

## Twenty Things Physicians and Patients Should Question

1

### Don't do an inherited thrombophilia evaluation for women with histories of pregnancy loss, fetal growth restriction (FGR), preeclampsia and abruption.

Scientific data supporting a causal association between either methylenetetrahydrofolate reductase (MTHFR) polymorphisms or other common inherited thrombophilias and adverse pregnancy outcomes, such as recurrent pregnancy loss, severe preeclampsia and FGR, are lacking. Specific testing for antiphospholipid antibodies, when clinically indicated, should be limited to lupus anticoagulant, anticardiolipin antibodies and beta 2 glycoprotein antibodies.

2

### Don't place a cerclage in women with short cervix who are pregnant with twins.\*

Women with a short cervical length who are pregnant with twins are at very high risk for delivering preterm, but the scientific data, including a meta-analysis of data published on this issue, shows that cerclage in this clinical situation not only is not beneficial, but may in fact be harmful, i.e., associated with an increase in preterm births.

#### *\*Recommendation Withdrawn*

*This statement is being withdrawn based on recently published data that provides equipoise on the use of cerclage in patients with twin gestations and short cervix. The first study was a retrospective cohort of twin pregnancies with a cervix <2.5cm or cervix dilated > 1cm that demonstrated a decrease in the rate of spontaneous preterm birth <32 weeks of gestation with cerclage compared to those managed expectantly, especially in patients with cervical dilation. In a multicenter open-label randomized controlled trial, twin gestation with asymptomatic cervical dilation (defined as <5cm) between 16 and 23 6/7 of weeks gestation who received a physical exam indicated cerclage was observed to have a 50% decrease in preterm birth at <28 weeks of gestation and 78% reduction in perinatal mortality. These recent data are not an indication to recommend this intervention, however, is sufficient to remove any recommendation against it.*

3

### Don't make irreversible decisions based on the results of cell-free DNA screening test.

False positive and false negative results occur with cell-free DNA screening. Any positive cell-free DNA screening result should be confirmed with invasive diagnostic testing prior to a termination of pregnancy. If cell-free DNA screening is performed, adequate pretest counseling must be provided to explain the benefits and limitations.

4

### Don't screen for fetal growth restriction (FGR) with Doppler blood flow studies.

Studies that have attempted to screen pregnancies for the subsequent occurrence of FGR have produced inconsistent results. Furthermore, no standards have been established for the optimal definition of an abnormal test, best gestational age for the performance of the test or the technique for its performance. However, once the diagnosis of FGR is suspected, the use of antenatal fetal surveillance, including umbilical artery Doppler flow studies, is beneficial.

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### Don't use progestogens for preterm birth prevention in uncomplicated multifetal gestations.

The use of progestogens has not been shown to reduce the incidence of preterm birth in women with uncomplicated multifetal gestations.

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### Don't perform routine cervical length screening for preterm birth risk assessment in asymptomatic women before 16 weeks of gestation or beyond 24 weeks of gestation.

The predictive ability of cervical length measurement prior to 16 weeks of gestation for preterm birth risk assessment is limited. It should be performed, when indicated, between 16 and 24 weeks of gestation. Routine cervical length screening for preterm birth risk assessment in asymptomatic women beyond 24 weeks of gestation has not been proven to be effective.

7

### Don't perform antenatal testing on women with the diagnosis of gestational diabetes who are well controlled by diet alone and without other indications for testing.

Monitoring of glucose levels and maintaining adequate glycemic control for gestational diabetes are paramount to decreasing adverse outcomes, including stillbirth. If nutritional modification and glucose monitoring alone control maternal glycemic status such that pharmacological therapy is not required, the risk of stillbirth due to uteroplacental insufficiency is not increased. Thus, the use of routine antepartum testing (e.g. biophysical profile (BPP) or nonstress test (NST)) in the absence of other co-morbidities is not indicated.

8

### Don't place women, even those at high-risk, on activity restriction to prevent preterm birth.

There are no studies documenting an improvement in outcomes in women at risk for preterm birth who are placed on activity restriction, including bed rest. There are multiple studies documenting untoward effects of routine activity restriction on the mother and family, including negative psychosocial effects. Therefore, activity restriction should not be routinely prescribed as a treatment to reduce preterm birth.

9

### Don't order serum aneuploidy screening after cfDNA aneuploidy screening has already been performed.

Serum biochemistry and cell free DNA (cfDNA) are both screening tests for fetal aneuploidy. When low-risk results have been reported on either test, there is limited clinical value of also performing the other screen. While serum screening may identify some aneuploidies not detected by cfDNA, the yield is too low to justify this test if cfDNA screening has already been performed.

10

### Don't perform maternal serologic studies for cytomegalovirus and toxoplasma as part of routine prenatal laboratory studies.

Routine serologic screening of pregnant women for CMV and toxoplasmosis is not recommended due to poor predictive value of these tests and potential for harm due to false positive results. Serologic screening during pregnancy for both diseases should be reserved for situations in which there is clinical or ultrasound suspicion of maternal or fetal infection.

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### Don't recommend diagnostic testing following sonographic identification of an isolated echogenic intracardiac focus (EIF) or choroid plexus cyst (CPC) in women with low-risk aneuploidy screening results.

The concept of using ultrasonographic soft markers for aneuploidy, such as EIF and CPC, was introduced in an era that predated screening for Down syndrome based on factors other than maternal age. Because the sensitivity of cell free (cfDNA) screening for Down syndrome approaches 99%, the residual risk for Down syndrome is very low in patients who have a negative cfDNA screening test result. Given the low a priori risk, the presence of an isolated EIF or CPC is unlikely to increase the detection rate for aneuploidy to any measurable degree. In addition, for a woman with an isolated EIF or CPC on a second-trimester ultrasound in the setting of any negative first- or second-trimester aneuploidy screening test result, a reasonable approach is to consider the presence of the isolated finding as a normal variant. Recent guidelines from the Society for Maternal-Fetal Medicine state that diagnostic testing should not be recommended to patients solely for the indication of an isolated EIF or CPC in the setting of a negative cfDNA screening test result or a negative first- or second-trimester screening test result.

12

### Don't perform serial cervical length measurement following cerclage placement.

Although progressive cervical shortening after cerclage placement increases the risk of preterm birth, neither overall cervical length nor the length below the stitch correlates well with outcomes. Most importantly, there are currently no additional treatment options for a short cervix after cerclage (e.g., reinforcement suture does not improve outcomes). Although there may be theoretical psychological benefits to the patient and provider to visualize the stitch, there are insufficient data to suggest a clinical benefit of routine post-cerclage serial cervical length measurement.

13

### Don't test women for MTHFR mutations.

MTHFR is responsible for the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate. Genetic variant C677T and A1286C have been associated with a mild decrease in enzymatic activity, which in the setting of reduced folate levels has been found to be a risk factor for hyperhomocysteinemia. Although hyperhomocysteinemia is a risk factor for cardiovascular disease and venous thrombosis, its cause is multifactorial and independent of the MTHFR genotype, even in homozygotic individuals. Despite earlier (mostly case control) studies that found an association between the MTHFR genotype and adverse outcomes, recent studies of more robust design have not replicated these findings. Due to the lack of evidence associating genotype independently with thrombosis, recurrent pregnancy loss, or other adverse pregnancy outcomes, MTHFR genotyping should not be ordered as part of a workup for thrombophilia.

14

### Don't screen asymptomatic pregnant women for subclinical hypothyroidism.

Subclinical hypothyroidism (SCH) is defined as an elevated serum TSH level in the presence of a normal free T4 level and is found in 2% to 5% of otherwise healthy pregnant women. SCH is unlikely to progress to overt hypothyroidism during pregnancy. While some authorities and organizations have recommended routine screening for all pregnant women and subsequent treatment with levothyroxine, two recent, large (>100,000 women) prospective randomized clinical trials of screening and treatment for SCH demonstrated no effect of treatment on offspring IQ at age 5 years. Because treatment for SCH has not resulted in a beneficial effect on outcomes, routine screening for SCH is not currently recommended. Targeted screening for women at risk for overt hypothyroidism is still appropriate.

15

### Don't use amniotic fluid index to make a diagnosis of oligohydramnios (in the third trimester).

Amniotic fluid volume can be measured using either the amniotic fluid index (AFI) or the deepest vertical pocket (DVP). Diagnosis of oligohydramnios based on an AFI of <5 cm has been found to lead to a greater number of obstetric interventions without a significant benefit in improving perinatal outcomes when compared to use of a DVP of <2 cm for diagnosis.

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### Don't perform routine cell-free DNA screening for microdeletions.

Cell-free DNA screening for the common aneuploidies is associated with a high detection rate and low false-positive rate. This screening test is also now offered for a small number of microdeletion syndromes. Most of these microdeletions are extremely rare. Given the very low prevalence of these conditions, most positive test results will be false positives, and the positive predictive value of the test is very low. Moreover, data are lacking for the performance of microdeletion screening, which can add substantially to the costs of this test.

17

### Don't perform routine midtrimester serum biomarker risk stratification for preterm birth or preeclampsia in asymptomatic patients.

Routine midtrimester biomarker risk stratification for preterm birth (e.g., various cytokines) and preeclampsia (e.g., placental growth factor (PIGF), soluble FMS-like tyrosine kinase-1 (sFlt-1)) in asymptomatic pregnant women is not recommended due to its limited utility and poor predictive value, respectively. Importantly, employing interventions (eg, low-dose aspirin) based on screening results have not been shown to improve maternal or fetal outcomes. Furthermore, there is the potential to expose many women to unnecessary prophylactic intervention(s).

18

### Don't recommend delivery in a nondiabetic patient for suspected macrosomia before 39 0/7 weeks of gestation.

Recommendations regarding the optimal timing of delivery seek to balance maternal and perinatal risks. Delivery before 39 0/7 weeks of gestation without medical indication has been associated with increased adverse perinatal outcomes compared with those at or beyond 39 weeks of gestation. For suspected macrosomia, the accuracy of estimated fetal weight using sonographic and clinical estimates is inherently imprecise. In addition, the data comparing delivery to expectant management for suspected macrosomia are inconsistent with regard to reducing the risk of shoulder dystocia, especially when weighed against the harms of early delivery. Given the imprecision in fetal weight assessment, the increase in adverse perinatal outcomes, and the limited data demonstrating benefit, delivery before 39 weeks of gestation is not recommended for suspected macrosomia in nondiabetic patients.

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### Don't routinely exclude women with two prior low transverse cesarean deliveries from having the choice to undertake a trial of labor after cesarean.

Although in some studies, women with two prior cesarean deliveries who attempt a trial of labor after cesarean have a higher rate of complications than women with one prior cesarean delivery, the absolute risk of any major complication remains low and the chance of achieving a vaginal birth are similar to those who have one prior cesarean. Given the risk of maternal morbidity and placenta accreta spectrum associated with multiple repeat cesarean deliveries, a trial of labor should remain an option for women with two prior low transverse cesarean deliveries.

20

### Don't perform 3rd trimester Group B streptococcus (GBS) culture in patients with GBS bacteriuria during pregnancy.

Group B streptococcus (GBS) bacteriuria at levels of  $10^5$  CFU/mL or greater, either symptomatic or asymptomatic, warrants acute treatment during pregnancy and indicates the need for intrapartum antibiotic prophylaxis at the time of birth, and thus no additional rectovaginal culture later in pregnancy is necessary. Identification of asymptomatic bacteriuria with GBS during pregnancy at a level less than  $10^5$  CFU/mL does not require maternal treatment during the antepartum period but is an indication for intrapartum prophylaxis at the time of birth.

# How This List Was Created

As a national medical specialty society, the Society for Maternal-Fetal Medicine relies on the input of any number of its committees in the development of various documents. In the case of the items included in this list, the Publications Committee reviewed the literature and evidence from SMFM's published documents for possible topics. For SMFM's first set of five recommendations a sub-group of the Committee initially developed a list of 10 items that the Committee then ranked for the top five with input and suggestions by the Society's Executive Committee. For SMFM's second set of recommendations, the sub-group of the Committee developed a list of 12 items that the Committee then ranked for the top five, again soliciting input and suggestions by the Society's Executive Committee. For SMFM's third set of five recommendations, the sub-group of the Publications Committee developed a list of 10 items that the Committee ranked for the top five, again soliciting input and suggestions by the Society's Executive Committee. For SMFM's fourth set of five recommendations, the sub-group of the Publications Committee developed a list of 7 items that the Committee ranked for the top five, again soliciting input and suggestions by the Society's Executive Committee. The final lists have been reviewed and approved by the Society's Document Review Committee and Executive Committee.

SMFM's disclosure and conflict of interest policy can be found at [www.smfm.org](http://www.smfm.org).

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The Society for Maternal-Fetal Medicine (SMFM) is a society of physicians and scientists who are dedicated to the optimization of pregnancy and perinatal outcomes. SMFM was established in 1977 and is the membership organization for obstetricians/gynecologists who have additional formal education and training in maternal-fetal medicine. There are currently about 2,000 active members of SMFM. The Society hosts an annual scientific meeting in which new ideas and research in the area of maternal-fetal medicine are presented. The Society is also an advocate for improving public policy and expanding research funding and opportunities in the area of maternal-fetal medicine.

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