Clinical Features. Rupture of an aneurysm leading to clinically significant subarachnoid hemorrhage is most frequent in the fifth decade and is slightly more frequent in females. Overall, in about 1.3% of individuals aneurysms will rupture over the course of 1 year, but the risk is higher for larger aneurysms. For example, aneurysms greater than 10 mm in diameter have a roughly 50% risk of bleeding per year. Rupture may occur at any time, but in about one third of cases it is associated with acute increases in intracranial pressure, such as with straining at stool or sexual orgasm. Blood under arterial pressure is forced into the subarachnoid space and affected individuals are stricken with a sudden, excruciating headache ("the worst headache I've ever had") and rapidly lose consciousness. Between 25% and 50% of patients die with the first rupture, but patients who survive often improve and recover consciousness in minutes. Repeat bleeding is common in survivors and unpredictable in timing. With each episode of bleeding, the prognosis is worse.

The clinical consequences of blood in the subarachnoid space can be separated into acute events, occurring within hours to days after the hemorrhage, and late sequelae associated with the healing process. In the first few days after a subarachnoid hemorrhage, regardless of the etiology, there is an increased risk of additional ischemic injury from vasospasm affecting vessels bathed in the extravasated blood. This problem is of greatest significance in cases of basal subarachnoid hemorrhage, in which vasospasm can involve major vessels of the circle of Willis. Various mediators have been proposed to have a role in this process, including endothelins, nitric oxide, and arachidonic acid metabolites. In the healing phase of subarachnoid hemorrhage, meningeal fibrosis and scarring occur, sometimes leading to obstruction of CSF flow as well as interruption of the normal pathways of CSF resorption.

Vascular Malformations

Vascular malformations of the brain are classified into four principal groups: arteriovenous malformations, cavernous malformations, capillary telangiectasias, and venous angiomas. Of these, the first two are the types associated with risk of hemorrhage and development of neurologic symptoms.

MORPHOLOGY

Arteriovenous malformations (AVM) may involve vessels in the subarachnoid space, in the brain or both. This tangled network of wormlike vascular channels has prominent, pulsatile arteriovenous shunting with high blood flow. They are composed of greatly enlarged blood vessels separated by gliotic tissue, often showing evidence of prior hemorrhage. Some vessels can be recognized as arteries with duplication and fragmentation of the internal elastic lamina, while others show marked thickening or partial replacement of the media by hyalinized connective tissue.

Cavernous malformations consist of distended, loosely organized vascular channels arranged back to back with collagenized walls of variable thickness. There is usually no brain parenchyma between vessels in this type of malformation. They occur most often in the cerebellum, pons, and subcortical regions, in decreasing order of frequency, and are "low-flow" channels that do not participate in arteriovenous shunting. Foci of old hemorrhage, infarction, and calcification frequently surround the abnormal vessels. **Capillary telangiectasias** are microscopic foci of dilated, thin-walled vascular channels separated by relatively normal brain parenchyma that occur most frequently in the pons. **Venous angiomas** (varices) consist of aggregates of ectatic venous channels. **Foix-Alajouanine disease** (angiodysgenetic necrotizing myelopathy) is a venous angiomatous malformation of the spinal cord and overlying meninges, most often in the lumbosacral region, associated with ischemic injury to the spinal cord and slowly progressive neurologic symptoms.

Clinical Features. Arteriovenous malformations are the most common type of clinically significant vascular malformation. Males are affected twice as frequently as females. The lesion often presents between the ages of 10 and 30 years as a seizure disorder, an intracerebral hemorrhage, or a subarachnoid hemorrhage. The most common site is the territory of the middle cerebral artery, particularly its posterior branches. Large arteriovenous malformations occurring in the newborn period can lead to congestive heart failure because of shunt effects, especially if the malformation involves the vein of Galen. Cavernous malformations are unique among this class of lesion in that familial forms are relatively common. Multiplicity of lesions is a hallmark of familial cases, which are inherited as a highly penetrant autosomal dominant trait.

KEY CONCEPTS

Cerebrovascular Diseases

- *Stroke* is the clinical term for acute-onset neurologic deficits resulting from hemorrhagic or obstructive vascular lesions.
- Cerebral infarction follows loss of blood supply and can be widespread or focal, or affect regions with the least robust vascular supply (boundary zones).
- Focal cerebral infarcts are most commonly embolic; with subsequent dissolution of an embolism and reperfusion, a nonhemorrhagic infarct can become hemorrhagic.
- Primary intraparenchymal hemorrhages typically are due to either hypertension (most commonly in white matter, deep gray matter, or posterior fossa contents) or cerebral amyloid angiopathy.
- Spontaneous subarachnoid hemorrhage usually is caused by a structural vascular abnormality, such as an aneurysm or arteriovenous malformation.

Infections

Infection may damage the nervous system directly through injury of neurons or glia by the infectious agent, or indirectly through microbial toxins, the destructive effects of the inflammatory response, or the result of immune-mediated mechanisms. There are four principal routes by