whether the patient has an associated life-threatening condition (Box 205.1).

### IDIOPATHIC OR IMMUNE THROMBOCYTOPENIC PURPURA

#### EPIDEMIOLOGY

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by isolated thrombocytopenia. The estimated incidence is 100 cases per 1,000,000 patients, and half of the cases are seen in children. In children, the gender distribution is equal, whereas in adults, women are three times more likely to be affected than are men. ITP is defined as chronic if it lasts for longer than 6 months. Eighty percent of children with ITP have the acute form, whereas 80% of adults with ITP develop the chronic illness.

#### PATHOPHYSIOLOGY

Thrombocytopenia in ITP is primarily the result of accelerated platelet destruction. Autoantibodies bind to platelet antigens and thus lead to accelerated clearance by macrophages found primarily in the spleen and the liver. This increased clearance is magnified by decreased production caused by intramedullary destruction of platelets and megakaryocyte inhibition. Thrombocytopenia, in turn, leads to bleeding through loss of the integrity of the vascular wall and deficits in thrombus formation.

#### PRESENTING SIGNS AND SYMPTOMS

ITP is classically described as occurring after a prodromal infection. This presentation accounts for 60% of cases in patients 1 to 10 years of age. Outside this age range, thrombocytopenia occurs without any preceding symptoms and is often found incidentally.

Patient's symptoms of bleeding depend on the severity of the thrombocytopenia. Patients with platelet counts higher than 50,000/mm$^3$ are asymptomatic. Patients with platelet counts lower than 50,000/mm$^3$ may report easy bruising with...
ICH is the major cause of mortality in patients with ITP. The mortality rate of patients with ITP and ICH is greater than 50%.4

ICH is the major cause of mortality in patients with ITP. The mortality rate of patients with ITP and ICH is greater than 50%.4 Atraumatic ICH secondary to ITP is rare, estimated to occur in 0.1% to 1% of patients with ITP. In one report of patients with ICH, 70% had platelet counts lower than 10,000/mm^3.5 Despite the rarity of this complication, patients with ITP and any cranial or neurologic complaint should be evaluated for ICH.

### Differential Diagnosis and Medical Decision Making

Primary and secondary forms of immune-mediated destruction of platelets are recognized. ITP generally refers solely to the primary form of this disease. The secondary form is associated with rheumatic disease, connective tissue disorders, malignant disease, drug exposure, immune deficiencies, and infections, including human immunodeficiency virus infection and hepatitis C. Because no specific diagnostic criteria exist for ITP, it is a diagnosis of exclusion.

The importance of pursuing alternative diagnoses is highlighted by the associated morbidity and mortality of the other diagnoses. The patient's history can point toward an alternate cause of the thrombocytopenia. Constitutional symptoms such as fever or weight loss suggest malignant disease or infection. Recent initiation of medications such as heparin, clopidogrel, or vancomycin may indicate drug-induced thrombocytopenia.

In ITP the remainder of the laboratory evaluation should be within normal limits. Thrombocytopenia with other abnormalities suggests alternative diagnoses. For example, thrombocytopenia with anemia is found in patients with thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS). Thrombocytopenia and additional cytopenias are found in leukemia and myelodysplastic disorders. Thrombocytopenia and coagulation abnormalities are found in disseminated intravascular coagulation (DIC).

The peripheral blood smear should be examined. The smear can differentiate true thrombocytopenia from spurious causes of thrombocytopenia such as platelet clumping, platelet satellitism, and abnormally large platelets. Furthermore, the peripheral blood smear can identify manifestations of the primary cause of thrombocytopenia, such as schistocytes in TTP-HUS, evidence of parasitic infections, or findings suggestive of leukemia.

In the patient with suspected ITP, the physician must identify the degree of any bleeding complications. A careful skin examination can quantify the degree of petechiae or bruising. Rectal examination can identify gastrointestinal bleeding. Additionally, any intracranial symptoms, especially in the context of trauma, should be evaluated by computed tomography for possible ICH.

Patients with a history of ITP often have relapses. Most adults with ITP have one or more relapses, commonly during a steroid taper. Relapses are also seen in patients treated with intravenous immune globulin (IVIG) after steroids have failed. Patients with an ITP relapse are treated in the same manner as patients with an initial presentation of ITP. Patients with ITP relapse should also have a nonemergency surgical consultation for possible splenectomy.

### Treatment

ITP is treated by immunomodulation. The first-line treatment is with parenteral steroids. Most patients presenting with ITP...
are well and do not need treatment in the ED and can be managed with an early referral to a hematologist. Treatment should be started in patients who are ill, have bleeding complications, need emergency surgery, or have severe thrombocytopenia.

Initiation of treatment should be coordinated with a hematologist, for several reasons. Early leukemia can manifest with isolated thrombocytopenia, especially in pediatric patients. Leukemia should also be considered in adults who have prominent and persistent constitutional symptoms. In a patient who is presenting with leukemia, empiric steroids can lead to alteration of the bone marrow aspirate that causes difficulty and delay in diagnosis.

Steroids are usually started at a dose 1 to 1.5 mg/kg of prednisone per day. IVIG (usual dose of 1 g/kg) is reserved for infants and patients with severe disease or internal bleeding. Anti-D immune globulin is used as an adjunct in Rh-positive patients (usual dose of 75 mcg/kg). Patients with a recurrence of ITP are treated in the same manner as patients with an initial presentation of ITP and should be considered for escalation of therapy. Patients who have chronic or refractory ITP should be considered for splenectomy. The rate of remission of ITP after splenectomy in children is 70% to 80%. The remission rate in adults is unpredictable, ranging from 60% to 70%. Platelet transfusion leads to a rapid but transient increase in platelet count and is therefore indicated only in certain settings, such as in patients with bleeding complications, patients undergoing emergency surgery, and those with severe thrombocytopenia.

**FOLLOW-UP, NEXT STEPS OF CARE, AND PATIENT EDUCATION**

Most patients with suspected ITP are treated and managed as outpatients. However, patients with severe thrombocytopenia—defined as a platelet count lower than 10,000/mm³, patients with head trauma, and those with bleeding complications—should be admitted. Patients should be considered for admission if their platelet count is lower than 30,000/mm³, if they work in a profession (e.g., construction) in which trauma is inevitable, or if the diagnosis is in question. Ultimately, disposition should be based on the patient’s appearance, the severity of thrombocytopenia, comitant use of antiplatelet agents, and the patient’s access to expeditious follow-up.

Patients who are managed as outpatients should be advised to avoid any antiplatelet agents. Patients, especially children, should limit their activities in situations associated with possible trauma (e.g., construction work, contact sports, gym class). Discharge instructions should instruct patients to return if they have any signs of bleeding, abdominal pain, trauma, or neurologic symptoms.

**THROMBOTIC MICROANGIOPATHIES**

**PERSPECTIVE**

The thrombotic microangiopathies are a group of disorders characterized by intravascular aggregation of platelets that leads to organ ischemia. These disorders include TTP and HUS. Although the two diseases have different names, they share a common mechanism, as well as overlapping clinical features. TTP and HUS are generally believed to lie on a spectrum of disease, as opposed to being distinct clinical entities. Therefore, they are discussed together.

**EPIDEMIOLOGY**

TTP and HUS are rare diseases. TTP has an estimated prevalence of 4 to 11 cases per million people, and HUS has an incidence of 1 to 10 cases per 100,000. TTP is associated with black race, female sex, and obesity. Pregnant and peripartum patients account for 12% to 25% of patients with TTP.

Despite the rarity, TTP and HUS are associated with significant morbidity and mortality. Untreated TTP has a mortality rate of 90%. and adults with typical HUS have a 45% mortality rate. Children less than 10 years of age have a 15% chance of developing HUS in the setting of diagnosed Escherichia coli O157:H7 infection. Although 90% of children with typical Shiga toxin–associated HUS recover with supportive care, they have a 12% rate of death or permanent end-stage renal disease and a 25% incidence of hypertension and proteinuria. Shiga toxin–associated HUS is the most common cause of acute renal failure in childhood, and it accounts for 4.5% of pediatric patients who undergo long-term renal replacement therapy. Commonly cited risk factors for developing HUS include antibiotic administration, use of antimotility agents, and age younger than 10 years.

**PATHOPHYSIOLOGY**

The underlying process of the thrombotic microangiopathies is organ dysfunction resulting from intravascular aggregation of platelets that leads to consumptive thrombocytopenia and organ ischemia from thrombosis. The platelet aggregation, in turn, causes mechanical destruction of red blood cells and microangiopathic, nonimmunologic anemia.

In classic HUS, the inciting event is typically an infection with Shiga toxin–releasing bacteria, most commonly E. coli O157:H7 and non-O157:H7 subtypes. The toxin produced by the bacteria is systemically absorbed, thus leading to widespread microvascular injury and consequent thrombosis. For unknown reasons, most cases of thrombosis in HUS occur in the renal vasculature. Ten percent of cases of HUS are atypical and are not triggered by Shiga toxin. The triggers in atypical HUS include pregnancy, autoimmune disorders, drug toxicity, malignant disease, drug reactions, and preceding infections.

Most patients with TTP have an acquired deficit in the protease ADAMTS-13 that is typically caused by autoantibody destruction. This deficit in ADAMTS-13 leads to the inability to cleave von Willebrand factor multimers and causes intravascular platelet aggregation and thrombosis. Genetic susceptibility to the development of TTP has been described but is not well characterized. Although most patients with TTP are characterized as having idiopathic TTP, ADAMTS-13 antibodies have also been associated with medications (e.g., quinine, ticlopidine, clopidogrel), pregnancy, autoimmune disorders, direct drug toxicity, and hematopoietic stem cell
TTP is treated with plasma exchange, which is thought to work by both removing the autoantibodies against ADAMTS-13 and replacing ADAMTS-13 activity.

**PRESENTING SIGNS AND SYMPTOMS**

The presenting symptoms of both TTP and HUS depend on the severity of the organ dysfunction, the anemia, and the thrombocytopenia. TTP is classically defined by the pentad of thrombocytopenia, anemia, neurologic abnormalities, renal failure, and fever. Fever is typically low grade and is not usually a prominent feature of the syndrome. The neurologic abnormalities in TTP can range from seizures and fluctuating focal deficits to transient confusion. Patients with HUS typically present with signs and symptoms of renal failure including oliguria or anuria, edema, and hypertension. Ninety percent of patients with HUS have typical HUS, with a prodrome of watery diarrhea, which becomes bloody on the third day of illness, that is caused by a Shiga toxin–producing bacterial infection. Despite the distinctions made between TTP and HUS, 25% of patients with HUS can have neurologic abnormalities, and patients with TTP often have renal failure. When both renal impairment and neurologic dysfunction are present, the patient is considered to have TTP if the neurologic abnormalities are prominent and HUS if renal failure is prominent. In both diseases, patients can have symptoms caused by thrombosis and ischemia in any organ, including the heart, bowel, lungs, and pancreas, as well as having symptoms caused by anemia or thrombocytopenia.

Despite the classic descriptions of both TTP and HUS, the most common symptoms are nonspecific. Patient typically present with complaints of abdominal pain, nausea, vomiting, and weakness and are frequently misdiagnosed as having gastroenteritis, sepsis, or transient ischemic attack. Even when the diagnosis is made, 10% of patients with an initial diagnosis of TTP in one report were eventually found to have sepsis or systemic cancer.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

Making the diagnosis of TTP-HUS is challenging. Clinical suspicion is essential. The diagnosis is clinical, with no “gold standard” findings, and the signs and symptoms can be subtle, especially early in the disorder. These are also rare conditions that have clinical overlap with sepsis and DIC. The importance of making the diagnosis is emphasized by the 90% mortality rate of TTP and the knowledge that plasma exchange is a curative treatment.

Several elements of the patient’s history should alert the clinician to the possibility of TTP-HUS. HUS should be considered in children with symptoms of renal failure after a diarrheal illness. TTP should be considered in patients presenting after initiating antiplatelet agents, especially in the first 3 to 14 days. Although TTP is considered an acute illness, one fourth of patients report symptoms for several weeks before diagnosis.

TTP has been described in patients of all ages, but it is seen primarily in adults. The diagnosis of TTP should be considered in any patient with thrombocytopenia and anemia without a readily apparent cause. The anemia of TTP is microangiopathic hemolytic anemia, which is associated with schistocytes and elevated lactate dehydrogenase levels. The hemolysis is nonimmunologic and therefore should elicit a negative Coombs test result. The dyad of thrombocytopenia and microangiopathic hemolytic anemia, with or without renal or neurologic abnormalities, is sufficient to establish the diagnosis of TTP and to start plasma exchange. Additional signs of hemolysis include elevated serum lactate dehydrogenase levels secondary to red blood cell fragmentation and organ ischemia, an elevated reticulocyte count, and low hemoglobin levels. These patients should have no coagulation abnormalities.

Because of the clinical overlap and the divergent treatment of sepsis, DIC, and TTP-HUS, the physician should focus on the distinguishing features. Fever is part of the pentad of TTP but tends to be low grade. High fevers, associated with rigors, or the identification of an infectious source, point toward sepsis. A new coagulation abnormality suggests DIC as the cause of thrombocytopenia and anemia.

Pregnant and peripartum patients with suspected TTP are a diagnostic and clinical challenge. Pregnant patients account for a large percentage of cases of TTP, and clinical overlap exists between TTP and preeclampsia-HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome. Clinically, the two diseases have vastly divergent treatment. Patients with TTP and preeclampsia-HELLP have thrombocytopenia, microangiopathic anemia, renal disease, and neurologic abnormalities. Both diseases are seen primarily in the second and third trimesters. Distinguishing features include more severe hypertension in preeclampsia. The renal dysfunction in patients with preeclampsia is typically proteinuria, compared with the frank renal failure and oliguria seen in TTP-HUS. The thrombocytopenia in preeclampsia tends to be milder and corrects rapidly after delivery. The neurologic abnormalities in preeclampsia are typically headache, scotoma, and seizure, unlike the cerebrovascular accident or mental status change seen in TTP. Pregnant patients with possible TTP should have care coordinated among obstetrics, hematology, and nephrology.

Examination of the peripheral blood smear can be useful in patients with suspected TTP-HUS. In addition to identifying schistocytes, it can differentiate true thrombocytopenia from spurious causes of thrombocytopenia, as well as identifying alternative diagnoses such as leukemia. Hematology and nephrology should be involved in these cases to coordinate plasma exchange and dialysis.

**TREATMENT**

The treatment for TTP is plasma exchange. Plasma exchange halts the thrombosis by removing the autoantibodies against ADAMTS-13 and replacing the ADAMTS-13. Plasma exchange should start within 24 hours of presentation. If plasma exchange is not available or will be severely delayed, plasma infusion at 30 mL/kg/day may be attempted. Immunosuppression with glucocorticoids is used as an adjunct in patients with idiopathic ITP and in patients who have exacerbations after plasma exchange is stopped or in patients who have a relapse after remission. The dose of prednisone is 1 to 2 mg/kg/day. Some weak evidence indicates that additional
immunosuppression with cyclophosphamide or vincristine may be beneficial, but it is not routinely recommended.\textsuperscript{3} When clopidogrel or ticlopidine is the suspected cause, the medication must be discontinued.

The treatment of HUS varies among patient populations. The treatment of children with typical Shiga toxin–associated HUS centers around aggressive supportive care, including fluid and electrolyte management, blood pressure management, red blood cell transfusion, and dialysis when indicated. Plasma exchange or plasma infusion is not routinely indicated for the treatment of typical HUS. Plasma exchange should be considered in patients with HUS that is not associated with Shiga toxin–associated diarrhea,\textsuperscript{16} in adults, in patients with neurologic abnormalities, and in those who are very ill.\textsuperscript{7}

**FOLLOW-UP, NEXT STEPS OF CARE, AND PATIENT EDUCATION**

All patients with TTP-HUS should be admitted to the hospital for further management. Even if patients appear well, TTP has no outpatient management. Patients with HUS need electrolyte and fluid management. Patients should be admitted to telemetry beds because of the possibility of myocardial ischemia.

Patients should be educated about the possibility of long-term sequelae, including renal failure, permanent neurologic disability, and myocardial dysfunction, as well as the possibility of relapse. The long-term prognosis depends on various factors, including age, degree of organ dysfunction, prompt treatment with plasma exchange, and length of time undergoing dialysis. Children universally do better than adults. Young children with typical (Shiga toxin diarrhea–associated) HUS have the best prognosis of all patients with TTP-HUS. Patients with typical HUS are unlikely to have a recurrence, whereas patients with idiopathic TTP have a 50% relapse rate.\textsuperscript{8}

**DRUG-INDUCED THROMBOCYTOPENIA**

**EPIDEMIOLOGY**

The diagnosis of drug-induced thrombocytopenia is challenging. More than 150 drugs have been implicated (Box 205.2),\textsuperscript{21} but the epidemiology is not well characterized because of the dual lack of consistent, high-quality reporting and diagnostic criteria. This rare disease has an estimated incidence of 10 cases per 1,000,000 patients, but it occurs more frequently in hospitalized patients and in older persons.\textsuperscript{22} Reported incidences of thrombocytopenia induced by specific medications have ranged from 0.0003% with quinine to 1% with gold salts and abciximab. This diagnosis is important to consider because the only effective treatment is discontinuation of the medication. Drug-induced thrombocytopenia does not respond to immunomodulation, as do conditions such as ITP.

Heparin-induced thrombocytopenia (HIT) must be considered separately from all other forms of drug-induced thrombocytopenia. HIT is more common than other drug-induced thrombocytopenias, with an incidence as high as 5% in high-risk populations.\textsuperscript{23} Additionally, it has a much higher rate of both morbidity and mortality from thrombotic complications, which can persist after the heparin is discontinued and platelet levels return to normal. The risk of developing thrombocytopenia is 10 times higher in patients who are exposed to unfractionated heparin, when compared with those receiving low-molecular-weight heparin.\textsuperscript{24,11}

**PATHOPHYSIOLOGY**

In drug-induced thrombocytopenia, the drop in platelets is an immunologic process. The drugs themselves are not immunogenic. When the drug is bound to the platelet, however, the drug-platelet complex induces antibody production. The key feature of most of these antibodies is that they are not true autoantibodies because they do not bind to the platelet if the drug is not bound. Very rarely, drugs can induce true autoantibodies that can bind to the platelet in the absence of the drug. This phenomenon is most commonly seen during treatment with gold salts, but it also occurs with procainamide, sulfonamides, and interferon-\(\alpha\) and -\(\beta\).\textsuperscript{22}

Binding of the antibodies to the platelet or the platelet-drug complex leads to immune destruction of the platelet and thrombocytopenia through the reticuloendothelial system, primarily in the spleen. In addition to the immune destruction of the platelets, the antibodies in HIT lead to platelet activation, which causes thrombosis.

**PRESENTING SIGNS AND SYMPTOMS**

Most patients with drug-induced thrombocytopenia, including HIT, are asymptomatic. Patients presenting with bleeding complications are common in platelet dysfunction. These complications include findings such as petechiae, easy bruising, epistaxis, and other mucocutaneous bleeding. The typical time course is 5 to 7 days after exposure to a new medication. Patients previously sensitized to a medication can have a dramatic and rapid drop in platelets. The development of HIT can, in rare circumstances, be remote from the drug exposure.
In contrast to the other type of drug-induced thrombocytopenia, 20% to 50% of patients with HIT present with thrombotic complications. Of these thromboses, 70% are venous, and 30% are arterial. The clinical presentation of patients with thrombotic complications from HIT depends on the vascular bed that is involved. The venous thromboses are most commonly deep vein thromboses and pulmonary emboli, but they also include cerebral and adrenal venous thromboses. The arterial thromboses are reported in the limbs, aorta, cerebral, and coronary vasculatures.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

The thrombocytopenia of HIT can either be absolute (<150,000/mm³) or relative (decrease of >50% from baseline.) Patients almost universally have detectable levels of antibodies against platelet factor 4. Other drugs with drug-induced thrombocytopenia do not have readily available testing for drug-platelet antibodies.

Because immunologic testing is not often available or available in a timely fashion, the diagnosis and initial management must often be empiric. Drug-induced thrombocytopenia should resolve within several days of discontinuation of the medication.

**TREATMENT**

The most important therapeutic intervention is discontinuation of the offending medication. Most of these antibodies have activity against the platelets only when the drug is bound, thus stressing the importance of identification and discontinuation of the drug. In most patients, the thrombocytopenia resolves without further intervention.

Patients with severe thrombocytopenia or bleeding should be treated with platelet transfusion. Immunomodulating medications such as corticosteroids, IVIG, and plasma transfusion have been tried, without any conclusive evidence supporting their efficacy.

Patients with thromboses from HIT must be treated with direct thrombin inhibitors (e.g., lepirudin, argatroban, bivalirudin). When choosing among these medications, the physician must consider that lepirudin and bivalirudin are renally excreted, whereas argatroban is hepatically metabolized. This distinction is especially important because of the high rate of iatrogenic bleeding complications. Furthermore, because lepirudin is highly immunogenic, patients with recurrent HIT should not be treated with lepirudin more than once. Warfarin monotherapy in active HIT is contraindicated, but warfarin may be started in patients with platelet counts higher than 150,000/mm³ and therapeutic levels of anticoagulation. Care should be taken to remove all sources of heparin, including catheter ports and dialysis tubing.

**FOLLOW-UP, NEXT STEPS OF CARE, AND PATIENT EDUCATION**

The determination of disposition of a patient with suspected drug-induced thrombocytopenia should start with a search for other conditions that cause thrombocytopenia, most importantly sepsis. Next, the implications of discontinuing the medication and the question whether an acceptable alternative exists must be considered. Patients treated as outpatients should have urgent follow-up to evaluate for signs of bleeding and serial blood counts to ensure the resolution of the thrombocytopenia.

**THROMBOCYTOSIS**

**EPIDEMIOLOGY**

Thrombocytosis is usually an incidental finding in a patient in the ED. Most patients have secondary thrombocytosis, from an acute or chronic condition such as infection or malignant disease. Even in the extremes of thrombocytosis with platelet counts greater than 1,000,000/mm³, 88% of patients have reactive thrombocytosis.

The other main cause of thrombocytosis is essential thrombocythemia (ET), which is one of the myeloproliferative disorders. ET is a relatively rare disease with an estimated incidence of 2.5 cases per 100,000 patients. In contrast to reactive thrombocytosis, patients with ET are prone to both bleeding and thrombotic complications.

**PATHOPHYSIOLOGY**

Platelet production and homeostasis are primarily controlled by the effects of thrombopoietin on the megakaryocytes. Thrombocytosis can either be primary or secondary. In primary thrombocytopenia (ET), the thrombocytosis results from the clonal proliferation of megakaryocytes. Secondary thrombocytosis is caused by the effects of various catechols and cytokines, as well as increased production of thrombopoietin in the liver in response to inflammatory stimuli.

**PRESENTING SIGNS AND SYMPTOMS**

Thrombocytosis is typically an incidental finding. Because most patients with thrombocytosis have secondary thrombocytosis, the presenting symptoms relate to the underlying condition and not to the thrombocytosis itself. The underlying conditions can be transient or sustained. Secondary thrombocytosis can be caused by a clinically occult process such as malignant disease or a chronic inflammatory condition. Patients with secondary thrombocytosis do not have any thrombotic or bleeding sequelae even in the extremes of thrombocytopenia unless it is a sequela of the underlying disorder.

Patients with ET can present with both bleeding and thrombotic complications. Thrombotic complications are more common that bleeding complications, with a ratio of 11:1, and arterial thrombosis is more common than venous thrombosis, with a ratio of 3:1.

The bleeding complications are similar to those seen with thrombocytopenia and qualitative platelet disorders. Findings may include petechiae, hematuria, and gastrointestinal bleeding. Counterintuitively, these bleeding complications are more likely to occur in the extremes of thrombocytosis.
The thrombotic complications of ET are common. Fifty percent of patients with ET have at least one thrombotic complication in the first 9 years from diagnosis. The thrombotic complications have an unusual distribution. In addition to deep vein thromboses, patients are at risk for developing venous thromboses of the cerebral, hepatic, and portal veins. Most arterial complications are cerebrovascular, accounting for symptoms ranging from migraine-like symptoms to transient ischemic attack and stroke. Despite its relative rarity, ET is classically associated with digital ischemia and erythromelalgia, which is characterized by patchy burning or throbbing pain in the extremities. Associated skin findings range from mottling, to erythema, to absent. Erythromelalgia can progress to gangrene and necrosis if it is not treated. In addition, patients with ET are at extreme risk for pregnancy-related complications, including fetal growth retardation and recurrent spontaneous abortions, because of placental thromboses.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

No known signs, symptoms, or laboratory findings distinguish ET from secondary thrombocytosis. Because of the lack of diagnostic criteria, ET is a diagnosis of exclusion, and the initial diagnosis and treatment should be focused on excluding an underlying cause of secondary thrombocytosis. ET can be secondary to acute and chronic conditions, medication reactions, stress, and clinically occult conditions. Tests such as C-reactive protein and erythrocyte sedimentation rate, as well as fecal occult blood testing, can point toward an underlying inflammatory or malignant condition.

The main differentiating feature between secondary and ET is that secondary thrombocytosis does not have associated thrombotic or bleeding complications attributable to the thrombocytosis. Even so, that primary disease process can put the patient at increased risk for both thrombotic and bleeding sequelae. Patients with ET are at risk for spontaneous transformation of the disorder into acute leukemia. The main clue to leukemic transformation is involvement of multiple cell lines.

**TREATMENT**

Treatment of ET depends on the presentation. Patients with ET are commonly receiving a combination of aspirin and cytoreductive therapy. Typical agents include hydroxyurea, anagrelide, or interferon-α. Hydroxyurea is teratogenic, and the safety of interferon-α in pregnancy is not known, so patients with ET and newly diagnosed pregnancy should be counseled appropriately.

Patients with symptomatic ET must be treated aggressively. Patients with arterial thrombotic complications should have a combination of aspirin and cytoreductive therapy with hydroxyurea, anagrelide, or interferon-α. In addition, patients should be considered for platelet pheresis especially if they have cerebral and digital ischemia. ED initiation of treatment for asymptomatic patients with suspected ET is not indicated. Patients should be referred to hematology and to their primary care physician for further evaluation.

Patients with secondary thrombocytosis do not need any specific treatment for the thrombocytosis. Diagnostic work-up and treatment should all be directed toward the underlying condition.

**FOLLOW-UP, NEXT STEPS OF CARE, AND PATIENT EDUCATION**

Patients with known ET with either thrombotic or hemorrhagic complications should be admitted. Patients with asymptomatic thrombocytosis that has no clear underlying cause can be treated as outpatients, with coordination with their physicians and a hematologist. Patients with suspected ET should be instructed to return to the ED for any neurologic complaints or unexplained burning or throbbing pain in the extremities or bleeding.

**SUGGESTED READINGS**


**REFERENCES**

References can be found on Expert Consult @ [www.expertconsult.com](http://www.expertconsult.com).
REFERENCES