Preconception Care: In the Continuum of Women's Healthcare

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Abstract

The goals of preconception care are (1) to identify potential risks to the mother, fetus, and pregnancy, (2) to educate the women about these risks and provide options for intervention and management, and (3) to initiate interventions to provide optimal maternal, fetal, and pregnancy outcomes. Preconception counseling involves interventions that include health education and counseling related to reproductive risks and optimizing the control of medical disorders. If pregnancy is not desired, then contraceptive options should be discussed as preconception care begins with family planning to optimize the timing and intention of pregnancy. As such, all reproductive-age women should develop a reproductive health plan. Evidence supports an association between preconception counseling and positive changes in maternal behavior before and during pregnancy.

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Contents

1 Introduction

Preconception care is primary prevention and a preconception appointment is an integral first step toward a healthy pregnancy. The goal of preconception counseling is the reduction of potential harm and the recognition of modifiable risk factors related to pregnancy. Most pregnancies are uncomplicated with favorable maternal and fetal outcomes. However, optimizing health literacy before conception allows a woman to further reduce risk. More so, preconception care stratifies pregnancies on a continuum of low to high risk and allows women who could benefit from early intervention to possibly reduce pregnancy complications and/or birth defects. The early initiation of care relies on counseling about potential pregnancy risks and preventative strategies that are provided **before** conception.

Preconception counseling should be incorporated into any visit with a reproductive-age woman, as nearly half of all pregnancies in the United States are unplanned (Henshaw 1998). The challenge of preconception care lies in addressing pregnancy planning for women who seek any medical care and to screen and educate all reproductively capable women on an ongoing basis to identify potential maternal and fetal risks and hazards to pregnancy before and between pregnancies.

1.1 Definition and Rationale of Preconception Care

The Centers for Disease Control and Prevention (CDC) has defined preconception care as "a set of interventions that aim to identify and modify medical, behavioral, and social risks to a woman's health or pregnancy outcome through prevention and management" (Johnson et al. 2006). In addition, they define the following goals for improving preconception care:

1. Improving the knowledge, attitudes, and behaviors of women related to preconception health.
2. Assure that all reproductive-age women receive preconception care, including evidence-based risk screening, health promotion, and interventions that will enable them to enter pregnancy in optimal health.
3. Reduce risks indicated by a previous adverse pregnancy outcome through preconception interventions to prevent or minimize recurrent adverse outcomes.
4. Reduce the disparities in adverse pregnancy outcomes.

Preconception care begins with family planning to optimize timing and intention of pregnancy. To assess the effectiveness of preconception counseling to increase planned pregnancies and reduce unintended pregnancies, the effects of a preconception care program instituted in a low-income health department clinic were reviewed (Moos et al. 1996). Over 400 women who were given preconception counseling demonstrated a 50% greater likelihood of their subsequent pregnancies being intended, compared with women who received healthcare but no counseling, and a 65% greater likelihood compared with women with no healthcare or counseling prior to pregnancy.

Optimizing maternal health and nutritional status prior to pregnancy and early gestation is important because organogenesis begins within weeks of fertilization. By the time most women realize they are pregnant, 1–2 weeks after the first missed period, organogenesis has started and many prevention strategies, such as folic acid to prevent neural-tube defects (NTDs) or glycemic control to prevent adverse pregnancy outcomes, are suboptimal in effect even if initiated ACOG (2005).

Several organizations have focused on the optimization of health before conception, resulting in the development of clinical recommendations and educational materials available for providers and patients (see Table 1) (see http://www.acog.org/

Table 1 Core consideration during preconception counseling

Core considerations addressed during preconception counseling include, but are not limited, to the following:	
1.	Reproductive life plan
2.	Family history
3.	Maternal genetic conditions
4.	Infections and immunizations
5.	Chronic medical conditions
6.	Medications
7.	Environmental exposures
8.	Weight
9.	Nutrition
10.	Age
11.	Assisted reproductive technologies
12.	Social and lifestyle issues

Resources-And-Publications/Committee-Opinions/Committee-on-Gynecologic-Practice/The-Importance-of-Preconception-Care-in-the-Continuum-of-Womens-Health-Care#resources).

2 Reproductive Life Plan

To encourage preconception planning, the CDC offers a tool for healthcare professional to encourage patients to think about their reproductive goals and make a plan to facilitate these goals (http://www.cdc.gov/preconception/documents/rlphealthproviders.pdf). At every medical encounter, providers should ask a series of questions to formulate a reproductive life plan:

Questions to ask your patient: **Do you plan to have any (more) children at any time in your future?** *Open-ended question that allows branching.*

If They Answer YES

1. **How many children would you like?** Encourages woman to consider that there are choices about the number of children she has.
2. **How long would you like to wait until you or your partner become pregnant?** Encourages a woman to visualize her own future. Short interpregnancy intervals are associated with adverse fetal outcomes, including low birth weight and preterm birth.
3. **What family planning method do you plan to use until you or your partner are ready to become pregnant?** Gives the woman an opportunity to formulate a personal strategy. Slightly more than half of unintended pregnancies occur among women who were not using any method of contraception in the month they conceived.
4. **How sure are you that you will be able to use this method without any problems?** Encourages the woman to match her method choice to her lifestyle. Contraception can be highly effective if used appropriately; however, no method is perfect. In addition to nonuse of contraception, unintended pregnancies occur due to imperfect use of contraception (43%) and method failure (5%) (Frost et al. 2008).

If They Answer NO

1. **What family planning method will you use to avoid pregnancy?** Gives an opportunity to formulate and communicate a personal strategy to achieve plan.
2. **How sure are you that you will be able to use this method without any problems?** Encourages recognition that methods can have problems and to consider matching method choice to personal circumstances.
3. **Peoples' plans change. Is it possible that you or your partner could ever decide to become pregnant?** Relays the message that plans can change and that it is okay, but deliberate decisions about becoming pregnant are possible and desirable.

Action plan: Creating a reproductive health plan requires an ongoing conscientious assessment of the desirability of a future pregnancy, determination of steps that need to be taken either to prevent or to plan for and optimize a pregnancy, and evaluation of current health status and other issues relevant to the health of a pregnancy.

If pregnancy is not desired, current contraceptive use and options should be discussed to identify the most appropriate and effective method for her. Preconception and interpregnancy care are components of a larger healthcare goal that optimizes the health of every woman.

2.1 Components of Preconception Counseling

The first task of preconception counseling is obtaining a thorough history. There are several questionnaires and forms available for this purpose. Of special note in the history is a very thorough gynecologic and obstetrical history, which is essential to a preconception visit. For example, a detailed history of sexually transmitted infections, current medication use, and uterine malformations may decrease the risk of recurrent pregnancy loss. In a woman with a previous stillbirth, a detailed medical and obstetrical history, evaluation of previous stillbirth, and understanding of recurrence risk may help in the management of subsequent pregnancy. Additionally, reviewing the menstrual history is an opportunity to evaluate a woman's knowledge of menstrual physiology, determine endocrinologic comorbidities, and offer counseling about how she might plan a pregnancy.

3 Family History

Family history plays a critical role in assessing the risk of inherited medical conditions and single gene disorders. The US Surgeon General's Family History Initiative was launched in 2004 with the goal of educating healthcare providers and patients about the value of using a family history as a screening tool in clinical care (Yoon and Scheuner 2004). The preconception consultation is an optimal time to review the family history and discuss the option of undergoing carrier screening for genetic conditions. It is important to obtain the family history of both the patient and her partner, including their ethnic backgrounds, and any adverse pregnancy outcomes as a couple, or with other partners. Positive responses will need to be followed up by appropriate risk assessment, testing, and genetic counseling if needed (Table 2).

Any genetic counseling and testing that can be completed before conception is beneficial to the couple, and allows a broader array of options and greater time for decision-making. Some communities with high prevalence of carrier status even advocate for testing prior to considering pregnency (JGDC 2015). Because of counseling, couples may decide not to conceive, or they may consider using an egg donor or obtaining a preimplantation genetic screening. A patient who has had a past adverse pregnancy outcome or has a family history of other adverse pregnancy outcomes might be at increased risk of these disorders. Because both genetic and environmental factors may contribute to some of these outcomes, advising a patient that she is at increased risk of an adverse pregnancy outcome based on family history might motivate her to reduce her environmental risk (Dolan and Moore 2007).

Table 2 Red flags for genetic conditions (2011; NCHPEG 2015)

Family history of a known or suspected genetic condition
Ethnic predisposition to certain genetic disorders
Consanguinity
Multiple affected family members with the same or related disorders
Earlier than expected age of onset of disease
Diagnosis in less-often-affected sex
Multifocal or bilateral occurrence of disease (often cancer) in paired organs
Disease in the absence of risk factors or after application of preventive measures
One or more major malformations
Developmental delays or mental retardation
Abnormalities in growth
Recurrent pregnancy losses

Table modified from Family history as a risk assessment tool. Committee Opinion No. 478. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:747–50

4 Maternal Genetic Conditions

Patients with genetic conditions will benefit from a preconception evaluation with their obstetrician, geneticist, maternal–fetal medicine (MFM) specialists, or appropriate subspecialists to optimize their care. Precise identification of maternal genetic conditions in the preconception period is important to review maternal health risks and offspring morbidities associated with pregnancy, to counsel the patient regarding mode of inheritance, partner carrier screening, assessment of

genetic condition risk in the offspring, and the availability of prenatal diagnosis or preimplantation genetic screening (Table 3). The need for a multidisciplinary approach to care will vary with the patient's condition, but all patients should create a plan that addresses possible adverse effects of a pregnancy on the condition and of the condition on a pregnancy.

Table 3 Overview of select maternal genetic conditions in pregnancy

Genetic condition	Mode of inheritance	Key features
Pulmonary		
Cystic fibrosis	Autosomal recessive	Sinopulmonary disease, obstructive lung disease, recurrent infections, gastrointestinal and nutritional deficiencies, obstructive azo0spermia, salt-loss syndromes, diabetes, and pancreatic insufficiency
Cardiac		
Marfan syndrome	Autosomal dominant	Aortic root enlargement with risk of dissection; mitral valve prolapse; ectopia lentis; myopia; skeletal manifestations, including joint laxity and pectus abnormalities; dural ectasia; and lung bullae
Neurocutaneous		
Neurofibromatosis type 1	Autosomal dominant	Café au lait spots, inguinal and axillary freckling, neurofibromas, Lisch nodules, learning disabilities, scoliosis, and optic nerve and central nervous system gliomas
Tuberous sclerosis	Autosomal dominant	Skin abnormalities – hypomelanotic macules, facial angiofibromas, shagreen patches, fibrous facial plaques, and ungual fibromas Bran findings – cortical tubers, subependymal nodules, and seizures Kidney issues – angiomyolipomas, cysts, and renal cell carcinomas Heart and lung issues – rhabdomyomas, arrhythmias, and lymphangioleiomyomatosis
Renal		
Autosomal dominant polycystic kidney disease	Autosomal dominant	Renal cysts; liver and other organ cysts; vascular malformations, including intracranial aneurysms; abdominal wall hernias; hypertension; renal insufficiency; aortic root dilation with risk of dissection; and mitral valve prolapse
Metabolic		
Classic phenylketonuria (PKU)	Autosomal recessive	Children born to women with PKU on unrestricted diets at risk of intellectual disability, microcephaly, and congenital heart defects Universal newborn screening for PKU in the United States Before conception, patients should consume a low-protein diet and use a phenylalanine-free medical formula to achieve plasma phenylalanine concentrations of 120–320 μmol/L
Noonan syndrome	Autosomal dominant	Short stature; characteristic facial features; congenital heart defects, including pulmonic stenosis, lymphatic dysplasias; intellectual disability of varied degree; pectus deformity; varied coagulation defects; and renal abnormalities
Myotonic dystrophy type 1	Autosomal dominant – trinucleotide repeat disorder	Three types: 1. Mild (cataract and mild myotonia) 2. Classical (muscle weakness, myotonia, cataracts, and cardiac conduction abnormalities) 3. Congenital (severe hypotonia, respiratory failure, intellectual disability, and early death)

Table modified from Identification and Referral of Maternal Genetic Conditions in Pregnancy. Committee Opinion No. 643. American College of Obstetricians and Gynecologists. 2015 Oct;126(4):e49–51

For some genetic conditions associated with significant maternal morbidity and mortality, consideration should be given to avoiding pregnancy altogether and providing appropriate family planning, contraception counseling, and viable alternatives via assisted reproductive technologies (ART) (e.g., donor gametes or surrogacy). Patients with complex medical conditions may require treatment with medications that have potential teratogenic effects. Patients should be counseled that medications should not be discontinued until a thorough discussion with the appropriate members of the multidisciplinary team has been done to review the risks, benefits, and therapeutic alternatives. In some circumstances, the treatment adjustments need to be made before conception to minimize reproductive risks. Patients with established causative mutations for a genetic condition, and who desire prenatal genetic testing, should be offered preimplantation genetic screening with in vitro fertilization (IVF) by a reproductive endocrinologist or prenatal diagnostic testing after pregnancy is established.

5 Infections and Immunizations

Certain infections during pregnancy can cause **birth defects** and pregnancy complications. Many infections can be prevented by proper immunizations or education on hygiene. Preconception immunization of women to prevent diseases is generally preferred to vaccination in pregnancy; however, only live-virus vaccines can be of any theoretical risk to the fetus.

Two vaccinations are of particular importance while planning for and during pregnancy: influenza and pertussis. **Influenza** can cause significant morbidity and mortality in pregnancy. It is therefore critically important that all providers of reproductive-age women advocate for influenza vaccination, provide the influenza vaccine to their pregnant patients, and receive the influenza vaccine themselves every season ACOG (2014). Influenza vaccines should be given in inactivated, single-dose, intramuscular form during pregnancy. Women planning pregnancy should also be counseled on the importance of receiving a dose of the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine during *each* pregnancy, ideally between 27 and 36 weeks' gestation. Lastly, women are often immune to measles, mumps, and rubella (MMR), poliomyelitis, and varicella through childhood-conferred immunization or exposures.

The increased understanding of the link between Zika virus and fetal neurological effects adds another discussion to preconception counseling. Since the rate of vertical transmission is not known, the CDC recommends that women diagnosed with Zika, or who have had possible exposure, wait at least 8 weeks after their exposure or onset of symptoms before attempting conception. Male partners should wait at least 6 months after their symptoms to have unprotected intercourse (Petersen et al. 2016). Women residing in endemic areas are currently encouraged to possibly delay pregnancy, after a reproductive life plan discussion with a physician knowledgeable about Zika (Simeone et al. 2016).

Immune globulin or vaccination against poliomyelitis, yellow fever, typhoid, or hepatitis may be indicated for travels to endemic areas.

Additional infectious disease screening includes:

1. **Rubella**: Screening for anti-rubella IgG identifies rubella nonimmune women who should be offered vaccination. If serologic testing demonstrates that they are susceptible, women should be vaccinated with rubella vaccine before conception occurs. If preconception counseling is not possible, patients should have serologic testing to document rubella immunity status at the time of their first prenatal appointment. Women who are susceptible to rubella should be counseled to avoid exposure to other individuals who may have viral exanthems.
2. **Hepatitis B**: Universal screening of pregnant women for hepatitis B virus has been recommended by the CDC since 1988. Women with social or occupational risk for exposure to hepatitis B, such as healthcare providers, should be counseled and offered vaccination.
3. **Pneumococcus**: The pneumococcal polysaccharide vaccine is recommended for all adults

with conditions that increase the risk of invasive pneumococcal disease, which includes immunocompetent women with underlying health conditions (chronic heart, lung, or liver disease, diabetes mellitus, alcoholism, cochlear implants, and cigarette smoking), anatomic asplenia, and immunocompromised persons. Ideally, this vaccine would be given preconceptionally, but the indications for administration are not different in pregnancy.

4. **Tuberculosis**: Patients at risk for tuberculosis should be tested with a subcutaneous purified protein derivative (PPD) challenge. If the patient has a history of bacillus Calmette-known-positive skin testing, quantiferon-Gold can be used as an alternative. Preconception treatment for latent TB infection can be ordered as indicated.
5. **Parvovirus B19:** Parvovirus IgG testing may be offered preconceptionally to teachers and childcare workers.
6. **Chickenpox**: Screening for varicella IgG should be performed if a positive history of prior chickenpox cannot be obtained. The varicella zoster virus vaccine is now recommended for all nonimmune adults. The VZV vaccine is a live-virus vaccine that should be given at least 30 days prior to conception. Nonimmune women can be counseled regarding post-exposure prophylaxis during pregnancy.
7. **HIV**: ACOG recommends that all pregnant women should be screened for **HIV** infection as early as possible during each pregnancy using the opt-out approach. Repeat HIV testing in the third trimester is recommended for women in areas with high HIV incidence or prevalence and women known to be at risk of acquiring HIV infection ACOG (2015). If the diagnosis of HIV infection is established, the woman should be linked into ongoing care with a specialist in HIV care for comanagement.
8. **Sexually transmitted infections**: Sexually transmitted infections (STIs) can affect women's ability to become pregnant and cause infections that affect pregnancy outcomes. Common STIs are chlamydia, gonorrhea, genital herpes, trichomoniasis, hepatitis B, and syphilis, and HIV. Testing for STIs before pregnancy gives the women the opportunity to possibly avoid a poor pregnancy outcome. Preconception testing for the following STIs is currently recommended for all: HIV, as above, and chlamydia and gonorrhea for women 25 years or younger or if they are older than 25 years with risk factors. A wider panel of STIs, including syphilis and hepatitis C, can be tested in women at high risk, such as sex workers or intravenous drug abusers.

6 Chronic Medical Conditions

Preconception care should include an ascertainment of medical conditions. Obtaining consultation and ongoing close collaboration with other specialist may be indicated. Briefly, some common or serious medical conditions that impact or are impacted by pregnancy are discussed below by system.

1. **Neurologic**

Seizure disorders. Seizure disorders are the most common neurologic disease to affect pregnant women, and both the disease and its treatments can adversely affect pregnancy. Approximately one-third of women with a seizure disorder will experience more frequent seizures in pregnancy. Poorly controlled seizure disorder has been associated with miscarriages, low birth weight, developmental disabilities, microcephaly, and hemorrhagic disease of the newborn (Hadar et al. 2015). Seizure disorders increase the risk of congenital anomalies, whether or not the mother is taking antiepileptic drugs (AEDs). Generally, obstetricians and neurologists will recommend that patients planning pregnancy should be managed on the most effective AED, ideally monotherapy at the lowest possible drug dose, for their seizures and will not make changes to AEDs for the purpose of reducing teratogenic risk with the exception of valproate. Low folate levels in women with epilepsy are associated with an increased risk of major fetal malformations. Furthermore, given the increased rates of NTDs with many AEDs, supplementation with 4.0 mg of folic

acid (versus 0.4 mg recommended to all women of childbearing potential) should be initiated at least 1 month before conception and continued in the first trimester in women with a seizure disorder.

Multiple sclerosis. Multiple sclerosis (MS) is an immune-mediated demyelinating disease of the CNS typically characterized by relapses and remissions of neurologic deficits. MS occurs with a 3:2 ratio of females to males and a peak incidence of 30 years of age. Fortunately, pregnancy does not appear to affect the type or severity of exacerbation and may even have a protective effect against relapses. However, higher rates of relapse in the postpartum period have been reported. Long-term disability due to MS is not altered by pregnancy. There are no accepted guidelines for recommending for or against pregnancy in women with MS, and each patient's MS history and current neurologic deficits should be considered independently. A multidisciplinary approach is required, combining the expertise of MFM and neurology. Medication adjustments may be recommended prior to pregnancy.

2. **Cardiovascular**

Hypertension. Chronic hypertension affects 3–5% of women of reproductive age ACOG (2015). Hypertension is a common comorbidity of diabetes and is found in 20–30% of women who have had diabetes for longer than 10 years. Chronic hypertension in pregnancy is associated with higher rates of preterm birth, placental abruption, intrauterine growth restriction, preeclampsia, and fetal demise. Women with chronic hypertension are at risk of worsening hypertension and end-organ damage, and 20–25% of women with hypertension develop superimposed preeclampsia during pregnancy. Treating severe hypertension (systolic blood pressure of 160 mmHg or higher, or diastolic blood pressure of 110 mmHg or higher) improves pregnancy outcomes (Sibai and Anderson 1986), but goal blood pressure range remains contested. Caring for women of reproductive age with hypertension should include educating them about the risks of hypertension during pregnancy.

Women with long-standing hypertension who are planning pregnancy should be assessed for retinopathy, renal disease, and ventricular hypertrophy. Blood pressure medications that are safe for pregnancy should be added sequentially until target blood pressure levels are achieved. Such agents include long-acting calcium channel blockers, selected beta-adrenergic blockers, and methyldopa. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) are contraindicated in pregnancy because of associated teratogenicity. Women treated with these agents should use effective contraception or be converted to safer agents prior to conception. Women taking statins should also be advised to discontinue them under the guidance of a provider.

Congenital cardiac disease: As more women with congenital cardiac disease, both corrected and uncorrected, reach reproductive age, preconception counseling and family planning for this unique category of women becomes increasingly important. Pregnancy and its associated changes in cardiovascular physiology can pose significant risks to women with congenital heart disease. These women require a multidisciplinary approach with both cardiology and MFM preconceptionally.

3. **Pulmonary**

Asthma. Asthma complicates approximately 4–8% of pregnancies (Kwon et al. 2003). Women with poorly controlled asthma before pregnancy and at conception are more likely to experience worsening symptoms with pregnancy. The goal of asthma treatment in pregnancy is to maintain adequate oxygenation of the fetus by preventing hypoxic episodes in the mother (Dombrowski and Schatz 2008). Preconception care should focus on optimizing asthma control with medications, and identifying and reducing exposure to allergens. Patients should be counseled on smoking cessation and avoidance of secondhand smoke exposure. Asthma self-management skills, including self-monitoring with peak flow monitors, correct use of inhalers, and following a

plan for long-term management of asthma and promptly handling signs of worsening asthma enhances asthma control. Inhaled corticosteroids are first-line controller therapy for persistent asthma during pregnancy. Influenza vaccination is of even more importance in women with asthma as concomitant infectious comorbidity can lead to significant respiratory decompensation.

4. **Gastroinsteninal**

   Inflammatory bowel disease. Women with inflammatory bowel disease (IBD) (Crohn's disease and ulcerative colitis), should address disease control, medications, and nutritional status preconceptionally as IBD affects women in their reproductive years. IBD does not decrease fertility; however, fertility in patients with IBD is possibly affected by active disease, medications, and prior surgeries. Women with IBD may experience worse obstetrical and pregnancy-related outcome compared to the general population, even with the disease in remission (Cornish et al. 2007). As such, optimizing the preconception disease burden can attenuate risk. The course of IBD during pregnancy is determined by the activity of the disease at conception. Hence, patients in remission at the time of conceptions are likely to remain in remission during pregnancy. In contrast, up to 70% of women with active disease at conception will have continued or worsening symptoms (Getahun et al. 2014). The choice of anti-inflammatory and immunosuppressive medications during pregnancy should be based on the safety profile of the medication, as well as the risk of relapse of IBD if the medication is discontinued.

5. **Renal**

   Lupus nephritis. Women with systemic lupus erythematosus (SLE), particularly lupus nephritis, have a better pregnancy prognosis if their disease has been quiescent for at least 6 months prior to pregnancy and they have normal or near-normal renal function. Active SLE at the time of conception is a strong predictor of adverse maternal and obstetrical outcomes. Disease flares with pregnancy are difficulty to decouple from the physiologic changes of pregnancy versus disease hallmarks. Most SLE medication can be continued during pregnancy, but some (such as some anti-inflammatories and methotrexate) will need to be discontinued under the guidance of a physician. The most important aspects of preconception counseling with SLE is to determine whether pregnancy may present an unacceptable high maternal or fetal risk to optimize interventions that can decrease risk, and to adjust medications that are known to be harmful to the fetus.

6. **Hematological and immune**

   Thrombophilia. Confirmed inherited or acquired thrombophilia places women at a higher risk of thromboembolic complications during pregnancy because of the inherent hypercoagulable state of pregnancy. These coagulation factor changes include resistance to activated protein C in the second and third trimester; decrease in protein S activity due to a reduction in total and free protein S antigen; increase in fibrinogen and factors II, VII, VIII, and X; and increases in levels and activity of fibrinolytic inhibitors, thrombin fibrinolytic inhibitor, and plasminogen activator inhibitor (Lockwood 1999). The goal of screening and treatment of appropriate women with specific inherited thrombophilias is the prevention of maternal venous thromboembolism (VTE). Risk and treatment of VTE depend on the type of inherited thrombophilia and a personal or family history of thrombosis. Preconceptional consultation with hematology and MFM is recommended.

7. **Endocrine**

   Diabetes. The goal of preconception diabetes management is to achieve a glycosylated hemoglobin (A1c) level within the normal range before conception, in order to prevent or minimize the postconception sequelae of diabetes: miscarriage, congenital anomaly, macrosomia, polyhydramnios, preterm labor, shoulder dystocia, birth injury, and postnatal metabolic instability of the newborn. A secondary goal is to reduce the risks associated with in utero fetal programming, including future pediatric and adult metabolic syndrome

in the offspring. For this goal to be achieved, glycemic control must be instituted early and aggressively (Bellamy et al. 2009), and appropriate contraception would ideally be used until the patient is ready.

Diabetes affects nearly 10% of women of reproductive age, and about 1% of pregnancies are complicated by pregestational diabetes (Bellamy et al. 2009). Glucose is known to be teratogenic at high levels, and rates of congenital fetal anomalies are directly related to glycemic control in the first trimester. Optimal glycemic control during organogenesis reduces rates of congenital malformations. Pregnancy and associated nausea and vomiting can also lead to higher rates of hypoglycemia, decreased hypoglycemic awareness, increased rates of diabetic ketoacidosis, and the progression of diabetic retinopathy and nephropathy (Metzger et al. 2008).

Preconception counseling improves pregnancy outcomes in women with diabetes and should include educating women about the impact of diabetes on pregnancy outcomes and the impact of pregnancy on diabetes, optimizing glycemic control, screening for vascular complications of diabetes, evaluating medication use, and encouraging effective family planning. For patients who have had diabetes for 10 years or longer, evaluation for baseline electrocardiogram, echocardiogram, microalbuminuria, and serum creatinine should be considered. Because microvascular disease can progress during pregnancy, ophthalmic and podiatric examinations are also recommended.

Thyroid disease. Thyroid disease can significantly impact pregnancy outcomes, as uncontrolled thyrotoxicosis and hypothyroidism are associated with adverse pregnancy outcomes. Hypothyroidism affects 2.5% of women of reproductive age. Hypothyroidism in the first trimester is associated with cognitive impairment in children. Hypothyroidism in pregnant women increases the risk of preterm birth, low birth weight, placental abruption, and fetal death (Fitzpatrick and Russell 2010).

Women who are adequately treated before pregnancy and those diagnosed and treated early in pregnancy have no increased risk of perinatal morbidity. It is essential to monitor women on thyroid replacement therapy. During pregnancy, thyroid replacement dosages typically need to be increased every 4–6 weeks' gestation, possibly by 30% or more. Universal screening for thyroid disease in pregnancy is not recommended because identification and treatment of maternal subclinical hypothyroidism has not been shown to result in improved neurocognitive function in offspring ACOG (2005). The first-line screening test used to assess thyroid status in patients at risk is measurement of the TSH level.

Hyperthyroidism can result in significant maternal and neonatal morbidity, and outcomes correlate with disease control (Stagnaro-Green and Pearce 2012). Patients with Graves' disease should be evaluated for the presence of thyroid-stimulating immunoglobulins.

8. **Mental health**

   Depression. Approximately 10–15% of women of reproductive age are affected by depression. Untreated mood disorders in pregnancy can be potentially serious, with approximately 40–50% of untreated patients experiencing an episode of decompensation and 15% are at risk for suicidal ideation. Untreated depression may increase the risk of adverse pregnancy outcomes, such as stillbirth, IUGR, preterm delivery, low Apgar scores, STIs, and substance abuse. Patients should be counseled that the risk of uncontrolled psychiatric disease typically outweighs the theoretical risk of medications during pregnancy, and therefore medications should be continued if medically indicated. Close co-surveillance with her mental health provider is important before, during, and after pregnancy.

9. **Oral**

   Dental disease: Pregnancy may results in physiological changes in the oral cavity: pregnancy gingivitis, tooth mobility, tooth erosion, dental caries, and periodontitis (ACOG 2013). Dental caries and periodontal diseases are common and may be associated with

pregnancy complicates, such as preterm delivery; thus, referral to a dentist is appropriate. Patients should be reassured that prevention, diagnosis, and treatment of oral health conditions, including shielded dental X-rays and local anesthesia, are safe during pregnancy. Delaying treatment could result in more complex problems. Preconception counseling and evaluation by dentist is a good time to reinforce oral health maintenance such as fluoridated toothpaste for brushing twice a day, flossing, limiting sugary drinks, and dental visits twice a year.

7 Medications

The woman's preconception medications should be reviewed and altered to avoid teratogenicity, when clinically appropriate and feasible. Evaluation of exposure to medications includes over-the-counter and prescription medications, herbs, and supplements. Of note, in December 2014, the FDA published the Pregnancy and Lactation Labeling Rule or final rule (PLLR), which changed the labeling requirements for prescription drugs. This removed the pregnancy letter categories and created descriptive subsections for pregnancy exposure and risk, lactation, and effects to reproductive potential. Labeling changes began in June 2015, for all new drug submissions. Previously approved drugs will gradually switch to the new labeling. The rule does not affect over-the-counter drug labeling.

Since the conversion to the PLLR labeling has not yet fully taken effect, we will discuss medications using the standing terminology. Traditionally, FDA pregnancy categories X and D should be avoided.

Important medications to discuss include:

1. **Statins**: Category X. Should be discontinued before conception.
2. **Isoretinonin**: Category X. Should be discontinued before conception.
3. **Warfarin**: Category X. Should be discontinued before conception except with a mechanical heart valve.
4. **ACE inhibitors and ARBs**: Category C in first trimester and category D in second and third trimesters. Should be discontinued before conception.
5. **Oral anti-glycemic agents**: Metformin and acarbose are classified as category B, although systematic data on safety are lacking. All other agents are category C drugs. The potential risks and benefits of oral antidiabetic agents in the preconception period should be carefully weighed.
6. **Antiepiletic drugs (AEDs)**: Valproate (category D) is associated with neural-tube defects as well as craniofacial, limb, and cardiac abnormalities. Carbamazepine (category D) exposure has been associated with facial dysmorphism and fingernail hypoplasia. Data on second-generation AEDs are still limited. Women should continue AEDs that control their epilepsy, ideally as a monotherapy at the lowest effective dose.
7. **Psychotropic medications**: Some psychiatric medications are of concern for teratogenesis; however, untreated psychiatric illness is also associated with poor pregnancy outcomes, including premature birth, low birth weights, and fetal growth restriction. Treatment of bipolar disorder with lithium has been associated with increased incidence of heart defects. During pregnancy, a fetal echocardiogram is recommended for women taking lithium in the first trimester. Most selective serotonin reuptake inhibitors (SSRIs) are considered safe; however, paroxetine early in pregnancy has been associated with an increased risk of heart defects, and an FDA advisory notes a possible association between late-term SSRI use and persistent pulmonary hypertension in the newborn. SSRI use in pregnancy should be individualized, balancing the risks of maternal depression and potential fetal effects.
8. **Contraceptives**: No evidence indicates teratogenicity from oral contraceptive or contraceptive implant use.

Resources for Medications During Pregnancy

- LactMed www.toxnet.nlm.nih/gov/cgi-bin/sis/htmlgen?LACT

- OBPharmacopoeia: http://www.perinatology.com/Reference/OBPharmacopoeia-Public/PharmacopoeiaTOC-public.htm
- ReproTox: https://reprotox.org/
- Briggs Drugs in Pregnancy and Lactation textbook

Resources for Information on Potential Teratogens

- National Library of Medicine (NLM), sis.nlm.nih.gov/
- Reproductive Toxicology Center (ReproTox), www.reprotox.org
- Teratogen Information System (TERIS Catalog) http://depts.washington.edu/terisweb/teris/
- Organization of Teratology Information Specialists (OTIS), www.OTISPregnancy.org
- The Hospital for Sick Children, Toronto, Canada, http://www.motherisk.org/women/drugs.jsp
- Pediatric Environmental Health Specialty Units (PEHSU), www.pehsu.net/aboutus.html

8 Environmental Exposures

Questions about women's work, hobbies, pets, and home environment can identify potentially toxic exposures, such as mercury, pesticides, lead, and endocrine-disrupting chemicals (phthalates, bisphenol A, polybrominated diethyl ethers) (McDiarmid et al. 2008). In additional to occupational exposures, mercury may be found in fish and skin-lightening creams. Lead exposure can come from paint (pre-1970), imported cosmetics, food additives, medicine, and clay (Sathyanarayana et al. 2012). Exposure to outdoor cats and their fecal matter can increase risk of toxoplasmosis. These are all potential modifiable risk factors.

9 Weight

In the United States, 26% of women 20–39 years of age are overweight, defined as body mass index (BMI) of 25–29.9 kg/m^2, and prevalence rates continue to rise. Obese (BMI above 30 kg/m^2) and underweight women (BMI $<$18.5 kg/m^2) are at risk for adverse pregnancy outcomes. Women who are overweight or obese are at risk of diabetes, gestational diabetes, hypertension, macrosomia, cesarean delivery, and thromboembolism. Low prepregnancy BMI is associated with preterm birth and low birth weight. Low body weight is also associated with nutrient deficiencies, osteoporosis, amenorrhea, infertility, and arrhythmias. Women with low BMIs should be assessed for eating disorders and counseled about how being underweight can affect their health and pregnancy (ACOG 2013). Nutritionist referrals may be beneficial.

Recommendations for obese (BMI $>$30 kg/m^2) women (ACOG 2013): Preconception counseling for obese women who are pregnant or planning a pregnancy includes the following:

- Preconception assessment and counseling
- Evaluation for sequelae of obesity
- Documentation of current and goal weight and BMI
- Provision of specific information concerning the maternal and fetal risks of obesity in pregnancy
- Encouragement to undertake a monitored weight-reduction program
- Nutrition consultation
- Evaluation for prior history of bariatric surgery or candidacy for bariatric intervention

9.1 Bariatric Surgery

Managing a patient who has had bariatric surgery ideally involves a planned pregnancy, coordination with the bariatric surgery team, and preconception nutritional counseling. Bariatric surgery is available for patients with a BMI $>$40 kg/m^2 (or $>$35 kg/m^2 with comorbidities) (Xanthakos and Inge 2006). The roux-en-Y gastric bypass (65%) or adjustable gastric banding (24%) (Xanthakos and Inge 2006) aims to cause weight loss by restricting food intake, food malabsorption, or both.

All bariatric surgery candidates should undergo contraceptive options and preconception

counseling. Ideally, women will use contraception for the first 12–18 months postoperatively to minimize the pregnancy risk during the initial rapid weight loss period. Rare complications of bariatric surgery carried out during pregnancy include intestinal obstruction, gastrointestinal hemorrhage, hernias, anastomotic leaks, and band complications.

Screening for diabetes will also be potentially limited by dumping syndrome. In these patients with possible underlying insulin resistance, evaluation for pregestational diabetes or insulin resistance may help elucidate further pregnancy risk. At their preconception visit, women with a history of bariatric surgery should obtain a laboratory measure of baseline nutritional status which includes complete blood count (CBC), iron studies, albumin level, ferritin levels, vitamin B1 (thiamine) level, vitamin B12 level, calcium and phosphorus levels, and 25-hydroxyvitamin D levels. Additionally, it is important to appropriately treat nutritional deficiencies throughout pregnancy with close monitoring of weight changes. A caveat is that in the setting of restrictive surgeries, attention should be placed that any medication prescribed should ideally be less than 10 mm. A helpful patient handout:

http://contemporaryobgyn.modernmedicine.com/sites/default/files/images/ContemporayOBGYN/SMFM_bariatric_patient_handout.pdf

9.2 Weight Gain

The recommended weight gain for pregnancy is based on prepregnancy BMI. Pregnant women require 15% more calories than nonpregnant women, usually 300–500 kCal more per day, depending on the patient's weight and activity. The total weight gain recommended is 25–35 lb for women with a normal BMI. Underweight women may gain 40 lb or more, and overweight women should limit weight gain to <25 lb or less. Three to six pounds is typically gained in the first trimester, and 0.5–1.0 lb per week is gained in the last two trimesters of pregnancy. Inadequate weight gain is associated with an increased risk of low birth weight in infants. Total weight gain in obese patients can be as low as 11 lb. Preconception education for ideal pregnancy weight gain and dietary changes can help set realistic expectations for intended mothers.

Institute of Medicine Weight Gain Recommendations for Pregnancy (2009, 2013)

Prepregnancy weight category	Body mass index	Recommended range of total weight (lb)	Recommended rates of weight gain† in the 2nd and 3rd trimesters (lb) (mean range [lb/wk])
Underweight	<18.5	28–40	1 (1–1.3)
Normal weight	18.5–24.9	25–35	1 (0.8–1)
Overweight	25–29.9	15–25	0.6 (0.5–0.7)
Obese	>30	11–20	0.5 (0.4–0.6)

10 Nutrition

Dietary allowances for most vitamins and minerals increase with pregnancy and are adequately supplied in a well-balanced diet. The recommendations listed below are for singleton gestations. Requirements need to be adjusted with multiple gestations. Increased iron is needed for both the fetus and the mother. Consumption of iron-containing foods should be encouraged, and iron supplements may be prescribed during pregnancy. The 30-mg elemental iron supplement is contained in approximately 150 mg of ferrous sulfate, 300 mg of ferrous gluconate, and 100 mg of ferrous fumarate. Prenatal calcium requirement is 1,200 mg per day.

After the establishment of a pregnancy, and during subsequent prenatal visits, nutrition should continue to be discussed as discussions revolve around the avoidance of unpasteurized cheeses and deli meats to avoid the risk of exposure to *Listeria monocytogenes.* Excess use of multivitamin and supplements containing vitamin A should be avoided because the estimated dietary intake of vitamin A for most women in the United States is sufficient. Vitamin A is teratogenic in humans at dosages of more than 20,000–50,000 IU daily. Women with a history of anorexia or bulimia may benefit from nutrition and psychological counseling before conception.

10.1 Folic Acid

The initiation of folic acid supplementation at least 1 month before pregnancy reduces the incidence of NTDs, such as spina bifida and anencephaly (Czeizel and Dudas 1992). Folic acid supplementation of 400 mcg (0.4 mg) daily started before pregnancy and continued until 6–12-week postconception reduces the rate of neural-tube defects by nearly 75%. Women receiving preconception counseling from their physicians are five times more likely to take folic acid before conception (Elsinga et al. 2008). Unless contraindicated by the presence of pernicious anemia, women who have previously carried a fetus with an NTD, have epilepsy, or are taking folic acid antagonist should take 4.0 mg of folic acid daily (Wilson et al. 2003).

11 Exercise

Conditioned pregnant women usually can continue to exercise throughout gestation, with appropriate modifications (ACOG 2002). There are no data to suggest that exercise is deleterious during pregnancy. One caveat is that as pregnancy progresses, balance problems and joint relaxation may predispose to orthopedic injury. A woman should be advised not to exercise to exhaustion, and she should augment heat dissipation and fluid replacement. She should avoid supine positions, activities requiring good balance, and extreme weather conditions. In the absence of obstetric or medical complications, moderate physical activity can maintain cardiovascular and muscular fitness throughout pregnancy and the postpartum period. No data suggests that moderate aerobic exercise is harmful to the mother or fetus. Certain obstetric complications may lead to recommendations to further modify or decrease activity, and these will be determined by her obstetrics provider during the pregnancy.

12 Age

In the United States, 10% of pregnancies occur in women after 35 years of age. Older woman are more likely to obtain preconceptional counseling. After age 35, there is an increased risk for obstetrical complications, chromosomal abnormalities, and perinatal morbidity and mortality (Cunningham and Leveno 1995). Older women with multiple chronic medical conditions or who are in poor physical condition usually have readily apparent risks. For the physically fit woman without medical problems the risks are much lower. Fetal risks associated with advanced maternal age stem primarily from (1) indicated preterm delivery for maternal complications such as hypertension and diabetes, (2) spontaneous preterm delivery, (3) fetal growth disorders related to chronic maternal disease or multifetal gestation, (4) fetal aneuploidy, (5) increased risk of multiple gestations, and (6) pregnancies resulting from use of ART. Most researchers have found that fetal aneuploidy is the only congenital abnormality related to maternal age.

13 Assisted Reproductive Technologies

About 1% of births in the United States are a result of ART (Wright et al. 2005). Couples with fertility problems (10% of couples in the developed world) seeking treatment with ART should receive the same baseline preconception counseling as women without fertility problems. Underlying disorders leading to primary or secondary infertility, such as congenital Müllerian anomalies, endocrinologic abnormalities, or recurrent pregnancy loss, may require more focused preconception counseling. Additional counseling should address ART success rates and the possible risks associated with ART. As reviewed above, a woman's age decreases her success of achieving a live birth after 35 years old, with decreasing ovarian reserve. This holds true for ART. Singleton gestations conceived by ART may have lower birth weights and possibly carry an increase in imprinting disorders (Camprubi et al. 2013) and congenital cardiac anomalies. The major risk of ovarian stimulation (clomiphene citrate and letrozole) is multiple gestations. About one-third of live births delivered by ART have more than one infant, and twins represent 85% of these

multiple-birth children (Grainger et al. 2006). There are more complications in multiple gestations, which include the morbidities associated with preterm delivery. The risks of higher-order multiples should be discussed prior to ART therapy, including the patient and partner's preferences for selective reduction procedures.

14 Social and Lifestyle History

A detailed social and lifestyle history should be obtained to identify potentially risky behavior and exposures that may compromise pregnancy outcome and to identify social, financial, and psychological issues that could affect pregnancy planning.

All patients should be asked about alcohol, tobacco, and other drug uses:

1. **Alcohol** is a known teratogen, and a clear dose-response relationship exists between alcohol use and fetal effects. The American Academy of Pediatrics identifies prenatal exposure to alcohol as the leading preventable cause of birth defects and intellectual and neurodevelopmental disabilities in children and recommends complete abstinence from alcohol during pregnancy (Williams and Smith 2015).
2. **Marijuana** is the illicit drug most commonly used during pregnancy, with estimated prevalence rates of 2–5%. Cannabinoids have been associated with impaired neurodevelopment and emotional dysregulation, and women should be encouraged to discontinue prior to pregnancy (2015).
3. **Cocaine** has also been identified as a teratogen, as well as a cause of prematurity, abruptio placentae, and intrauterine growth restriction.
4. **Tobacco** use has been identified as the leading preventable cause of low birth weight. At least 11% of pregnant women in the United States smoke. Nicotine is considered teratogenic and a modifiable lifestyle with extensive counseling on smoking cessation, intensive smoking reduction program, and nicotine replacement therapy. If substance addiction is present, a structured recovery plan is needed to effect behavioral change.

Pregnancy can exacerbate interpersonal problems and is a time of increased risk from an abusive partner. Victims of domestic violence should be identified before they conceive. They are most likely to be abused during pregnancy than at other times. Approximately 37% of abused women are assaulted during their pregnancy, resulting in possible abruptio placentae, antepartum hemorrhage, fetal fractures, rupture of internal organs, and preterm labor. Information about community, social, and legal resources should be made available to women who are abused and a plan devised for dealing with an abusive partner.

The preconception interview is also an appropriate time to discuss insurance coverage and financial difficulties. Many women and couples do not know their eligibility or may lack medical insurance coverage altogether. Referral for medical assistance programs, such as the Women, Infants, and Children's (WIC) program, should be part of preconception planning. WIC is a supplemental food and nutrition program for pregnant women, new moms, and children under the age of five. Through the WIC program, women receive financial assistance in purchasing food, counseling and information on health eating, breastfeeding support, and information and referrals to health and community resources. WIC state agency contacts are available at http://www.fns.usda.gov/wic-state-agency-contacts.

15 Cancer Survivors

Pregnancy risks for women who are cancer survivors vary based on the cancer and the treatment received. For example, a woman who has been on a cardiotoxic chemotherapy (i.e., adriamycin) or has received chest radiation needs an assessment of her cardiac function prior to pregnancy. Preconception evaluation should be modified based on oncological therapy. Baseline liver and renal function tests should be performed, as chemotherapy can be hepatotoxic and/or nephrotoxic. Prior chemotherapy and radiation do not confer any increased risk of adverse pregnancy outcomes, genetic conditions, or childhood cancers (Green

et al. 2002). However, prior radiation to the abdomen and pelvis has been associated with an increased rate of miscarriage and poor pregnancy outcomes (Signorello et al. 2010). There is an increased risk of cancer in the offspring of women with hereditary cancer syndromes, such as BRCA or hereditary nonpolyposis colorectal cancer. These women should have a preconception visit with a genetic counselor.

Young women who may be receiving chemotherapeutic agents that may render her infertile should also be referred to reproductive endocrinologist and infertility specialists to discuss ovarian preservation prior to therapy.

16 Prenatal Care

An often-overlooked effect of preconception counseling is to educate woman about the importance of early prenatal care and more so accurate dating of pregnancy. Accurate dating of a pregnancy improves outcomes and is a public health imperative. As such, an accurately assigned estimated due date (EDD) is among the first evaluations during prenatal care.

Methods for EDD. The American College of Obstetricians and Gynecologists, the American Institute of Ultrasound in Medicine, and the Society for Maternal-Fetal Medicine make the following recommendations regarding the method for estimating gestational age and due date (2014):

- Ultrasound measurement of the embryo or fetus in the first trimester is the most accurate method to establish or confirm gestational age.
- If pregnancy resulted from ART, the ART-derived gestational age should be used to assign the EDD.
- As soon as data from the last menstrual period (LMP), the first accurate ultrasound examination, or both are obtained, the gestational age and the EDD should be determined, discussed with the patient, and documented clearly in the medical record. Subsequent changes to the EDD should be reserved for rare circumstances, discussed with the patient, and documented clearly in the medical record.
- For the purposes of research and surveillance, the best obstetric estimate, rather than estimates based on the LMP alone, should be used as the measure for gestational age.

Following the establishment of an accurate EDD, the first prenatal visits involves a discussion of the risks, benefits, and alternatives of various methods of prenatal screening and diagnostic testing, including the option of no testing, which should occur with all patients. Genetic disease screening can suggest increased risk for specific diseases such as muscular dystrophy, fragile X, or Down syndrome, for which genetic counseling should be offered. Information about screening versus diagnostic tests, such as chorionic villus sampling or amniocentesis, can be explained. In some instances, genetic counseling may result in a decision to forego pregnancy or to use ART. In addition to the above, the first prenatal visit includes obtaining baseline prenatal labs: blood type, Rh status, antibody screen, CBC, Rubella, RPR, HBsAg, HIV, urine culture, Pap test, and gonorrhea and chlamydia (if indicated).

Any further discussion about prenatal care is beyond the scope of this chapter.

17 Summary

The goals of preconception care are:

- To identify potential risks to the mother, fetus, and pregnancy.
- To educate the women about these risks, provide option for intervention and management.
- Initiate interventions to provide optimal maternal, fetal and pregnancy outcomes.

Preconception counseling involves interventions that include health promotion and counseling related to reproductive health risks, optimizing the control of medical disorders, and referral, when appropriate. If pregnancy is not desired, then contraceptive options should be discussed. As such, all reproductive-age women should develop a **reproductive health plan**. Evidence supports an association between preconception counseling and

positive changes in maternal behavior before pregnancy, particularly with respect to folic acid intake, improved glycemic control, and reduction in alcohol intake and tobacco use.

Resources: Online resources on preconception care:

- Centers for Disease Control and Prevention http://www.cdc.gov/preconception/freematerials-health-edu.html
- March of Dimes http://www.marchofdimes.org/pregnancy/your-checkup-before-pregnancy.aspx
- Perinatal Foundation http://www.perinatalweb.org/index.php?page=shop.product_details&flypage=shop.flypage&product_id=16&category_id=2&option=com_virtuemart&Itemid=280
- American College of Obstetricians and Gynecologists http://www.acog.org/Resources_And_Publications/Committee_Opinions/Committee_on_Gynecologic_Practice/The_Importance_of_Preconception_Care_in_the_Continuum_of_Womens_Health_Care

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