Preconception care can help ensure a healthy maternal and fetal outcome through risk assessment and patient counseling. The primary areas of risk assessment include past obstetrical and gynecological history, past medical history focusing on history of chronic illnesses and infectious diseases, family history of genetic disease, and psychosocial history.

Patient counseling is focused on areas of nutrition and lifestyle. For most patients a well-balanced diet containing approximately 2300 kcal/day will provide adequate nutrition during pregnancy. For normal-weight pregnant teenagers, a daily intake of 2400 kcal or more is recommended. The diet should provide for an increased intake of certain nutrients, specifically protein, calcium, iron, and folic acid. Important lifestyle considerations include assessing social support systems and counseling regarding smoking cessation and alcohol abstinence during pregnancy.

Women over the age of 35 should be counseled about the increased risks associated with advanced maternal age. However, it is important to emphasize that the increase in complication risk is modest and the majority of women over 35 have normal, healthy pregnancies.
Prenatal Care

The primary goal of prenatal care is to provide a healthy maternal and fetal pregnancy outcome. Prenatal care involves appropriate pregnancy planning, education, risk assessment, and clinical monitoring throughout each trimester of pregnancy. Pregnancy is typically divided into three trimesters lasting approximately 13 weeks each. The vast majority of pregnancies proceed without major maternal or fetal morbidity and mortality.

The First Antenatal Visit

There are 3 key areas to address during the first prenatal visit:
1) Diagnosis of pregnancy
2) Maternal and fetal health assessment
3) Development of a plan for continued obstetrical care

These goals are accomplished with a thorough history, physical and routine investigations.

Confirmation of pregnancy

A β-hCG test should be performed if pregnancy is suspected, as it is the most sensitive and specific indicator of pregnancy. A positive urine or serum test of β-hCG supports the diagnosis of pregnancy. By 10–12 weeks gestation, fetal heart tones can usually be detected with a Doppler stethoscope, which provides firm evidence of pregnancy. If heart tones are not heard by 12–13 weeks, ultrasonography should be performed to determine viability, location, and/or dates. The expected delivery date is approximately 280 days after the woman’s last period, plus or minus 2 weeks, assuming the mother can accurately offer you the date. It can easily be calculated using Naegele’s rule.

**NAEGELE’S RULE:**  
Expected Delivery Date = LMP + 1 week – 3 months + 1 year

The extent of the history will vary depending on the level of preconception care provided. It should include: past medical history, obs/gyn history, family history and psychosocial assessment.

Routine investigations for a patient who has a confirmed pregnancy should be based around assessing maternal and fetal health. The physician may also wish to obtain additional data to assess risks associated with the pregnancy and plan appropriate management. For example, it is common to order screening tests for gonorrhea and chlamydia, particularly in patients with a history of pelvic infections, physical symptoms suggestive of pelvic infection, a history of multiple sexual partners, or a history of preterm labor. A culture for herpes is indicated in patients with genital lesions suggestive of herpes, and TB skin testing is recommended for patients at risk. A sickle cell test is recommended for women of African-American or Caribbean descent. While the TORCH screen was routine in the past, newer guidelines recommend screening for toxoplasmosis and cytomegalovirus be omitted.

An assessment of common complaints during pregnancy as well as a screen for complications such as visual changes and first trimester bleeding should also be conducted. The many signs and symptoms of pregnancy include: ammenorrhea, fatigue, weak or numb extremities, nausea, vomiting, breast sensitivity/tenderness, more frequent urination, constipation, abdominal distention, and increased vaginal discharge. It is important to discuss the appropriate management of these symptoms and reassure the expectant mother that these symptoms are normal.
Subsequent Antenatal Care

Following the first antenatal visit, subsequent care involves monitoring fetal growth and maternal health as well as continued risk assessment. The average woman makes 14 prenatal visits during her pregnancy. The first visit should occur within the first 12 weeks of gestation. The typical visit schedule is 1 visit every 4 weeks during the first 28 weeks of gestation; 1 visit every 2 weeks until 36 weeks gestation, and weekly visits thereafter.

Each prenatal visit should include:
- reconfirmation of gestational age
- BP check
- symphysis-fundal height (SFH)
- fetal heart rate (FHR) measurement
- Leopold maneuvers to assess fetal position (after 24 weeks)

It is necessary to understand all pertinent maternal and fetal risk factors in order to assess for risk of complications during prenatal visits. A thorough history is an essential to risk assessment. As the patient’s risk status may change during the course of the pregnancy, it is important to inform patients regarding the signs and symptoms that may signal the development of potentially dangerous conditions such as preeclampsia/eclampsia, placental abnormality, GDM, IUGR, multiple gestation, and preterm labor. These conditions will be discussed briefly in this guide.

The options for prenatal screening should be discussed during antenatal visits. These will be covered later in these notes.

Apart from routine investigations such as urine dipstick, CBC, and infection screening, tests specific to patients in certain risk groups (e.g. diabetic mothers and those at risk STDs) are conducted at various stages throughout pregnancy.

Lastly, the patient should be asked about her concerns with regard to the pregnancy, and every attempt made to assess and allay any anxiety she may express. Reduction of anxiety may enhance the emotional and physical well-being of the pregnant patient.

Immunizations During Pregnancy

Immunizations during pregnancy are often delayed or avoided due to concerns about their safety. Generally, attenuated virus vaccines, such as MMR or varicella, should be avoided during pregnancy due to the possibility of fetal infection and malformation. However, there is no evidence that any of the currently approved vaccines are fetotoxic, teratogenic or have resulted in specific adverse pregnancy outcomes. The following vaccines should be used in pregnancy for the same indications as in non-pregnant patients: tetanus toxoid, hepatitis A or B vaccines, inactivated polio, and pneumococcal vaccine. Influenza vaccine is recommended for all pregnant women who will be beyond 14 weeks gestation during the influenza season, as population studies have shown increased morbidity and hospitalization rates for pregnant women who develop influenza during T3 or postpartum.
Nutrition during Pregnancy

A well-balanced diet of approximately 2300-2400 kcal/day will provide adequate nutrition for the mother and the fetus during pregnancy. Patients should be advised to increase intake of protein, calcium, iron and folic acid to ensure proper health of both parties.

Folic Acid and Iron

The daily dose of folic acid that should be taken starting at 3 months prior to conception is 0.4-1.0 mg. If the patient has previously given birth to a baby with a neural tube defect, then the dose should be 4 mg and be taken in combination with vitamin B12 until 10-12 weeks, at which she can begin taking a prenatal multivitamin with 0.4mg of folic acid for the rest of the pregnancy and lactation. A maternal or prenatal vitamin is recommended rather than a normal multi-vitamin to ensure adequate folic acid intake. Alternatively, a standard multi-vitamin plus a folic acid pill may be taken. Specific iron supplementation is controversial – the incidence of anemia during pregnancy is >30% - this should be screened for and treated if necessary.

Alcohol Intake During Pregnancy

While there is no appreciable risk with an occasional alcoholic drink during pregnancy, it is best to advise women not to drink at all throughout pregnancy, especially during the period of time around conception. If for some reason the woman must drink occasionally, it is acceptable, and if she drank but did not know about the pregnancy, she should not be made to feel guilty. However, excessive drinking is associated with fetal alcohol syndrome, mental development and physical growth retardation as well as CNS disorders.

Vegetarians

Vegetarians may have some difficulty getting adequate amounts of protein (at least 40-60 grams/day), as well as vitamin B12, and iron. For that reason, it is important to ensure these patients have enough protein in their diet and recommend that these patients take maternal vitamins. Vegans may also have some difficulty meeting recommended calcium intake (>3 servings/day); for these patients you may consider referral to a dietitian.

Weight Gain

Appropriate weight gain during pregnancy is 10 lbs by 20 weeks and a total of 25-35 lbs during the entire pregnancy. In following the patient you should expect to see a gain of one pound every two weeks for the first half of the pregnancy and then 1.5 pounds every two weeks in the second half. There is a general consensus that the woman who enters pregnancy substantially underweight is at greater risk and should gain a greater amount of weight during the pregnancy. Although authorities do not agree about the optimum weight gain for the patient who is overweight, there is strong support for the view that the overweight patient may not need to gain as much as the patient who begins pregnancy at normal weight. A patient should therefore not “eat for two” as the average patient needs only 300 extra calories a day (about 1 tuna sandwich). Remind patients they are eating to support a baby, not a full extra person.

Recommended Dietary Changes to Decrease Benign Complaints of Pregnancy

The discussion of appropriate diet during pregnancy should include information regarding the use of dietary measures to decrease symptoms such as nausea, constipation, and heartburn. The patient should be encouraged to increase her intake of liquids and to add bulk-containing foods to her diet if she is troubled by constipation. Nausea may be relieved by keeping small amounts of food in the stomach at all times. Heartburn may be alleviated by eliminating fluids with meals and restricting fluid intake to before meals or 2 hours after meals. The patient should be cautioned against lying down immediately after eating, and she may be advised to take a low-sodium non-aluminum antacid if the symptoms are distressing.
## Investigations and Screening

It is important to conduct the appropriate investigations during each trimester in order to effectively monitor the health of the mother and fetus. Below is a table outlining recommended tests to be ordered at each trimester.

<table>
<thead>
<tr>
<th>Trimester</th>
<th>Purpose</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Trimester</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rh Blood Type and Screen</td>
<td>Determine blood-Ag incompatibility</td>
<td>A</td>
</tr>
<tr>
<td>HCT, Hb</td>
<td>Screen for anemia</td>
<td>B</td>
</tr>
<tr>
<td>Hb electrophoresis (if indicated)</td>
<td>Screen for hemoglobinopathies</td>
<td>B</td>
</tr>
<tr>
<td>Rubella Ab titre</td>
<td>Determine rubella immunization status</td>
<td>A</td>
</tr>
<tr>
<td>VDRL</td>
<td>Screen for syphilis infection</td>
<td>A</td>
</tr>
<tr>
<td>HIV</td>
<td>Screen for HIV infection</td>
<td>A</td>
</tr>
<tr>
<td>Varicella</td>
<td>Screen for varicella Abs if patient has not had chicken pox.</td>
<td>A</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Screen for Hepatitis B infection</td>
<td>A</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>Screen for n. gonorrhea infection</td>
<td>B</td>
</tr>
<tr>
<td>Pap Smear</td>
<td>Screen for cervical cancer</td>
<td>A</td>
</tr>
<tr>
<td>Ultrasound at 11-14 weeks</td>
<td>Confirmation of dates, screen for nuchal translucency (NT)</td>
<td>-</td>
</tr>
<tr>
<td>Chorionic Villus Sampling, if indicated, at 11-13 weeks</td>
<td>Diagnostic prenatal test, indicated w positive prenatal screen, maternal age &gt;35 or positive family hx for a genetic disorder</td>
<td>-</td>
</tr>
<tr>
<td>First Trimester Screen, optional, scheduled between 11-14 weeks</td>
<td>Early prenatal screening, includes 1 blood sample (PAPP-A) and U/S screen for increased NT</td>
<td>A</td>
</tr>
<tr>
<td>Integrated Prenatal Screen, optional, (first blood sample and US at 11-14 weeks)</td>
<td>Early prenatal screening that includes U/S screen for increased nuchal translucency (11-14 weeks) and 2 blood samples: • PAPP-A at 11-14 weeks • aFP, B-hCG and estriol testing at 15-20 weeks</td>
<td>A</td>
</tr>
<tr>
<td>Serum Integrated Prenatal Screening (SIPS), optional (first blood sample at 11-14 weeks)</td>
<td>Early prenatal screening that includes two blood samples: • PAPP-A at 11-14 weeks • aFP, B-hCG and estriol testing at 15-20 weeks</td>
<td>A</td>
</tr>
<tr>
<td>Urine Culture</td>
<td>Screen for bacteriuria</td>
<td>A</td>
</tr>
<tr>
<td><strong>Second Trimester</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rh screen</td>
<td>If mother tested Rh negative, to prevent blood-Ag incompatibility</td>
<td>A</td>
</tr>
<tr>
<td>Ultrasound at 16-20 weeks</td>
<td>Anatomical survey</td>
<td>-</td>
</tr>
<tr>
<td>Integrated Prenatal Screen, optional (second blood sample taken in T 2)</td>
<td>Prenatal screening that includes U/S screen for increased nuchal translucency (11-14 weeks) and 2 blood samples: • PAPP-A at 11-14 weeks • aFP, B-hCG and estriol testing at 15-20 weeks</td>
<td>A</td>
</tr>
<tr>
<td>Serum Integrated Prenatal Screening (SIPS), optional (second blood sample taken in T 2)</td>
<td>Prenatal screening that includes two blood samples: • PAPP-A at 11-14 weeks • aFP, B-hCG and estriol testing at 15-20 weeks</td>
<td>A</td>
</tr>
<tr>
<td>Maternal Serum Screen (MSS) aka Triple Screening or Quadruple Screening at 15-20 weeks</td>
<td>Later prenatal screening, offered to women who have their first prenatal visit after 14 weeks of gestation. Includes 1 blood sample: aFP, B-hCG and estriol test (quadruple screen also includes dimeric inhibin A [DIA]A)</td>
<td>A</td>
</tr>
<tr>
<td>Amniocentesis at 15-22 weeks</td>
<td>Diagnostic test, indicated with positive screen, women &gt; 35 or with family history of genetic disorders</td>
<td>-</td>
</tr>
<tr>
<td><strong>Third Trimester</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational Diabetes Mellitus (GDM) testing at 24-28 weeks</td>
<td>Identify mothers with GDM</td>
<td>C</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Only if indicated e.g. third trimester bleed</td>
<td>-</td>
</tr>
<tr>
<td>Hb or Hct determination</td>
<td>Identify anemia</td>
<td></td>
</tr>
<tr>
<td>GBS culture at 35-37 weeks</td>
<td>Identify maternal carriers of group B streptococcus</td>
<td>B</td>
</tr>
<tr>
<td>Repeat gonorrhea, syphilis, chlamydia, hepatitis, and HIV tests</td>
<td>Repeat in women at high risk of infection</td>
<td>A</td>
</tr>
<tr>
<td>Rh prophylaxis at 28 weeks</td>
<td>In the Rh(d)-negative patient, 300 mg of Rh immune globulin (RhIg) should be given IM</td>
<td>A</td>
</tr>
</tbody>
</table>
**Prenatal Screening**

All women are offered some form of prenatal screening. Screening can help facilitate psychological adjustment to fetus with a congenital defect or inform therapeutic decision-making.

The prenatal screening options available include:

- **Early prenatal screening options:** First Trimester Screening (FTS), Integrated Prenatal Screen (IPS) or Serum Integrated Prenatal Screening (SIPS)
- **Later prenatal screening options:** Maternal Serum Screen (MSS) aka Triple Screen/Quadruple Screen

It is suggested that all women, especially women with an increased risk of congenital malformation/disease (previously affected pregnancy, positive family history, advanced maternal age), undergo some form of prenatal screening. If screening is positive, then women can undergo diagnostic tests such as CVS or amniocentesis. While women with an increased risk of congenital malformation or disease can choose to have CVS or amniocentesis without prior screening, it is recommended that some form of screening be performed first as they give a better estimate of risk than age alone. A negative screen can be reassuring and allow avoidance of an invasive diagnostic test.

**Ultrasound**

Ultrasonography (U/S) is an important first step in evaluating fetal abnormalities. U/S is reliable after 4-6 weeks gestation and provides valuable information about gestational age, number of fetuses and placental location. U/S is helpful in the diagnosis of hydatidiform mole and missed abortion. It is particularly useful in the differentiation of ectopic vs. intrauterine pregnancy, when used in conjunction with B-hCG and progesterone levels.

Ultrasound is normally performed during twice during the prenatal period. The first ultrasound is performed between week 11-14 of gestation to screen for nuchal translucency and confirm dates. A second ultrasound is performed between weeks 16-20 to assess fetal anatomy. Subsequent ultrasounds are performed on a case-by-case basis. Ultrasound is frequently used and is safe; there are no known cases of U/S-induced harm to pregnant women or their fetuses.

**Maternal Serum Screen (MSS)**

The most important risk associated with advanced maternal age is the chromosomal abnormality trisomy 21, also known as Downs syndrome. The MSS is a later prenatal screening test that screens for T21, T18, T13 and other fetal abnormalities. The MSS is also known as a “triple screen” because it is a serological test for hCG, alpha fetoprotein (aFP), and unconjugated estriol. The MSS should be offered between 15-20 weeks gestation for those with high-risk pregnancies. If the results indicate increased risk of chromosomal abnormalities, then amniocentesis at 15-22 weeks can be done to definitively rule in or out chromosomal abnormalities. The quad screening includes the triple screen and also the hormone inhibin A.

If levels of hCG are increased, a patient is thought to be at increased risk for Downs syndrome whereas decreased levels suggest trisomy 18 or 13. Decreased levels of aFP suggest increased risk of T21, fetal demise, incorrect dates, or trophoblastic disease. Increased levels of aFP suggest open neural tube defects. Low levels of estriol correlate with increased incidence of T21. Increased levels of inhibin A are associated with increased risk of Downs syndrome.

**Integrated Prenatal Screen (IPS)**

IPS involves two blood samples and an U/S to screen for increased nuchal translucency. The first blood sample is taken at 11-14 weeks gestation and measures levels of Pregnancy Associated Plasma Protein A (PAPP-A). Low levels of PAPP-A are associated with decreased risk of trisomy 13, 18 and 21. The second blood sample is the triple screen, done between 15-20 weeks. IPS rules out 90% of cases of trisomy 21.
**Chorionic Villus Sampling (CVS)**

CVS is a diagnostic test for chromosomal or genetic disorders. Testing is conducted at 11-13 weeks gestation and consists of transabdominal or transvaginal sampling of the chorionic villus sampling for karyotyping purposes. The test is recommended in patients with a family history of or previous child with a chromosomal abnormality. The test does not provide any information regarding neural tube defects. CVS testing carries a 1/100 chance of fetal loss.

**Amniocentesis**

Amniocentesis is a diagnostic test that involves sampling the amniotic fluid around the fetus at 15-22 weeks of gestation. The fluid provides cell samples for karyotype and amniotic fluid levels of AFP. The test is indicated in situations of advanced maternal age, two or more previous spontaneous abortion, IPS or MSS is positive, or if there is concern of a congenital disorder. A variety of conditions can be diagnosed using amniocentesis such as CF, Tay Sachs, sickle cell anemia, phenylketonuria, Downs syndrome, and neural tube defects. The risk of fetal loss is approximately 1/200.

**Specific Tests**

Specific testing for inherited disorders (e.g. thalassemia) are indicated with positive family hx.

**Complications of Pregnancy**

**Benign Complications**

The most common benign complaint in pregnancy is nausea and vomiting, experienced most frequently during early pregnancy. Other common benign complaints include: leg cramps, hyper/hypothyroidism, tiredness and sleep disturbance, dizziness, frequent urination, nosebleeds and bleeding gums, constipation, varicose veins and hemorrhoids.

<table>
<thead>
<tr>
<th>Recommendations for Nausea and Vomiting in Pregnancy (NVP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dietary and lifestyle changes should be liberally encouraged and women should be counseled to eat whatever appeals to them.</td>
</tr>
<tr>
<td>• Patients should avoid foods that cause nausea, eat small frequent meals, try dry crackers, and/or eating before getting out of bed. Avoiding fried and heavily seasoned foods may help.</td>
</tr>
<tr>
<td>• Milk can cause nausea and vomiting; since there is no need for the extra calcium before 16 weeks, milk can be omitted from the diet during this time.</td>
</tr>
<tr>
<td>• Alternative therapies, such as ginger supplementation, acupuncture and acupressure, may also be beneficial.</td>
</tr>
<tr>
<td>• Medications can be given as per the algorithm for pharmacological treatment of NVP (see table on page 16). When NVP is refractory to initial pharmacotherapy, investigation of other potential causes should be undertaken.</td>
</tr>
<tr>
<td>• If the morning sickness is accompanied by persistent severe vomiting, weight loss or ketonuria, the patient may have hyperemesis gravidarum, a condition which may warrant treatment with intravenous fluids, additional antiemetics, and consideration of hospitalization.</td>
</tr>
</tbody>
</table>

**Vaginal Discharge**

Many patients complain of increased vaginal discharge during pregnancy. If this becomes problematic, investigate with culture and microscopic techniques to r/o bacterial vaginosis, trichomoniasis, or STIs. Increased vaginal discharge may signal preterm cervical changes or labor and may warrant vaginal examination.

**Urinary Complaints**

Urinary frequency is a common complaint in early pregnancy, stemming from increased pressure on the bladder from the uterus and increased GFR. Urinary complaints are also common during T3 as the presenting part descends into the pelvis. Urinary complaints (e.g., dysuria or urgency) may indicate urinary tract infection (UTI) and should be investigated by microscopic examination of the
urine and culture. UTI has been associated with a significant increase in preterm contractions, preterm labor, prematurity, fetal loss, and chronic pyelonephritis following pregnancy, and should be treated with antibiotic therapy followed by a post-treatment culture. Antibiotic selection should be based on the results of a culture and sensitivity testing, any patient history of drug reactions, and the stage of the pregnancy. Signs and symptoms of pyelonephritis (i.e., fever and flank pain) warrant antibiotic therapy and hospitalization until the woman is afebrile and asymptomatic, with antimicrobial prophylaxis for the remainder of the pregnancy.

**Serious Complications of Pregnancy**

The major complications associated with pregnancy can be classified according to the trimester of most likely occurrence. *Spontaneous abortions*, or miscarriages, are the most common complication of the first trimester (T1) and should be suspected in the event of a T1 bleed. The vast majority of spontaneous abortions occur during T1, however, they also occur during the early second trimester. All patients who are Rh negative should receive Rh immunoglobulin in the event of a bleed during pregnancy. *Preeclampsia* and other placental complications are the most common complications associated with the third trimester of pregnancy.

**Serious Complications During the First Trimester**

Bleeding during T1 can signal a serious complication. The differential for T1 bleeding includes:

<table>
<thead>
<tr>
<th>Spontaneous Abortion</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Implantation bleed (benign)</td>
<td></td>
</tr>
<tr>
<td>Spontaneous abortion (miscarriage)</td>
<td></td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td></td>
</tr>
<tr>
<td>Molar pregnancy</td>
<td></td>
</tr>
<tr>
<td>Cervicitis</td>
<td></td>
</tr>
</tbody>
</table>

Work-up for a first trimester bleed should include *vitals, a pelvic exam* (checking for open or closed cervical os, rupture of membranes), *FHR, U/S and B-hCG*. In a normal pregnancy, B-hCG doubles every 48 hrs. All Rh negative patients should receive Ig to prevent isoimmunization.

### Spontaneous Abortion

Spontaneous abortion is the natural termination of a fetus before 20 weeks of gestation. Types of spontaneous abortion include threatened, missed, inevitable, incomplete, complete, and septic.

- A D/C is indicated if products of pregnancy are retained.
- It is very important to provide counseling after a miscarriage.
- The most common cause of spontaneous abortion is a chromosomal abnormality.
- Reassure the patient that physical activity such as sex and exercise do not cause a spontaneous abortion, however, sexual activity should be discontinued if bleeding occurs.

### Ectopic Pregnancy

A patient with an ectopic pregnancy presents with amenorrhea, abdominal pain/cramping, signs and symptoms of pregnancy, and possibly an adnexal mass.

- U/S and serial B-hCG are the most important investigations.
  - If B-hCG is > 1500 mIU/ml (the discriminatory zone of b-hCG level at which all intrauterine pregnancies should be visible on transvaginal US) and there is no intrauterine gestational sac, ectopic is very likely.
  - If B-hCG is > 6000 mIU/ml with no intrauterine gestational sac, a presumptive diagnosis of ectopic pregnancy is made.
- Primary treatment is surgical – radical laparotomy.
- Rhogamm is given to Rh negative women.
- Methotrexate can be given if: patient is stable, no FHR and ectopic is <3.5cm.
Serious Complications During the Second Trimester
Complications occurring in T2 include spontaneous abortion and IUGR.

IUGR (Intrauterine Growth Retardation) IUGR occurs when a fetus weighs less than the 10th percentile for its gestational age. IUGR should be suspected when the fetus does not display predicted growth during weeks 20-36. With IUGR, there is a high risk for stillbirth and other complications. Close surveillance is required as the decision of when to deliver is complex.

Risk factors include: previous hx of IUGR, chronic maternal disease, maternal age > 35, fetal genetic disorder, smoking, drug/alcohol abuse, placental problems, infection

Serious Complications of the Third Trimester
Serious complications of T3 that should be monitored include T3 bleeding, hypertensive disorders of pregnancy, gestational diabetes and group B streptococcal infection.

Third Trimester Bleeding
T3 bleeding is commonly caused by placenta previa, placental abruption and “bloody show”. “Bloody Show” is a benign cause of bleeding that occurs due to cervical dilatation. Placenta previa and placental abruption are two serious complications that present with T3 bleeding.

<table>
<thead>
<tr>
<th>Presentations</th>
<th>Placenta Previa</th>
<th>Placental Abruption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation</td>
<td>Bright red, painless bleeding (70%), some cramping (20%), no symptoms (10%)</td>
<td>Triad of painful dark red bleeding (66%) with increased uterine tone/hyperactivity (&gt;30%) and fetal distress (&gt;50%) Occurs in 1/200 pregnancies</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>Advanced maternal age, prior uterine scar, multiparity, prior placenta previa, smoking</td>
<td>Maternal hypertension (44%), multiparity, previous hx of abruption, trauma, smoking, cocaine, alcohol</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Confirm with U/S (sensitivity 95%) Pelvic exam is contraindicated</td>
<td>A clinical diagnosis based on presentation + risk factor assessment, exclusion of other causes via U/S May not be confirmed until delivery when placenta is found to have a blood clot.</td>
</tr>
<tr>
<td>Sequelae</td>
<td>Risk of maternal morbidity is &lt;1%, risk of fetal morbidity -8%. Fetal complications include low birth weight, birth defects, breathing difficulties, anemia requiring transfusion.</td>
<td>Risk of maternal death is low, but patient may require transfusions, and shock and DIC is possible. Risk of death for the fetus is 1/500 and accounts for 15% of all newborn deaths. If the baby survives, 15% have neurological and behavioural problems due to decreased oxygen to the brain.</td>
</tr>
</tbody>
</table>
| Management    | • Treat for shock if present  
• C-section delivery if bleeding is severe, regardless of gestation  
• Expectant management in outpatient setting if preterm gestation, no fetal distress and no hemorrhage is present  
• C-section delivery if minimal bleeding and > 37 weeks | For mild bleeding with an immature fetus < 36 wks that is not in compromise (normal FHR), the patient can be managed on an outpatient basis after initial hospitalization.  
• Follow-up is in the form of serial FHR and U/S  
• In all other cases, delivery is indicated  
• Vaginal delivery is preferred after 36 wks  
• C-section is indicated if there is a threat to fetal or maternal life  
• FFP for associated coagulopathy |
Management of Vaginal Bleeding
The first step in the management of a vaginal bleeding is to stabilize the patient. Next, gestational age should be determined; if >20wks, pelvic examination is absolutely contraindicated until an U/S is performed first to rule out placental previa! However, if the gestational age is <20wks, a speculum exam is appropriate. Ultrasound is indicated in a third trimester bleed in order to rule out the presence of placenta previa. Rh immunization is only unnecessary if paternity is certain and the father and mother are both Rh negative. Otherwise, the mother should be immunized following any episode in which antibodies may have crossed from baby to mother (such as labour, threatened or real abortion, amniocentesis, or third trimester bleed).

Hypertension in Pregnancy
Maternal blood pressure measurements should be taken at every prenatal visit to monitor for rises in blood pressure that could signal preeclampsia. Preeclampsia and hypertension is usually most common in the third trimester due the physiological changes in blood pressure that occur during pregnancy. Early in the first trimester, there is a fall in blood pressure caused by vasodilation. Vasodilation results from the action of local mediators, such as prostacyclin and nitric oxide. This reduction in blood pressure primarily affects the diastolic pressure, and a drop of 10 mm Hg is usual by 13-20 weeks’ gestation. Blood pressure continues to fall until 22-24 weeks. After this, there is a gradual increase in blood pressure until term, when blood pressure returns to the level it was before pregnancy. Towards the end of the second trimester of pregnancy and in the third trimester, blood pressure should not be measured with the woman lying supine because the enlarged uterus may obstruct venous return.

The 3 main types of hypertensive disease in pregnancy are gestational hypertension (BP > 140/90 after 20wks), chronic hypertension (BP > 140/90 before 20wks), and preeclampsia (increased BP + proteinuria, usually after 20wks)

Pharmacotherapy for hypertension during pregnancy
Diastolic blood pressure (DBP) greater than 110 mm Hg is associated with increased risk of placental abruption and intrauterine growth retardation, while systolic blood pressure (SBP) greater than 160 mm Hg increases risk of maternal intracerebral hemorrhage.

Pregnant patients should be started on an antihypertensive if SBP is > 160 mm Hg or DBP is > 100-105 mm Hg.

Methyldopa is the first-line treatment for persistent hypertension in pregnancy because it has been used for decades without reports of serious adverse effects to the fetus or children up to the age of 7 years. Patients taking the drug should be warned that it can cause sedation, which may limit the dose used. The drug may cause liver transaminases to rise (in up to 5% of women) or a positive Coomb's test (although haemolytic anaemia is uncommon). You should not give methyldopa to women with a prior history of depression, because of the increased risk of postnatal depression.

Nifedipine is a second-line choice because it does not have the long safety record of methyldopa, although it has been used extensively in later pregnancy. Nifedipine is popular for treating hypertension in pregnancy. It is safe at any stage of gestation. You should avoid sublingual nifedipine to minimize the risk of sudden maternal hypotension and fetal distress, caused by placental hypoperfusion. Giving concomitant magnesium sulphate can exacerbate abrupt hypotension.

Hydralazine is also a second line choice because, despite its extensive use in pregnancy, it does not have the long safety record of methyldopa. Hydralazine is safe throughout pregnancy, although there have been reports of lupus-like syndromes in the mother and neonate. Hydralazine is more frequently used as an infusion for treating acute severe hypertension.
**Labetalol**, a beta-adrenergic blocker, can be used as a first-line agent to manage hypertension in pregnancy. The other beta-blockers (acebutolol, metoprolol, pindolol and propranolol) are second-line options. In the past, beta-adrenergic blockers have been highlighted as a class of antihypertensives associated with an increased risk of intrauterine growth retardation. Atenolol in particular has often been singled out and *atenolol should be avoided because it may impair fetal growth in utero*. However, in a recent meta-analysis of published data from randomised trials, the presence of intrauterine growth retardation appeared not to be related to the antihypertensive used. While contraindicated during pregnancy, atenolol can be used as a first-line antihypertensive medication post-partum.

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**Contraindicated antihypertensives during pregnancy include atenolol, ACEi and ARBs.**

**ACE inhibitors and ARBs** should not be utilized during pregnancy as they have adverse effects on fetal development and growth. It is important to note that ACE inhibitors and ARBs are fetotoxic, not teratogenic. A fetotoxic drug interferes with the subsequent growth and development of the fetus; a teratogenic substance is one that interferes with the formation of major body structures during the first trimester, during the period of organogenesis. Conceiving while taking these agents appears to be safe, but all women of childbearing age treated with these drugs should stop them within the first trimester if they become pregnant. The greatest risk to the fetus appears to be associated with exposure in the third trimester, but the earlier the drug is stopped, the better.

**Preeclampsia**

Preeclampsia classically presents as a triad of increased blood pressure, proteinuria and edema. However, diagnosis of pre-eclampsia is based only on *a rise in blood pressure during pregnancy together with >0.3 g proteinuria in 24 hours*. Edema is no longer included because it is not specific. Preeclampsia may also present as isolated intrauterine growth restriction.

Overall, pre-eclampsia complicates 5–6% of pregnancies, but this figure increases to up to 25% in women with pre-existing hypertension. The presence of mild pre-existing hypertension approximately doubles the risk of pre-eclampsia and increases the risk of abruption of the placenta and restriction of growth in the fetus. In general, when blood pressure is controlled, these women do well and have outcomes similar to women without hypertension. However, when chronic hypertension is severe (diastolic blood pressure >110 mm Hg before 20 weeks' gestation) the risk of pre-eclampsia is as high as 46%.

Delivery remains the ultimate treatment for preeclampsia. Management before the onset of labor includes close monitoring of maternal and fetal status. Management during delivery includes seizure prophylaxis with magnesium sulfate and, if necessary, medical management of hypertension.

Women with preeclampsia should be counseled about future pregnancies. In nulliparous women with preeclampsia before 30 weeks of gestation, the recurrence rate for the disorder may be as high as 40 percent in future pregnancies, while multiparous women have even higher rates of recurrence.
Gestational Diabetes
Women with gestational diabetes are often asymptomatic, so routine screening for GDM at 24-28 weeks gestation is recommended, unless the patient fulfills the criteria for low risk. Routine screening is a 50 g oral glucose challenge test with a threshold of 7.8 mmol/L. If screening is positive, then the patient undergoes a diagnostic test – either the 100 g or 75 g oral glucose tolerance test. If GDM is diagnosed, then the patient should be reevaluated with a 75 g oral glucose tolerance test at 6-12 weeks postpartum in order to determine if she has persistent glucose intolerance.

Risk factors for GDM include advanced maternal age, obesity, and previous child with large birth weight (>9.5 lbs). Possible adverse effects associated with GDM include perinatal mortality, pre-eclampsia, macrosomia, brachial plexus injury and neonatal metabolic complications such as hypoglycemia, hypocalcemia, and hyperbilirubinemia.

Management of GDM involves glucose control through dietary modification (choosing low glycemic index foods, having small, frequent meals) and checking fasting glucose at each visit. Patients should be counseled to maintain tight glucose control, as it is essential to prevent maternal and fetal morbidity and mortality.

Group B Streptococcal Infection
Women with Group B streptococcal (GBS) infections are often asymptomatic. Approximately 15-40% of all pregnant women are GBS colonized. GBS is the number one cause of neonatal sepsis, so it is important to screen for GBS in all pregnant women at 35-37 weeks. If cultures are positive, the patient is treated with IV antibiotics once labour begins or if their membranes rupture early. All pregnant women with an infant previously infected with GBS or any woman with documented GBS bacteriuria should also be treated with IV antibiotics during labour.

The first-line treatment is penicillin G 5 million units IV, then 2.5 million every 4 hours. If penicillin G is unavailable, then ampicillin can be used. If the patient is allergic to penicillin (but not at risk of anaphylaxis), cefazolin 2g IV can be used instead. If the patient is allergic to penicillin and is at risk of anaphylaxis, clindamycin 900 mg IV q8h or erythromycin 500 mg IV q6h can be given.

Criteria for Low Risk of GDM
- Maternal age < 25
- Caucasian or member of other ethnic group with low prevalence of diabetes
- Pregnant body mass index (BMI) ≤ 27
- No previous history of GDM or glucose intolerance
- No family history of diabetes in first-degree relatives
- No history of GDM-associated adverse pregnancy outcomes
**Hyper and Hypothyroidism in Pregnancy**

During pregnancy, thyroid function is affected by two hormones, B-hCG and estrogen. Both these hormones result in increased thyroid hormone levels. B-hCG is similar to TSH and stimulates the thyroid to produce more thyroid hormone, while higher estrogen levels stimulate increased production of thyroid-binding globulin, which transports thyroid hormone into the blood. As a result of the increased thyroid hormone levels, in about 20% of normal women, TSH levels decrease to less than the lower limit of normal. Women who have the highest hCG concentrations have the greatest reduction in TSH. In most pregnant women, this change has minimal clinical consequences.

Plasma iodide levels decrease as a result of fetal iodide use and increased maternal renal clearance. In about 15 percent of pregnant women, these lower iodide levels are associated with an increase in thyroid gland size. Ultrasound measurement of thyroid glands in more than 600 women who did not have thyroid disease confirmed a mean increase in size of 18%; the gland returns to normal in the postpartum period. Despite the change in size of the gland, none of the women had abnormal thyroid function tests. However, an enlarged thyroid detected on physical exam should be evaluated.

Rarely, hyperemesis gravidarum is associated with biochemical hyperthyroidism (undetectable TSH level, elevated FTI, or both). The relation is hypothesized to be due to high levels of hCG which can trigger severe nausea and vomiting, as well as result in increased thyroid hormone levels. The condition is rarely associated with clinical hyperthyroidism, no treatment is usually required and the condition usually resolves by 20 weeks gestation.

**Pharmacological treatment of Hyperthyroidism in Pregnancy**

In Canada, methimazole is more often used. A study that compared the use of propylthiouracil (PTU) with methimazole during pregnancy found the incidence of major malformations were similar—3% with PTU and 2.7% with methimazole. Continue medications throughout the postpartum period because exacerbation of Graves’ disease is common during this time. Both PTU and methimazole are considered to be compatible with breastfeeding and should be taken just after nursing. Thyroidectomy should be reserved for women who do not respond to thioamide therapy. Treatment with iodine 131 (I-131) is contraindicated in pregnant women. As with other surgeries during pregnancy, if thyroidectomy is necessary, it should be performed in the second trimester.

The goal of treatment of hyperthyroidism during pregnancy is to keep the patient euthyroid with free T4 (fT4) in the upper limit of normal so as not to cause fetal or neonatal hypothyroidism. Neonatal thyrotoxicosis can occur in approximately 1% of infants who are born to mothers who have Graves’ disease, secondary to transplacental passage of maternal Abs. This process can occur in cases where the mother remains euthyroid throughout the pregnancy or has had surgical or radioactive I-131 treatments before pregnancy. The risk for neonatal disease in women who have had surgical or radioactive I-131 treatments is even higher because they do not require thioamides, which can cross the placenta and have a beneficial suppressive effect. For these reasons, maternal thyroid stimulating immunoglobulin (TSI) levels should be checked at the onset of pregnancy and during T3. As well, all newborns are screened for TSH after 24 hours of age, in order to screen for hypothyroidism and neonatal hyperthyroidism.

**Complications associated with hyper and hypothyroidism**

Both excess and deficient thyroid hormone levels are risk factors for preeclampsia. As well, maternal hypothyroidism is associated with severe neuropsychological deficits in the fetus. The fetus is solely dependent on maternal T4 until 12 weeks gestation, where it begins to produce its own thyroid hormones. After 12 weeks gestation, the fetus continues to depend on maternal T4 to supplement its own thyroid hormone production. Children born to women with untreated high serum TSH at 17 weeks’ gestation had 7-point lower IQs than matched controls. The lack of T4 is most detrimental to neuropsychological development during the first trimester; however, treating maternal hypothyroidism even at a later stage is beneficial for neonatal outcome. A recent cohort study found that infant neurodevelopment was not adversely affected by hypothyroxinemia during the first trimester if fT4 concentrations were subsequently corrected.

There is some controversy as whether maternal hypothyroidism should be monitored using fT4 or TSH levels. There are also no defined reference ranges for normal serum fT4 or TSH levels. Consequently, it is the clinician’s decision to decide the ideal serum levels of fT4 and TSH in pregnancy. In Ontario, TSH levels are used to monitor thyroid function in pregnant patients with hypothyroidism. Levothyroxine (L-T4) is the first-line treatment for hypothyroid pregnant patients as it is considered safe and effective, is not teratogenic and is compatible with breastfeeding.
Sexually Transmitted Infections in Pregnancy

Sexually transmitted infections active or contracted during pregnancy can result in significant complications, including poorer pregnancy outcomes (lower gestational age at delivery, preterm prolonged rupture of membranes) and poorer newborn health (as a result of vertical transmission). As a result, screening for sexually transmitted infections is an important component of prenatal care. Prenatal counseling should involve assessing risk factors for increased susceptibility for contracting a sexually transmitted infection.

The following are recommendations from the Public Health Agency of Canada (as of Jan 2010):

- At the first prenatal visit, all pregnant women should be:
  - Offered HIV counseling and testing
  - Screened for hepatitis B surface antigen (HBsAg)
  - Screened for Chlamydia trachomatis and Neisseria gonorrhoeae
  - Screened for syphilis
- All pregnant women should be evaluated for STI risk factors prior to and during pregnancy. Any woman with ongoing risk factors for STI acquisition should be considered for rescreening each trimester
- If an STI is diagnosed in pregnancy, appropriate treatment, taking the pregnancy into consideration, should be prescribed.
- Due to the potential for decreased efficacy of treatments during pregnancy, both the patient and her sexual partner(s) should be followed to ensure therapeutic success.

Chlamydia, gonorrhea, syphilis, trichomoniasis, and bacterial vaginosis can be treated and cured with antibiotics during pregnancy. Note that special caution is required to safely treat STIs in pregnancy. See page 14 and 15 for a chart with specific rates of transmission, recommendations and treatments for infections of concern (herpes, hepatitis B, hepatitis C, chlamydia, gonorrhea, syphilis) during pregnancy.

Women who are HIV+ positive should be initiated on highly active antiretroviral therapy (HAART) to prevent vertical transmission. Suppression of viral loads prior to delivery, along with intrapartum HAART and 6 weeks of neonatal antiretroviral therapy, reduces risk of vertical transmission from 25% to less than 1%. Due to the complexity of associated with the use of antiretrovirals in pregnancy, management should involve an HIV specialist.

Contraindicated (absolute or relative) medications in pregnancy

- Erythromycin estolate
- Sulfamethoxazole
- Fluoroquinolones
- Podophyllin/podophylloxyxin/5-fluorouracil/imiquimod
- Doxycycline/tetracycline/minocycline
- Gamma benzene hexachloride/lindane
- Interferons
- Ribavirin
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<th>Risk of transmission and possible sequelae</th>
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| Chlamydial infection| • No consistent association with adverse pregnancy outcomes (preterm birth or PROM)  
• Vertical transmission in 50% of vaginal deliveries by infected mothers, can also occur in c-sections where membranes are intact  
• Of neonates that acquire infection, 20% develop conjunctivitis, 20% develop pneumonia | • Screen for C. trachomatis at first prenatal visit  
• Repeat screening in T3 for women at high risk  
• Pregnant women and their sexual partners should be treated and undergo f/u testing to ensure cure. | • Amoxicillin 500 mg PO tid for 7 days or erythromycin base 500 mg PO qid for 7 days  
• azithromycin 1 g PO in a single dose if poor compliance is suspected  
• Condoms or abstinence recommended during treatment until f/u tests are negative. |
| Gonococcal infection| • Possible sequelae include endometritis, pelvic sepsis, ophthalmia neonatorum, systemic neonatal infection | • Screen for N. gonorrhea at first prenatal visit  
• Treatment for C. trachomatis should be initiated with dx of N. gonorrhea due to high probability of co-infection  
• F/u to ensure cure | • Cefixime 400 mg PO in single dose  
• Alternatives:  
  • Ceftriaxone 125 mg in single dose  
  • Spectinomycin 2g IM in a single dose  
• Condoms or abstinence is recommended until treatment of both partners is complete |
| Syphilis            | • Infectious syphilis can lead to fetal infection w stillbirth, preterm birth, congenital abnormalities and active disease at delivery  
• Transmission occurs transplacentally > 14 weeks or at delivery  
• Untreated primary or secondary syphilis has a transmission risk of up to 100%  
• Early latent infection has 40% transmission risk  
• Untreated late latent syphilis has transmission rate of <10%.  
• Treated syphilis has a transmission rate of 1.8% | • Screen all pregnant patients in T1  
• For those with high risk or in areas with heterosexual outbreaks, repeat at 28-32 weeks and at delivery  
• Add treponemal enzyme immunoassay (EIA), a treponemal test for IgG/IgM antibodies, to VDRL test in women considered to be at high risk.  
• Any woman delivering a stillborn infant at > 20 weeks gestation should be screened for syphilis. | • Treatment during pregnancy is the penicillin regimen appropriate for the presenting stage.  
• No alternatives for treatment of syphilis during pregnancy  
• Those with penicillin allergy should be desensitized and then treated with penicillin.  
• In the second half of pregnancy, a U/S fetal evaluation for congenital syphilis (hepatomegaly, ascites, hydrops) can be done. If congenital syphilis is likely, manage with an obstetric specialist. |
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| **Hepatitis B**           | • Transmission to infant occurs at delivery, not transplacentally  
• Mothers who are acutely infected with HBV, or are carriers, can transmit to their infant  
• Vertical transmission rates can be as high as 90% depending on the stage of maternal infection, in absence of intervention                                                                                     | • If the patient is newly HBsAg-positive, consider testing for HIV, hepatitis B e antigen, hepatitis B core antibody, HBV DNA, hepatitis A IgM and hepatitis C antibodies. If positive for any of the above, assess liver transaminases and function.  
• * if the mother is at risk of acquiring hepatitis B, there is no contraindication to HBIG or HBV vaccine in pregnancy.                                                                 | • Administration of hepatitis B immunoglobulin (HBIG) immediately after birth and hepatitis B vaccine w/i 12 hours of birth to the neonate, followed by 2 vaccine doses at 1 and 6 months, can prevent 95% of cases  
• Complete a f/u HBsAg at 1-2 months, after completion of vaccine series, to document adequate immune response.                                                                                                                             |
| **Hepatitis C**           | • Risk of vertical transmission is 7.9% - not known if c-section reduces vertical transmission.                                                                                                                                                                                                 | • Patients with hepatitis C should be referred to a hepatitis C specialist.                                                                               | • Current treatments available for HCV infection are C/I in pregnancy (interferon-alpha, ribavirin)                                                                                                                                                                                                                                                                                                           |
| **Genital Herpes Simplex Virus** | • Both HSV-1 and HSV-2 can cause genital lesions, and be transmitted vertically  
• Primary infection is associated with vertical transmission rates of 30-50% if occurring in the second half of pregnancy.  
• Women with previous infections have a 2-4% risk of transmitting the infection to their baby.  
• Neonatal HSV is associated with significant mortality and morbidity – including cutaneous, CNS and disseminated disease (pneumonitis, encephalitis)                                                                 | • No evidence to screen or treat women with no history of genital herpes, with partners who also have no history.  
• Provide risk-reduction counseling (abstinence or condoms) to reduce risk of primary infection                                                                                                                                             | • Primary infections in pregnancy should be treated with acyclovir 200 mg PO five times per day for 5-10 days  
• Consider c-section for delivery, esp. if infection is in late T3.  
• If genital lesions or prodromal symptoms are present during delivery, c-section is recommended.  
• These measures reduce but do not eliminate the risk of vertical transmission  
• For women w/ recurrent infections:  
  • those with an outbreak in the past year should be given prophylaxis at 36 weeks gestation until delivery with acyclovir or valacyclovir                                                                                                                                                                                                 |
Figure 1. Algorithm for treatment of nausea and vomiting of pregnancy: If no improvement, proceed to next step.

- **Add any of the following:**
  - chlorpromazine 10 to 25 mg every 4 to 6 h PO or IM or 50 to 100 mg every 6 to 8 h PR
  - metoclopramide 5 to 10 mg every 8 h IM or PO
  - ondansetron 4 to 8 mg every 6 to 8 h PO
  - prochlorperazine 5 to 10 mg every 6 to 8 h IM or PO
  - promethazine 12.5 to 25 mg every 4 to 6 h IM, PO, or PR

- **Start rehydration treatment:**
  - IV fluid replacement (per local protocol)
  - multivitamin IV supplementation
  - dimenhydrinate 50 mg (in 50 mL of saline, over 20 min) every 4 to 6 h IV

- **Add any of the following:**
  - chlorpromazine 25 to 50 mg every 4 to 6 h IV
  - metoclopramide 5 to 10 mg every 8 h IV
  - prochlorperazine 5 to 10 mg every 6 to 8 h IV
  - promethazine 12.5 to 25 mg every 4 to 6 h IV

- **Add 1 of the following:**
  - methylprednisolone 15 to 20 mg every 8 h IV or 1 mg/h continuously up to 24 h
  - ondansetron 8 mg over 15 min every 12 h IV or 1 mg/h continuously up to 24 h

**NOTE**
- Use of this algorithm assumes that other causes of NVP have been ruled out. At any step, when indicated, consider total parenteral nutrition.
- At any time you can add any or all of the following:
  - pyridoxine (vitamin B6) 25 to 50 mg every 8 h PO
  - ginger root powder, capsules, or extract up to 1000 mg/d, and
  - acupressure or acupuncture at acupuncture P6.

* Study showed that up to 8 tablets daily did not increase baseline risk for major malformations or any other adverse effects. Monitor for potential side effects of Diclectin and other H<sub>1</sub> blockers.

† No study has compared various fluid replacements for NVP.

‡ Safety of up to 200 mg/d of 86 has been confirmed.

§ Ginger products are not standardized.

‖ Steroids are not recommended during the first 10 wk of pregnancy because of possible increased risk for oral clefts.