



OTHER CANCERS IN PREGNANCY

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CLASSIFICATION

Gynecologic Cancer

- *Vulvar Cancer
- *Vaginal Cancer
- *Endometrial Cancer
- *Fallopian Tube Cancer
- *Gestational Trophoblastic Neoplasia

Non Gynecologic Cancer

- *Melanoma
- *Colorectal Cancer
- *Hematological Malignancies
- *Thyroid Cancer



VULVAR CANCER

- *Fewer than 50 cases of invasive cancer of the vulva associated with pregnancy have been reported in the literature.
- *Incidence 1 per 8000-20000 deliveries.
- *The most common of these are **invasive epidermoid carcinomas** followed by melanomas, sarcomas, and adenoid cystic adenocarcinomas.



VULVAR CANCER

- *The majority of patients have been between **25 and 35** years of age
- *With the **increasing frequency of the diagnosis of CIS** of the vulva, the occurrence of preinvasive disease with pregnancy is common today.
- ***Adequate biopsies** of the most suspicious areas are essential to **rule out invasive disease**.
- *The presence of intraepithelial neoplasia should not prohibit vaginal delivery!!



MANAGEMENT

- *First, second, and early third trimesters is usually treated as indicated in nonpregnant patients.
- *T1 lesions should be managed by **radical wide excision** with ipsilateral groin dissection if the depth of invasion is larger than 1 mm.
- *Larger and more deeply invasive tumors require a radical vulvectomy and bilateral inguinofemoral lymphadenectomy.
- *When the diagnosis is made after 36 weeks of gestation, we recommend a wide local excision with definitive surgery postponed until the postpartum period.



MANAGEMENT

- *Women treated during pregnancy may be **allowed to attempt vaginal delivery** provided the vulvar wounds are well healed!!
- *Patients with high-risk surgicopathologic features warranting adjuvant radiation should undergo cesarean delivery as soon as fetal pulmonary maturation can be documented.
- *After delivery of the baby, **the ovaries should be transposed to the paracolic gutters**, and pelvic or groin irradiation (or both) can be administered postpartum.



VAGINAL CANCER

- *Cancer of the vagina has been found mainly in women **older than 50 years.**
- ***Clear cell adenocarcinoma** of the vagina alleged to be associated with the **diethylstilbestrol-exposed offspring!!**
(Young women??)
- *The diagnosis of vaginal cancer during pregnancy is exceptionally uncommon.



VAGINAL CANCER

*Senekjian and colleagues described 16 women who were pregnant when stage 1 and 2 clear cell adenocarcinoma of the vagina (Gynecol Oncol, 1986).

- Long-term survivors
- maternal hormone history
- symptoms
- stage
- location
- predominant histologic or cell type
- greatest tumor diameter
- surface area
- depth of invasion
- grade
- number of mitoses

no significant differences were observed when 408 never-pregnant (age-corrected) patients.



VAGINAL CANCER

- *Primary SCC of the vagina discovered during pregnancy is exceedingly rare.
- *Accordingly literature primary invasive SCC of the vagina complicating pregnancy, with an overall survivorship rate of 38%, similar to what is observed in nonpregnant patients.



MANAGEMENT

- *The pregnancy should be disregarded if the diagnosis is made in the first or early second trimester.
- *If the pregnancy is late second or third trimester, the decision for appropriate time of intervention depends on the preferences of the patient and the oncologist.
- *The impact of a delay in therapy on the prognosis is impossible to predict.
- *There is extensive involvement of the vagina by any lesion, one should seriously consider evacuation of the uterus by a hysterotomy or cesarean section and institution of appropriate radiation therapy.



ENDOMETRIAL CANCER

- *Most of the reported cases have been diagnosed at examination of uterine contents obtained by curettage for elective pregnancy termination or spontaneous abortion.
- *They are usually incidental findings noted in surgical specimens.





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Case Report

Endometrial carcinoma in septate uterus detected 6 months after full-term delivery: case report and review of the literature

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*29 patients

*11 of whom were older than 35 years.

*Twenty-one of the 29 cases had no or minimal myometrial invasion

•18 of which were histologically FIGO grade I, and three were FIGO grade II.

*This patient subsequently conceived, and after delivery at term, she underwent a total abdominal hysterectomy.

*Pathologic examination of the uterus revealed **a persistent well differentiated endometrioid adenocarcinoma limited to the endometrium.**

ENDOMETRIAL CANCER

- *Most cases of endometrial carcinoma associated with pregnancy are characterized by well-differentiated tumors, an endometrioid histology with no or minimal myometrial invasion, and favorable outcome, consistent with the typical clinicopathologic features of type I endometrial carcinoma that develops in obese women.
- *It has been hypothesized that the elevated serum progesterone level during pregnancy inhibits the growth of endometrial carcinoma cells, and this may contribute to the good outcomes!!!



FALLOPIAN TUBE CANCER

- *Direct extension of an ovarian tumor or from an endometrial carcinoma(**Secondarily involved**).
- *Primary fallopian tube cancer is the least common gynecologic tumor.
- *The mean age ranges from 50 to 55 years.
- *The usual **watery, blood-tinged vaginal discharge** would be obviated in pregnancy because at 12 weeks of gestation.



FALLOPIAN TUBE CANCER

*Several instances are reported in the literature of incidental findings of CIS of the tube noted in specimens submitted after postpartum tubal ligation.

*Management(CIS)

-total abdominal hysterectomy with bilateral salpingo-oophorectomy

-simple removal of the fallopian tubes!

***Primary choriocarcinoma of the fallopian tube** may be associated with ectopic pregnancy. In these scenarios, the **biologic behavior is very aggressive, with distant metastases manifesting in 75% of cases.**



GESTATIONAL TROFOBLASTIC NEOPLASIA

- *Molar pregnancy may coexist with a normal gestation in 1 of 20,000 to 100,000 pregnancies
- *Coordinated care among the obstetrician, perinatologist, neonatologist, and gynecologic oncologist must ensue.
- *These pregnancies are associated with a higher incidence of complications such as fetal death, vaginal bleeding, preeclampsia, and persistent GTN after evacuation.



Research letters

*77 twin pregnancies

*53 women continued their pregnancies

*23 spontaneously aborted(<24 w)

*20 livebirths

***The rate of persistent GTN requiring chemotherapy was not different** in women undergoing early pregnancy termination compared with those who did not terminate!!

Outcome of twin pregnancies with complete hydatidiform mole and healthy co-twin

Neil J Sebire, Marianne Foskett, Fernando J Paradinas, Rosemary A Fisher, Ros J Francis, Della Short, Edward S Newlands, Michael J Seckl

We assessed 77 twin pregnancies, comprising complete hydatidiform mole (CHM) and healthy co-twin, to ascertain the risks to the mother and baby of continuing the pregnancy, versus termination. 24 women with histologically confirmed CHM and healthy co-twin pregnancies decided to have a termination. 53 women continued with their pregnancies, though two had to have terminations because of severe pre-eclampsia, and 23 spontaneously aborted (<24 weeks' gestation). 28 pregnancies lasted 24 weeks or more, resulting in 20 livebirths. Chemotherapy to eliminate persistent gestational trophoblastic disease (pGTD) was required in three of 19 women (16%; 95% CI 3–39) who terminated their pregnancies in the first trimester, and in 12 of 58 (21%; 95% CI 11–33%) who continued their pregnancies. CHM and healthy co-twin pregnancies have a high risk of spontaneous abortion, but about 40% result in livebirths, without significantly increasing the risk of pGTD.

Lancet 2002; 359: 2165–66

pGTD in women undergoing early terminations with that of patients electing to continue their pregnancies with the modified Fisher's exact test. (Comparison of proportions test, two independent proportions; Arcus Quickstat Biomedical version 1.1, Research Solutions, UK.)

Figure 1 shows the course and outcome of 77 of 126 pregnancies histologically confirmed as CHM and co-twin. 19 women had an abortion after first-trimester diagnosis, and five decided to terminate their pregnancies after diagnosis at 15–22 weeks' gestation. 53 women chose to continue their pregnancies: two had to have abortions because of severe pre-eclampsia at 16–18 weeks' gestation; 23 (43%, 95% CI 31–60) pregnancies resulted in spontaneous abortion or intrauterine death before 24 weeks' gestation, one of which showed co-twin placental mesenchymal dysplasia. 28 women reached 24 weeks' gestation (fetal viability). Eight fetal deaths happened; seven intrauterine at 24–35 weeks' gestation (one of whom showed co-twin placental mesenchymal dysplasia) and

MELANOMA

- ***Cutaneous melanoma** is the most common malignancy encountered during pregnancy.
- *Melanoma is with 6%, the **fifth most common** cancer, diagnosed during pregnancy
- *The average age of patients with melanoma is 45 years, and **35% of women** will be diagnosed during childbearing years.



MELANOMA

Pregnancy possible effects?

1. Pregnancy increases the risk of developing malignant melanoma.
2. Pregnancy worsens the prognosis.
3. Future pregnancies have an adverse effect both on prognosis and on recurrence.
4. Oral contraceptives and hormone replacement therapy are contraindicated in women with a history of melanoma because of theoretic stimulatory effects of hormones on melanocytes.

None of these claims are **substantiated by the medical literature.



Effect of Pregnancy on Survival in Women With Cutaneous Malignant Melanoma

Marko B. Lens, Inger Rosdahl, Anders Ahlbom, Bahman Y. Farahmand, Ingrid Synnerstad, Bernt Boeryd, and Julia A. Newton Bishop

A B S T R A C T

Purpose

An adverse influence of pregnancy on the risk of death in women with cutaneous melanoma was suggested historically by anecdotal reports. Previous studies included small numbers of women observed for short periods.

Methods

Using data from the Swedish National and Regional Registries, we performed a retrospective cohort study of all Swedish women who were diagnosed with cutaneous melanoma during their reproductive period, from January 1, 1958, to December 31, 1999. The relationship between pregnancy status at the diagnosis of melanoma and overall survival was examined in multivariable proportional-hazards models.

Results

The cohort comprised 185 women (3.3%) diagnosed with melanoma during pregnancy and 5,348 (96.7%) women of the same childbearing age diagnosed with melanoma while not pregnant. There was no statistically significant difference in overall survival between pregnant and nonpregnant groups (log-rank χ^2 [r] = 0.84, $P = .361$). Pregnancy status at the time of diagnosis of melanoma was not related to survival in a multivariable Cox model in the 2,101 women (hazard ratio for death in the pregnant group was 1.08; 95% CI, 0.60 to 1.93). In the multivariable analysis, pregnancy status after diagnosis of melanoma was not a significant predictor of survival (hazard ratio for death in women who had pregnancy subsequent to the diagnosis of melanoma was 0.58; 95% CI, 0.32 to 1.05).

Conclusion

The survival of pregnant women with melanoma is not worse than the survival of nonpregnant women with melanoma. Pregnancy subsequent to the diagnosis of primary melanoma was not associated with an increased risk of death.

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Authors' disclosures of potential conflicts of interest are found at the end of this article.

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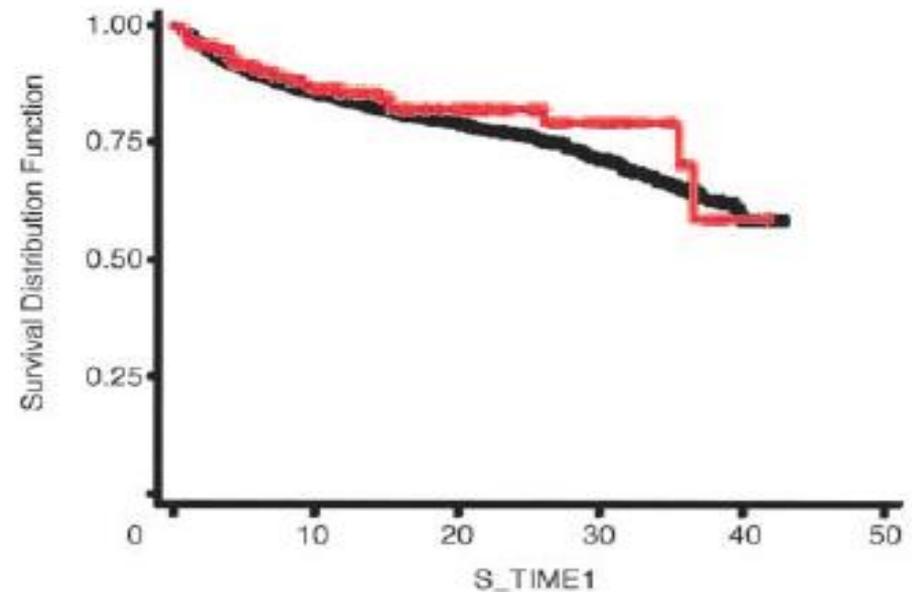


Table 2. Multivariable Cox Regression Analysis for the 2,101 Women With Melanoma for Whom We Knew Breslow Thickness, Clark's Level, and Tumor Site (results from the primary analysis)

| Variable | HR | 95% CI | P |
|---|------|--------------|---------|
| Pregnancy at the time of diagnosis of primary melanoma* | 1.08 | 0.60 to 1.93 | .804 |
| Breslow thickness (per additional category) | 2.16 | 1.80 to 2.58 | < .0001 |
| Axial site v limb site of primary melanoma | 2.51 | 1.78 to 3.56 | < .0001 |
| Clark's level (> 3 v ≤ 3) | 1.39 | 0.92 to 2.14 | .12 |
| Age (per year increase) | 1.02 | 0.99 to 1.05 | .06 |

Abbreviation: HR, hazard ratio.

*Pregnant women at the time of diagnosis of melanoma versus non-pregnant women at the time of diagnosis of melanoma.



Conclusion

The survival of pregnant women with melanoma is not worse than the survival of nonpregnant women with melanoma. Pregnancy subsequent to the diagnosis of primary melanoma was not associated with an increased risk of death.

MANAGEMENT

- *A changing skin lesion should be subjected to an **excisional biopsy**.
- *Early diagnosis of stage I disease often leads to curative therapy. Irrespective of pregnancy, treatment of melanoma is related to depth and stage.
- *Lesions **smaller than 1 mm** in thickness usually require a **wide, deep local excision** with a 1-cm margin
- *Between 1 mm and 4 mm need a 2-cm margin of excision.



MANAGEMENT

- *In pregnant women presenting **with metastatic disease**, the decision regarding termination of pregnancy and initiation of systemic therapy should be **individualized** according to the prognosis and the patient's wishes.
- *There is **very limited experience with the use of interferon!**
- *The newer agents such as **ipilimumab** (a monoclonal antibody targeting CTLA-4) and **vemurafenib** (a mitogenactivated protein [MAP] kinase inhibitor) are classified as category C and D for use in pregnancy and hence **currently not recommended.**



FETUS AND MELANOMA

- *Melanomas constitute **nearly 50% of all tumors** that metastasize to the placenta and account for **nearly 90% of those that metastasize to the fetus.**
- *Pregnant women with advanced or recurrent disease should undergo ultrasound examination during pregnancy for assessment of any obvious fetal tumor masses.
- *Attention should be directed to placental thickness, the fetal liver, and the size of the fetal spleen.



COLORECTAL CANCER

- *Colorectal cancer in pregnancy is a rare event, with a reported incidence of 0.008% (1 in 13,000 pregnancies).
- *Approximately 300 cases have been reported in the literature.
- *The mean age at diagnosis of colorectal cancer in pregnancy is 31 years (range, 16 to 48 years)
- *The diagnosis is particularly difficult because the common signs and symptoms of colon cancer are often attributed to the pregnancy. This results in advanced stages of the disease at diagnosis, with a correspondingly poor prognosis (abdominal pain, anemia, nausea, vomiting, constipation, abdominal mass).



COLORECTAL CANCER

Diagnosis

- *Pregnancy is a **relative contraindication** to colonoscopy.
- *Possible adverse effects of colonoscopy in pregnant women include **placental abruption** from mechanical pressure on the uterus, fetal exposure to potential teratogenic medications, and fetal injury resulting from maternal hypoxia or hypotension.



MANAGEMENT

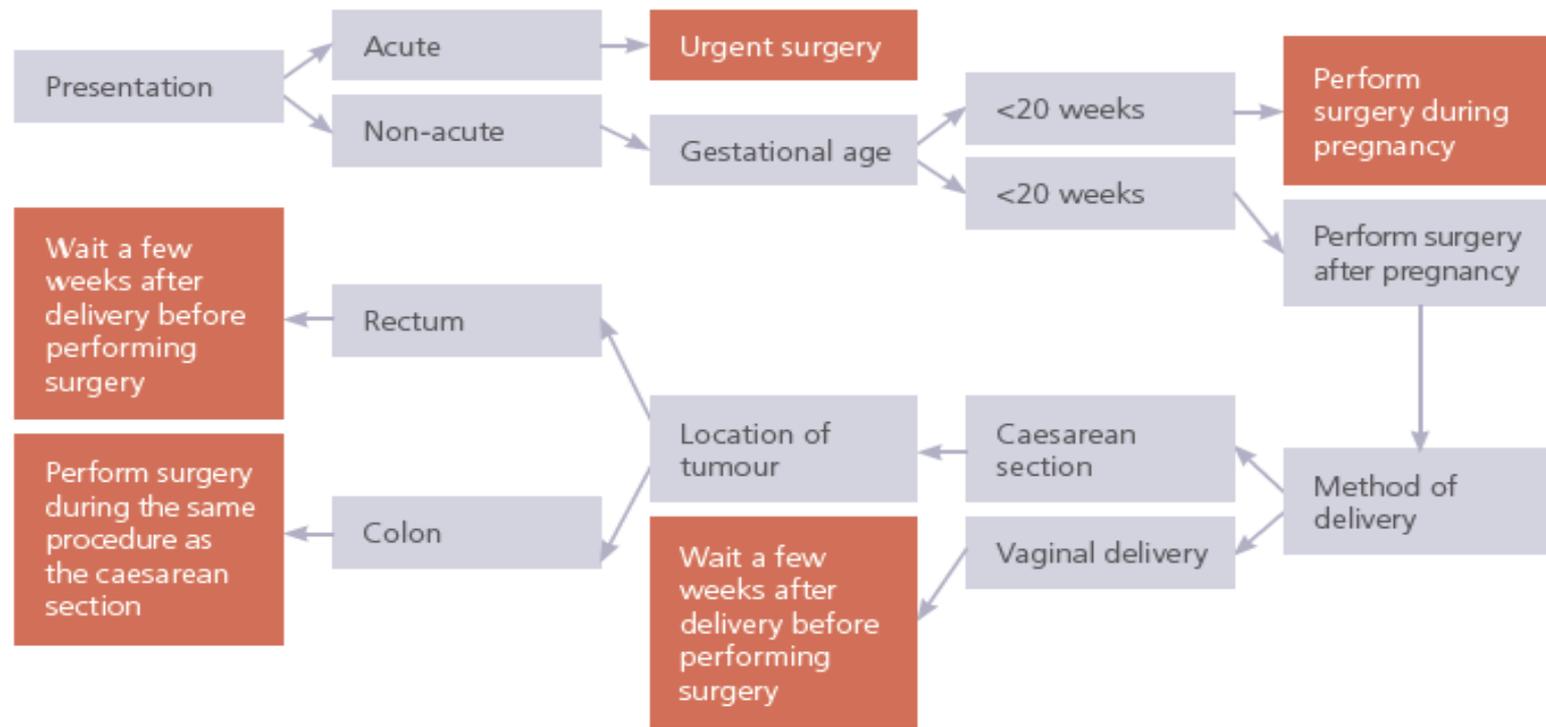
- *Management of colorectal cancer in pregnancy is influenced by the **gestational age, tumor stage, and need for elective or emergent surgery**. There are no universally accepted guidelines for treatment.
- *Colorectal cancer is diagnosed in the first 20 weeks of pregnancy, the recommended treatment is surgical removal of the tumor.
- *The diagnosis is made after 20 weeks of pregnancy, surgery may be delayed until the fetal prognosis has improved. The patient should be fully informed about these risks before making a decision to postpone surgery.



MANAGEMENT

Figure 1

Flow chart showing surgical management of CRC in pregnancy.



MANAGEMENT

- *Colorectal cancer in pregnancy may be complicated by ovarian metastases, which are reported in 25% of pregnant patients but in only 3% to 8% of nonpregnant patients(Mason et al. 1981)
- **Prophylactic bilateral salpingo-oophorectomy(spontaneous abortion??)
- **Bilateral wedge biopsies of the ovaries may be performed during surgery for pathologic examination and subsequent removal if the ovaries are involved.
- *Colorectal cancer in pregnancy is associated with a poor prognosis(delay diagnosis and advanced stage!!)



HEMATOLOGICAL MALIGNANCIES

1-Leukemia

2-Lymphoma

a)Hodgkin

b)non-Hodgkin



LEUKEMIA

- *Leukemia is estimated to occur in 1 in 75,000-100000 pregnancies.
- *AML accounting for more than 60% of reported cases.
- *In pregnant patients, persistent fever, weight loss, lymphadenopathy, or an abnormal differential on the complete blood count should prompt an investigation and raise the clinician's suspicion for leukemia.
- *Acute leukemia often very ill, and the primary concern is to save the pregnant woman's life through induction chemotherapy or radiotherapy.
- *Chronic myelogenous leukemia in pregnancy, however, can be managed similar to Hodgkin disease, with a justifiable delay in definitive treatment of several weeks if indicated.



MANAGEMENT

*Potential risks from acute leukemia and its treatment during pregnancy include **preterm delivery, low birth weight, disseminated intravascular coagulation, and maternal or fetal bleeding and infection** due to thrombocytopenia and neutropenia.



Acute Leukemia during Pregnancy

A Report on 37 Patients and a Review of the Literature

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⁷ Service d'Hématologie, Hôpital Henri Mondor, Créteil, France.

BACKGROUND. Acute leukemia (AL) requiring cytotoxic treatment occurring during pregnancy poses a very difficult therapeutic dilemma.

METHODS. By means of a mail questionnaire, information on a series of 37 patients with a diagnosis of AL during pregnancy was collected from 13 French centers between December 1988 and November 2003.

RESULTS. Thirty-one patients had acute myeloid leukemia (AML), and 6 patients had acute lymphoblastic leukemia (ALL). Nine patients were diagnosed during the first trimester, 10 patients were diagnosed during the second trimester, and 18 patients were diagnosed during the third trimester. Fifteen pregnancies ended with therapeutic or spontaneous abortion. There were 13 normal deliveries, including 1 gemellary pregnancy, and 9 Cesarean sections. Twenty-three healthy babies survived from the 37 pregnancies, of whom 15 babies had been exposed to chemotherapeutic agents. A complete remission was achieved in 34 patients. Eleven women had severe extrahematologic complications during the induction remission course. The median disease-free survival (DFS) was not reached, with a 5-year DFS of 54%. Ten patients developed recurrent disease. Overall, 12 of 37 pregnant women died from leukemia.

CONCLUSIONS. Pregnancy does not affect the course of AL. In the first trimester, termination of pregnancy should be discussed because of the potential fetal consequences of chemotherapy. Chemotherapy treatment during the second or third trimester may not require termination of pregnancy, because as remission of AL and delivery of a normal infant are likely to be obtained. *Cancer* 2005;104:110-7. © 2005 American Cancer Society.

KEYWORDS: acute leukemia, pregnancy, chemotherapy, remission.

- *%24 patients presented first trimester,%27 second and %49 third trimester.
- *Chemotherapy was initiated immediately.
- *Therapeutic abortion recommended to those women presenting in the first trimester.
- *3-year disease-free survival rate reached 65%, which was similar to the rate for the nonpregnant population.

HODGKIN LYMPHOMA

- *Peak incidence between the ages of **18 and 30 years**.
- *Hodgkin disease in pregnancy occurs in approximately **1 in 6000** deliveries.
- *Young women diagnosed with Hodgkin disease are **usually asymptomatic**.
- *The **nodular sclerosis subtype** of Hodgkin disease is the most common subtype encountered in pregnancy and carries a favorable prognosis.
- *Pregnancy itself does not appear to adversely affect the course of the disease, and **interruption of pregnancy** during the course of the disease is **not definitely indicated**.



HODGKIN LYMPHOMA

- *Present recommendations are based on the assumptions that **radiotherapy** is the mainstay of treatment of **early-stage** disease
 - *Combination chemotherapy is the primary treatment of advanced-stage disease with **parenchymal organ involvement**, and a combination of the two is required for patients with bulky disease (eg, a large mediastinal mass) or **generalized abdominal lymph node involvement**.
 - *Aggressive therapy has resulted in considerable improvement in overall survival rates for patients with Hodgkin disease.
- 

NON HODGKIN LYMPHOMA

- *Most women with NHL in association with pregnancy have an **aggressive histologic subtype and advanced-stage disease**, possibly as a result of a delay in diagnosis in many cases.
- *An **unexpectedly high incidence of breast, uterine, cervical, and ovarian involvement** among pregnant women has been noted when NHL is associated with pregnancy, with the predilection for these organs attributed to hormonal influences and increased blood flow to these organs.
- *Overall, the prognosis for all patients with NHL is **worse than** the prognosis for patients with **Hodgkin** disease.



THYROID CANCER

- *Papillary, follicular, and anaplastic carcinomas are the most common primary thyroid malignant neoplasms, with medullary carcinoma accounting for only 5%.
- *The disease usually manifests as a relatively asymptomatic nodular mass in the thyroid gland.
- *Papillary and follicular thyroid carcinomas are two to three times more common in women than in men (5.5 vs. 2.4 per 100,000, respectively). This female predominance is especially notable during the reproductive years!!



MANAGEMENT

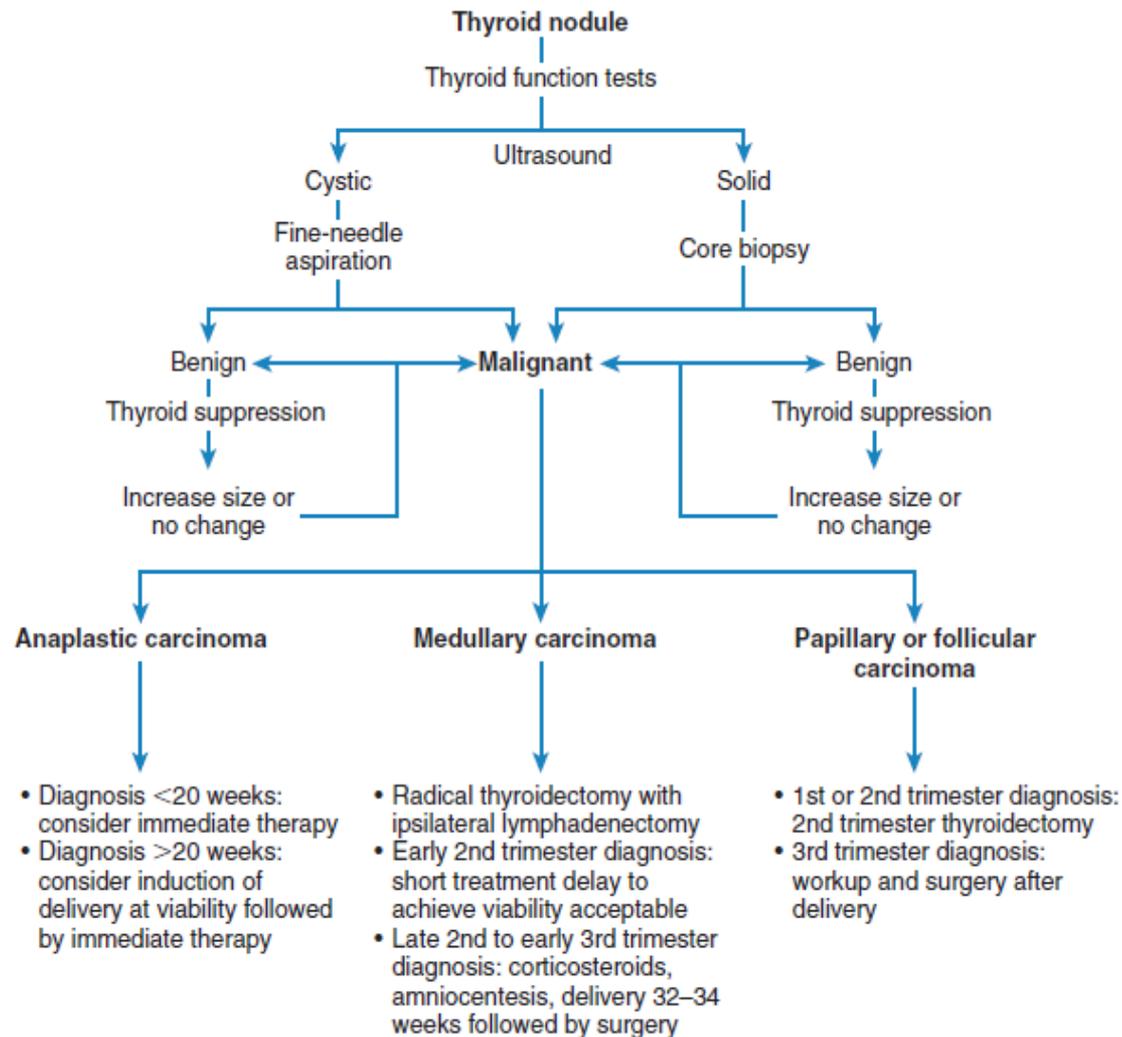


FIGURE 15.17 Management algorithm for the thyroid nodule and thyroid cancer in pregnancy.

MANAGEMENT

Endocrine Society Guidelines for the management of thyroid dysfunction during pregnancy and postpartum.

1. Thyroid nodules measuring 1 cm or larger should be evaluated by FNA biopsy.
2. Individuals with nodules that are malignant or show rapid growth should be offered surgery in the second trimester of pregnancy.
3. It may be appropriate for patients with follicular neoplasia or early-stage papillary thyroid cancers to wait until postpartum for thyroidectomy because these lesions are not expected to progress rapidly and the risk of surgery may outweigh the benefits of immediate intervention.
4. Patients with known thyroid cancer should maintain a low but measurable TSH and normal thyroxine (T4) values on levothyroxine while pregnant.
5. RAI (radioactive iodine) therapy should not be provided to women who are breastfeeding.
6. After RAI therapy, women should wait 6 to 12 months before becoming pregnant.



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*Cancer in Pregnancy Textbook, ESGO, 2018



THANK YOU FOR YOUR ATTENTION

