What's new in obstetrics and gynecology

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The following represent additions to UpToDate from the past six months that were considered by the editors and authors to be of particular interest. The most recent What's New entries are at the top of each subsection.

PRENATAL OBSTETRICS

Pessary placement for short cervical length does not reduce preterm birth (July 2023)

Previous meta-analyses of randomized trials comparing use of a cervical pessary versus no pessary (with or without vaginal progesterone) for asymptomatic patients at high risk for preterm birth (PTB) have found that a pessary did not result in a statistically significant reduction in spontaneous PTB; however, the trials had many limitations. In a recent well-designed randomized trial of over 500 patients with cervical length <20 mm, placement of an Arabin pessary at 16 to 23 weeks of gestation also demonstrated no benefit over usual care; the rate of PTB or fetal death <37 weeks was nearly the same for both groups [1]. Strengths of this trial were inclusion of a very high-risk population, exclusion of patients with a history of PTB, and routine use of vaginal progesterone in both groups. These findings further support our practice of not using a pessary to reduce PTB in patients with a short cervix. (See "Cervical insufficiency", section on 'Pessary'.)

Impact of warning signs about cannabis use (June 2023)

The rising prevalence of cannabis use has raised questions regarding best methods of public education about potential risks of use during pregnancy. In a study that surveyed pregnant and recently pregnant women residing in states with legal recreational cannabis, point-of-sale

warning signs about risks of cannabis use in pregnancy were not associated with reduced pregnancy use [2]. Although 42 percent of pregnant users agreed that warning signs give important information, 32 percent thought they scare people too much, only 30 percent trusted the information in the signs, and only 26 percent believed signs stop people from using cannabis during pregnancy. This study highlights the need for obstetric providers to provide education about potential risks of cannabis use during pregnancy. (See "Substance use during pregnancy: Overview of selected drugs", section on 'Perceived lack of risk'.)

Early pregnancy diagnosis of gestational diabetes (June 2023)

The benefit of treating gestational diabetes (table 1) diagnosed before 20 weeks of gestation has not been established. In a trial comparing immediate treatment of such patients versus retesting at 24 to 28 weeks and starting treatment at that time if diagnostic criteria are met, immediate treatment did not reduce rates of large-for-gestational age infants or pregnancy-related hypertension [3]. These findings have prompted stakeholders to review their early pregnancy diabetes screening protocols. Treatment of overt diabetes (table 2) diagnosed in early pregnancy is still recommended. (See "Gestational diabetes mellitus: Screening, diagnosis, and prevention", section on 'Management of patients after an early pregnancy GTT'.)

Anticoagulation does not prevent recurrent pregnancy loss in patients with inherited thrombophilia (June 2023)

Increasing data support the lack of benefit of anticoagulation for improving live birth rates among patients with an inherited thrombophilia who have experienced recurrent pregnancy loss. In one of the largest randomized trials, which included 326 such patients, treatment with low molecular weight heparin (LMWH) throughout pregnancy did not improve live birth, miscarriage, preterm birth, or small for gestational age birth rates compared with standard care [4]. In pregnant patients with an inherited thrombophilia, we use LMWH to prevent venous thromboembolism, as described in the tables (table 3A-B). (See "Inherited thrombophilias in pregnancy", section on 'Anticoagulation'.)

Disease relapse among pregnant SLE patients (June 2023)

Patients with systemic lupus erythematosus (SLE) are known to have a higher risk of relapse during pregnancy. In a multivariate analysis of pregnancies in patients with SLE, patients with a low C4 prior to conception had an increased risk of relapse during pregnancy [5]. Moreover, patients who experienced flare during pregnancy were more likely to have a low C4 during each trimester compared with patients who did not flare. Pregnant SLE patients with a low C4 may benefit from closer disease monitoring throughout pregnancy. (See "Pregnancy in women with systemic lupus erythematosus", section on 'Exacerbation of SLE'.)

New guidelines on pregnancy/postpartum mental health screening (May 2023)

Updated guidelines from the American College of Obstetricians and Gynecologists now suggest screening patients for depression and anxiety at the initial prenatal visit, later in pregnancy, and at postpartum visits using a standardized, validated tool [6]. Updated guidelines on treatment and management of mental health conditions include screening for bipolar disorder before initiating pharmacotherapy for anxiety or depression, if not previously done [7]. Perinatal Psychiatry Access Programs are a useful resource for obstetric providers managing these patients. (See "Prenatal care: Initial assessment", section on 'History' and "Overview of the postpartum period: Normal physiology and routine maternal care", section on 'Screening'.)

Obstetric outcomes of transgender men (May 2023)

Transgender men are capable of pregnancy, but their obstetric outcomes have not been well studied. A United States database study comparing birth outcomes of nearly 2000 transgender men with 2.7 million cisgender people reported similar rates of severe morbidity and preterm birth for both groups [8]. Transgender men experienced lower rates of cesarean birth despite an overall increased prevalence of chronic medical conditions, anxiety, and depression. While study limitations included potential gender misclassification and a low frequency of severe morbidity, we discuss these reassuring findings with transgender men desiring or experiencing pregnancy. (See "Sexual and gender minority women (lesbian, gay, bisexual, transgender, plus): Medical and reproductive care", section on 'Transgender individuals'.)

Cerclage placement at 24 to 27 weeks of gestation (May 2023)

Cerclage placement at 24 to 28 weeks of gestation is controversial because of concerns that efficacy has not been proven and procedure-related complications may lead to an extremely preterm birth (PTB). In a meta-analysis of individual patient-level data from four randomized trials of cerclage versus no cerclage in 131 singleton pregnancies at 24+0/7 to 26+6/7 weeks of gestation, cerclage did not result in statistically significant reductions in PTB <37, 34, 32, or 28 weeks nor improvement in any neonatal outcome [9]. PTB <37 weeks was not reduced even in subgroups with cervical length ≤15 mm or ≤10 mm. However, confidence intervals were wide, and modest benefits or harms cannot be excluded. In the absence of reassuring data of efficacy and safety, we do not perform cerclage at ≥24 weeks of gestation. (See "Transvaginal cervical cerclage", section on 'Upper and lower gestational age thresholds for cerclage placement'.)

Biomarker test approved for predicting preeclampsia progression (May 2023)

In stable patients with a hypertensive disorder of pregnancy, it is difficult to predict when severe features of preeclampsia (sFP) will develop. Assessment of the antiangiogenic factor,

soluble fms-like tyrosine kinase 1 (sFlt-1), and the proangiogenic factor, placental growth factor (PlGF), in maternal blood may be useful. In the PRAECIS study of hospitalized patients with a hypertensive disorder of pregnancy between 23+0 and 34+6 weeks of gestation, those with sFlt-1:PlGF below the threshold had <5 percent chance of developing sFP within two weeks, while those above the threshold had a 65 percent chance of developing sFP [10]. Based on these findings, in May 2023, the US Food and Drug Administration approved use of the sFlt-1:PlGF test for pregnant patients hospitalized for a hypertensive disorder of pregnancy [11]. Clinicians may find use of this test along with other laboratory tests and clinical assessments helpful for managing these patients. (See "Preeclampsia: Antepartum management and timing of delivery", section on 'Inpatient versus outpatient care'.)

Caffeine consumption and congenital anomalies (May 2023)

The safety of caffeine consumption during pregnancy is an ongoing concern. An update of the 1997-2011 US National Birth Defects Study compared children born with versus without congenital anomalies stratified by maternal self-reported pre- and early pregnancy caffeine intake and found associations with 10 congenital anomalies [12]. However, causality is unlikely given the lack of dose-response relationships, small effect size (odds ratios 1.2 to 1.7), residual confounding, retrospective subjective ascertainment of caffeine consumption, likelihood of chance due to the large number of estimates, and other study limitations. We continue to suggest that individuals who are attempting to conceive or pregnant limit caffeine consumption to less than 200 to 300 mg per day until more conclusive data are available. (See "Caffeine: Effects on reproductive outcomes in females", section on 'Congenital anomalies'.)

Interruption of endocrine therapy for an attempt at pregnancy after breast cancer (May 2023)

There are few data informing the risks of interrupting adjuvant endocrine therapy for breast cancer survivors desiring pregnancy. In a study in 516 patients with early breast cancer who had received adjuvant endocrine therapy for 18 to 30 months and desired pregnancy, endocrine therapy was interrupted upon enrollment, and pregnancy occurred in 74 percent [13]. The three-year rate of breast cancer events was 8.9 percent, which was similar to the rate in an external control group who met study entry criteria aside from desire for pregnancy and treatment interruption (9.2 percent). These data suggest that endocrine therapy interruption for pregnancy does not increase short-term risks of breast cancer recurrence, but longer-term data are required. We typically advise women to wait for at least two years before attempting pregnancy to ensure that the patient does not have early cancer recurrence prior to a pregnancy attempt. (See "Approach to the patient following treatment for breast cancer", section on 'Fertility and pregnancy after breast cancer'.)

Vitamin B12 supplementation does not reduce preterm birth (April 2023)

Cohort studies have reported that lower maternal vitamin B12 levels (particularly gross deficiency) are associated with a higher risk of preterm birth, suggesting that supplementation may improve pregnancy outcome. However, in a placebo-controlled randomized trial of vitamin B12 supplementation during pregnancy conducted in Nepal in which most participants were at least marginally vitamin B12 deficient, supplementation did not improve gestational age at birth or birth weight [14]. For individuals with vitamin B12 deficiency, which is uncommon in the United States, vitamin B12 supplementation is indicated for maternal health. It is administered parenterally if malabsorption is the cause and orally to those with normal absorption. (See "Nutrition in pregnancy: Dietary requirements and supplements", section on 'Vitamin B12'.)

Respiratory syncytial virus vaccination in pregnancy (April 2023)

Respiratory syncytial virus (RSV) is a major cause of morbidity and mortality in infants; however, no RSV vaccines are approved for use in pregnancy in the United States. In a phase 3 placebo-controlled randomized trial including almost 7000 pregnant people between 24 and 36 weeks of gestation, a single intramuscular injection of RSV prefusion F protein-based vaccine reduced the rate of severe RSV-associated lower respiratory tract illness in infants up to 180 days after birth [15]. The rate of nonsevere RSV-associated illness also trended lower. Rates of preterm birth trended higher in the vaccinated compared with unvaccinated group, but this was not statistically significant. These data suggest effective passive immunity in infants. The US Food and Drug Administration is reviewing an application for approval of this vaccine. (See "Immunizations during pregnancy", section on 'Vaccines under investigation'.)

FDA withdraws approval for Makena (April 2023)

In 2002, the US Food and Drug Administration (FDA) approved use of Makena (generic name hydroxyprogesterone caproate) during pregnancy for prevention of recurrent spontaneous preterm birth (sPTB) based on data from a randomized trial, but required a postmarketing trial for confirmation of benefit. In 2023, additional analysis of data from these two trials and other data led the FDA to withdraw its approval of Makena for preventing recurrent sPTB [16]. Pregnant people currently taking Makena may continue or discontinue treatment; the FDA did not identify any harms for either approach. However, medication supply may be limited. Vaginal progesterone does not appear to be an effective alternative for prevention of recurrent PTB; therefore, no pharmacologic prophylaxis is available for this purpose. (See "Progesterone supplementation to reduce the risk of spontaneous preterm labor and birth", section on 'Singleton pregnancy with prior preterm birth'.)

Malaria prevention regimens and pregnancy outcomes in East Africa (March 2023)

Intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) is important for reducing malaria-associated adverse birth outcomes, but dihydroartemisinin-piperaquine (DP) is a promising alternative in areas with SP resistance. A randomized trial of nearly 4700 pregnant women without human immunodeficiency virus (HIV) infection in East Africa randomly assigned participants to receive IPTp with: SP alone, DP alone, or DP with azithromycin [17]. Compared with SP alone, DP resulted in a 41 percent reduction in clinical malaria but a higher composite rate of adverse pregnancy outcomes (low birth weight, small for gestational age, preterm birth, death: 28 versus 23 percent). Thus, while DP-IPTp may have superior antimalarial effects in areas with SP resistance, SP-IPTp may have other benefits on pregnancy outcomes. Further study of malaria prevention tools in areas with SP resistance is needed. (See "Malaria in pregnancy: Prevention and treatment", section on 'Intermittent preventive treatment in pregnancy (IPTp)'.)

Intrauterine transfusion for alpha thalassemia major (March 2023)

Alpha thalassemia major (ATM; loss of all four alpha globin genes) is usually incompatible with live birth unless intrauterine transfusions (IUT) are performed. In a series of 19 pregnancies with prenatally diagnosed ATM, all 14 fetuses treated with >2 IUT survived to delivery, while the 5 fetuses who did not receive IUT died in utero or shortly after birth [18]. Earlier initiation of IUT correlated with higher neurodevelopmental scores. For patients electing to proceed with fetal therapy, IUT should be initiated as soon as technically possible (18 weeks at most fetal treatment centers). (See "Alpha thalassemia major: Prenatal and postnatal management", section on 'Intrauterine transfusions'.)

Timing of aspirin discontinuation in preeclampsia prophylaxis (March 2023)

The optimal time to discontinue aspirin use for preventing preeclampsia is unclear, and practice varies. In a randomized trial in Spain, patients at high risk of preterm preeclampsia based on a first-trimester screening algorithm began aspirin 150 mg daily before 14 weeks of gestation [19]. Blood angiogenic factors were measured at 24 to 28 weeks, and those at low preeclampsia risk based on these results discontinued aspirin prophylaxis. The rates of preterm and term preeclampsia and most adverse outcomes were not significantly different for the two groups, but the early discontinuation group had less minor antepartum bleeding (7.6 versus 12.3 percent). These findings warrant further study. They are not generalizable to populations such as the United States, where angiogenic factor testing is unavailable, a lower dose of aspirin (81 mg) is commonly used, and the population is more diverse. (See "Preeclampsia: Prevention", section on 'Dose'.)

Romiplostim for ITP during pregnancy (February 2023)

Initial therapies for immune thrombocytopenia (ITP) during pregnancy (glucocorticoids and intravenous immune globulin [IVIG]) are usually effective and considered safe. In contrast, data on thrombopoietin receptor agonists (TPO-RAs) has been lacking. In a new study involving 92 pregnancies with romiplostim exposure, adverse pregnancy outcomes were similar to the general population [20]. In pregnant individuals, we generally reserve TPO-RAs for refractory ITP or for those who cannot take glucocorticoids or IVIG. Individuals who become pregnant while taking a TPO-RA should have an individualized risk assessment. (See "Thrombocytopenia in pregnancy", section on 'ITP therapies'.)

ART selection during pregnancy (February 2023)

The United States Department of Health and Human Services issued new recommendations on the selection and continuation of antiretroviral therapy (ART) during pregnancy [21]. The major practical changes include:

● Atazanavir and raltegravir are no longer preferred ART agents during pregnancy but are reasonable alternative agents if preferred agents cannot be used.

● Patients who become pregnant while on the injectable cabotegravir-rilpivirine regimen can now continue the regimen throughout pregnancy with frequent viral load monitoring (every one to two months).

● For patients who acquire HIV despite using cabotegravir as part of an HIV pre-exposure prophylaxis (PrEP) regimen, ritonavir-boosted darunavir is preferred over dolutegravir for ART initiation during pregnancy.

Our approach is consistent with these recommendations, which take into account a patient's preferences regarding use of ART that have less data on pregnancy and also consider the effect of newer ART agents used in PrEP. (See "Antiretroviral selection and management in pregnant individuals with HIV in resource-rich settings", section on 'Selecting the third drug'.)

Removal of X-waiver requirement to prescribe buprenorphine for opioid use disorder (February 2023)

Previously, in order to prescribe buprenorphine for opioid use disorder (OUD) in the United States, clinicians had to apply for a federally required DATA Waiver (X-Waiver). In January 2023, the Consolidated Appropriations Act of 2023 removed this requirement and allowed clinicians with schedule III authority on their Drug Enforcement Administration (DEA) registration to prescribe buprenorphine for OUD treatment if permitted by applicable state law [22]. We believe this change will encourage buprenorphine prescribing and thus prevent opioid

overdose. (See "Acute opioid intoxication in adults", section on 'Prevention of recurrent opioid overdose'.)

Screening for alcohol use during pregnancy (February 2023)

Although universal screening for alcohol use during pregnancy is advised, evidence suggests that screening and follow-up care remain suboptimal. An analysis of 2017 and 2019 United States Behavioral Risk Factor Surveillance Systems data noted that approximately 20 percent of pregnant patients were not asked about alcohol consumption at their most recent visit and, of those who were asked and reported alcohol use, only 16 percent were advised to stop or reduce their consumption [23]. We advise continued education for both patients and clinicians about the risks of alcohol use during pregnancy and encourage universal screening for pregnant persons. (See "Alcohol intake and pregnancy", section on 'Screening during pregnancy'.)

INTRAPARTUM AND POSTPARTUM OBSTETRICS

Intravenous iron during pregnancy (May 2023)

Oral iron is generally used to treat iron deficiency in pregnancy, especially during the first trimester. However, intravenous (IV) iron may be indicated in some cases and has the advantage of providing the entire dose in a single infusion. In a new open-label trial from Malawi that randomly assigned 862 pregnant individuals at a median gestational age of 22 weeks with hemoglobin <10 g/dL to receive IV or oral iron, the IV iron group had a lower incidence of iron deficiency at all time points and a lower incidence of anemia that reached statistical significance at some time points [24]. IV iron is especially useful for severe anemia and later in pregnancy when rapid repletion is needed. (See "Anemia in pregnancy", section on 'Oral versus IV iron'.)

Multicomponent intervention for postpartum hemorrhage (May 2023)

Postpartum hemorrhage (PPH) is a major cause of maternal morbidity and mortality globally. In a randomized trial comparing a multicomponent intervention for PPH versus usual care in nearly 100,000 vaginal births at secondary-level hospitals across Africa, using a calibrated blood-collection drape and a bundle of first-line treatments (eg, uterine massage, uterotonic medications, tranexamic acid) reduced the composite outcome (blood loss ≥1000 mL, laparotomy for bleeding, maternal death from bleeding) by 60 percent (1.6 versus 4.3 percent) [25]. The efficacy of the intervention likely derived from improved detection of PPH coupled with consistent implementation of the evidence-based treatment bundle. Although the trial was

conducted in low- and middle-income countries, a similar approach has been suggested for high-income countries. (See "Overview of postpartum hemorrhage", section on 'Early recognition, assessment, and intervention'.)

Family well-being after gestational carrier pregnancy (April 2023)

Data on child and family psychological well-being after gestational carrier pregnancy has been limited to studies with short-term follow-up. Now, a longitudinal study that administered standardized interviews and questionnaires to 65 mothers and 20-year-old children conceived with assisted reproductive technology (ART), including 22 with gestational carrier pregnancy, reported similar outcomes in young adult psychological adjustment, maternal well-being (measured by anxiety and depression), and couple relationship quality for the ART and 52 unassisted conception groups [26]. This study provides the longest psychological follow-up data of ART families and shows that their well-being, including those who used a gestational carrier, appears to be at least as good as natural conception families. (See "Gestational carrier pregnancy", section on 'Psychological'.)

Race-based differences in screening for substance use in pregnancy (April 2023)

Substance use disorders are an underdiagnosed problem with significant medical implications during pregnancy. In a study that used logistic regression models including race and history of substance use and adjusting for age and other factors, Black patients with a history of substance use had a higher predicted probability of undergoing urine toxicology testing at delivery than comparable White patients, but White patients had a higher predicted probability of a positive test result [27]. This study highlights the need for universal screening of pregnant people for substance use to avoid differential testing for a problem that is known to impact patients of all ages, races/ethnicities, and socioeconomic demographics. (See "Substance use during pregnancy: Screening and prenatal care", section on 'Concerns for bias'.)

Prophylactic tranexamic acid at cesarean birth (April 2023)

Administration of tranexamic acid to patients having a postpartum hemorrhage reduces mortality due to bleeding, but a benefit from routine prophylactic administration at cesarean is uncertain. In a randomized trial including 11,000 patients undergoing cesarean birth at 31 hospitals, administration of tranexamic acid immediately after umbilical cord clamping slightly reduced rates of "maternal death or transfusion" and "intraoperative blood loss >1 L" compared with placebo, but the reductions were not statistically significant [28]. The tranexamic acid group was less likely to need intervention in response to bleeding complications and had a slightly smaller decrease in hemoglobin levels. One UpToDate author administers prophylactic tranexamic acid before making the skin incision for cesarean, which may be more effective. (See

"Management of the third stage of labor: Prophylactic pharmacotherapy to minimize hemorrhage", section on 'Effectiveness'.)

Hemolytic disease of the fetus and newborn due to anti-M (April 2023)

Hemolytic disease of the fetus and newborn (HDFN) due to maternal alloantibodies against the M antigen (anti-M) is usually mild, but severe HDFN can occur when the alloantibody is a high-titer IgG (or a mixture of IgM and IgG) that is active at 37°C. In a new series of 17 infants with HDFN due to anti-M, fetal or neonatal anemia was severe enough in 14 cases to warrant transfusion, even when maternal antibody titers were higher at 4°C than at 37°C [29]. The risk of low birthweight and premature birth was increased relative to infants with HDFN caused by antibodies against RhD and ABO antigens. This series is a reminder that severe fetal anemia can complicate pregnancies with anti-M. (See "Management of non-RhD red blood cell alloantibodies during pregnancy", section on 'MNS'.)

Preventing postpartum overdose (April 2023)

Overdose is a leading cause of pregnancy-related deaths in the year following delivery. In a population-based study of individuals with Medicaid insurance in the United States (2006 to 2013), those with opioid use disorder (OUD) had a high incidence of opioid overdose death compared with the general obstetric population (118 versus 5 per 100,000 deliveries); their all-cause postpartum death rate was also high (316 versus 51 per 100,000 deliveries) [30]. However, postpartum use of medication for OUD (MOUD) was associated with a 60 percent reduction in the odds of opioid overdose death. We follow patients with OUD closely and continue MOUD postpartum to support retention in treatment of OUD and prevent return to use. (See "Opioid use disorder: Overview of treatment during pregnancy", section on 'Continue MOUD'.)

Ventilatory support of critically ill pregnant patients with COVID-19 (March 2023)

Limited data are available in pregnant females who are critically ill with COVID-19. In a cohort study of 91 such patients, lung mechanics and ventilatory parameters during advanced respiratory support were similar to nonpregnant patients with COVID-19 [31]. Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score was the only risk factor for invasive mechanical ventilation. Fetal delivery was induced in nearly two-thirds of patients and mainly for maternal reasons. Delivery did not improve ventilatory parameters other than the arterial oxygen tension to fraction of inspired oxygen ratio. These findings suggest that the approach to advanced respiratory support for critically ill patients with COVID-19 is similar for pregnant and nonpregnant patients. (See "Critical illness during pregnancy and the peripartum period", section on 'COVID-19'.)

Extending low molecular weight heparin until closer to delivery (March 2023)

Some obstetricians replace low molecular weight (LMW) heparin with unfractionated heparin at 36 to 37 weeks of gestation to improve the patient's chances of receiving neuraxial anesthesia for labor and delivery, if desired. However, an analysis of data from the Highlow trial of LMW heparin prophylaxis in pregnancy found that most patients were eligible for neuraxial anesthesia at the unplanned onset of labor, including 82 percent of patients on low-dose and 61 percent of patients on intermediate-dose LMW heparin [32]. Numbers of eligible patients were higher for planned labor (93 and 81 percent). These results support extended use of LMW heparin prophylaxis to 39 weeks or even until onset of labor in many individuals. (See "Use of anticoagulants during pregnancy and postpartum".)

Prophylactic antibiotics before vaginal birth (February 2023)

Antibiotic prophylaxis to reduce the risk of postpartum maternal infection is standard practice before cesarean birth but not for laboring patients planning to give birth vaginally. However, in a randomized trial among nearly 30,000 patients ≥28 weeks of gestation in early labor planning a vaginal birth in seven low- and middle-income countries (LMIC), a single 2-gram oral dose of azithromycin reduced the composite risk of maternal sepsis or death compared with placebo (1.6 versus 2.4 percent) [33]. Neonatal sepsis and death rates were unchanged. A similar trial in different LMIC reported a reduction in maternal sepsis that was not statistically significant (0.1 versus 0.2 percent) [34]. Based on these findings, we would consider use of azithromycin prophylaxis in LMIC with clinical settings that mirror the first trial's setting, but not in other countries or clinical settings. (See "Labor and delivery: Management of the normal first stage", section on 'Interventions unlikely to be beneficial'.)

Feeding and antiretroviral prophylaxis for infants born to mothers with HIV (February 2023)

The United States Department of Health and Human Services (DHHS) issued updated guidelines on breastfeeding and antiretroviral prophylaxis for infants born to mothers with HIV [21]:

- Patients who are virologically suppressed and have been on ART consistently through at least the third trimester and at delivery can now consider breastfeeding after discussing the risks and benefits with their clinician. The guidelines continue to strongly recommend against breastfeeding for individuals without virologic suppression.
- Formula-fed infants who are at very low risk of HIV acquisition (full-term and born to mothers who maintained viral suppression on at least 10 consecutive weeks of ART during pregnancy and delivery without adherence concerns) can receive only 2 weeks of zidovudine instead of the previously recommended 4 to 6 weeks. For breastfed infants

who are at low risk of HIV acquisition at birth, the guidelines recommend six weeks of zidovudine.

We are in agreement with these recommendations. (See "Intrapartum and postpartum management of pregnant women with HIV and infant prophylaxis in resource-rich settings", section on 'Breastfeeding'.)

OFFICE GYNECOLOGY

Cabergoline after second-trimester pregnancy loss or termination (June 2023)

Breast symptoms (engorgement, tenderness, milk leakage) after second-trimester pregnancy loss or termination are common, but pharmacotherapy to suppress engorgement and lactation is limited. In a randomized placebo-controlled trial of approximately 70 patients with pregnancy loss or termination at 18 to 26 weeks of gestation, cabergoline (1 mg orally within four hours of fetal expulsion/extraction) substantially reduced breast symptoms on days 2 through 14 of follow-up [35]. Side effects were similar between groups, but the trial was not powered to detect small differences. When counseling patients about breast symptoms after second-trimester pregnancy loss or termination, we discuss the option of cabergoline as well as nonpharmacologic measures (eg, ice, compression with a tight sports bra, avoiding breast stimulation). (See "Overview of second-trimester pregnancy termination", section on 'Postprocedure considerations' and "Overview of the postpartum period: Normal physiology and routine maternal care", section on 'Breast engorgement'.)

Prednisone use during in vitro fertilization (May 2023)

Prednisone is often used during in vitro fertilization (IVF) to improve the chances of implantation, and thereby live birth, in patients with a prior unsuccessful embryo transfer. However, a randomized trial comparing oral prednisone with placebo in over 700 patients <38 years of age with two or more unsuccessful embryo transfers reported similar live birth rates in both groups after frozen-thawed embryo transfer [36]. We do not prescribe prednisone during IVF cycles, including for patients with prior unsuccessful embryo transfer. (See "In vitro fertilization: Overview of clinical issues and questions", section on 'No proven effect'.)

Surgical management of incomplete miscarriage (April 2023)

Hysteroscopic resection of retained intrauterine tissue after miscarriage has been proposed as an alternative to vacuum aspiration because it may preserve fertility better. However, a randomized trial comparing the two procedures in 563 patients found similar live birth rates

and median times to conception for both procedures at two years' follow-up [37]. Hysteroscopic resection required additional equipment, took longer, and could not be completed in all cases. We continue to use vacuum aspiration to manage patients with retained products of conception. (See "Pregnancy loss (miscarriage): Counseling and comparison of treatment options and discussion of related care", section on 'Surgical management'.)

Combination medical therapy not superior to methotrexate alone for treating ectopic pregnancy (March 2023)

Ectopic pregnancy is usually treated with surgery or methotrexate (MTX) alone, but use of MTX with another medication (eg, gefitinib, mifepristone) has been described. In a randomized trial comparing a single dose of MTX plus seven days of either gefitinib or placebo in over 300 patients with tubal ectopic pregnancy, both groups had similar rates of surgical intervention, time to pregnancy resolution, subsequent doses of MTX, and serious complications [38]. However, more patients in the gefitinib group experienced diarrhea and rash. In our practice, we do not use combination medical therapy because MTX alone is effective, and combination therapy increases side effects and cost. (See "Ectopic pregnancy: Methotrexate therapy", section on 'Role of combined drug therapy'.)

OTHER GYNECOLOGY

Assisted reproductive technology outcomes in euthyroid women with thyroid peroxidase (TPO) antibodies (March 2023)

A 2022 meta-analysis of observational studies showed higher rates of adverse assisted reproductive technology (ART) outcomes in euthyroid women with, compared to without, thyroid peroxidase (TPO) antibodies, although the findings were limited by the low quality of the evidence [39]. In a subsequent retrospective study of 449 TPO antibody-positive and 2945 antibody-negative Chinese women undergoing in vitro fertilization or intracytoplasmic sperm injection, there was no difference in oocyte retrieval, fertilization, embryo utilization, blastocyst formation, pregnancy rate, or live birth rate between the two groups [40]. Although the new study was larger than most previous studies and attempted to control for numerous potential confounding factors, it was retrospective in design and has similar limitations as previous observational studies. The association between thyroid autoimmunity and adverse ART outcomes remains uncertain. (See "Overview of thyroid disease and pregnancy", section on 'Pregnancy outcomes'.)

REFERENCES

1. Hoffman MK, Clifton RG, Biggio JR, et al. Cervical Pessary for Prevention of Preterm Birth in Individuals With a Short Cervix: The TOPS Randomized Clinical Trial. JAMA 2023; 330:340.
2. Roberts SCM, Zaugg C, Biggs MA. Association of Mandatory Warning Signs for Cannabis Use During Pregnancy With Cannabis Use Beliefs and Behaviors. JAMA Netw Open 2023; 6:e2317138.
3. Simmons D, Immanuel J, Hague WM, et al. Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy. N Engl J Med 2023; 388:2132.
4. Quenby S, Booth K, Hiller L, et al. Heparin for women with recurrent miscarriage and inherited thrombophilia (ALIFE2): an international open-label, randomised controlled trial. Lancet 2023; 402:54.
5. Crisafulli F, Andreoli L, Zucchi D, et al. Variations of C3 and C4 Before and During Pregnancy in Systemic Lupus Erythematosus: Association With Disease Flares and Obstetric Outcomes. J Rheumatol 2023.
6. Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum: ACOG Clinical Practice Guideline No. 4. Obstet Gynecol 2023; 141:1232.
7. Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum. Obstet Gynecol 2023; 141:1262.
8. Stroumsa D, Moniz MH, Crissman H, et al. Pregnancy Outcomes in a US Cohort of Transgender People. JAMA 2023; 329:1879.
9. Gulersen M, Lenchner E, Nicolaides KH, et al. Cervical cerclage for short cervix at 24 to 26 weeks of gestation: systematic review and meta-analysis of randomized controlled trials using individual patient-level data. Am J Obstet Gynecol MFM 2023; 5:100930.
10. Thadhani R, Lemoine E, Rana S, et al. Circulating Angiogenic Factor Levels in Hypertensive Disorders of Pregnancy. NEJM Evid 2022.
11. Thermo Fisher Scientific Announces FDA Clearance of Breakthrough Immunoassays to Aid i n the Risk Assessment of Preeclampsia. Thermo Fisher Scientific. Available at: https://newsr oom.thermofisher.com/newsroom/press-releases/press-release-details/2023/Thermo-Fishe r-Scientific-Announces-FDA-Clearance-of-Breakthrough-Immunoassays-to-Aid-in-the-Risk-A ssessment-of-Preeclampsia/default.aspx (Accessed on May 19, 2023).
12. Williford EM, Howley MM, Fisher SC, et al. Maternal dietary caffeine consumption and risk of birth defects in the National Birth Defects Prevention Study, 1997-2011. Birth Defects Res 2023; 115:921.

13. Partridge AH, Niman SM, Ruggeri M, et al. Interrupting Endocrine Therapy to Attempt Pregnancy after Breast Cancer. N Engl J Med 2023; 388:1645.
14. Hysing M, Strand TA, Chandyo RK, et al. The effect of vitamin B12-supplementation on actigraphy measured sleep pattern; a randomized control trial. Clin Nutr 2022; 41:307.
15. Kampmann B, Madhi SA, Munjal I, et al. Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants. N Engl J Med 2023; 388:1451.
16. Makena (hydroxyprogesterone caproate injection) Information. U.S. Food and Drug Administration (FDA). Available at: https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/makena-hydroxyprogesterone-caproate-injection-information (Accessed on April 06, 2023).
17. Madanitsa M, Barsosio HC, Minja DTR, et al. Effect of monthly intermittent preventive treatment with dihydroartemisinin-piperaquine with and without azithromycin versus monthly sulfadoxine-pyrimethamine on adverse pregnancy outcomes in Africa: a double-blind randomised, partly placebo-controlled trial. Lancet 2023; 401:1020.
18. Schwab ME, Lianoglou BR, Gano D, et al. The impact of in utero transfusions on perinatal outcomes in patients with alpha thalassemia major: the UCSF registry. Blood Adv 2023; 7:269.
19. Mendoza M, Bonacina E, Garcia-Manau P, et al. Aspirin Discontinuation at 24 to 28 Weeks' Gestation in Pregnancies at High Risk of Preterm Preeclampsia: A Randomized Clinical Trial. JAMA 2023; 329:542.
20. Bussel JB, Cooper N, Lawrence T, et al. Romiplostim use in pregnant women with immune thrombocytopenia. Am J Hematol 2023; 98:31.
21. Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States. https://clinicalinfo.hiv.gov/en/guidelines/perinatal/whats-new-guidelines (Accessed on February 08, 2023).
22. Substance Abuse anda Mental Health Services Administration. Removal of DATA Waiver (X-Waiver) Requirement. https://www.samhsa.gov/medications-substance-use-disorders/removal-data-waiver-requirement (Accessed on February 07, 2023).
23. Luong J, Board A, Gosdin L, et al. Alcohol Use, Screening, and Brief Intervention Among Pregnant Persons - 24 U.S. Jurisdictions, 2017 and 2019. MMWR Morb Mortal Wkly Rep 2023; 72:55.
24. Pasricha SR, Mwangi MN, Moya E, et al. Ferric carboxymaltose versus standard-of-care oral iron to treat second-trimester anaemia in Malawian pregnant women: a randomised

controlled trial. Lancet 2023; 401:1595.

25. Gallos I, Devall A, Martin J, et al. Randomized Trial of Early Detection and Treatment of Postpartum Hemorrhage. N Engl J Med 2023; 389:11.
26. Golombok S, Jones C, Hall P, et al. A longitudinal study of families formed through third-party assisted reproduction: Mother-child relationships and child adjustment from infancy to adulthood. Dev Psychol 2023; 59:1059.
27. Jarlenski M, Shroff J, Terplan M, et al. Association of Race With Urine Toxicology Testing Among Pregnant Patients During Labor and Delivery. JAMA Health Forum 2023; 4:e230441.
28. Pacheco LD, Clifton RG, Saade GR, et al. Tranexamic Acid to Prevent Obstetrical Hemorrhage after Cesarean Delivery. N Engl J Med 2023; 388:1365.
29. He Y, Gao W, Li Y, et al. A single-center, retrospective analysis of 17 cases of hemolytic disease of the fetus and newborn caused by anti-M antibodies. Transfusion 2023; 63:494.
30. Suarez EA, Huybrechts KF, Straub L, et al. Postpartum Opioid-Related Mortality in Patients With Public Insurance. Obstet Gynecol 2023; 141:657.
31. Vasquez DN, Giannoni R, Salvatierra A, et al. Ventilatory Parameters in Obstetric Patients With COVID-19 and Impact of Delivery: A Multicenter Prospective Cohort Study. Chest 2023; 163:554.
32. Bistervels IM, Wiegers HMG, Áinle FN, et al. Onset of labor and use of analgesia in women using thromboprophylaxis with 2 doses of low-molecular-weight heparin: insights from the Highlow study. J Thromb Haemost 2023; 21:57.
33. Tita ATN, Carlo WA, McClure EM, et al. Azithromycin to Prevent Sepsis or Death in Women Planning a Vaginal Birth. N Engl J Med 2023; 388:1161.
34. Roca A, Camara B, Bognini JD, et al. Effect of Intrapartum Azithromycin vs Placebo on Neonatal Sepsis and Death: A Randomized Clinical Trial. JAMA 2023; 329:716.
35. Henkel S, Johnson SA, Reeves MF, et al. Cabergoline for Lactation Inhibition After Second-Trimester Abortion or Pregnancy Loss A Randomized Controlled Trial. Obstet Gynecol 2023; 141:1115.
36. Sun Y, Cui L, Lu Y, et al. Prednisone vs Placebo and Live Birth in Patients With Recurrent Implantation Failure Undergoing In Vitro Fertilization: A Randomized Clinical Trial. JAMA 2023; 329:1460.
37. Huchon C, Drioueche H, Koskas M, et al. Operative Hysteroscopy vs Vacuum Aspiration for Incomplete Spontaneous Abortion: A Randomized Clinical Trial. JAMA 2023; 329:1197.
38. Horne AW, Tong S, Moakes CA, et al. Combination of gefitinib and methotrexate to treat tubal ectopic pregnancy (GEM3): a multicentre, randomised, double-blind, placebo-

controlled trial. Lancet 2023; 401:655.

39. Busnelli A, Beltratti C, Cirillo F, et al. Impact of Thyroid Autoimmunity on Assisted Reproductive Technology Outcomes and Ovarian Reserve Markers: An Updated Systematic Review and Meta-Analysis. Thyroid 2022; 32:1010.
40. Rao M, Zeng Z, Zhang Q, et al. Thyroid Autoimmunity Is Not Associated with Embryo Quality or Pregnancy Outcomes in Euthyroid Women Undergoing Assisted Reproductive Technology in China. Thyroid 2023; 33:380.

Topic 8350 Version 12127.0

GRAPHICS

IADPSG and ADA criteria for a positive two-hour 75-gram oral glucose tolerance test for the diagnosis of gestational diabetes

Two-hour 75-gram oral glucose tolerance test thresholds	
Fasting	92 mg/dL (5.1 mmol/L)
OR	
One hour	180 mg/dL (10 mmol/L)
OR	
Two hour	153 mg/dL (8.5 mmol/mol)

The diagnosis of gestational diabetes mellitus is made at 24 to 28 weeks of gestation when ≥1 plasma glucose value is at or above these thresholds.

IADPSG: International Association of the Diabetes and Pregnancy Study Groups; ADA: American Diabetes Association.

Graphic 61208 Version 20.0

American Diabetes Association criteria for the diagnosis of diabetes

1. A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.* **OR**
2. FPG ≥126 mg/dL (7 mmol/L). Fasting is defined as no caloric intake for at least 8 hours.* **OR**
3. 2-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.* **OR**
4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

A1C: glycated hemoglobin; NGSP: National Glycohemoglobin Standardization Program; DCCT: Diabetes Control and Complications Trial; FPG: fasting plasma glucose; OGTT: oral glucose tolerance test.

* In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

Graphic 61853 Version 18.0

Approach to anticoagulation for pregnant individuals with inherited thrombophilia

Clinical setting		Antepartum management	Postpartum management
Lower-risk thrombophilia*	With personal history of previous VTE	Unprovoked VTE or VTE associated with a hormonal risk factor: Anticoagulation (low-dose heparin)	Anticoagulation (low-dose heparin)
		VTE associated with a nonhormonal temporary provoking risk factor and no other risk factors for VTE: No antepartum anticoagulation	Anticoagulation (low-dose heparin)
	No personal history of VTE	Surveillance for VTE without anticoagulation. Anticoagulation may be warranted for individual patients with additional factors that place them at greater risk of thrombosis (eg, prolonged immobility, first-degree relative with unprovoked VTE under age 50 years).	Anticoagulation (low-dose heparin) for patients who have a cesarean birth
Higher-risk thrombophilia¶	With previous VTE and on long-term anticoagulation	Anticoagulation (therapeutic-dose heparin)	Anticoagulation (therapeutic-dose heparin)
	With previous VTE not on long-term anticoagulation	Anticoagulation (intermediate- or therapeutic-dose heparin)	Anticoagulation (intermediate- or therapeutic-dose heparin)
	No personal history of previous VTE and not on chronic anticoagulation	Anticoagulation (low- or intermediate-dose heparin)	Anticoagulation (intermediate-dose heparin)

Low molecular weight heparin is generally preferred to use of unfractionated heparin. Refer to UpToDate content regarding use proximate to labor and birth. Postpartum anticoagulation can generally be started 4 to 6 hours after a vaginal birth or 6 to 12 hours after a cesarean birth, unless

there is significant bleeding or risk for significant bleeding. It is generally continued for six weeks postpartum in patients who did not have a VTE during the pregnancy and who do not have indications for chronic anticoagulation.

VTE: venous thromboembolism; FVL: factor V Leiden; PGM: prothrombin G20210A gene mutation; AT: antithrombin.

* Lower-risk thrombophilias include heterozygosity for FVL or PGM and heritable deficiencies of protein C or protein S.

¶ Higher-risk thrombophilias include AT deficiency, homozygosity for FVL or PGM mutation, double heterozygosity for FVL and PGM, and protein C deficiency in combination with another hereditary defect. Some women with heterozygous deficiencies may be at higher risk based on their personal and family history.

Graphic 95707 Version 12.0

Heparin dosing during pregnancy

Indication	Dose level	Type of heparin	Dosing for specific agents
VTE prevention	Low dose (also called prophylactic dose) May require modifications for extremes of body weight	LMW heparin	Enoxaparin 40 mg SUBQ once daily **or** Dalteparin 5000 units SUBQ once daily
		UFH	5000 units SUBQ every 12 hours
	Intermediate dose*	LMW heparin	Enoxaparin 40 mg SUBQ once daily, increase as pregnancy progresses to 1 mg/kg once daily **or** Dalteparin 5000 units SUBQ once daily, increase as pregnancy progresses to 100 units/kg once daily
		UFH	First trimester: 5000 to 7500 units SUBQ every 12 hours Second trimester: 7500 to 10,000 units SUBQ every 12 hours Third trimester: 10,000 units SUBQ every 12 hours
VTE treatment	Therapeutic dose	LMW heparin	Enoxaparin 1 mg/kg SUBQ every 12 hours **or** Dalteparin 100 units/kg SUBQ every 12 hours
		UFH	Can be given as a continuous IV infusion or SUBQ dose every 12 hours. Titrated to keep the aPTT in the therapeutic range.

This table applies to VTE in pregnant individuals, with the exception of individuals with a prosthetic heart valve, which is discussed separately in UpToDate.

- **Dose level** – Prevention typically uses low or intermediate dose, but therapeutic dose may be used for prevention in selected cases (eg, individuals with recurrent unprovoked thrombotic

events [with or without hereditary thrombophilia or antiphospholipid antibody syndrome] who are receiving long-term anticoagulation with warfarin or a direct oral anticoagulant such as rivaroxaban 20 mg daily or apixaban 5 mg twice daily).

- **Choice of agent** – LMW heparin is recommended for most patients. UFH is used when there may be a need for rapid discontinuation, such as for delivery or perioperatively or in individuals with severely reduced kidney function (eg, CrCl <30 mL/min). Only one heparin product is given at any point in time. Confirm the absence of preservatives (eg, benzyl alcohol) in the heparin product chosen.

Refer to UpToDate for anticoagulation indications, choice of dose level, duration of pharmacologic therapy, and timing of switches between LMW heparin and UFH.

VTE: venous thromboembolism; LMW: low molecular weight; SUBQ: subcutaneously; UFH: unfractionated heparin; IV: intravenous; aPTT: activated partial thromboplastin time; ACCP: American College of Chest Physicians; ACOG: American College of Obstetricians and Gynecologists; CrCl: creatinine clearance.

* Our "intermediate" dose level differs from that used in society guidelines (eg, ACCP, ACOG). Some clinicians prefer to use a different "intermediate" dose level such as enoxaparin 40 mg SUBQ every 12 hours; however, this entails a significant increase in the number of injections over the course of the pregnancy.

Courtesy of Kenneth A Bauer, MD.

Graphic 140440 Version 3.0

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Conflict of interest policy

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