Hypertensive Disorders of Pregnancy

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15.1 Introduction

Hypertensive disorders of pregnancy complicate approximately 10 % of pregnancies and are considered one of the leading causes of maternal and fetal morbidity and mortality. There are an estimated 50,000–60,000 preeclampsia-related deaths per year worldwide. Hypertensive disorders can either predate pregnancy (i.e., chronic hypertension) or be specific to pregnancy (i.e., gestational hypertension and preeclampsia) [1–4].

Chronic hypertension is more common in patients over the age of thirty. The prevalence of chronic hypertension ranges from 4.6 to 22.3 % among those between the ages of 30 and 39 as opposed to 0.6–2 % in those between the ages of 18 and 29. As more women delay childbearing and with the increased use of egg donation (Fig. 15.1) and assisted reproduction infertility treatment (Fig. 15.2), the average age of pregnancy is increasing. As a result, chronic hypertension and its complications will certainly be encountered more often in pregnancy. This will inevitably increase the incidence of preeclampsia. Approximately 25 % of chronic hypertensive patients will develop preeclampsia during pregnancy compared to 4 % without underlying hypertension. Preeclampsia is associated with even greater maternal and fetal risks, rendering the pregnancies of patients with both chronic underlying hypertension and preeclampsia to be at very high risk [1, 2, 5].

Elevated blood pressures (BP) initially encountered in the first and early second trimester, especially those occurring prior to 20 weeks of gestation, are usually a result of chronic hypertension (Fig. 15.3). When hypertension is encountered early in pregnancy, this is usually due either to a known hypertensive disorder or previously undiagnosed chronic hypertension rather than a pregnancy-induced pathology. Hypertension predating pregnancy can be either primary hypertension or secondary hypertension. In primary/essential hypertension, an underlying cause is not found. However, in secondary hypertension, an underlying etiology is identified. If secondary hypertension is suspected, further investigation is warranted, as the majority of secondary causes are potentially treatable [1, 2, 5].

Understanding the classification and management of hypertensive disorders is essential. It is critical to identify those patients with underlying hypertensive disorders in pregnancy as they are at greater risk for complications. Some women with underlying hypertensive disorders may require outpatient treatment with medications, urgent treatment in the hospital setting, transfer to a higher level of care, or in some cases termination of pregnancy. Identifying those pregnant patients with hypertensive disorders early and treating them accordingly allow for an overall reduction in maternal and perinatal morbidity and mortality [1].

15.2 Establishing the Diagnosis of Hypertension in Pregnancy

Hypertension can easily be missed, as blood pressure elevation is usually silent and asymptomatic. A diagnosis can occur only when hypertension is elicited on physical exam. There is a physiologic decrease in blood pressure in early pregnancy, which may normalize previously elevated blood pressure. This

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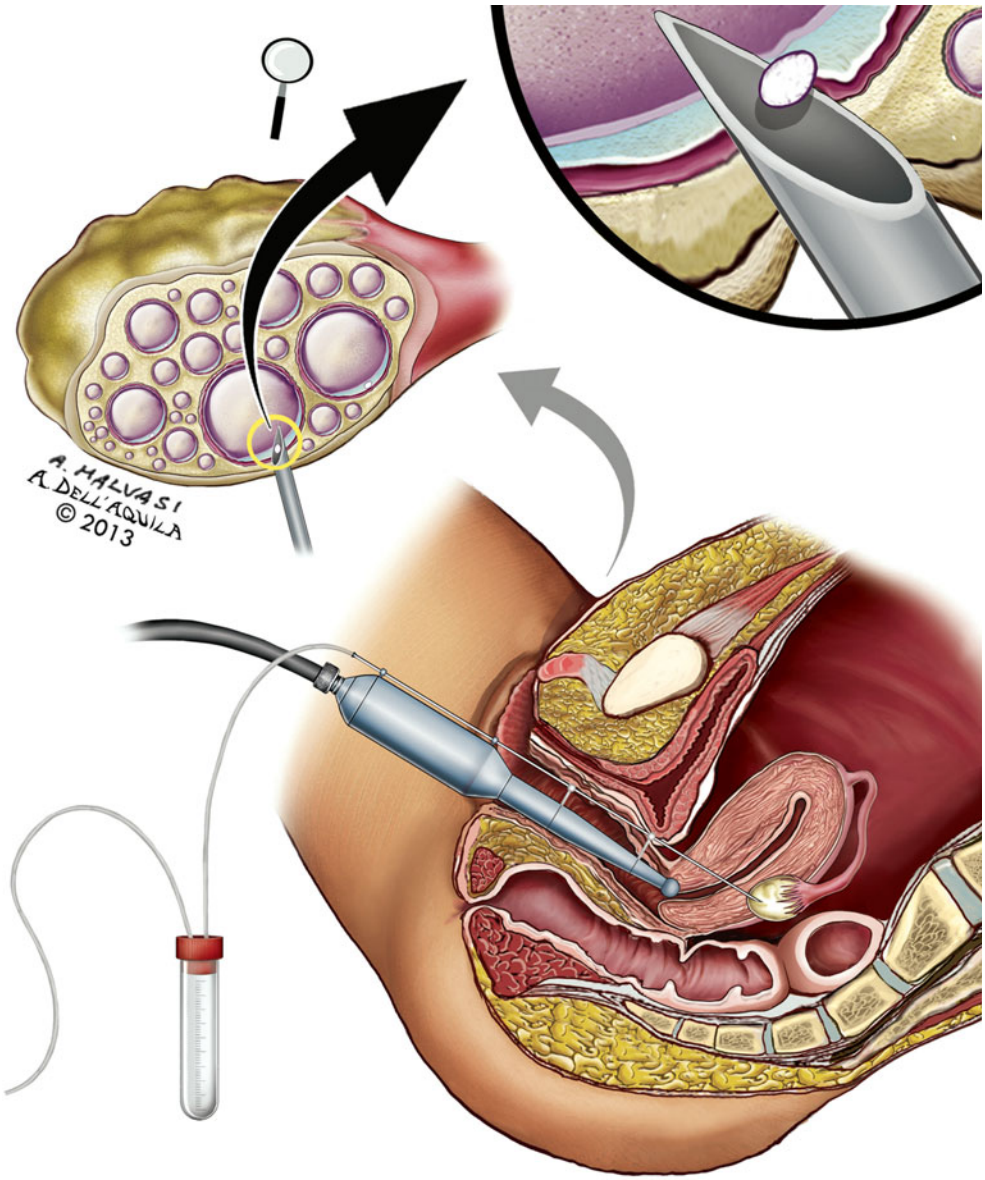

Fig. 15.1 The figure represents an ovarian pickup

physiologic decrease in blood pressure may mask preexisting hypertension, particularly before 16 weeks of gestation [1, 5].

15.2.1 Definition

Hypertension in pregnancy is defined as either a systolic blood pressure of greater than or equal to 140 mmHg *OR* a diastolic BP of greater than or equal to 90 mmHg (Fig. 15.4). In order to establish the diagnosis of hypertension, one must have at least two elevated blood pressure measurements taken correctly at least 4 h apart [1, 2, 5].

Blood pressure elevation is further classified into mild versus severe. Hypertension is considered mild until systolic and/or diastolic levels reach or exceed 160 mmHg and 110 mmHg, respectively. In the setting of persistent severe-range blood pressures, a diagnosis of severe hypertension can be made without waiting 4 h. More importantly, therapy can be initiated promptly when severe-range blood pressure elevations are persistent [1].

White coat hypertension, defined as elevated BPs in the presence of a healthcare provider, is found in up to 15 % of individuals outside of pregnancy. White coat hypertension may lead to a false diagnosis of hypertension. It is suspected when the reported BP measurement at home is less than the BP measurements in the hospital or office. In the setting of suspected white coat hypertension, ambulatory blood pressure monitoring is recommended [1].

15.2.2 Optimal Measurement of Blood Pressure

Measuring blood pressure correctly is crucial in establishing the diagnosis of hypertension. Inaccurate BP measurements can lead to an inappropriate diagnosis. Inaccurate high BP readings could lead to the false diagnosis of a hypertensive

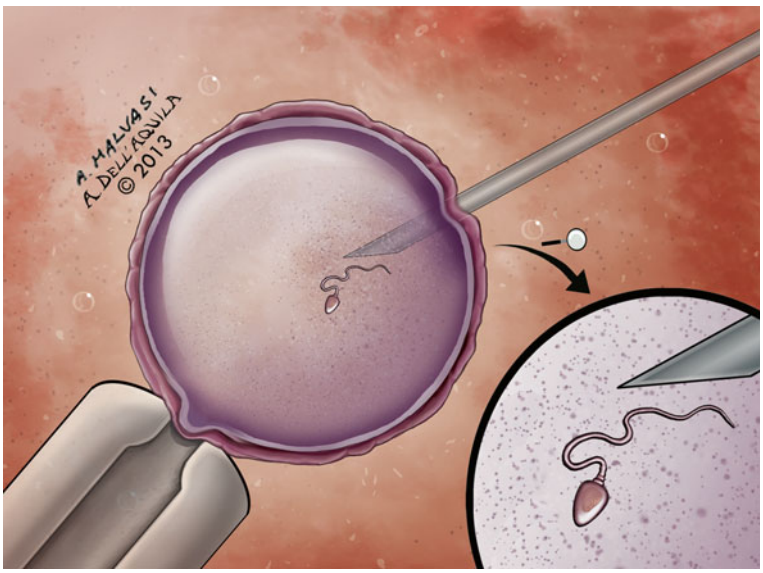

Fig. 15.2 The figure shows the intracytoplasmic sperm injection (ICSI) technique

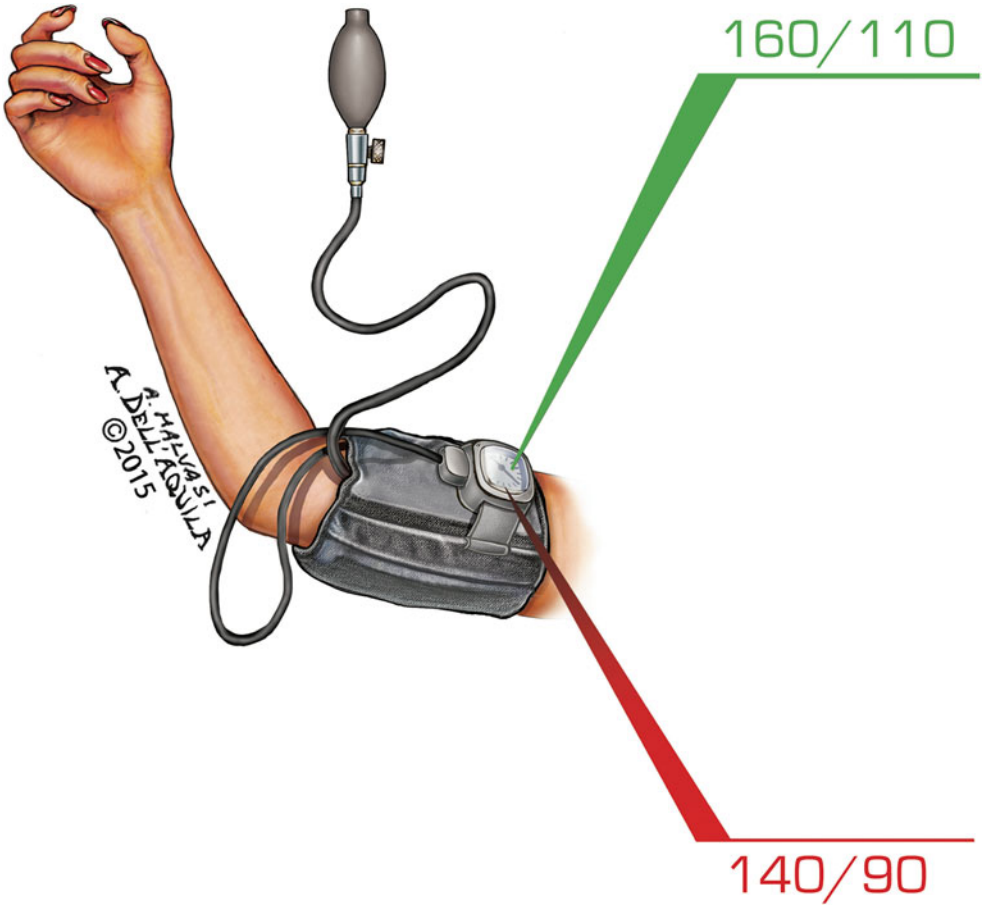

Fig. 15.3 A patient underwent blood pressure measurement, referring a chronic hypertension

pregnancy. Inaccurately low BP measurements can label a patient as normotensive when he/she is actually hypertensive. Below are some of the important requirements needed for obtaining accurate blood pressure measurements [6–10]:

- Proper cuff size
- Patient comfortably seated
- Back supported
- Legs uncrossed

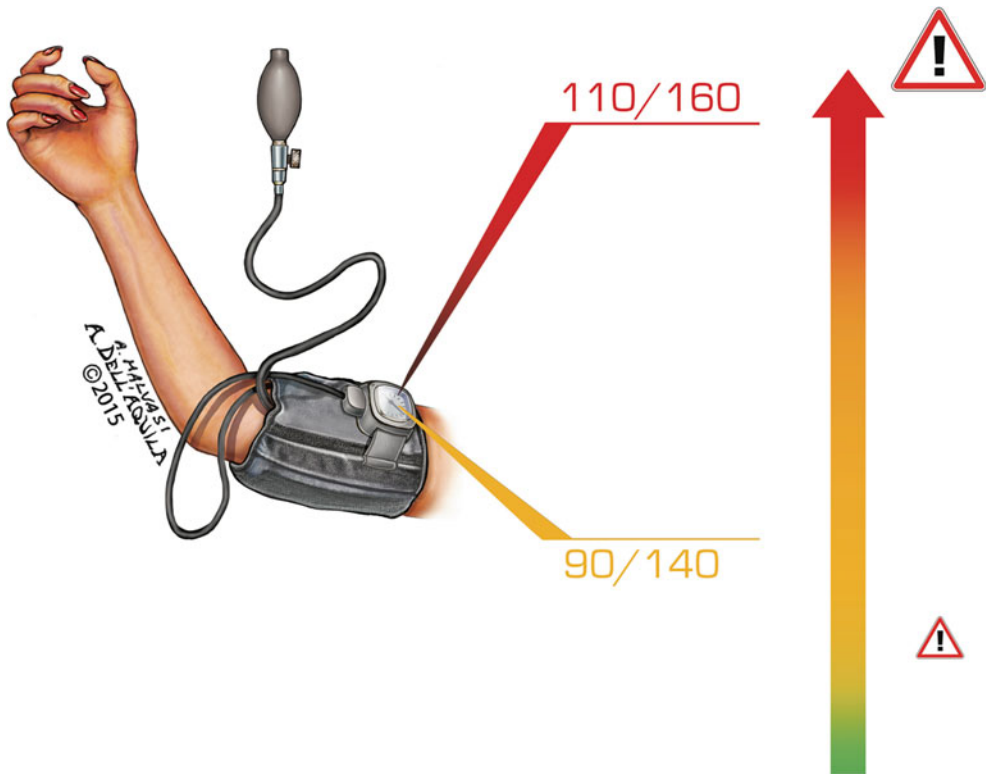

Fig. 15.4 Hypertension in pregnancy is defined as either a systolic blood pressure of greater than or equal to 140 mmHg or a diastolic BP of greater than or equal to 90 mmHg. The systolic and diastolic numbers reversed

The arm should be supported so that the middle of the cuff on the upper arm is at the level of the right atrium.

The patient should be instructed to relax and not talk.

If the BP is elevated, at least 5 min should lapse before a repeat blood pressure is retaken.

The BP cuff should be placed with the bladder midline over the brachial artery pulsation, and the arm should be without restrictive clothing.

15.3 Evaluation of Hypertension in Early Pregnancy

Early recognition of hypertension in pregnancy, establishing the extent of organ damage, and identifying comorbidities are of paramount importance. These can only be achieved by conducting a thorough history and physical exam, ordering the appropriate laboratory tests and imaging studies, and making appropriate referrals. This ensures proper management of the patient, which will help decrease maternal and fetal risks.

Paying attention to the patient's history (medical, surgical, obstetrical, family, and social) as well as abnormal physical exam findings may yield valuable information in establishing the correct diagnosis and management options. Spending enough time with patients and giving them the opportunity to express their concerns and ask questions help establish a strong and healthy patient-physician relationship. This relationship allows further building of trust and confidence, which may allow patients to share vital information that may have otherwise remained uncovered. Reviewing the patient's medication list is of equal importance, as this helps minimize the potential for teratogen exposure.

Laboratory evaluation is another important step when taking care of patients with hypertensive disorders. Obtaining lab tests on patients with chronic hypertension as well as those in whom blood pressure elevation is initially encountered in the first half of pregnancy serves two main purposes. First, it helps to assess the extent of end-organ damage and severity of disease and to investigate coexisting comorbidities. Second, it enables us to establish a baseline for comparison purposes later in pregnancy. The baseline labs are especially helpful in distinguishing a chronic hypertension exacerbation from superimposed preeclampsia. As mentioned earlier, the distinction between the two is very important as the complication rates and management differ dramatically.

The appropriate labs and studies should be obtained at the first prenatal visit or prior to pregnancy if possible.

The recommended labs and studies include the following [1, 2]:

- Urinalysis, urine culture, and a quantitative assessment of urine protein (i.e., 24-h urine collection or a protein/creatinine ratio)

- Renal function tests
- CBC with platelet count
- Glucose
- Electrolytes
- Uric acid and liver enzymes
- Thyroid-stimulating hormone (TSH) level
- EKG and possible echocardiogram

Establishing an accurate gestational age and due date in a hypertensive patient is imperative given the high likelihood that fetal growth restriction may occur and/or early delivery may be required. Performing a dating ultrasound as early as possible is highly recommended [1, 2].

Ideally, patients with chronic hypertension planning to become pregnant should be seen for preconception counseling. The extent of end-organ damage should be evaluated at this time, as pregnancy risks and recommendations may change depending on severity of disease.

Patients should be counseled about the risks pregnancy poses and the expectations during the pregnancy. Patients should also be changed to pregnancy safe medications when possible and folic acid supplementation should be started. Appropriate vaccines should also be recommended at this time [1, 2].

15.4 Classification of Hypertensive Disorders in Pregnancy

Four major hypertensive disorders occur in pregnancy [1] (Table 15.1):

A. Chronic (preexisting) hypertension
B. Gestational hypertension
C. Preeclampsia-eclampsia/hemolysis, elevatedliver enzymes and low platelet count (HELLP) syndrome
D. Preeclampsia-eclampsia superimposed upon chronic hypertension

Table 15.1 Etiologies of hypertensive disorders in pregnancy

Pregnancy specific	Nonspecific
Gestational hypertension	Essential hypertension
Preeclampsia	Renal disease
Preeclampsia superimposed on chronic hypertension	Obstructive sleep apnea
	Cushing syndrome
HELLP syndrome	Renal artery stenosis
Gestational trophoblastic disease	Pheochromocytoma
Mirror syndrome	Coarctation of the aorta
	Primary aldosteronism
	Thyroid dysfunction
	Lupus flare
	Drugs and medications

15.5 Chronic Hypertension

Chronic hypertension is defined as blood pressure elevation that predates pregnancy. If blood pressure is unknown prior to pregnancy and elevation is discovered prior to 20 weeks of gestation, the presumed diagnosis is chronic hypertension. However, to make an absolute diagnosis of chronic hypertension in this instance, elevated blood pressures must be demonstrated beyond 12-week postpartum [1].

15.6 Gestational Hypertension

Gestational hypertension is a pregnancy-specific diagnosis. Gestational hypertension is defined as new-onset blood pressure elevations that occur after 20 weeks of gestation in the absence of proteinuria and preeclampsia diagnostic criteria (see below).

Gestational hypertension is a pregnancy-specific transient hypertensive disorder that begins during pregnancy and resolves within 6–12 weeks postpartum. Persistence of BP elevation beyond 6–12 weeks postpartum is indicative of chronic hypertension. Even though gestational hypertension is transient in nature, it can be an indicator of future hypertensive disease [1, 2, 5].

15.7 Preeclampsia/Eclampsia/HELLP Syndrome

Similar to gestational hypertension, the spectrum of preeclampsia-eclampsia and HELLP syndrome is also a pregnancy-specific condition and usually occurs in the latter part of pregnancy (after 20 weeks of gestation). However, unlike gestational hypertension, the hypertension associated with preeclampsia is accompanied by new-onset proteinuria. Proteinuria is defined as the excretion of greater than or equal to 300 mg of protein in a 24-h urine collection or a protein/creatinine ratio in a single void of greater than or equal to 0.3 (each measured as mg/dL). A urine dipstick of 1+ or greater may be used if the other quantitative methods are not available; however, this method has high false-positive and false-negative rates [1].

Recent changes to the diagnostic criteria have made it possible to diagnose preeclampsia in the absence of proteinuria. In addition to acute hypertension, when there is evidence of thrombocytopenia, renal insufficiency, abnormal liver function tests, pulmonary edema, and/or cerebral/visual symptoms, the diagnosis of preeclampsia can be made even in the absence of proteinuria (Table 15.2) [11].

As preeclampsia is a progressive disorder, it is no longer classified as mild or severe. Preeclampsia is now classified as either preeclampsia with severe features or preeclampsia

Table 15.2 The diagnostic criteria for preeclampsia

Blood pressure	Greater than or equal to 140 mmHg systolic or greater than or equal to 90 mmHg diastolic on two occasions at least 4 h apart after 20 weeks of gestation in a woman with previously normal blood pressure
	Greater than or equal to 160 mmHg systolic or greater than or equal to 110 mmHg diastolic; hypertension can be confirmed with a short interval (15 min) to facilitate timely antihypertensive therapy
And	
Proteinuria	Greater than or equal to 300 mg per 24-h urine collection
	Protein/creatinine ratio greater than or equal to 0.3
	Dipstick reading of 1+ (use only if other quantitative methods are unavailable)
Or in the absence of proteinuria, new-onset hypertension with new onset of any of the following:	
Thrombocytopenia	Platelet count less than 100,000/uL
Renal insufficiency	Serum creatinine concentrations greater than 1.1 mg/dl or a doubling of the serum creatinine concentration in the absence of other renal diseases
Impaired liver function	Elevated blood concentrations of liver transaminases to twice normal concentration
Pulmonary edema	
Cerebral or visual changes	

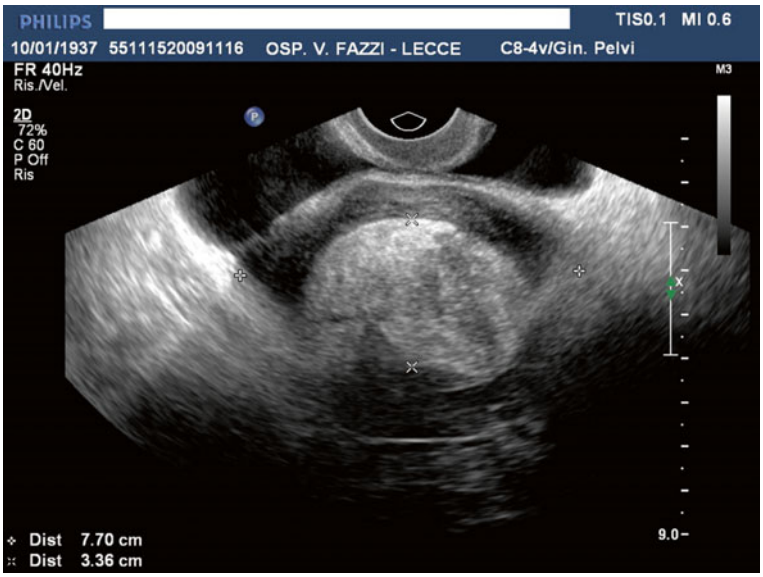

Fig. 15.5 Ultrasonographic transversal image of uterus with gestational trophoblastic disease (GTD) or hydatidiform mole (hyperechogenic part of uterus)

without severe features. Fetal growth restriction and massive proteinuria (>5 g/24 h) are no longer considered diagnostic criteria for severe disease [1].

After the diagnosis of preeclampsia is made, disease severity is assessed. Management options will depend on both the severity of the disease and the gestational age at diagnosis. As preeclampsia is seldom encountered in the first half of pregnancy, detailed management options will not be discussed in this chapter [1]. The development of preeclampsia prior to 20 weeks is extremely rare. If preeclampsia occurs in the first half of pregnancy, the diagnosis of either gestational trophoblastic disease (GTD) or mirror syndrome should be considered. A beta-human chorionic gonadotropin (hCG) and ultrasound should be performed promptly.

GTD or hydatidiform mole (Fig. 15.5) can present with all the typical hallmarks of preeclampsia including hypertension, end-organ damage, and proteinuria. Rare cases of eclampsia have also been reported. Preeclampsia as a sequelae of GTD is more often a result of complete molar pregnancies (46XX or XY); however, preeclampsia can occur with partial moles (69XXX or XXY) and choriocarcinoma (Fig. 15.6) as well. Preeclampsia associated with GTD has declined over the past 40 years secondary to earlier diagnosis and treatment. The mainstay of diagnoses of GTD is via beta-HCG levels and ultrasound. The treatment of GTD is either by uterine evacuation (Fig. 15.7) or hysterectomy, depending on the patient's desire for future fertility. Some patients will also require chemotherapy depending on disease persistence and extent. Similar to preeclampsia that occurs in the latter part of pregnancy, evacuation of uterine contents results in resolution of the preeclampsia disease process [12–23].

Mirror syndrome, also known as Ballantyne syndrome, is a rare condition defined as the development of preeclampsia-

like symptoms in association with fetal hydrops. This syndrome can manifest early in pregnancy and be associated with severe signs and symptoms (features) of preeclampsia. Cases of eclampsia have also been reported. The gestational age at diagnosis usually ranges from 22.5 to 27.8 weeks of gestation. Maternal edema, which occurs commonly and is often impressive, is said to mirror the hydropic fetus. According to a systemic review conducted by Braun et al. that included 56 reported cases, edema was encountered most commonly and seen in 80–100% of patients. Blood pressure elevation and proteinuria were found in 78 % and 20–56 % of patients, respectively. The majority of cases were attributed to fetal malformations (Fig. 15.8) and fetal or placental tumors (Fig. 15.9) (37.5 %) followed by Rh isoimmunization (29 %). Twin-to-twin transfusion syndrome accounted for 18 % of cases and viral infections accounted for 16 % of the cases [2, 24–30].

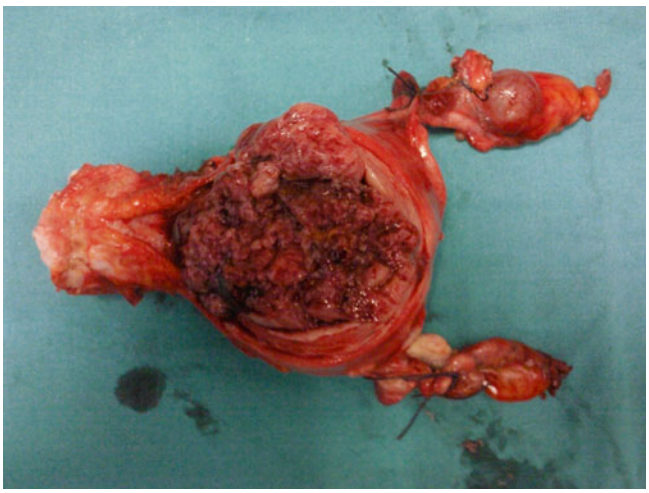

Fig. 15.6 Uterine hysterectomy for a choriocarcinoma (showed by opening of anterior uterine wall)

Patients with mirror syndrome experience some of the signs and symptoms of preeclampsia as described above. However, some of the lab abnormalities and ultrasound findings found in patients with mirror syndrome differ from those with preeclampsia. Hemodilution and polyhydramnios are found in patients with mirror syndrome as opposed to the findings of hemoconcentration and oligohydramnios seen in patients with preeclampsia. Consultation with a maternal-fetal medicine subspecialist is recommended as treatment options may vary depending on the cause of the fetal hydrops and the severity of the disease. Delivery may be the recommended treatment for some patients with mirror syndrome. Resolution of maternal symptoms usually occurs within 4.8–13.5 days after delivery [25, 27–30].

Eclampsia, the occurrence of new-onset grand mal seizures in a pregnant woman that cannot be attributed to another cause, is a severe manifestation of preeclampsia. Unfortunately, occurrence of seizures cannot be predicted by the level of blood pressure elevation, proteinuria, or degree of derangement of laboratory values [1, 2].

The only known curative treatment for eclampsia is delivery after stabilization. In the absence of contraindication such as severe renal compromise, intravenous magnesium sulfate is recommended to stop ongoing seizure activity and prevent further seizures.

Diazepam (Valium) or phenytoin (Dilantin) can be used with caution if magnesium sulfate is unavailable or contraindicated or if seizures recur; however, these medications are less effective than magnesium sulfate [1, 2].

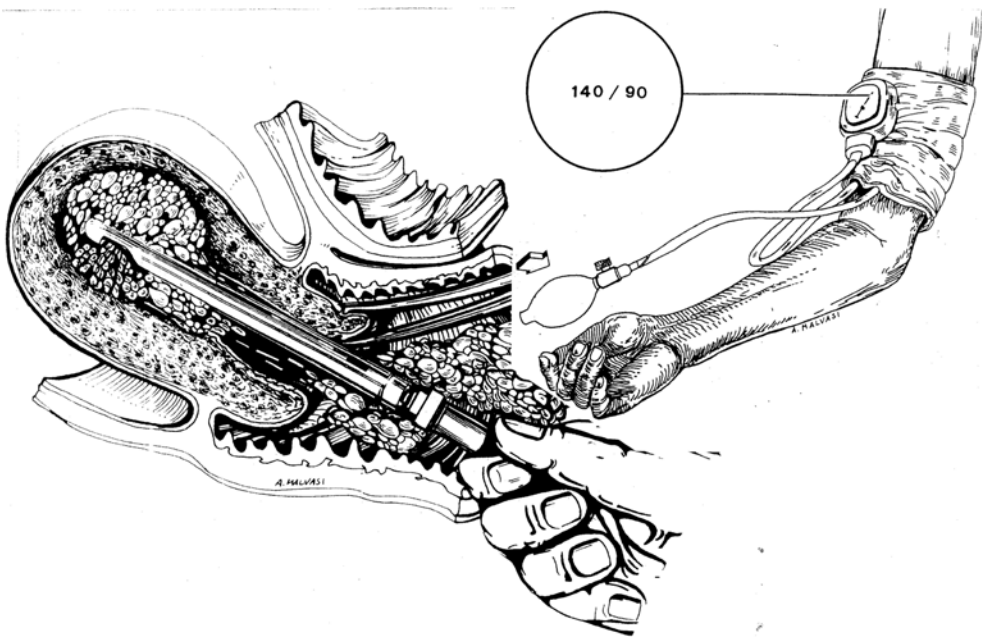

Fig. 15.7 The image shows a uterine evacuation, by Karman cannula, for gestational trophoblastic disease (GTD) or hydatidiform mole

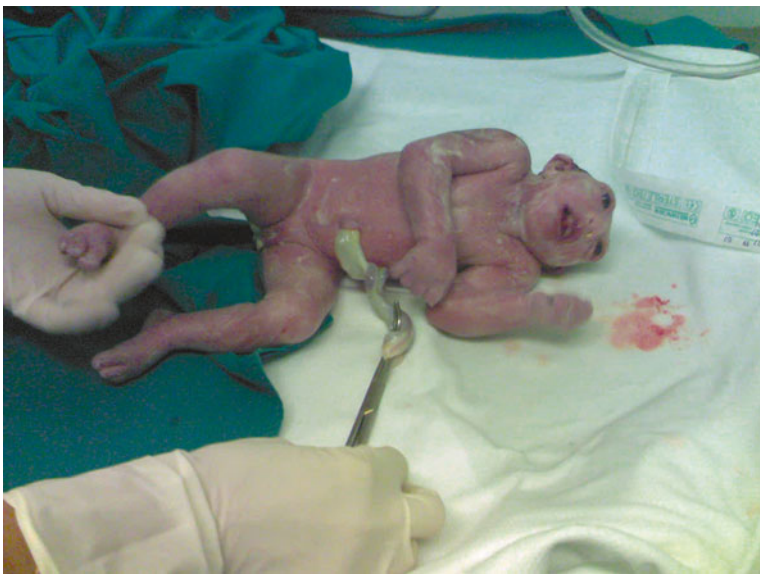

Fig. 15.8 Photos of anencephalic fetuses born to the 34th week in a patient with severe hypertension, polyhydramnios, and abruptio placenta

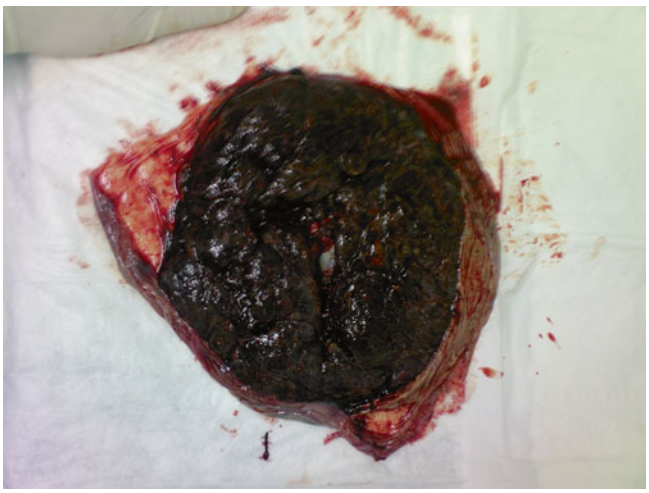

Fig. 15.9 Placenta with placental tumor (with atypical vascular invasion and atypical hyperplasia)

HELLP syndrome is a specific form of preeclampsia/eclampsia that is characterized by the presence of (Fig. 15.10):

- Hemolysis
- Elevated liver enzymes
- Low platelet count

Like preeclampsia, HELLP syndrome is usually a disease of the third trimester.

When HELLP syndrome occurs in the first half of pregnancy, it is most commonly associated with other etiologies such as antiphospholipid syndrome or molar pregnancy. Infrequently, HELLP syndrome can occur prior to 25 weeks of gestation without any secondary contributing factors [31–35].

Delivery is the only definitive cure for HELLP syndrome. Delivery should be undertaken soon after initial maternal stabilization for women with HELLP syndrome regardless of gestational age or likelihood of fetal viability [1].

Maternal stabilization involves treatment of severe-range blood pressures and magnesium sulfate for seizure prophylaxis. Consideration should be given to administration of dexamethasone per the Mississippi protocol [35, 36].

Like previously mentioned, when preeclampsia, eclampsia, or HELLP syndrome is encountered prior to the gestational age of fetal viability, delivery is recommended shortly after initial maternal stabilization.

Delivery is recommended for the safety and well-being of the mother. This can be accomplished either medically or surgically. The mode of delivery is dependent on the gestational age of the fetal-maternal condition, patient preference, and availability of resources.

Regardless of choice, the goal is to achieve a safe and efficient delivery [1, 37, 38].

Distinguishing preeclampsia apart from a lupus flare can pose a diagnostic dilemma, since a lot of overlap exists between the two (i.e., hypertension, proteinuria, and edema). Usually, lupus flares are associated with a low serum complement, rising levels of anti-DsDNA antibody, and erythrocyte casts. Normal complement swings the pendulum in favor of preeclampsia as does rapid worsening of symptoms. When symptoms occur prior to 20 weeks, a lupus flare is more likely to be the correct diagnosis [2, 39, 40].

15.8 Chronic Hypertension with Superimposed Preeclampsia

Patients with chronic hypertension are at increased risk of developing preeclampsia during the course of pregnancy. It is reported that up to one in four pregnant patients with

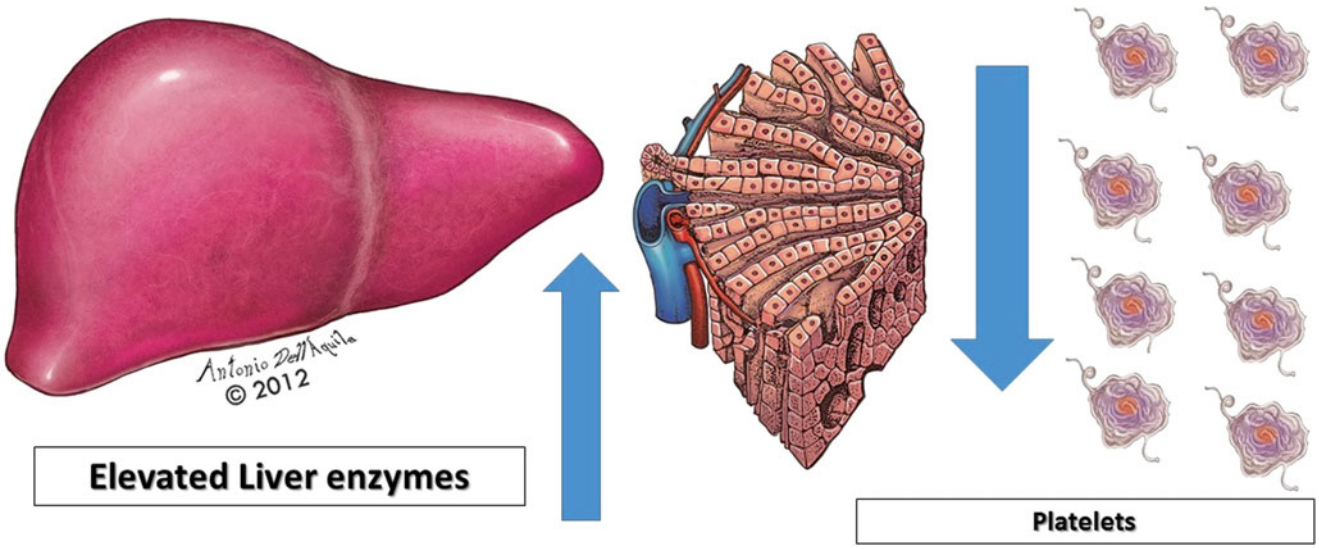

Fig. 15.10 HELLP syndrome is a specific form of preeclampsia/eclampsia that is characterized by hemolysis, elevated liver enzymes, and low platelet count

chronic hypertension will develop superimposed preeclampsia at some point during pregnancy [1, 5].

Establishing the diagnosis of superimposed preeclampsia is challenging, as it is often difficult to distinguish worsening chronic hypertension from developing preeclampsia. Differentiating the two is essential as management options and maternal and fetal complications differ. The diagnosis of superimposed preeclampsia is likely in the following scenarios [1]:

A sudden increase in BP that was previously well controlled or increases in antihypertensive medication(s) required to control blood pressure

New-onset proteinuria or sudden increase in proteinuria in a woman with known proteinuria before or in early pregnancy

The above distinguishing features only highlight the importance of obtaining baseline labs and blood pressure measurements as early as possible in pregnancy. The baseline labs, BP measurements, and 24-h urine protein collection are essential to serve as a baseline for comparison later during gestation.

15.9 Screening for Secondary Causes

Secondary hypertension accounts for approximately 5–10% of hypertensive disorders outside of pregnancy. It is important for the clinician to consider the possibility of secondary causes of hypertension in early pregnancy hypertension as the underlying etiology is often treatable. Secondary causes of hypertension need to be considered in certain pregnant women, and if the etiology is found and corrected, pregnancy outcomes will often improve [1, 2, 10].

Healthcare providers need to pay close attention to patients' symptoms, physical exam findings, imaging studies, and/or lab evaluations that may indicate a secondary cause of hypertension. One must remember that the symptoms may be vague or subtle. It is also important to review the patient's medications and diet, as certain medications and dietary supplements may be responsible for the elevated blood pressures.

Some of the findings on history and physical exam that should prompt further workup include [1, 2, 10]:

- Age less than 35 in non-obese, non-African-American women without a family history of hypertension
- Difficult to control blood pressures despite multiple medications and patient compliance
- Strong family history of renal disease
- Flushing and sweating
- Elevated serum creatinine (>1.1 mg/dl)
- Non-medication-induced hypokalemia (potassium <3.0 mEq/l)
- Renal bruit on abdominal auscultation
- Arm-to-leg systolic blood pressure measurement discrepancy or absent femoral pulses

Once secondary hypertension is suspected, referral to a hypertension specialist is recommended as the diagnostic tests and criteria are not well agreed upon and can vary. It is also worthy to note that apart from suspected renovascular hypertension and pheochromocytoma, which are associated with adverse pregnancy outcomes, there is a tendency to delay thorough evaluation and definitive treatment until postpartum.

This minimizes the diagnostic risk and eliminates the diagnostic confusion that can occur from the overlap between these conditions and the physiologic changes of pregnancy [1, 2].

Listed below are some commonly encountered secondary causes of hypertension (Table 15.1).

15.9.1 Kidney Disease

Renal disease (Fig. 15.11) is the most common identifiable cause of secondary hypertension. It significantly affects pregnancy. Renal disease is associated with adverse maternal and fetal outcomes, which is proportional to the degree of kidney damage. Renal disease is often associated with either a strong family history or comorbidities known to cause kidney damage (e.g., diabetes mellitus and systemic lupus erythematosus). Evidence of chronic kidney disease is elicited via abnormal kidney function tests (elevated serum creatinine) or proteinuria. Once proteinuria is identified, it needs to be quantified. A renal ultrasound should be also performed. Referral to a specialist is advised [1, 2].

15.9.2 Thyroid Dysfunction

Thyroid dysfunction should be suspected in the presence of any suggestive symptoms of either hypothyroidism (e.g., bradycardia, cold intolerance, constipation, weight gain) or hyperthyroidism (e.g., tachycardia, heat intolerance, weight loss) (Fig. 15.12). A TSH level should be checked if thyroid dysfunction is suspected. TSH is considered sensitive for both hypo- and hyperthyroidism, and management should then be directed accordingly. Interestingly, hypothyroidism mainly affects the diastolic blood pressure, while hyperthyroidism exerts an effect on the systolic blood pressure [10, 41].

15.9.3 Primary Aldosteronism

Suspicion for this condition should be raised in the presence of both hypertension and non-medication-induced hypokalemia. The initial recommended test is the measurement of both aldosterone and renin. The aldosterone/renin ratio is then calculated. If this condition is suspected, referral to an endocrinologist is strongly recommended [10, 42, 43].

15.9.4 Obstructive Sleep Apnea

Secondary hypertension can be attributed to obstructive sleep apnea (OSA) (Fig. 15.13). This should be suspected in obese patients or in those that have apneic episodes during sleep or constantly complain of daytime sleepiness. Sometimes, the only complaint is the partner reporting loud snoring. Diagnosis is made through a sleep study [10, 44].

15.9.5 Cushing Syndrome

Suspicion for this condition should be raised in the presence of any of the following physical findings: buffalo hump, central obesity, moon facies, and striae. It is important to ask

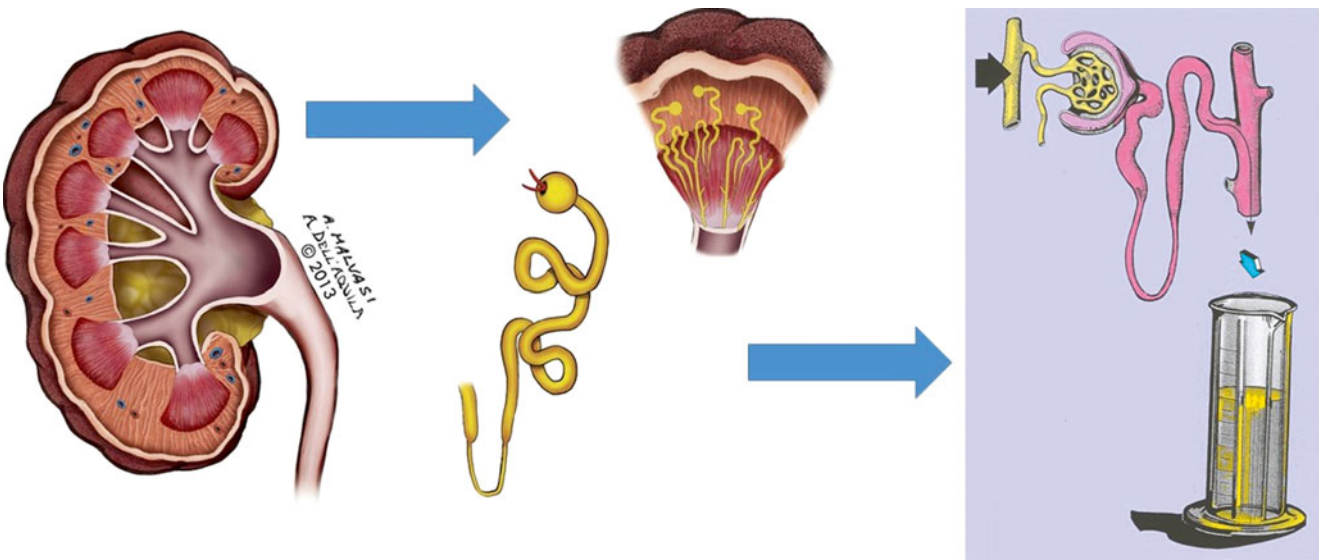

Fig. 15.11 Renovascular hypertension: kidney on the *left*, pathological nephron in the *center*, proteinuria and abnormal kidney function on the *right*

about medication history to rule out iatrogenic causes of hypercortisolism. Initial tests include 24-h urine cortisol, low-dose dexamethasone or late-night salivary cortisol tests. Evaluation is best left to endocrinologists when this condition is suspected [10].

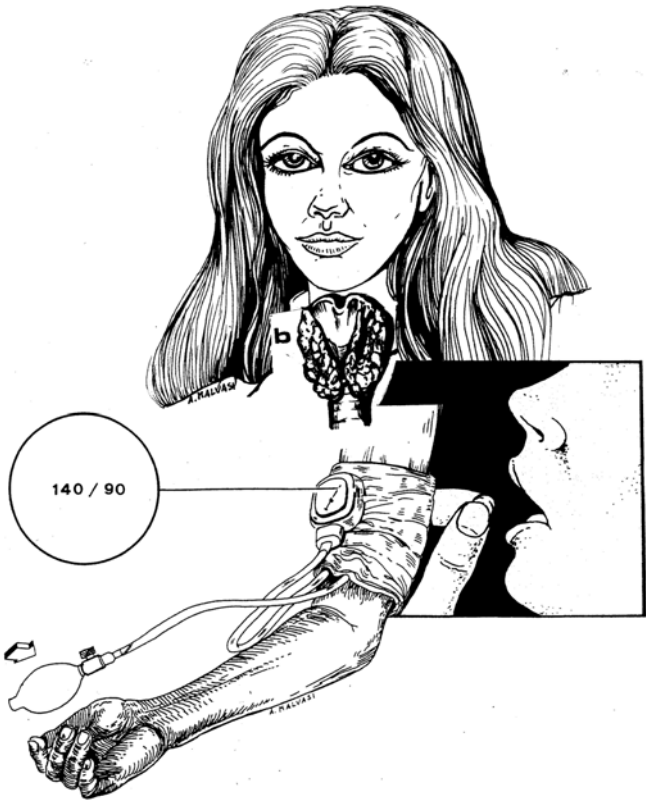

Fig. 15.12 Pregnant with hyperthyroidism and hypertension

15.9.6 Renal Artery Stenosis

This condition should be suspected when a renal artery bruit is auscultated on physical exam. The bruit is an audible high-pitched holosystolic renal artery bruit (Fig. 15.14). Detection of such a bruit has a relative risk of five for renal artery stenosis and should be followed by imaging studies. Commonly used imaging modalities include a CT scan, MRI, and Doppler studies. The risks and benefits of contrast use should be taken into consideration when choosing the modality [1, 2, 10].

15.9.7 Pheochromocytoma

This condition (Fig. 15.15) is associated with flushing, sweating, palpitations, headache, syncope, and labile blood pressures. Testing is done either via measuring metanephrines in a 24-h urine sample or measurement of free metanephrines in the plasma. The treatment is surgical excision of the tumor. If suspected in pregnancy, evaluation and treatment should be undertaken during pregnancy to help minimize the risks associated with an untreated pheochromocytoma [1, 2, 10].

15.9.8 Coarctation of the Aorta

The clue to this diagnosis (Fig. 15.16) lies in the discrepancy between blood pressures at certain anatomic sites (Fig. 15.17). The classic finding includes hypertension in the upper extremities along with low or unobtainable blood pressure in the lower extremities. Delayed femoral pulses may also be found. Imaging is the diagnostic modality of choice and usually is in the form of an MRI. Treatment in pregnancy is recommended after consultation with a specialist [1, 2, 10].

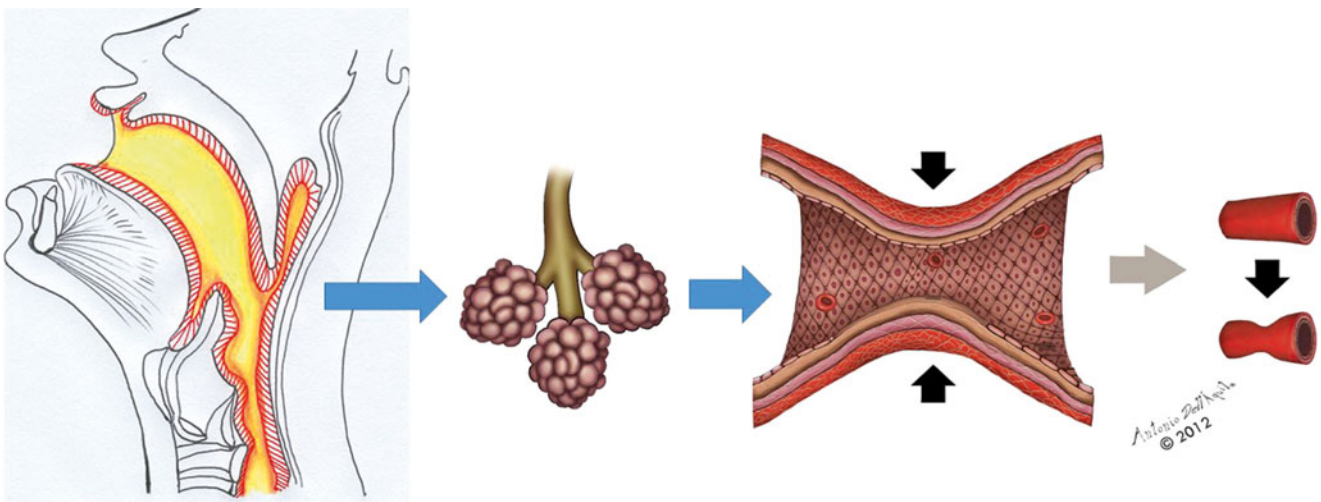

Fig. 15.13 Pregnant with obstructive sleep apnea: on the *left,* apneic episodes during sleep or constantly complain of daytime sleepiness; in the middle, an obstructed pulmonary alveolus; on the *right,* a vasospasm

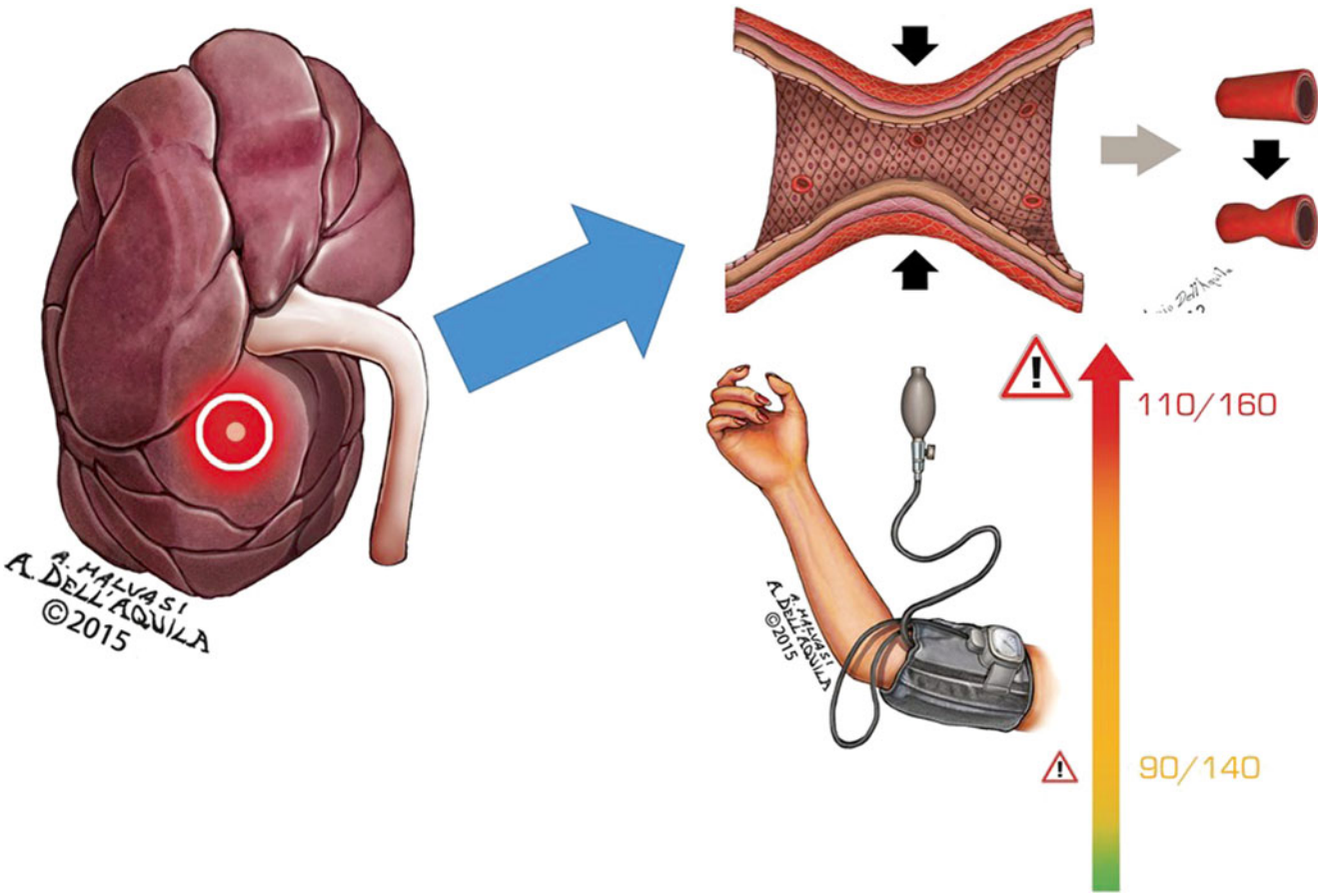

Fig. 15.14 The renal stenosis with hypertension

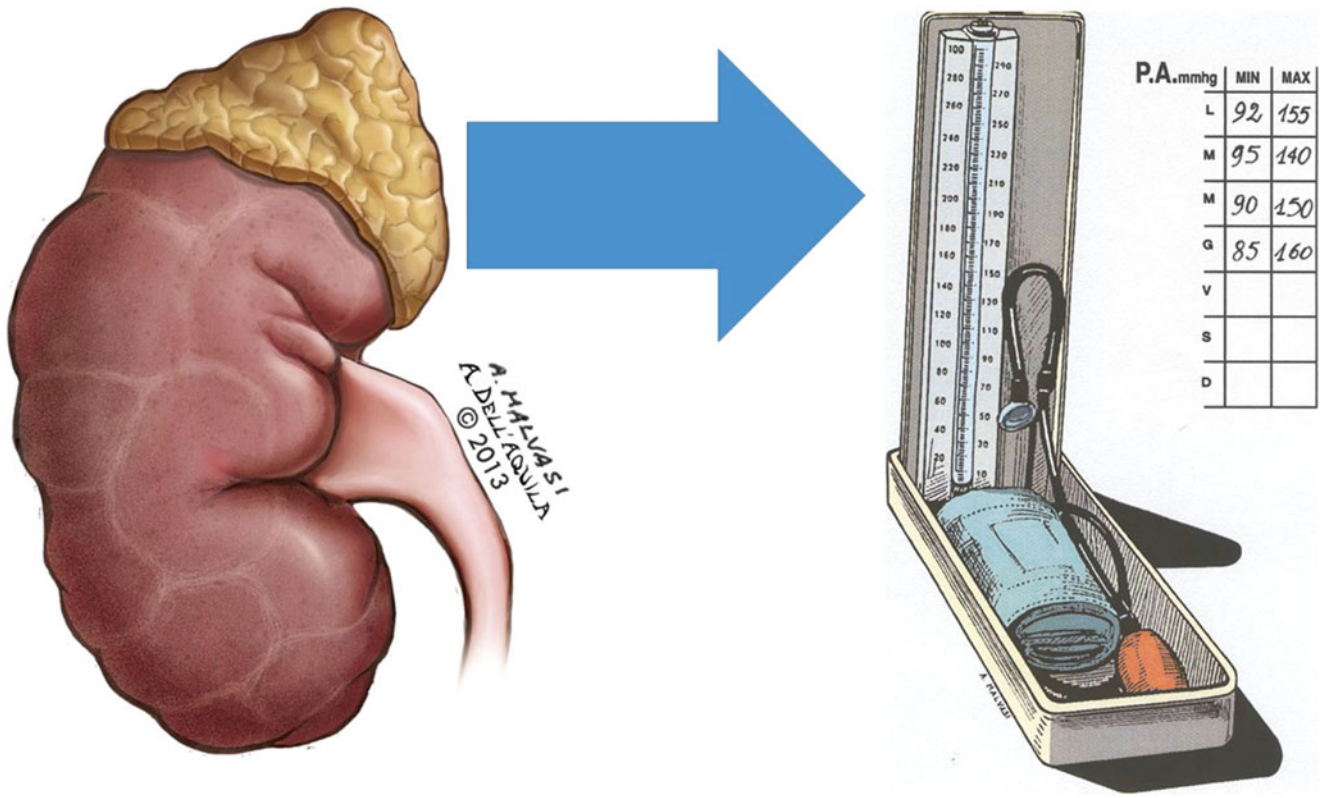

Fig. 15.15 A pheochromocytoma causing hypertension

15.9.9 Drugs and Medications

It is important to ask about medications, supplements, and illicit drug history (Fig. 15.18). Prescription, over-the-counter, and herbal medications may contribute to blood pressure changes. Illicit drugs may also cause acute hypertension.

Some drugs known to affect blood pressure include decongestants (pseudoephedrine), psychiatric medications (TCAs and SSRIs), nonsteroidal anti-inflammatory medications, and steroids. Illicit drugs such as amphetamines and cocaine may cause elevated blood pressures. Herbal medications like ginseng also affect blood pressure. Licorice is also known to cause hypertension as well as hypokalemia [2, 10, 45].

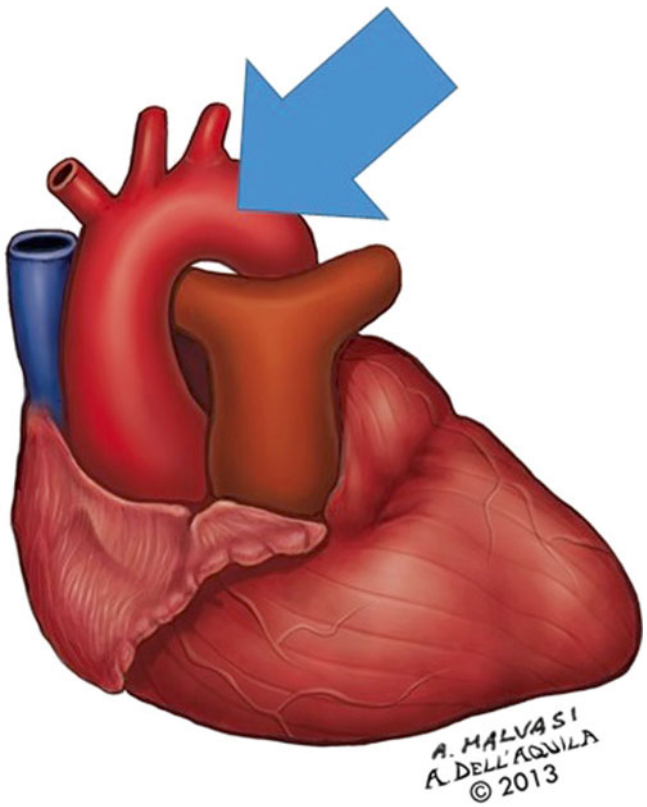

Fig. 15.16 A coarctation of the aorta

15.10 Management of Hypertensive Disorders in Pregnancy

Management strategies are multifaceted and are aimed at preventing complications. However, hypertensive disorders of pregnancy are high risk and complications often occur albeit appropriate treatment. It is critical to know and recognize the various complications that may occur in hypertensive disorders of pregnancy so timely treatment can be initiated. The management of hypertension in pregnancy depends on the type of hypertensive disorder, severity of hypertension, gestational age, maternal comorbidities, and maternal and fetal status.

Outside of pregnancy, weight loss, exercise, and dietary modifications have been shown to improve blood pressure, decrease complication rates and disease progression. The outcomes of these regimens have not been clearly demonstrated in pregnancy in part due to the lack of quality studies. At the present time, the American College of Obstetricians and Gynecologists (ACOG) task force does not recommend weight loss or extremely low sodium diets (<100 mEq/d) in the management of chronic hypertension in pregnancy. The ACOG task force also does not recommend sodium restriction, bed rest, or the restriction of physical activity for the primary prevention of preeclampsia [1].

Pregnant women with persistent severe-range blood pressures defined as a systolic blood pressure of 160 mmHg or higher and/or a diastolic of 105 mmHg or higher require immediate treatment utilizing intravenous labetalol, hydrala-

Fig. 15.17 The coarctation of the aorta clinical diagnosis: discrepancy between blood pressures at certain anatomic sites

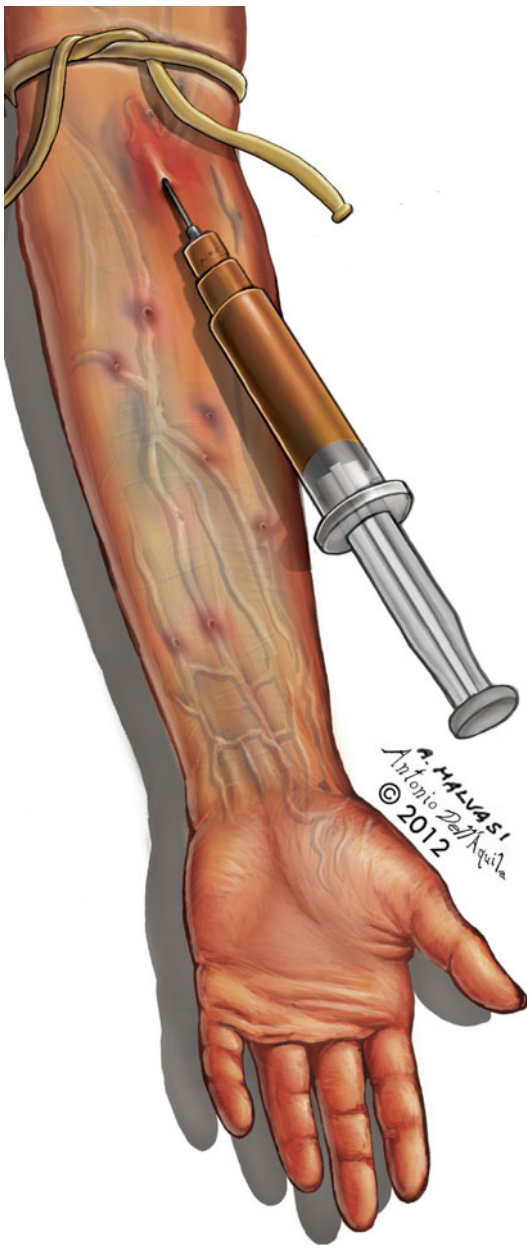

Fig. 15.18 Arm of addict patient injecting illicit drugs during pregnancy

zine, or oral nifedipine as described in ACOG Committee Opinion 623 [46]. However, controversy exists surrounding the management of mild blood pressure elevation in pregnancy. The optimal blood pressure needed to treat in order to decrease adverse maternal and fetal outcomes in pregnancy remains elusive.

Evidence is conflicting and non-conclusive regarding the management of mild blood pressure elevations. Anukumah et al. reported an improvement in adverse maternal and fetal outcomes when blood pressure was lowered below 140/90 mmHg [1, 2, 47]. There was an overall reduction in preterm birth, preeclampsia, and small for gestational age infants. However, a 2007 Cochrane review (46 trials, 4282 pregnant women) did not show improvement in the aforementioned outcomes. This meta-analysis did see improvement in the rate of progression to severe disease [1, 2, 48].

The decision to initiate therapy ultimately depends upon the benefit-to-risk ratio. Does the maternal benefit of treatment outweigh the potential fetal risk of the medication? Secondary to the lack of conclusive evidence showing clear benefit of treatment of mild range blood pressures and the concerns about the safety and possible teratogenic effect of treatment, the majority opinion recommends against initiating antihypertensive therapy with mild blood pressure elevations (140–159 mmHg/90–104 mmHg) unless other comorbidities exist. This recommendation mainly stems from the lack of strong evidence showing benefit of treatment, rather than the teratogenic potential of treatment. This recommendation may change as new studies emerge [1, 2, 5].

Patients already on antihypertensive medications should continue them as long as the medication is considered safe to use in pregnancy (Fig. 15.19); otherwise, a safer alternative should be chosen. Ideally, this should be done during preconception counseling or as early as possible in pregnancy to minimize teratogenic potential [1, 2].

For the nonurgent treatment of hypertension (long-term control) in pregnancy, the following medications are considered first line [1, 2]:

- Methyldopa (oral)
- Labetalol (oral)
- Nifedipine (oral)

Diuretics should be used as second-line medications due to their potential effect on plasma volume. If diuretics are part of a prepregnancy program of blood pressure control, their use can be continued during pregnancy. The initiation of diuretics as adjunctive therapy with antihypertensives poses a hazard to the fetus when there is evidence of placental insufficiency. Angiotensin-converting enzyme inhibitors (ACE-i) and angiotensin receptor blockers (ARB) should be avoided in pregnancy secondary to the association with fetal renal agenesis and dysfunction [1, 2, 49–54].

In the instance where urgent blood pressure control is needed (immediate control), the choice of medications depends upon the clinical setting, medication availability, and the comfort level of the provider. In the rare occurrence that blood pressure is not controlled using the recommended medications (see below), consultation with a specialist is advised. The recommended medications include [1, 46, 55]:

- Labetalol (IV)
- Hydralazine (IV)
- Nifedipine (oral)

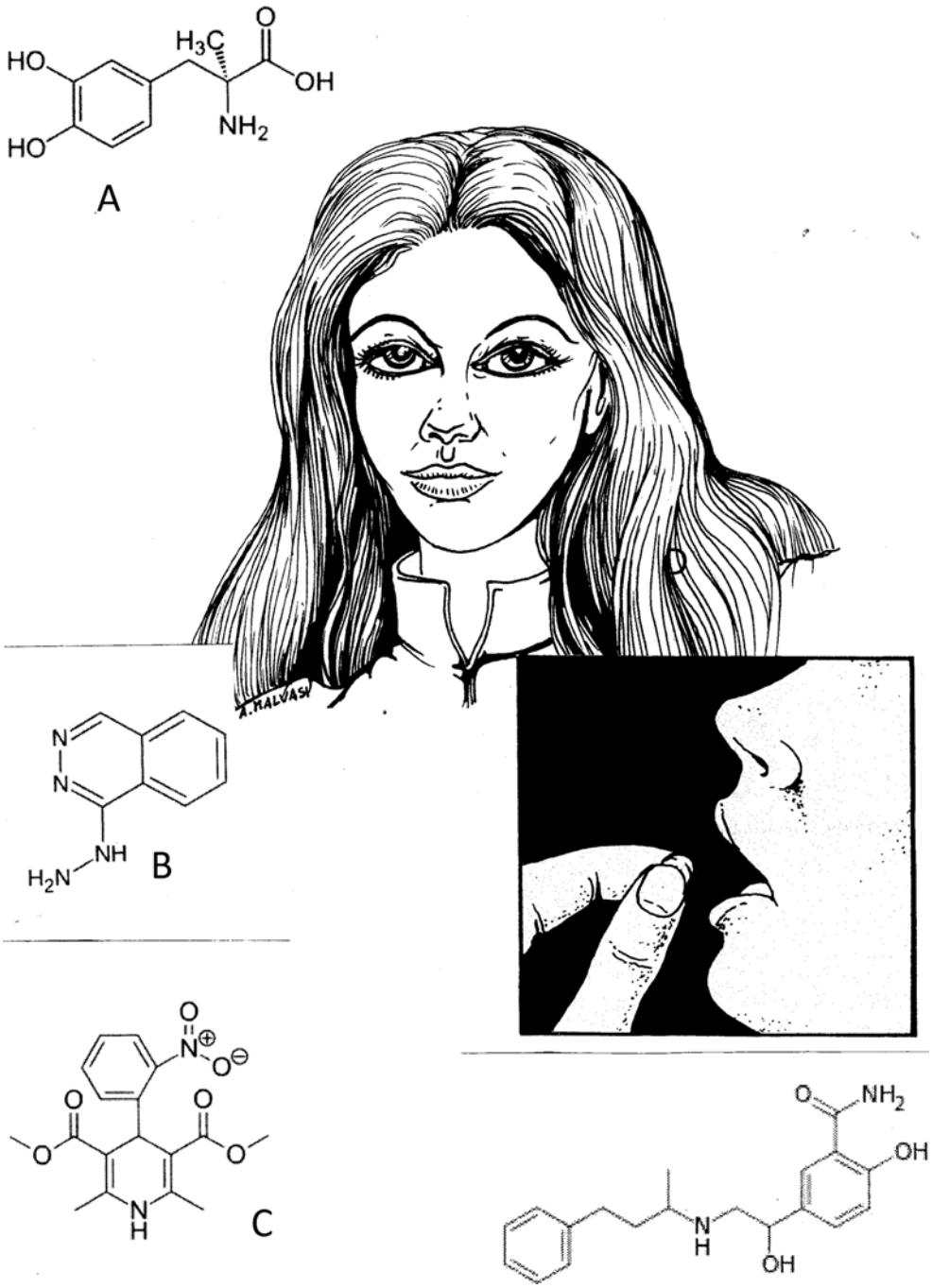

Fig. 15.19 The common gestational drugs in hypertension: (**a**) methyldopa; (**b**) hydralazine; (**c**) nifedipine; (**d**) labetalol

15.10.1 Methyldopa

Methyldopa is a central-acting alpha agonist. It has a long track record of safety and is the only drug that demonstrates safety with long-term follow-up of children. Methyldopa may be less effective in controlling severe-range blood pressures than the other recommended antihypertensive medications. It is not recommended for urgent control of blood pressures [56, 57].

15.10.2 Labetalol

Labetalol is a combined alpha- and beta-blocker. It can be safely used in pregnancy for the treatment of both acute and chronic blood pressure elevation. Concern for fetal growth restriction does exist; however, studies are inconclusive and contradictory with the majority of evidence not showing an association [2, 58–62].

15.10.3 Nifedipine

Nifedipine is a calcium channel blocker that is commonly used as first-line treatment of hypertension in pregnancy. Nifedipine should be used with caution in patients receiving magnesium sulfate as there is a theoretical risk of hypotension and neuromuscular blockade when combined [1, 63].

15.10.4 Hydralazine

Hydralazine is a peripheral vasodilator that is very effective in the urgent treatment of blood pressure elevation. Hydralazine can cause reflex tachycardia as a result of peripheral vasodilation [1, 2].

15.11 Adverse Maternal and Fetal Outcomes

Pregnant woman with elevated blood pressure is at an increased risk of many adverse pregnancy outcomes, both maternal and fetal. The development of such complications varies depending on many factors such as the duration of chronic hypertension, extent of end-organ damage, compliance with prenatal care, and disease severity [1, 2, 5].

With that in mind, the rate of development of superimposed preeclampsia and abruptio placenta can range anywhere from 10 to 50 % and 0.7–10 %, respectively. Some maternal complications are potentially life threatening and include hemorrhagic stroke (Fig. 15.20), heart failure (Fig. 15.21), pulmonary edema (Fig. 15.22), hypertensive encephalopathy, retinopathy and acute renal failure, or acceleration of end-organ damage. The risk of cesarean delivery (odds ratio [OR] 2.7 with a 95 % confidence interval [2.4–3.0]) and postpartum hemorrhage increases (OR 2.2; 95 % CI, 1.4–3.7), as does that of gestational diabetes (OR 1.8; 95 % CI) when compared to their non-hypertensive counterparts [1, 2, 5, 64–70].

In the presence of maternal hypertension, preterm delivery rates also rise and are reported to be as high as 70 % with severe hypertension and between 12 and 34 % in less severe disease. Small for gestational age (SGA) is also more frequently encountered and varies with disease severity (8–15.5 % for mild and 31–40 % for severe). An overall fourfold increase in perinatal mortality is also noted [1, 2, 5, 67–71].

Another contributor to morbidity is the potential for teratogen exposure for those on antihypertensive medications. When preeclampsia results in preterm delivery or if preeclampsia has occurred in more than one pregnancy, low-dose aspirin administration initiated by the end of the first trimester is recommended in subsequent pregnancies [1].

Fig. 15.20 A pregnant patient with cerebral hemorrhagic stroke

15.12 Summary and Conclusions

Hypertension in pregnancy is a commonly encountered major contributor to maternal and fetal morbidity and mortality. Etiologies, prognoses, outcomes, and management are varied. Establishing the correct diagnosis in a timely fashion allows for appropriate management of the patient and pregnancy, which is instrumental in achieving the best outcome for both mother and fetus. Knowing when to look for secondary causes of hypertension is of equal importance as these can be life threatening and potentially curable. Further studies are needed to establish the blood pressure that is associated with adverse outcome in pregnancy, and until studies emerge, it is only recommended to treat severe-range blood pressures.

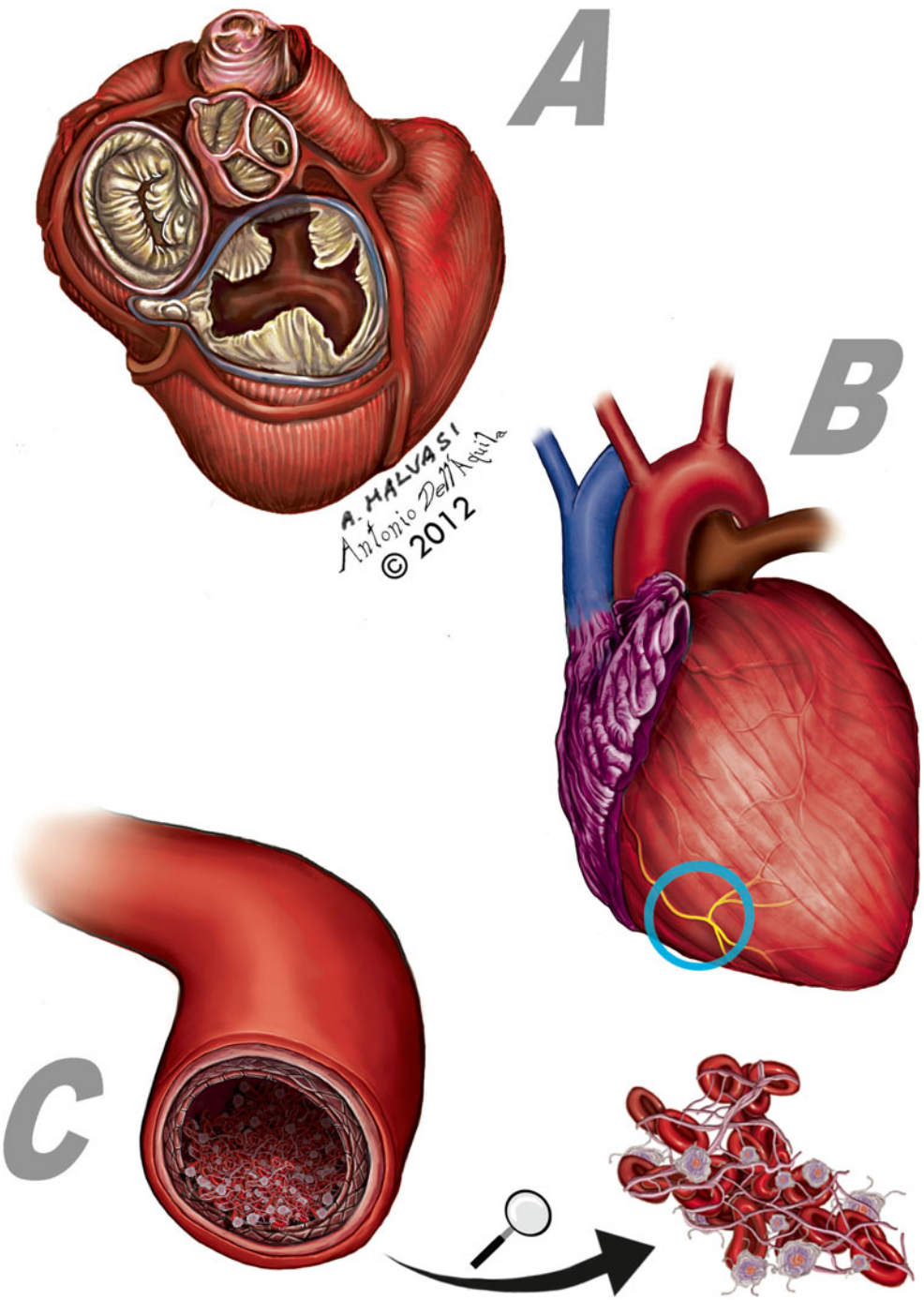

Fig. 15.21 Illustration of heart failure with sequencing phenomena (from the *top* to *bottom*)

Fig. 15.22 Pregnant patient with pulmonary edema

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