Thrombocytopenia in pregnancy

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INTRODUCTION — Evaluation and management of thrombocytopenia during pregnancy and postpartum may be challenging because there are many potential causes, some directly related to the pregnancy and some unrelated. For many of the causes there are no diagnostic laboratory tests. Management options may have the potential for serious complications for both mother and fetus and may require urgent decisions about delivery, and there may be concerns about fetal thrombocytopenia.

This topic reviews our approaches to determining the cause of thrombocytopenia in a pregnant woman and to management during pregnancy and delivery, which in some cases cannot wait for full diagnostic evaluation.

Additional information on the diagnosis and management of specific conditions that cause thrombocytopenia is presented in more detail separately:

- **Immune thrombocytopenia (ITP)** – (See "Immune thrombocytopenia (ITP) in adults: Clinical manifestations and diagnosis".)
- **Drug-induced thrombocytopenia** – (See "Drug-induced immune thrombocytopenia".)
- **Preeclampsia** – (See "Preeclampsia: Clinical features and diagnosis".)
- **HELLP syndrome** – (See "HELLP syndrome".)
- **Disseminated intravascular coagulation** – (See "Disseminated intravascular coagulation during pregnancy".)
- **Acquired, autoimmune thrombotic thrombocytopenic purpura (TTP)** – (See "Acquired TTP: Clinical manifestations and diagnosis".)
- **Hereditary TTP** – (See "Hereditary thrombotic thrombocytopenic purpura (TTP)".)
- **Complement-mediated thrombotic microangiopathy (C-TMA)** – (See "Complement-mediated hemolytic uremic syndrome".)

DEFINITION AND INCIDENCE — Thrombocytopenia is defined as a platelet count below the lower limit of the normal range (typically, <150,000/microL). In almost all uncomplicated pregnancies, platelet counts remain within the normal range (150,000 to 450,000/microL). Platelet counts may be slightly lower in women with twin compared with singleton pregnancies. Some studies have documented a statistically significant decrease of the platelet count, still within the normal range, as pregnancy progresses, which may reflect physiologic gestational changes [1-3]. (See 'Gestational thrombocytopenia (GT)' below.)

The frequency of maternal thrombocytopenia at delivery is generally considered to be 5 to 7 percent (table 1) [4-6]. When a more stringent platelet count threshold is used (eg, platelet count <100,000/microL), the incidence is <1 percent [7]. Early in pregnancy, the frequency is lower.

LIST OF CAUSES — The causes of thrombocytopenia during pregnancy vary with the duration of gestation, from early in the first trimester through delivery, the severity of thrombocytopenia, and the patient's clinical status [8-10]. In a retrospective series of 199 pregnant women with moderate to severe thrombocytopenia (platelet count <100,000/microL), the main causes were as follows [11]:

- Gestational thrombocytopenia (GT) – 59 percent
- Preeclampsia with severe features/HELLP syndrome – 22 percent (includes patients classified as having the HELLP syndrome [hemolysis, elevated liver function tests, and low platelets])
- Immune thrombocytopenia (ITP) – 11 percent
- Other causes – 8 percent (includes antiphospholipid syndrome, disseminated intravascular coagulation, dilutional thrombocytopenia, myeloproliferative neoplasm)

Selected causes categorized by gestational age and platelet count are listed in the table (table 2). The discussion of causes that follows is organized starting with the most common condition, GT, and ending with less common, non-pregnancy-related disorders.

Gestational thrombocytopenia (GT) — Gestational thrombocytopenia (GT), also called incidental thrombocytopenia of pregnancy, is a benign, self-limited condition that requires no additional evaluation or treatment [12-14]. GT accounts for the vast majority of all thrombocytopenias discovered during pregnancy, and almost all cases of thrombocytopenia in women with uncomplicated pregnancies. GT may occur during the first trimester, but it becomes more common as gestation progresses, with the highest frequency at the time of delivery, when the frequency is 5 to 7 percent (table 1) [6,9,15].

GT typically is characterized by the following [7,16]:

- Most common at delivery, but can occur at any time during pregnancy
- Mild thrombocytopenia (≥80,000/microL, typically 100,000 to 150,000/microL)
- No increased bleeding or bruising
- No associated abnormalities on CBC
- No fetal or neonatal thrombocytopenia

GT is a diagnosis of exclusion. The diagnosis of GT is accepted if the woman has mild thrombocytopenia (platelet count 100,000 to 150,000/microL), especially during late pregnancy and at delivery, with no other associated findings on complete blood count (CBC) or physical examination. In our experience, platelet counts below 80,000/microL are extremely unlikely to be due to GT [17]. GT resolves postpartum, but in some women the return to a normal platelet count requires more than six weeks. A normal prepregnancy platelet count is helpful but not always available. A history of mild thrombocytopenia during a previous pregnancy supports the diagnosis of GT [9].

GT requires no treatment and no change of normal prenatal care and management of delivery. No diagnostic testing is necessary because a platelet count >100,000/microL causes no risk for the mother.

The mechanism(s) of GT has not been documented, but it may be assumed to be a physiologic adaptation of pregnancy, related to the increased plasma volume, pooling or consumption of platelets in the placenta, or other physiologic changes that occur in uncomplicated pregnancies [17].

Immune thrombocytopenia (ITP) — Immune thrombocytopenia (ITP) occurs in approximately 1 to 3 in 10,000 pregnancies; only a subset of these have platelet counts <50,000/microL [18]. This is approximately 10-fold greater than the incidence of ITP in the general population, estimated to be 3 in 100,000 adults [19]. The increased frequency of ITP diagnosed during pregnancy may reflect more frequent CBC testing during pregnancy and the increased incidence of autoimmune disorders in young women, and possibly unmasking of mild ITP due to the increased platelet turnover in pregnancy. (See "Immune thrombocytopenia (ITP) in adults: Clinical manifestations and diagnosis", section on 'Epidemiology'.)

ITP may occur during any trimester. The severity of thrombocytopenia is variable and may change during the pregnancy, although for many patients the platelet count remains stable. For individuals with a prior history of ITP, the platelet count may decline further during pregnancy and improve after delivery [20].

As in non-pregnant individuals, the risk of bleeding is greater with platelet counts <20,000 to 30,000/microL, although there is no absolute platelet count threshold above which bleeding does not occur. This was illustrated in a long-term study involving 119 pregnancies in 92 women over the course of 11 years [21]. Most pregnancies were uneventful, but there was moderate bleeding in 21 patients (18 percent; described as epistaxis or mucous membrane bleeding) and severe bleeding in 4 patients (3 percent; described as hematuria or gastrointestinal). Most deliveries were vaginal, and one-fourth of the infants had thrombocytopenia. (See 'Neonatal testing' below.)

ITP is an autoimmune condition in which antiplatelet autoantibodies interfere with platelet production and cause destruction of circulating platelets. However, tests for antiplatelet antibodies are neither sensitive nor specific. The diagnosis of ITP is based only on the exclusion of other causes of thrombocytopenia. Therefore, in a pregnant woman with mild thrombocytopenia (platelet count 100,000 to 150,000/microL), GT and ITP cannot be distinguished. The diagnosis of GT is much more likely than ITP in such patients because the frequency of GT is 100-fold greater than the frequency of ITP during pregnancy. (See "Immune thrombocytopenia (ITP) in adults: Clinical manifestations and diagnosis".)

Preeclampsia with severe features/HELLP — The terminology for "preeclampsia with severe features" and "HELLP syndrome" (co-occurrence of microangiopathic **h**emolytic anemia, **e**levated **l**iver function tests, and **l**ow **p**latelet count) is complex and evolving.

Both terms ("preeclampsia with severe features" and "HELLP") describe a pregnant woman who is acutely ill with thrombocytopenia and who requires delivery to halt the disease process. There is substantial overlap between these syndromes, but it is possible to have HELLP without hypertension (thus, by definition, the patient does not have preeclampsia) and it is also possible to have preeclampsia with severe features without all of the manifestations of HELLP. Thus, we will use the combined term "preeclampsia with severe features/HELLP" in the following discussion.

- **Preeclampsia** – Preeclampsia is a common complication of pregnancy, occurring in approximately 5 percent of pregnant women. Preeclampsia is manifested by hypertension and proteinuria or new onset hypertension and end-organ dysfunction with or without proteinuria after 20 weeks of gestation (ie, mid-second trimester) in a previously normotensive woman (table 3). (See "Preeclampsia: Clinical features and diagnosis", section on 'Definitions of pregnancy-related hypertensive disorders'.)

  Preeclampsia is associated with thrombocytopenia in approximately 15 percent of cases, and with severe thrombocytopenia (platelet count <50,000/microL) in under 5 percent, with the likelihood of thrombocytopenia correlating with the severity of disease.

  In 1 percent of cases, preeclampsia can be associated with a constellation of findings including more severe hypertension (often with severe headache and/or visual symptoms), liver function abnormalities and epigastric pain, and thrombocytopenia; this condition has been designated as "preeclampsia with severe features" (table 4) [10,22]. A platelet count <100,000/microL is a criterion for preeclampsia with severe features (table 4) [15,22]. Preeclampsia with severe features is also associated with microangiopathic hemolytic anemia with one or more of the following: schistocytes on the blood smear, increased lactate dehydrogenase (LDH), increased bilirubin, and decreased haptoglobin; these features also raise the possibility of thrombotic microangiopathy syndromes such as thrombotic thrombocytopenic purpura. (See 'Thrombotic microangiopathy (TMA)' below.)

  The presence of seizures changes the diagnosis to eclampsia. (See "Eclampsia".)

- **HELLP** – The name HELLP syndrome has been used for decades; this syndrome may not require the presence of hypertension or proteinuria. By definition HELLP syndrome includes thrombocytopenia and evidence of microangiopathic hemolytic anemia. In a review of case series of women with preeclampsia with severe features/HELLP syndrome, the median nadir platelet counts were 43,000 to 57,000/microL. However, among individual women, the lowest platelet counts were 6000 to 15,000/microL [23]. (See "HELLP syndrome".)

Findings of preeclampsia with severe features and/or HELLP syndrome typically become apparent in the latter part of the third trimester and progress until delivery (table 5); however, in some patients, symptoms begin in the latter half of the second trimester, and in other women the signs of preeclampsia may not occur until after delivery.

Preeclampsia with severe features and HELLP syndrome are managed with delivery as soon as possible. It is necessary to gauge the relative likelihood of these conditions that are treated by delivery versus other conditions for which delivery does not result in improvement and other urgent treatments are required, such as sepsis related to a non-obstetric infection, TTP, or complement-mediated TMA. (See 'Management decisions' below.)

DIC — Disseminated intravascular coagulation (DIC) is a systemic process in which coagulation and fibrinolysis become activated within the vasculature, often massively. This can lead to depletion of clotting factors and platelets, with severe bleeding as well as increased risk of thrombosis. There is always an underlying cause that initiates systemic activation of the clotting cascade. Causes of DIC in pregnancy include abruptio placentae, retained dead fetus, amniotic fluid embolism, septic abortion, and others. Patients may have severe hemorrhage and/or diffuse oozing. There may be microangiopathic hemolytic anemia with schistocytes on the blood smear. Typically the prothrombin time (PT) and activated partial thromboplastin time (aPTT) are prolonged; the fibrinogen is low, and the plasma D-dimer is elevated.

Management of DIC involves identifying and treating the underlying cause; in some cases this may require delivery (eg, retained dead fetus, abruption), whereas in others the primary treatment may involve antibiotics (eg, sepsis from a non-obstetric infection) or other therapies (eg, therapy for a malignancy). Transfusions may be needed while bleeding is being controlled. (See "Disseminated intravascular coagulation during pregnancy", section on 'Maternal management'.)

Acute fatty liver of pregnancy — Acute fatty liver of pregnancy (AFLP) is a form of liver injury that typically occurs in the third trimester. The major clinical findings relate to fatty infiltration of the liver and include nausea, vomiting, and abdominal pain. The platelet count may be decreased. If liver function is severely impaired, the PT and aPTT will be prolonged, and the fibrinogen may be low. AFLP is discussed in more detail separately. (See "Acute fatty liver of pregnancy".)

Thrombotic microangiopathy (TMA) — Thrombotic microangiopathies (TMAs) include a number of conditions in which platelet microthrombi form in small vessels and lead to organ damage. There are several primary TMAs including thrombotic thrombocytopenic purpura (TTP), complement-mediated TMA (C-TMA), and Shiga toxin-mediated hemolytic uremic syndrome (ST-HUS). TTP and C-TMA can be hereditary or acquired. (See "Approach to the patient with suspected TTP, HUS, or other thrombotic microangiopathy (TMA)".)

For patients with hereditary TTP, pregnancy confers a great risk for an acute, severe episode of TTP [24]. For patients in remission from acquired, autoimmune TTP, pregnancy may also increase the risk of relapse, but the frequency is low [25]. For patients with C-TMA, pregnancy and the postpartum period are also a risk for triggering an acute episode of severe acute kidney injury [26].

The only defining clinical features of the TMA syndromes are microangiopathic hemolytic anemia (MAHA), which is inferred from the presence of schistocytes on the peripheral blood smear (picture 1), and thrombocytopenia, which can be severe (table 5). Severe acute kidney injury is the most important presenting abnormality in patients with C-TMA. Other findings that may be present include neurologic symptoms ranging from mild headache to seizures and transient focal abnormalities. Although fever has been described as a manifestation of TTP, this was most commonly seen in the pre-plasma exchange era; fever almost always indicates a systemic infection [27].

The TMA syndromes can occur during any trimester, but they are more commonly seen during late pregnancy or postpartum. Persistence or worsening of thrombocytopenia, MAHA, and ongoing end-organ injury for more than three days after delivery is considered by some experts to be strongly suggestive of a TMA, since preeclampsia with severe features almost always begins to recover before this time.

Despite the overlapping clinical presentations, different TMAs have differing pathophysiologies and require different treatments. TMAs are potentially life-threatening, so it is important to make the most accurate diagnosis possible and in many cases to treat presumptively for the most serious of these while pursuing diagnostic testing. (See "Approach to the patient with suspected TTP, HUS, or other thrombotic microangiopathy (TMA)", section on 'Overview of primary TMA syndromes'.)

Many women with TMA during pregnancy deliver healthy term infants. However, intrauterine fetal death may occur from placental infarction caused by thrombosis of the decidual arterioles. These complications are discussed separately. (See "Acquired TTP: Initial treatment", section on 'Acquired TTP during pregnancy' and "Hereditary thrombotic thrombocytopenic purpura (TTP)", section on 'Pregnancy'.)

TTP — Thrombotic thrombocytopenic purpura (TTP) is associated with severely reduced activity of ADAMTS13, a protease that cleaves very large von Willebrand factor (VWF) multimers on endothelial cells. ADAMTS13 may be reduced because of a neutralizing autoantibody (acquired, autoimmune TTP) or an inherited mutation in the *ADAMTS13* gene (hereditary TTP). (See "Acquired TTP: Clinical manifestations and diagnosis" and "Hereditary thrombotic thrombocytopenic purpura (TTP)".)

A significant proportion of patients with hereditary TTP have their first presentation of disease during pregnancy, but acquired TTP is more common than hereditary TTP and thus more likely in a pregnant patient without a family history of TTP. A 2012 series of 42 patients with a first episode of TTP during pregnancy found three-fourths were due to acquired TTP and one-fourth to hereditary TTP [24]. A 2014 series of 35 women from the United Kingdom TTP registry who presented with new onset TTP during pregnancy documented acquired TTP in 12 (34 percent) and hereditary TTP in 23 (66 percent) [28].

Features suggestive of TTP include thrombocytopenia and schistocytes combined with severe neurologic findings (although half of patients with TTP have no or only minor neurologic abnormalities); and absence of features of DIC (eg, absence of coagulation abnormalities). As noted above, TTP can occur during any trimester or postpartum. In a series of 166 pregnancies complicated by TTP, the median onset was at 23 to 24 weeks of gestation, with two-thirds presenting in the first and second trimesters and one-third presenting in the third trimester [29].

The diagnosis of TTP relies on a thorough clinical assessment combined with a finding of ADAMTS13 activity <10 percent. As in non-pregnant patients, the clinical assessment is vital to the diagnosis, because results of ADAMTS13 activity testing often are not immediately available. In contrast to severe ADAMTS13 deficiency, moderately reduced ADAMTS13 activity (eg, activity between 10 and 50 percent) can be seen in many systemic disorders and is not specific for (or indicative of) TTP. ADAMTS13 activity decreases during pregnancy, related to the increased levels of VWF, and may fall below 50 percent in many pregnant women near term (but not below 10 percent, which is typical of TTP) [30]. These issues are discussed in more detail separately. (See "Acquired TTP: Clinical manifestations and diagnosis", section on 'Reduced ADAMTS13 activity' and "Acquired TTP: Clinical manifestations and diagnosis", section on 'Diagnostic testing' and "Pathophysiology of acquired TTP and other primary thrombotic microangiopathies (TMAs)", section on 'TTP pathogenesis'.)

The clinical course of TTP is not affected by delivery, intravenous immune globulin (IVIG), or eculizumab. The most important treatment is urgent plasma exchange (PEX) therapy, which removes the autoantibody to ADAMTS13 and supplies functional ADAMTS13 in the replacement plasma. For patients known to have hereditary TTP, plasma infusion is sufficient for treatment because it supplies ADAMTS13. Platelet transfusion should be reserved for treatment of severe bleeding in a patient with TTP due to the potential increased risk of thrombosis, but platelets should not be withheld in a bleeding patient due to concerns about this risk. (See "Acquired TTP: Initial treatment", section on 'Initiation of PEX for a presumptive diagnosis of TTP' and "Hereditary thrombotic thrombocytopenic purpura (TTP)", section on 'Pregnancy'.)

With appropriate monitoring and therapy, outcomes for pregnancy-associated TTP are usually successful. In a review of cases from the United Kingdom TTP registry, 10 women known to have hereditary TTP who were actively monitored and treated during pregnancy had 15 live births, and six women with acquired TTP had six pregnancies; there were no maternal or fetal deaths, and all deliveries were in the third trimester [28].

Complement-mediated TMA — Complement-mediated TMA (C-TMA), also called complement-mediated HUS or "atypical HUS," is a disorder in which patients have increased activation of complement on endothelial cells. We avoid the term atypical HUS because it is nonspecific. Patients with dysregulated complement can develop microthrombi in small vessels throughout the vasculature; the kidney is often affected. Complement may be dysregulated because of a neutralizing autoantibody or an inherited mutation in a complement regulatory gene such as complement factor H (*CFH*). (See "Acute kidney injury (acute renal failure) in pregnancy" and "Complement-mediated hemolytic uremic syndrome", section on 'Genetic mutations'.)

Many patients with hereditary C-TMA have their first presentation of disease during pregnancy or postpartum. C-TMA presents very similarly to HELLP syndrome and TTP, and the differentiation among C-TMA, HELLP, and TTP can often be challenging. Key diagnostic features include microangiopathic hemolytic anemia, thrombocytopenia, and increasing serum creatinine. ADAMTS13 activity is not severely deficient in C-TMA (activity is ≥10 percent) and stool studies are negative for Shiga toxin-producing organisms. Often, patients with C-TMA are thought to have HELLP syndrome, but instead of improving within one to two days of delivery the patient's clinical status and renal function worsens. Limited data suggest that the platelet count is not severely decreased in C-TMA, and overt neurologic abnormalities are rare. Most patients have severe kidney injury requiring dialysis.

The clinical course of C-TMA is not affected by delivery. In fact, the postpartum period may be the time of greatest risk for the occurrence of C-TMA [26]. The most important treatment is anti-complement therapy to stop the process, and supportive care for renal failure that may include dialysis. Anti-complement therapy (eg, with eculizumab) should be initiated promptly if C-TMA is considered the most likely diagnosis, because end-stage renal disease may occur rapidly if the process goes unchecked. Additional information about anti-complement therapies, including therapies under development, is presented separately. (See "Complement-mediated hemolytic uremic syndrome", section on 'Treatment'.)

Fetal effects of anti-complement therapy in C-TMA have not been well studied. However, experience with the use of eculizumab in paroxysmal nocturnal hemoglobinuria (PNH) does not appear to show evidence of increased fetal risks. (See "Treatment and prognosis of paroxysmal nocturnal hemoglobinuria", section on 'Pregnancy'.)

ST-HUS — Shiga toxin-mediated hemolytic uremic syndrome (ST-HUS) is a disorder in which enteric infection with an organism that produces the toxin (eg, enterohemorrhagic *Escherichia coli*, *Shigella*); the kidneys are commonly affected. The mechanism(s) by which the toxin produces a TMA are incompletely understood. (See "Approach to the patient with suspected TTP, HUS, or other thrombotic microangiopathy (TMA)", section on 'Overview of primary TMA syndromes'.)

Patients with ST-HUS typically have severe abdominal pain and diarrhea, which is typically overtly bloody, as their major symptom. There may be a history of eating improperly prepared food or a recent outbreak, but almost all cases are sporadic. MAHA and thrombocytopenia are present and often accompanied by renal insufficiency. Fever and neurologic symptoms may also be present but are not always seen. These features are similar to those seen in children, in whom ST-HUS is much more common.

The diagnosis of ST-HUS is made based on clinical features, microangiopathic hemolytic anemia, thrombocytopenia, and demonstration of an implicated diarrheal organism. Stool testing for Shiga toxin-secreting bacteria (eg, *E. coli* 0157:H7, *Shigella dysenteriae*) and for Shiga toxin itself should be performed. Most patients will have been tested for and found to have normal or only mildly reduced ADAMTS13 activity and normal or nonspecifically reduced complement levels. Management involves supportive care, similar to children. (See "Treatment and prognosis of Shiga toxin-producing Escherichia coli (STEC) hemolytic uremic syndrome (HUS) in children".)

Causes of thrombocytopenia not triggered by the pregnancy — Some conditions associated with thrombocytopenia are discovered incidentally during the pregnancy. These include systemic lupus erythematosus (SLE), medications that cause immune thrombocytopenia, heparin-induced thrombocytopenia (HIT), cancer, infection, liver disease, hypersplenism, deficiency of vitamin B12/folate/copper, or inherited platelet disorders. Most of these causes of thrombocytopenia are rare during pregnancy, with the exception of SLE, which may be more common than several of the conditions discussed above such as TMAs. These are discussed in separate topic reviews:

- **SLE** – Pregnancy is associated with risk for acute "flares" of SLE. These flares may be associated with thrombocytopenia as well as other cytopenias and/or manifestations of SLE. (See "Hematologic manifestations of systemic lupus erythematosus", section on 'Thrombocytopenia'.)
- **Antiphospholipid syndrome** – Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by arterial and venous thromboembolism and pregnancy morbidity. A small subset of these individuals have catastrophic APS (CAPS), with widespread thrombotic disease. (See "Clinical manifestations of antiphospholipid syndrome", section on 'Catastrophic APS'.)
- **Medications**
  - **Drug-induced ITP** – (See "Drug-induced immune thrombocytopenia", section on 'Commonly implicated drugs'.)
  - **HIT** – (See "Use of anticoagulants during pregnancy and postpartum", section on 'Suspected heparin-induced thrombocytopenia' and "Clinical presentation and diagnosis of heparin-induced thrombocytopenia", section on 'Evaluation'.)
  - **Drug-induced TMA** (eg, from quinine) – (See "Drug-induced thrombotic microangiopathy".)
- **Cancer** – (See "Approach to the adult with unexplained thrombocytopenia", section on 'Causes of thrombocytopenia'.)
- **Infections**
  - **Hepatitis C virus (HCV)** – (See "Extrahepatic manifestations of hepatitis C virus infection".)
  - **Human immunodeficiency virus (HIV)** – (See "Hematologic manifestations of HIV infection: Thrombocytopenia and coagulation abnormalities".)
  - **Other infectious organisms** – (See "Approach to the adult with unexplained thrombocytopenia", section on 'Causes of thrombocytopenia'.)
- **Liver disease** – (See "Hemostatic abnormalities in patients with liver disease", section on 'Thrombocytopenia and platelet dysfunction' and "Acute fatty liver of pregnancy" and "HELLP syndrome".)
- **Deficiency of vitamin B12, copper, or (extremely rarely) folate** – (See "Treatment of vitamin B12 and folate deficiencies" and "Clinical manifestations and diagnosis of vitamin B12 and folate deficiency".)
- **Inherited disorders**
  - **Inherited platelet disorders** – (See "Congenital and acquired disorders of platelet function".)
  - **Type II von Willebrand disease (VWD)** – (See "Clinical presentation and diagnosis of von Willebrand disease".)

DETERMINING THE LIKELY CAUSE(S)

Overview of the evaluation — In many cases, pregnancy imposes additional urgency on determining the cause of thrombocytopenia and additional management decisions related to the potential for complications that may affect the patient and the fetus. The diagnostic evaluation and interventions for the most likely cause(s) of the findings must often be performed simultaneously. Early involvement of experts in high-risk obstetrics, hematology, and other appropriate specialists (eg, nephrology when renal failure is present; infectious diseases when sepsis is suspected) is advised.

Selected causes categorized by trimester and platelet count are shown in the table (table 2) and discussed above. (See 'List of causes' above.)

Our approach to distinguishing among these causes, as described in the following sections, is consistent with a 2013 pocket guide on thrombocytopenia in pregnancy and a practice guideline on immune thrombocytopenia (ITP) from the American Society of Hematology and a 2010 international consensus panel [31-33]. Additional information concerning thrombocytopenic conditions including drug-induced thrombocytopenia, ITP, and thrombotic thrombocytopenic purpura (TTP) can be found on a website maintained and updated by Dr. James N George at the University of Oklahoma Health Sciences Center: www.ouhsc.edu/platelets [34].

As noted above, our approach to the evaluation takes into account the severity of thrombocytopenia, clinical presentation (table 6), and trimester. Helpful information includes the following:

- Course of the pregnancy so far, including presence or absence of complications.
- Symptoms of infection such as fever and chills.
- New daily medications within the past three weeks, or occasional medications taken immediately before symptoms occurred.
- Personal or family history of excessive bleeding, bruising, pregnancy complications, or known thrombotic microangiopathy (TMA) syndrome.
- Systemic lupus erythematosus or other autoimmune disorder.
- History of liver disease.
- Timing of the drop in platelet count (which trimester, how rapidly).
- Presence of anemia more severe than expected for the stage of pregnancy.
- Abnormalities of the peripheral blood smear, such as abnormal white blood cells or nucleated red blood cells.

Isolated, asymptomatic thrombocytopenia; platelets >80,000 — Almost all pregnant women with relatively mild or incidentally discovered thrombocytopenia (eg, platelet count between 80,000 and 150,000/microL) without other cytopenias or major clinical findings will have gestational thrombocytopenia (GT). The only other common cause to consider may be ITP; however, ITP with mild thrombocytopenia requires no treatment and therefore the management is observation, as for GT.

Other, uncommon causes of isolated, mild thrombocytopenia include conditions that may have preceded the pregnancy or developed during the pregnancy but remained clinically silent, such as systemic lupus erythematosus (SLE), inherited thrombocytopenia, bone marrow disorders such as myelodysplasia, human immunodeficiency virus (HIV), liver disease, hypersplenism, nutrient deficiencies (eg, vitamin B12, folate, copper), and type II von Willebrand disease. These conditions account for <1 percent of cases. (See 'Causes of thrombocytopenia not triggered by the pregnancy' above.)

Evaluation for these conditions includes a personal and family history for bleeding disorders; review of the complete blood count (CBC) for other cytopenias and morphologic abnormalities in white blood cells, red blood cells, and platelets.

Pseudothrombocytopenia due to in vitro platelet clumping can be misinterpreted as true thrombocytopenia. Pseudothrombocytopenia should be excluded by reviewing the blood smear and, if necessary, repeating the platelet count using a tube containing citrate or heparin rather than EDTA as the anticoagulant. This and other testing for causes of thrombocytopenia not directly related to pregnancy are discussed separately. (See "Approach to the adult with unexplained thrombocytopenia".)

HIV testing is appropriate for all patients if not done already. Testing early in each pregnancy is routine in the United States. (See "Prenatal care: Initial assessment", section on 'Human immunodeficiency virus' and "Screening and diagnostic testing for HIV infection", section on 'Routine screening'.)

As noted above, it is not possible (or necessary) to distinguish between GT and ITP during pregnancy as long as the thrombocytopenia is relatively mild (eg, platelet count >80,000/microL). Both of these conditions are diagnosed by excluding other causes of thrombocytopenia; there are no laboratory tests for either condition. GT can present at any time during pregnancy, but because CBCs are more likely to be performed later in the pregnancy, GT is more often recognized near term or at delivery. GT resolves after delivery, but it may require more than six weeks. ITP is often present before, during, and after the pregnancy, and the degree of thrombocytopenia is variable. If the platelet count drops below 80,000/microL, then ITP becomes the more likely diagnosis. If the history and/or examination suggest a cause other than GT or ITP, appropriate testing should be obtained. (See 'List of causes' above.)

After delivery, GT will resolve and ITP typically will persist, allowing a presumptive diagnosis to be made in most cases. The value of this is that patients with GT do not require any additional monitoring until or unless they become pregnant again. GT can recur with subsequent pregnancies, so it may be helpful to anticipate this possibility. If thrombocytopenia persists after pregnancy (eg, at the six-week follow-up), then ITP becomes the likely diagnosis. A less common condition such as an inherited platelet disorder may also be responsible. The evaluation, differential diagnosis, and management of ITP are discussed in detail separately. (See "Approach to the adult with unexplained thrombocytopenia" and "Immune thrombocytopenia (ITP) in adults: Clinical manifestations and diagnosis" and "Immune thrombocytopenia (ITP) in adults: Initial treatment and prognosis".)

Monitoring of mild thrombocytopenia, management as delivery nears, and neonatal platelet count testing are discussed below. (See 'Management decisions' below.)

Acutely ill, platelets <80,000, bleeding, thrombosis, or other major findings — The major causes of pregnancy-associated thrombocytopenia that present with acute systemic illness and/or severe thrombocytopenia or bleeding include preeclampsia with severe clinical features, disseminated intravascular coagulation (DIC), and thrombotic microangiopathies (TMAs; eg, thrombotic thrombocytopenic purpura [TTP] or complement-mediated TMA [C-TMA]) (table 5). Other possible diagnoses include conditions not specifically related to the pregnancy such as systemic lupus erythematosus (SLE), sepsis, severe ITP, drug-induced thrombocytopenia (DITP), catastrophic antiphospholipid syndrome (APS) or, rarely, other conditions such as malignancy or severe liver disease.

Preeclampsia with severe clinical features and HELLP syndrome (hemolysis, elevated liver function tests, and low platelets) is significantly more common than DIC, and DIC is significantly more common than the TMAs (approximate incidences, 1 in 100, 1 in 1000, and 1 in 100,000, respectively) [35]. (See "Disseminated intravascular coagulation during pregnancy", section on 'Prevalence'.)

In a patient with SLE, it can be challenging (and may not be possible) to distinguish a flare of SLE from preeclampsia with severe features. This evaluation is presented separately. (See "Pregnancy in women with systemic lupus erythematosus", section on 'Preeclampsia versus lupus nephritis'.)

The evaluation to determine the cause includes review of the CBC to assess for other cytopenias (eg, leukopenia, anemia out of proportion to the stage of pregnancy) and the red blood cell indices; review of the peripheral blood smear to detect schistocytes or abnormal white blood cells, prothrombin time (PT) and activated partial thromboplastin time (aPTT), and fibrinogen level; metabolic panel with renal function and hepatic function tests; urinalysis, lactate dehydrogenase (LDH) and bilirubin to assess hemolysis; and, if the PT, aPTT, and/or fibrinogen level are abnormal, D-dimer. At least one additional platelet count measurement should be obtained in order to identify a declining trend (and its tempo).

Features that help to narrow down to the most likely (or most dangerous) cause in the symptomatic or severely thrombocytopenic patient include the following:

- Isolated thrombocytopenia – Severe ITP, drug-induced ITP
- Fever, chills – Infection, DIC
- Severe hypertension – Preeclampsia with severe clinical features/HELLP, possible TMA
- Hypotension – Bleeding, DIC
- Neurologic findings – Possible central nervous system bleeding, preeclampsia, DIC, TTP
- Bloody diarrhea – ST-HUS, possible TMA
- Hemolytic anemia (drop in hemoglobin, increased LDH and bilirubin) – Preeclampsia with severe clinical features, DIC, TTP
- Schistocytes on the blood smear – TTP, C-TMA, preeclampsia with severe clinical features/HELLP, possibly DIC
- Leukopenia or leukocytosis – Infection, possibly DIC
- Prolonged PT and aPTT, low fibrinogen – DIC, severe liver disease
- Rapidly increasing creatinine – C-TMA, ST-HUS, DIC
- Elevated liver function tests – Preeclampsia with severe clinical features/HELLP, acute fatty liver of pregnancy (AFLP), infection (eg, viral illness)
- Hypoglycemia – AFLP
- Proteinuria – Preeclampsia/HELLP

The most important diagnostic distinctions to make are between conditions that are treated by delivery and those that are not, especially if the patient is not at term (algorithm 1). If a TMA is considered likely, the major decisions are whether to initiate plasma exchange or anti-complement therapies; a TMA will not resolve with

delivery alone.

Early communication between the obstetrician, anesthesiologist, and consulting hematologist is advised when there are questions about the diagnosis or possible need for urgent interventions.

MANAGEMENT DECISIONS

Treatment of bleeding or severe thrombocytopenia — The risk of severe bleeding due to thrombocytopenia only increases substantially with platelet counts below 50,000/microL. For women with platelet counts of 50,000 to 100,000/microL, increased bleeding may occur with invasive procedures, but will not occur spontaneously. For women with platelet counts <50,000 and severe bleeding (bleeding into a closed space, bleeding requiring transfusion, bleeding that will not stop) or bleeding that is expected to become severe, platelet transfusion should be given immediately, regardless of the underlying cause of thrombocytopenia. (See "Clinical and laboratory aspects of platelet transfusion therapy", section on 'Actively bleeding patient'.)

Platelet transfusions are not appropriate for women without active bleeding, unless surgery and/or delivery is imminent.

The platelet count threshold for a non-bleeding pregnant woman nearing delivery or a procedure depends on the expected mode of delivery or type of procedure. In the absence of bleeding, we use the following thresholds:

- **Vaginal delivery** – Transfuse to a platelet count of 30,000/microL
- **Cesarean delivery** – Transfuse to a platelet count of 50,000/microL
- **Neuraxial anesthesia** – (See 'Neuraxial anesthesia' below.)
- **Invasive procedure** – (See "Clinical and laboratory aspects of platelet transfusion therapy", section on 'Preparation for an invasive procedure'.)

The safety of these thresholds is supported by data from a review of 119 pregnancies associated with immune thrombocytopenia (ITP), 17 of 110 women (15 percent) had platelet counts <50,000/microL at delivery [21]. Hemorrhagic complications in these women were uncommon and did not correlate with the platelet count. None of the women with platelet counts <50,000/microL had blood loss greater than one liter; the greatest blood loss was in four women with platelet counts between 54,000 and 321,000/microL. Individuals with other causes of thrombocytopenia that are also associated with platelet dysfunction may require higher platelet counts, and clinical judgement is required to incorporate the cause of thrombocytopenia and the bleeding risk for the specific patient.

If therapy is needed to raise the platelet count in a woman with ITP, glucocorticoids or intravenous immune globulin (IVIG) approximately one week prior to a scheduled delivery. If the platelet count is <20,000 to 30,000/microL at the time of delivery and therapy is needed to raise the platelet count, platelet transfusions should be used. (See 'ITP therapies' below.)

There are no data comparing vaginal delivery versus cesarean delivery for women with ITP, and we reserve cesarean delivery for standard obstetrical considerations [14]. This practice is consistent with guidelines published by the American Society of Hematology, the British Society of Haematology, and an international consensus report [14,31,32]. (See "Cesarean delivery: Preoperative planning and patient preparation", section on 'Indications'.)

Both forceps and vacuum-assisted delivery are relatively contraindicated in the setting of severe maternal thrombocytopenia. However, if operative vaginal delivery is performed, we use forceps rather than vacuum-assisted delivery because the potential harms of vacuum-assisted delivery are greater for the fetus than those with forceps if there is fetal thrombocytopenia. The complications of operative vaginal delivery are described in more detail separately.

We do not attempt to measure the fetal platelet count prior to delivery, and we avoid placing a fetal scalp electrode if the maternal platelet count is <80,000/microL. Measurement of the neonatal platelet count may be appropriate in some cases, as described in the next section. (See 'Neonatal testing' below.)

Of note, the indications for platelet transfusions in patients with TTP or heparin-induced thrombocytopenia (HIT) are the same as for other women with thrombocytopenia; platelet transfusions should be reserved for bleeding that is clinically important or for prevention of bleeding with an invasive procedure or delivery. (See "Clinical and laboratory aspects of platelet transfusion therapy", section on 'TTP or HIT'.)

In conditions in which platelets are being destroyed, the increase in platelet count with transfusion will only be temporary, and additional interventions directed at the underlying disorder are also needed:

- ITP – Glucocorticoids or IVIG. (See 'ITP therapies' below.)
- TTP – Plasma exchange. (See 'Need for plasma exchange or anti-complement therapy' below.)
- C-TMA – Anti-complement therapy. (See 'Need for plasma exchange or anti-complement therapy' below.)
- HIT – Cessation of all heparin exposure and anticoagulation with a non-heparin anticoagulant (eg, fondaparinux). (See 'Anticoagulation for HIT' below.)
- Other drug-induced thrombocytopenias – Cessation of drug exposure. (See "Drug-induced immune thrombocytopenia", section on 'Management'.)

Frequency of platelet count monitoring — The frequency of platelet count monitoring is greater for those with more severe thrombocytopenia, with the specific interval individualized for the patient and altered as needed depending on the platelet count trend.

The following provides a general guide:

- Severely ill patients (eg, those with HELLP) may require platelet count monitoring as often as every four to six hours.
- Daily monitoring is appropriate for most patients who are hospitalized due to maternal illness, although women with gestational thrombocytopenia (GT) and mild, stable thrombocytopenia who are hospitalized for an unrelated illness such as hyperemesis or asthma may not need daily platelet counts. Sometimes the frequency can be decreased depending on the patient's level of stability.
- For those with mild to moderate thrombocytopenia, which is likely due to GT, or less commonly to ITP, we generally monitor the platelet count once per trimester or once per month (depending on the absolute platelet count and platelet count trend), and assess the platelet count at 36 to 37 weeks to plan for a possible need for treatment near delivery.
- Routine obstetrical management is appropriate for women with platelet counts >100,000/microL.

Need for urgent/emergent delivery — The need for delivery depends on the underlying cause, which may not be definitively determined. The most challenging cases are those in which the cause is not entirely clear. In a preterm gestation, as long as mother and fetus appear stable, completing a thorough evaluation before making decisions for delivery is important, as several of the etiologies can be addressed, allowing the pregnancy to safely progress to term. If the mother and/or fetus is unstable, and steps taken for stabilization do not allow a detailed evaluation, then delivery may be the best choice. In such cases, antenatal glucocorticoids should be given prior to delivery if possible (see "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery"). At term, delivery may be warranted to facilitate evaluation of the underlying cause more efficiently.

Conditions treated by delivery — Thrombocytopenic conditions that are treated by delivery include the following, management of which is discussed in detail separately:

- **Preeclampsia with severe features or HELLP syndrome** – (See "Preeclampsia: Management and prognosis" and "HELLP syndrome", section on 'Management'.)
- **Disseminated intravascular coagulation (DIC)** (when due to retained dead fetus or intra-amniotic infection) – (See "Disseminated intravascular coagulation during pregnancy", section on 'Maternal management'.)

Conditions not treated by delivery — Conditions that are not treated by delivery include:

- **Thrombotic thrombocytopenic purpura (TTP)** – (See "Acquired TTP: Initial treatment" and "Hereditary thrombotic thrombocytopenic purpura (TTP)", section on 'Management'.)
- **Complement-mediated thrombotic microangiopathy (C-TMA)** – (See "Complement-mediated hemolytic uremic syndrome", section on 'Treatment'.)
- **Drug-induced thrombocytopenia** – (See "Drug-induced immune thrombocytopenia", section on 'Management' and "Management of heparin-induced thrombocytopenia".)
- **DIC** (when due to a non-obstetric cause such as malignancy or extrauterine infection) – (See "Clinical features, diagnosis, and treatment of disseminated intravascular coagulation in adults", section on 'Treatment'.)

Need for plasma exchange or anti-complement therapy — Plasma exchange therapy (PEX) is urgent initial treatment for TTP, and anti-complement therapy is urgent initial treatment indicated for C-TMA. TTP and C-TMA can usually be distinguished by the degree of kidney injury. Acute kidney injury with an increasing serum creatinine causing anticipation of dialysis is typical of C-TMA and very rarely occurs in patients with TTP.

PEX and monoclonal antibodies to complement components cannot be initiated simultaneously, unless the monoclonal antibody is repeated daily (instead of weekly) following each PEX procedure, because PEX removes the antibody.

Both PEX and anti-complement therapy carry risks of potentially serious adverse effects and are costly. (See "Acquired TTP: Initial treatment", section on 'Acquired TTP during pregnancy' and "Complement-mediated hemolytic uremic syndrome", section on 'Adverse effects'.)

Thus, we reserve PEX and anti-complement therapy for individuals with strong supporting evidence for TTP or C-TMA, respectively [23,36]. This includes the following features (see "Approach to the patient with suspected TTP, HUS, or other thrombotic microangiopathy (TMA)", section on 'Initial evaluation (all patients)'):

- Thrombocytopenia and microangiopathic hemolytic anemia (MAHA).
- Lack of evidence of an alternative cause of thrombocytopenia and MAHA.
  - No obvious malignancy by physical examination.
  - No obvious DIC by coagulation testing.
  - No obvious drug-induced cause by history.
  - No obvious acute liver disease or autoimmune disease by examination and laboratory testing.
  - No previous hypotension as a cause of acute tubular necrosis and acute kidney injury.

MAHA and thrombocytopenia are characteristic features of preeclampsia with severe features, which typically resolves within three days following delivery. Persistence of MAHA and thrombocytopenia for more than three days postpartum is also consistent with TTP or C-TMA, but delivery should not be performed solely to establish this finding and therapy should not be delayed until after delivery if one of these TMAs is strongly suspected.

Decisions regarding the likelihood of TTP and C-TMA may be complex and may require the involvement of multiple specialists. We advise early involvement of the consulting hematologist, nephrologist (if appropriate), and laboratory personnel, as well as the anesthesiologist should these therapies be ineffective and emergent delivery required. These considerations are discussed separately. (See "Approach to the patient with suspected TTP, HUS, or other thrombotic microangiopathy (TMA)", section on 'Key distinguishing features among the primary TMA syndromes' and "Complement-mediated hemolytic uremic syndrome", section on 'Clinical manifestations'.)

Need for other medications

ITP therapies — The management of ITP during pregnancy is generally the same as ITP in a non-pregnant patient, in that the goal of therapy is to reduce the risk of bleeding, not to normalize the platelet count. In individuals who are not bleeding, therapy to raise the platelet count typically is indicated only if the platelet count is below 20,000 to 30,000/microL or if the patient requires a higher count for an invasive procedure. Therapy may also be appropriate at a higher platelet count if the patient has a history of bleeding at a higher count, or if there are other factors that increase the risk of bleeding [16,31,32]. In contrast, some patients with ITP who have persistent platelet counts less than 30,000/microL may not require treatment during pregnancy if they were not receiving it prior to conception, except in preparation for delivery.

Decisions about the need for ITP therapy during pregnancy should be based on maternal indications, as there is no evidence that administration of ITP therapies to the mother increases the fetal platelet count or improves neonatal outcomes. This lack of effect on fetal/neonatal platelet counts is illustrated by the following:

- A 2012 Cochrane review identified only a single trial from 1990 that evaluated neonatal platelet counts in pregnancies associated with maternal ITP in which the mothers were randomly assigned to receive or not receive ITP therapy [37]. This trial initially included 41 pregnancies in 38 women randomly assigned to receive betamethasone 1.5 mg daily for two weeks, but only 28 were evaluable [38]. Of these, there were no significant differences in the frequency of neonatal thrombocytopenia in the betamethasone-treated mothers versus controls (seven and six infants; 64 versus 57 percent) or in the frequency of neonatal bleeding (three and two infants; 21 versus 14 percent). All of the bleeding was mild (eg, cephalohematoma associated with forceps use).
- In a retrospective review of 98 pregnancies in which therapy was administered for ITP, approximately half were treated with glucocorticoids and half with intravenous immune globulin (IVIG) [39]. Outcomes were similar with both therapies, including maternal platelet count increases (seen in approximately 40 percent in both groups) and bleeding risks, neonatal platelet counts or bleeding, and method of delivery. There were no maternal deaths or critical maternal bleeding.

When therapy is indicated, we usually use a glucocorticoid as initial therapy. High-dose dexamethasone (typical dose, 40 mg per day for four days) and prednisone (typical dose, 1 mg/kg per day for two weeks followed by a gradual taper) are both effective; dexamethasone may have fewer adverse effects. (See "Immune thrombocytopenia (ITP) in adults: Initial treatment and prognosis", section on 'Glucocorticoids'.)

The choice of glucocorticoid in pregnancy thus depends on whether the goal is to minimize fetal exposure or to treat both the mother and the fetus:

- When delivery is not imminent (eg, during early pregnancy and/or when preterm birth is not expected), prednisone is preferable because there is less fetal exposure [40]. (See "Safety of antiinflammatory and immunosuppressive drugs in rheumatic diseases during pregnancy and lactation", section on 'Glucocorticoids'.)

- If the patient is a candidate for therapy to improve neonatal outcomes related to preterm birth, then dexamethasone or betamethasone given antenatally can serve to treat both preterm birth and ITP. (See "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery".)

IVIG may also be appropriate, either in addition to or instead of a glucocorticoid, especially if there is a need to raise the platelet count more rapidly. If therapy is needed to raise the platelet count prior to delivery or neuraxial anesthesia, it should be initiated approximately one week in advance if possible, to allow time for maximal efficacy and platelet count retesting. The increase in platelet count with IVIG is usually temporary.

Typical times for these therapies to take effect are as follows [32,41]:

- IVIG – 1 to 3 days for initial response, 2 to 7 days to peak response.

- Dexamethasone – 2 to 14 days for initial response, 4 to 28 days to peak response.

- Prednisone – 4 to 14 days for initial response, 7 to 28 days to peak response.

Additional information about the administration and dosing of glucocorticoids and IVIG for ITP is discussed separately. (See "Immune thrombocytopenia (ITP) in adults: Initial treatment and prognosis", section on 'First-line therapies'.)

Outcomes in pregnant women with ITP have been described in retrospective studies. In general, the use of any type of therapy to raise the platelet count is reported in 30 to 40 percent of pregnancies, and serious complications are rarely seen [21,39]. The pediatrician should be informed about the possibility of neonatal thrombocytopenia, which may develop several days after delivery, as discussed below. (See 'Neonatal testing' below.)

We generally avoid splenectomy, rituximab, and thrombopoietin receptor agonists during pregnancy due to concerns about maternal and fetal adverse effects [32]. However, we have used rituximab in pregnant women, and these therapies may be appropriate in selected individuals.

- Immunoglobulins do not cross the placenta until the second trimester, with a linear increase in the amount of transfer as pregnancy progresses [42,43]. Thus, rituximab therapy in the first trimester should be without adverse effects. Review of a global rituximab drug safety database identified 153 pregnancies associated with rituximab exposure for which outcomes were known. Of these, 90 (59 percent) resulted in live births; 22 (14 percent) were associated with premature birth; 11 neonates (7 percent) had hematologic abnormalities; one neonate died at age six weeks; and two infants had congenital malformations [44]. Of note, most of these pregnancies were confounded by concomitant use of teratogenic agents and other maternal conditions (eg, lymphoma). (See "Safety of antiinflammatory and immunosuppressive drugs in rheumatic diseases during pregnancy and lactation", section on 'Rituximab'.)

- Splenectomy may be required for a patient with severe thrombocytopenia and bleeding who is unresponsive to glucocorticoids, IVIG, and rituximab, but splenectomy later during pregnancy becomes a greater risk as the uterus becomes larger.

- The safety of thrombopoietin receptor agonists (eg, romiplostim, eltrombopag) during pregnancy is unknown. These agents stimulate platelet production by activating the platelet thrombopoietin receptor; they also may stimulate other hematopoietic cells. Registries have been established by the manufacturers to document pregnancy outcomes when these agents are inadvertently given to pregnant women. (See "Immune thrombocytopenia (ITP) in adults: Second-line and subsequent therapies", section on 'Thrombopoietin receptor agonists' and "Clinical applications of thrombopoietic growth factors".)

- A form of recombinant human thrombopoietin (rhTPO) is available in China. When administered to 31 pregnant women with ITP who had platelet counts <30,000/microL that could not be increased by glucocorticoids, IVIG, or platelet transfusions (ie, treatment-refractory ITP), this rhTPO agent was well tolerated and was not associated with adverse effects in the newborns [45]. Platelet counts normalized in 10 and increased in an additional 13 (overall response rate, 74 percent).

If a woman taking rituximab or a thrombopoietin receptor agonist (eg, romiplostim) becomes pregnant, discussion regarding the necessity of continuing the medication in the setting of limited fetal risk data versus the use of alternative medications should be individualized. (See "Safety of antiinflammatory and immunosuppressive drugs in rheumatic diseases during pregnancy and lactation", section on 'Rituximab'.)

Anticoagulation for HIT — As mentioned above, heparin-induced thrombocytopenia (HIT) is extremely rare in pregnancy. If HIT is suspected or confirmed, all heparin exposure should be eliminated and presumptive therapy with a non-heparin anticoagulant should be initiated. The evaluation and management of HIT, and options for anticoagulation during pregnancy, are discussed in detail separately. (See "Clinical presentation and diagnosis of heparin-induced thrombocytopenia" and "Management of heparin-induced thrombocytopenia" and "Use of anticoagulants during pregnancy and postpartum", section on 'Alternatives to heparin'.)

Antibiotics — Broad spectrum antibiotics are appropriate for patients with a presumed infectious cause of thrombocytopenia, either due to severe bacterial infection or DIC.

The choice of antibiotic depends on the site of infection and likely organisms, as discussed in separate topic reviews. As examples:

- Pyelonephritis – (See "Urinary tract infections and asymptomatic bacteriuria in pregnancy", section on 'Acute pyelonephritis'.)

- Pneumonia – (See "Treatment of respiratory infections in pregnant women", section on 'Pneumonia'.)

- Septic thrombophlebitis – (See "Septic pelvic thrombophlebitis", section on 'Treatment'.)

- Intra-amniotic infection – (See "Intra-amniotic infection (clinical chorioamnionitis or triple I)", section on 'Antibiotic therapy'.)

Neuraxial anesthesia — There is a lack of high-quality data regarding what constitutes a safe platelet count for placement of a neuraxial catheter, and the threshold may differ for different patients and different thrombocytopenic disorders. It is also worth noting that of the numerous pregnant women who have epidural anesthesia without platelet count testing, some will predictably be mildly thrombocytopenic and not counted in case series [46].

As a general rule, epidural anesthesia is considered to be safe if the platelet count is above 50,000 to 80,000/microL [47-49]. Depending on the cause and severity of thrombocytopenia, platelet transfusion and/or other therapies may be indicated two or more days prior to placement of a neuraxial catheter.

Practice patterns vary, and it is important to discuss options for neuraxial analgesia or anesthesia with the consulting anesthesiologist prior to delivery in patients with thrombocytopenia. Obstetricians should be familiar with policies at their institution and preferences of the treating anesthesiologist. This subject is discussed in more detail separately. (See "Adverse effects of neuraxial analgesia and anesthesia for obstetrics", section on 'Neuraxial analgesia and low platelets'.)

For women with presumed diagnosis of ITP who are near term and have a platelet count just below the "acceptable" limit for regional anesthesia, a brief treatment course with a glucocorticoid such as dexamethasone, 40 mg daily for up to four days in order to increase the patient's platelet count into the acceptable range may be used, with the understanding that there is little evidence to support this practice. Compared with prednisone, dexamethasone has better efficacy in raising the platelet count and fewer adverse effects, and crosses the placenta, which may improve the fetal platelet count (if low) and aid in lung maturation, although either

dexamethasone or prednisone can be used (see "Immune thrombocytopenia (ITP) in adults: Initial treatment and prognosis", section on 'Glucocorticoids'). Practitioners and their patients should decide the risks and benefits of giving glucocorticoids to raise the platelet count prior to delivery on a case-by-case basis. (See 'ITP therapies' above.)

The range of outcomes from placement of a neuraxial catheter in pregnant women with ITP was illustrated in a retrospective series of 119 pregnant women with ITP over a 10-year period, for whom data on analgesia were available for all but one [21]. Of the 42 women who received epidural anesthesia, none had a complication related to the catheter placement. Platelet counts were <100,000/microL in 19 women (45 percent), <75,000/microL in six women (14 percent), and <50,000/microL in one woman (2 percent).

Neonatal testing — Settings in which testing of the neonatal platelet count is prudent include the following:

- Maternal ITP.
- Neonatal thrombocytopenia in a previous pregnancy. (See "Causes of neonatal thrombocytopenia" and "Neonatal alloimmune thrombocytopenia: Parental evaluation and pregnancy management".)
- Indications unrelated to maternal platelet count, such as bleeding or petechiae/ecchymoses in the infant; congenital anomalies associated with thrombocytopenia; trisomy 21, 18, or 13; or neonatal infections such as cytomegalovirus or rubella. These are discussed in detail separately. (See "Clinical manifestations, evaluation, and management of neonatal thrombocytopenia".)

The risk of neonatal thrombocytopenia in women with gestational thrombocytopenia (GT) is difficult to determine, as there are no tests that can distinguish GT from ITP, and women in some series may have been misclassified [50]. If we are confident in the diagnosis of GT (eg, if previous pregnancies were associated with maternal thrombocytopenia that resolved after delivery), then we do not routinely obtain a neonatal platelet count. If the diagnosis of GT versus ITP is unclear, it may be reasonable to treat as ITP until further information becomes available.

The overall risk of thrombocytopenia in infants born to mothers with ITP has been estimated to be in the range of 10 to 15 percent; severe thrombocytopenia is possible but much less common. In the series of 119 pregnancies associated with maternal ITP, 31 of 109 infants (28 percent) had platelet counts below 150,000/microL [21]. Of these, six infants (6 percent) had counts <20,000/microL, five had counts between 20,000 and 50,000, and the remainder had counts >50,000/microL. One infant had an intracerebral hemorrhage, which was not clearly due to thrombocytopenia; the infant was born at 29 weeks of a twin gestation, and the platelet count nadir was 135,000/microL on the day after delivery. There were two fetal deaths, one unrelated to thrombocytopenia and one a stillbirth at 27 weeks associated with extensive fetal hemorrhage and severe maternal thrombocytopenia. Smaller series have found similar rates of thrombocytopenia and similar platelet count distributions [51-59].

There does not appear to be a strong correlation between maternal platelet count and neonatal platelet count in ITP [21]. Risk factors for neonatal thrombocytopenia include a previous history of neonatal thrombocytopenia, prior splenectomy, severe thrombocytopenia (eg, <50,000/microL) at some point during the pregnancy, and possibly a maternal platelet count <100,000/microL at the time of delivery [21,51,54,55,60,61]. As noted above, there is no evidence that ITP therapy for the mother raises the fetal platelet count. (See 'ITP therapies' above.)

When neonatal testing is performed, it should be done after delivery, typically by cord blood platelet count using clean venipuncture of a cord vessel rather than draining blood from the cord [31]. Platelet count testing by scalp blood sampling or cordocentesis is not recommended because these procedures are associated with adverse events and have not been demonstrated to improve outcomes. Percutaneous umbilical cord blood sampling carries an increased risk of fetal hemorrhage that is considered to be greater than the risk of severe neonatal intracerebral hemorrhage from thrombocytopenia (approximately 2 percent versus 1 percent) [14,21,31,51,62]. Fetal scalp blood sampling has been abandoned because it is technically difficult and frequently results in spuriously low platelet counts [14,16,31,51].

Based on our experience, if the neonate's platelet count is low (<150,000/microL), a repeat platelet count the next day is appropriate to be confident that the platelet count is stable or increasing. The neonatal platelet count may decrease up to several days after birth (typical nadir, between days 2 to 5 postpartum) [53]. The mechanism is thought to involve passage of maternal antiplatelet antibodies to the fetal circulation, with gradual acquisition of infant splenic function within the first few days after birth that leads to destruction of antibody-sensitized platelets. Management of the thrombocytopenic neonate is discussed separately. (See "Clinical manifestations, evaluation, and management of neonatal thrombocytopenia", section on 'Management'.)

Postpartum — The patient's postpartum course depends on the cause of thrombocytopenia. In some cases in which the diagnosis was unclear, the postpartum course is helpful in clarifying the diagnosis, and the diagnosis in turn guides postpartum management.

- Thrombocytopenia is expected to resolve postpartum in women with GT, preeclampsia/HELLP syndrome, and DIC for which the cause has been corrected.
  - In GT the maternal platelet count often returns to normal within two to four weeks following delivery but may not be normal until six to eight weeks [13,63]. We check a platelet count at the six-week postpartum visit, and repeat the count in another one to two weeks only if the six-week count remains low. Recurrence during subsequent pregnancies is not uncommon, typically to a similar platelet count as previously seen [13,50].
  - In preeclampsia/HELLP, the maternal thrombocytopenia may first occur at or after delivery, but in all women there should be at least a beginning recovery of the platelet count within one to three days postpartum. Of note, the platelet count may initially worsen before it improves. For those with stable preeclampsia and thrombocytopenia, we initially check the platelet count daily until it begins rising and then again at the six-week postpartum visit. For those with HELLP, we check the count every 6 to 12 hours until it begins to show stability or improvement.
  - In women with DIC at term, recovery from thrombocytopenia is related to correction of the underlying cause of the DIC. Most causes associated with pregnancy, such as placental abruption, will be corrected by delivery, although others may not be corrected. Sepsis requires appropriate identification of the infectious organism, treatment with antibiotics, and control of the source, with possible surgical removal. We check the platelet count daily (or more often, if clinical features warrant) until it begins to show stability or improvement. The causes of DIC in pregnancy, their management, and expected postpartum course are discussed in more detail separately. (See "Disseminated intravascular coagulation during pregnancy".)
- Thrombocytopenia caused by TTP or C-TMA may worsen or first occur during the postpartum period. We check the maternal platelet count every 6 to 12 hours until it begins to show stability or improvement.
- Thrombocytopenia caused by a condition unrelated to the pregnancy such as an inherited platelet disorder or ITP will be present postpartum.

For patients with stable or worsening thrombocytopenia following delivery, diagnostic evaluation should be pursued as done for non-pregnant patients. (See "Approach to the adult with unexplained thrombocytopenia".)

Indications for platelet count testing in the neonate are described above. (See 'Neonatal testing' above.)

Recurrence in future pregnancies — The recurrence of thrombocytopenia in future pregnancies depends on the underlying etiology. As examples:

- Our experience corroborates published reports that show GT often recurs in future pregnancies.

- Acquired autoimmune TTP has a low but possible risk of recurrence with a subsequent pregnancy [25]. Our practice is to follow women with acquired TTP who are asymptomatic with frequent blood counts throughout their pregnancy but with no prophylactic treatment. (See "Acquired TTP: Management following recovery from an acute episode and during remission", section on 'Pregnancy after an episode of TTP'.)

- In contrast, hereditary TTP has a high likelihood of recurring during subsequent pregnancies unless appropriate prophylaxis with plasma infusion is provided [24,64].

SOCIETY GUIDELINE LINKS — Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Immune thrombocytopenia (ITP) and other platelet disorders".)

SUMMARY AND RECOMMENDATIONS

- Mild thrombocytopenia (platelet count 100,000 to 150,000/microL) is seen in approximately 5 to 7 percent of pregnancies, most commonly near term or at delivery; platelet counts <100,000/microL are much less common (on the order of 1 percent). (See 'Definition and Incidence' above.)

- By far the most common cause of thrombocytopenia in pregnancy is gestational thrombocytopenia (GT), a benign, physiologic condition that requires no evaluation or treatment (table 2). The next most, but far less common, is immune thrombocytopenia (ITP), an autoimmune condition in which autoantibodies interfere with platelet production and cause destruction of circulating platelets. GT and ITP can occur at any stage of the pregnancy; platelet counts in GT gradually decrease during gestation. Both are diagnoses of exclusion. (See 'Gestational thrombocytopenia (GT)' above and 'Immune thrombocytopenia (ITP)' above.)

- Less common conditions associated with severe thrombocytopenia and acute systemic illness include the overlapping syndromes of preeclampsia with severe clinical features and HELLP (hemolysis, elevated liver function tests, and low platelets), disseminated intravascular coagulation (DIC), and thrombotic microangiopathies (TMAs) such as thrombotic thrombocytopenic purpura (TTP) and complement-mediated TMA (C-TMA). These conditions are all rare and potentially life-threatening. (See 'Preeclampsia with severe features/HELLP' above and 'DIC' above and 'Thrombotic microangiopathy (TMA)' above.)

- Other rare causes of thrombocytopenia that may be discovered incidentally during the pregnancy include systemic lupus erythematosus (SLE), catastrophic antiphospholipid syndrome, medications that cause immune thrombocytopenia, heparin-induced thrombocytopenia (HIT), cancer, infection, liver disease, hypersplenism, deficiency of vitamin B12/folate/copper, or inherited platelet disorders. (See 'Causes of thrombocytopenia not triggered by the pregnancy' above.)

- The majority of pregnant women with relatively mild or incidentally discovered thrombocytopenia (platelet count between 80,000 and 150,000/microL) without other cytopenias or major clinical findings will have GT (table 2). It generally is not possible or necessary to distinguish GT from mild ITP because both are diagnoses of exclusion and neither requires therapy. In individuals who are acutely ill, preeclampsia with severe clinical features is significantly more common than DIC, and DIC is significantly more common than the TMAs (table 5). Laboratory testing to narrow the diagnosis is discussed above. (See 'Determining the likely cause(s)' above.)

- Platelet transfusions may be required for women with severe thrombocytopenia who are bleeding, require a procedure, or are nearing delivery. Platelet count thresholds are provided above. (See 'Treatment of bleeding or severe thrombocytopenia' above.)

- Management depends on the underlying cause (or most likely cause) of thrombocytopenia (algorithm 1):

  - Delivery effectively treats some conditions such as preeclampsia with severe features, HELLP syndrome, and DIC and/or sepsis due to retained dead fetus or intra-amniotic infection. (See 'Need for urgent/emergent delivery' above.)

  - TTP is treated with plasma exchange, and C-TMA is treated with anti-complement therapy. (See 'Need for plasma exchange or anti-complement therapy' above.)

  - Not all patients with ITP require treatment. For those who do, glucocorticoids or intravenous immune globulin (IVIG) are used. (See 'ITP therapies' above.)

  - HIT is treated with cessation of all heparin and administration of a non-heparin anticoagulant. Infection/sepsis is managed with antibiotics and sepsis protocols. (See 'Anticoagulation for HIT' above and 'Antibiotics' above.)

- Additional management issues related to neuraxial anesthesia, delivery, neonatal testing, and postpartum care are discussed above. (See 'Neuraxial anesthesia' above and 'Neonatal testing' above and 'Postpartum' above and 'Recurrence in future pregnancies' above.)

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Topic 6681 Version 30.0

GRAPHICS

Incidence of maternal thrombocytopenia in 15,471 consecutive women admitted for labor and delivery, 1986-1992

Mother's health status (percent of all 15,471 women)	Maternal platelet count <150,000/microL (percent)
Normal - 13,925 (90%)	**756 (5%)***
Preeclampsia - 1414 (9%)	216 (15%)
ITP - 46 (0.3%)	31 (67%)
Systemic lupus erythematosus - 55 (0.4%)	8 (15%)
At risk for neonatal alloimmune thrombocytopenia¶ - 18 (0.1%)	3 (17%)
Other hematologic and medical disorders$^{\Delta}$ - 13 (0.1%)$^{\Delta}$	13 (100%)

Refer to UpToDate topic on thrombocytopenia in pregnancy for further discussion.

* These women most likely had gestational thrombocytopenia (GT). Two-thirds of them had platelet counts of 130,000 to 150,000/microL.
¶ These women had maternal-paternal platelet alloantigen mismatch diagnosed because of a previous thrombocytopenic fetus (15 women) or were sisters of women who had infants with alloimmune thrombocytopenia.
Δ The other hematologic or medical disorders were not further specified.

Data from: Burrows RF, Kelton JG, N Engl J Med 1993; 329:1463.

Graphic 81684 Version 5.0

Causes of thrombocytopenia in pregnancy

Gestational age	Incidental finding of asymptomatic thrombocytopenia (platelet count 80,000 to 149,000/microL)	Platelet count <80,000/microL
≤20 weeks	▪ Most often GT ▪ ITP cannot be excluded, but no evaluation or management would be required ▪ Occurrence of other disorders not different from non-pregnant patients	▪ Not GT ▪ May be ITP ▪ Occurrence of other disorders not different from non-pregnant patients
>20 weeks, at delivery, and postpartum	▪ Almost always GT ▪ ITP cannot be excluded, but no evaluation or management would be required ▪ Occurrence of other disorders not different from non-pregnant patients	▪ Almost never GT ▪ If asymptomatic, ITP likely ▪ If hypertension, preeclampsia ▪ If symptoms of systemic illness as well as MAHA: • HELLP syndrome, if LFTs increased • DIC, if coagulation abnormalities present; suspect sepsis • C-TMA, if AKI is severe • TTP, if transient focal neurologic abnormalities occur The frequency of these disorders increases with gestation, with a peak occurrence at delivery and the first postpartum week.

Some disorders are listed in both columns because patients with these disorders may have mild or severe thrombocytopenia. Refer to UpToDate topics for details of the diagnostic evaluation and immediate management interventions while determining the diagnosis.

GT: gestational thrombocytopenia; ITP: immune thrombocytopenia; TTP: thrombotic thrombocytopenic purpura; MAHA: microangiopathic hemolytic anemia; HELLP: hemolysis, elevated liver function tests, and low platelets; LFTs: liver function tests; DIC: disseminated intravascular coagulation; C-TMA: complement-mediated thrombotic microangiopathy; AKI: acute kidney injury.

Graphic 111435 Version 1.0

Criteria for the diagnosis of preeclampsia

Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two occasions at least four hours apart after 20 weeks of gestation in a previously normotensive patient
If systolic blood pressure is ≥160 mmHg or diastolic blood pressure is ≥110 mmHg, confirmation within minutes is sufficient
and
Proteinuria ≥0.3 g in a 24-hour urine specimen or protein/creatinine ratio ≥0.3 (mg/mg) (30 mg/mmol)
Or dipstick ≥1+ if a quantitative measurement is unavailable
OR
Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two occasions at least four hours apart after 20 weeks of gestation in a previously normotensive patient with the new onset of any of the following (with or without proteinuria):
Platelet count <100,000/microL
Serum creatinine >1.1 mg/dL (97.2 micromol/L) or doubling of the creatinine concentration in the absence of other renal disease
Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory
Pulmonary edema
Cerebral or visual symptoms (eg, new-onset and persistent headaches not responding to usual doses of analgesics*; blurred vision, flashing lights or sparks, scotomata)

Superimposed preeclampsia is defined by the new onset of proteinuria, significant end-organ dysfunction, or both after 20 weeks of gestation in a woman with chronic/preexisting hypertension. For women with chronic/preexisting hypertension who have proteinuria prior to or in early pregnancy, superimposed preeclampsia is defined by worsening or resistant hypertension (especially acutely) in the last half of pregnancy or development of signs/symptoms of the severe end of the disease spectrum.

* Response to analgesia does not exclude the possibility of preeclampsia.

Adapted from: American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013; 122:1122.

Graphic 79977 Version 28.0

In a patient with preeclampsia, the presence of one or more of the following indicates a diagnosis of "preeclampsia with severe features"

Symptoms of central nervous system dysfunction:
New-onset cerebral or visual disturbance, such as: ▪ Photopsia, scotomata, cortical blindness, retinal vasospasm ▪ Severe headache (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy ▪ Altered mental status
Hepatic abnormality:
Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis or serum transaminase concentration ≥2 times the upper limit of the normal range, or both
Severe blood pressure elevation:
Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg on two occasions at least four hours apart while the patient is on bedrest (antihypertensive therapy may be initiated upon confirmation of severe hypertension, in which case criteria for severe blood pressure elevation can be satisfied without waiting until four hours have elapsed)
Thrombocytopenia:
<100,000 platelets/microL
Renal abnormality:
Progressive renal insufficiency (serum creatinine >1.1 mg/dL [97.2 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease)
Pulmonary edema

In contrast to older criteria, the 2013 criteria do not include proteinuria >5 g/24 hours and fetal growth restriction as features of severe disease.

Adapted from: Hypertension in pregnancy: Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013; 122:1122.

Graphic 76975 Version 18.0

Comparison of typical clinical features and specific management of disorders associated with a platelet count <80,000/microL occurring after 20 weeks gestation

Clinical feature	Preeclampsia/HELLP	TTP	C-TMA	ITP	Hemorrhage/DIC	Sepsis/DIC
Incidence	100 in 10,000 pregnancies	1 in 10,000 pregnancies	Unknown. May be similar to TTP.	3 in 10,000 pregnancies	2 in 10,000 pregnancies	1 in 10,000 pregnancies
Time of occurrence	By definition, occurs after 20 weeks of gestation; more common near term and within three days postpartum	May occur throughout pregnancy, but most common near term and several weeks postpartum	May occur throughout pregnancy, but most common postpartum	Any time during pregnancy	Most commonly at delivery and postpartum	Most commonly at delivery and postpartum
Vital signs	Hypertension, by definition, BP ≥160/110	Normal BP, fever may be present but is rare	Hypertension due to AKI	Normal, unless hypotension and tachycardia from bleeding	Hypotension, tachycardia (may have been transient)	Fever, hypotension, tachycardia
Neurologic abnormalities	Headache, vision changes. Less commonly eclamptic seizures, PRES, stroke.	Severe in 41% (transient focal defects, seizure, stroke); minor in 30%	None	None	Probably none	Probably none
Microangiopathic hemolysis/schistocytes	Moderate	Severe	Moderate	None	Variable	Variable
Kidney injury	Usually mild, but severe AKI is possible. Dialysis is rarely required.	Usually mild or absent; severe AKI requiring dialysis in <5%	Severe, typically dialysis is required	None	Severe ATN, reversible	May have ATN, reversible
Liver function tests: ALT, AST	From normal to markedly increased	Normal or slightly increased	Normal	Normal	May be markedly increased	May be increased
Typical course following delivery	Stabilization or improvement within 48 hours	No stabilization or improvement within 48 hours	Increasing serum creatinine	Most unchanged, but may improve after delivery	Recovery after source of hemorrhage corrected	Recovery after appropriate treatment
Specific management	Delivery of infant is curative	Plasma exchange, immunosuppression if acquired autoimmune TTP suspected. If hereditary TTP is strongly suspected, plasma infusion is sufficient	Anti-complement agent	Glucocorticoids, IVIG, and maybe additional immunosuppressive agents	Identify and correct source of hemorrhage. May require additional laparotomy.	Antibiotics

The incidence of preeclampsia with severe features is 1 case per 100 pregnancies. The incidence of TTP during pregnancy is estimated from data from the Oklahoma TTP Registry (frequency of TTP during pregnancy), and the CDC (birth rate per population).

PE/HELLP: preeclampsia/hemolysis, elevated liver enzymes, low platelets; TTP: thrombotic thrombocytopenic purpura; C-TMA: complement-mediated thrombotic microangiopathy; ITP: immune thrombocytopenia; DIC: disseminated intravascular coagulation; PRES: posterior reversible encephalopathy syndrome; AKI: acute kidney injury; ATN: acute tubular necrosis; AST: aspartate aminotransferase; ALT: alanine aminotransferase; IVIG: intravenous immune globulin; CDC: US Centers for Disease Control and Prevention.

Courtesy of James N George, MD and Jennifer J McIntosh, DO, MS.

Graphic 111517 Version 4.0

Peripheral smear in microangiopathic hemolytic anemia showing presence of schistocytes

Peripheral blood smear from a patient with a microangiopathic hemolytic anemia with marked red cell fragmentation. The smear shows multiple helmet cells (arrows) and other fragmented red cells (small arrowhead); microspherocytes are also seen (large arrowheads). The platelet number is reduced; the large platelet in the center (dashed arrow) suggests that the thrombocytopenia is due to enhanced destruction.

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 70851 Version 8.0

Normal peripheral blood smear

High-power view of a normal peripheral blood smear. Several platelets (arrows) and a normal lymphocyte (arrowhead) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor (dashed arrow) should equal one-third of its diameter.

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 59683 Version 4.0

Clinical features and diagnosis of thrombocytopenic conditions in pregnancy

Disorder	Onset during pregnancy	Diagnosis
Pseudothrombocytopenia	Any time	Examine blood smear for platelet clumps, or giant platelets. Repeat platelet count in citrate or heparin anticoagulant. Usually caused by agglutinins dependent upon EDTA, the standard anticoagulant for blood counts.
Gestational thrombocytopenia (GT)	Typically late in gestation, frequency increases as term approaches	Based on five criteria: 1. Mild thrombocytopenia (most 100,000 to 150,000/microL, rarely <80,000/microL) 2. No thrombocytopenia outside of pregnancy 3. Occurs late in gestation 4. No fetal/neonatal thrombocytopenia 5. Postpartum resolution
Immune thrombocytopenia (ITP)	Any time	Presence of isolated thrombocytopenia with no evidence for alternative etiologies. May be indistinguishable from gestational thrombocytopenia if mild and occurs late during pregnancy. Platelet count may improve after delivery.
Preeclampsia with severe features	After 20 weeks gestation	Systolic or diastolic hypertension plus proteinuria
HELLP syndrome (hemolysis, elevated liver function tests, and low platelets)	After 20 weeks gestation	Diagnostic criteria for preeclampsia are present in 85% of cases. Hemolysis: Microangiopathic hemolytic anemia with schistocytes, with other signs of hemolysis: increased serum LDH and indirect bilirubin, decreased haptoglobin Elevated liver function tests (eg, AST, ALT), typically ≥twice normal Low platelets: Platelet count ≤100,000/microL
Thrombotic thrombocytopenic purpura (TTP)	Typically late in gestation, frequency increases as term approaches. May occur after delivery.	Thrombocytopenia and microangiopathic hemolytic anemia without an alternative etiology. May be indistinguishable from severe preeclampsia or HELLP syndrome. Severe neurologic abnormalities and acute renal failure support the diagnosis of TTP. Persistent abnormalities ≥3 days after delivery also support the diagnosis of TTP.
Drug-induced immune thrombocytopenia (DITP) (except heparin)	Any time	Complete history of drug ingestion, including non-prescription drugs and herbal remedies. Focus on drugs taken intermittently, or regularly for more than one week. Thrombocytopenia typically resolves in five to seven days after stopping the drug.
Heparin-induced thrombocytopenia (HIT)	Any time	Suspected in patients who have thrombocytopenia (or >50% decrease in platelet count) and who have begun heparin within previous 5 to 10 days. Thrombocytopenia is typically mild; arterial or venous thrombi are commonly present. ELISA assay for heparin-dependent antibodies is sensitive; measurement of heparin-induced platelet serotonin release is more specific.
Antiphospholipid syndrome (APS)	Any time	Requires one clinical and one laboratory criterion: **Clinical:** 1. Adverse pregnancy outcome: ≥3 losses <10 weeks gestation or ≥1 loss ≥10 weeks gestation, <34 week delivery secondary to preeclampsia or placental insufficiency 2. Arterial or venous thrombosis **Laboratory:** Demonstration of the persistent presence of at least one of the following antiphospholipid antibodies: 1. Lupus anticoagulant 2. Anticardiolipin antibody 3. Anti-β2 glycoprotein-I

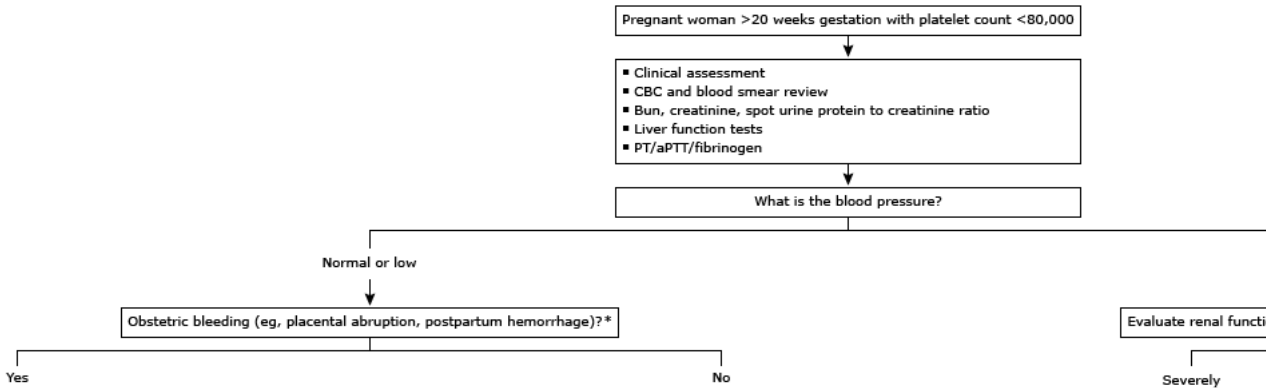
Refer to UpToDate for additional details of the clinical features.

EDTA: ethylenediaminetetraacetic acid; LDH: lactate dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

Courtesy of James N George, MD and Eric J Knudtson, MD.

Graphic 53727 Version 9.0

Approach to a pregnant woman beyond 20 weeks gestation with a platelet count below 80,000/microL



This algorithm does not substitute for the clinical judgment of the treating obstetrician and hematologist. Platelet transfusions are indicated for patients with active bleeding, with thrombosis. Early involvement of the appropriate consulting specialist is advised. The threshold platelet count of 80,000/microL was chosen to exclude women with gesta UpToDate topics on thrombocytopenia in pregnancy and specific conditions for additional possible causes of thrombocytopenia and information about management.

CBC: complete blood count; PT: prothrombin time; aPTT: activated partial thromboplastin time; MAHA: microangiopathic hemolytic anemia; AKI: acute kidney injury; DIC: di immune thrombocytopenia; TTP: thrombotic thrombocytopenic purpura; C-TMA: complement-mediated thrombotic microangiopathy; HELLP: hemolysis, elevated liver functio function tests; IVIG: intravenous immune globulin; PEX: plasma exchange.

* Severity of bleeding and source must be evaluated.

¶ Gestational thrombocytopenia is extremely unlikely if the platelet count is <80,000/microL.

Δ Genetic testing for complement mutations may be appropriate for some patients. Refer to UpToDate for details.

Graphic 111837 Version 2.0

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