Continued research is needed regarding the management of breast and cervical cancer during pregnancy in order to optimize treatments and to further our understanding of these disease processes.

Watanabe, Y., M. Tsuritani, et al. (2009). "Radical hysterectomy for invasive cervical cancer during pregnancy: a retrospective analysis of a single institution experience." Eur J Gynaecol Oncol **30**(1): 79-81.

PURPOSE: To evaluate long-term prognosis and patient safety for a radical hysterectomy in pregnant women with invasive cervical cancer. PATIENTS AND METHODS: We retrospectively analyzed 12 cases of radical hysterectomy (RH) performed for invasive cervical cancer during pregnancy. Four patients underwent RH with the fetus in situ and another eight patients underwent RH followed by cesarean section. RESULTS: The median treatment period was 17 weeks of gestation (range: 9 to 39), the mean blood loss was 550.1 +/- 162.5 g (range: 275 to 850). Pelvic lymph node metastases were observed in three patients and parametrial invasion was observed in one patient. Although one patient experienced a recurrence at the vaginal stump, all patients were alive at a median follow-up interval of 105 months (range: 61 to 234). CONCLUSION: RH during pregnancy can be safely performed even with the fetus in situ and a subsequent cesarean section.

Weisz, B., D. Meirow, et al. (2004). "Impact and treatment of cancer during pregnancy." Expert Rev Anticancer Ther **4**(5): 889-902.

Cancer is the second most common cause of death in the reproductive years and complicates up to one in 1000 pregnancies. When cancer is diagnosed during pregnancy, the management strategy must take into account both the mother and developing fetus. In this article, the four most common malignancies diagnosed in pregnant patients--cervical and breast cancer, malignant melanoma and lymphoma--will be reviewed, with an emphasis on the impact of the

diagnosis and management on the pregnant patient and the developing fetus.

Wijaya, R., W. S. Yong, et al. (2007). "Managing breast cancer diagnosed in first trimester pregnancy: a case report." Ann Acad Med Singapore **36**(12): 1024-7.

INTRODUCTION: Breast cancer is the most common malignancy in pregnant women, occurring at a rate of about 1 in 3000 pregnancies. Unfortunately, this will sometimes occur during the first trimester of pregnancy and this situation warrants discussion of management options with regard to the mother and child, especially with the current trend of deferring child bearing to a later age. CLINICAL PICTURE: We present a 34-year-old primigravida who had a breast lump prior to confirmation of her pregnancy and received her diagnosis of invasive breast cancer at 7 weeks' amenorrhoea. The oncologic management options of this pregnant patient with breast cancer are discussed. TREATMENT: The patient eventually opted to undergo wide excision of the breast cancer with sentinel lymph node biopsy and possible axillary clearance together with termination of her pregnancy. RESULTS: The patient successfully underwent surgery for her breast cancer and was subsequently treated with adjuvant therapy as per normal protocol for a non-pregnant patient. CONCLUSION: The management of breast cancer and pregnancy occurring concurrently is a complex problem fraught with many dilemmas for both the medical team, the patient and her family. The option chosen must involve a multidisciplinary team and have full informed consent of the patient.

Wilczynski, J. R., J. Kalinka, et al. (2008). "The role of T-regulatory cells in pregnancy and cancer." Front Biosci **13**: 2275-89.

The acceptance of paternally-derived alloantigens during pregnancy and escape from host immunosurveillance by cancer are based on similar immunological mechanisms. Among them both natural and peripherally-induced T CD4+ CD25+ Foxp3+ and Tr1 regulatory cells (Tregs) play important role. Interactions of Tregs with other immunocytes including dendritic cells, mechanisms of Tregs recruitment and their suppressive properties in cancer and pregnancy have been presented in this paper. Despite the fact that mechanisms of Treg regulation are still in progress, there is a hope for use of Tregs-related immunotherapy in clinical practice, and the first attempts of such management have already been described. However, more information about the function of Tregs cells is needed to provide safe treatment devoid of potential side-effects. Resolving the secrets of Tregs cells will probably offer new options of cancer treatment and will help to improve the management of pregnancy failure.

Wo, J. Y. and A. N. Viswanathan (2009). "Impact of radiotherapy on fertility, pregnancy, and neonatal outcomes in female cancer patients." Int J Radiat Oncol Biol Phys **73**(5): 1304-12.

PURPOSE: Radiation has many potential long-term effects on cancer survivors. Female cancer patients may experience decreased fertility depending on the site irradiated. Oncologists should be aware of these consequences and discuss options for fertility preservation before initiating therapy. METHODS AND MATERIALS: A comprehensive review of the existing literature was conducted. Studies reporting the outcomes for female patients treated with cranio-spinal, abdominal, or pelvic radiation reporting fertility, pregnancy, or neonatal-related outcomes were reviewed. RESULTS: Cranio-spinal irradiation elicited significant hormonal changes in women that affected their ability to become pregnant later in life. Women treated with abdomino-pelvic radiation have an increased rate of uterine dysfunction leading to miscarriage, preterm labor, low birth weight, and placental abnormalities. Early menopause results from low-dose ovarian radiation. Ovarian transposition may decrease the rates of ovarian dysfunction. CONCLUSIONS: There is a dose-dependent relationship between ovarian radiation therapy (RT) and premature menopause. Patients treated with RT must be aware of the impact of treatment on fertility and explore appropriate options.

Woo, J. C., T. Yu, et al. (2003). "Breast cancer in pregnancy: a literature review." Arch Surg **138**(1): 91-8; discussion 99.

HYPOTHESIS: Breast cancer in pregnancy will increase as more women postpone childbearing until later in life. OBJECTIVE: To review the literature on diagnosis, staging, treatment, and prognosis. DESIGN AND METHODS: Articles were obtained from MEDLINE (1966-present) using the keywords breast, cancer, carcinoma, and pregnancy. Additional articles were sought using the references of those obtained. A total of 171 articles were found, 125 in English. More than 100 were reviewed, including 7 prospective and 40 retrospective studies, 6 case reports, and at least 47 review articles on various aspects of pregnancy and cancer. Data extraction was performed by 1 reviewer. RESULTS: Diagnostic delays are shorter than in the past but remain common. Mammography has a high false-negative rate during pregnancy. Biopsy or needle aspiration are needed for diagnosis and cannot be postponed until after delivery. Pregnancy-associated cancers tend to occur at a later stage and be estrogen receptor-negative. However,

they carry a similar prognosis to other breast cancers when matched for stage and age. Although modified radical mastectomy is the traditional treatment, breast-conserving therapy is increasingly common. Therapeutic radiation is contraindicated, but chemotherapy is relatively safe after the first trimester. Tamoxifen should be avoided in the first trimester and possibly beyond. CONCLUSIONS: Physicians should perform a thorough breast examination at the first prenatal visit and maintain a high index of suspicion for cancer. Patients who wish to continue their pregnancies have a growing array of treatment options.

Yang, W. T., M. J. Dryden, et al. (2006). "Imaging of breast cancer diagnosed and treated with chemotherapy during pregnancy." Radiology **239**(1): 52-60.

PURPOSE: To retrospectively assess mammography, high-frequency-transducer ultrasonography (US), and color Doppler US for the initial and subsequent evaluation of breast cancer diagnosed and treated with chemotherapy during pregnancy. MATERIALS AND METHODS: A retrospective study of clinical records between January 1989 and December 2003 of women with breast cancer diagnosed and treated with chemotherapy during pregnancy was performed after waiver of informed consent was obtained. The study was approved by an institutional review board and was HIPAA compliant. Mammograms and sonograms were reviewed by two mammographers using the Breast Imaging Reporting and Data System (BI-RADS) mammographic and US lexicon. US assessment of the regional lymph node basins, including the axillary, infraclavicular, internal mammary, and supraclavicular regions, was documented. US was used to evaluate response to therapy in the breast and the regional lymph nodes in women who underwent neoadjuvant chemotherapy. RESULTS: Twenty-three women with 24 cancers that were imaged prior to surgery with mammography (n = 3), US (n = 4), or mammography and US (n = 17) were included in the study. The histologic diagnosis of the primary tumor was invasive ductal cancer in 22 lesions, and the diagnosis was invasive carcinoma in the two other cancers. The median age in this study was 34 years (range, 24-45 years). Of the 20 women who underwent preoperative mammography, findings were positive for malignancy in 18 of 20 (90%) cancers despite dense breast parenchymal patterns (BI-RADS types 3 and 4). A mass in all 21 cancers (100%) was depicted in the 20 women who underwent breast and nodal US. US correctly depicted axillary metastasis in 15 of 18 women who underwent US nodal assessment. Of the 12 patients who were evaluated for response to chemotherapy, US demonstrated complete response in two patients, partial response in three, stable findings in one, and progression of disease in six. CONCLUSION: Breast cancer diagnosed during pregnancy is mammographically evident despite dense parenchymal background. US, when performed, demonstrates all masses and provides information regarding response to neoadjuvant chemotherapy.

Yarali, H., G. Bozdag, et al. (2004). "A successful pregnancy after intracytoplasmic sperm injection and embryo transfer in a patient with endometrial cancer who was treated conservatively." Fertil Steril **81**(1): 214-6.

OBJECTIVE: To describe a patient with polycystic ovary syndrome (PCOS) conceiving with intracytoplasmic sperm injection (ICSI) and embryo transfer after conservative treatment of early stage endometrial cancer. DESIGN: Case report. SETTING: Tertiary center for assisted reproductive technologies.A 32-year-old woman with PCOS, primary infertility of 4 years duration, and grade 1 endometrioid endometrial cancer. INTERVENTION(S): Assessment of myometrial invasion and extrauterine spread with magnetic resonance imaging (MRI) and explorative laparotomy. High-dose progestin treatment and ICSI and embryo transfer. MAIN OUTCOME MEASURE(S): Successful take-home baby and no residual endometrial cancer. RESULT(S): A healthy normal female infant with a birth weight of 1740 g was born by cesarean section at 30 weeks' gestation. No residual cancer was detected at the follow-up curettage performed 2 months after the delivery. CONCLUSION(S): Conservative uterus-preserving treatment may be considered in patients with early stage endometrial cancer. Assisted reproductive technologies may be used in such patients for immediate achievement of pregnancy.

Yasmeen, S., R. Cress, et al. (2005). "Thyroid cancer in pregnancy." Int J Gynaecol Obstet **91**(1): 15-20.

OBJECTIVE: To compare stage at diagnosis, treatment and survival among pregnant women with thyroid cancer to non-pregnant women with thyroid cancer, and to assess the impact of treatment on maternal and perinatal outcomes. METHODS: A database containing maternal and newborn discharge records linked to the California Cancer Registry was queried to obtain information on all thyroid cancers from 1991-1999. Women with thyroid cancer occurring during pregnancy were compared to age-matched non-pregnant women with thyroid cancer. RESULTS: 595 cases of thyroid cancers were identified (129 antepartum and 466 postpartum).

About 64% of thyroid cancers were diagnosed at stage 2 among pregnant women versus 58% among non-pregnant controls. The odds of thyroid cancer were 1.5 times higher among Asian/Pacific Islanders than among Non-Hispanic White women. Pregnancy had no significant effect on mortality after diagnosis of thyroid cancer. Thyroidectomy during pregnancy was not associated with adverse maternal or neonatal outcomes. CONCLUSIONS: Thyroid cancer discovered during or after pregnancy does not appear to have a significant impact on the prognosis of the disease.

Yasuda, M., Y. Terai, et al. (2009). "Successful pregnancy after conservative surgery for stage IA endometrial cancer in a young woman." Fertil Steril **91**(3): 936 e13-5.

OBJECTIVE: To report a case of successful pregnancy after conservative surgery for stage 1A endometrial cancer. DESIGN: Case report. SETTING: University hospital. PATIENT(S): A 33-year-old woman who was diagnosed with stage IA endometrial cancer. INTERVENTION(S): Conservative surgery and chemotherapy. MAIN OUTCOME MEASURE(S): Clinical outcome. RESULT(S): After administering medroxyprogesterone acetate (MPA) for 6 weeks, hysterofiberscopy showed that the restricted lesions still remained. A partial resection of the lesions was therefore performed. The patient delivered a girl by cesarean section after the surgery. CONCLUSION(S): Conservative surgery after MPA treatment may be a new treatment option for patients who wish to preserve their fertility.

Yildirim, Y., N. Erkan, et al. (2009). "Perforated gastric cancer complicating early postpartum period of pregnancy." Acta Chir Belg **109**(4): 534-7.

BACKGROUND: An unique association of gastric cancer with pregnancy and puerperium is rare. CASE: A 29-year-old woman had complained of epigastric pain, postprandial vomiting and weight loss during the last 3 months of pregnancy. She first applied to our centre for premature rupture of membranes at the 38th week of gestation and underwent an emergency caesarean section because of umblical cord prolapsus. The patient developed generalised abdominal pain, distention and fever on the 2nd postpartum day. She was operated on due to acute abdomen. During surgery, generalised peritonitis with a gastric ulcer perforation at the corpus was found. The perforation area was repaired primarily. Pathological examination revealed gastric adenocarcinoma. Definitive surgery was carried out 2 weeks later. The patient received 6 cycles of adjuvant chemotherapy. After completing chemotherapy the patient was re-explored because of developing intestinal obstruction. In surgical exploration, a disseminated peritonitis carcinomatosa and extensive adhesions were observed and the patient was therefore evaluated as incurable. Postoperatively, the patient developed a high output intestinal fistula which could not be treated with palliative care. The patient died 6 months after initial diagnosis of gastric cancer. CONCLUSION: When peritonitis symptoms exist in a postpartum woman in addition to other peritonitis causes, malignant gastro-intestinal perforations such as gastric cancer perforation should be kept in mind.

Yoshida, M., H. Matsuda, et al. (2009). "Successful treatment of gastric cancer in pregnancy." Taiwan J Obstet Gynecol **48**(3): 282-5.

OBJECTIVE: Gastric cancer during pregnancy is rare, and even in Japan where a high rate of gastric cancers are reported, only 0.016% of pregnant women suffer from this disease. Generally, the cancer is already advanced at the time of detection and the prognosis for the woman is usually extremely poor. Moreover, prioritizing treatment of the woman often results in a premature birth. CASE REPORT: We report a case of gastric cancer in a 32-year-old pregnant woman, gravida 6, para 4. The mother and the neonate had good prognoses after early diagnosis, cesarean delivery and surgery. CONCLUSION: Diagnosis of gastric cancer in pregnant women is often delayed even when they are symptomatic, because the symptoms are taken to be symptoms of hyperemesis or expansion of the uterus. However, since the nausea and vomiting arising from hyperemesis generally improves by the 20th week of gestation, the presence of protracted digestive symptoms in the second trimester calls for prompt investigation of digestive disorders. This case highlights the importance of early detection of gastric cancer for a positive prognosis, considering the rapidity with which gastric cancer advances in pregnancy.

Zambelli, A., G. A. Prada, et al. (2008). "Erlotinib administration for advanced non-small cell lung cancer during the first 2 months of unrecognized pregnancy." Lung Cancer **60**(3): 455-7.

Although several antineoplastic agents have been proven to be safe for the fetus after the organogenesis period, there is limited information on their use during the first trimester of pregnancy. Herein we report the first case of a patient with metastatic lung cancer treated with erlotinib during the first 2 months of an unrecognized pregnancy. A 30-year-old woman was diagnosed with stage IV non-small cell lung cancer with bone and lung metastasis. The patient received 4 months of palliative cisplatin/gemcitabine chemotherapy and

biphosphonates. After 12 months the disease progressed and the patient received erlotinib 100 mg/day. During this period the patient became pregnant. Since she recalled the date of her last menstrual period at about 15 days prior to the start of the therapy, we did consider the possibility of conception at the time of the first day of erlotinib administration. Informed about the risk for the fetus due to erlotinib, the patient stopped anticancer treatment. After 42 weeks of regular gestation, cesarean section was performed, delivering a 3490 g female new-born with no evidence of congenital malformations. The disease evaluation performed with thoracic CT scan, after 1 month from the childbirth, showed a progressive lung metastasis and erlotinib treatment was resumed at the dose of 150 mg/day.

Zamperini, P., B. Gibelli, et al. (2009). "Pregnancy and thyroid cancer: ultrasound study of foetal thyroid." Acta Otorhinolaryngol Ital **29**(6): 339-44.

Thyroid cancer is the most common endocrine malignancy, more frequently diagnosed in young women during childbearing age and approximately 10% of all thyroid cancers are diagnosed during pregnancy or in the early post-partum period. Thyroid cancer in young people has generally an excellent prognosis, and survival among women with thyroid cancer diagnosed during pregnancy may not differ from that in age-matched non-pregnant women with similar cancer. Pregnancy after treatment of thyroid carcinoma requires both maternal and foetal controls. Of utmost importance is to ensure adequate maintenance of maternal levels of levothyroxine, needed by both the foetal central nervous system for its normal maturation and the mother to avoid possible recurrence or spread of the disease. In the present investigation, to confirm normal foetal growth and foetal thyroid development, an ultrasound study of the foetal thyroid was performed in 40 full term pregnancies in 32 women receiving levothyroxine treatment for previously treated thyroid cancer. In patients undergoing either suppressive or substitutive levothyroxine treatment, foetal thyroid growth was noted to be normal in all the cases, newborn thyroid status was always normal, and the incidence of maternal morbidity was not influenced. In the present study group, pregnancy does not appear to compromise mother's disease-free interval, nor to be compromised by thyroid cancer treatment. Results of the present study confirm that regular adjustment of levothyroxine treatment is of utmost importance for both maternal and foetal well-being and that foetal thyroid ultrasound study may add useful and reassuring data about child well-being.

Zanetti-Dallenbach, R., S. Tschudin, et al. (2006). "Psychological management of pregnancy-related breast cancer." Breast **15 Suppl 2**: S53-9.

The comprehensive care of a pregnant patient in whom breast cancer is diagnosed presents a challenge to the biomedical and psychological competence of the medical team. Illustrated by a case presentation the different phases of psychological care are delineated and discussed: the confrontation with the diagnosis of a life-threatening disease in a situation in which the beginning of a future life is celebrated. Special attention is given to breaking bad news, the establishment of a stable and trustful physician-patient relationship, communicating risk and to the extremely difficult decision-making process regarding termination or continuation of pregnancy (shared decision-making). The delicate balance between oncological care for the mother with a high-risk disease and a high-risk pregnancy and neonatal care for the foetus is outlined, including regular talks about emotions and concerns.

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