Preeclampsia: Clinical features and diagnosis

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INTRODUCTION

Preeclampsia is a multisystem progressive disorder characterized by the new onset of hypertension and proteinuria or the new onset of hypertension and significant end-organ dysfunction with or without proteinuria in the last half of pregnancy or postpartum (table 1). It is caused by placental and maternal vascular dysfunction and resolves after birth over a variable period of time. Although approximately 90 percent of cases present in the late preterm (≥34 to <37 weeks), term, or postpartum period and have good maternal, fetal, and newborn outcomes, the mother and child are still at increased risk for serious morbidity or mortality. The remaining 10 percent of cases have an early presentation (<34 weeks), which is associated with a higher risk of maternal and fetal or newborn complications than preeclampsia at term and carries the additional high risks associated with moderately preterm, very preterm, or extremely preterm birth. Long-term, patients with preeclampsia are at increased risk for developing cardiovascular and renal disease.

This topic will discuss the clinical features, diagnosis, and differential diagnosis of preeclampsia. Other important issues related to this disease are reviewed separately:

- (See "Preeclampsia: Pathogenesis".)
- (See "Preeclampsia: Antepartum management and timing of delivery".)
- (See "Early pregnancy prediction of preeclampsia".)

- (See "Preeclampsia: Prevention".)

DEFINITIONS/DIAGNOSTIC CRITERIA

The major hypertensive disorders that occur in pregnant patients are described below and summarized in the table (table 2) [1,2].

Criteria for hypertension — During pregnancy, hypertension is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Severe hypertension is defined as systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg.

Chronic hypertension is defined as hypertension that precedes pregnancy or is present on at least two occasions before the 20th week of gestation or persists longer than 12 weeks postpartum. It can be primary or secondary to a variety of medical disorders. (See "Overview of hypertension in adults", section on 'Definitions'.)

The American College of Cardiology and the American Heart Association have endorsed a lower threshold for diagnosing hypertension in nonpregnant patients (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg). Some have suggested that this definition may also be appropriate for pregnant patients [3]. However, it has not been widely studied, would increase the incidence of hypertension in pregnancy by about 10 percent, and would increase potentially unnecessary testing, hospitalization, and intervention in the absence of a proven benefit.

Preeclampsia, eclampsia, and HELLP

- **Preeclampsia** refers to the new onset of hypertension and proteinuria **or** the new onset of hypertension and significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation or postpartum in a previously normotensive patient (table 1) [2,4-6]. It is important to note that the diagnosis can still be made in the absence of proteinuria if the new-onset hypertension is accompanied by specific signs or symptoms of significant end-organ dysfunction, as listed in the table.

  The diagnosis of **preeclampsia with severe features (formerly severe preeclampsia)** is made in the subset of patients with preeclampsia who have severe

hypertension and/or specific signs or symptoms of significant end-organ dysfunction that signify the severe end of the preeclampsia spectrum. The specific criteria for diagnosis are listed in the table (table 3).

In 2013, the American College of Obstetricians and Gynecologists removed proteinuria as an essential criterion for the diagnosis of preeclampsia (hypertension plus signs of significant end-organ dysfunction are sufficient for diagnosis). They also removed massive proteinuria (5 g/24 hours) and fetal growth restriction (FGR) as possible features of severe disease because massive proteinuria has a poor correlation with outcome, and FGR is managed similarly whether or not preeclampsia is diagnosed. Oliguria was also removed as a characteristic of severe disease. The International Society for the Study of Hypertension in Pregnancy continues to include FGR as one of the criteria that can establish a diagnosis of preeclampsia in a patient with new-onset hypertension after 20 weeks of gestation since both preeclampsia and growth restriction are manifestations of a primary placental disorder [7].

- **Eclampsia** refers to the occurrence of a grand mal seizure in a patient with preeclampsia in the absence of other neurologic conditions that could account for the seizure. (See "Eclampsia".)

- **HELLP syndrome** (**h**emolysis, **e**levated **l**iver enzymes, **l**ow **p**latelets) is a subtype of preeclampsia with severe features in which hemolysis, elevated liver enzymes, and thrombocytopenia are predominant features. Hypertension, central nervous system dysfunction, and/or renal dysfunction may also be present. The majority of patients, but not all, have hypertension (82 to 88 percent, although in some cases the increase in blood pressure may be subtle initially) and/or proteinuria (86 to 100 percent) [8]. Rare patients have neither; other diagnoses associated with similar laboratory abnormalities should be excluded before making the diagnosis of HELLP in these atypical patients. (See "HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets)".)

- **Preeclampsia superimposed upon chronic hypertension** – Preeclampsia is considered superimposed when it occurs in a patient with preexisting chronic hypertension (see 'Criteria for hypertension' above). It 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 after 20 weeks of gestation or postpartum in a patient with chronic hypertension (table 3).

Gestational hypertension — Gestational hypertension refers to hypertension without proteinuria or other signs/symptoms of preeclampsia-related end-organ dysfunction that develops after 20 weeks of gestation. Ten to 25 percent of these patients may ultimately develop signs and symptoms of preeclampsia. Development of proteinuria upgrades the diagnosis to preeclampsia. Even without proteinuria, patients who develop severe hypertension or other features of severe disease (table 3) are managed in the same way as those with preeclampsia with severe features.

True gestational hypertension should resolve by 12 weeks postpartum. If it persists beyond 12 weeks postpartum, the diagnosis is "revised" to chronic hypertension that was masked by the physiologic decrease in blood pressure that occurs in early pregnancy. If it resolves postpartum and signs and symptoms of preeclampsia did not develop, the diagnosis can be "revised" to transient hypertension of pregnancy. (See "Gestational hypertension".)

INCIDENCE

In a systematic review, 4.6 percent (95% CI 2.7-8.2) of pregnancies worldwide were complicated by preeclampsia [9]. The incidence in the United States is approximately 5 percent [10]. Variations in incidence among countries reflect, at least in part, differences in the maternal age distribution and proportion of nulliparous pregnant patients in the population [11]. (See 'Risk factors' below.)

Preeclampsia is less common before 34 weeks of gestation. In one population-based study, the incidence before and after 34 weeks was 0.3 and 2.7 percent, respectively [12].

RISK FACTORS

Risk factors for preeclampsia are listed in the table (table 4) and apply to both early-onset and late-onset disease. The magnitude of risk depends on the specific factor and is described below for selected risk factors evaluated in systematic reviews [13,14]. A past

history of preeclampsia, preexisting hypertension, pregestational diabetes, multifetal gestation, chronic kidney disease, and some autoimmune diseases (antiphospholipid syndrome, systemic lupus erythematosus) carry the highest relative risk (RR).

- A **past history of preeclampsia** increases the risk of developing preeclampsia in a subsequent pregnancy eightfold compared with patients without this history (RR 8.4, 95% CI 7.1-9.9) [14].

  The severity of preeclampsia strongly impacts this risk. Patients with severe features of preeclampsia in the second trimester are at greatest risk of developing preeclampsia in a subsequent pregnancy: Recurrence rates of 25 to 65 percent have been reported [15-18]. By comparison, patients with preeclampsia without severe features in their first pregnancy develop preeclampsia in 5 to 7 percent of second pregnancies [19,20]. Patients who had a normotensive first pregnancy develop preeclampsia in less than 1 percent of second pregnancies.

- **Preexisting medical conditions**:

  - **Pregestational diabetes** (RR 3.7, 95% CI 3.1-4.3) [14] – This increase has been related to a variety of factors, such as underlying renal or vascular disease, obesity, high plasma insulin levels/insulin resistance, and abnormal lipid metabolism [21].

  - **Chronic hypertension** (RR 5.1, 95% CI 4.0-6.5) [14] – Although chronic hypertension (when defined as blood pressure ≥140/90 mmHg) increases the risk of preeclampsia fivefold compared with patients without this risk factor, chronic hypertension is uncommon in reproductive-age females and thus accounts for only 5 to 10 percent of preeclampsia cases [22].

    Increasing data suggest that patients with contemporary definitions of hypertension are also at increased risk for preeclampsia [13,23-26]. There appears to be a dose-response relationship between blood pressure and preeclampsia that becomes clinically significant when blood pressure reaches the elevated level (systolic blood pressure 120 to 129 mmHg and diastolic blood pressure <80 mmHg), increases with stage 1 hypertension (systolic blood pressure 130 to 139 mmHg and/or diastolic blood pressure 80 to 89 mmHg), and increases further with stage 2 hypertension (systolic blood pressure ≥140 mmHg

or diastolic blood pressure ≥90 mmHg) [25,26].

- Some autoimmune disorders, such as **systemic lupus erythematosus** (RR 1.8, 95% CI 1.5-2.1) and **antiphospholipid syndrome** (RR 2.8, 95% CI 1.8-4.3), increase the risk for developing preeclampsia [14]. The reasons for this relationship are not clear but may include multiple mechanisms involving inflammation, microangiopathy, increased platelet turnover, and kidney dysfunction.

- **Prepregnancy overweight or obesity** (body mass index >25 kg/m^2 [RR 2.1, 95% CI 2.0-2.2] and >30 kg/m^2 [RR 2.8, 95% CI 2.6-3.1]) [14] – The risk of preeclampsia doubles with each 5 to 7 kg/m^2 increase in prepregnancy body mass index [27]. This relationship persisted in studies that excluded patients with chronic hypertension, diabetes mellitus, multiple gestations, or after adjustment for other confounders. Although overweight and obesity increase the risk of preeclampsia only two- to threefold, overweight and obesity are highly prevalent worldwide and thus cumulatively account for over 40 percent of preeclampsia cases [22].

- **Chronic kidney disease** (RR 1.8, 95% CI 1.5-2.1) [14] – The risk varies depending on the degree of reduction of glomerular filtration rate and the presence or absence of hypertension. In some studies, as many as 40 to 60 percent of patients with advanced chronic kidney disease (stages 3, 4, 5) were diagnosed with preeclampsia in the latter half of pregnancy [28,29].

- **Multifetal pregnancy** (RR 2.9, 95% CI 2.6-3.1) [14] – In three large series, preeclampsia occurred in 5 percent of singleton, 8 to 13 percent of twin, and 11 percent of triplet gestations [30-33], although rates over 20 percent in multiple gestations are commonly reported in small series [34].

- **Nulliparity** (RR 2.1, 95% CI 1.9-2.4) [14] – It is unclear why the nulliparous state is consistently found to be the most prevalent predisposing factor for preeclampsia [14]. One theory is that the immune system of nulliparous individuals has had limited exposure to paternal antigens, and this lack of desensitization may play a role in the pathogenesis of the disease. Epidemiologic data support this theory: Protection from preeclampsia in subsequent pregnancies is either reduced or eliminated if there is a change in paternity, patients using barrier methods of contraception are at increased risk, and risk is reduced with increased duration of

sexual activity before pregnancy [35]. However, the notion that the risk of preeclampsia is increased in a subsequent pregnancy with a new partner has been challenged by data suggesting that a longer interval between pregnancies may be the reason for the increased risk with a new partner [36].

- A **family history of preeclampsia** in a first-degree relative increases the risk for preeclampsia (RR 2.90, 95% CI 1.70-4.93) [13], suggesting a heritable mechanism in some cases [37,38]. The occurrence and severity of the disease appear to be influenced primarily by maternal factors, but the paternal contribution to fetal genes may play a role in defective placentation and subsequent preeclampsia.

  A patient who was born preterm, low birth weight, or small for gestational age also appears to be at increased risk of developing gestational hypertension or preeclampsia when they become pregnant [39]. Preeclampsia, preterm birth, low birth weight, and small for gestational age can be different manifestations of a heritable tendency for abnormal placental development. (See "Preeclampsia: Pathogenesis", section on 'Genetic factors'.)

- **Prior pregnancy complications associated with placental insufficiency** – Fetal growth restriction (RR 1.4, 95% CI 0.6-3.0), abruption (RR 2.0, 95% CI 1.4-2.7), and stillbirth (RR 2.4, 95% CI 1.7-3.4) can be different manifestations of placental insufficiency [14]. They are risk factors for preeclampsia, and preeclampsia is a risk factor for developing these disorders.

- **Advanced maternal age** (maternal age ≥35: RR 1.2, 95% CI 1.1-1.3; maternal age ≥40: RR 1.5, 95% CI 1.2-2.0) [14] – Older patients tend to have additional risk factors, such as obesity, diabetes mellitus, and chronic hypertension, that predispose them to developing preeclampsia.

  Whether adolescents are at higher risk of preeclampsia is more controversial. One systematic review estimated that the prevalence of preeclampsia/eclampsia in adolescent pregnancies was 6.7 percent [40] and another did not find an association between adolescence and risk for preeclampsia [13], but the results are not conclusive given the heterogeneity of the included studies. (See "Effects of advanced maternal age on pregnancy".)

- **Use of assisted reproductive technology** is a risk factor in large cohort studies

(pooled rate 6.2 percent, 95% CI 4.7-7.9; RR 1.8, 95% CI 1.6-2.1) [14]. However, multivariate logistic regression analysis attenuates this association, and propensity analysis further weakens it [41]. In addition, one study reported the risk for hypertensive disorders of pregnancy was increased with both autologous or donor oocyte frozen embryo transfer and fresh donor oocyte embryo transfer, but not with autologous oocyte-fresh embryo transfer [42].

Of note, patients who smoke cigarettes have a **lower** risk of preeclampsia than nonsmokers. (See "Cigarette and tobacco products in pregnancy: Impact on pregnancy and the neonate", section on 'Preeclampsia'.)

OVERVIEW OF PATHOPHYSIOLOGY

The pathophysiology of preeclampsia likely involves both maternal and fetal/placental factors. In a normal pregnancy, the myometrial and decidual vasculature at the placental implantation site remodels such that the terminal part of the spiral arterioles is wide open, resulting in a high-capacity, low-resistance system to provide optimal maternal-fetal nutrient and oxygen exchange. In preeclampsia, however, shallow placentation and failure of the spiral arteries to remodel early in pregnancy, weeks to months before development of clinical manifestations of the disease, results in suboptimal uteroplacental blood flow and relatively hypoxic trophoblast tissue [43,44]. An exaggerated state of oxidative stress develops in the placenta, which in turn adversely affects villous angiogenesis [45]. As pregnancy advances, the pathologic placenta increasingly secretes antiangiogenic factors (soluble fms-like tyrosine kinase-1 [sFlt-1] and endoglin) into the maternal circulation that bind vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), which results in widespread maternal vascular inflammation, endothelial dysfunction, and vascular injury, leading to hypertension, proteinuria, and the other clinical manifestations of preeclampsia [46,47]. (See "Preeclampsia: Pathogenesis".)

It has been proposed that there are several subtypes of preeclampsia, with a variety of pathophysiological pathways leading to maternal and fetal mortality and morbidity [48]. The most commonly described subtypes of preeclampsia are characterized as early onset (<34 weeks of gestation) and late onset (≥34 weeks of gestation). The clinical features overlap, but the spectrum of disease and outcomes differ: Early-onset disease has been associated with more severe placental and maternal/fetal clinical findings and, in turn,

poorer maternal/fetal outcomes [49,50]. For this reason, it has been hypothesized that the two phenotypes have different origins and pathophysiologies [49,51,52]. Other possible subtypes include gestational hypertension and preeclampsia with versus without fetal growth restriction. However, these differences can also be explained by biological variation in the disease process.

SCREENING AND RISK REDUCTION

At the first prenatal visit, screening for traditional risk factors for preeclampsia is routinely performed because identifying patients at high risk of developing the disease and treating them with low-dose aspirin throughout pregnancy can reduce this risk. Candidates for low-dose aspirin therapy and the effectiveness of this therapy are reviewed separately. (See "Early pregnancy prediction of preeclampsia", section on 'Routine regular prenatal blood pressure measurement' and "Preeclampsia: Prevention", section on 'Candidates'.)

At subsequent provider visits, the body of evidence supports continuing to screen for preeclampsia by measuring blood pressure at every encounter [53,54]. Although preeclampsia is not typically diagnosed before 20 weeks, measuring blood pressures before 20 weeks establishes a baseline for comparison later in pregnancy. (See 'Accurate assessment of blood pressure' below.)

The value of any laboratory or imaging test for screening and subsequent intervention has not been established (see "Early pregnancy prediction of preeclampsia"). Although it is customary to test for proteinuria at each prenatal visit, this practice has not been rigorously evaluated and proven to improve outcomes [54]. We suggest performing a urinalysis to test for proteinuria at the first prenatal visit to establish a baseline and, given the possibility for false-positive and false-negative results, repeating the test only in those who develop hypertension. By contrast, testing for proteinuria should be performed at each visit in patients with hypertension as proteinuria changes the diagnosis to preeclampsia. Once a diagnosis of preeclampsia is established, testing for proteinuria is no longer diagnostically or prognostically useful. (See "Evaluation of proteinuria in pregnancy and management of nephrotic syndrome" and "Evaluation of proteinuria in pregnancy and management of nephrotic syndrome", section on 'Semiquantitative' and "Evaluation of proteinuria in pregnancy and management of nephrotic syndrome", section on 'Quantitative'.)

CLINICAL PRESENTATION

Typical presentation — One-third of affected patients are nulliparous, and most of the remainder are at high risk for the disease because of overweight/obesity, prior preeclampsia, chronic hypertension, multifetal pregnancy, chronic kidney disease, or pregestational diabetes [14]. Approximately 85 percent of affected patients present with new-onset hypertension and proteinuria at ≥34 weeks of gestation, sometimes during labor [55,56]. Approximately 10 percent develop these signs and symptoms at <34 weeks of gestation (ie, early-onset preeclampsia) [55] and rarely as early as 20 to 22 weeks. In approximately 5 percent of preeclampsia cases, the signs and symptoms are first recognized postpartum (ie, postpartum preeclampsia), usually within 48 hours of birth [57-59].

The degree of maternal hypertension and proteinuria as well as the presence/absence of other clinical manifestations of the disease, which represent the severe end of the disease spectrum (alarm findings), are highly variable and described in detail below [60]. (See 'Spectrum of disease' below.)

Alarm blood pressure and symptoms — Approximately 25 percent of patients with preeclampsia develop severe hypertension and/or one or more of the following nonspecific symptoms, which characterize the severe end of the disease spectrum. Severe hypertension and/or alarm symptoms signify the need for urgent evaluation, prompt treatment to reduce blood pressure below the severe level, and possible birth (see 'Patient evaluation' below):

- Persistent and/or severe headache
- Visual abnormalities (scotomata, photophobia, blurred vision, or temporary blindness [rare])
- Upper abdominal, retrosternal, or epigastric pain
- Altered mental status (confusion, altered behavior [agitation])
- New dyspnea, orthopnea

Upper abdominal, retrosternal, or epigastric pain may be the presenting symptom of preeclampsia and reflux is common in pregnant individuals, especially at night; therefore, a high index of suspicion is important to make a timely diagnosis of preeclampsia rather than reflexively ascribing these symptoms to gastroesophageal reflux.

Rare and atypical presentations

Onset <20 weeks — Most cases of preeclampsia presenting before 20 weeks of gestation are associated with a complete or partial molar pregnancy or antiphospholipid syndrome (APS). (See "Hydatidiform mole: Epidemiology, clinical features, and diagnosis", section on 'Preeclampsia <20 weeks of gestation' and "Antiphospholipid syndrome: Obstetric implications and management in pregnancy".)

In rare cases, the diagnosis of preeclampsia with severe features has been made before 20 weeks after other disorders with similar findings have been excluded. These disorders include lupus nephritis, thrombotic thrombocytopenic purpura (which may be hereditary), and hemolytic-uremic syndrome, as well as molar pregnancy and APS. (See "Hypertensive disorders in pregnancy: Approach to differential diagnosis".)

Hydrops-related Mirror syndrome is most common between 22 and 28 weeks, but rare cases have presented before 20 weeks [61,62]. (See "Nonimmune hydrops fetalis", section on 'Mirror syndrome'.)

Onset or exacerbation of symptoms >2 days postpartum — Delayed-onset or late postpartum preeclampsia can be defined as signs and symptoms of the disease leading to readmission more than two days but less than six weeks after birth [59], although various other definitions have been used. Headache is the most common reason for presentation to a health care provider and affected nearly 70 percent of patients in two large studies [59,63]. Shortness of breath was also relatively common, affecting 20 to 30 percent of patients.

Signs and symptoms can be atypical; for example, the patient may have thunderclap headaches alternating with mild headaches or intermittent hypertension. Other etiologies for the signs and symptoms should be considered, such as reversible cerebral vasoconstriction syndrome or impending stroke [64-67]. (See "Overview of thunderclap headache" and "Reversible cerebral vasoconstriction syndrome".)

Risk factors for delayed postpartum preeclampsia appear to be similar to those for the typical cases of preeclampsia [59,68,69], and some patients have no risk factors.

In a retrospective cohort study including 152 patients with delayed postpartum preeclampsia, 63.2 percent had no antecedent diagnosis of hypertensive disease in the

current pregnancy whereas 18.4 percent had preeclampsia, 9.2 percent had chronic hypertension, 4.6 percent had gestational hypertension, and 4.6 percent had preeclampsia superimposed upon chronic hypertension during the peripartum period [59]. Of these patients, 14.5 percent developed postpartum eclampsia and their most common presenting symptom was headache, which occurred in 70 percent of patients.

Severe features of preeclampsia without hypertension — It is uncommon for patients to exhibit the severe features of preeclampsia without hypertension, but this may be observed in 15 percent of patients with HELLP syndrome (which some consider a variant of preeclampsia and others consider a separate disorder) and in some patients with eclampsia (a possible sequelae of preeclampsia). It is possible that in such patients, blood pressure is increased above baseline but does not meet diagnostic criteria for hypertension, similar to what has been described in the syndrome of posterior reversible encephalopathy [70]. (See "Eclampsia", section on 'Can eclampsia be predicted and prevented?' and "HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets)".)

Isolated hypertension — Patients with new onset of mild hypertension but no other criteria for preeclampsia or an underlying disease associated with hypertension are given the diagnosis of gestational hypertension. These patients should be followed closely since 15 to 25 percent will subsequently develop the full diagnostic criteria for preeclampsia. (See "Gestational hypertension", section on 'Risk of progression to preeclampsia'.)

Isolated proteinuria — Isolated gestational proteinuria may occur before the diagnostic criteria for preeclampsia have manifested [71]. We are unaware of prospective studies describing this finding, but in a retrospective study of 95 pregnant patients with new-onset isolated proteinuria who were followed to term, preeclampsia developed in 22 percent: antepartum or intrapartum in 13 patients and postpartum in 8 patients [72].

PATIENT EVALUATION

All pregnant patients with new-onset hypertension or worsening hypertension after 20 weeks of gestation should be evaluated for preeclampsia. Patients with severe hypertension and/or symptoms suggestive of severe disease, such as cerebral or visual symptoms, epigastric pain, or dyspnea, require hospitalization for initial maternal and fetal evaluation and management. Asymptomatic patients with nonsevere hypertension may be followed closely as outpatients provided they are seen frequently and the

maternal and fetal status is stable. The decision to monitor patients in the hospital versus in an outpatient setting should be made on a case-by-case basis, taking into consideration both medical and social issues. (See "Preeclampsia: Antepartum management and timing of delivery".)

Accurate assessment of blood pressure — An appropriate, standardized technique for blood pressure measurement is critically important both in the office and at home. This technique is reviewed separately. (See "Treatment of hypertension in pregnant and postpartum patients", section on 'Technique for accurate measurement of blood pressure'.)

Laboratory tests — We obtain the following laboratory tests when preeclampsia is suspected:

- Complete blood count with platelets
- Serum creatinine level
- Liver chemistries (aspartate aminotransferase [AST], alanine aminotransferase [ALT]) and bilirubin
- Urinary protein determination (protein to creatinine ratio in a random urine specimen or 24-hour urine collection for total protein)

In patients with abnormal liver chemistries, additional laboratory testing includes lactate dehydrogenase (LDH) level.

Coagulation studies (prothrombin time, partial thromboplastin time, fibrinogen) are not routinely obtained but are indicated in patients with additional complications, such as abruptio placentae, severe bleeding, thrombocytopenia, or severe liver dysfunction.

In patients with acute upper abdominal or epigastric pain or those found to have severe liver dysfunction, glucose, amylase, lipase, and ammonia levels can help in differential diagnosis. (See "Hypertensive disorders in pregnancy: Approach to differential diagnosis".)

Assessment of fetal status — Fetal status is assessed concurrently with the maternal evaluation or post-diagnosis, depending on the degree of concern when the mother is evaluated. At a minimum, a nonstress test or biophysical profile is performed, if appropriate for gestational age. Ultrasound is indicated to evaluate amniotic fluid volume and estimate fetal weight given the increased risk for oligohydramnios and fetal growth

restriction (FGR).

Indications for neurology consultation — The neurology service should be consulted to evaluate patients with neurologic deficits/abnormal neurologic examination, ocular signs and symptoms, or a severe persistent headache that does not respond to repeat doses of acetaminophen and initial routine management of preeclampsia.

The complaint of the sudden onset of severe headache ("worst headache of my life") is sufficiently characteristic of subarachnoid hemorrhage that this symptom should prompt neurology consultation and consideration of imaging. The headache is lateralized in 30 percent of patients and may or may not be associated with a brief period of altered consciousness, collapse, nausea or vomiting, preretinal subhyaloid hemorrhages, and meningismus. (See "Aneurysmal subarachnoid hemorrhage: Clinical manifestations and diagnosis".)

Measurement of angiogenic factors — Measurement of urinary or plasma antiangiogenic factors, such as soluble fms-like tyrosine kinase-1 (sFlt-1), and angiogenic factors, such as placental growth factor (PlGF), or their ratios may be useful for distinguishing preeclampsia from other hypertensive-proteinuric disorders or for determining whether a patient with some of the manifestations of preeclampsia but not meeting diagnostic criteria requires medical intervention, such as hospitalization or birth.

Tests for measurement of angiogenic factors are commercially available in some countries (not the United States) but are generally still considered investigational [73-75]. However, in the United Kingdom, the National Institute for Health and Care Excellence 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 [76]. They suggested use of any of four specific tests (DELFIA Xpress PlGF 1-2-3, DELFIA Xpress sFlt-1/Xpress PlGF1-2-3 ratio, Elecsys immunoassay sFlt-1/PlGF ratio, Triage PlGF test), not repeating testing if initial testing is negative.

The International Society for the Study of Hypertension in Pregnancy practice guideline states that assessment of angiogenic imbalance could be performed (if available) and if present (reduced PlGF <5th percentile for gestational age or increased sFlt/PlGF ratio [eg, >38 by the Roche assay]) would strengthen the clinical diagnosis, but should not be used as a sole criterion for diagnosing preeclampsia [77]. It is important to note that these tests are not approved for use in the United States and are not recommended by the American

College of Obstetricians and Gynecologists (ACOG) or the Society for Maternal-Fetal Medicine (SMFM). (See "Preeclampsia: Pathogenesis", section on 'sFlt-1, VEGF, PlGF'.)

In our opinion, the clinical utility of these tests remains unclear. Although some prospective studies and trials [78-81] demonstrated that angiogenic markers have a high negative predictive value and thus can be useful in ruling out preeclampsia and reducing the time to diagnosis, the value of early accurate diagnosis alone without a concomitant improvement in maternal and/or neonatal outcome is questionable. In a meta-analysis of studies examining the performance of sFlT-1, PlGF, or the sFlT-1/PlGF ratio in predicting adverse outcomes in patients with suspected or confirmed preeclampsia, both PlGF and the sFlt-1/PlGF ratio demonstrated pooled area under the summary receiver operating characteristic curve values from 0.68 to 0.87 for predicting composite adverse maternal and perinatal outcomes, preterm birth, and fetal growth restriction, but very high heterogeneity of the population sampled coupled with differences in study methodology, study quality, and the outcomes measured limited conclusions regarding the prognostic value of these biomarkers in clinical practice [82].

SPECTRUM OF DISEASE

Potential clinical findings

Hypertension — All patients with preeclampsia have hypertension, but a small proportion of those with HELLP and rare patients with eclampsia do not meet current diagnostic criteria for hypertension. It is generally the earliest clinical finding and the most common clinical clue to the presence of the disease. The blood pressure usually rises gradually, reaching the hypertensive range (defined as ≥140/90 mmHg) sometime in the third trimester, often after the 37th week of gestation [55]. Blood pressures are often around 135/85 mmHg in the one to two weeks before reaching the hypertensive range. However, in some patients, hypertension develops rapidly, before 34 weeks of gestation, or postpartum.

Pheochromocytoma is a rare cause of hypertension during pregnancy and may be difficult to distinguish from preeclampsia. (See "Hypertensive disorders in pregnancy: Approach to differential diagnosis", section on 'Pheochromocytoma'.)

Hypertension is due to increased peripheral vascular resistance. Cardiac output usually is

normal for pregnancy, except in a minority of patients in whom preeclampsia is complicated by peripartum cardiomyopathy. Some patients with onset near term have decreased vascular resistance and increased cardiac output.

Epigastric, upper abdominal, or retrosternal pain — Epigastric, upper abdominal, or retrosternal pain, when present, is a cardinal symptom of the severe end of the disease spectrum. It is characterized by severe constant pain that often begins at night, usually maximal in the low retrosternum or epigastrium, but may radiate to the right hypochondrium or back [83]. Nausea and vomiting sometimes also occur, but when persistent and associated with loss of appetite, fatty liver of pregnancy should be ruled out. (See "Acute fatty liver of pregnancy".)

On examination, the liver may be tender to palpation due to stretching of Glisson's capsule from hepatic swelling or bleeding. Liver rupture or hemorrhage is rare but should be suspected when there is sudden onset of right upper quadrant pain associated with a decrease in blood pressure.

Acute pancreatitis is a rare complication of preeclampsia [84] and can mimic the epigastric pain of preeclampsia [85]. (See "Hypertensive disorders in pregnancy: Approach to differential diagnosis", section on 'Medical and surgical disorders associated with elevated blood pressure, headache, and/or abdominal pain'.)

Neurologic

Headache — Headache, when present, is a feature of the severe end of the disease spectrum. It may be temporal, frontal, occipital, or diffuse [86,87]. The pain usually has a throbbing or pounding quality but may be piercing. Although not pathognomonic, a feature that suggests preeclampsia-related headache rather than another type of headache is that it persists despite administration of over-the-counter analgesics, and it may become severe (ie, incapacitating, "the worst headache of my life"). However, resolution of the headache with analgesics does not exclude the possibility of preeclampsia. The American College of Obstetricians and Gynecologists' criteria for preeclampsia-related headache are "new-onset headache unresponsive to medication and not accounted for by alternative diagnoses or visual symptoms" [2].

The mechanism for headache, as well as other cerebrovascular symptoms of preeclampsia, is poorly understood. Cerebral edema and ischemic/hemorrhagic changes

in the posterior hemispheres observed on computed tomography and magnetic resonance imaging help to explain, but do not fully account for, the clinical findings [88,89]. These findings may result from generalized endothelial cell dysfunction, leading to vasospasm of the cerebral vasculature in response to severe hypertension, or they may result from loss of cerebrovascular autoregulation, leading to areas of both vasoconstriction and forced vasodilation. Thus, they could represent a form of posterior reversible leukoencephalopathy syndrome (PRES) [70,90,91]. PRES is typically associated with severe hypertension but can also occur with rapid increases in blood pressure in patients with endothelial damage and also in patients with only mildly elevated blood pressure [92]. (See "Reversible posterior leukoencephalopathy syndrome" and "Eclampsia", section on 'Clinical findings'.)

Acetaminophen is commonly used to treat headache. Doses ≤2 g/day can be administered to patients with mild hepatic or renal insufficiency, but it is contraindicated in patients with severe hepatic or renal impairment.

Visual symptoms — Visual symptoms, when present, are also symptoms of the severe end of the disease spectrum. They are caused, at least in part, by retinal arteriolar spasm, impaired cerebrovascular autoregulation, and cerebral edema [70,93]. Symptoms include blurred vision, photopsia (flashing lights or sparks), and scotomata (dark areas or gaps in the visual field) [94-96]. Diplopia or amaurosis fugax (blindness in one or both eyes) may also occur. Visual disturbances in preeclampsia may be manifestations of PRES [91].

Cortical blindness is rare and typically transient [97]. Blindness related to retinal pathology, such as retinal artery or vein occlusion, retinal detachment, optic nerve damage, retinal artery spasm, and retinal ischemia, may be permanent [98].

Mental status changes — Mental status changes include confusion and altered behavior, such as agitation.

Stroke — Stroke leading to death or disability is the most serious complication of preeclampsia/eclampsia and is responsible for approximately 36 percent of pregnancy-associated stroke [99]. Most strokes in this setting are hemorrhagic and preceded by severe headache and severe and fluctuating blood pressure levels (especially severe systolic hypertension), but ischemic strokes also occur [100,101]. Eclamptic seizures occur in some, but not all, cases. Risk factors for hemorrhagic stroke in patients with

preeclampsia include persistent severe hypertension associated with significant headache and/or seizures. Lowering blood pressure can reduce the risk. (See "Cerebrovascular disorders complicating pregnancy", section on 'Preeclampsia, eclampsia, and HELLP'.)

Generalized hyperreflexia — Hyperreflexia is a common finding. Sustained ankle clonus may be present.

Seizure — In some patients, the combination of hypertension and endothelial activation results in posterior reversible

encephalopathy syndrome (PRES), manifested as headaches, scotomata, scintillations, and seizure. Seizure in a preeclamptic patient upstages the diagnosis to eclampsia. Eclamptic seizures develop in 1 in 400 patients with preeclampsia without severe features and in 1 in 50 patients with preeclampsia with severe features. Histopathologic correlates include brain hemorrhage, petechiae, edema, vasculopathy, ischemic damage, microinfarcts, and fibrinoid necrosis [102,103]. Neuroimaging consistent with PRES may be seen [104]. (See "Eclampsia", section on 'Clinical findings'.)

Pulmonary edema — Pulmonary edema is a feature of the severe end of the disease spectrum and was observed in approximately 10 percent of 63 cases of preeclampsia with severe features in a prospective study [105]. Symptoms may include shortness of breath, cough, wheezing, anxiety/restlessness, chest pain, palpitations, or excessive perspiration. The symptom complex of dyspnea, chest pain, and/or decreased (≤93 percent) oxygen saturation by pulse oximetry is predictive of adverse maternal outcome (maternal death and hepatic, central nervous system, renal, cardiorespiratory, and hematologic morbidities) [106].

The etiology of pulmonary edema in preeclampsia is multifactorial [107-110]. Excessive elevation in pulmonary vascular hydrostatic pressure combined with decreased plasma oncotic pressure may produce pulmonary edema in some patients, particularly in the postpartum period. However, not all preeclamptic patients with pulmonary edema demonstrate this phenomenon. Other causes of pulmonary edema are capillary leak from endothelial activation, left heart failure, acute severe hypertension, and iatrogenic volume overload. There may be some overlap between preeclampsia and peripartum cardiomyopathy as the two disorders may coexist [111,112]. (See "Peripartum cardiomyopathy: Etiology, clinical manifestations, and diagnosis".)

Oliguria — Patients with preeclampsia commonly have transient oliguria (less than 100 mL over 4 hours) in labor or the first 24 hours postpartum. Patients at the severe end of the disease spectrum may have urine output <500 mL/24 hours. Oliguria in preeclampsia is due to contraction of the intravascular space secondary to vasospasm, leading to increased renal sodium and water retention, as well as intrarenal vasospasm [113]. The glomerular filtration rate (GFR) may fall by over 25 percent. (See "Acute kidney injury in pregnancy", section on 'Preeclampsia with or without HELLP'.)

Rarely, patients with preeclamptic liver disease develop polyuria due to transient diabetes insipidus of pregnancy. The mechanism in these cases is decreased degradation of vasopressinase due to hepatic dysfunction. (See "Polyuria and diabetes insipidus of pregnancy".)

Generalized edema — Many pregnant individuals have peripheral edema whether or not they have preeclampsia. However, sudden and rapid weight gain (eg, >5 lb/week [2.3 kg/week]) and facial edema are more common in patients who develop preeclampsia; thus, these findings warrant diagnostic evaluation for the disease. Generalized edema in preeclampsia may be due to capillary leak from endothelial damage and/or increased sodium retention that may be related to glomerular endotheliosis and proteinuria.

Abruptio placentae — Abruption can be a life-threatening event for the mother and/or fetus. It occurs in less than 1 percent of pregnancies with preeclampsia without severe features but 3 percent of those with severe features [114]. It has been attributed to ischemia-reperfusion injury in maternal uteroplacental vessels. (See "Acute placental abruption: Pathophysiology, clinical features, diagnosis, and consequences" and "Acute placental abruption: Management and long-term prognosis".)

Potential laboratory findings

- **Proteinuria** – Proteinuria in preeclampsia can be defined as any of the following [2]:
    - ≥0.3 g protein in a 24-hour urine specimen. The completeness of the 24-hour urine collection can be estimated from creatinine excretion, which should be 15 to 20 mg/kg (133 to 177 micromol/kg) of lean body weight in females. (See "Assessment of urinary protein excretion and evaluation of isolated non-nephrotic proteinuria in adults", section on '24-hour versus spot urine collection'.)

- Random urine protein to creatinine ratio ≥0.3 mg protein/mg creatinine (30 mg/mmol) (some clinicians opt to confirm presence of ≥0.3 g protein with a 24-hour collection).

  The urine protein concentration in a spot sample is measured in mg/dL and is divided by the urine creatinine concentration, also measured in mg/dL. This value can be used to estimate the 24-hour protein excretion (calculator 1) [115-123].

- Protein ≥2+ on a paper test strip dipped into a fresh, clean voided midstream urine specimen (only if one of the above quantitative methods is not available. (2+ is equivalent to 100 to 300 mg/dL and performs better than 1+, which does not accurately detect or exclude the protein threshold for preeclampsia [124]).

Measurement of proteinuria is discussed in detail separately. (See "Evaluation of proteinuria in pregnancy and management of nephrotic syndrome", section on 'Assessment of proteinuria'.)

Proteinuria generally increases as preeclampsia progresses, but increased urinary protein excretion may be a late finding [125,126]. It usually remains <5 g/day, but levels >10 g/day may be seen. Preeclampsia is the most common cause of severe proteinuria in pregnancy.

Proteinuria is due, in part, to impaired integrity of the glomerular filtration barrier and altered tubular handling of filtered proteins (hypofiltration) leading to increased nonselective protein excretion [127]. Both size and charge selectivity of the glomerular barrier are affected [128]. Using special studies, podocyturia (urinary excretion of podocytes) has been observed in patients with preeclampsia [129,130]. Urinary shedding of podocytes may indicate podocyte loss from the glomerulus, which may lead to a disruption of the glomerular filtration barrier and consequent proteinuria. Deficient vascular endothelial growth factor (VEGF) signaling appears to account, at least in part, for these findings. (See "Preeclampsia: Pathogenesis", section on 'Role of systemic endothelial dysfunction in clinical findings'.)

Kidney histology is reviewed below. (See 'Potential histologic findings' below.)

- **Elevated creatinine** – The physiologic increase in GFR during a normal pregnancy results in a decrease in serum creatinine concentration, which falls by an average of

0.4 mg/dL (35 micromol/L) to a range of 0.4 to 0.8 mg/dL (35 to 70 micromol/L). The serum creatinine concentration in patients with preeclampsia generally remains in this range or only slightly elevated. A creatinine level >1.1 mg/dL (97.3 micromol/L) concentration indicates the severe end of the disease spectrum. Some guidelines also include doubling of the patient's baseline creatinine in the absence of other renal disease as indicative of the severe end of the disease spectrum. Although creatinine levels remain <1.5 mg/dL (133 micromol/L) in most patients, preeclampsia is the most common cause of acute kidney injury in pregnancy. (See "Acute kidney injury in pregnancy", section on 'Preeclampsia with or without HELLP'.)

The rise in serum creatinine is due primarily to a fall in GFR; renal plasma flow also decreases but to a lesser degree.

- **Thrombocytopenia** – A platelet count less than 150,000/microL occurs in approximately 20 percent of patients with preeclampsia [2]. The severe end of the disease spectrum is characterized by a platelet count less than 100,000/microL.

  Thrombocytopenia is the most common coagulation abnormality in preeclampsia. Microangiopathic endothelial injury and activation result in formation of platelet and fibrin thrombi in the microvasculature. Accelerated platelet consumption leads to thrombocytopenia; immune mechanisms may also play a role [131].

- **Hemolysis** – Schistocytes and helmet cells on the peripheral blood smear (picture 1A-B) suggest microangiopathic hemolysis, which is a finding in severe disease. Elevation in the serum indirect bilirubin level also suggests hemolysis. Elevations in lactate dehydrogenase are usually related to liver dysfunction but can be due to hemolysis or both.

- **Hemoconcentration** – Hemoconcentration may result from contraction of the intravascular space secondary to vasospasm as well as capillary leaking. Hematocrit typically increases (range 36 to 43 percent in one study [132]). When both hemolysis and hemoconcentration occur concurrently, the effects on hematocrit may negate each other, resulting in a normal value.

- **Coagulation studies** – The prothrombin time, partial thromboplastin time, and fibrinogen concentration are not usually affected by preeclampsia unless there are additional complications, such as severe thrombocytopenia, abruptio placentae,

severe bleeding, or severe liver dysfunction [133,134].

- **Elevated liver chemistries** – Liver chemistries are increased in patients at the severe end of the disease spectrum, which is characterized by elevated transaminase levels (defined as twice the upper limit of normal for the local laboratory). Abnormalities in liver chemistries are due to reduced hepatic blood flow from periportal and sinusoidal fibrin deposition and microvesicular fat deposition, potentially resulting in ischemia, necrosis, and periportal hemorrhage [135,136]. Infrequently, subcapsular hematoma, hepatic failure, or rupture occurs.

  Elevation in the serum indirect bilirubin level suggests hemolysis.

- **Hyperuricemia** – The association between hyperuricemia and preeclampsia has been known for decades. The cause is most likely related to a reduction in GFR. However, the increase in serum uric acid is often greater than expected for mild reductions in GFR, leading to the hypothesis that decreased tubular secretion or increased reabsorption in the proximal renal tubules plays a role [137].

  Although meta-analyses have concluded that uric acid levels are not an accurate predictor of complications associated with preeclampsia [138-140], this issue remains controversial because of inconsistency among studies. For example, data from a prospective international study of patients admitted to the hospital with preeclampsia showed that serum uric acid corrected for gestational age is clinically useful in predicting adverse perinatal, but not maternal, outcomes [141].

- **Other**

  - **Troponin** – Several studies have reported that cardiac troponin I can be elevated above the normal threshold [142]. A very small subgroup of patients with severe preeclampsia may develop myocardial damage or global diastolic dysfunction [143]. Therefore, troponin I levels should be obtained when clinically indicated, such as when the patient complains of chest pain suggestive of myocardial ischemia or new electrocardiogram changes are observed [144,145].

  - **Urine sediment** – The urine sediment is typically benign.

  - **Lipids** – Total cholesterol and triglyceride levels are higher than in normotensive pregnant patients [146,147].

- **Neutrophilia** – The white blood count may be slightly higher due to neutrophilia.

- **Hypocalciuria** – Hypocalciuria has been attributed to increased tubular reabsorption of calcium [148-150]. Lower levels of parathyroid hormone, compared with normal pregnancy, have also been reported [151].

Potential sonographic findings

- **Fetal ultrasound** – Preeclampsia that develops clinically before term is often associated with suboptimal fetal growth due to reduced uteroplacental perfusion [152] (see 'Overview of pathophysiology' above). Fetal growth restriction (FGR) may be accompanied by oligohydramnios due to redistribution of the fetal circulation away from the kidneys and toward more vital organs, particularly the brain (see "Oligohydramnios: Etiology, diagnosis, and management in singleton gestations"). By contrast, preeclampsia that develops clinically at term tends to be associated with growth that is appropriate for gestational age and normal amniotic fluid volume; in some cases, the fetus may be large for gestational age [153-158].

  Fetal hydrops is rarely observed and is the cause rather than the result of preeclampsia. Hydrops of any etiology can be associated with preeclampsia-like symptoms and is called Mirror syndrome. (See "Nonimmune hydrops fetalis", section on 'Mirror syndrome'.)

- **Uterine and umbilical artery Doppler** – Increased impedance to flow in the uterine arteries due to uteroplacental maldevelopment is manifested by elevation of the pulsatility index accompanied by uterine artery notching on uterine artery Doppler velocimetry. However, this finding is neither sensitive nor specific for preeclampsia. (See "Early pregnancy prediction of preeclampsia", section on 'Uterine artery Doppler velocimetry'.)

  Increased resistance in placental blood vessels is reflected by rising Doppler indices of the umbilical artery. Absent and reversed end diastolic flow are the most severe abnormalities and are associated with a poor perinatal outcome. (See "Doppler ultrasound of the umbilical artery for fetal surveillance in singleton pregnancies".)

- **Maternal hemodynamic imaging studies** – Preeclampsia can be associated with a highly variable hemodynamic profile, including cardiac failure [159-163]. Changes in

cardiac function and morphology may be seen on echocardiography at an asymptomatic early stage and progress with increasing disease severity [164]. Preeclampsia does not affect the myocardium directly, but the heart responds to physiologic changes induced by the disease. Left ventricular ejection fraction usually remains within normal limits [165], but reductions in longitudinal, circumferential, and radial systolic strain have been observed [166]. The decrement in left ventricular performance has been attributed to a physiologic response to increased afterload [159,165,166], but other factors may play a role since systolic strain was depressed in preeclamptic patients compared with pregnant patients with nonproteinuric hypertension and similar resting blood pressure [166].

The high afterload in preeclampsia is associated with elevated cardiac filling pressures, reflected by fourfold higher concentrations of natriuretic peptides in patients with preeclampsia compared with pregnant patients who are normotensive or who have chronic hypertension [160].

Intravascular volume may be reduced in preeclampsia (especially with severe features) compared with a normal pregnancy [167]. There is no evidence of underfilling of the arterial circulation; rather, the reduced volume appears to be a consequence of vasoconstriction from enhanced responses to vasoactive substances. Activation of the renin angiotensin aldosterone system (RAAS) increases vascular tone and renal reabsorption of sodium and water. In normal pregnancy, despite lower blood pressure compared with the nonpregnant state, the RAAS is upregulated, an appropriate physiologic response to vasodilation. Sensitivity to angiotensin II is reduced [168]. In contrast, in multiple studies of patients with preeclampsia, levels of renin and angiotensin I and II were reduced compared with normal pregnancy and sensitivity to angiotensin II was increased, consistent with vasoconstriction, reduced sodium excretion, and possibly some overfilling of the circulation, and similar to what is observed in acute glomerulonephritis [169,170].

Potential histologic findings

- **Placenta** – Abnormalities in the placenta are believed to be a critical feature of the preeclampsia syndrome; however, many findings are nonspecific. In blinded studies, the pooled prevalence of villous lesions in preeclamptic and normal pregnancies was 42 and 19 percent, respectively, and the pooled prevalence of vascular lesions was 39

and 10 percent, respectively [171].

The parenchymal finding most characteristically associated with preeclampsia on routine hematoxylin and eosin staining is acute atherosis (ie, fibrinoid necrosis of the vessel wall with an accumulation of lipid-laden "foamy" macrophages and a mononuclear perivascular infiltrate). Cytotrophoblast invasion of the interstitial uterine compartment is frequently shallow, with incomplete invasion and remodeling of spiral arteries in many places [172]. This maldevelopment of the uteroplacental circulation can result in reduced placental perfusion, leading to placental infarcts, villous hypoplasia, and, in some cases, the clinical sequelae of FGR. Research studies using more advanced techniques (eg, special stains) have described additional findings (eg, reduced uterine natural killer cells in the decidua).

Placental histology is described in detail separately. (See "The placental pathology report", section on 'Preeclampsia'.)

- **Kidney** – The renal histologic changes described in patients with preeclampsia who have had kidney biopsies, and in autopsy specimens obtained from patients who died of eclampsia, are termed "glomerular endotheliosis." Light and electron microscopy of glomerular endotheliosis show endothelial cell swelling, loss of fenestrations, and occlusion of capillary lumens (picture 2A-B) [173]. Foot process effacement is not a prominent feature, despite marked proteinuria.

  Glomerular endotheliosis shares some histologic features with nonpreeclamptic thrombotic microangiopathies [173], except thrombi are rare in preeclampsia (although fibrin deposition may be observed by immunofluorescence microscopy). Patients treated with anti-VEGF chemotherapy have also been found to have glomerular endotheliosis, along with hypertension and proteinuria [174]. Rarely, it may be present without proteinuria and in nonpregnant females [175,176].

DIFFERENTIAL DIAGNOSIS

When evaluating patients for possible preeclampsia, it is generally safer to assume that new-onset hypertension in pregnancy is due to preeclampsia, even if all 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.

However, several other disorders can manifest some or many of the signs and symptoms of preeclampsia.

Causes of hypertension in pregnancy that are unrelated to the pregnant state include chronic hypertension (either primary or secondary), chronic kidney disease, acute kidney injury, other medical disorders (eg, pheochromocytoma, some neurologic disorders, some endocrine disorders [eg, hyperthyroidism]), and use/withdrawal of some drugs. Most pregnant patients with hypertension and thrombocytopenia and/or elevated transaminases have preeclampsia with severe features; alternative diagnoses to consider include HELLP syndrome, 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). Differential diagnosis is reviewed separately. (See "Hypertensive disorders in pregnancy: Approach to differential diagnosis".)

NATURAL HISTORY/COURSE OF DISEASE

Overview — Preeclampsia can be a progressive disease. Although most patients develop signs of the disease in late pregnancy with gradual worsening until birth, in approximately 25 percent of patients, especially those with early-onset preeclampsia, hypertension becomes severe and/or signs and symptoms of significant end-organ damage become apparent over a period of days to weeks. It is important to note that severe sequelae (significant end-organ dysfunction, death) can occur in patients without severe hypertension. Chest pain, dyspnea, and low platelet count appear to be particularly predictive of fatal or life-threatening complications [177].

Although, in some patients, signs and symptoms of preeclampsia are first recognized postpartum (ie, postpartum preeclampsia), usually within 48 hours of birth, resolution of the maternal signs and symptoms of the disease occurs variably in the postpartum period, with some symptoms disappearing in a matter of hours (eg, headache), while others may take weeks or months (eg, proteinuria). Typically, mobilization of third-space fluid and diuresis begin within 48 hours postpartum. Hypertension may worsen during the first, and occasionally the second, postpartum week but normalizes in most patients within four weeks postpartum [178]. Rarely, hypertension persists beyond three months. Proteinuria usually begins to improve within a few days; however, in patients with several

grams of protein excretion, complete resolution may take weeks to months [179].

Even though it is not clear why signs and symptoms of preeclampsia may be first recognized or worsen after birth, postpartum preeclampsia is not caused by large fragments of retained placenta. Patients with postpartum preeclampsia may represent a subgroup of patients who had subclinical preeclampsia before birth, delayed clearance of antiangiogenic factors, or activation of the complement system after birth [180,181]. In addition, mobilization of extracellular fluid into the intravascular system can lead to volume load hypertension and cerebral vasoconstriction [64]. Curettage may slightly accelerate the fall of the soluble fms-like tyrosine kinase-1 (sFlt-1) concentration by removing residual cytotrophoblast in the decidua basalis; however, randomized trials have reported conflicting data as to the value of curettage for hastening recovery from preeclampsia and eclampsia [182-185], and progression of prepartum preeclampsia to postpartum eclampsia has been reported after cesarean hysterectomy [186]. Consequently, we do not recommend postpartum curettage in clinical practice.

Risk of maternal death — Patients with preeclampsia are at an increased risk for life-threatening obstetric or medical complications. Worldwide, 10 to 15 percent of direct maternal deaths (ie, resulting from obstetric complications of pregnancy) are associated with preeclampsia/eclampsia [187].

In the United States, preeclampsia/eclampsia is one of the four leading causes of maternal death, along with hemorrhage, cardiovascular conditions, and thromboembolism [188-190]. Among maternal deaths in the US that occurred during delivery hospitalization (2017 to 2019), approximately one-quarter had documented pregnancy-associated hypertension (gestational hypertension, preeclampsia, eclampsia, chronic hypertension with superimposed preeclampsia) and one-third had documented hypertension (chronic, pregnancy-associated, or unspecified) [191]. In previous US studies, there was approximately one maternal death due to preeclampsia/eclampsia per 100,000 live births, with a case-fatality rate of 6.4 deaths per 10,000 cases [192,193].

Fetal complications — For the fetus, preeclampsia can lead to growth restriction and oligohydramnios as well as medically or obstetrically indicated preterm birth. Fetal growth restriction results from inadequate placentation, usually with early-onset preeclampsia. As a result, perinatal morbidity and mortality are increased, with the highest risk in pregnancies with onset of preeclampsia before 34 weeks of gestation. Late-onset

preeclampsia may not affect fetal growth. (See 'Potential sonographic findings' above.)

Long-term outcomes — Long-term maternal prognosis (recurrence risk, risk for related obstetric complications in future pregnancies, risk for cardiovascular and renal disease in later life) and long-term prognosis for offspring are reviewed separately. (See "Preeclampsia: Intrapartum and postpartum management and long-term prognosis", section on 'Prognosis'.)

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

- Beyond the Basics topics (see "Patient education: Preeclampsia (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Definitions and diagnosis**

  - **Major hypertensive disorders of pregnancy** – In a hypertensive pregnant patient, the four major hypertensive disorders related to pregnancy are preeclampsia, chronic hypertension, preeclampsia superimposed upon chronic hypertension, and gestational hypertension. Diagnostic criteria are summarized in the table (table 2). The approach to diagnosis of these disorders is shown in the algorithm (algorithm 1). (See 'Definitions/diagnostic criteria' above.)

  - **Diagnostic criteria for preeclampsia** – The diagnosis of preeclampsia is based on the new onset of hypertension and proteinuria or the new onset of hypertension and significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation in a previously normotensive patient (table 1). Severe hypertension or signs of significant end-organ dysfunction characterize the severe end of the disease spectrum (table 3). (See 'Definitions/diagnostic criteria' above.)

  - **Differential diagnosis** – Several other disorders can manifest some or many of the signs and symptoms of preeclampsia. Causes of hypertension include chronic hypertension, chronic renal disease, pheochromocytoma, and use/withdrawal of some drugs. Hypertension with thrombocytopenia and/or elevated transaminases may be caused by acute fatty liver of pregnancy, thrombotic microangiopathy, systemic lupus erythematosus (SLE), or antiphospholipid syndrome (APS). (See "Hypertensive disorders in pregnancy: Approach to differential diagnosis".)

- **Risk factors** – At the first prenatal visit, patients should be evaluated for traditional risk factors for preeclampsia (table 4) to identify those at high risk for developing the disease. Patients at highest risk are those with a past history of preeclampsia, multiple gestation, type 1 or type 2 diabetes, chronic hypertension, chronic kidney disease, or autoimmune disease with potential vascular complications (APS, SLE). Moderate risk factors include nulliparity, obesity, and family history of preeclampsia in a mother or sister. (See 'Risk factors' above.)

- **Use of low-dose** aspirin **prophylaxis for high-risk patients** – Patients at high risk for developing preeclampsia are offered low-dose aspirin therapy beginning in the second trimester and continuing until birth to reduce their risk of developing preeclampsia. (See "Preeclampsia: Prevention", section on 'Candidates'.)

- **Screening** – At all provider visits throughout pregnancy, routine measurement of blood pressure to identify patients with preeclampsia is required. The value of any laboratory or imaging test as a screening tool, including routine assessment of proteinuria at each visit, has not been established. (See 'Screening and risk reduction' above.)

- **Typical presentation and course of disease** – The gradual development of hypertension and proteinuria in the last half of pregnancy is usually due to preeclampsia, particularly in a nulliparous patient. These findings typically become apparent after 34 weeks of gestation and progress until birth, but some patients develop symptoms earlier in gestation, intrapartum, or postpartum.

  Patients with preeclampsia are at increased risk for life-threatening events, including placental abruption, acute kidney injury, cerebral hemorrhage, hepatic failure or rupture, pulmonary edema, stroke, cardiac failure, and progression to eclampsia. (See 'Spectrum of disease' above and 'Overview' above and 'Risk of maternal death' above.)

  The fetus in preeclamptic pregnancies is at increased risk for growth restriction and medically or obstetrically indicated preterm birth. (See 'Fetal complications' above.)

  Delivery of the placenta always results in complete resolution of the maternal signs and symptoms of the disease over a variable period of time. (See 'Clinical presentation' above and 'Natural history/course of disease' above.)

  - **Atypical presentations** – Atypical presentations of preeclampsia include onset before 20 weeks of gestation or after the second postpartum day. Some patients initially present with gestational hypertension or proteinuria alone. Others present with significant end-organ dysfunction and minimal or even absent hypertension or proteinuria; these patients are typically classified as HELLP syndrome (hemolysis, elevated liver enzymes, low platelets). (See 'Rare and

atypical presentations' above.)

- **Diagnostic evaluation**

  - **Laboratory** – Patients with suspected preeclampsia should have a complete blood count with platelets, creatinine level, liver chemistries, and determination of urinary protein excretion. (See 'Laboratory tests' above and 'Potential laboratory findings' above.)

  - **Fetal status** – Fetal status is assessed concurrently or postdiagnosis, depending on the degree of concern when the mother is evaluated. At a minimum, a nonstress test or biophysical profile is performed if appropriate for gestational age. Ultrasound is indicated to evaluate amniotic fluid volume and estimate fetal weight given the increased risk for oligohydramnios and fetal growth restriction. (See 'Assessment of fetal status' above and 'Potential sonographic findings' above.)

  - **Consultation** with the neurology service is generally indicated in patients with neurologic deficits/abnormal neurologic examination, which may include ocular signs and symptoms or a severe persistent headache that does not respond to repeat doses of acetaminophen and initial routine management of preeclampsia. (See 'Indications for neurology consultation' above.)

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GRAPHICS

Criteria for the diagnosis of 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 (mg/mg) (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 renal 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 woman with chronic hypertension. It 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 after 20 weeks of gestation in a woman with chronic hypertension.

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

Graphic 79977 Version 37.0

Definitions for the hypertensive disorders of pregnancy

Gestational hypertension	▪ New onset of systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on at least 2 occasions 4 hours apart after 20 weeks of gestation in a previously normotensive individual **And:** ▪ No proteinuria ▪ No severe features of preeclampsia (thrombocytopenia, renal insufficiency, elevated liver transaminases, pulmonary edema, cerebral or visual symptoms)
Preeclampsia	▪ New onset of systolic blood pressure ≥140 mmHg 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 **or** systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy **And:** ▪ 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]) **Or, in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:** ▪ Thrombocytopenia (platelet count <100,000/microL) ▪ Renal insufficiency (serum creatinine of >1.1 mg/dL [97 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease) ▪ Impaired liver function as indicated by liver transaminase levels at least twice the normal concentration ▪ Pulmonary edema ▪ Persistent cerebral or visual symptoms
Preeclampsia with severe features	**Any of these findings in a patient with preeclampsia:** ▪ Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg on 2 occasions at least 4 hours apart (unless antihypertensive therapy is initiated before this time) ▪ Thrombocytopenia (platelet count <100,000/microL) ▪ 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 ▪ Progressive renal insufficiency (serum creatinine concentration >1.1 mg/dL [97 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease) ▪ Pulmonary edema ▪ Persistent cerebral or visual disturbances
Eclampsia	▪ In a patient with preeclampsia, generalized seizures that cannot be attributed to other causes
HELLP syndrome	▪ Presence of Hemolysis, Elevated Liver enzymes, and Low Platelet count; 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 before 20 weeks of gestation. Hypertension that is first diagnosed during pregnancy and persists for at least 12 weeks post-delivery is also considered chronic hypertension. • The blood pressure criteria are systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or both. Ideally, this diagnosis is based on at least 2 elevated blood pressure measurements taken at least 4 hours apart. In the setting of severe hypertension, the diagnosis can be confirmed in a shorter interval to facilitate timely treatment.
Chronic hypertension with superimposed preeclampsia*	**Any of these findings in a patient with chronic hypertension:** ▪ A sudden increase in blood pressure that was previously well-controlled or an escalation of antihypertensive therapy to control blood pressure ▪ New onset of proteinuria or sudden increase in proteinuria in a patient with known proteinuria before or early in pregnancy
Chronic hypertension with superimposed preeclampsia with severe features	**Any of these findings in a patient with chronic hypertension and superimposed preeclampsia:** ▪ Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg despite escalation of antihypertensive therapy ▪ Thrombocytopenia (platelet count <100,000/microL) ▪ 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 ▪ New-onset or worsening renal insufficiency ▪ Pulmonary edema

	▪ 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.

Courtesy of Arun Jeyabalan, MD, MSCR, and Jacob Larkin, MD.

Graphic 127246 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: ▪ Photopsia, scotomata, cortical blindness, retinal vasospasm ▪ Severe headache (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy 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 or severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis
Thrombocytopenia:
<100,000 platelets/microL
Renal abnormality:
Renal insufficiency (serum creatinine >1.1 mg/dL [97.2 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease)
Pulmonary edema

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 27.0

Clinical factors that have been associated with an increased risk of developing preeclampsia

Nulliparity
Preeclampsia in a previous pregnancy
Age >40 years or <18 years
Family history of preeclampsia
Chronic hypertension
Chronic renal disease
Autoimmune disease (eg, antiphospholipid syndrome, systemic lupus erythematosus)
Vascular disease
Diabetes mellitus (pregestational and gestational)
Multifetal gestation
Obesity
Minority racial or ethnic group or otherwise disadvantaged
Hydrops fetalis
Poorly controlled hyperthyroidism
Patient themself was small for gestational age
Fetal growth restriction, abruptio placentae, or fetal demise in a previous pregnancy
Prolonged interpregnancy interval if the previous pregnancy was normotensive; if the previous pregnancy was preeclamptic, a short interpregnancy interval increases the risk of recurrence
Male partner-related factors (new male partner, limited sperm exposure [eg, previous use of barrier contraception])
In vitro fertilization
Obstructive sleep apnea
Elevated blood lead level
Posttraumatic stress disorder

By comparison, smoking decreases the risk of preeclampsia, and Asian females and Hispanic females have a lower risk of preeclampsia than White females and a much lower risk than Black females.

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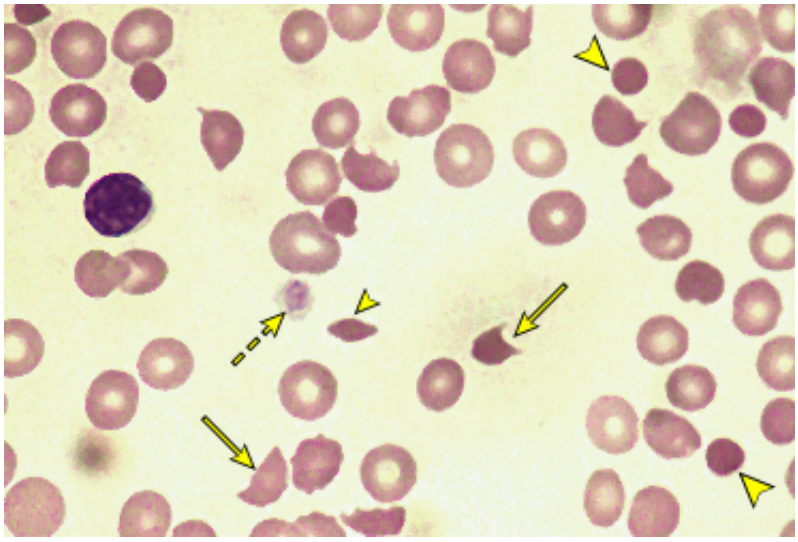
Peripheral smear in microangiopathic hemolytic anemia showing presence of schistocytes

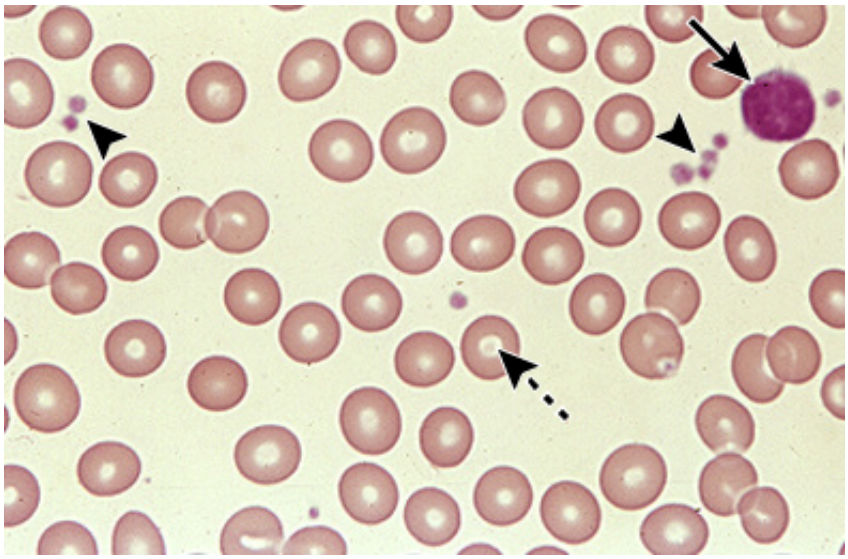


Peripheral blood smear from a patient with a microangiopathic hemolytic anemia with marked red cell fragmentation. The smear shows multiple helmet cells (arrows) and other fragmented red cells (small arrowhead); microspherocytes are also seen (large arrowheads). The platelet number is reduced; the large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

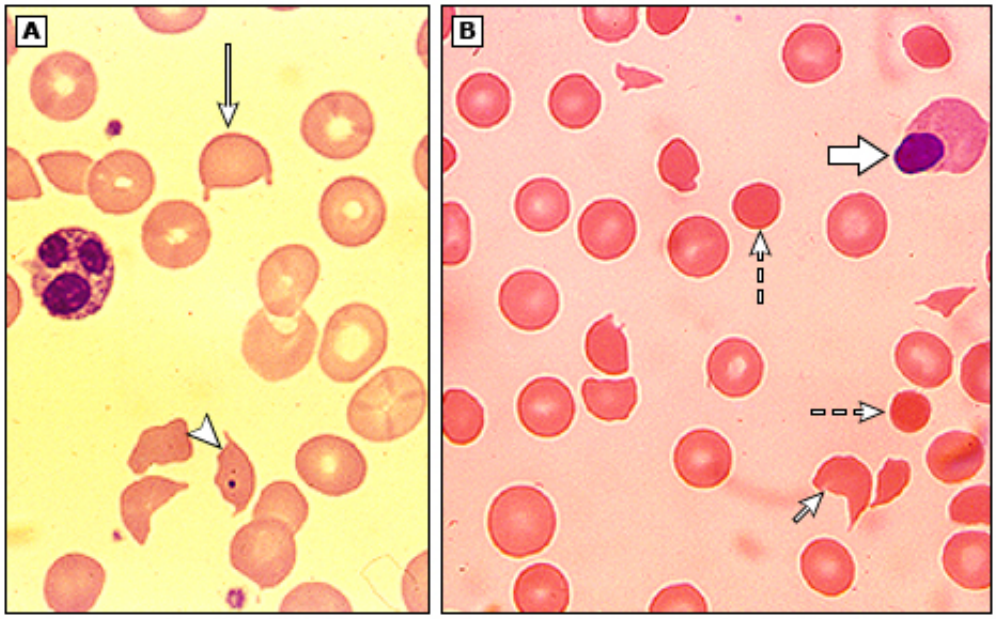


High-power view of a normal peripheral blood smear. Several platelets (arrowheads) and a normal lymphocyte (arrow) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor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

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 59683 Version 5.0

Helmet cells in microangiopathic hemolytic anemia

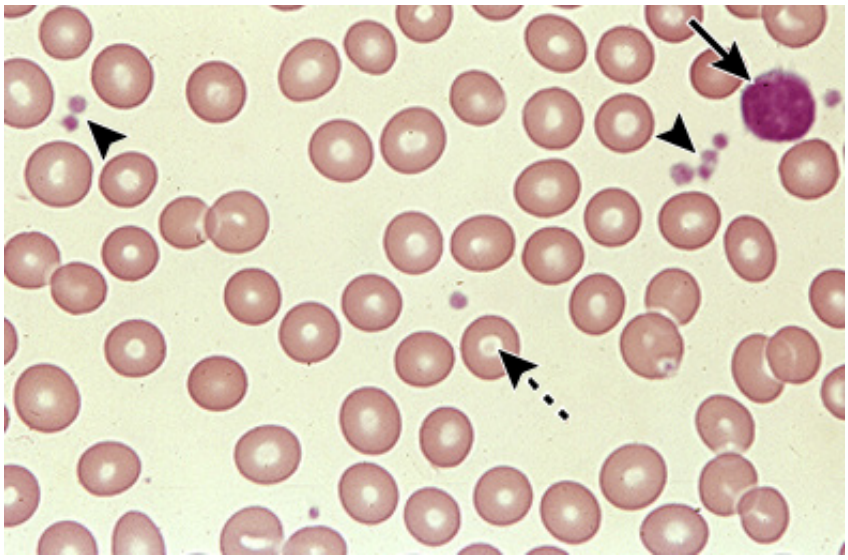


Peripheral smears from two patients with microangiopathic hemolytic anemia, showing a number of red cell fragments (ie, schistocytes), some of which take the form of combat (arrow), bicycle (arrowhead), or football (short arrow) "helmets." Microspherocytes are also seen (dashed arrows), along with a nucleated red cell (thick arrow).

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 50715 Version 5.0

Normal peripheral blood smear

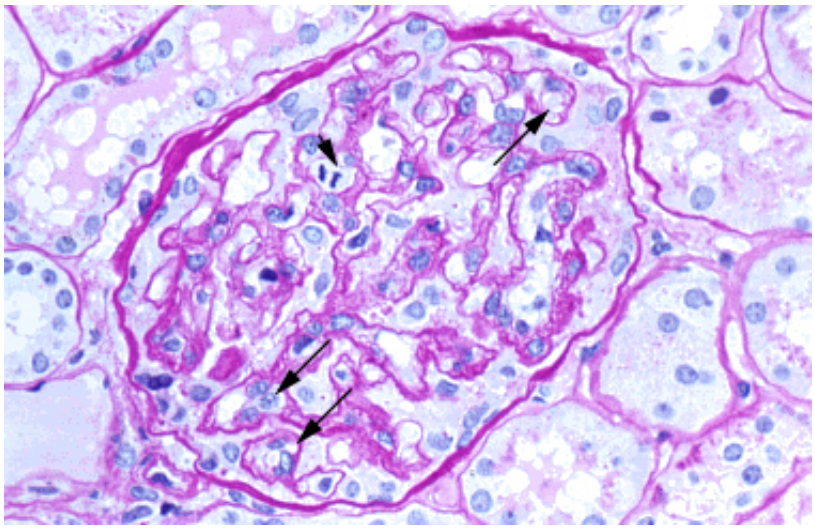


High-power view of a normal peripheral blood smear. Several platelets (arrowheads) and a normal lymphocyte (arrow) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor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

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 59683 Version 5.0

Preeclampsia

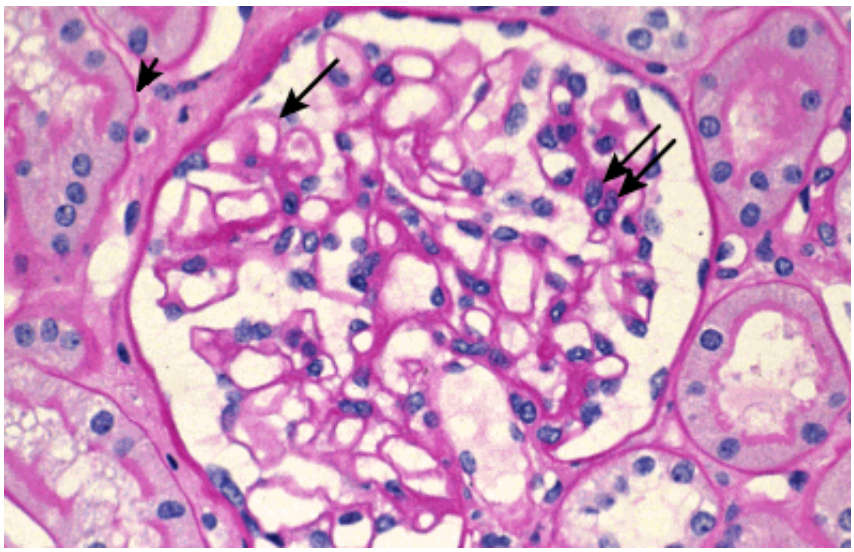


Light micrograph in preeclampsia showing glomerular endotheliosis. The primary changes are swelling of damaged endothelial cells, leading to partial closure of many of the capillary lumens (arrows). Mitosis within an endothelial cell (short arrow) is a sign of cellular repair.

Courtesy of Helmut Rennke, MD.

Graphic 78879 Version 3.0

Normal glomerulus



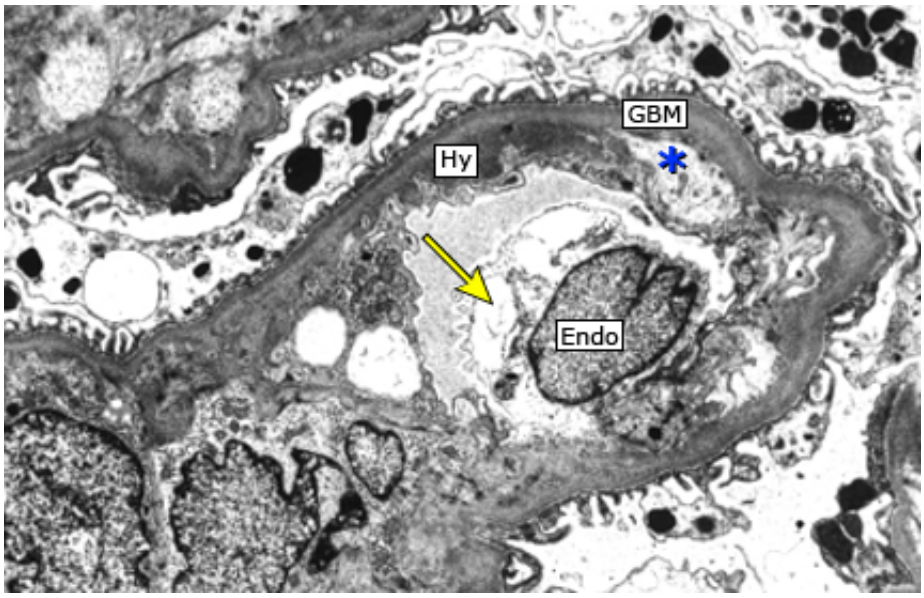
Light micrograph of a normal glomerulus. There are only one or two cells per capillary tuft, the capillary lumens are open, the thickness of the glomerular capillary wall (long arrow) is similar to

that of the tubular basement membranes (short arrow), and the mesangial cells and mesangial matrix are located in the central or stalk regions of the tuft (arrows).

Courtesy of Helmut G Rennke, MD.

Graphic 75094 Version 6.0

Preeclampsia

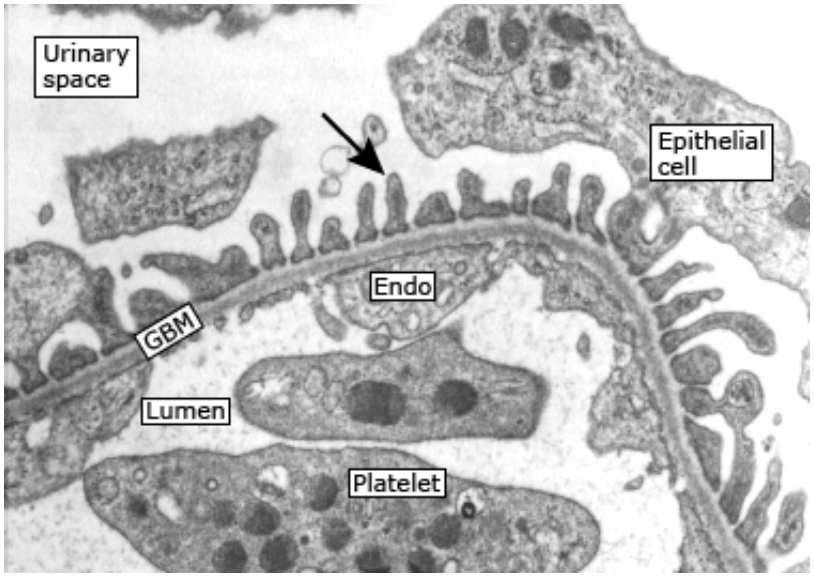


Electron micrograph in preeclampsia showing narrowing of the capillary lumen due to expansion of the mesangium, swelling of the endothelial (Endo) cell cytoplasm (arrow), and subendothelial deposition of hyaline (Hy) material, which represents large macromolecules such as immunoglobulin M. The damaged endothelial cell has become partially separated (*) from the glomerular basement membrane (GBM).

Courtesy of Helmut Rennke, MD.

Graphic 59970 Version 4.0

Electron micrograph of a normal glomerulus

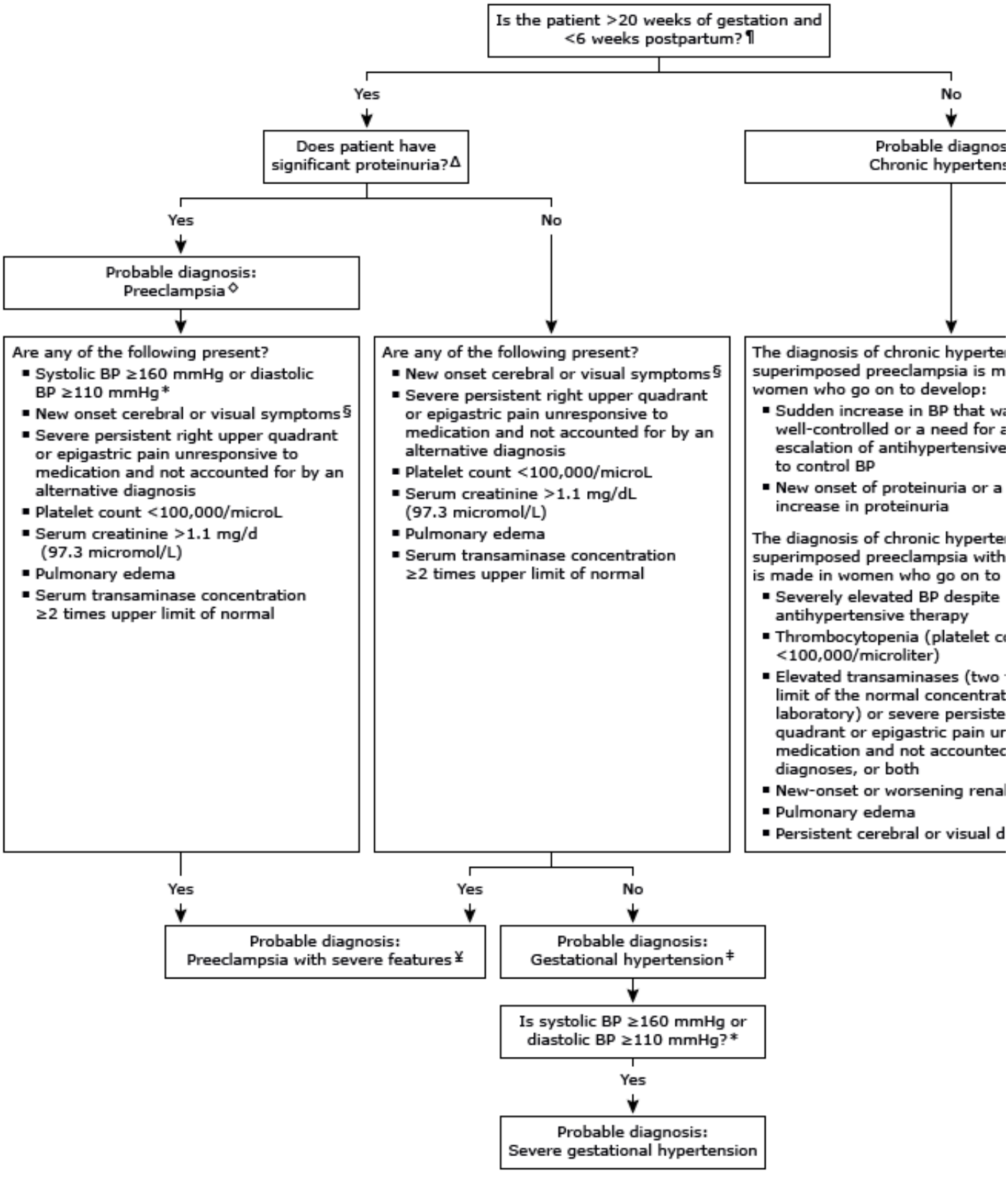


Electron micrograph of a normal glomerular capillary loop showing the fenestrated endothelial cell (Endo), the glomerular basement membrane (GBM), and the epithelial cells with its interdigitating foot processes (arrow). The GBM is thin, and no electron-dense deposits are present. Two normal platelets are seen in the capillary lumen.

Courtesy of Helmut G Rennke, MD.

Graphic 50018 Version 7.0

Diagnostic evaluation of a pregnant or postpartum woman with persisten 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,

chronic hypertension may be normotensive at their first few prenatal visits. Later in pregnancy, when pressure returns to its prepregnancy baseline, they may appear to be developing preeclampsia or ges hypertension if there are no documented prepregnancy blood pressure measurements.

BP: blood pressure.
* Blood pressure should be elevated on at least two occasions at least four hours apart. However, if sy pressure is ≥160 mmHg or diastolic pressure is ≥110 mmHg, confirmation after a short interval, ever minutes, is acceptable to facilitate timely initiation of antihypertensive therapy.
¶ The onset of preeclampsia and gestational hypertension is almost always after 20 weeks of gestatic Preeclampsia before 20 weeks of gestation may be associated with a complete or partial molar pregn hydrops. Postpartum preeclampsia usually presents within two days of delivery. The term "delayed po preeclampsia" is used for signs and symptoms of the disease leading to readmission more than two c than six weeks after delivery.
Δ Significant proteinuria is defined as ≥0.3 g in a 24-hour urine specimen or protein/creatinine ratio ≥ (30 mg/mmol) in a random urine specimen or dipstick ≥1+ if a quantitative measurement is unavailab
◇ Almost all women with the new onset of hypertension and proteinuria at this gestational age or po preeclampsia, but a rare patient may have occult renal disease exacerbated by the physiologic chang pregnancy. An active urine sediment (red and white cells and/or cellular casts) is consistent with a pro glomerular disorder but not a feature of preeclampsia. Women with chronic hypertension who had p prior to or in early pregnancy may develop superimposed preeclampsia. This can be difficult to diagn definitively, but should be suspected when blood pressure increases significantly (especially acutely) i of pregnancy/postpartum or signs/symptoms associated with the severe end of the disease spectrum
§ Photopsia (flashes of light), scotomata (dark areas or gaps in the visual field), blurred vision, or temp blindness (rare); severe headache (ie, incapacitating, "the worst headache I've ever had") or headache and progresses despite analgesic therapy; altered mental status. Seizure occurrence upgrades the dia 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. (in UpToDate topic "Preeclampsia: Clinical manifestations and diagnosis.") The prepregnancy history, r spectrum of laboratory abnormalities, and additional presence of signs and symptoms not typically a preeclampsia help in making the correct diagnosis, which is not always possible during pregnancy.
In addition, a variety of medical disorders may be associated with hypertension and one or more of tl symptoms that occur in women with preeclampsia with severe features. These patients can usually b distinguished from patients with preeclampsia by taking a detailed history, performing a thorough ph examination, and obtaining relevant laboratory studies.
‡ In contrast to preeclampsia, gestational hypertension is not associated with end-organ involvement proteinuria nor the symptoms or laboratory findings of preeclampsia are present. Refer to UpToDate gestational hypertension.

Graphic 119141 Version 2.0

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. **Vanessa A Barss, MD, FACOG** No relevant financial relationship(s) with ineligible companies to disclose.

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