HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets)

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INTRODUCTION

HELLP is an acronym that refers to a syndrome in pregnant and postpartum individuals characterized by hemolysis with a microangiopathic blood smear, elevated liver enzymes, and a low platelet count. It probably represents a severe form of preeclampsia (table 1A-B), but the relationship between the two disorders remains controversial. HELLP may be a separate disorder from preeclampsia because as many as 15 to 20 percent of patients with HELLP do not have antecedent hypertension or proteinuria [1-3].

Birth eventually leads to resolution of signs and symptoms of HELLP. Maternal complications are primarily related to bleeding, which can include hepatic hemorrhage. Neonatal complications are primarily related to the gestational age at birth, which is commonly preterm.

This topic will focus on the clinical presentation, diagnosis, differential diagnosis, and management of HELLP syndrome. Preeclampsia is reviewed in detail separately.

- (See "Preeclampsia: Clinical features and diagnosis".)
- (See "Preeclampsia: Antepartum management and timing of delivery".)
- (See "Preeclampsia with severe features: Delaying delivery in pregnancies remote from term".)

PREVALENCE

Prevalence ranges from 0.1 of normotensive pregnancies to 1.0 percent of pregnant people with preeclampsia without severe features, depending on the diagnostic criteria used.

RISK FACTORS

- Previous history of HELLP. (See 'Recurrence in subsequent pregnancies' below.)
- Several genetic variants have been associated with an increased risk for HELLP in research studies [4]. (See 'Pathogenesis' below.)

In contrast to preeclampsia, nulliparity is **not** a risk factor for HELLP [5]. Multiparous individuals account for ≥50 percent of affected patients.

PATHOGENESIS

The pathogenesis of HELLP is unclear. If it is a severe form of preeclampsia, it likely has the same origin (see "Preeclampsia: Pathogenesis"). If it is a separate entity, it can still have a similar origin (eg, shallow placentation), but for unknown reasons it may then diverge along a different pathway in which hepatic inflammation and activation of the coagulation system exceeds that in preeclampsia [4,6,7].

A subset of HELLP may be related to thrombotic microangiopathy caused by complement dysregulation (ie, complement-mediated thrombotic microangiopathy [CM-TMA]), which may be treatable without prompt fetal delivery. In a case report of a patient with severe early HELLP, treatment with eculizumab, a targeted inhibitor of complement protein C5, was associated with marked clinical improvement and complete normalization of laboratory parameters for 16 days, after which HELLP recurred [8]. The authors chose this intervention based on the hypothesis that preeclampsia with severe features/HELLP is a systemic inflammatory disorder mediated by the complement cascade and the observation that pregnant individuals with pathogenic variants in complement regulatory proteins appear to be at increased risk for developing preeclampsia with severe features [9]. Further research of possible benefits and harms is needed before such a clinical approach becomes advisable [10].

In less than 2 percent of patients with HELLP, the underlying etiology appears to be related to fetal long-chain 3-hydroxyacyl CoA dehydrogenase (LCHAD) deficiency [11,12]. In one case series, all six pregnancies with fetal LCHAD deficiency developed severe maternal liver disease

(HELLP or acute fatty liver of pregnancy [AFLP]) [13]. These complications probably were not due to chance or maternal heterozygosity for LCHAD deficiency alone because three other pregnancies with unaffected fetuses among these mothers were uncomplicated. In another case series in which 19 fetuses had LCHAD deficiency, 15 mothers (79 percent) developed AFLP or HELLP syndrome during their pregnancies [14]. Although these findings inform theories about the pathogenesis of HELLP, evaluation for genetic variants associated with LCHAD deficiency has no role in clinical management of patients with HELLP. (See "Acute fatty liver of pregnancy", section on 'Fetal long-chain 3-hydroxyacyl CoA dehydrogenase (LCHAD) deficiency'.)

PATHOPHYSIOLOGY

Microangiopathy and activation of intravascular coagulation can account for all of the laboratory findings in HELLP syndrome (see 'Laboratory criteria for diagnosis' below). Hepatic histology may show microvascular fibrin deposition, neutrophilic infiltrate, fatty infiltration, lobular necrosis, and periportal hemorrhage (picture 1) [15]. Although kidney dysfunction is not an essential diagnostic criterion, microvascular dysfunction may also occur in the kidney and may increase its vulnerability to an ischemic insult [16].

PATIENT PRESENTATION

Signs and symptoms — HELLP has a variable presentation; the frequency of typical signs and symptoms is shown in the table (table 2) [17]. Symptoms typically present over a short period of time and progressively worsen.

Most patients have upper abdominal pain, which is probably the most common symptom. It may be localized to the midepigastrium, right upper quadrant, or below the sternum and the area may be tender on physical examination [18]. The pain is often severe and usually constant but may be fluctuating and colicky. Many patients also have nausea, vomiting, and generalized malaise, which may be mistaken for a nonspecific viral illness or viral hepatitis, particularly if the serum aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) levels are markedly elevated. Less common symptoms include headache, visual changes, jaundice, and ascites.

On physical examination, hypertension (defined as blood pressure ≥140/90 mmHg) and proteinuria are present in approximately 85 percent of cases, but it is important to note that either or both may be absent in patients with HELLP [17].

Serious maternal morbidity may be present at initial presentation or develop shortly thereafter. This includes placental abruption, acute kidney injury, pulmonary edema, subcapsular or intraparenchymal liver hematoma, and retinal detachment [18]. Disseminated intravascular coagulation (DIC), if present, is usually associated with abruption, severe peripartum bleeding, or fulminant liver failure. (See 'Maternal outcome' below.)

Thrombocytopenia-related bleeding (mucosal, hematuria, petechial hemorrhages, ecchymosis) is an unusual presentation [17].

Gestational age at onset — Symptoms typically develop between 28 and 37 weeks of gestation, but onset in the late second trimester or at term/postpartum is also common. In a series including over 440 pregnancies complicated by HELLP, 70 percent of cases occurred before birth, approximately 80 percent of these occurred before <37 weeks, approximately 20 percent occurred before 28 weeks, and <3 percent occurred at 17 to 20 weeks [18].

In the 30 percent of cases that occurred postpartum, most were diagnosed within 48 hours after birth, but occasionally as long as seven days; 80 percent had evidence of preeclampsia before birth. Why some cases of HELLP and preeclampsia develop postpartum is unknown and confusing since expulsion of the placenta initiates resolution of the disease in most patients.

DIAGNOSTIC EVALUATION

In pregnant individuals with characteristic symptoms of HELLP (eg, right upper quadrant/midepigastric pain, nausea, vomiting, malaise) and/or new-onset hypertension in the second half of pregnancy or first postpartum week, we order the laboratory tests needed to establish/exclude the diagnosis of HELLP. Because in rare cases of preeclampsia severe persistent upper abdominal pain may precede laboratory abnormalities by several hours, repeating the laboratory tests in four to six hours may be helpful unless another cause for the pain has been determined [19].

Laboratory work-up includes [17]:

- Complete blood count
- Peripheral smear
- Aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin
- Creatinine

A lactate dehydrogenase (LDH) level (as a marker for hemolysis) is needed to make a diagnosis of HELLP in some diagnostic protocols, thus it should be obtained at the same time as the initial

laboratory work-up or secondarily in patients with elevated aminotransferases. In patients with elevated aminotransferases, the author of this topic obtains haptoglobin and LDH levels and coagulation studies (fibrinogen, prothrombin time, activated partial thromboplastin time). The coagulation studies are obtained to rule out acute fatty liver of pregnancy (AFLP) in the absence of abruption and severe thrombocytopenia.

DIAGNOSIS

The diagnosis of HELLP is based upon the presence of all of the laboratory abnormalities comprising its name (hemolysis with a microangiopathic blood smear [fragmented red blood cells; ie, schistocytes, burr cells], elevated liver enzymes, and low platelet count) in a pregnant/postpartum patient.

Pregnant/postpartum patients who have some of the typical laboratory abnormalities but do not have all of the laboratory criteria described below are considered to have partial HELLP (eg, cases without hemolysis have been termed ELLP) [5]. These patients may progress and eventually meet all laboratory criteria.

Laboratory criteria for diagnosis

Tennessee classification — The author of this topic requires the presence of all the following criteria to diagnose HELLP (called Tennessee classification) [20]:

- Hemolysis, established by at least two of the following:
  - Peripheral smear with schistocytes and burr cells (picture 2).
  - Serum bilirubin ≥1.2 mg/dL (20.52 micromol/L).
  - Low serum haptoglobin (≤25 mg/dL) or lactate dehydrogenase (LDH) ≥2 times the upper level of normal (based on laboratory-specific reference ranges).
  - Severe anemia unrelated to blood loss. (Severe anemia in pregnancy can be defined as hemoglobin level <8 to 10 g/dL, depending on the trimester). (See "Anemia in pregnancy", section on 'Definition of anemia'.)
- Elevated liver enzymes:
  - Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥2 times the upper level of normal (based on laboratory-specific reference ranges). (The use of twice the upper limit of normal threshold was chosen, in part, to avoid problems related to differences in assays, which may result in an elevated absolute value in one hospital that is considered near normal in another).

- Low platelets: <100,000 cells/microL

In HELLP, an elevated LDH level is a nonspecific marker that can be associated with severe hemolysis, acute hepatocellular injury, or both. The total bilirubin level is increased as a result of an increase in the indirect (unconjugated) fraction from hemolysis. Haptoglobin level is a specific marker of hemolysis: 25 mg/dL provides the best cutoff between hemolytic and nonhemolytic disorders. (See "Diagnosis of hemolytic anemia in adults", section on 'High LDH and bilirubin; low haptoglobin'.)

Other diagnostic criteria

- **ACOG** – The American College of Obstetricians and Gynecologists (ACOG) suggests slightly different diagnostic criteria and acknowledges the absence of clinical consensus among experts [21]. ACOG requires all of the following for diagnosis of HELLP:
  - LDH ≥600 international units/L
  - AST and ALT elevated more than twice the upper limit of normal
  - Platelet count <100,000 cells/microL
- **Mississippi classification** – Some clinicians use the Mississippi classification system, which is based on severity of thrombocytopenia [22]:
  - Class 1 – Platelet count ≤50,000 cells/microL plus LDH >600 international units/L and AST or ALT ≥70 international units/L
  - Class 2 – Platelet count >50,000 but ≤100,000 cells/microL plus LDH >600 international units/L and AST or ALT ≥70 international units/L
  - Class 3 – Platelet count >100,000 but ≤150,000 cells/microL plus LDH >600 international units/L and AST or ALT ≥40 international units/L

DIFFERENTIAL DIAGNOSIS

HELLP may occasionally be confused with other diseases complicating pregnancy. The four major disorders in differential diagnosis are acute fatty liver of pregnancy (AFLP), thrombotic thrombocytopenic purpura (TTP), pregnancy-related complement-mediated thrombotic microangiopathy (CM-TMA), and systemic lupus erythematosus. Distinguishing features of HELLP and these other disorders are shown in the tables (table 3A-B).

There is also overlap with preeclampsia with severe features, which may not be a separate disease [23,24]. In HELLP, angiopathy (including thrombotic microangiopathy and microangiopathic hemolytic anemia) and liver dysfunction are marked, and the magnitude of hypertension is not highly correlated with the level of angiopathy and liver dysfunction. By contrast, most cases of severe preeclampsia have severe hypertension; thrombocytopenia and liver dysfunction, although present, are not as markedly abnormal as in HELLP. However, the clinical and histologic features are so similar that establishing the correct diagnosis may not be possible; furthermore, HELLP can occur concurrently with these disorders.

Likewise, SARS-CoV-2 infection during pregnancy has been associated with a significant increase in the odds of preeclampsia with severe features, eclampsia, and HELLP [25]. The laboratory abnormalities of COVID-19 and HELLP can overlap, making diagnosis of HELLP difficult in infected patients. (See "COVID-19: Overview of pregnancy issues", section on 'Risk of preeclampsia'.)

Differential diagnosis is discussed in more detail separately. (See "Hypertensive disorders in pregnancy: Approach to differential diagnosis".)

MANAGEMENT

Our general approach is shown in the algorithm (algorithm 1).

Site of care — Because of the potential for life-threatening maternal complications (eg, liver rupture, acute kidney injury, disseminated intravascular coagulation [DIC]), which can develop rapidly and necessitate preterm birth, patients with HELLP should be managed at a tertiary care center with appropriate levels of maternal and neonatal intensive care, when possible. (See 'Maternal outcome' below and 'Fetal/neonatal outcome' below.)

The risk for serious morbidity correlates with increasing severity of maternal symptoms and laboratory abnormalities [22,26]. In a report of four patients with aspartate aminotransferase (AST) levels >2000 international units/L and lactate dehydrogenase (LDH) levels >3000 international units/L, all had disordered mental status, jaundice, intense hemolysis, and severe hypertension; one had multiorgan failure; and two died [26].

Treatment of severe hypertension — Severe hypertension, if present, requires prompt administration of one or more of the antihypertensive medications in this table (table 4) to reduce the risk of stroke. The approach to antihypertensive therapy is the same as that for preeclampsia (algorithm 2). (See "Treatment of hypertension in pregnant and postpartum patients", section on 'Acute therapy of severe hypertension'.)

In hemodynamically stable patients, intravenous fluids are administered conservatively, as in patients with preeclampsia. (See "Preeclampsia: Intrapartum and postpartum management and long-term prognosis", section on 'Fluids'.)

Hepatic imaging in patients with severe right upper quadrant/epigastric pain — These patients may have hepatic bleeding or hepatic swelling portending liver rupture. The pain may be associated with hypotension and tachycardia; shoulder, chest, back, or neck pain; dyspnea or pain on inspiration; nausea/vomiting; and/or abdominal distention beyond that expected for the pregnant state [27-29]. In the overall population of patients with HELLP, the incidence of subcapsular hematoma is estimated to be 0.9 to 1.6 percent [18,30]. The aminotransferases in patients with hepatic bleeding are usually modestly elevated, but values of 4000 to 5000 international units/L can occasionally be seen.

Because of the poor correlation between the magnitude of laboratory abnormalities and liver histology [15], patients with severe symptoms (eg, persistent severe midepigastric pain not responding to opioids, tenderness on liver palpation, shoulder or neck pain, pain on inspiration) should undergo an appropriate imaging study expeditiously to look for hepatic bleeding, even if liver enzymes are not severalfold above the normal range, and to assess for other pathology [20,27,28]. Bedside ultrasound screening (focused assessment with sonography for trauma [FAST]) is a good initial study, followed by formal ultrasound examination and computed tomography (CT) or magnetic resonance imaging (MRI), when needed for clinical decision making. Imaging using CT (image 1 and image 2) or MRI (image 3 and image 4) is more accurate than ultrasound for detecting a liver hematoma and rupture but may not be as readily available and CT exposes the fetus to ionizing radiation. This is not an issue with noncontrast MRI, which is felt to be safe for the fetus. Issues regarding CT, MRI, and contrast in pregnant and lactating patients are discussed in more detail separately. (See "Diagnostic imaging in pregnant and lactating patients".)

Management of hepatic bleeding — Hepatic bleeding may remain contained or the liver may rupture, resulting in hemorrhage into the peritoneal cavity. Rupture is a life-threatening complication for both the mother and fetus, especially if diagnosis and treatment are delayed.

- The patient should be supported with volume replacement and transfusion of blood and blood products, as needed.
    - We transfuse red blood cells if the hemoglobin is <7 g/dL and/or if the patient has ecchymosis, severe hematuria, or suspected abruption.
    - Actively bleeding patients with thrombocytopenia should be transfused with platelets. Platelet transfusion may be indicated to prevent excessive bleeding during birth if the

platelet count is less than 20,000 cells/microL, but the threshold for prophylactic platelet transfusion in this setting is controversial. The decision depends on patient-specific factors; consultation with the hematology service may be helpful. It is also useful to notify the blood bank that platelet transfusions may be required.

If cesarean birth is planned, platelet transfusion may be required. Some experts recommend platelet transfusion to achieve a preoperative platelet count greater than 40,000 to 50,000 cells/microL [17], but the minimum count before a neuraxial procedure is controversial and depends on factors in addition to platelet concentration. (See "Platelet transfusion: Indications, ordering, and associated risks", section on 'Preparation for an invasive procedure' and "Adverse effects of neuraxial analgesia and anesthesia for obstetrics", section on 'Neuraxial analgesia and low platelets'.)

- Prompt cesarean birth is indicated when the patient is hemodynamically stable and severe anemia and coagulopathy, if present, have been corrected. We stabilize the patient before the cesarean, even in cases with nonreassuring fetal heart rate patterns or a low biophysical profile score. A team experienced in liver trauma surgery should be consulted during maternal stabilization and prior to delivery [31].

  A hematoma that is unruptured and not expanding on initial imaging may be managed conservatively. The appearance of the hematoma depends on the age of the hematoma and the duration of and extension of the bleed. Subacute blood on ultrasound is echogenic.

  Repeat ultrasound evaluation of the liver is performed 48 hours after the delivery. If liver findings remain stable, repeat imaging is performed again in one week and at six weeks postpartum. It may take months for a hematoma to resolve completely [20,27]. Patients with resolving laboratory abnormalities may be discharged home with outpatient follow-up.

- An expanding or ruptured hematoma requires operative management, which includes packing, drainage, hepatic artery ligation, and/or resection of affected areas of the liver. For patients with intractable hemorrhage despite these interventions, administration of recombinant factor VIIa has been successful in case reports [32]. Liver transplantation because of massive spontaneous hepatic rupture or acute liver failure has been life-saving in case reports [33-36].

- Similar considerations apply to postpartum patients with hepatic bleeding. Surgical intervention is always required for those with hemodynamic instability and generally required for those with persistent bleeding, increasing pain, or continued expansion of the

hematoma on serial ultrasound examinations [37]; however, percutaneous embolization of the hepatic arteries is a reasonable first-line therapy in patients who are hemodynamically stable [38,39].

DIC, pulmonary edema, or acute kidney injury — Patients with disseminated intravascular coagulation (DIC), pulmonary edema, or acute kidney injury should be stabilized using standard therapies.

- (See "Disseminated intravascular coagulation (DIC) during pregnancy: Clinical findings, etiology, and diagnosis" and "Disseminated intravascular coagulation (DIC) during pregnancy: Management and prognosis".)
- (See "Acute respiratory failure during pregnancy and the peripartum period", section on 'Pulmonary edema'.)
- (See "Acute kidney injury in pregnancy".)

Magnesium sulfate — Magnesium sulfate is initiated at the time of admission to the labor and delivery unit and continued for 24 hours postpartum to prevent maternal seizures. (See "Preeclampsia: Intrapartum and postpartum management and long-term prognosis", section on 'Seizure prophylaxis'.)

It also provides fetal/neonatal neuroprotection when administered to pregnancies <32 weeks of gestation. (See "Neuroprotective effects of in utero exposure to magnesium sulfate".)

Role of therapeutic plasma exchange — Therapeutic plasma exchange has no benefit in patients with HELLP, but is the mainstay of treatment for patients with thrombotic thrombocytopenic purpura (TTP). Because patients with HELLP and those with TTP have both microangiopathic hemolysis and thrombocytopenia, making the correct diagnosis and, in turn, initiating the appropriate treatment can be challenging. Differential diagnosis is discussed in more detail separately. (See "Hypertensive disorders in pregnancy: Approach to differential diagnosis", section on 'Thrombotic microangiopathy: TTP and HUS'.)

Delivery timing

Prompt delivery (preferred approach for most patients) — Delivery is the cornerstone of therapy for HELLP and is the only effective treatment. After maternal stabilization, the consensus among experts is that prompt delivery is indicated for pregnancies ≥34 weeks of gestation and pregnancies <34 weeks with severe complications (eg, abruption, hepatic bleeding, DIC, acute kidney injury, nonreassuring fetal status, pulmonary edema, fetal death, seizure, stroke) [17,40]. In pregnancies <34 weeks without severe complications, delivery can be

delayed for 48 hours for antenatal corticosteroid administration (see 'Delayed delivery for up to 48 hours in selected pregnancies <34 weeks' below). However, pregnancies that have not reached a stage of fetal maturity that ensures a reasonable chance of extrauterine survival after a course of steroids are delivered promptly since expectant management is associated with a high risk of developing maternal complications without significant improvement in perinatal prognosis.

We do not manage patients with HELLP syndrome expectantly at any gestational age and consider delaying delivery for more than 48 hours investigational. There are few studies on the outcome of expectant management of HELLP syndrome. In these studies, the laboratory abnormalities of HELLP syndrome reversed in a subset of patients managed expectantly, and serious maternal complications were uncommon with careful maternal monitoring and timely intervention. However, the aim of expectant management is to improve neonatal morbidity and mortality. There is no evidence demonstrating improvement in overall perinatal outcome with expectant management compared with pregnancies delivered after a course of antenatal corticosteroids and no maternal benefits from expectant management. The following studies support our approach:

- In a study that treated 128 patients with HELLP <34 weeks of gestation with volume expansion and pharmacologic vasodilation under invasive hemodynamic monitoring, delivery was necessitated in 22 out of 128 (17 percent) of patients within 48 hours; the remaining patients had a median prolongation of pregnancy of 15 days [41]. Although there was no maternal mortality or serious maternal morbidity and more than one-half (55 out of 102) of the patients had complete reversal of their laboratory abnormalities with expectant management, 11 fetal and 7 neonatal deaths occurred.

- In another series, 41 patients with HELLP <35 weeks of gestation were managed expectantly [42]. Delivery was required within 48 hours in 14 out of 41 (34 percent), the remaining patients had a median prolongation of pregnancy of three days, and more than one-half (15 out of 27) had compete reversal of their laboratory abnormalities [42]. However, there were 10 fetal deaths.

Delayed delivery for up to 48 hours in selected pregnancies <34 weeks — Delaying delivery for up to 48 hours for administration of a course of antenatal corticosteroids can improve neonatal outcome in pregnancies <34 weeks that have reached a stage of fetal maturity that ensures a reasonable chance of extrauterine survival, but this benefit must be balanced against the maternal risk of developing complications in an ongoing pregnancy [17,40]. Although a short delay in delivery for betamethasone administration does not appear to increase maternal or fetal morbidity or mortality [43], we advise not attempting to delay delivery beyond 48 hours

because disease progression usually occurs, sometimes with rapid maternal deterioration. Evidence of the efficacy of antenatal corticosteroids is reviewed separately. (See "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery", section on 'Evidence of efficacy'.)

We do not give betamethasone for fetal lung maturity in pregnancies with gestational age ≥34 weeks since no patients with HELLP were enrolled in randomized trials of the efficacy of steroids after 34 weeks. Furthermore, the marginal fetal benefit of steroids beyond 34 weeks is likely less than the maternal risk of expectant management. During administration of betamethasone, all patients are kept in the labor and delivery unit with continuous fetal monitoring. (See "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery", section on 'Long-term harms'.)

The author of this topic repeats the complete blood count (including platelet count) at 24 and 48 hours after administering steroids and more often if clinical deterioration is suspected. The American College of Obstetricians and Gynecologists (ACOG) recommends laboratory testing at least at 12-hour intervals until birth and in the postpartum period [21]. This information is useful when considering whether to administer red blood cell transfusions, whether neuraxial anesthesia can be performed safely (see "Adverse effects of neuraxial analgesia and anesthesia for obstetrics", section on 'Neuraxial analgesia and low platelets'), and whether platelet transfusion is indicated (See 'Management of hepatic bleeding' above.).

Choosing the route of birth — Vaginal birth is desirable in the absence of standard indications for cesarean birth (eg, breech, nonreassuring fetal status) and hepatic bleeding.

We induce patients with HELLP uncomplicated by hepatic bleeding regardless of gestational age when the cervix is favorable. When the cervix is unfavorable, we believe cesarean birth is probably preferable to induction in pregnancies less than 30 to 32 weeks of gestation, especially if signs of fetal compromise (growth restriction, oligohydramnios) are present. Induction of these pregnancies, even with use of cervical ripening agents, generally has a high failure rate and is often prolonged, thereby potentially exposing the mother and fetus to a higher risk of complications from severe HELLP syndrome [17]. (See "Induction of labor with oxytocin" and "Induction of labor: Techniques for preinduction cervical ripening".)

In patients with HELLP complicated by hepatic bleeding, we suggest cesarean birth because the increased intrabdominal pressure during vomiting and pushing can lead to further hepatic bleeding, even in patients who have undergone embolization by interventional radiology. Performing cesarean avoids this and allows visual evaluation of the source and amount of bleeding. Although the consequences of vaginal birth in patients with liver hematoma has not

been studied, cesarean birth has been recommended for patients with esophageal varices as most cases of maternal mortality due to variceal hemorrhage occurred during vaginal birth [44].

Anesthesia/analgesia — Thrombocytopenia and coagulation abnormalities may preclude use of neuraxial anesthesia for labor and birth. The minimum platelet count necessary to safely perform neuraxial anesthesia is unknown, and practice varies. Use of neuraxial and general anesthesia for these patients is reviewed separately. (See "Anesthesia for the patient with preeclampsia", section on 'Coagulation'.)

Opioids administered intravenously provide some pain relief without risk of maternal bleeding, which may occur with intramuscular administration or with placement of neuraxial anesthesia, removal of a neuraxial catheter, or placement of a pudendal nerve block. However, there is no contraindication to perineal infiltration of an anesthetic for performing an episiotomy or repairing the perineum. (See "Pharmacologic management of pain during labor and delivery".)

Performing cesarean birth and exploring the abdomen — If preoperative imaging was not performed in a patient with findings suggestive of liver hematoma, we perform a midline skin incision and very gently palpate the liver to assess for the presence of an unruptured hematoma, after extracting the fetus and placenta.

Because of the increased risk of subfascial and wound hematoma in patients with thrombocytopenia who undergo cesarean birth, the author of this topic places a subfascial drain and leaves the skin incision open for the first 48 postoperative hours [3]. Some surgeons place a subfascial and/or suprafascial drain and close the incision with staples, so it is easy to open partially if a hematoma develops. The management of the abdominal wall incision after cesarean should be individualized, depending on the surgeon's assessment of risk of hematoma/seroma development.

Is there a role for dexamethasone in treatment of HELLP? — We do not treat patients with HELLP syndrome with dexamethasone. The two largest, randomized, double-blind, placebo-controlled trials evaluating the use of dexamethasone to improve maternal outcome in patients with HELLP syndrome did not establish a benefit [45,46], in contrast to initial observational studies and small randomized trials that suggested more rapid improvement in maternal laboratory and clinical parameters [47-50].

In a meta-analysis of 11 trials (550 participants) comparing corticosteroid treatment with placebo/no treatment in HELLP, steroid administration did not lead to a convincing reduction in maternal death (risk ratio [RR] 0.95, 95% CI 0.28-3.21), maternal death or severe maternal morbidity (RR 0.27, 95% CI 0.03-2.12), or perinatal/infant death (RR 0.64, 95% CI 0.21-1.97), but

the standardized mean difference in platelet count favored the steroid group (0.67, 95% CI 0.26-1.10) [51].

The use of dexamethasone rather than betamethasone to promote fetal pulmonary maturity is a separate issue. (See "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery", section on 'Betamethasone or dexamethasone?'.)

POSTPARTUM

All of the signs and symptoms of HELLP, including subcapsular hematoma and liver rupture, can initially appear in the postpartum period [52]. Management is similar to that of HELLP diagnosed before birth, except fetal status no longer needs to be considered.

Maternal care — Patients who are critically ill or at substantial risk for developing serious complications can benefit from transfer to an intensive care setting, rather than a postpartum unit. Potential indications for intensive monitoring include threatened or actual liver rupture or fulminant liver failure, disseminated intravascular coagulation (DIC), acute kidney injury, massive transfusion, transfusion-related acute lung injury, and cardiac ischemia or cardiomyopathy.

Supportive care may involve oxygenation and ventilation (ie, supplemental oxygen or mechanical ventilation), sedation, pain control, hemodynamic support (ie, vasopressors), intensive monitoring, volume management (ie, intravenous fluids or diuretics), nutritional support, stress ulcer prophylaxis, and venous thromboembolism prophylaxis. (See "Critical illness during pregnancy and the peripartum period".)

Laboratory monitoring — Laboratory results may initially worsen in the 48 hours following birth (eg, platelet count usually decreases by 40 percent/day, hematocrit falls, and liver enzymes increase) [53], which is the reason that the American College of Obstetricians and Gynecologists (ACOG) recommends laboratory testing at least at 12-hour intervals in the postpartum period [21]. We stop checking laboratory values once they are clearly beginning to stabilize. In the absence of bleeding or complications related to HELLP, there is no benefit for further serial evaluation of platelet counts or liver enzymes. Although liver enzymes return to normal or substantially decrease by the fourth postpartum day [45,46,53,54], in one report, total bilirubin levels were elevated in 20 percent of patients who had liver function tests checked 3 to 101 months after giving birth [55].

An upward trend in platelet count and a downward trend in lactate dehydrogenase (LDH) concentration are usually seen by the fourth postpartum day in the absence of complications. In a series of 158 patients with HELLP syndrome, platelet counts decreased until 24 to 48 hours after birth, while serum LDH concentration usually peaked at this time [53]. In all patients who recovered, a platelet count greater than 100,000 cells/microL was achieved by the sixth postpartum day or within 72 hours of the platelet nadir. Others have reported similar findings [54]. The platelet count rebound can overshoot; one group reported values of 413,000 to 871,000 cells/microL [56].

If the platelet count continues to fall and LDH continues to rise after the fourth postpartum day, then diagnoses other than HELLP syndrome (eg, primary thrombotic microangiopathy) should be considered [21]. However, recovery can be delayed in patients with particularly severe HELLP, such as those with DIC, platelet count less than 20,000 cells/microL, renal dysfunction, or ascites [17,57]. These patients are at risk of developing pulmonary edema and acute kidney injury.

OUTCOME AND PROGNOSIS

Maternal outcome — The outcome for patients with HELLP is generally good; however, serious complications are relatively common. In the author's series of 437 patients with HELLP syndrome at a tertiary care facility, the following complications were observed [18]:

- Bleeding – 55 percent required transfusions with blood or blood products; 2 percent required laparotomies for major intraabdominal bleeding
- Disseminated intravascular coagulation (DIC) – 21 percent
- Placental abruption – 16 percent
- Acute kidney injury – 8 percent
- Pulmonary edema – 6 percent
- Subcapsular liver hematoma (or hepatic rupture) – 1 percent
- Retinal detachment – 1 percent
- Intracerebral hemorrhage – <1 percent
- Death – 1 percent

Many of these complications are interdependent (eg, abruption is a common obstetric etiology of DIC, which, in turn, may induce acute kidney injury, which may lead to pulmonary edema; massive bleeding from the liver, postpartum uterine atony, or lacerations could also lead to DIC).

Additional complications that have been reported in other series include adult respiratory distress syndrome, sepsis, stroke, cerebral hemorrhage and edema, and hepatic infarction (in patients with antiphospholipid syndrome) [5,58,59]. Wound complications secondary to bleeding and hematomas are common in patients with thrombocytopenia.

HELLP with or without acute kidney injury does not affect long-term kidney function [60,61]. Similarly, there are no ongoing hepatic sequelae following recovery from hepatic bleeding with/without rupture.

Fetal/neonatal outcome — The neonatal and long-term prognoses are most strongly associated with gestational age at birth and birth weight [62-70]. Preterm birth is common (70 percent; with 15 percent of births before 27 weeks) [62]. Leukopenia, neutropenia, and thrombocytopenia may be observed in the neonate but appear to be related to fetal growth restriction, preterm birth, and maternal hypertension rather than HELLP [64]. Maternal HELLP does not affect fetal/neonatal liver function.

The overall perinatal mortality rate is 7 to 20 percent; complications of preterm birth, fetal growth restriction, and abruption are the leading causes of perinatal death [17,63]. The severity of hemolysis, liver disfunction, and thrombocytopenia does not correlate with the risk of fetal demise.

Recurrence in subsequent pregnancies — The risk of recurrent HELLP was about 4 percent for patients who were normotensive before onset of the syndrome, in a long-term study of 139 patients with subsequent pregnancies [71]. However, these patients were at increased risk for other placenta-mediated obstetric complications. In a meta-analysis of individual patient data from 512 patients with HELLP who became pregnant again, 7 percent developed HELLP, 18 percent developed preeclampsia, and 18 percent developed gestational hypertension in a subsequent pregnancy [72].

In a subsequent Norwegian registry-based study of 577 patients with HELLP in their first pregnancy and then a second pregnancy, 24 percent developed hypertensive disorders of pregnancy that included either HELLP syndrome, preeclampsia, pregnancy-induced hypertension, or eclampsia in the second pregnancy compared with 3.6 percent of patients with no HELLP in their first pregnancy [73]. The study did not provide results for recurrent HELLP syndrome alone. The risk of recurrence of hypertensive disorders of pregnancy was higher in patients with preterm versus term HELLP in the first pregnancy (30.3 versus 16.5 percent).

Prevention — There is no evidence that any therapy prevents recurrent HELLP syndrome, but data are limited. The author considers HELLP syndrome a form of severe preeclampsia and prescribes low-dose aspirin during the second and third trimesters in future pregnancies to

reduce the risk of preeclampsia. Evidence for use of low-dose aspirin for prevention of preeclampsia is discussed separately. (See "Preeclampsia: Prevention", section on 'Low-dose aspirin'.)

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: Hypertensive disorders of pregnancy".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: HELLP syndrome (The Basics)" and "Patient education: High blood pressure and pregnancy (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Clinical presentation** – The most common clinical presentation of HELLP syndrome (hemolysis with a microangiopathic blood smear, elevated liver enzymes, and low platelet count) is abdominal pain and tenderness in the midepigastrium, right upper quadrant, or below the sternum (table 2). Most cases are diagnosed between 28 and 36 weeks of gestation, but symptoms may present up to seven days postpartum. (See 'Patient presentation' above.)

- **Diagnosis** – The diagnosis of HELLP is based on the presence of all of the following criteria (Tennessee classification) (see 'Diagnosis' above):
  - Hemolysis, established by at least two of the following:
    - Peripheral smear with schistocytes and burr cells (picture 2)
    - Serum bilirubin ≥1.2 mg/dL (20.52 micromol)
    - Low serum haptoglobin or lactate dehydrogenase (LDH) ≥2 times the upper level of normal (based on laboratory-specific reference ranges)
    - Severe anemia, unrelated to blood loss
  - Elevated liver enzymes:
    - Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥2 times the upper level of normal (based on laboratory-specific reference ranges)
  - Low platelets: <100,000 cells/microL
- **Differential diagnosis** – The four major disorders in differential diagnosis are acute fatty liver of pregnancy (AFLP), thrombotic thrombocytopenic purpura (TTP), pregnancy-related hemolytic-uremic syndrome, and systemic lupus erythematosus. All have features that overlap with HELLP (table 3A-B). (See 'Differential diagnosis' above.)
- **Management** – The initial steps are to assess the mother and fetus and stabilize patients who are unstable. Because of the potential for life-threatening maternal complications, which can develop rapidly and necessitate preterm birth, patients with HELLP should be managed at a tertiary care center with appropriate levels of maternal and neonatal intensive care. Our general approach to management is shown in the algorithm (algorithm 1). (See 'Management' above.)
  - **Severe hypertension** – Severe hypertension, if present, requires prompt administration of one or more of the antihypertensive medications in this table (table 4) to reduce the risk of stroke. The approach to antihypertensive therapy is the same as that for preeclampsia (algorithm 2). This approach and supporting evidence is available separately. (See "Treatment of hypertension in pregnant and postpartum patients", section on 'Acute therapy of severe hypertension'.)
  - **Hepatic imaging and management of hepatic bleeding** – Patients with severe right upper quadrant/epigastric pain should undergo hepatic imaging as the pain may be due to hepatic bleeding, which may remain contained or rupture the liver capsule. Management of hepatic bleeding involves volume replacement and transfusion of

blood and blood products, as needed. Prompt cesarean delivery is indicated once the patient is hemodynamically stable and severe anemia and coagulopathy, if present, have been corrected.

A hematoma that is unruptured and not expanding may be managed conservatively. An expanding or ruptured hematoma requires operative management, which includes packing, drainage, hepatic artery ligation, and/or resection of affected areas of the liver. A team experienced in liver trauma surgery should be consulted during maternal stabilization and prior to delivery. (See 'Hepatic imaging in patients with severe right upper quadrant/epigastric pain' above.)

- Magnesium sulfate – Magnesium sulfate is initiated at the time of admission to the labor and delivery unit and continued for 24 to 48 hours postpartum to prevent maternal seizures. It also provides fetal/neonatal neuroprotection. The use of magnesium sulfate for these indications and evidence of efficacy of magnesium sulfate are available separately. (See "Preeclampsia: Intrapartum and postpartum management and long-term prognosis", section on 'Seizure prophylaxis' and "Neuroprotective effects of in utero exposure to magnesium sulfate".)

- **Timing of delivery**

  - **Pregnancies with serious complications** – Pregnancies with serious maternal or fetal complications (eg, abruption, hepatic bleeding, disseminated intravascular coagulation [DIC], acute kidney injury, nonreassuring fetal status, pulmonary edema) require prompt delivery. (See 'Prompt delivery (preferred approach for most patients)' above.)

  - **Pregnancies ≥34 weeks without serious complication** – For pregnancies ≥34 weeks of gestation without serious maternal or fetal complications, we suggest prompt delivery rather expectant management (**Grade 2C**). In this population, the potential risks of preterm birth or iatrogenic term birth are outweighed by the risk of developing serious complications associated with HELLP syndrome. (See 'Prompt delivery (preferred approach for most patients)' above.)

  - **Pregnancies <34 weeks without serious complications**

    - For pregnancies <34 weeks without serious maternal or fetal complications and at a stage of fetal maturity that ensures a reasonable chance of extrauterine survival, we suggest delaying delivery for 48 hours for administration of a course of antenatal corticosteroids rather than prompt delivery (**Grade 2C**). (See 'Delayed

delivery for up to 48 hours in selected pregnancies <34 weeks' above and 'Prompt delivery (preferred approach for most patients)' above.)

- For preterm pregnancies that have not reached a stage of fetal maturity that ensures a reasonable chance of extrauterine survival, we suggest prompt delivery (**Grade 2C**). Expectant management is associated with a high risk of developing maternal complications without significant improvement in perinatal prognosis. (See 'Prompt delivery (preferred approach for most patients)' above.)

- **Route of birth** – Vaginal birth is desirable in the absence of standard indications for cesarean birth and hepatic bleeding (see 'Choosing the route of birth' above). However:

  - For pregnancies less than 30 to 32 weeks with an unfavorable cervix, we suggest cesarean birth (**Grade 2C**). These patients are likely to have a prolonged induction if vaginal birth is attempted.

  - For patients with hepatic bleeding, we suggest cesarean birth (**Grade 2C**). The intrabdominal pressure during vomiting and pushing can lead to further hepatic bleeding.

- **Outcome/prognosis**

  - **Maternal** – The outcome for mothers with HELLP syndrome is generally good, but serious complications such as abruption, acute kidney injury, subcapsular liver hematoma or hepatic rupture, pulmonary edema, hemorrhage, retinal detachment, and death may occur. (See 'Maternal outcome' above.)

    Future pregnancies are at increased risk for developing HELLP, preeclampsia, and gestational hypertension. (See 'Recurrence in subsequent pregnancies' above.)

  - **Pediatric** – The short-term and long-term pediatric prognoses are primarily related to the gestational age at delivery and birth weight. Maternal HELLP does not affect fetal/neonatal liver function. (See 'Fetal/neonatal outcome' above.)

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Topic 6778 Version 68.0

GRAPHICS

Diagnostic criteria for preeclampsia

Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on at least 2 occasions at least 4 hours apart after 20 weeks of gestation in a previously normotensive patient AND the new onset of 1 or more of the following*:
▪ Proteinuria ≥0.3 g in a 24-hour urine specimen or protein/creatinine ratio ≥0.3 (30 mg/mmol) in a random urine specimen or dipstick ≥2+ if a quantitative measurement is unavailable
▪ 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 kidney disease
▪ Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory
▪ Pulmonary edema
▪ New-onset and persistent headache not accounted for by alternative diagnoses and not responding to usual doses of analgesics¶
▪ Visual symptoms (eg, blurred vision, flashing lights or sparks, scotomata)

Preeclampsia is considered superimposed when it occurs in a patient with chronic hypertension. Superimposed preeclampsia is characterized by worsening or resistant hypertension (especially acutely), the new onset of proteinuria or a sudden increase in proteinuria, and/or significant new end-organ dysfunction in a patient with chronic hypertension. It typically occurs after 20 weeks of gestation or postpartum.

Definitions/diagnostic criteria for preeclampsia are generally similar worldwide except the International Society for the Study of Hypertension in Pregnancy definition also includes signs of uteroplacental dysfunction (eg, fetal growth restriction, abnormal angiogenic markers, abnormal umbilical artery Doppler, abruption, fetal demise).

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* If systolic blood pressure is ≥160 mmHg and/or diastolic blood pressure is ≥110 mmHg, confirmation within minutes is sufficient.

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

Adapted from:

1. *American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin No. 222: Gestational Hypertension and Preeclampsia. Obstet Gynecol 2020; 135:e237.*
2. *Magee LA, Brown MA, Hall DR, et al. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. Pregnancy Hypertens 2022;*

27:148.

Graphic 79977 Version 39.0

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

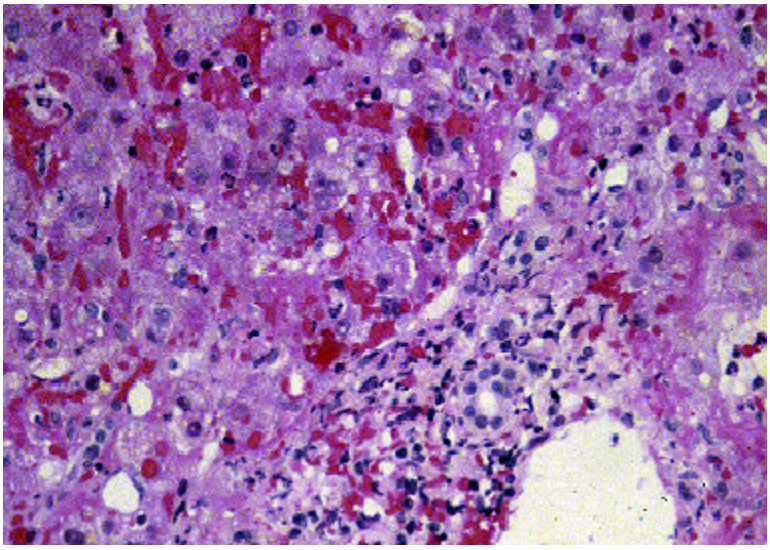
Severe blood pressure elevation:
Systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg on 2 occasions at least 4 hours apart while the patient is on bedrest; however, antihypertensive therapy generally should be initiated upon confirmation of severe hypertension, in which case criteria for severe blood pressure elevation can be satisfied without waiting until 4 hours have elapsed
Symptoms of central nervous system dysfunction:
New-onset cerebral or visual disturbance, such as: ▪ Photopsia, scotomata, cortical blindness, retinal vasospasm **and/or** ▪ Severe headache (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy with acetaminophen and not accounted for by alternative diagnoses
Hepatic abnormality:
▪ Impaired liver function not accounted for by another diagnosis and characterized by serum transaminase concentration >2 times the upper limit of the normal range **and/or** ▪ Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis
Thrombocytopenia:
▪ Platelet count <100,000 platelets/microL
Kidney function impairment:
▪ Serum creatinine >1.1 mg/dL [97.2 micromol/L] **and/or** ▪ Doubling of the serum creatinine concentration in the absence of other kidney disease
Pulmonary edema

Reference:

1. *American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin No. 222: Gestational Hypertension and Preeclampsia. Obstet Gynecol 2020; 135:e237.*

Graphic 76975 Version 29.0

HELLP syndrome



Liver biopsy from a patient with HELLP syndrome. The zones immediately adjacent to the portal triads show collections of red blood cells, without inflammation or necrosis of hepatocytes.

HELLP: hemolysis, elevated liver enzymes, and low platelets.

Courtesy of Caroline A Riely, MD.

Graphic 69691 Version 2.0

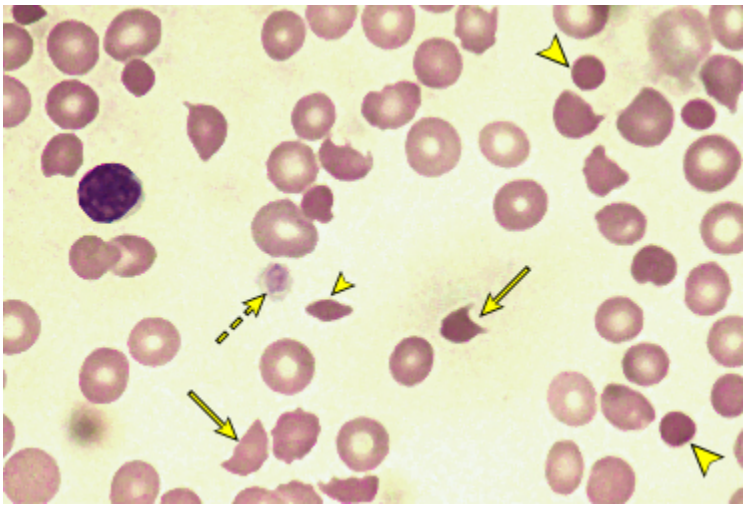
Reported frequency of signs and symptoms of HELLP syndrome

Sign/symptom	Frequency (%)
Proteinuria	86 to 100
Malaise	90 to 100
Hypertension	82 to 88
Right upper quadrant/epigastric pain	40 to 90
Nausea, vomiting	29 to 84
Headache	33 to 61
Visual changes	10 to 20
Jaundice	5

HELLP: hemolysis, elevated liver enzymes, and low platelets.

Graphic 64665 Version 4.0

Peripheral smear in microangiopathic hemolytic anemia showing presence of schistocytes

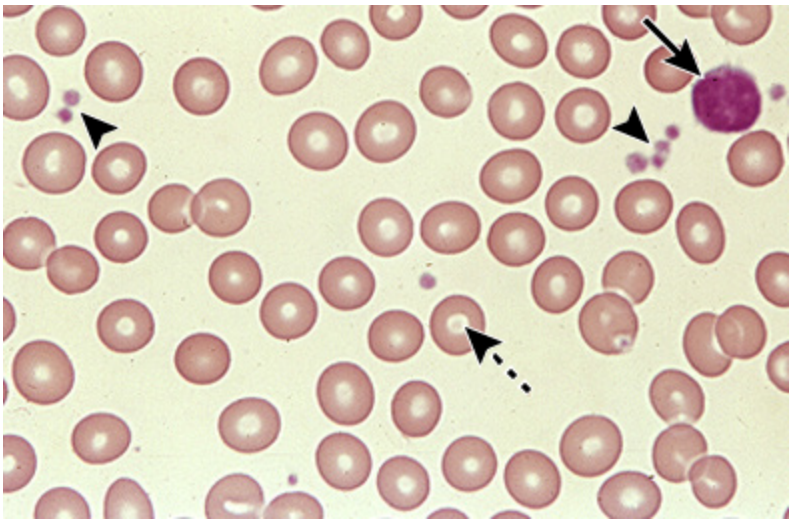


Peripheral blood smear from a patient with a microangiopathic hemolytic anemia with marked red cell fragmentation. The smear shows multiple helmet cells (arrows) and other fragmented red cells (small arrowhead); microspherocytes are also seen (large arrowheads). The platelet number is reduced; the large 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 (arrowheads) and a normal lymphocyte (arrow) 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 5.0

Frequency of various signs and symptoms among imitators of preeclampsia

Signs and symptoms	HELLP syndrome, percent	AFLP, percent	TTP, percent	HUS, percent	Exacerbation of SLE, percent
Hypertension	85	50	20 to 75	80 to 90	80 with APA, nephritis
Proteinuria	90 to 95	30 to 50	With hematuria	80 to 90	100 with nephritis
Fever	Absent	25 to 32	20 to 50	NR	Common during flare
Jaundice	5 to 10	40 to 90	Rare	Rare	Absent
Nausea and vomiting	40	50 to 80	Common	Common	Only with APA
Abdominal pain	60 to 80	35 to 50	Common	Common	Only with APA
Central nervous system	40 to 60	30 to 40	60 to 70	NR	50 with APA

HELLP: hemolysis, elevated liver enzymes, low platelets; AFLP: acute fatty liver of pregnancy; TTP: thrombotic thrombocytopenic purpura; HUS: hemolytic uremic syndrome; SLE: systemic lupus erythematosus; APA: antiphospholipid antibodies with or without catastrophic antiphospholipid syndrome; NR: values not reported; common: reported as the most common presentation.

Graphic 64296 Version 11.0

Frequency and severity of laboratory findings among imitators of preeclampsia

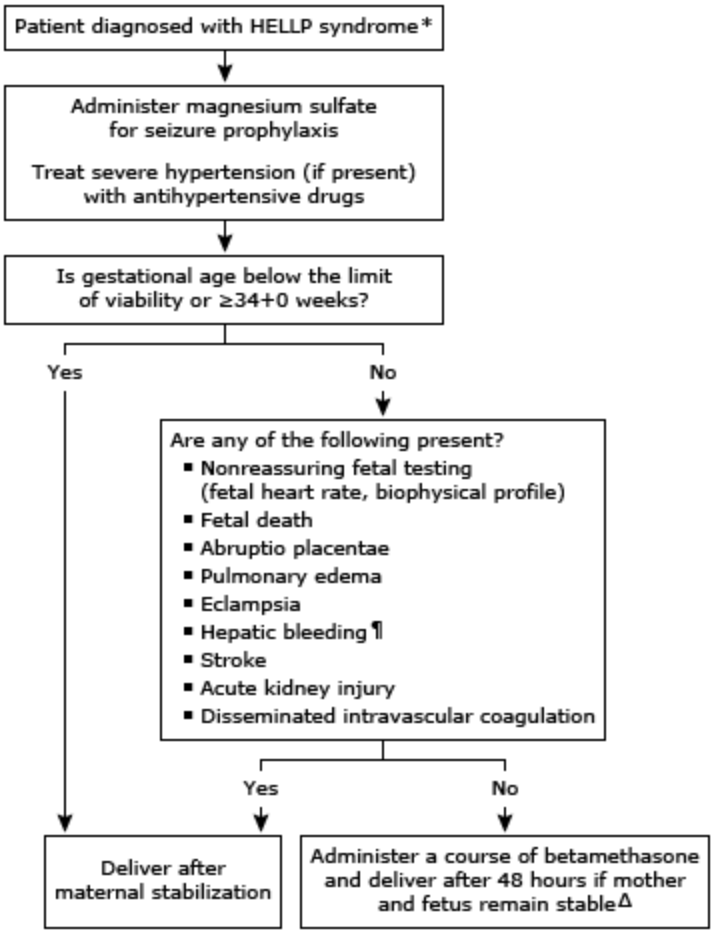
Laboratory findings	HELLP syndrome	AFLP	TTP	HUS	Exacerbation of SLE
Thrombocytopenia (less than 100,000/mm^3)	More than 20,000	More than 50,000	20,000 or less	More than 20,000	More than 50,000
Hemolysis (%)	50 to 100	15 to 20	100	100	14 to 23 in patients with APA
Anemia (%)	Less than 50	Absent	100	100	14 to 23 in patients with APA
DIC (%)	Less than 20	50 to 100	Rare	Rare	Rare
Hypoglycemia (%)	Absent	50 to 100	Absent	Absent	Absent
VW factor multimers (%)	Absent	Absent	80 to 90	80	Less than 10
ADAMTS13 less than 5% (%)	Absent	Absent	33 to 100	Rare	Rare
Impaired renal function (%)	50	90 to 100	30	100	40 to 80
LDH (international units/L)	600 or more	Variable	More than 1000	More than 1000	May be elevated in patients with APA and liver involvement
Elevated ammonia (%)	Rare	50	Absent	Absent	Absent
Elevated bilirubin (%)	50 to 60	100	100	NA	Less than 10
Elevated transaminases (%)	100	100	Usually mild*	Usually mild*	In patients with APA and liver involvement

HELLP: hemolysis, elevated liver enzymes, low platelets; AFLP: acute fatty liver of pregnancy; TTP: thrombotic thrombocytopenic purpura; HUS: hemolytic uremic syndrome; SLE: systemic lupus erythematosus; APA: antiphospholipid antibodies with or without catastrophic antiphospholipid syndrome; DIC: disseminated intravascular coagulopathy; VW: von Willebrand; ADAMTS13: von Willebrand factor-cleaving metalloprotease; LDH: lactic dehydrogenase; NR: values not reported.

* Levels less than 100 international units/L.

Graphic 65674 Version 13.0

Management of patients with HELLP syndrome



HELLP: hemolysis, elevated liver enzymes, and low platelets; LDH: lactate dehydrogenase; AST: aspartate transaminase; ALT: alanine transaminase.

* Criteria for HELLP:

- Hemolysis, established by at least 2 of the following:
  - Peripheral smear with schistocytes and burr cells
  - Serum bilirubin ≥1.2 mg/dL (20.52 micromol)
  - Low serum haptoglobin (≤25 mg/dL) or LDH ≥2 times the upper level of normal (in the local laboratory)
  - Severe anemia, unrelated to blood loss
- Elevated liver enzymes:
  - AST or ALT ≥2 times the upper level of normal (in the local laboratory)
- Low platelets: <100,000 cells/microL

¶ Patients with severe epigastric or right upper quadrant pain should undergo an appropriate imaging study expeditiously to evaluate for hepatic bleeding, even if liver enzymes are not severalfold above the normal range.

Δ The mother and fetus should be closely monitored during this period. Refer to UpToDate content on HELLP syndrome.

Graphic 121602 Version 1.0

Antihypertensive medications for urgent blood pressure control in pregnancy

Drug	Initial dose	Follow-up
Labetalol	20 mg IV gradually over 2 minutes.	Repeat BP measurement at 10-minute intervals: ▪ If BP remains above target level at 10 minutes, give 40 mg IV over 2 minutes. ▪ If BP remains above target level at 20 minutes, give 80 mg IV over 2 minutes. ▪ If BP remains above target level at 30 minutes, give 80 mg IV over 2 minutes. ▪ If BP remains above target level at 40 minutes, give 80 mg IV over 2 minutes. Cumulative maximum dose is 300 mg. If target BP is not achieved, switch to another class of agent. Hold dose if heart rate <60 beats per minute.
	A continuous IV infusion of 1 to 2 mg/minute can be used instead of intermittent therapy or started after 20 mg IV dose. Requires use of programmable infusion pump and continuous noninvasive monitoring of blood pressure and heart rate (reduce/discontinue infusion if heart rate <60 beats per minute).	Adjust dose within this range to achieve target blood pressure. Cumulative maximum dose is 300 mg. If target BP is not achieved, switch to another class of agent.
Hydralazine	5 mg IV gradually over 1 to 2 minutes.* Adequate reduction of blood pressure is less predictable than with IV labetalol.	Repeat BP measurement at 20-minute intervals: ▪ If BP remains above target level at 20 minutes, give 5 or 10 mg IV over 2 minutes, depending on the initial response. ▪ If BP remains above target level at 40 minutes, give 5 to 10 mg IV over 2 minutes, depending on the previous response.

		Cumulative maximum dose is 20 to 30 mg per treatment event. If target BP is not achieved, switch to another class of agent.
Nicardipine (parenteral)	The initial dose is 5 mg/hour IV by continuous infusion titrated up to 15 mg/hour to achieve target BP 130 to 150/80 to 100 mmHg. The effect of dose titrations may not be observed for 5 to 15 minutes; rapid titration should be avoided to minimize risk of overshooting dose. Requires use of a programmable infusion pump and continuous noninvasive monitoring of blood pressure and heart rate.	Adjust dose within this range to achieve target BP.
Nifedipine immediate release*	10 mg orally.	Repeat BP measurement at 20-minute intervals: ▪ If BP remains above target at 20 minutes, give 10 or 20 mg orally, depending on the initial response. ▪ If BP remains above target at 40 minutes, give 10 or 20 mg orally, depending on the previous response. If target BP is not achieved, switch to another class of agent.
Nifedipine extended release	30 mg orally.	If target BP is not achieved in 1 to 2 hours, another dose can be administered. If target BP is not achieved, switch to another class of agent.

IV: intravenous; BP: blood pressure; FHR: fetal heart rate.

* We caution against use of immediate-release oral nifedipine, although some obstetric guidelines have endorsed its use as a first-line option for emergency treatment of acute, severe hypertension in pregnancy or postpartum (other options were labetalol and hydralazine), particularly when IV access is not in place. In most cases, use of immediate-release oral nifedipine will be safe and well tolerated; however, there is a risk of an acute, precipitous fall in blood pressure, which may result in a reduction in uteroplacental perfusion. The immediate-release preparations are also associated

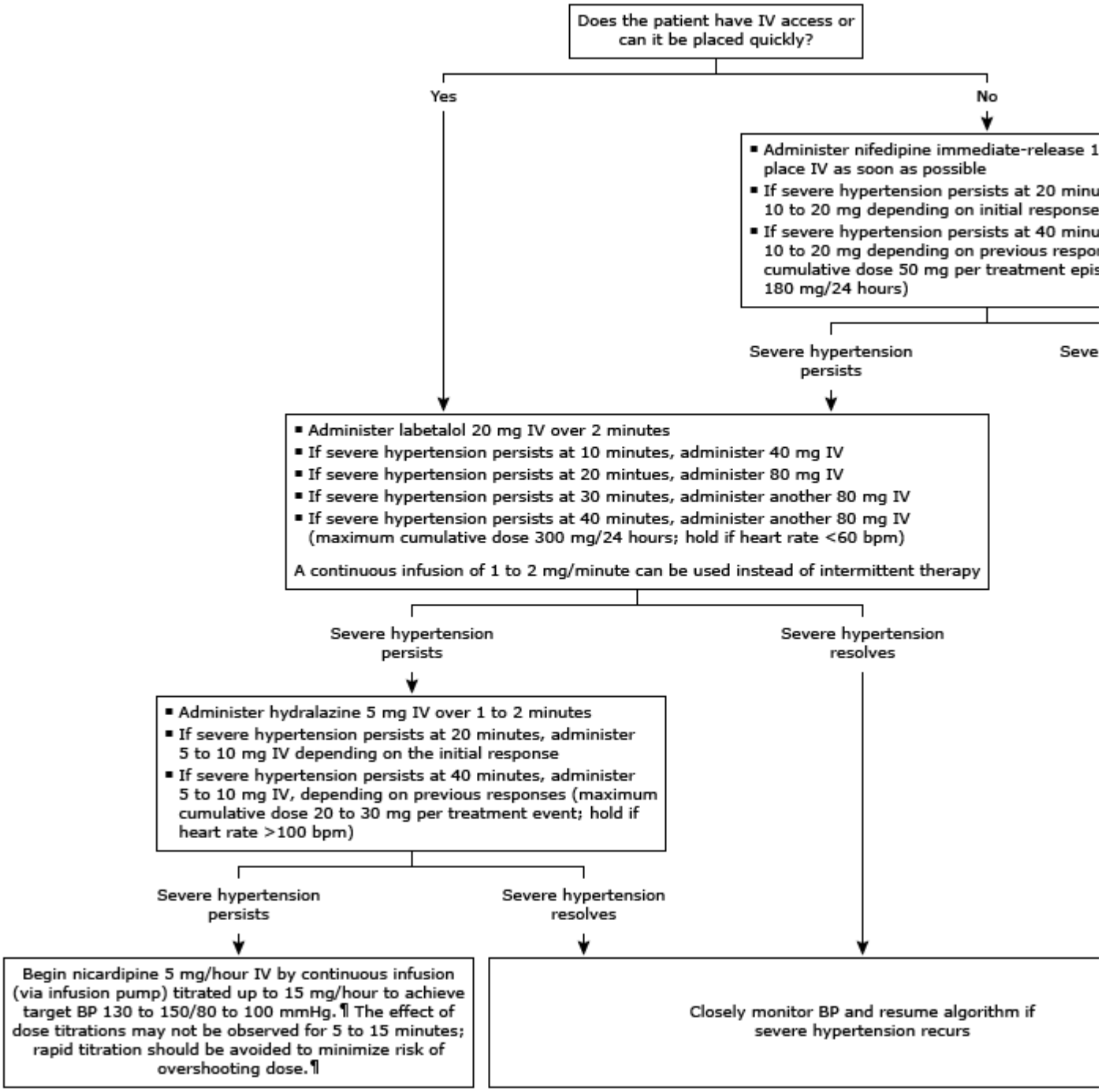
with a higher incidence of headache and tachycardia. In nonpregnant adults, the package insert states that "nifedipine capsules should not be used for the acute reduction of blood pressure."

Adapted from:

1. *American College of Obstetricians and Gynecologists. Gestational hyertension and preeclampsia. Practice Bulletin, Number 222. Obstet Gynecol 2020; 135:e237.*
2. *Bernstein PS, Martin JN Jr, Barton JR, et al. National Partnership for Maternal Safety: Consensus Bundle on Severe Hypertension During Pregnancy and the Postpartum Period. Obstet Gynecol 2017; 130:347.*

Graphic 110261 Version 14.0

Management of inpatient pregnant people with acute severe hypertension due preeclampsia (systolic blood pressure ≥160 mmHg and/or diastolic blood press mmHg)*



Mean arterial pressure should not be reduced by more than 25% over two hours, systolic blood pressure sh reduced below 130 mmHg, and diastolic blood pressure should not be reduced below 80 mmHg. Blood pres range of 130 to 150/80 to 100 mmHg are ideal. During treatment, heart rate and blood pressure should be r closely. If delivery will not occur for days to weeks, maintenance therapy can be initiated, if required, with or antihypertensive drugs. Refer to UpToDate content for additional information on treatment of hypertension pregnancy.

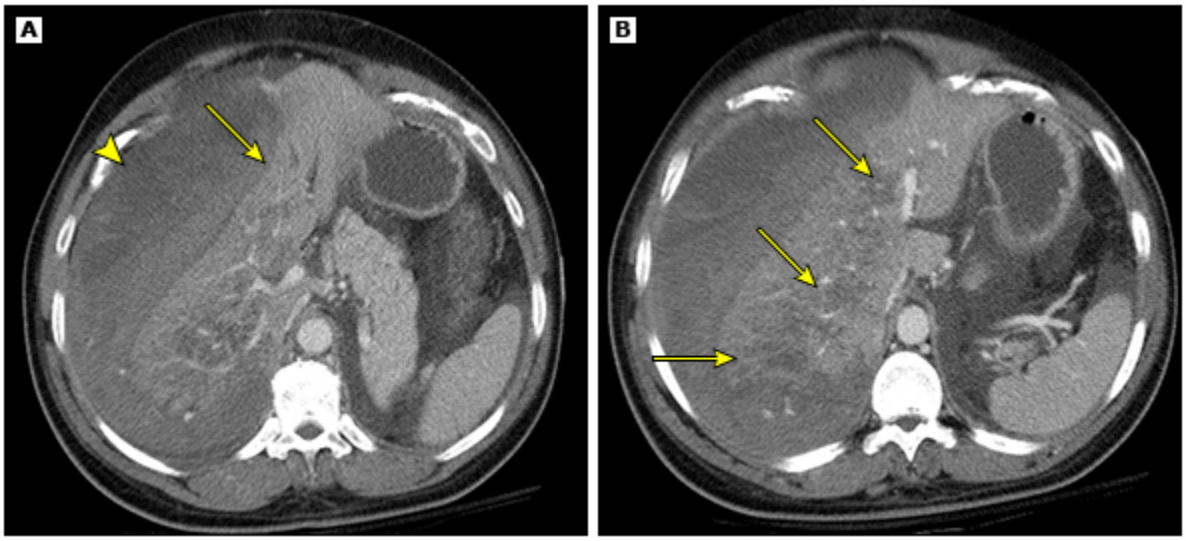
IV: intravenous; bpm: beats per minute; BP: blood pressure; mmHg: millimeters of mercury.

* Severe hypertension should be confirmed with a second BP reading within 15 minutes to facilitate initiatio antihypertensive therapy.

¶ The American College of Obstetricians and Gynecologists (ACOG) considers use of intravenous hydralazine intravenous labetalol, and oral nifedipine similarly effective and safe. Dosing is slightly different from the do algorithm. ACOG guidance does not describe use of nicardipine or reserve immediate-release nifedipine for without intravenous access.

Graphic 134292 Version 3.0

Liver infarction subcapsular hematoma HELLP syndrome on CT scan



(A) An axial CT scan through the upper abdomen shows a large subcapsular hematoma compressing the liver (arrow).

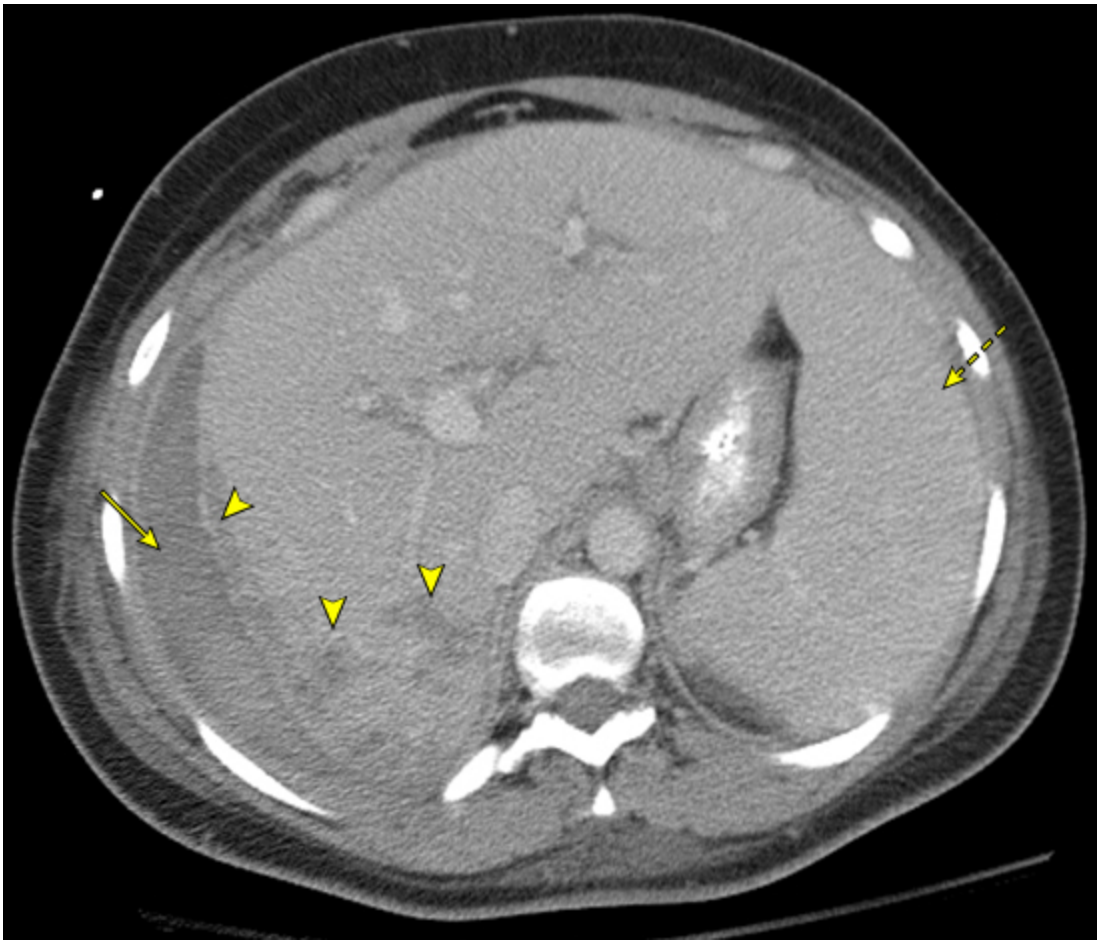
(B) This image shows a large and irregular perfusion defect involving the right lobe and part of the left lobe of the liver (arrows).

CT: computed tomography; HELLP: hemolysis, elevated liver enzymes, and low platelets.

Courtesy of Jonathan B Kruskal, MD, PhD.

Graphic 89900 Version 2.0

Liver infarction HELLP syndrome on CT scan



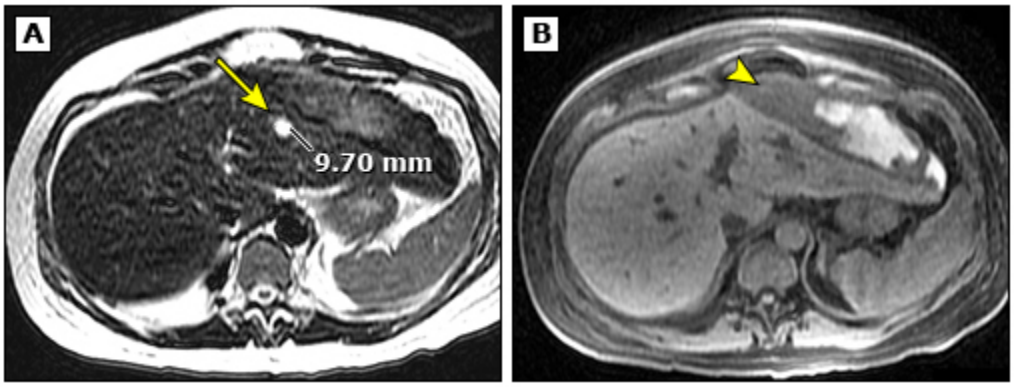
An axial CT scan through the upper abdomen shows multiple perfusion defects (arrowheads) in the posterior aspect of the right lobe of the liver. A subcapsular hematoma is present (arrow). The spleen is enlarged (dashed arrow).

CT: computed tomography; HELLP: hemolysis, elevated liver enzymes, and low platelets.

Courtesy of Jonathan B Kruskal, MD, PhD.

Graphic 89901 Version 2.0

Subcapsular liver hematoma on MRI



These MRIs are from a patient with HELLP syndrome and a subcapsular liver hematoma.

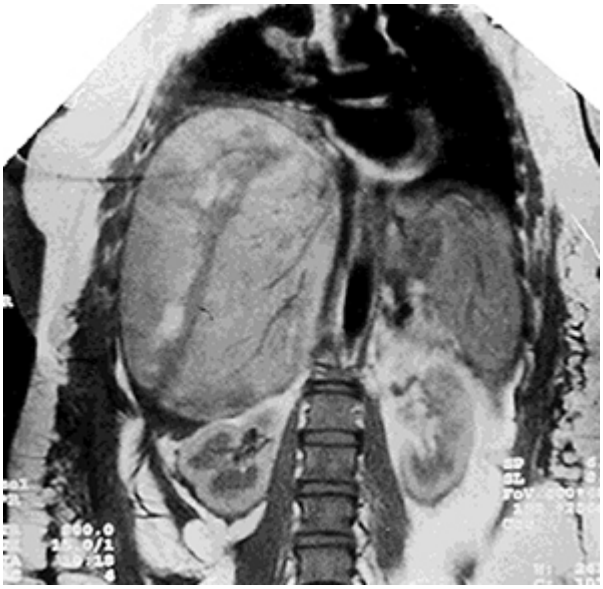
(A) The T2-weighted image shows a 9 mm hyperintense focus (arrow) that could represent a small laceration or a hepatic cyst.

(B) The T1-weighted image shows an adjacent subcapsular hematoma (arrowhead) with both hyperintense and hypointense components reflecting a complex solid thrombus. The subcapsular hematoma was estimated as occupying less than 10% of the liver surface.

MRI: magnetic resonance imaging; HELLP: hemolysis, elevated liver enzymes, and low platelets.

Graphic 86843 Version 4.0

Hepatic hematoma with rupture



Magnetic resonance image from a pregnant patient with hepatic hematoma with rupture. This cut shows collected blood under the hepatic capsule running from the dome of the liver down along the right side, pushing the remaining normal parenchyma toward the midline.

Reproduced with permission from Barton JR, Sibai BM, Am J Obstet Gynecol 1996; 174:1820.

Graphic 68521 Version 4.0

Contributor Disclosures

Baha M Sibai, MD No relevant financial relationship(s) with ineligible companies to disclose. **Charles J Lockwood, MD, MHCM** No relevant financial relationship(s) with ineligible companies to disclose. **Keith D Lindor, MD** Consultant/Advisory Boards: Pliant [DSMB member]. All of the relevant financial relationships listed have been mitigated. **Vanessa A Barss, MD, FACOG** No relevant financial relationship(s) with ineligible companies to disclose.

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