A. OVERVIEW AND EPIDEMIOLOGY
Cerebral venous thrombosis, including venous sinus thrombosis and cortical vein thrombosis, is a relatively rare cause of stroke. The annual incidence is estimated to be 3-7 cases per million people. It is more common among young women and children. Though it can cause devastating injury to the brain, most patients have a good prognosis if it is recognized and treatment is initiated early.

B. PATHOPHYSIOLOGY
Multiple etiologic factors are associated with the development of cerebral venous thrombosis. Usually an inciting factor (Table 1) occurs in a patient with one or more predisposing risk factors (Table 2). These act through the common pathways of thrombosis of hypercoaguability and hemoconcentration, direct injury or inflammation of the vessel, venous stasis and obstruction of flow. Two distinct mechanisms are responsible for the manifestations of injury. Thrombosis of the cortical veins causes localized vasogenic edema, venous infarction with cytotoxic edema, and hemorrhage. Thrombosis of the large venous sinuses obstructs venous drainage leading to impaired CSF absorption through the arachnoid villi and intracranial hypertension without hydrocephalus.

C. CLINICAL FEATURES
The onset of symptoms can be acute, subacute or chronic. Headache is the most common presenting symptom of cerebral venous thrombosis, present in nearly 90% of patients. Other common presenting symptoms include focal or generalized seizure (40%), focal motor weakness (37%), encephalopathy or change in mental status (22%), vision loss (13%), diplopia (13%), stupor or coma (13%). The particular constellation of symptoms and exam findings reflects the extent to which the cortical veins (seizure and focal neurologic symptoms) and large venous sinuses (elevated intracranial pressure, bihemispheric symptoms) are involved. Papilledema is present in 25-30% of patients. Thrombosis of the deep cerebral veins (vein of Galen, straight sinus, internal cerebral veins) can produce a spectrum from mild cognitive disturbances to coma. Thrombosis of the cavernous sinus produces a characteristic syndrome of orbital pain, proptosis, chemosis and variable dysfunction of cranial nerves III, IV, V, and VI.

D. DIAGNOSIS
The key to the diagnosis of venous sinus thrombosis is maintaining a high degree of clinical suspicion in the setting of common presenting symptoms.
Head CT: Non-contrast head CT may be normal in a large number of patients and cannot exclude a diagnosis of cerebral venous thrombosis. Suspicious findings include cerebral edema, findings suggestive of bilateral infarction or infarction in a non-arterial distribution, intracerebral or subarachnoid hemorrhage. Hyperdense thrombosed cortical veins or hyperdensities within the venous sinuses can sometimes be seen.

CT Venography (CTV): CT venography with multiplanar reformatting has a sensitivity of 95% when compared with digital subtraction angiography. CT venography is advantageous because it is widely available and can be performed quickly. It is less expensive than MRI and less invasive than conventional angiography. Disadvantages include radiation exposure and administration of intravenous contrast.

MRI/MRV: MRI in combination with MR venography (MRV) is highly sensitive for the diagnosis of cerebral venous thrombosis. Abnormal T1 and T2 signal within the venous sinus in conjunction with absence of normal flow through the venous sinus on MRV confirms the diagnosis of venous thrombosis. The age of the thrombus determines the T1 and T2 signal characteristics.

Catheter Angiography (DSA): Either CTV or MRI/MRV are usually adequate for the diagnosis or exclusion of cerebral venous thrombosis. Digital subtraction angiography (DSA) may be necessary for identification of an isolated cortical vein thrombosis without venous sinus involvement or for the diagnosis or characterization of dural arteriovenous fistula associated with a cerebral venous thrombosis.

Evaluation of Etiology and Predisposing Factors: After a diagnosis of cerebral venous thrombosis is made, attention must be shifted to the evaluation of potential etiologies and predisposing factors. Evaluation for meningitis, sinusitis, otitis, or mastoiditis should be performed in patients with evidence of infection. Laboratory evaluation of prothrombotic states should be considered including: antiphospholipid antibodies, protein C and S, antithrombin III, plasma homocysteine, factor V leiden mutation, and prothrombin gene mutation.

E. TREATMENT

Anticoagulation: The cornerstone of treatment for cerebral venous thrombosis is the initiation of anticoagulation to prevent extension of the thrombosis and support spontaneous thrombus resolution. Though there is concern about the safety of anticoagulation in the presence of cerebral hemorrhage and venous infarction, a metaanalysis of 2 randomized controlled trials demonstrated a pooled relative risk reduction for death or dependency and no new symptomatic intracranial hemorrhages after initiation of anticoagulation. 6,7,8 Most importantly, no patients demonstrated worsening intracranial hemorrhage after initiation of systemic anticoagulation.
The American Heart Association recommends:
For patients with CVT, unfractionated heparin or low molecular weight heparin is reasonable even in the presence of hemorrhagic infarction (Class IIa, Level B). Continuation of oral anticoagulation is reasonable for 3-6 months followed by antiplatelet therapy (Class IIa, Level C).9

The European Federation of Neurological Societies (EFNS) recommends:
Patients with CVT without contraindications for anticoagulation should be treated either with body weight-adjusted subcutaneous low molecular weight heparin or dose adjusted intravenous heparin with an at least doubled aPTT. Concomitant ICH related to CVT is not a contraindication for heparin therapy.10

**Thrombolytics and Endovascular Treatment options:** Numerous case reports have described the use of localized thrombolytic administration as well as mechanical clot disruption as a potential treatment option for cerebral venous thrombosis.11,12,13 No evidence exists from controlled trials to establish efficacy or safety of these therapies.14 The use of localized administration of urokinase or rtPA in conjunction with systemic anticoagulation may be promising. However, the appropriate agent, dose, route of administration and clinical situation have yet to be defined. An increased risk of intracranial hemorrhage is the most commonly reported complication.15 Thrombolytic and endovascular treatment should be limited to select patients who decline despite anticoagulation and should be performed only in centers with sufficient expertise in neuro-endovascular interventions.

**Seizures:** Patients with CVT are at risk of seizures, especially those with focal edema, venous infarcts and hemorrhage.16 Prophylactic anticonvulsants may be considered in patients with CVT, especially in those at high risk of seizure.

**Intracranial Pressure:** CVT causes elevated intracranial pressure by two separate mechanisms. First, intracranial hemorrhage, edema and infarction can lead to localized mass effect. Second, impairment of venous outflow causes decreased reabsorption of CSF, communicating hydrocephalus and intracranial hypertension. Hyperosmolar therapy with mannitol or hypertonic saline should be administered to patients at risk for cerebral herniation. There is no data to support the use of corticosteroids and they pose a theoretical risk of exacerbating thrombosis. CSF diversion by lumbar puncture or ventriculostomy may be required for patients with communicating hydrocephalus and intracranial hypertension. This is especially true of patients with symptoms of headache and vision loss from sub-acute and chronic CVT. Surgical intervention including resection of hemorrhagic infarction or decompressive craniectomy may be necessary.17,18 Anticoagulation should be resumed as soon as possible following surgical intervention.
REFERENCES


**Excellent reviews on the topic

Table 1
Inciting events causing cerebral venous thrombosis:
- Trauma
- Injury to the jugular vein (catheterization)
- Neurosurgical procedures
- Lumbar puncture
- Meningitis and CNS infections
- Otitis/Mastoiditis/Sinusitis
- Systemic infection
- Dehydration

Table 2
Predisposing risk factors for cerebral venous thrombosis:
- Genetic prothrombotic states
- Acquired prothrombotic states (Antiphospholipid antibodies, hyperhomocysteinemia, nephritic syndrome)
- Pregnancy or puerperium
- Systemic inflammatory diseases and vasculitis
- Oral contraceptives and hormone replacement therapy
- CNS, hematological, or other malignancy