IN THE NAME OF GOD

CEREBROVASCULAR DISEASES

Abnormalities of the cerebrovascular circulation include strokes—both ischemic and hemorrhagic, as well as anatomical anomalies, such as arteriovenous malformations and aneurysms. The current endemic of obesity in this country, along with concomitant increases in heart disease, hypertension, and diabetes, has also resulted in increased stroke prevalence (Centers for Disease Control and Prevention, 2012). Women have a higher lifetime risk of stroke than men as well as higher associated mortality rates (Martínez-Sánchez, 2011; Roger, 2012). Moreover, pregnancy increases the immediate and lifetime risk of both ischemic and hemorrhagic stroke (Jamieson, 2010; Jung, 2010).

Stroke is relatively uncommon in pregnant women, but it contributes disparately to maternal mortality rates. Reported incidences of strokes in pregnancy range from 1.5 to 71 per 100,000 pregnancies (James, 2005; Kuklina, 2011; Scott, 2012). The incidence is increasing as measured by pregnancy-related hospitalizations for stroke (Callaghan, 2008; Kuklina, 2011).

Importantly, most are associated with hypertensive disorders or heart disease. Almost 9 percent of the pregnancy-related mortality rate in the United States is due to cerebrovascular accidents, with a third being associated with preeclampsia (Berg, 2010b).

Risk Factors

Most strokes in pregnancy manifest either during labor and delivery or in the puerperium. In a study of 2850 pregnancy-related strokes, approximately 10 percent developed antepartum, 40 percent intrapartum, and almost 50 percent postpartum (James, 2005). Several risk factors—unrelated and related to pregnancy—have been reported from studies that included more than 10 million pregnancies. These include older age; migraines, hypertension, obesity, and diabetes; cardiac disorders such as endocarditis, valvular prostheses, and patent foramen ovale; and smoking. Those related to pregnancy include hypertensive disorders, gestational diabetes, obstetrical hemorrhage, and cesarean delivery. By far, the most common risk factors are pregnancy-associated hypertensive disorders. As noted, one third of strokes are associated with gestational hypertension, and there is a three- to eightfold increased risk of stroke in hypertensive compared with normotensive women (Scott, 2012; Wang, 2011). Women with preeclampsia undergoing general anesthesia may be at higher risk of stroke compared with those given neuraxial anesthesia (Huang, 2010). Another risk factor for peripartum stroke is cesarean delivery, which increases the risk 1.5-fold compared with vaginal delivery (Lin, 2008).

are unclear as related to risk for stroke. Although cerebral blood flow *decreased* by 20 percent from midpregnancy until term, importantly, it *increased* significantly with gestational hypertension (Zeeman, 2003, 2004b). Such hyperperfusion would at least intuitively be dangerous in women with certain vascular anomalies.

Ischemic Stroke

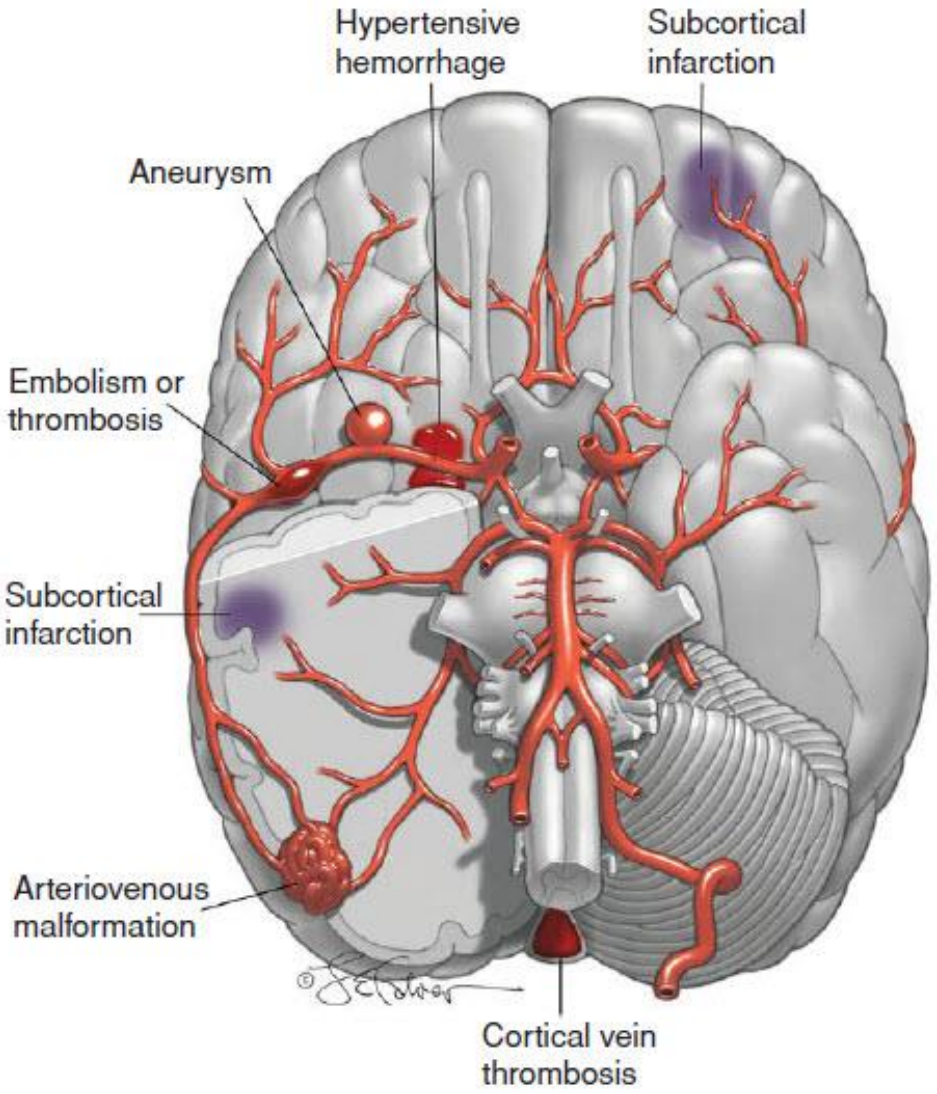
Acute occlusion or embolization of an intracranial blood vessel causes cerebral ischemia, which may result in death of brain tissue (Fig. 60-1). The more common associated conditions and etiologies of ischemic stroke are shown in Table 60-3. A transient ischemic attack (TIA) is caused by reversible ischemia, and symptoms usually last less than 24 hours. Patients with a stroke usually have a sudden onset of severe headache, hemiplegia or other neurological deficits, or occasionally, seizures. Focal neurological symptoms accompanied by an aura usually signify a first-episode migraine (Liberman, 2008).

Evaluation of an ischemic stroke includes echocardiography and cranial imaging with CT, MR, or angiography. Serum lipids are measured with the caveat that their values are distorted by normal pregnancy (Appendix, p. 1291). Antiphospholipid antibodies and lupus anticoagulant are sought—these cause up to a third of ischemic strokes in otherwise healthy young women (Chap. 59, p. 1173). Also, tests for sickle-cell syndromes are completed when indicated. With a thorough evaluation, most causes can be identified, although treatment is not always available. Some of these include cardiac-associated embolism, vasculitis, or vasculopathy such as Moyamoya disease (Ishimori, 2006; Miyakoshi, 2009; Simolke, 1991).

Preeclampsia Syndrome

In reproductive-age women, a significant proportion of pregnancy-related ischemic strokes are caused by gestational hypertension and preeclampsia syndrome (Jeng, 2004). As shown in Figure 60-1, areas of subcortical perivascular edema and petechial hemorrhage may progress to cerebral infarction (Aukes, 2007, 2009; Zeeman, 2004a). Although these are usually clinically manifest by an eclamptic convulsion, a few women will suffer a symptomatic stroke from a larger cortical infarction (Chap. 40, p. 742).

Other conditions with findings similar to pre-eclampsia include *thrombotic microangiopathies* (Chap. 56, p. 1116) and the *reversible cerebral vaso-constriction syndrome* (Chap. 40, p. 743). The latter, which is also termed *postpartum angiopathy*, can cause extensive cerebral edema with necrosis as well as widespread infarction with areas of hemorrhage (Katz, 2014; Ramnarayan, 2009; Singhal, 2009).


Hypertensive hemorrhage
Subcortical infarction
Aneurysm
Embolism or thrombosis
Subcortical infarction
Arteriovenous malformation
Cortical vein thrombosis

Cerebral Embolism

These strokes usually involve the middle cerebral artery (see Fig. 60-1). They are more common during the latter half of pregnancy or early puerperium (Lynch, 2001). The diagnosis can be made with confidence only after thrombosis and hemorrhage have been excluded. The diagnosis is more certain if an embolic source is identified. Hemorrhage may be more difficult to exclude because embolization and thrombosis are both followed by hemorrhagic infarction. Paradoxical embolism is an uncommon cause, even considering that more than a fourth of adults have a patent foramen ovale through which right-sided venous thromboemboli are deported (Kizer, 2005; Scott, 2012). Foraminal closure may not improve outcomes in these patients, however, this procedure has been performed during pregnancy (Dark, 2011; Furlan, 2012). Assorted cardioembolic causes of stroke include arrhythmias—especially atrial fibrillation, valvular lesions, mitral valve prolapse, mural thrombus, infective endocarditis, and peripartum cardiomyopathy.

Management of embolic stroke in pregnancy consists of supportive measures and antiplatelet therapy. Thrombolytic therapy and anticoagulation are controversial issues at this time (Kizer, 2005; Li, 2012).

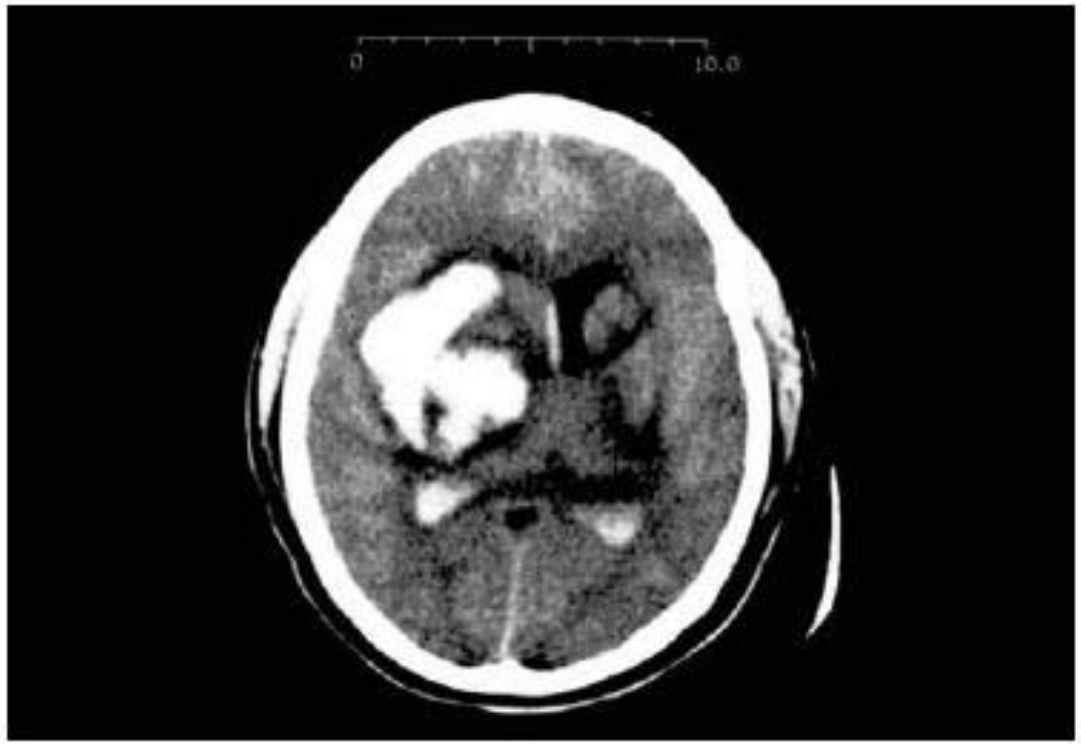
Cerebral Artery Thrombosis

Most thrombotic strokes affect older individuals and are caused by atherosclerosis, especially of the internal carotid artery. Many are preceded by one or more transient ischemic attacks. Thrombolytic therapy with *recombinant tissue plasminogen activator—rt-PA* or *alteplase* is recommended within the first 3-hour window if there is measurable neurological deficit and if neuroimaging has excluded hemorrhage. This can be used in pregnancy. A principal risk is hemorrhagic transformation of an ischemic stroke in approximately 5 percent of treated patients (van der Worp, 2007).

TABLE 60-3. Some Associated Disorders or Causes of Ischemic and Hemorrhagic Strokes During Pregnancy or the Puerperium

Ischemic Stroke	Hemorrhagic Stroke
Preeclampsia syndrome	Chronic hypertension
Arterial thrombosis	Preeclampsia syndrome
Venous thrombosis	Arteriovenous malformation
Lupus anticoagulant	Saccular aneurysm
Antiphospholipid antibodies	Angioma
Thrombophilias	Cocaine, methamphetamines
Migraine induced	Vasculopathy
Paradoxical embolus	
Cardioembolic	
Sickle hemoglobinopathy	
Arterial dissection	
Vasculitis	
Moyamoya disease	
Cocaine, amphetamines	

From Smith, 2012; Yager, 2012.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Cerebral Venous Thrombosis

In a 10-center study in the United States, 7 percent of cerebral venous thromboses were associated with pregnancy (Wasay, 2008). Even so, pregnancy-associated cerebral venous thrombosis is rare in developed countries, and reported incidences range from 1 in 11,000 to 1 in 45,000 pregnancies (Lanska, 1997; Simolke, 1991). In the Nationwide Inpatient Sample of more than 8 million deliveries, James and associates (2005) observed that venous thrombosis caused only 2 percent of pregnancy-related strokes (Saposnik, 2011). There are numerous predisposing causes, and the greatest risk is in late pregnancy and the puerperium.

Thrombosis of the lateral or superior sagittal venous sinus usually occurs in the puerperium and often in association with preeclampsia, sepsis, or thrombophilia (see Fig. 60-1). It is more common in patients with inherited thrombophilias, lupus anticoagulant, or antiphospholipid antibodies (Chaps. 52, p. 1029 and 59, p. 1173). Headache is the most common presenting symptom, neurological deficits are common, and up to a third of patients have convulsions (Wasay, 2008). Diagnosis is with MR venography (Saposnik, 2011).

Management includes anticonvulsants for seizures, and although heparinization is recommended by most, its efficacy is controversial (de Freitas, 2008; Saposnik, 2011; Smith, 2012). Antimicrobials are given if there is septic thrombophlebitis, and fibrinolytic therapy is reserved for those women failing systemic anticoagulation. The prognosis for venous thrombosis in pregnancy is better than in nonpregnant subjects, and mortality rates are less than 10 percent (McCaulley, 2011). The recurrence rate is 1 to 2 percent during a subsequent pregnancy (Mehraein, 2003).

Recurrence Risk of Ischemic Stroke

Women with previous ischemic stroke have a low risk for recurrence during a subsequent pregnancy unless a specific, persistent cause is identified. Lamy and colleagues (2000) followed 37 women who had an ischemic stroke during pregnancy or the puerperium, and none of their 24 subsequent pregnancies was complicated by another stroke. In another study of 23 women who had prepregnancy strokes from a variety of causes, there were 35 subsequent pregnancies without a stroke recurrence (Coppage, 2004). Finally, in a follow-up study of 1770 nonpregnant women with antiphospholipid-related ischemic stroke, investigators reported no difference in the recurrence risk as long as preventative treatment was given with warfarin or aspirin (Levine, 2004). In another study of nonpregnant subjects, low-dose aspirin following venous thromboembolism decreased the risk of a subsequent stroke (Brighton, 2012).

Currently, there are no firm guidelines regarding prophylaxis in pregnant women with a stroke history (Helms, 2009). The American Heart Association stresses the importance of controlling risk factors such as hypertension and diabetes (Furie, 2011). Women with antiphospholipid antibody syndrome or certain cardiac conditions should be considered for prophylactic anticoagulation as discussed in Chapters 49 (p. 979) and 59 (p. 1175).

Hemorrhagic Stroke

The two distinct categories of spontaneous intracranial bleeding are intracerebral and subarachnoid hemorrhage. The symptoms of a hemorrhagic stroke are similar to those of an ischemic stroke. Their differentiation is only possible with CT or MR imaging (Morgenstern, 2010).

Intracerebral Hemorrhage

Bleeding into the brain parenchyma most commonly is caused by spontaneous rupture of small vessels previously damaged by chronic hypertension as depicted in Figure 60-1 (Qureshi, 2001; Takebayashi, 1983). Thus, pregnancy-associated hemorrhagic strokes such as the one shown in Figure 60-2 are often associated with chronic hypertension and superimposed preeclampsia (Cunningham, 2005; Martin, 2005). Because of its location, this type of hemorrhage has much higher morbidity and mortality rates than does subarachnoid hemorrhage (Morgenstern, 2010). Chronic hypertension is uniquely associated with *Charcot-Bouchard microaneurysms* of the penetrating branches of the middle cerebral artery. Pressure-induced rupture causes bleeding in the putamen, thalamus, adjacent white matter, pons, and cerebellum. In the 28 women described by Martin and associates (2005), half died and most survivors had permanent disabilities. This cautions for the importance of proper management for gestational hypertension—especially systolic hypertension—to prevent cerebrovascular pathology (Chap. 40, p. 761).

Subarachnoid Hemorrhage

In a study of 639 cases of pregnancy-related subarachnoid hemorrhage from the Nationwide Inpatient Sample, the incidence was 5.8 per 100,000 pregnancies, with half being postpartum (Bateman, 2012). These bleeds are more likely caused by an underlying cerebrovascular malformation in an otherwise normal patient (see Fig. 60-1). Ruptured saccular or "berry" aneurysms cause 80 percent of all subarachnoid hemorrhages. The remaining cases are caused by a ruptured arteriovenous malformation, coagulopathy, angiopathy, venous thrombosis, infection, drug abuse, tumors, or trauma. Such cases are

uncommon, and a ruptured aneurysm or angioma or bleeding from a vascular malformation has an incidence of 1 in 75,000 pregnancies. Although this frequency is not different from that in the general population, the mortality rate during pregnancy is reported to be as high as 35 percent.

Intracranial Aneurysm. Approximately 2 to 5 percent of adults have this lesion (see Fig. 60-1). Fortunately, only a small percentage rupture—approximately 0.1 percent for aneurysms < 10 mm and 1 percent for those > 10 mm (Smith, 2008). Most aneurysms identified during pregnancy arise from the circle of Willis, and 20 percent are multiple (Stoodley, 1998). Pregnancy does not increase the risk for aneurysmal rupture. However, because of their high prevalence, they are more likely to cause subarachnoid bleeding than other causes (Hirsch, 2009; Tiel Groenestege, 2009). Aneurysms are more likely to bleed during the second half of pregnancy—only approximately 20 percent bleed during the first half (Dias, 1990).

The cardinal symptom of a subarachnoid hemorrhage from an aneurysm rupture is sudden severe headache, accompanied by visual changes, cranial nerve abnormalities, focal neurological deficits, and altered consciousness. Patients typically have signs of meningeal irritation, nausea and vomiting, tachycardia, transient hypertension, low-grade fever, leukocytosis, and proteinuria. Prompt diagnosis and treatment may prevent potentially lethal complications. The American Heart Association recommends noncontrast cranial CT imaging as the first diagnostic test, although MR imaging may be superior (Chalela, 2007; Connolly, 2012).

Treatment includes bed rest, analgesia, and sedation, with neurological monitoring and strict blood pressure control. Repair of a potentially accessible aneurysm during pregnancy depends in part on the recurrent hemorrhage risk versus surgical risks. At least in nonpregnant patients, the risk of subsequent bleeding with conservative treatment is 20 to 30 percent for the first month and then 3 percent per year. The risk of rebleeding is highest within the first 24 hours, and recurrent hemorrhage leads to death in 70 percent.

Early repair is done by surgical clipping of the aneurysm or by endovascular coil placement completed using fluoroscopic angiography yet attempting to limit radiation exposure. For women remote from term, repair without hypotensive anesthesia seems optimal. For women near term, cesarean delivery followed by aneurysm repair is a consideration, and we have successfully done this in several cases. For aneurysms repaired either before or during pregnancy, most allow vaginal delivery if remote from aneurysmal repair. A problem is what defines "remote," and although some recommend 2 months, the time for complete healing is unknown. For women who survive subarachnoid hemorrhage, but in whom surgical repair is not done, we agree with Cartlidge (2000) and recommend against bearing down—put another way, we favor cesarean delivery.

Arteriovenous Malformations. These are congenital focal abnormal conglomerations of dilated arteries and veins with subarteriolar disorganization (see Fig. 60-1). They lack capillaries and have resultant arteriovenous shunting. Although

unclear, the risk of bleeding may increase with gestational age. When arteriovenous malformations (AVMs) bleed, half do so into the subarachnoid space, whereas half are intraparenchymal with subarachnoid extension (Smith, 2008). They are uncommon and are estimated to occur in 0.01 percent of the general population. Bleeding does not appear to be more likely during pregnancy (Finnerty, 1999; Horton, 1990). AVMs are correspondingly rare during pregnancy, and in the study from Parkland Hospital, there was only one AVM in nearly 90,000 deliveries (Simolke, 1991).

Treatment of AVMs in nonpregnant patients is largely individualized. There is no consensus whether all those that are accessible should be resected. It also depends on whether the lesion is symptomatic or an incidental finding; its anatomy and size; presence of associated aneurysm, which is found in up to 60 percent; and especially, whether or not the lesion has bled. After hemorrhage, the risk of recurrent bleeding in unrepaired lesions is 6 to 20 percent within the first year, and 2 to 4 percent per year thereafter (Friedlander, 2007; Smith, 2008). The mortality rate with a bleeding AVM is 10 to 20 percent. In pregnancy, the decision to operate is usually based on neurosurgical considerations, and Friedlander (2007) recommends strong consideration for treatment if bleeding occurs. Because of the high risk of recurrent hemorrhage from an unresected or inoperable lesion, we favor cesarean delivery. An unusual case of spontaneous regression of a cerebral AVM has been described (Couldwell, 2011).

Thank