# Hypertensive disorders in pregnancy: Approach to differential diagnosis

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## INTRODUCTION

The four major hypertensive disorders that occur in pregnant women are ( table 1):

- Preeclampsia (and related disorders: eclampsia and HELLP [hemolysis, elevated liver enzymes, low platelets] syndrome)
- Gestational hypertension
- Chronic hypertension
- Preeclampsia superimposed on chronic hypertension

An accurate diagnosis, when possible, can be helpful for making management decisions (eg, timing of delivery, need for antiseizure prophylaxis) and assessing maternal prognosis (eg, risk for progression in the current pregnancy, recurrence risk in future pregnancies, long-term maternal health risks).

In addition to distinguishing among these four causes of hypertension, health care providers may also need to consider other medical disorders (eg, glomerulonephritis or thrombotic microangiopathies) that share clinical and/or laboratory features with the hypertensive disorders in pregnancy.

In the United Kingdom, the National Institute for Health and Care Excellence (NICE) suggests offering PlGF-based tests, which should be used with standard clinical assessment, to help rule in or rule out preeclampsia in patients suspected of the disorder between 20+0 and 36+6 weeks of gestation [ 75]. A health technology assessment from Ontario Health concluded

PlGF-based biomarker testing as an adjunct to standard clinical assessment likely improves prediction of preeclampsia [1]. A PlGF-based test was approved by the US Food and Drug Administration in 2023 for use in pregnant patients hospitalized with hypertension to predict progression to preeclampsia with severe features within two weeks. (See "Preeclampsia: Clinical features and diagnosis", section on 'Role of measurement of angiogenic markers'.)

## DIAGNOSTIC CRITERIA FOR THE FOUR MAJOR HYPERTENSIVE DISORDERS IN PREGNANCY

The four major hypertensive disorders in pregnant patients can be distinguished by their diagnostic criteria ( table 1), which have distinct characteristics despite overlap ( table 2 and algorithm 1) [2,3].

In a series including nearly four million delivery hospitalizations, 11 percent had a hypertension-related diagnosis, including 4.7 percent with preeclampsia, 3.8 percent with gestational hypertension, 1.7 percent with chronic hypertension, and 0.6 percent with unspecified hypertension [4]. Of the 176,925 deliveries with preeclampsia/eclampsia, approximately 47 percent were mild or unspecified preeclampsia, 37 percent were preeclampsia with severe features or HELLP, 1.4 percent were eclampsia, and 15 percent were preeclampsia superimposed upon chronic hypertension.

Diagnostic criteria, clinical findings, and management of the hypertensive disorders of pregnancy are reviewed in detail separately.

- (See "Preeclampsia: Clinical features and diagnosis" and "Preeclampsia: Antepartum management and timing of delivery" and "Preeclampsia: Intrapartum and postpartum management and long-term prognosis".)
- (See "Eclampsia".)
- (See "HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets)".)
- (See "Gestational hypertension".)
- (See "Chronic hypertension in pregnancy: Prenatal and postpartum care".)

## DIFFERENTIAL DIAGNOSIS AMONG PATIENTS WHOSE PRIMARY FINDING IS HYPERTENSION

**Chronic hypertension versus preeclampsia** — In a prospective study that measured blood pressure in 1000 pregnant individuals across gestation, blood pressure gradually fell after 6

weeks of gestation, reached a nadir between weeks 16 and 20, and then gradually increased to prepregnancy levels by term [5]. Because of the reduction in blood pressure that typically occurs early in pregnancy, an individual with preexistent hypertension may be normotensive when first seen by the obstetric provider. Later in pregnancy, when their blood pressure returns to its prepregnancy baseline, they may appear to be developing preeclampsia if no prepregnancy blood pressure measurements have been documented and are available for comparison.

In this setting, the factors described below can be helpful in establishing the likely diagnosis. However, when evaluating pregnant patients with hypertension, it is generally safer to assume that new-onset hypertension in pregnancy is due to preeclampsia, even if all of the diagnostic criteria are not fulfilled and the blood pressure is only mildly elevated since preeclampsia may progress to eclampsia or other severe forms of the disease in a short period of time. Clinicians should be mindful that:

- Hypertension occurring before the 20$^{th}$ week is usually due to chronic hypertension rather than preeclampsia; however, in rare cases it could be the first manifestation of preeclampsia. This is more likely to occur in patients who become pregnant at >40 years of age in association with in vitro fertilization and multifetal gestation. It also could be the first manifestation of pheochromocytoma.

- Proteinuria is usually present and increases over time in preeclampsia, occasionally reaching the nephrotic range (greater than 3 g per day); by comparison, protein excretion is usually normal or less than 1 g/day in women with chronic hypertension. Hypertensive nephrosclerosis, a complication of poorly treated chronic hypertension, is associated with very modest proteinuria (1 to 2 g/day) but rarely occurs in young people [6]. (See "Clinical features, diagnosis, and treatment of hypertensive nephrosclerosis".)

- Preeclampsia is more common in nulliparas than multiparas, and it is uncommon in multiparas with previously normotensive pregnancies in the absence of change in paternity. (See "Preeclampsia: Clinical features and diagnosis", section on 'Risk factors'.)

- Preeclampsia is more common in older (>40 years) than younger nulliparas, although older individuals (nulliparous or multiparous) are also more likely to have chronic hypertension. (See "Preeclampsia: Clinical features and diagnosis", section on 'Risk factors'.)

**Chronic hypertension versus superimposed preeclampsia** — Reproductive-age individuals with chronic hypertension typically have no proteinuria unless they have chronic kidney disease; therefore, new proteinuria suggests development of superimposed preeclampsia. A serum urate (uric acid) level may also help to distinguish chronic hypertension (urate generally not elevated) from superimposed preeclampsia (urate often elevated) [3,7,8].

**Exacerbation of chronic kidney disease versus preeclampsia** — Reproductive-age individuals with chronic hypertension and mild proteinuria (up to 1 to 2 g/day) prior to or in early pregnancy likely have chronic kidney disease (CKD). During pregnancy, worsening hypertension and/or proteinuria may represent an exacerbation of the underlying disease; this is commonly seen in patients with diabetic nephropathy. Increased proteinuria in the absence of hypertension commonly occurs in pregnant individuals with baseline proteinuria and is usually due to the physiologic hyperfiltration associated with pregnancy.

However, patients with CKD are also at increased risk for superimposed preeclampsia [9,10]. The ability to accurately distinguish among these possibilities is important as management and complications are different. Quantification of proteinuria and measurement of serum chemistries early in pregnancy are helpful in order to interpret changes that may occur as pregnancy progresses. Factors that can be helpful in establishing the likely diagnosis include the following:

- Laboratory evidence suggestive of exacerbation of CKD includes the presence of findings specific for disease activity (eg, low complement levels in a patient with systemic lupus erythematosus, urinalysis consistent with a proliferative glomerular disorder [red and white cells and/or cellular casts]). An active urine sediment is not a feature of preeclampsia. An elevated creatinine (>1.2 mg/dL [106 micromol/L]) without significant hypertension or proteinuria is suggestive of CKD and would be very atypical for preeclampsia. (See "Pregnancy in patients with nondialysis chronic kidney disease".)

- In the first half of pregnancy, worsening hypertension and/or proteinuria is likely due to CKD rather than preeclampsia, which typically develops after 20 weeks and usually in the third trimester.

- In the last half of pregnancy, superimposed preeclampsia should be suspected when hypertension significantly worsens (especially acutely) or signs/symptoms ( table 3) associated with the severe end of the preeclampsia spectrum develop.

**Gestational hypertension versus preeclampsia** — Gestational hypertension is diagnosed in a pregnant patient with all of the following: new onset of hypertension at ≥20 weeks of gestation, normal urine protein excretion for pregnancy, and absence of the signs and symptoms of end-organ dysfunction associated with preeclampsia with severe features ( table 3). The absence of both proteinuria and signs and symptoms of end-organ dysfunction distinguish gestational hypertension from preeclampsia. Some patients (10 to 25 percent) with gestational hypertension ultimately develop signs and symptoms of preeclampsia. Patients who develop severe gestational hypertension have rates of pregnancy complications comparable to those of patients with preeclampsia with severe features, thus the two groups are managed similarly. (See "Gestational hypertension" and "Preeclampsia: Antepartum management and timing of delivery".)

### Autonomic overactivity

**Pheochromocytoma** — Pheochromocytoma is a rare cause of hypertension during pregnancy and may be difficult to distinguish from preeclampsia because hypertension and headache occur with both disorders. Symptoms of pheochromocytoma that help to make this distinction include generalized sweating, palpitations, tremor, pallor, dyspnea, generalized weakness, and panic attack-type symptoms. Some patients with pheochromocytoma have an elevated blood glucose level (impaired fasting glucose, apparent type 2 diabetes mellitus). Antepartum diagnosis is important because intrapartum maternal and fetal mortality are high without appropriate treatment. (See "Clinical presentation and diagnosis of pheochromocytoma", section on 'Pheochromocytoma in pregnancy'.)

### Other medical disorders

- Hypertension can be a manifestation of severe autonomic dysfunction related to a primary neurologic disorder, such as Guillain-Barré syndrome, paroxysmal sympathetic hyperactivity, multiple system atrophy syndrome, or acute spinal cord injury. (See "Evaluation and treatment of hypertensive emergencies in adults", section on 'Sympathetic overactivity resulting in hypertensive emergencies'.)

- Hypertension with tachycardia can be a sign of hyperthyroidism. (See "Overview of the clinical manifestations of hyperthyroidism in adults".)

- Hypertension with hypercalcemia can be a sign of hyperparathyroidism. (See "Primary hyperparathyroidism: Clinical manifestations".)

- Cushing's syndrome and primary aldosteronism are other endocrine disorders associated with hypertension. Cushing's syndrome has multiple characteristic signs and symptoms due to excess glucocorticoids ( table 4). The classic presenting signs of primary aldosteronism are hypertension and hypokalemia. (See "Epidemiology and clinical manifestations of Cushing syndrome", section on 'Hypertension' and "Pathophysiology and clinical features of primary aldosteronism", section on 'Hypertension'.)

**Drugs** — Acute hypertension can be caused by use of drugs that can produce a hyperadrenergic state, such as cocaine, amphetamine(s), and phencyclidine; withdrawal of short-acting antihypertensive medications (especially clonidine, propranolol, or other beta blockers); and ingestion of sympathomimetic agents (eg, tyramine-containing foods in patients who take chronic monoamine oxidase inhibitors).

## DIFFERENTIAL DIAGNOSIS AMONG PATIENTS WITH HYPERTENSION AND THROMBOCYTOPENIA OR ELEVATED TRANSAMINASES

Most pregnant patients with hypertension and thrombocytopenia and/or elevated transaminases have preeclampsia with severe features; alternative diagnoses to consider are discussed below.

**HELLP versus preeclampsia with severe features** — In HELLP, hemolysis, elevated liver enzymes, and thrombocytopenia are the predominant features rather than hypertension or central nervous system or kidney dysfunction, which can also occur. In those cases of HELLP that do have severe hypertension, the magnitude of blood pressure elevation may not correlate with the level of angiopathy and liver dysfunction. By comparison, most cases of preeclampsia with severe features have severe hypertension, and when thrombocytopenia and liver dysfunction are also present, they are not as markedly abnormal as in HELLP. (See "HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets)".)

HELLP may represent a subtype of preeclampsia with severe features or it may be a separate disorder. The subtype concept is supported by the observation that the majority of patients with HELLP also have hypertension (82 to 88 percent) and/or proteinuria (86 to 100 percent) [11]. However, because rare patients have neither hypertension nor proteinuria, some authorities have opined that HELLP syndrome is a separate disorder. In these rare atypical patients, the other diagnoses associated with similar laboratory abnormalities discussed below should be excluded before making the diagnosis of HELLP.

**Other disorders** — Although preeclampsia with severe features/HELLP is the most common cause of hypertension, thrombocytopenia, and abnormal liver and kidney chemistries in pregnant patients, the following conditions should be considered and excluded, if possible. The clinical and histologic features of preeclampsia with severe features/HELLP and these disorders are so similar that establishing the correct diagnosis may not be possible; furthermore, preeclampsia with severe features/HELLP can occur concurrently with these disorders.

Signs, symptoms, and laboratory findings in these disorders are compared in the tables ( table 5A-B).

Gestational thrombocytopenia is a common self-limited condition that requires no additional evaluation or treatment. It is a diagnosis of exclusion in pregnant patients with mild thrombocytopenia (platelet count 100,000 to 150,000/microL), especially during late pregnancy and at delivery, who have no other laboratory abnormalities and a normal history and physical examination. (See "Thrombocytopenia in pregnancy", section on 'Gestational thrombocytopenia (GT)'.)

**Acute fatty liver of pregnancy** — There is considerable overlap between acute fatty liver of pregnancy (AFLP) and preeclampsia with severe features/HELLP ( table 5A-B). In one study, approximately one-half of AFLP patients based on the Swansea criteria (which identify the most severe spectrum of the disease) also fulfilled criteria for HELLP syndrome [12].

Although the initial management of both preeclampsia with severe features/HELLP and AFLP is similar (ie, supportive care and delivery), it is important to differentiate between the two disorders, if possible, because patients with AFLP can rapidly develop liver failure, encephalopathy, and severe hypoglycemia. In one series of 46 patients who developed liver disease during pregnancy sufficiently severe to require admission to a liver failure unit, 70 percent had AFLP, and 15 percent had HELLP [13]. Most of the remaining patients had liver disease that was unrelated to pregnancy.

- In the authors' experience, serum fibrinogen level is the most important laboratory test to differentiate between the two conditions. A fibrinogen level below 300 mg/dL is the rule in patients with AFLP, whereas in the absence of abruption or massive hemorrhage, it is rare to have a fibrinogen level below 300 mg/dL in preeclampsia with severe features/HELLP.

- Like preeclampsia with severe features/HELLP, AFLP typically presents in the third trimester, but the diagnosis has been made as early as 22 weeks and as late as four days after delivery.

- Like preeclampsia with severe features/HELLP, the initial symptoms of AFLP are often nonspecific (eg, anorexia, nausea, vomiting, abdominal pain, malaise, and headache).

- Many patients with AFLP have hypertension, with or without proteinuria, possibly due to coexistent preeclampsia; however, hypertension is more common in preeclampsia with severe features/HELLP than in AFLP (in one review, 80 to 100 percent of cases versus 26 to 70 percent of cases [14]).

- Low-grade fever can be present in AFLP but does not occur in preeclampsia with severe features/HELLP.

- AFLP is associated with more serious liver dysfunction: Hypoglycemia (which may be severe), elevated serum ammonia level, and prolongation of the prothrombin time (PT) and activated partial thromboplastin time (aPTT) are common features, while unusual in preeclampsia with severe features/HELLP.

- AFLP is also usually associated with more significant kidney dysfunction compared with preeclampsia with severe features/HELLP.

AFLP can be confirmed by diagnostic liver biopsy, but this is rarely performed because the information gained would not change management and the procedure exposes the mother and pregnancy to additional risks. Furthermore, AFLP and preeclampsia with severe features/HELLP share several common histologic features [14].

Of note, patients with AFLP are more likely than those with preeclampsia with severe features/HELLP to have offspring with an inherited defect in mitochondrial beta-oxidation of fatty acids, such as long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency, short-chain acyl-coenzyme A dehydrogenase deficiency, or carnitine palmitoyltransferase I deficiency [15-19]. However, this information is not typically available during differential diagnosis and is not highly sensitive or specific. (See "Acute fatty liver of pregnancy".)

**Thrombotic microangiopathy: TTP and HUS** — (See "Diagnostic approach to suspected TTP, HUS, or other thrombotic microangiopathy (TMA)", section on 'Key distinguishing features among the primary TMA syndromes'.)

- **Thrombotic thrombocytopenic purpura (TTP)** – The distinction between TTP and preeclampsia with severe features/HELLP is important for therapeutic and prognostic reasons. Plasma exchange (PEX) is the treatment of choice and life-saving for acquired TTP occurring during pregnancy but is not useful for treatment of preeclampsia with severe features/HELLP. The decision to initiate plasmapheresis will depend on a combination of factors: the severity of thrombocytopenia, the trend in change in platelet count, and the trend in change in lactate dehydrogenase (LDH) levels after delivery. TTP may relapse years after pregnancy whereas preeclampsia with severe features/HELLP is only associated with pregnancy and the postpartum state. (See "Immune TTP: Initial treatment" and "Immune TTP: Management following recovery from an acute episode and during remission".)

  - TTP is similar to preeclampsia with severe features/HELLP in that severe thrombocytopenia, severe anemia, and elevated LDH levels are common to both disorders ( table 5A-B) [20-24]. Time of onset may suggest one disorder over the other. The onset of TTP tends to be earlier in gestation than the onset of preeclampsia with severe features/HELLP: Approximately 12 percent of TTP in pregnancy occurs in the first trimester, 56 percent in the second trimester, and 33 percent in the third trimester/postpartum, whereas preeclampsia with severe features/HELLP does not occur before 20 weeks of gestation and most cases are diagnosed in the third trimester [25]. Early preeclampsia before 20 weeks is a characteristic of hereditary TTP. (See "Hereditary thrombotic thrombocytopenic purpura (hTTP)", section on 'Pregnancy'.)

  - The presence of proteinuria and hypertension prior to onset of laboratory abnormalities favors the diagnosis of preeclampsia with severe features/HELLP over

TTP.

- In TTP, aspartate aminotransferase and alanine aminotransferase are minimally elevated or normal, in contrast to significant elevations in preeclampsia with severe features/HELLP [26].
- In TTP, the percentage of schistocytes on peripheral smear is often higher than in preeclampsia with severe features/HELLP (2 to 5 percent versus less than 1 percent) [26].
- TTP is always associated with severe platelet consumption whereas prolongation of the PT and aPTT is typically absent. Moderate to severe platelet consumption is a characteristic of HELLP and is often present in severe preeclampsia, and, like TTP, prolongation of the PT and aPTT is typically absent in both.
- In TTP, LDH levels are markedly elevated (often >1000 IU/L and as high as 2000 or 3000 IU/L) [27], whereas they are usually modestly increased in preeclampsia with severe features/HELLP, although fulminant cases can have LDH levels that are as high as those seen in TTP.
- Severe *ADAMTS13* deficiency (activity <10 percent) is consistent with a diagnosis of TTP but not of preeclampsia with severe features/HELLP; however, this testing may take several days, and in patients with a presumptive diagnosis of TTP, urgent therapy with PEX should be initiated. Early involvement of the consulting hematologist to assist with diagnosis and management, including transfer to a facility capable of performing PEX, is advised. (See "Diagnosis of immune TTP", section on 'Reduced ADAMTS13 activity'.)

- **Hemolytic-uremic syndrome (HUS)** – Pregnancy-related atypical HUS is rare, usually develops postpartum, and may be a complement-mediated disorder triggered by pregnancy [28-30]. Both HUS and preeclampsia with severe features/HELLP are characterized by thrombocytopenia and hemolysis. However:
  - In HUS, kidney injury progresses postpartum and is much more prominent: 71 percent of patients required dialysis at diagnosis in one series [30]. In preeclampsia with severe features/HELLP, kidney injury usually begins to improve within 72 hours of birth.
  - In HUS, the liver is not severely affected (transaminases may be normal or mildly elevated).

  One group found that a serum creatinine ≥1.9 mg/d or LDH ≥1832 U/L were good thresholds for differentiating pregnancy-related HUS from HELLP syndrome [31]. Serum

creatinine levels were ≥1.9 mg/dL in 98 percent of HUS cases compared with 2 percent of HELLP cases, serum LDH levels were ≥1832 U/L in 77 percent of HUS cases compared with 0 percent of HELLP cases, and when evaluated together, the combination of serum creatinine ≥1.9 mg/dL and LDH ≥600 U/L showed the greatest utility as this was seen in 91 percent of HUS cases compared with 0 percent of HELLP cases. Median hemoglobin values in HUS and HELLP were 6.7 and 9 g/dL, respectively; median platelet counts were 41,000 and 67,000 cells/microliter, respectively; median creatinine levels were 5.6 and 0.8 g/dL, respectively; and median LDH levels were 2750 and 662 U/L, respectively.

(See "Diagnostic approach to suspected TTP, HUS, or other thrombotic microangiopathy (TMA)", section on 'Key distinguishing features among the primary TMA syndromes'.)

**Systemic lupus erythematosus** — In patients with systemic lupus erythematosus (SLE), it can be difficult to distinguish a flare from preeclampsia with severe features/HELLP, particularly in patients with lupus hepatitis or nephritis ( table 5A-B). (See "Gastrointestinal manifestations of systemic lupus erythematosus", section on 'Hepatic involvement'.)

- SLE flares are likely to be associated with hypocomplementemia and increased titers of anti-DNA antibodies; in comparison, complement levels are usually, but not always, normal or increased in preeclampsia.
- SLE kidney flares are often associated with increases in proteinuria and/or hematuria and significant elevations in serum creatinine level whereas hypertension, although present, may be less pronounced compared with preeclampsia with severe features/HELLP.
- In SLE, hemolytic anemia is relatively rare (most patients have anemia of chronic disease) whereas it is common in preeclampsia with severe features/HELLP.
- Thrombocytopenia is common to both SLE and preeclampsia with severe features/HELLP: Mild thrombocytopenia (platelet counts between 100,000 and 150,000/microL) has been noted in 25 to 50 percent of patients with SLE; platelet counts <50,000/microL occur in approximately 10 percent of SLE patients. (See "Hematologic manifestations of systemic lupus erythematosus".)
- Acute onset, accelerated hypertension is more likely to be due to preeclampsia with severe features/HELLP than to an SLE flare. (See "Pregnancy in women with systemic lupus erythematosus".)

**Antiphospholipid syndrome** — Hypertension, proteinuria, thrombocytopenia, and other signs of significant end-organ dysfunction are clinical manifestations of antiphospholipid syndrome (APS) in adults. In pregnant individuals, a preterm birth of a morphologically normal newborn before 34 weeks of gestation due to severe preeclampsia, eclampsia, or

features consistent with placental insufficiency may be a manifestation of APS. (See "Clinical manifestations of antiphospholipid syndrome" and "Diagnosis of antiphospholipid syndrome".)

We believe antiphospholipid antibody (aPL) testing is not indicated to exclude APS in all patients in whom preeclampsia with severe features is suspected before 34 weeks, but we suggest it for those in whom APS is suspected based on additional findings (eg, thrombotic event, livedo reticularis [lace-like purplish discoloration of the skin], stillbirth). The absence of laboratory evidence of aPL excludes APS. Management of pregnant patients with APS or aPL alone is reviewed separately. (See "Antiphospholipid syndrome: Obstetric implications and management in pregnancy".)

## DIFFERENTIAL DIAGNOSIS AMONG PATIENTS WHOSE PRIMARY FINDING IS PROTEINURIA

The differential diagnosis in patients in whom proteinuria is the prominent finding includes kidney disease (eg, acute or chronic kidney disease, diabetic kidney disease) and preeclampsia. (See "Proteinuria in pregnancy: Diagnosis, differential diagnosis, and management of nephrotic syndrome", section on 'Differential diagnosis of proteinuria'.)

## DIFFERENTIAL DIAGNOSIS OF OTHER SIGNS/SYMPTOMS OF PREECLAMPSIA WITH SEVERE FEATURES

**Medical and surgical disorders associated with elevated blood pressure, headache, and/or abdominal pain** — Patients with a medical or surgical disorder can usually be distinguished from those with preeclampsia with severe features/HELLP by taking a detailed history, performing a thorough physical examination, and obtaining relevant laboratory studies.

Patients with migraine, gastroesophageal reflux, peptic ulcer disease, gastritis, hepatitis, appendicitis, cholecystitis, pancreatitis, or other causes of head or abdominal pain ( table 6A-E) may develop elevated blood pressures and/or other signs/symptoms associated with preeclampsia with severe features/HELLP. In contrast to preeclampsia with severe features/HELLP:

- Patients with disseminated herpes simplex and septic shock may have clinical and laboratory findings consistent with HELLP syndrome or acute fatty liver of pregnancy (AFLP); however, they usually have fever and no hypertension.
- Thrombocytopenia typically does not occur with any of these disorders.

- Migraine is associated with recurrent headaches and no associated laboratory abnormalities. A typical attack progresses through four phases: the prodrome, the aura, the headache (which is usually unilateral, throbbing, or pulsatile), and the postdrome. (See "Pathophysiology, clinical manifestations, and diagnosis of migraine in adults" and "Headache during pregnancy and postpartum", section on 'Migraine'.)

- Gastroesophageal reflux and peptic ulcer disease are associated with abdominal pain but not with the laboratory abnormalities. Pain associated with reflux will improve if stomach acid levels are reduced. (See "Clinical manifestations and diagnosis of gastroesophageal reflux in adults" and "Medical management of gastroesophageal reflux disease in adults" and "Peptic ulcer disease: Clinical manifestations and diagnosis".)

- Acute viral gastroenteritis is associated with fever and diarrhea. (See "Acute viral gastroenteritis in adults".)

- Hepatitis can be definitively diagnosed based on serologic testing. (See "Hepatitis A virus infection in adults: Epidemiology, clinical manifestations, and diagnosis" and "Hepatitis B virus: Screening and diagnosis in adults" and "Clinical manifestations, diagnosis, and treatment of acute hepatitis C virus infection in adults".)

- Acute appendicitis is often associated with fever and leukocytosis. Pain is often in the lower right quadrant or midabdomen. The appendix often appears abnormal on imaging. (See "Acute appendicitis in pregnancy".)

- Acute cholecystitis is often associated with fever and leukocytosis and typically develops in a patient with a history of symptomatic gall stones. The gall bladder is abnormal on imaging. (See "Gallstone diseases in pregnancy".)

- Intrahepatic cholestasis of pregnancy is strongly associated with pruritus. The diagnosis is confirmed when pruritus is associated with elevated total serum bile acid levels, elevated aminotransferases, or both, and diseases that may produce similar laboratory findings and symptoms have been excluded. (See "Intrahepatic cholestasis of pregnancy".)

- Acute pancreatitis is associated with epigastric pain often radiating to the back, elevation in serum lipase or amylase to three times or greater than the upper limit of normal, and characteristic findings on imaging. (See "Clinical manifestations and diagnosis of acute pancreatitis".)

- Pulmonary embolism is characterized by dyspnea and pleuritic chest pain and characteristic findings on imaging. (See "Pulmonary embolism in pregnancy: Clinical presentation and diagnosis".)

## 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".)

## SUMMARY AND RECOMMENDATIONS

- **Pregnancy-related hypertensive disorders** – The diagnostic criteria for the four major hypertensive disorders in pregnant people are described in the table ( table 1). Despite some similar findings, the disorders can be distinguished as shown in the following table and algorithm ( table 2 and algorithm 1). (See 'Diagnostic criteria for the four major hypertensive disorders in pregnancy' above and 'Differential diagnosis among patients whose primary finding is hypertension' above.)

- **Nonpregnancy-related hypertensive disorders** – These include chronic hypertension; chronic kidney disease and other secondary causes of hypertension (eg, pheochromocytoma, primary aldosteronism, Cushing's disease, hyperthyroidism); other medical disorders with symptoms (eg, headaches, abdominal pain) similar to preeclampsia; and use/withdrawal of some drugs. (See 'Differential diagnosis among patients whose primary finding is hypertension' above.)

- **General principles of differential diagnosis**

  - When evaluating pregnant individuals with hypertension, it is generally safer to assume that new-onset hypertension in pregnancy is due to preeclampsia, even if all of the diagnostic criteria are not fulfilled and the blood pressure is only mildly elevated, since preeclampsia may progress to eclampsia or other severe forms of the disease in a short period of time. (See 'Differential diagnosis among patients whose primary finding is hypertension' above.)

  - Most pregnant individuals with hypertension and thrombocytopenia and/or elevated transaminases have preeclampsia with severe features. Alternative diagnoses to consider include HELLP syndrome (Hemolysis, Elevated liver enzymes, Low Platelets; which may be a subtype of preeclampsia), acute fatty liver of pregnancy (AFLP), thrombotic microangiopathy (eg, thrombotic thrombocytopenic purpura [TTP], hemolytic-uremic syndrome [HUS]), systemic lupus erythematosus (SLE), and antiphospholipid syndrome (APS).

    The clinical and histologic features of preeclampsia with severe features/HELLP and these disorders are so similar that establishing the correct diagnosis may not be

possible; furthermore, preeclampsia with severe features/HELLP can occur concurrently with these disorders. Laboratory findings in these disorders are compared in the tables ( table 5A-B). (See 'Differential diagnosis among patients with hypertension and thrombocytopenia or elevated transaminases' above.)

- Patients with a medical or surgical disorder can usually be distinguished from those with preeclampsia with severe features/HELLP by taking a detailed history, performing a thorough physical examination, and obtaining relevant laboratory studies. Patients with migraine, gastroesophageal reflux, peptic ulcer disease, gastritis, hepatitis, appendicitis, cholecystitis, pancreatitis, or other causes of head or abdominal pain ( table 6A-E) may develop elevated blood pressures and/or other signs/symptoms associated with preeclampsia with severe features/HELLP. (See 'Medical and surgical disorders associated with elevated blood pressure, headache, and/or abdominal pain' above.)



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Topic 126975 Version 12.0

## GRAPHICS

### Definitions/diagnostic criteria for the hypertensive disorders in pregnancy

| | |
|---|---|
| **Gestational hypertension** | ▪ New onset of systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on at least 2 occasions 4 hours apart after 20 weeks of gestation in a previously normotensive individual<br>**And:**<br>▪ No proteinuria<br>▪ No signs/symptoms of preeclampsia-related end-organ dysfunction (eg, thrombocytopenia, renal insufficiency, elevated liver transaminases, pulmonary edema, cerebral or visual symptoms) |
| **Preeclampsia** | ▪ New onset of 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 individual. Patients with systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg should have blood pressure confirmed within a short interval (minutes) to facilitate timely administration of antihypertensive therapy.<br>**And:**<br>▪ Proteinuria (≥300 mg per 24-hour urine collection [or this amount extrapolated from a timed collection], or protein:creatinine ratio ≥0.3, or urine dipstick reading ≥2+ [if other quantitative methods are not available]).<br>**In a patient with new-onset hypertension without proteinuria, the diagnosis of preeclampsia can still be made if any features of severe disease are present.** |
| **Preeclampsia with severe features** | **In a patient with preeclampsia, presence of any of the following findings are features of severe disease:**<br>▪ Systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg on 2 occasions at least 4 hours apart (unless antihypertensive therapy is initiated before this time)<br>▪ Thrombocytopenia (platelet count <100,000/microL)<br>▪ Impaired liver function as indicated by liver transaminase levels at least twice the normal concentration or severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both<br>▪ Progressive renal insufficiency (serum creatinine concentration >1.1 mg/dL [97 micromol/L] or doubling of the serum creatinine concentration in the absence of other renal disease)<br>▪ Pulmonary edema<br>▪ Persistent cerebral or visual disturbances |
| **Eclampsia** | ▪ A generalized seizure in a patient with preeclampsia that cannot be attributed to other causes |

| | |
|---|---|
| **HELLP syndrome** | ▪ **H**emolysis, **E**levated **L**iver enzymes, and **L**ow **P**latelets. Hypertension may be present (HELLP in such cases is often considered a variant of preeclampsia). |
| **Chronic (preexisting) hypertension** | **Hypertension diagnosed or present before pregnancy or on at least two occasions before 20 weeks of gestation. Hypertension that is first diagnosed during pregnancy and persists for at least 12 weeks postpartum is also considered chronic hypertension.**<br>▪ Blood pressure criteria during pregnancy are:<br>• Systolic ≥140 mmHg and/or diastolic ≥90 mmHg<br>▪ Prepregnancy and 12 weeks postpartum blood pressure criteria are:<br>• Stage 1 – Systolic 130 to 139 mmHg or diastolic 80 to 89 mmHg<br>• Stage 2 – Systolic ≥140 mmHg or diastolic ≥90 mmHg |
| **Chronic hypertension with superimposed preeclampsia*** | **Any of these findings in a patient with chronic hypertension:**<br>▪ A sudden increase in blood pressure that was previously well-controlled or an escalation of antihypertensive therapy to control blood pressure<br>▪ New onset of proteinuria or a sudden increase in proteinuria in a patient with known proteinuria before or early in pregnancy<br>▪ Significant new end-organ dysfunction consistent with preeclampsia after 20 weeks of gestation or postpartum |
| **Chronic hypertension with superimposed preeclampsia with severe features** | **Any of these findings in a patient with chronic hypertension and superimposed preeclampsia:**<br>▪ Systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg despite escalation of antihypertensive therapy<br>▪ Thrombocytopenia (platelet count <100,000/microL)<br>▪ Impaired liver function as indicated by liver transaminase levels at least twice the normal concentration or severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both<br>▪ New-onset or worsening renal insufficiency<br>▪ Pulmonary edema<br>▪ Persistent cerebral or visual disturbances |

* Precise diagnosis is often challenging. High clinical suspicion is warranted given the increase in maternal and fetal-neonatal risks associated with superimposed preeclampsia.

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*Adapted from:*

1. *Gestational hypertension and preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol 2020; 135:e237.*
2. *Report of the National High Blood Pressure Education Program Working Group on high blood pressure in pregnancy. Am J Obstet Gynecol 2000; 183:S1.*

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Graphic 127246 Version 7.0

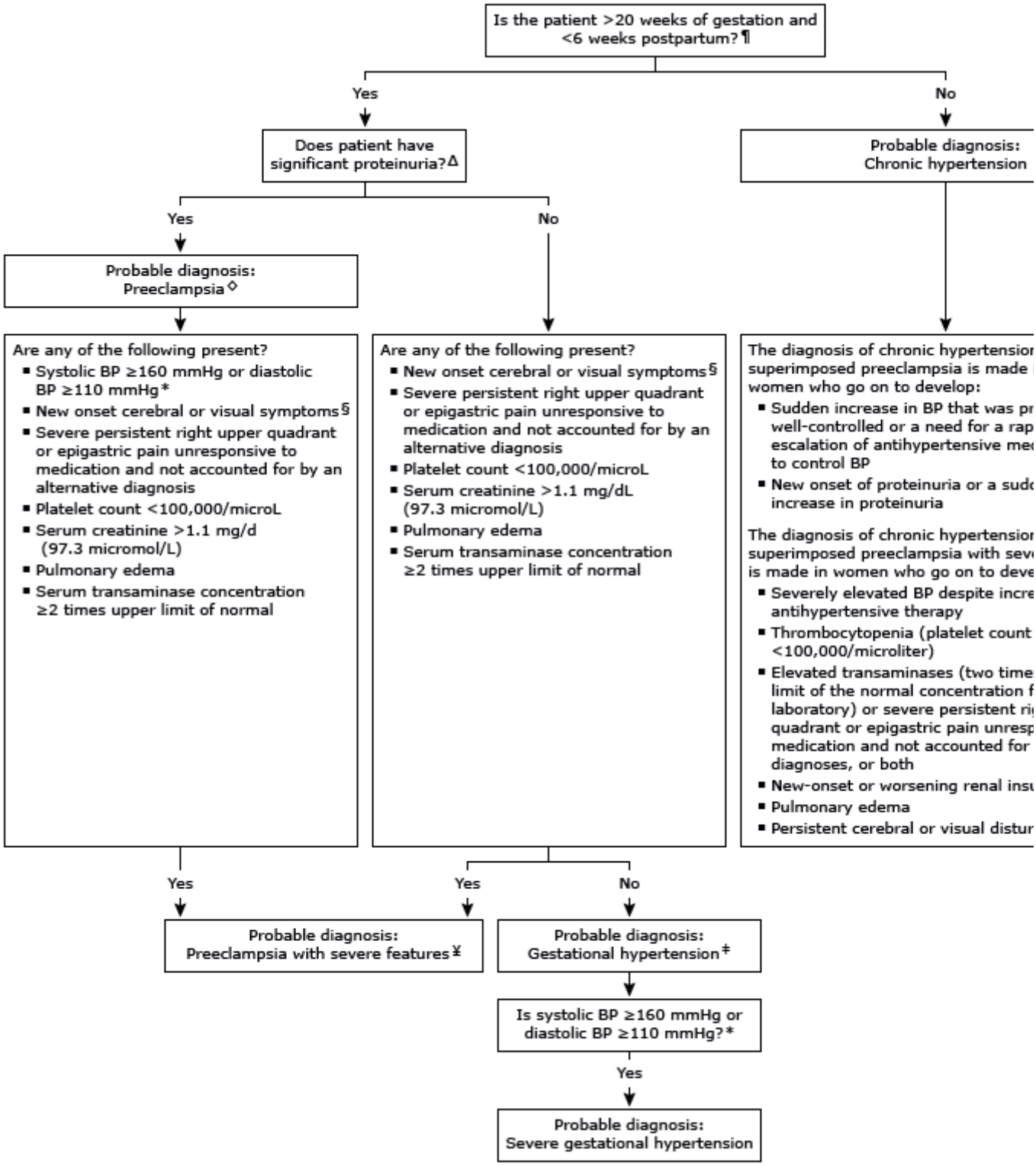
## Comparison of the major hypertensive disorders that occur in pregnant women

| | Normotension before pregnancy | Hypertension during pregnancy (%) | Proteinuria | Thrombocytopenia and/or increased transaminases |
|---|---|---|---|---|
| Preeclampsia | Yes | 100 | Usually present | Variable, depending on whether preeclampsia is at the severe end of the disease spectrum |
| HELLP | Yes | 82 to 88 | Usually present | 100% |
| Gestational hypertension | Yes | 100 | No | No |
| Chronic hypertension | No | 100 | Variable | No |
| Preeclampsia superimposed on chronic hypertension | No | 100 | Usually present | Variable, depending on whether preeclampsia is at the severe end of the disease spectrum |

HELLP: hemolysis, elevated liver enzymes, low platelets.

Graphic 127053 Version 1.0

## Diagnostic evaluation of a pregnant or postpartum woman with persistent s blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg*




A reduction in blood pressure early in pregnancy is a normal physiologic occurrence. For this reason, wo chronic hypertension may be normotensive at their first few prenatal visits. Later in pregnancy, when the pressure returns to its prepregnancy baseline, they may appear to be developing preeclampsia or gestat hypertension if there are no documented prepregnancy blood pressure measurements.

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BP: blood pressure.

* Blood pressure should be elevated on at least two occasions at least four hours apart. However, if systo pressure is ≥160 mmHg or diastolic pressure is ≥110 mmHg, confirmation after a short interval, even wi minutes, is acceptable to facilitate timely initiation of antihypertensive therapy.

¶ The onset of preeclampsia and gestational hypertension is almost always after 20 weeks of gestation. Preeclampsia before 20 weeks of gestation may be associated with a complete or partial molar pregnanc hydrops. Postpartum preeclampsia usually presents within two days of delivery. The term "delayed postp preeclampsia" is used for signs and symptoms of the disease leading to readmission more than two days than six weeks after delivery.

Δ Significant proteinuria is defined as ≥0.3 g in a 24-hour urine specimen or protein/creatinine ratio ≥0.3 (34 mg/mmol) in a random urine specimen or dipstick ≥1+ if a quantitative measurement is unavailable.

◇ Almost all women with the new onset of hypertension and proteinuria at this gestational age or postp preeclampsia, but a rare patient may have occult renal disease exacerbated by the physiologic changes o pregnancy. An active urine sediment (red and white cells and/or cellular casts) is consistent with a prolife glomerular disorder but not a feature of preeclampsia. Women with chronic hypertension who had prote prior to or in early pregnancy may develop superimposed preeclampsia. This can be difficult to diagnose definitively, but should be suspected when blood pressure increases significantly (especially acutely) in th of pregnancy/postpartum or signs/symptoms associated with the severe end of the disease spectrum de

§ Photopsia (flashes of light), scotomata (dark areas or gaps in the visual field), blurred vision, or tempora blindness (rare); severe headache (ie, incapacitating, "the worst headache I've ever had") or headache tha and progresses despite analgesic therapy; altered mental status. Seizure occurrence upgrades the diagn eclampsia.

¥ The differential diagnosis of preeclampsia with severe features includes but is not limited to:

- Antiphospholipid syndrome
- Acute fatty liver of pregnancy
- Thrombotic thrombocytopenic purpura (TTP)
- Hemolytic uremic syndrome (HUS)

The laboratory findings in these disorders overlap with those in preeclampsia with severe features. (Refe in the UpToDate topic on the clinical manifestations and diagnosis of preeclampsia.) The prepregnancy h magnitude and spectrum of laboratory abnormalities, and additional presence of signs and symptoms n associated with preeclampsia help in making the correct diagnosis, which is not always possible during p

In addition, a variety of medical disorders may be associated with hypertension and one or more of the s symptoms that occur in women with preeclampsia with severe features. These patients can usually be distinguished from patients with preeclampsia by taking a detailed history, performing a thorough physi examination, and obtaining relevant laboratory studies.

‡ In contrast to preeclampsia, gestational hypertension is not associated with end-organ involvement, sc proteinuria nor the symptoms or laboratory findings of preeclampsia are present. Refer to UpToDate top gestational hypertension.

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Graphic 119141 Version 3.0

## 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:<br>▪ Photopsia, scotomata, cortical blindness, retinal vasospasm<br>**and/or**<br>▪ 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<br>**and/or**<br>▪ 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]<br>**and/or**<br>▪ 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

## Signs and symptoms of Cushing syndrome

| More common | Less common |
| --- | --- |
| ▪ Decreased libido<br>▪ Obesity/weight gain<br>▪ Plethora<br>▪ Round face<br>▪ Menstrual changes<br>▪ Hirsutism<br>▪ Hypertension<br>▪ Ecchymoses<br>▪ Lethargy, depression<br>▪ Dorsal fat pad<br>▪ Abnormal glucose tolerance | ▪ ECG abnormalities or atherosclerosis<br>▪ Striae<br>▪ Edema<br>▪ Proximal muscle weakness<br>▪ Osteopenia or fracture<br>▪ Headache<br>▪ Backache<br>▪ Recurrent infections<br>▪ Abdominal pain<br>▪ Acne<br>▪ Female balding |

ECG: electrocardiogram.

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Graphic 111525 Version 7.0

## 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.

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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.

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Graphic 65674 Version 13.0

## Causes of epigastric abdominal pain

| Epigastric | Clinical features | Comments |
|---|---|---|
| Acute myocardial infarction | May be associated with shortness of breath and exertional symptoms. | Consider particularly in patients with risk factors for coronary artery disease. |
| Acute pancreatitis | Acute-onset, persistent upper abdominal pain radiating to the back. | |
| Chronic pancreatitis | Epigastric pain radiating to the back. | Associated with pancreatic insufficiency. |
| Peptic ulcer disease | Epigastric pain or discomfort is the most prominent symptom. | Occasionally, discomfort localizes to one side. |
| Gastroesophageal reflux disease | Associated with heartburn, regurgitation, and dysphagia. | |
| Gastritis/gastropathy | Abdominal discomfort/pain, heartburn, nausea, vomiting, and hematemesis. | Variety of etiologies including alcohol and nonsteroidal antiinflammatory drugs (NSAIDs). |
| Functional dyspepsia | The presence of one or more of the following: postprandial fullness, early satiation, epigastric pain, or burning. | Patients have no evidence of structural disease. |
| Gastroparesis | Nausea, vomiting, abdominal pain, early satiety, postprandial fullness, and bloating. | Most causes are idiopathic, diabetic, or postsurgical. |

Graphic 106200 Version 2.0

## Causes of right upper quadrant (RUQ) abdominal pain

| RUQ | Clinical features | Comments |
|---|---|---|
| **Biliary** | | |
| Biliary colic | Intense, dull discomfort located in the RUQ or epigastrium. Associated with nausea, vomiting, and diaphoresis. Generally lasts at least 30 minutes, plateauing within one hour. Benign abdominal examination. | Patients are generally well-appearing. |
| Acute cholecystitis | Prolonged (>4 to 6 hours) RUQ or epigastric pain, fever. Patients will have abdominal guarding and Murphy's sign. | |
| Acute cholangitis | Fever, jaundice, RUQ pain. | May have atypical presentation in older adults or immunosuppressed patients. |
| Sphincter of Oddi dysfunction | RUQ pain similar to other biliary pain. | Biliary type pain without other apparent causes. |
| **Hepatic** | | |
| Acute hepatitis | RUQ pain with fatigue, malaise, nausea, vomiting, and anorexia. Patients may also have jaundice, dark urine, and light-colored stools. | Variety of etiologies include hepatitis A, alcohol, and drug-induced. |
| Perihepatitis (Fitz-Hugh-Curtis syndrome) | RUQ pain with a pleuritic component, pain is sometimes referred to the right shoulder. | Aminotransferases are usually normal or only slightly elevated. |
| Liver abscess | Fever and abdominal pain are the most common symptoms. | Risk factors include diabetes, underlying hepatobiliary or pancreatic disease, or liver transplant. |
| Budd-Chiari syndrome | Symptoms include fever, abdominal pain, abdominal distention (from ascites), lower extremity edema, jaundice, gastrointestinal bleeding, and/or hepatic encephalopathy. | Variety of causes. |
| Portal vein thrombosis | Symptoms include abdominal pain, dyspepsia, or | Clinical manifestations depend on extent of obstruction and |

| | | |
|---|---|---|
| | gastrointestinal bleeding. | speed of development. Most commonly associated with cirrhosis. |

Graphic 106199 Version 3.0

## Causes of left upper quadrant (LUQ) abdominal pain

| LUQ | Clinical features | Comments |
|---|---|---|
| Splenomegaly | Pain or discomfort in LUQ, left shoulder pain, and/or early satiety. | Multiple etiologies. |
| Splenic infarct | Severe LUQ pain. | Atypical presentations common. Associated with a variety of underlying conditions (eg, hypercoagulable state, atrial fibrillation, and splenomegaly). |
| Splenic abscess | Associated with fever and LUQ tenderness. | Uncommon. May also be associated with splenic infarction. |
| Splenic rupture | May complain of LUQ, left chest wall, or left shoulder pain that is worse with inspiration. | Most often associated with trauma. |

Graphic 106201 Version 2.0

## Causes of lower abdominal pain

| Lower abdomen | Localization | Clinical features | Comments |
|---|---|---|---|
| Appendicitis | Generally right lower quadrant | Periumbilical pain initially that radiates to the right lower quadrant. Associated with anorexia, nausea, and vomiting. | Occasional patients present with epigastric or generalized abdominal pain. |
| Diverticulitis | Generally left lower quadrant, although right-sided symptoms are not uncommon | Pain usually constant and present for several days prior to presentation. May have associated nausea and vomiting. | Clinical presentation depends on severity of underlying inflammatory process and whether or not complications are present. |
| Nephrolithiasis | Either | Pain most common symptom, varies from mild to severe. Generally flank pain, but may have back or abdominal pain. | Cause symptoms as stone passes from renal pelvis to ureter. |
| Pyelonephritis | Either | Associated with dysuria, frequency, urgency, hematuria, fever, chills, flank pain, and costovertebral angle tenderness. | |
| Acute urinary retention | Suprapubic | Present with lower abdominal pain and discomfort; inability to urinate. | |
| Cystitis | Suprapubic | Associated with dysuria, frequency, urgency, and hematuria. | |
| Infectious colitis | Either | Diarrhea as the predominant symptom, but may also have associated abdominal pain, which may be severe. | Patients with *Clostridioides difficile* infection can present with an acute abdomen and peritoneal signs in the setting of perforation and fulminant colitis. |

| | | | |
|---|---|---|---|
| Testicular torsion | Can begin in lower abdomen, localizing to side ipsilateral to testicle | Often associated with nausea and vomiting. | Usually in boys or adolescents. |

Graphic 106202 Version 5.0

## Pelvic causes of abdominal pain in women

| Pelvic causes of abdominal pain in women | Lateralization | Clinical features | Comments |
|---|---|---|---|
| Ectopic pregnancy | Either side or diffuse abdominal pain | Vaginal bleeding with abdominal pain, typically six to eight weeks after last menstrual period. | Patients can present with life-threatening hemorrhage if ruptured. |
| Pelvic inflammatory disease | Lateralization uncommon | Characterized by the acute onset of lower abdominal or pelvic pain, pelvic organ tenderness, and evidence of inflammation of the genital tract. Often associated with cervical discharge. | Wide spectrum of clinical presentations. |
| Ovarian torsion | Localized to one side | Acute onset of moderate-to-severe pelvic pain, often with nausea and possibly vomiting, in a woman with an adnexal mass. | Generally not associated with vaginal discharge. |
| Ruptured ovarian cyst | Localized to one side | Sudden-onset unilateral lower abdominal pain. The classic presentation is sudden onset of severe focal lower quadrant pain following sexual intercourse. | Generally not associated with vaginal discharge. |
| Endometriosis | | Associated with dysmenorrhea, pelvic pain, dyspareunia, and/or infertility, but other symptoms may also be present (eg, bowel or bladder symptoms). | Patients may present with one symptom or a combination of symptoms. |
| Acute endometritis | | Most often preceded by pelvic inflammatory disease. | Diagnostic criteria the same as pelvic inflammatory disease. |
| Chronic endometritis | | Present with abnormal uterine bleeding, which may consist of intermenstrual bleeding, spotting, postcoital bleeding, menorrhagia, or amenorrhea. Vague, crampy lower | |

| | | | |
|---|---|---|---|
| | | abdominal pain accompanies the bleeding or may occur alone. | |
| Leiomyomas (fibroids) | | Symptoms related to bulk or infrequently acute pain from degeneration or torsion of pedunculate tumor. Pain may be associated with a low-grade fever, uterine tenderness on palpation, elevated white blood cell count, or peritoneal signs. | |
| Ovarian hyperstimulation | | Abdominal distention/discomfort, nausea/vomiting, and diarrhea. More severe cases can have severe abdominal pain, ascites, intractable nausea, and vomiting. | Women undergoing fertility treatment. |
| Ovarian cancer | | Abdominal or pelvic pain. May have associated symptoms of bloating, urinary urgency or frequency, or difficulty eating/feeling full quickly. | |
| Ovulatory pain (Mittelsmerz) | | Occurs mid-cycle, coinciding with timing of ovulation. | May be right- or left-sided, depending on site of ovulation during that cycle. |
| Pregnancy and related complications* | | | |

* Refer to the UpToDate topics on abdominal pain.

Graphic 106204 Version 3.0

## Contributor Disclosures

**Phyllis August, MD, MPH** No relevant financial relationship(s) with ineligible companies to disclose. **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. **Lynn L Simpson, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Vanessa A Barss, MD, FACOG** No relevant financial relationship(s) with ineligible companies to disclose.

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