Occlusion or insufficiency of the venous drainage in the head and neck can cause a range of neurologic and ophthalmologic manifestations. Clinical features vary depending on the location and mechanism of occlusion.

CEREBRAL VENOUS THROMBOSIS

Our understanding of cerebral venous thrombosis (CVT) has greatly increased in recent years due primarily to improved radiographic methods of diagnosis (1,2). Prior to the advent of modern neuroimaging, estimates of the incidence of cerebral venous thrombosis (CVT) relied largely on autopsy series (3,4). More recent studies that employ radiographic techniques have demonstrated a higher incidence of this disorder than previously appreciated and have led to a greater awareness of cases at the milder end of the spectrum (5–11a). Despite these advances in recognition, the diagnosis of CVT remains challenging due to its wide range of clinical expression and some aspects of treatment remain controversial.

ANATOMY AND PHYSIOLOGY

The cerebral venous system consists of superficial and deep veins, all of which ultimately drain into the major dural venous sinuses and from these into the internal jugular veins (Fig. 45.1). The superficial veins drain the outer 2 cm of cerebral cortex; the deep veins drain blood from the deep hemispheric white matter, basal ganglia, and diencephalon. The superficial veins are thin-walled, lacking a muscular wall and valves. They are inconstant, lack well-defined vascular territories, and are not readily visualized with neuroimaging. By contrast, the deep cerebral veins are larger, constant, and identifiable on imaging studies (12,13).

The dural venous sinuses are often divided into two groups: the posterosuperior group consisting of the superior and inferior sagittal, straight, lateral (transverse), sigmoid, tentorial and occipital sinuses; and the anteroinferior group comprised of the cavernous, intercavernous, basilar, sphenoparietal, and the superior and inferior petrosal sinuses. Situated between the two layers of the dura mater, the dural sinuses are devoid of valves and are lined by endothelial cells and by connective tissue that is continuous with that of the veins that drain into them. In addition to receiving blood from the superficial and deep venous systems, the dural sinuses may also communicate with extracranial structures. Thus, the superior sagittal sinus is connected via emissary veins to scalp veins, the lateral sinus to middle ear and mastoid veins, and the cavernous sinus to orbital and facial veins. The superior sagittal sinus drains most of the cerebral cortex; the lateral sinus drains the posterior fossa, posterior cerebral hemispheres, and cerebellum; and the cavernous sinus receives the ophthalmic veins along with drainage from the anterior base of the brain via the middle cerebral vein and sphenoparietal sinus. Anatomic variations of the lateral sinuses are common, e.g., the right side is dominant in the majority of individuals. Normal variants are sometimes misinterpreted as sinus occlusion (14). In addition, blood flow in the lateral sinuses may decrease secondary to increased
intracranial pressure (ICP) simulating sinus stenosis (15). Thrombosis most commonly affects the superior sagittal sinuses (SSS) and lateral sinuses (LS) (9,11). These sinuses contain most of the arachnoid granulations into which cerebrospinal fluid (CSF) absorption occurs (Fig. 45.2). In most cases of thrombosis more than one venous structure is affected.

Pathologic changes depend on the location, degree of propagation of the clot, and extent of collateral venous drainage. Severe SSS thrombosis causes bilateral hemorrhagic infarction of the cortex and adjacent white matter (Fig. 45.3). Venous infarction is characterized macroscopically by pallor with multiple petechial hemorrhages which may become confluent. Edema is characteristic and may occur in the absence of infarction.

**CLINICAL FEATURES**

The clinical manifestations of CVT are extremely varied, depending on several factors. These include the site of obstruction (superficial or deep veins or dural sinuses); and the extent, the rate of occlusion (1,11a,16,17), the underlying etiology, and the overall health or fragility of the patient (18). Thrombosis of cerebral veins is more likely to cause focal deficits due to infarction, whereas isolated involvement of dural sinuses more commonly produces increased intracranial pressure in the absence of focal signs. The rate of obstruction is often related to the underlying cause; for example, tumorous compression of a venous structure usually occurs slowly whereas thrombosis due to coagulopathy is typically more apoplectic. If obstruction is sufficiently slow to allow the development of adequate collateral drainage, symptoms and signs may be quite minimal. In general, infants and elderly or debilitated patients tend to fare worse in terms of morbidity and mortality (11a,19).

The time course in patient with CVT is quite variable (2). Acute onset (symptoms less than 48 hours) is found in about one-third of cases (7,11), but is considerably more common in puerperal cases (9). Subacute onset (from 48 hours to 30 days) is observed in approximately 40% of cases, and chronic onset (progression for more than 30 days) in one-fourth to one-third.
Figure 45.2. Arachnoid granulations. (Courtesy of Kathleen Digre, MD.)

Figure 45.3. Paraneoplastic thrombosis of the superior sagittal sinus. The patient was a 63-year-old woman with known carcinoma of the breast who developed headache, left hemiparesis, and left homonymous hemianopia. She subsequently died of the effects of her tumor. A, Coronal sections through the brain show three large areas of hemorrhagic infarction in the distribution of the veins of Trouard on both sides and the vein of Labbé on the right. B, Serial sections through the superior sagittal sinus show complete occlusion of the sinus by organized thrombus. In some sections, the thrombus can be seen extending into the parasagittal cortical veins. (From Hickey WF, Garnick MB, Henderson IC, et al. Primary cerebral venous thrombosis in patients with cancer: A rarely diagnosed paraneoplastic syndrome. Am J Med 1982; 73:740–750.)
Symptoms and Signs

Headache is the most common symptom of CVT, reported as the presenting symptom in 61–73% of cases and occurring overall in 80% (1,7,9,11a,16). Headaches are typically persistent and often worse when recumbent. They may be localized or diffuse and range in severity. In most cases there are other neurologic signs and symptoms, although occasionally headache may occur in isolation (7,20). The mechanism by which headache occurs in CVT is probably multi-factorial, including elevated ICP, distention of pain-sensitive dural nerve endings, and chemical meningitis due to hemorrhage.

Focal neurologic deficits occur at some time during the course in approximately 60% of patients and are the initial manifestation in 15% (9). Type and pattern vary, including sensory and/or motor deficits, aphasia, and cerebellar signs. SSS thrombosis may cause bilateral deficits. Altered mental status is present in about half of patients with CVT (1) but is not usually the presenting symptom (9). In some cases decreased consciousness represents a post-ictal event. Seizures result from irritation of the cortex by superficial venous infarction, and affect up to 40% of patients (1).

Papilledema is identified in 50% of patients with CVT. Because it takes some time for disc edema to develop, this finding is much less common in those patients who present hyperacutely (7). Disc edema tends to be of higher grade in patients in whom CVT occurs acutely due to thrombosis, compared to those with venous occlusion due to compression (21). Vision is usually relatively normal early in the course but with persistent, severe papilledema, progressive optic neuropathy may supervene (21–23). In occasional cases vision is significantly reduced at the time of presentation (21) (Fig. 45.4). Detailed measurements of optic nerve function are not always feasible in the setting of acute CVT. Monitoring of optic nerve function ideally would include visual field testing since visual acuity may be preserved in the face of substantial peripheral loss. Assessment of pupillary reactivity may be helpful in this setting. Diplopia secondary to unilateral or bilateral sixth nerve palsy may occur and is more common in patients who suffer rapid and substantial increased ICP from thrombosis (21).

Homonymous hemianopic visual loss and cortical blindness may occur in patients with cortical venous infarction involving the posterior cerebral hemispheres (24). Positive visual phenomena may also occur in this setting (25,26).

Patterns of Presentation

Although there is a broad spectrum of signs and symptoms related to CVT, four main clinical patterns have been identified (1,7,20):

1. The most common pattern consists of focal signs, i.e., sensory or motor deficits, aphasia, homonymous hemia-

Figure 45.4. Results of visual field examination in four patients with venous sinus thrombosis who had substantial visual loss either at presentation or at follow-up (Humphrey automated perimetry in patients 5,7, and 12; Goldmann perimetry in patient 11). Worsening of the visual field occurred in both eyes of patient 5, in the right eye of patient 7, and in the left eye of patient 11. In patient 12 there was improvement in both eyes. (From Purvin VP, Trobe JD, Kosmorsky G. Neuro-ophthalmic features of cerebral venous obstruction. Arch Neurol 1995;52:880–885.)
Occlusion of superficial cerebral veins does not usually produce visual symptoms unless one or both occipital veins become occluded, resulting in a hemorrhagic venous infarction of one or both occipital lobes (24). Unilateral infarction is often associated with a homonymous visual field defect that is quite congruous when incomplete. Bilateral infarction may produce cortical blindness that usually, but not invariably, improves with time, or it may produce bilateral, congruous, homonymous visual field defects. Patients in whom a hemorrhagic infarction occurs in the parieto-occipital region may experience formed visual hallucinations in the affected homonymous hemifields (24–26).

Thrombosis of Deep Cerebral Veins

Thrombosis of the deep cerebral veins is often fatal (44,45). Patients with this condition usually suffer extensive hemorrhagic infarction of both thalami, the basal ganglia, the rostral mesencephalon, and the medial and lateral geniculate bodies (3,7,44–47) (Figs. 45.5 and 45.6). They typically present with acute coma accompanied by decerebrate posturing and extrapyramidal hypertonia. Women are more commonly affected than men and the time course is more rapidly declining than that of patients with dural sinus thrombosis (47). In contrast to dural CVT, seizures are uncommon in patients with deep cerebral vein thrombosis (47). Overall, the outcome in deep CVT is also worse than that of dural CVT. Mortality is considerably higher in this condition and patients who survive typically have extensive neurologic and cognitive sequelae.

Thrombosis of the Lateral Sinus

The symptoms and signs of thrombosis of the lateral sinus (LS) may be generalized, focal, or both (48). Some cases are septic, occurring in the setting of chronic otitis media (49–52) (Fig. 45.7). Infection spreads from the mastoid air

Figure 45.5. Massive cerebral hemorrhagic infarction from thrombosis of the internal cerebral veins and the straight and lateral sinuses. The patient was a 25-year-old woman with ulcerative colitis who was being treated with azathioprine. She also was taking an oral contraceptive agent. She presented with severe headache, right leg numbness, nausea, and vomiting. By the time she was admitted to the hospital, she was comatose, had decerebrate posturing to pinprick, and had roving eye movements associated with a skew deviation. She was treated with systemic corticosteroids but suffered a cardiorespiratory arrest 12 hours after admission. Coronal section through the cerebral hemispheres at the level of the basal ganglia shows a massive, bilateral, symmetric hemorrhagic infarction extending caudally to the mesencephalon and laterally to the striatum. The thalami and basal ganglia have been destroyed by the hemorrhage. (From Averback P. Primary cerebral venous thrombosis in young adults: Diverse manifestations of an underrecognized disease. Ann Neurol 1978;3:81–86.)
Figure 45.6. Straight sinus thrombosis. A. Sagittal phase contrast MRV shows complete absence of flow in the deep venous system. B. T2-weighted axial MRI demonstrates hyperintensity of the basal ganglia and thalami due to extensive venous infarction. (Courtesy of Dr. Benjamin Kuzma.)

Figure 45.7. Subacute septic lateral sinus and jugular vein thrombosis. This 43-year-old man developed headache and papilledema in the setting of chronic otitis media. Axial T2-weighted (left) and T1-weighted (right) MRI images obtained 2 weeks after onset of right ear pain and headache show effusion in the right mastoid (arrowhead) and clot in the right internal jugular vein, right lateral sinus, and torcular (arrows). (From Purvin V, Trobe J, Kosmorsky G. Neuro-ophthalmic features of cerebral venous obstruction. Arch Neurol 1995;52:880–885.)
cells to the dural sinus by direct invasion or via emissary veins (51). Other causes of septic LS thrombosis include infections of the scalp and parapharyngeal or retropharyngeal abscesses (6). The typical clinical picture is that of a patient with suppurative otitis who suddenly develops fever, chills, evidence of local inflammation in the region of the mastoid, and leukocytosis (53). Many patients develop neck pain and stiffness, and some also exhibit tenderness along the jugular vein on the side of the process (49,54,55). There may be some degree of associated ipsilateral facial weakness.

Unilateral abducens nerve paresis is frequently present and may result from several mechanisms. First, infection and thrombosis may extend to the inferior petrosal sinus and then to the abducens nerve which is located just above it as they both pass under the petroclinoid ligament. Second, the inferior petrosal sinus may not be thrombosed, but may simply be distended from the effects of the adjacent thrombosis of the lateral sinus. The distended inferior petrosal sinus compresses the abducens nerve upward against the petroclinoid ligament (56). In such cases, there may be severe ipsilateral facial pain, particularly around the eye (Gradenigo’s syndrome) (50,57,58). Finally, both unilateral and bilateral abducens nerve paresis may occur as non-localizing signs of increased ICP (59). This particular clinical picture was termed “otic hydrocephalus” by Symonds (60). Because the right lateral sinus (LS) is dominant in most individuals, most cases of isolated increased ICP due to LS thrombosis are caused by right-sided occlusion.

An unusual manifestation of LS thrombosis was described by Newman et al. (31), who reported two patients who experienced visual disturbances suggesting aseagalnic migraine. One patient experienced the sudden onset of intense colored photopsias in the central vision of both eyes. The photopsias slowly spread outward over several minutes until they affected the entire visual field. The positive visual phenomena resolved within 30 minutes, after which the patient was blind for some period of time. The second patient developed frequent episodes of visual blurring, lasting 10–30 minutes, associated with vertical wavy lines, teichopsias, and a sensation of pressure at the cranial vertex. Both patients had filling defects in the left lateral sinus.

Ocular signs other than those caused by increased ICP may occur when thrombosis of the LS extends anteriorly via the inferior petrosal sinus to the cavernous sinus (see later discussion).

**Thrombosis of the Superior Sagittal Sinus**

Aseptic thrombosis affects the superior sagittal sinus (SSS) more often than the other dural sinuses, apparently because of its high position, low pressure, and slow flow (61) (Fig. 45.8). Of 34 cases of aseptic dural sinus thrombosis evaluated by Bousser et al., 24 (71%) involved the SSS (6). The severity of clinical manifestations depends on which portion of the sinus is occluded. In general, the most severe signs and symptoms occur when the posterior portion of the sinus becomes occluded (Fig. 45.9). When only the anterior part is occluded, symptoms and signs may be minimal or absent, consisting of headache occasionally associated with nonspecific sensory symptoms (48). In cases with involvement of the posterior portion, the neurologic consequences can be devastating. Increased intracranial pressure can be isolated or may be accompanied by focal deficits, particularly weakness that typically affects the lower extremities early (62). Ocular signs and symptoms are generally referable to increased ICP. Thrombosis of the SSS is often associated with (LS) thrombosis.

![Figure 45.8. Superior sagittal sinus thrombosis due to essential thrombosis. This 66-year-old woman developed headaches, papilledema (A and B), and bilateral sixth nerve paresis. (Figure continues.)](image-url)
Figure 45.8. Continued. Sagittal (C) and axial (D) T1-weighted MRI scans obtained 3 weeks after onset of symptoms demonstrate hyperintense signal within the superior sagittal sinus. Laboratory evaluation disclosed a platelet count of 750,000. (From Purvin V, Trobe J, Kosmorsky G. Neuro-ophthalmic features of cerebral venous obstruction. Arch Neurol 1995; 52:880–885.)

Figure 45.9. Occlusion of the posterior superior sagittal sinus by a meningioma. This 60-year-old man developed progressive visual loss secondary to chronic papilledema. A, Sagittal MRI shows an ovoid midline mass that is isointense on T1-weighted images. B, Axial postcontrast images show intense enhancement of the tumor with mild surrounding edema.
Figure 45.10. Septic cavernous sinus thrombosis from facial infection. The patient was a 14-year-old girl who developed an abscess of the dorsum of the nose. She then developed fever and swelling of the nose, cheeks, frontal region, and both eyelids. Blood cultures were obtained, and antibiotic therapy was begun. Appearance of the patient 24 hours after starting systemic antibiotics shows marked, bilateral periorbital edema and bilateral proptosis. Cultures subsequently grew *Staphylococcus aureus* and neuroimaging studies were consistent with a diagnosis of septic cavernous sinus thrombosis. The patient slowly improved on antibiotic and anticoagulant therapy. (From Tveteras K, Kristensen S, Dommerby H. Septic cavernous and lateral sinus thrombosis: Modern diagnostic and therapeutic principles. J Laryngol 1988;102:877–882.)

Meningitis is the most common predisposing condition in cases of septic SSS thrombosis. In these cases, the infection probably spreads from the meninges to the SSS via the diplopic veins. Infections of the paranasal sinuses may also produce septic thrombosis of the SSS (6). Such infections spread from the ethmoid or maxillary sinuses to the SSS via ethmoidal veins (63). Infections of the frontal sinus with associated epidural abscess may result in cortical vein thrombosis, which may, in turn, be followed by thrombosis of the superior sagittal sinus.

**Thrombosis of the Cavernous Sinus**

Clinical presentations of cavernous sinus thrombosis are influenced by the mechanism of thrombosis, specifically whether the condition is infectious or aseptic. In most cases, signs and symptoms develop acutely, but subacute and chronic presentations also occur. Regardless of the underlying mechanism, most patients present with pain around the eye associated with a variety of orbital signs including proptosis, chemosis, ptosis and ophthalmoparesis (Fig. 45.10). Eyelid edema is especially prominent when the thrombosis is caused by facial, dental or ethmoidal infection (Fig. 45.11). Lid swelling may obscure neurogenic ptosis. Ophthalmoplegia often begins as an isolated ocular motor paresis, most commonly affecting the abducens nerve (64). Eventually, ophthalmoparesis may become severe and complete, and because of marked orbital congestion and proptosis it may be difficult to distinguish neurogenic and mechanical extra-ocular muscle limitation. In this setting the

Figure 45.11. Septic cavernous sinus thrombosis caused by Mucoraceae. The patient was a 49-year-old man with severe renal disease from chronic glomerulonephritis who was receiving hemodialysis. He developed generalized malaise associated with rhinorrhea, fever, and headache. His condition was unaffected by treatment with systemic antibiotics, and he developed right-sided periorbital swelling. He then suddenly lost vision in the right eye. When examined initially, he had no light perception in the right eye and 20/50 vision in the left eye. There was bilateral eyelid edema with a purplish hue, 5 mm of right proptosis, and bilateral conjunctival chemosis. The right eye had limited movement in all directions. There was a right, relative afferent pupillary defect, and the appearance of the right ocular fundus was consistent with an acute central retinal artery occlusion. A, CT scan, axial view, shows evidence of sinusitis and increased opacification of the right cavernous sinus (arrow). The patient subsequently developed a central retinal occlusion in the left eye. Despite treatment with antibiotics, he steadily deteriorated, and he died on the 7th hospital day. B, Histopathologic appearance of the right cavernous sinus, coronal section, shows thrombosis of the intracavernous portion of the right internal carotid artery (ICA). III, oculomotor nerve; IV, trochlear nerve; V, ophthalmic branch of the trigeminal nerve; VI, abducens nerve; PG, pituitary gland. (Figure continues.)
presence of definite levator weakness and/or pupillary dilation indicate a neurogenic mechanism. Spreading to the contralateral eye is also an indication that the ophthalmoplegia is due to neurogenic cavernous sinus involvement rather than restrictive orbitopathy. Corneal anesthesia or hypesthesia often occurs from damage to the first division of the trigeminal nerve in the cavernous sinus. Oculosympathetic dysfunction is probably common, but is generally masked by oculomotor nerve paresis. As venous stasis within the orbit increases, the ocular fundus may show increasing dilation of retinal veins and low-grade optic disc swelling.

Vision loss may occur in patients with cavernous sinus thrombosis due to neurotrophic keratopathy or optic neuropathy (65). In some patients, visual loss results from ischemic oculopathy caused by occlusion of the internal carotid or ophthalmic arteries, branch or central retinal artery occlusion, or ischemic optic neuropathy (66–71).

In cases of septic cavernous sinus, in addition to the above signs patients often manifest altered sensorium and more generalized headache with nausea and vomiting. Fever and leukocytosis are characteristic. Chills, diaphoresis, and tachycardia are inconstant findings. As the disease progresses, patients may show evidence of meningitis or brain abscess and seizures may occur (51). Laboratory abnormalities include a pronounced leukocytosis and positive blood cultures in most, but not all, patients. The CSF is abnormal in patients with associated meningitis, and the causative organism can often be isolated from the fluid in such cases. When septic cavernous sinus thrombosis occurs from sphenoid sinusitis or pharyngitis, obstructive signs are delayed, and the course is usually subacute or chronic (51,72–74).

A number of infectious processes may predispose a patient to developing septic thrombosis of the cavernous sinus (64,74,75). Infections of the face, especially those involving the medial third, continue to be the most frequent primary foci associated with septic cavernous sinus thrombosis (50,74,76–79). Bacteria entering the facial vein and pterygoid plexus from these sites may be carried to the cavernous sinus through the ophthalmic veins. Gram-positive bacteria, particularly Staphylococcus aureus, are the usual pathogens in this setting (50,51).

Sinusitis affecting the sphenoid and ethmoid air cells may cause septic thrombosis of the cavernous sinus (50,80–82). The sinusitis may be acute or chronic. When acute, sphenoid sinusitis causes cavernous sinus thrombosis, the predominant pathogens are gram-positive bacteria, including S. aureus, Streptococcus pneumoniae, and other aerobic as well as anaerobic streptococci (50). When chronic sinusitis causes cavernous sinus thrombosis, gram-negative rods, coagulase-negative staphylococci, and fungi such as Aspergillus and Mucoraceae are most often responsible (64,83,84) (Fig. 45.12).

Dental infections, usually affecting the maxillary teeth (66), cause about 10% of the reported cases of septic cavernous sinus thrombosis (74,85,86). The most common pathogens that produce odontogenic septic thrombosis of the cavernous sinus are streptococci, fusobacteria, and Bacteroides species (73).

Otitis media is no longer the common cause of septic cavernous sinus thrombosis it was in the pre-antibiotic era. Nevertheless, patients with bacterial or even fungal ear infections that are untreated, incompletely treated, or incorrectly treated occasionally develop septic thrombosis of the cavern-

Figure 45.11. Continued. C, Magnified view of thrombosis within the right internal carotid artery shows that it is composed of nonseptate, branching hyphae consistent with Mucoraceae. (From Johnson EV, Kline LB, Julian BA, et al. Bilateral cavernous sinus thrombosis due to mucormycosis. Arch Ophthalmol 1988;106:1089–1092.)

Figure 45.12. Septic cavernous sinus thrombosis. Severe bilateral proptosis, eyelid swelling, and conjunctival chemosis in an 82-year-old woman who developed septic cavernous sinus thrombosis from bacterial sinusitis. The patient was blind and had complete bilateral ophthalmoplegia. (From Daxecker F, Bicheler E. Beidseitiger Exophthalmus bei Sinus-cavernosus-Thrombose. Klin Monatsbl Augenheilkd 1983;182:235–236.)
Venous sinus that is directly related to the pathogen responsible for the ear infection (87,88).

Orbital cellulitis is rarely complicated by septic thrombosis of the cavernous sinus (68), even though the superior and inferior ophthalmic veins drain into the cavernous sinuses. The clinical manifestations of orbital cellulitis can, however, be difficult or impossible to differentiate from those of early cavernous sinus thrombosis.

The mortality rate for patients with septic cavernous sinus thrombosis is about 30%, regardless of the therapy (64,75,89). Survivors have a variety of neurologic deficits, usually from damage to the cranial nerves within the cavernous sinus. These deficits include diplopia from paresis of one or more of the ocular motor nerves; visual sensory dysfunction from optic neuropathy or central retinal artery occlusion (CRVO); and neurotrophic keratopathy, facial numbness, paresthesia, or pain from trigeminal neuropathy. Walsh and Hoyt (90) described a boy who developed secondary aberrant regeneration of the oculomotor nerve following a bout of septic cavernous sinus thrombosis. Full recovery occurs in less than 40% of patients who experience septic cavernous sinus thrombosis (50). Mortality rates are lower with aseptic cavernous sinus thrombosis and visual loss is less common.

Evaluation

Historically, conventional angiography has been considered the “gold standard” for the diagnosis of CVT. With continued technologic advances, however, noninvasive neuroimaging has become the primary method of diagnosing this condition (91,92). Both CT scanning (37,93–99) and MR imaging (100–108) can provide important information regarding localization, etiology, and severity of the disease process.

On nonenhanced CT scans, one may observe an abnormally high density in relation to a thrombosed superior sagittal (93) or straight (109) sinus (Fig. 45.13). However, this abnormal appearance is identifiable in only 5% of cases (2). Other changes seen on nonenhanced CT scans include diffuse cerebral swelling, single or multiple hemorrhages, areas of hemorrhagic infarction, and small ventricles (Figs. 45.14). An irregular, high-density area seen in the superficial portion of the hemisphere may represent a thrombosed cortical vein or dural sinus. Although this “cord sign” is rarely seen, it is considered to be diagnostic of cortical venous thrombosis (110,111). Following the intravenous administration of iodinated contrast material, other changes may be detected by CT scanning. The empty delta sign (also called the empty triangle sign) is one of the most important diagnostic criteria in a patient with suspected dural sinus thrombosis (112). This sign consists of a triangle of low density surrounded by a border of increased density (Fig. 45.15). It is caused by a clot within the sinus that is outlined by contrast material in the smaller collateral veins and in the wall of the sinus. The empty delta sign is most easily seen in patients with thrombosis of the posterior third of the superior sagittal sinus, where the CT is perpendicular to the sinus, but it can also be observed in patients with occlusion of the transverse and straight sinuses (95,112). Though highly characteristic of CVT, the empty delta sign is found in just 20–42% of cases, reflecting the relative insensitivity of CT in this condition (9,11,98). Overall, CT scanning appears normal in up to 40% of patients with CVT (20).

In contrast, MR imaging is an extremely sensitive modality for detecting CVT and has become the technique of choice for diagnosis and follow-up of CVT patients. MR imaging in patients with cerebral venous and dural sinus thrombosis reveals abnormalities in the veins and sinuses as well as in the brain parenchyma. At a very early stage there is absence of the normal flow void, and the occluded sinus appears isointense with brain parenchyma on T1-weighted images and hypointense on T2-weighted images (113,114) (Fig. 45.16). The hypointense signal in this setting may be mistaken for normal flow void (115). This phase lasts for only 3–4 days, after which the appearance of the thrombus undergoes evolution as oxyhemoglobin is converted to methemoglobin. In this phase the thrombus becomes hypointense, first on T1- and then on T2-weighted images. This intermediate pattern persists from day 4 or 5 through day 30 to 35 and thus is the most commonly observed MRI appearance (1,105) (Fig. 45.8). In the late stages, variable recanalization of the previously occluded vessel may result in reappearance of the flow void (116–119). After enhance-
Figure 45.14. Lateral sinus thrombosis producing a left parietal lobe hemorrhage. A, Unenhanced axial CT scan shows hemorrhage in the left parietal lobe. B, Unenhanced axial CT scan performed the next day shows increased hemorrhage with surrounding edema. C, T2-weighted axial MR image shows the extent of hemorrhage with surrounding edema. Note shift of midline from left to right. D, MR angiogram shows no flow in the left lateral sinus. (Courtesy of Dr. Douglas Nichols.)
ment with gadopentetate dimeglumine (gadolinium-DTPA) or a similar paramagnetic substance, enhanced T1-weighted images often demonstrate the empty delta sign (112,119). During the second month the majority of cases show an isointense signal on T1- and a hyperintense signal on T2-weighted images (Fig. 45.17). The sensitivity of MRI for detecting thrombus may be increased by the use of echoplanar T2-weighted sequences (120).

In addition to detecting thrombus in cerebral veins and sinuses, MR imaging identifies abnormalities in the brain parenchyma. These changes are different from those seen in arterial occlusive disease (121) and reflect the underlying pathophysiology. Mass effect without a bright signal on T2-weighted images is characteristic, suggesting that breakdown of the blood-brain barrier leading to vasogenic edema does not always occur. This initial swelling may be related to distention of a compliant venous bed with little or no increase in venous pressure. The swelling may persist for months or years (121). Further progression may be associated with mass effect with T2-weighted signal changes and ventricular dilation. As the venous pressure rises, bulk water is driven by the pressure gradient from the capillary bed into the interstitium. T2-weighted signal abnormalities are prone to develop in areas of poor venous drainage, such as the basal ganglia and thalamus. Transepidual reabsorption of CSF with hydrocephalus may develop. When elevated venous pressure exceeds the structural limit of the venous walls, rupture of veins causes a hematoma (Fig. 45.18).

Tsai et al. (122) measured venous sinus pressures in 11 patients with acute venous sinus thrombosis and found, based on clinical and neuroimaging findings, that the pressures correlated with five distinct stages of disease. In stage I, patients had headache, papilledema, weakness, changed mentation, and drowsiness. There were no parenchymal changes on MR imaging in this phase. The venous pressures in these cases were 14–17 mm Hg. In stage II, patients had increased headache, diplopia, seizures, decreased mentation, and extreme drowsiness. MR imaging showed changes consistent with cerebral edema. Venous pressures in these patients ranged from 20–25 mm Hg. In stage III, patients were obtunded with hemiparesis and seizures. MR imaging showed increased intensity of signal, with mild to moderate cerebral edema. Venous pressures ranged from 32–38 mm Hg. Stage IV patients were comatose and had hemiparesis and seizures. MR imaging showed severe cerebral edema but no other parenchymal changes. Venous pressures were 42–51 mm Hg. Stage V patients were comatose and re-
Figure 45.17. Chronic superior sagittal sinus thrombosis. This 55-year-old man had suffered superior sagittal sinus occlusion two months earlier. A, On sagittal T1-weighted images the clot appears isointense with brain. B, On axial T2-weighted images the clot appears hyperintense. C, Following contrast infusion extensive collateral circulation can be seen. (Courtesy of Dr. Benjamin Kuzma.)
Figure 45.18. Superior sagittal sinus thrombosis causing cerebral edema and hemorrhage. A, Cerebral angiogram, lateral view, shows occlusion of the superior sagittal sinus except for a portion of the middle third. B, T2-weighted axial MR image shows focal hemorrhage in the left parieto-occipital region. C, T1-weighted sagittal MR image shows position of hemorrhage. (Courtesy of Dr. John Huston.)
sponded only to deep pain. MR imaging showed marked cerebral edema, intraparenchymal hemorrhage, or both. No venous pressure measurements were obtained in these patients, but it was assumed that the venous pressures were greater than 50 mm Hg.

Recent advances in diffusion-weighted imaging (DWI) and related techniques have provided additional information concerning changes in brain parenchyma in CVT. In the setting of acute ischemia, cellular energy failure leads to cytotoxic edema, characterized by a shift of water molecules from the extracellular to the intracellular space. The resulting restricted diffusion of these water molecules is displayed as a bright signal on DWI and can be detected within minutes (123). The diffusion of water protons can be further quantitated by a parameter known as the apparent diffusion coefficient (ADC). Areas with restricted diffusion appear dark on ADC maps. Chronic infarcts and vasogenic edema, in contrast, appear bright on ADC maps. The combination of DWI and ADC mapping can discriminate between acute and chronic ischemia and between vasogenic and cytotoxic edema and represents a significant advance over conventional MRI. These techniques have been applied to the investigation of CVT in a number of reports (124–126) (Fig. 45.19). DWI is extremely sensitive to ischemic change in this setting, giving positive results in 17 of 18 cases in one study (126). In many cases a combination of cytotoxic and vasogenic edema is found (124,126). While one study of 12 patients with CVT found evidence of cytotoxic edema in 8 of 8 nonhemorrhagic lesions (125), another indicated that vasogenic edema seems to develop earlier and is more prominent than cytotoxic edema in this setting (127).

Chu et al. studied the DWI and ADC findings in patients

![Figure 45.19](https://example.com/figure.png)

**Figure 45.19.** Diffusion-weighted image (DWI) of venous infarction in a 30-year-old woman who suffered thrombosis of the internal cerebral veins related to eclampsia. A, Initial DWI, performed 10 days after onset of stroke, shows heterogeneous signal intensity (SI) in the left basal ganglia and high SI in the right basal ganglia. B, Apparent diffusion coefficient map indicates normal values in the area of very bright SI on DWI (solid arrows) and elevated values in the area of mildly bright SI on DWI (dotted arrows). C, Initial T2-weighted image shows high SI in the bilateral basal ganglia and left caudate hemorrhage. D, Follow-up T2-weighted image, performed 1 month later, demonstrates remnant high SI in the previously very bright area on DWI and otherwise normal findings. The patient eventually recovered with no residual disability. (From Chu K, Kang D-W, Yoon B-W, Roh J-K. Diffusion-weighted magnetic resonance in cerebral venous thrombosis. Arch Neurol 2001;58:1569–1576.)
with CVT and delineated three patterns of abnormality (128). The first, and most common, is a combination of vasogenic and cytotoxic edema appearing heterogeneous on DWI and normal or bright on ADC. The second consists of multifocal increased DWI signal and moderately decreased ADC values, thought to represent cytotoxic edema but correlating poorly with clinical deficits for reasons that are unclear. The third pattern is visualization of intravenous clot seen as a bright signal on DWI. The technique of MRI direct thrombus imaging (MRDTI) has been applied to the diagnosis of venous thrombosis in a variety of other sites as well (129).

The technique of perfusion-weighted imaging (PWI) has also been applied to the study of venous infarction (130,131). Measures of mean transit time (MTT) and relative cerebral blood volume (CBV) can be obtained using bolus injection of a paramagnetic contrast agent. In one study, five of six patients with CVT demonstrated increased MTT values without corresponding changes in CBV and ADC (131). On follow-up after clinical recovery, MTT prolongations had resolved, suggesting that this radiographic picture indicates a reversible insult, corresponding to the ‘ischemic penumbra.’ The combination of DWI and PWI studies may help both in the diagnosis of CVT (particularly in cases with atypical presentations [132]) and also in the management of these patients. In addition to information regarding staging, it is hoped that these studies will allow identification of brain areas that are likely destined for infarction within larger regions of potentially reversible ischemia, so that more aggressive treatment, with its attendant risks, can be reserved for those with potentially salvageable tissue (133).

Angiograph-like images of the intracranial vasculature can be obtained using CT or MR angiography. Helical cerebral CT venography provides excellent quality images of sinus thrombosis and may be easier to interpret with fewer artifacts than MRA (134). As a practical point, CT venography can be obtained immediately after noncontrast CT, which is often the first radiographic procedure performed in an emergency (Fig. 45.20) (1).

MR imaging enables direct visualization of clots as well as associated cerebral lesions and is less invasive than CT or conventional angiography. The most commonly used method for the diagnosis of CVT is the two-dimensional time-of-flight (TOF) technique (106) (Fig. 45.21). Advantages include a short acquisition time, good spatial resolution and a large covering volume (108). This technique, however, is prone to occasional false positives and negatives. Slow flow due to hypoplasia and signal loss secondary to in-plane blood flow may simulate thrombotic occlusion (109). Artifacts related to hemoglobin degradation products, which may appear hypointense on T2 spin echo images, may be mistaken for signal void due to flowing blood (105).

The 3-D contrast-enhanced magnetization-prepared rapid gradient-echo (MP-RAGE) technique was developed to further enhance the sensitivity and specificity of MRA (135,136). This modality is based on principles similar to those of CT venography but with lack of ionizing radiation and no need for iodinated contrast material. Also, postprocessing for CT venography is more time-consuming (136). In comparison to 2-D TOF-MRV, MP-RAGE was found to be superior because it is not affected by the angle between vessel and scan slab or flow velocity and because of its ability to simultaneously depict sinus, brain parenchyma, and lesions. Overall detectability of CVT was found to be higher with MP-RAGE. On the other hand, this technique requires a relatively longer scan time and the need for contrast administration (136). Furthermore, structures in sinuses may be mistaken for thrombus (e.g., septae, bands, and pachionian granulations); chronic CVT is not well visualized with this technique and may require TOF-MRV (136). Gadolinium-enhanced 3-D MR venography with auto-triggered elliptic centric-ordered sequence may represent a further refinement (137).

Doppler ultrasound techniques have a limited role in the diagnosis of CVT (1). Attempts have been made to assess the normal cerebral venous circulation using conventional transcranial Doppler ultrasound and transcranial color-coded duplex sonography (138–144). Thrombosis of the SSS has been associated with elevated venous blood velocities in the deep venous system (139) and with microembolic signals in the internal jugular vein (145). Sequential transcranial Doppler studies may allow for noninvasive monitoring of venous hemodynamics and collateral circulation in patients with CVT (139). Transcranial duplex sonography has limitations, however. In one study of 28 patients with CVT vs. 22 controls, this technique could not reliably distinguish thrombosis from hypoplasia or aplasia (146). Moreover, without the use of
Recent superior sagittal sinus thrombosis. This 22-year-old woman presented with a 3-day history of headache. A, T1-weighted sagittal MRI shows mildly hyperintense clot in the superior sagittal sinus. B, On time of flight MRV, this hyperintense signal creates a "shine through" artifact, which might be confused with normal flow. C, The phase contrast study, however, is diagnostic showing absence of flow in the superior sagittal sinus thrombosis with normal circulation in the deep venous system. (Courtesy of Dr. Benjamin Kuzma.)

A wide variety of conditions can cause CVT (1,2,147–149). These can be divided into congenital and acquired thrombophilias, abnormalities of blood flow, and disorders involving the vessel wall (see Table 45.1). In the pre-antibiotic era, septic CVT was relatively common, but in recent years prothrombotic states are more frequently identified.

A number of congenital thrombophilias have been associated with an increased risk of CVT. The most commonly

contrast media normal venous structures were identified in only 2 of 44 controls.

Cerebrospinal fluid (CSF) examination remains a useful diagnostic tool in CVT, and should always be performed in cases with isolated elevation of ICP without massive cerebral infarction or hemorrhage (2). In the majority of cases, the opening pressure is increased and the CSF profile is abnormal. However, in up to 40% of cases there is an elevated opening pressure with normal CSF constituents (1,20). CSF abnormalities consist of increased protein in approximately half of the cases, presence of red blood cells in two-thirds of the cases, and leukocytosis in one-third (1). A combination of all three abnormalities is found in 30–50% of cases (1). CSF examination may be diagnostic in cases of CVT secondary to infectious or neoplastic meningitis. In addition to its role in diagnosis, lumbar puncture is therapeutic in the management of increased ICP, particularly for preventing loss due to papilledema (20).
Table 45.1
Causes of Cerebral Venous Thrombosis

**Abnormalities of the Blood**

- **Hereditary thrombophilias**
  - Factor V Leiden mutation (150–157,441,442)
  - G20210A-prothrombin gene mutation (158,441,443,444)
  - Homocystinemia (1,161)
  - Antithrombin III (162,163)
  - Protein S (148,164,165,445,447)
  - Protein C (148,152,163,448,449)
  - Sickle cell disease (165)
- **Elevated factor VIII (176)**

**Acquired Coagulopathies**

- **Hematologic conditions**
  - Leukemia (450)
  - Lymphoma (148,451)
  - Essential thrombocytosis (21,452,453)
  - Polycythemia (4,454)
  - Anticardiolipin antibodies (1,16,150,159,160,455)
  - Paroxysmal nocturnal hemoglobinuria (456)
  - Cryofibrinogenemia (457)
  - Malignancy (458,459)
- **Gynecologic conditions**
  - Pregnancy (148)
  - Postpartum (148)
  - Oral contraceptives (6,460–462)
- **Metabolic derangements**
  - Nephrotic syndrome (463)
  - Thyrotoxicosis (464,465)
  - High altitude (457)
  - Inflammatory diseases
  - Ulcerative colitis (466)
  - Crohn’s disease (467,468)
  - Multiple sclerosis (469)
- **Medications**
  - Danazol (470)
  - Tamoxifen (471)
  - L-asparaginase (472)
  - IVIg (473)
  - Androgens (474)
  - Epoetin-α (475,476)
  - Ovarian hyperstimulation syndrome (268,270)
  - Heparin-induced thrombocytopenia (477)

**Abnormalities of Flow**

- **Compression**
  - Meningioma (21,228,478–480)
  - Glomus tumor (21,418)
  - Lymphoma (21,148,451)
  - Metastasis (21,481,482)
  - Intravenous catheterization (22,219,244,255–258,262)
- **Dehydration (163)**
  - Congenital heart disease (163,483)
  - Congestive heart failure (4,484)
  - Persistent pulmonary hypertension (163)
  - Dural arteriovenous malformation (148,485)

**Abnormalities of the Vessel Wall**

- **Local infection**
  - Trauma (4,17,486–488)
- **Surgical**
  - Neck dissection (21,22,228,231)
  - Ligation (21,22)
  - AVM embolization (21,489,490)
- **Vasculitis**
  - Behçet’s disease (21,491–494)
  - Sarcoidosis (495)
  - Wegener’s granulomatosis (148,496)
  - Systemic lupus erythematosus (148,497)
  - Carcinomatous infiltration (5,6)

- **Identified** have been the factor V Leiden mutation and the G20210A-prothrombin gene mutation (150–158). Other studies have found associations with antiphospholipid antibodies (1,7,150,159,160), hyperhomocysteinemia (1,161), antithrombin III deficiency (162,163), protein S or C deficiency (163,164), and sickle cell disease (165). Occasional patients harbor more than one such mutation (150,155) and in some patients a combination of congenital and acquired factors may cause thrombosis (166,167). The clinical corollary of this observation is that a full coagulation work-up should be undertaken in all patients with CVT even when an apparent inciting event, such as pregnancy, oral contraceptives, or recent surgery, has been identified (2) (Table 45.2).

Acquired procoagulant conditions that predispose to CVT include a variety of hematologic disorders such as leukemia, thrombocytosis, and polycythemia; hypercoaguable states due to gynecologic changes such as oral contraceptives, pregnancy, and puerperium; metabolic derangement such as nephrotic syndrome, thyrotoxicosis, and ulcerative colitis; and medication (e.g., danazol, IVIg, and tamoxifen).

Abnormalities of flow include systemic derangements that decrease perfusion such as dehydration, congenital heart disease, congestive heart failure, nephrotic syndrome, and sepsis. Local abnormalities of flow consist mainly of compressive lesions occluding venous structures. These are most commonly meningiomas or metastases intracranially (Fig. 45.9) and glomus tumors, lymphoma, or metastases in the neck (Figs. 45.22 and 45.23). Dural AVMs may also cause localized alterations in flow that precipitate venous thrombosis. Decreased flow in the transverse sinuses may also occur as a consequence of increased ICP (168). In such cases normal venous pressure and flow are restored following normalization of ICP (15).

Abnormalities of vessel walls include infectious etiologies and vasculitides such as Behçet’s disease, sarcoidosis, 

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**Table 45.2**

<table>
<thead>
<tr>
<th>Laboratory Evaluation for Patients with Suspected Hypercoagulable State</th>
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<tbody>
<tr>
<td>Inherited thrombophilias</td>
</tr>
<tr>
<td>Antithrombin III</td>
</tr>
<tr>
<td>Protein S and C</td>
</tr>
<tr>
<td>Activated protein C resistance (factor V Leiden mutation)</td>
</tr>
<tr>
<td>Prothrombin gene mutation</td>
</tr>
<tr>
<td>Homocysteine</td>
</tr>
<tr>
<td>Antiphospholipid antibodies (anticardiolipin antibodies and lupus anticoagulants)</td>
</tr>
<tr>
<td>Sickle cell disease</td>
</tr>
<tr>
<td>Acquired prothrombin states</td>
</tr>
<tr>
<td>Complete blood count with platelets</td>
</tr>
<tr>
<td>Prothrombin/partial thromboplastin</td>
</tr>
<tr>
<td>Fibrinogen</td>
</tr>
<tr>
<td>Serum protein electrophoresis</td>
</tr>
<tr>
<td>Renal function tests, proteinuria</td>
</tr>
<tr>
<td>Cryoglobulins</td>
</tr>
<tr>
<td>Search for malignancy</td>
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</tbody>
</table>
Figure 45.22. Jugular vein obstruction by tumor. This young man presented with low-grade headache and bilateral papilledema. He had undergone surgery for seminoma one year earlier. Evaluation revealed bulky cervical nodes causing bilateral jugular vein compression. Chemotherapy brought prompt shrinkage of these masses and resolution of the papilledema.

Wegener’s granulomatosis, and carcinomatous infiltration. Trauma and surgical procedures may also cause changes in vessel walls that lead to obstruction.

In about 10-20% of patients with thrombosis of cerebral veins or dural sinuses, the etiology cannot be determined, despite thorough evaluation (11a,43,97,169).

OUTCOME

The prognosis following CVT is variable, ranging from complete recovery to death. Older series reported a mortality of 30–50% (1,170) but more recent studies indicate a generally favorable outcome in the large majority of patients (171–176). In some reports this improved outcome has been attributed to earlier diagnosis and more widespread treatment with heparin (176), however one prospective univariate analysis showed no difference in outcome between those patients who were heparinized and those managed supportively (177). Studies of outcome that assess just mortality and independent status following CVT portray a more positive prognosis than those that record residual symptoms, neurologic and cognitive deficits, and ability to return to premorbid activities. Thus an overall good outcome was reported in 82–87.5% of patients following CVT in four separate studies (11a,173,174,176,177). However, Breteau et al. found residual symptoms in three-fourths of 48 survivors, including seizures in 7, motor deficits in 6, visual field loss in 5, and chronic headaches in 29 (172). In another study of patients who regained independence at least one year after a CVT, 29% had persistent cognitive impairments and 40% could not resume their previous level of economic activity (178). In a follow-up study of 34 patients who had suffered a CVT several years earlier, 10 suffered from persistent headaches and 3 had seizures, but none were found to have residual functional disability (175).

A number of factors have been associated with a poor clinical outcome including extremes of age, rapidity of onset, presence of focal neurologic deficits, an infectious or cancerous etiology, and evidence of hemorrhage (on neuroimaging or CSF examination), and thrombosis of the deep venous system (11a,43,171,172,179,180). The level of consciousness at presentation has been found to be strongly predictive of eventual outcome. In a series of 79 patients with CVT the overall mortality rate was 10%, but this figure increased to 53% in those with stupor or coma at initiation of treatment and dropped to zero in those with normal or only mildly impaired vigilance at entry (171).

In another study, patients who presented with the syndrome of isolated increased ICP had an overall excellent prognosis (172). A worsening course after admission has also been identified as a poor prognostic indicator (177).

In general, the prognosis for functional recovery is better than in patients with arterial stroke. Recovery may be due to recanalization of the venous thrombus or establishment of collateral drainage (1,10,173,181) (Fig. 45.17). Residual epilepsy has been reported in 10–30% of patients who had seizures during the acute stage (2). Seizures, when they occur, usually do so in the first year and are readily controlled with anti-epileptic drugs in most cases (1). Recurrent CVT appears to be infrequent: 11.7% in a series of 77 patients followed for a mean of 77.8 months (179). Recurrence during pregnancy is similarly uncommon. In a study of 22 pregnancies in 14 women with a prior history of CVT, none experienced recurrent CVT (182). Only five patients in this study received low-dose heparin as prophylaxis and so this represents largely the natural history in this condition. In some patients, CVT may lead to the later development of an arteriovenous malformation (1,183,184).

TREATMENT

Treatment of patients with CVT can be divided into management of symptoms, addressing etiologies, and antithrombotic measures (149,185). Some aspects of treatment remain controversial, in large part due to the variability in the clinical manifestations and outcome of this disorder (185–189).

Symptomatic treatments include airway and fluid support, management of seizures, and control of increased ICP and its consequences. Intubation and mechanical ventilation are required for more severe cases. Fluid support should be selected to avoid dehydration (which may further promote thrombosis) and maintain cerebral perfusion pressure without unduly elevating systolic blood pressure and thereby elevating the risk of intracerebral hemorrhage (2,185). To avoid
further increasing ICP, hypotonic solutions should be avoided.

Seizures should be treated as needed with appropriate anti-convulsants. There is no consensus on prophylactic treatment of seizures in this population.

Control of increased ICP is important both for preventing tentorial herniation and for protecting vision. Patients with extensive hemorrhagic venous infarction are at particularly high risk of herniation. Any patient with severe protracted papilledema is at risk for the development of optic atrophy. Measures to lower intracranial pressure include elevating the head of the bed, hyperventilation, and medications such as acetazolamide, mannitol, and glycerol. Surgical management may include external ventricular drainage, occasional surgical decompression, repeated lumbar punctures, and lumbo-peritoneal shunting. Performing surgical procedures in this setting generally requires temporarily halting anticoagulation and this poses some risk of increased thrombosis. Progressive visual loss due to papilledema can be addressed with optic nerve sheath fenestration, which is designed to protect the optic disc even in the face of persistent increased ICP (23). This procedure may bring prompt improvement of visual acuity and visual field in these patients. Unilateral surgery may be successful in improving papilledema in both eyes.

Treatment aimed at the underlying etiology of CVT most often consists of appropriate anti-microbial coverage in cases of septic thrombosis. Debridement of necrotic/infected tissue may be appropriate in selected cases. If an exogenous
A procoagulant factor is identified such agents as oral contraceptives, estrogen supplements, and certain medications should be stopped (166). Underlying medical conditions that may predispose to thrombosis, such as malignancy or collagen vascular disease, should likewise be treated.

Antithrombotic treatment usually consists of heparin acutely, switching to warfarin when the patient has stabilized. Although the use of heparin was at one time controversial, more recent data have established that the benefits of anticoagulation in terms of both morbidity and mortality outweigh the attendant risks of promoting or extending intracranial hemorrhage (185). This was confirmed in an initial randomized trial from Germany (188) that was halted after only 20 patients were enrolled because of the dramatic difference observed in the treated vs. control (placebo) group. Complete recovery occurred in eight patients treated with heparin vs. only one patient in the placebo group. There were no fatalities in the treated group vs. three in the placebo group. A subsequent larger European trial compared low molecular weight heparin to placebo in 60 patients (190). The poor (13%) outcome in the heparin-treated group compared favorably to the 21% poor outcome in the placebo group, however, the difference was not statistically significant. A subsequent meta-analysis of these two trials did indicate a 14% absolute risk reduction in mortality and 15% risk reduction in death or dependency (189). Additional studies have confirmed the efficacy and relative safety of anticoagulation for CVT although small sample sizes and large confidence intervals prevent the results from reaching statistical significance for individual series (149,191,192).

After a few days on heparin, most patients can be started on oral anticoagulation in order to reduce the risk of heparin-induced thrombocytopenia. The warfarin dose is usually adjusted to achieve an international normalized ratio (INR)

![Figure 45.24. A 16-year-old male with headaches and confusion. A, Initial head CT without contrast showed multiple hemorrhages in the left hemisphere. B, MRI of the brain demonstrated iso- and hypertense signals in the superior sagittal sinuses consistent with SSS thrombosis. Angiogram (C) and venogram (D) showed extensive thrombosis of the SSS. He was treated with intravenous heparin, but his neurological status deteriorated. E, He received intravenous tPA, and repeat angiogram 12 hours later showed opening of the superior sagittal sinus. He recovered rapidly and left the hospital 10 days later without neurological deficit. F, Repeat CT after thrombolysis showed mild worsening of the parenchymal hemorrhages. (Courtesy of Valérie Biousse, MD.)](image-url)
of between 2 and 3. The usual recommended duration of treatment is 3 months (185). In cases with a continued risk of thrombosis, such as inherited thrombophilias, malignancy, or chronic inflammatory disease, longer-term anti-coagulation is generally appropriate (149,187,191). Prophylactic low molecular weight heparin treatment is used during pregnancy and after delivery in those with a history of post-partum thrombosis (187).

Treatment with thrombolytic agents can be accomplished via peripheral intravenous or direct intrasinus infusion (193–209). Intrasinus infusion is usually accomplished through an indwelling catheter introduced via a transjugular approach. Agents utilized include urokinase, streptokinase, and tissue plasminogen activator (tPA). Although easier to administer, the peripheral intravenous route requires larger amounts of medication compared to selective sinus infusion and is thus associated with a higher risk of hemorrhagic complications (195). Time to onset of thrombolysis is also longer via the peripheral route. Locally administered thrombolytics also carry some risk of hemorrhage, particularly in those patients with pretreatment intracranial hemorrhage (149, 187,210). While local thrombolysis appears to be more effective in restoring flow compared to heparin, this method carries a higher risk of complications. Because of the relatively small number of patients treated and the variability in outcome, the risk-benefit ratio of this form of treatment remains unknown (185,209). The method of administration, relative merits of urokinase vs. tPA, and optimal dosage are also unclear. At present, there are no randomized controlled trials evaluating the relative safety and efficacy of thrombolytic therapy for CVT (209). Based on currently available data it is reasonable to treat initially with anticoagulation and symptomatic support, reserving antithrombotic therapy for patients who demonstrate worsening clinical status (185) (Fig. 45.24).

In cases of thrombotic failure, mechanical disruption of the clot (thrombectomy) can sometimes be performed via a microsnare (211) or AngioJet (a suction device) (212,213). The technique of sinus stenting has been used for stenotic vessels (214) and for recurrent thrombosis refractory to other treatment modalities (215). Other developing techniques include balloon angioplasty, intravascular laser, and intravascular ultrasound (216).

**JUGULAR VEIN OCCLUSION**

**CLINICAL MANIFESTATIONS**

Occlusion of the internal jugular may be asymptomatic or may produce a variety of systemic and ocular complications. Clinical manifestations are usually related to increased intracranial pressure. Cases with bilateral compromise of jugular outflow and those involving the dominant jugular venous drainage exhibit more severe signs and symptoms. Occlusion of the internal jugular vein may be asymptomatic when the nondominant side is affected. Swelling of the face and neck may occur, sometimes accompanied by neck pain and tenderness. The most serious systemic complications are pulmonary emboli (217–219), septic embolism, and septicemia (220).

Acute thrombosis or ligation of the internal jugular vein usually produces neuro-opthalmologic complications by its effect on ICP. Potts and Demarine reported a rise in pressure in the cisterna magna, subarachnoid space, and sagittal sinus during compression of the jugular vein in the dog (221). Stell and Maran (222) found that ligation of one internal jugular vein produced a 300% increase in ICP, whereas ligation of both internal jugular veins produced a 500% rise in ICP in experimental animals (223). Similar rises in ICP occur after ligation or occlusion of the internal jugular vein in humans (223). In most cases, simultaneous ligation of both jugular veins in humans produces an acute but only temporary rise in ICP. The ICP usually returns to normal within 2 weeks (224–226), presumably because of the relatively rapid development of adequate collateral intracranial venous circulation (227). Nevertheless, a prolonged increase in ICP may follow both unilateral or bilateral ligation of the internal jugular veins. In such cases, a pseudotumor cerebri-like syndrome may develop. Similar cases have been reported after both unilateral and bilateral radical neck dissection (21,228–233).

Isolated intracranial hypertension is not the only neuro-ophthalmologic complication of jugular vein occlusion. Anlyan et al. reported a fatal parieto-occipital venous infarction after a left-sided radical neck dissection (234). The patient had an anomalous aplastic lateral sinus on the right side, causing the brain to depend entirely on the left lateral sinus and left internal jugular vein for cerebral venous drainage. When the left internal jugular vein was ligated as part of the surgery, cerebral venous drainage was severely reduced, leading to the cerebral venous infarction.

A case of venous stasis retinopathy was reported by Gutteridge et al. in a patient without significant ipsilateral carotid artery disease but with occlusion of the ipsilateral internal jugular vein between the occipital tributary and the common facial tributary (235). The condition gradually resolved over several months. It is unclear if these two conditions were fortuitous or if an increase in venous back pressure from the occluded internal jugular vein somehow limited the ocular blood flow in much the same way as a carotid-cavernous sinus fistula.

Acute blindness may occur after bilateral radical neck dissection and ligation of the internal jugular veins (236–239). In nearly all cases, the blindness is not caused by increased ICP or by direct effects of ligation of the internal jugular vein, but by the effects of concomitant arterial occlusive disease, intraoperative or postoperative systemic hypotension with and without hemorrhage, or both. Such patients thus lose vision not from postpapilledema optic atrophy but from central retinal artery occlusion or ischemic optic neuropathy.
The diagnosis of internal jugular vein thrombosis is not difficult and can be made noninvasively by contrast-enhanced CT scanning, standard MR imaging, or MR angiography. It may also be readily diagnosed using ultrasonography which can be performed as a bedside procedure. Bessoudo et al. considered retrograde catheter venography to be the most definitive means of diagnosing this condition, but this procedure carries the risk of perforating a vein and dislodging a thrombus. Based on its high sensitivity and low risk, MR angiography appears to be the optimum noninvasive method of imaging this region.

CAUSES

Thrombosis of the jugular vein may result from a number of diverse clinical conditions (Table 1). In the postantibiotic era, infectious thrombosis of the jugular vein is uncommon. Septic thrombophlebitis of the internal jugular vein (IJV) was first described in 1936 by Lemierre and is sometimes referred to as Lemierre’s syndrome. It is usually caused by fulminant head and neck infections, particularly deep neck abscesses and pharyngitis. Additional causes include parotitis, dental manipulation, and injection of narcotics directly in the neck veins. The pathogens generally responsible for the septic thrombosis of the IJV include aerobic and anaerobic streptococci, staphylococci, pneumococci, and anaerobic Gram-positive bacilli.

Aseptic thrombosis of the internal jugular vein occurs in a variety of iatrogenic settings, including as a complication of central venous catheterization and secondary to placement of an endocardial pacemaker with a transvenous lead. The incidence of central venous access device-related thrombosis varies widely, from 2.3–63% depending on patient and device characteristics, and how cases are ascertained. Since most such thromboses are
asymptomatic, studies in which only symptomatic patients are investigated will yield lower numbers. In one prospective ultrasound study of 43 patients with hemato-oncological disease, 30% were found to have IJV catheter-related thrombosis (262). There was a strong correlation in this study between catheter thrombosis and catheter-related infection. In contrast, a similarly designed study also involving IJV catheters placed for delivery of chemotherapy found only four thromboses in 233 patients (1.5%), perhaps due to the routine use of low-dose heparin (257). An ultrasound study of 143 patients in whom an IJV catheter was placed for renal dialysis found a 25.9% prevalence of thrombosis (258). The only variable that correlated with the occurrence of thrombosis in this study was the number of catheters placed.

**OCCLUSION OF THE SUPERIOR VENA CAVA**

The superior vena cava may become obstructed from trauma, by neoplasm, or as a complication of certain shunting procedures for hydrocephalus. It also may become occluded by extension of a thrombus from the intracranial dural sinuses (261,271). Obstruction of the superior vena cava can also occur from fibrotic occlusion around a transvenous pacemaker (272).

**SUPERIOR OPHTHALMIC VEIN OCCLUSION**

The most common setting in which thrombosis of the superior ophthalmic vein (SOV) occurs is when a dural fistula of the cavernous sinus spontaneously closes. In this setting, a patient who may have had only mild proptosis, chemosis, and injection of the affected eye suddenly develops a worsening clinical picture characterized by increasing orbital signs accompanied by worsening of diplopia (274,275) (Fig. 45.25). Color Doppler imaging in such patients reveals occlusion of the SOV. Ocular pulse amplitudes in such patients gradually become reduced on the side of the fistula, indicating reduction in backflow of arterial blood through the venous system, and MR imaging shows complete or partial thrombosis of the superior ophthalmic vein (Fig. 45.26). The condition is self-limited, and the patient usually begins to improve within several days. Systemic corticosteroids may be useful in hastening improvement, but they are not needed unless orbital congestion is particularly severe, and intraocular pressure is significantly elevated. Topical antiglaucoma medications, particularly carbonic anhydrase inhibitors, should be used to lower intraocular pressure and prevent retinal arterial occlusion.

Additional associations include use of oral contraceptives (276,277), sinusitis (278,279), Tolosa-Hunt syndrome (280), and amyloidosis (281). SOV occlusion has also been reported as a complication of carotid cavernous sinus fistula coiling (282). Infectious SOV thrombosis occurs uncommonly (283). Because the inferior and superior ophthalmic veins lack valves, such infection may extend to the cavernous sinus and cause secondary thrombosis in this location (278).

Individual cases of isolated SOV occlusion have been verified by conventional angiography, MR imaging, or both. Boniuk reported four cases in which symptoms and signs of superior ophthalmic vein thrombosis included variable dilation and tortuosity of conjunctival vessels of the eye on the affected side, slight proptosis, injection of conjunctival and retinal veins, and a slightly higher intraocular pressure on the side of the lesion (284). Four additional cases of superior ophthalmic vein thrombosis were reported by Takahashi et al. (285). All four patients were over 60 years old and presented with signs of orbital congestion, including chemosis, proptosis, and dilation and tortuosity of conjunctival vessels. Venous stasis retinopathy and glaucoma were present in several of these cases. In all four cases, thrombosis of the superior ophthalmic vein was confirmed by orbital venography. Most likely these cases were caused by spontaneous, dural carotid cavernous fistulas (CCFs) that initially drained anteriorly and then closed spontaneously, resulting in acute occlusion of the superior ophthalmic vein.

**RETINAL VEIN OCCLUSION**

**CENTRAL RETINAL VEIN OCCLUSION**

Central retinal vein occlusion (CRVO) is a common ocular disorder with a prevalence of 1% overall (286) and 4% in individuals over age 49 (287). Most patients who develop this condition are over 50 years old, and 50–75% have associated hypertension, diabetes mellitus, renal disease, and/or hyperlipidemia (288–295). There is a strong association between CRVO and atherosclerotic disease of the central retinal artery (296,297). Atherosclerosis of the central retinal...
artery within the optic nerve, where it is adjacent to, and shares a common sheath with, the central retinal vein, presumably causes compression and irritative endothelial proliferation within the central retinal vein (298). Color Doppler imaging has demonstrated high vascular resistance in the central retinal artery, ophthalmic artery, and short posterior ciliary arteries of both affected and fellow eyes, suggesting that diffuse small-vessel disease may predate and contribute to the development of CRVO in some cases (299). Additional less common mechanisms for CRVO include mechanical compression, inflammation, or other abnormalities of vessel wall, and a variety of hypercoagulable states.

External compression of the central retinal vein can be caused by a space-occupying orbital lesion or by optic neuritis. Examples of mass lesions causing CRVO include melanocytoma of the optic disc (300) and optic disc drusen (301). Duker et al. reported five cases of optic neuritis associated with CRVO (302). Fluorescein angiography in these cases showed delayed venous filling with venous dilation and tortuosity. There was no evidence of capillary nonperfusion, macular edema, or macular hemorrhage. Presumably, pressure on the CRV from surrounding optic nerve swelling caused compromised blood flow. Winterkorn et al. described two patients with orbital pseudotumor (idiopathic orbital inflammation) who developed combined central retinal artery and central retinal vein occlusions, presumably from external compression of these vessels by inflamed orbital tissue (303).

Abnormalities of flow may account for some cases of CRVO. Schatz et al. described two patients with retinal AVMs who developed CRVO (304). The authors proposed that turbulent flow, high intravascular volume, and elevated arteriolar pressure led to vessel wall damage, thrombosis, and occlusion on the venous side. Dural CCFs may also be associated with CRVO via a similar mechanism. Komiyama et al. reported such a case and reviewed the findings in 14 other cases (305). These authors recommended close monitoring of patients with CFF in order to detect early stasis of the retinal veins in an effort to prevent the occurrence of CRVO in such cases.

Abnormalities of blood vessel walls that may lead to CRVO include vasculitides such as Behçet systemic lupus, sarcoidosis, tuberculosis, bacterial infiltration from septic thrombi, and moyamoya disease (288,306,307). Cases of CRVO due to infiltration by carcinomatous (308), lymphomatous (307), and leukemic meningitis are often accompanied by signs of central retinal artery occlusion. In some cases it is difficult to distinguish between inflammation in the vein wall and pressure from infiltration of the surrounding tissue as the underlying mechanism.

A variety of hereditary and acquired prothrombotic disorders have been associated with CRVO (309–314). Patients with CRVO have been found to have an increase in blood viscosity (288) and hematocrit (315) and fibrinogen levels (316) compared to controls. Testing for inherited coagulopathies has yielded mixed results. A correlation of CRVO with elevated plasma homocysteine levels has been found in several studies (317–319). Vine et al. reported elevated homocysteine in 21.6% of 74 patients, including 55% of the 9

patients with bilateral occlusion and 30% of those with ischemic CRVO (318). Similarly, El-Asrar et al. found hyperhomocysteinemia in 29 of 36 patients (63%) vs. 2 of 59 controls (3.4%) (319). In a smaller group of patients (N = 20), Brown et al. documented increased homocysteine in 75% (vs. 13% of controls) (320).

In contrast, several studies have found no association between Factor V Leiden and CRVO (321–324). When such testing is restricted to younger patients, however, such an association is more common. For example, Kuhli et al. found abnormalities in 17% of those CRVO patients under 45 years of age vs. 4.8% of young controls (325).

Deficiency of protein C was found in 6 of 14 patients with CRVO and 3 of 31 patients with BRVO in one study (326) and in 8 of 42 patients with RVO in another (316). Results of testing for protein S deficiency have been more varied including abnormally low levels in only 2 of 45 patients with RVO in one study (326) vs. positive results in 12 of 56 patients in another (316). Anecdotal associations with anti-thrombin III deficiency (316), prothrombin gene mutation (327,328), and platelet glycoprotein mutations (329,330) have also been reported.

The presence of antiphospholipid antibodies (APAs) has been found in some patients with CRVO. El-Asrar reported APAs in 15 of 57 patients with CRVO (vs. 3 of 74 controls) (316) and Adamczuk et al. in 13.5% of their patients (vs. 2.1% of controls) (309). Anticardiolipin antibodies were identified in 10 of 24 patients (43%) with CRVO and no other identifiable risk factors (331).

A number of other acquired prothrombotic conditions have been associated with CRVO in single case reports and small series, including polycythemia (332), essential thrombocytopathy (333), thrombocytopenic purpura (334), malignancy (335), dehydration (336), anorexia nervosa (337), systemic lupus, and pregnancy. Several medications have been implicated as a possible cause of CRVO including infliximab (338), intravenous immunoglobulin (339), rofecoxib (340), and α-interferon (341). In some cases the underlying disease for which these medications are used may be a contributory factor (e.g., hepatitis C, rheumatoid arthritis). CRVO secondary to heparin-induced antiheparin antibodies has also been reported (342).

Overall, the chance of identifying an underlying coagulopathy is considerably higher in those patients who lack the usual risk factors for CRVO, particularly age. In a group of 55 patients under the age of 56 years, Lahey et al. found at least one abnormal hematologic test in 27%, most commonly homocysteine and antiphospholipid antibodies (313). In some patients more than one thrombophilia is identified, and it has been suggested that several risk factors, both genetic and acquired, must be present for thrombosis to occur (343).

There appears to be an association between increased intraocular pressure and CRVO. In most cases, it is believed that increased pressure within the eye predisposes the patient to vein occlusion, possibly by producing a deformity in the wall of the central retinal vein, thus causing increased resistance to blood flow (344,345). In other cases, however, CRVO may induce increased intraocular pressure. In such cases, endothelial proliferation associated with retinal hem-
orrhage may cause a progressive increase in flow resistance. Some factor or mediator in the aqueous humor may then be formed by destruction of oxygen-deprived tissue or transferred through damaged vessels acting on outflow resistance, thus increasing the intraocular pressure (346).

Patients with CRVO usually complain of decreased vision in the affected eye. The loss of vision may occur suddenly without any preceding visual symptoms, or it may follow a period during which the patient has experienced transient episodes of blurred vision, flashes of light, or floaters. In some patients, the condition is asymptomatic, discovered during a routine ophthalmologic examination.

The clinical appearance of CRVO is characterized by dilated retinal veins and scattered intraretinal hemorrhages in both the posterior pole and the periphery. The retinopathy varies from a few small scattered retinal hemorrhages and perhaps a few cotton-wool spots (347) to a marked hemorrhagic retinopathy with both superficial and deep retinal hemorrhages (the classic “blood and thunder” retina) and blood in cystoid spaces within the macula (348) (Fig. 45.27). The optic disc may be normal or swollen in both mild and severe cases. When the retinal findings are severe and are associated with decreased vision in the eye, the diagnosis of CRVO is usually evident. However, patients with no significant visual loss and relatively minor retinal findings except for disc swelling and a few peripapillary and posterior pole hemorrhages may be thought to have unilateral papilledema, optic neuritis, or anterior ischemic optic neuropathy. Such patients may undergo an inappropriate evaluation for underlying neurologic disease.

**Figure 45.27.** Ophthalmoscopic appearance of central retinal vein occlusion in four different patients. Note varying degrees of optic disc hyperemia and swelling, intraretinal flame-shaped and blot hemorrhages, and peripapillary soft exudates (cotton-wool spots). All patients had markedly reduced central vision in the affected eye.
A particular type of CRVO has been termed “papillophlebitis,” a name that has generated some confusion (349–352). Some authors have used this term to indicate retinal vein occlusion or insufficiency that is due to inflammation. Specific systemic causes have included syphilis, periarteritis nodosa, Behçet’s disease, granulomatous vasculitis, typhoid vaccination, and multiple sclerosis (353). Others have used the term to denote nonischemic CRVO in younger individuals (e.g., under age 50) who lack vasculopathic risk factors (354). The thought here is that in these individuals the mechanism is likely to be inflammatory. In some cases the presence of vitreous cells and/or an apparent response to systemic corticosteroids seems to confirm an inflammatory process, but in many cases these features are lacking. To add to the confusion, the same clinical findings have also been classified as “benign retinal vasculitis” (355), “optic disc vasculitis” (356,357), “mild retinal and papillary vasculitis” (353), and “big blind spot syndrome” (358,359).

At one time the term “venous stasis retinopathy” was also used for this condition (360), however that term has now been generally adopted to indicate the retinal venous changes associated with ocular ischemic syndrome (361).

Figure 45.28. Etiology of central retinal vein occlusion. A, Section through center of optic nerve in a patient with a central retinal vein occlusion shows a patent central retinal artery (*), diffuse hemorrhage in the retrolaminar nasal portion of the nerve (arrows), and a fresh thrombus in the central retinal vein just posterior to the lamina cribrosa (arrowhead). B, In another case of central retinal vein occlusion, there is a recanalized thrombus (arrow) in the central retinal vein at the level of the lamina cribrosa. (From Green WR, Chan CC, Hutchins GM, et al. Central retinal vein occlusion: A prospective histopathologic study of 29 eyes in 28 cases. Retina 1981;1:27–55.)
guishing these two entities. First, optic disc swelling is never seen in the venous stasis retinopathy of carotid or ophthalmic artery occlusive disease, whereas it is a major feature in florid cases of CRVO and even in mild cases. Thus, if optic disc swelling is present, the patient has a CRVO and not the retinopathy of carotid disease. Second, while the appearance of the retinal veins is abnormal in both CRVO and venous stasis retinopathy, in CRVO the veins are engorged and tortuous, whereas in the retinopathy of carotid disease the veins become markedly irregular. Third, the hemorrhages, microaneurysms, and capillary dilations seen in CRVO tend to be distributed diffusely over the entire retina. In eyes with venous stasis retinopathy, however, these abnormalities are usually confined to the midperipheral retina, particularly in the superior temporal quadrant (Fig. 45.29). Fourth, patients with CRVO usually have normal and symmetric retinal artery pressures, whereas patients with venous stasis retinopathy have retinal artery pressures that are usually at least 50% less than that measured in the fellow eye.

The prognosis in patients with CRVO depends on the degree of retinal capillary perfusion, i.e., whether the condition is ischemic or nonischemic (294,345,360,373–375). Retinal capillary perfusion is best determined by a combination of clinical tests, fluorescein angiography, and electrophysiology (294,375–382). Determination of a relative afferent pupillary defect (RAPD) is a sensitive and reliable method to
distinguish an ischemic CRVO from a non-ischemic CRVO (383). In 90% of nonischemic CRVO eyes the RAPD was 3 log units or less; in 90% of ischemic eyes the RAPD was 1.2 log units or greater. No ischemic eyes were found to have less than a 6 log unit RAPD. When this clinical test is combined with electrophysiologo, perimetry, and visual acuity testing, the differentiation between these two forms of CRVO is usually straightforward. The ERG b-wave latency has been shown to be predictive of the future development of neovascularization (384) and reduced b-wave/a-wave ratios on an electroretinogram correlate well with dropout seen on fluorescein angiography (385). In one study the presence of optic disc edema was found to correlate with younger age, less severe non-perfusion and better visual acuity, and was thought to convey a better prognosis (386). This predictive value, however, was not confirmed in a study of CRVO prognostic factors by Hvarfner et al. (382).

Optical coherence tomography (OCT) has been found to be useful in detecting macular edema in eyes with CRVO, but unlike diabetic maculopathy, OCT findings do not correlate well with visual acuity (387). OCT has been useful in identifying optic disc traction and secondary localized retinal detachment which may contribute to poor visual outcome (388). Color Doppler imaging may demonstrate impaired central venous velocity in eyes with CRVO (389) and may help in distinguishing ischemic from nonischemic vein occlusion (390,391).

As might be expected, the visual prognosis for eyes with an ischemic CRVO is substantially worse than for eyes with a nonischemic CRVO. Eyes with ischemic CRVO have increased risk of experiencing acute and persistent visual loss from macular edema and subsequently developing neovascular glaucoma (392). Quinlan et al. reported that 57 of 61 eyes (93%) with an ischemic CRVO had final visual acuity less than or equal to 20/200 (393). Older patients with poor initial visual acuity have a particularly poor prognosis (394). Eyes with nonischemic CRVO may retain good vision throughout the course of the disease or they may recover vision as the process resolves (374,395–397). Quinlan et al. recorded a final visual acuity of 20/200 or less in 53 of 107 (50%) of eyes following nonischemic CRVO (393).

A CRVO that initially is nonischemic can become ischemic over time (398). According to Hayreh et al. (364), the probability of progression from a nonischemic to an ischemic CRVO in persons 45–65 years old is 6.7% at 6 months and 8.1% at 18 months. For patients 65 years or older, the probability of progression is 13.2% at 6 months and 18.8% at 18 months. Thus, older patients have a more substantial risk of progressing from an initially nonischemic to an ischemic CRVO over time. Such patients require extremely careful monitoring. Additional risk factors for progression to ischemic CRVO include male sex, number of systemic risk factors, and visual acuity (399).

A small percentage of patients who experience a CRVO will develop a second venous occlusive event in the same eye. Similarly, patients who experience a CRVO in one eye may develop a similar process in the fellow eye. According to Hayreh et al. (364), the cumulative probability of developing a second episode of CRVO or a BRVO in the same eye, is 2.5%, and in the fellow eye 11.9% within 4 years. Patients who experience a CRVO have also been found to have a higher risk of future morbidity and mortality due to cardiovascular disease (400,401).

Efforts to treat CRVO include both medical and surgical modalities (402). Isovolemic hemodilution (403), pentoxifylline—a drug that reduces blood viscosity (404), and steroids (405,406) have been tried in small studies without success. Systemic heparin, alone or combined with aspirin, brought no visual improvement in two studies (407,408). In a randomized series of 40 patients with CRVO, streptokinase (600,000 IU) followed by anticoagulants, vs. no treatment, improved visual outcome slightly but caused vitreous hemorrhage with blindness in 3 (15%) of 20 patients (409). Intravenous plasminogen activator plus aspirin seemed promising in 89 eyes with CRVO but the absence of randomization prevented any conclusion regarding effectiveness (410).

Supraselective intra-arterial fibrinolytic treatment has also been employed (411). Infusion of urokinase into the ophthalmic artery was followed by visual improvement at 48 hours in 6 of 26 eyes with CRVO (412). Eyes with a combined CRVO and CRAO and those with recent loss seemed most likely to benefit. No extraocular complications resulted from the procedure. Injection of tPA into a branch retinal vein has also been employed (413).

Intravitreal techniques for delivering medical treatment for CRVO have also been attempted. Intravitreal tissue plasminogen activator (tPA) was found to be safe in a preliminary study of 9 eyes (414), but in a larger study efficacy did not improve on the natural history of the condition (415). Intravitreal injection of triamcinolone has been used for the cystoid macular edema that results from CRVO (416) and found to be effective in 10 of 10 eyes (417).

High-intensity laser has been used to create chorioretinal anastomoses as a method for improving collateral venous drainage in CRVO (418). This procedure was technically successful in one-third of eyes and was associated with visual improvement (419). Using a modified technique, Leonard et al. reported development of at least 1 anastomosis in 19 of 19 treated eyes (420). All eyes maintained their nonischemic status over the period of follow-up and treatment complications were limited to localized preretal fibrosis.

A new technique for the treatment of CRVO developed by Opremcak and associates is based on the concept that this disorder is a form of ‘‘compartment syndrome’’ at the scleral outlet (421). Radial optic neurotomy consists of a small incision at the optic disc margin, usually nasally, across the scleral outlet (421). Radial optic neurotomy consists of a small incision at the optic disc margin, usually nasally, across the scleral outlet (421). Radial optic neurotomy consists of a small incision at the optic disc margin, usually nasally, across the scleral outlet (421). Radial optic neurotomy consists of a small incision at the optic disc margin, usually nasally, across the scleral outlet (421). Radial optic neurotomy consists of a small incision at the optic disc margin, usually nasally, across the scleral outlet (421).

In an initial report of 11 consecutive cases, all showed improvement by fundus exam and fluorescein angiography (421). In 10 of 11 cases visual acuity improved, including 8 with rapid improvement. In some cases neurotomy is followed by the development of optociliary venous anastomosis, which may portend a more favorable prognosis (423,424).

**BRANCH RETINAL VEIN OCCLUSION**

Occlusion of one or more of the retinal branch veins is a common cause of retinal vascular disease. This condition
equally affects men and woman, and usually occurs in pa-
tients from 60 to 70 years of age (425,426). It is typically
a unilateral condition; only about 10% of patients will de-
velop a BRVO occlusion in the fellow eye in the future.
There are no predictive features regarding such an occur-
rence, nor are there any known preventive measures (426).
BRVO usually occurs in patients with systemic hypertension
or atherosclerotic cardiovascular disease; however, there is
no firm evidence that any systemic disease plays a pathoge-
netic role in the condition (427). Occasional anecdotal re-
ports document the association of BRVO with some form
of thrombophilia (317,322,428–430).
The clinical manifestations of a BRVO usually occur
acutely. In most cases, a patient with previously normal vi-
sion suddenly develops blurred vision, a visual field defect,
or both. Ophthalmoscopy shows segmentally distributed in-

![Figure 45.30. Branch retinal vein occlusion in three patients. A, Acute branch retinal vein occlusion in the right eye. Note marked intraretinal hemorrhage that is primarily confined to the superotemporal quadrant of the right fundus. Several soft exudates (cotton-wool spots) are evident, and the occluded branch vein can be seen peripheral to the hemorrhage (arrowheads). B, A few months after an acute branch vein occlusion, the right ocular fundus in a second patient shows resolving intraretinal hemorrhage with the appearance of shunt vessels across the horizontal raphe. C, Many months after an acute branch retinal vein occlusion in a third patient, the right ocular fundus shows extensive hard exudates, multiple intraretinal hemorrhages, and peripapillary shunt vessels. (Courtesy of Dr. Stuart Fine.)](image-url)
traretinal hemorrhage (Fig. 45.30). With time, the hemorrhage resorbs, leaving a segmental distribution of retinal vascular abnormalities that may include capillary nonperfusion, capillary dilatation, microaneurysms, and formation of collateral retinal vessels (426).

There are three common vision-limiting complications of a BRVO: (a) macular edema, (b) macular nonperfusion, and (c) vitreous hemorrhage from neovascularization (434,426, 431–434). Although not evident clinically in most cases, serous retinal detachment was detected by optical coherence tomography in 10 (71.4%) of 14 eyes with BRVO and may play a role in visual loss (435). Visual acuity may also be reduced by macular hemorrhage, but in such cases, vision almost always improved as the hemorrhage resorbs.

There is no adequate medical therapy for a BRVO. Although there is an apparent association between systemic hypertension and loss of central vision from macular edema in this condition, control of hypertension does not improve visual outcome. Anticoagulant therapy has not been shown to be beneficial, and it is not recommended (426). Similarly, treatment with fibrinolytic agents does not appear to be helpful.

Patients with BRVO who develop reduced vision from macular edema may benefit from focal laser photocoagulation. A multicenter, randomized clinical trial supported by the National Institute of Health reported that argon laser photocoagulation can lessen the risk of subsequent vitreous hemorrhage, but in such cases, vision almost always improved as the hemorrhage resorbs.

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