Pathology
Neuronal migration is a complex, highly-regulated process integral to formation of normal cortical architecture that occurs throughout gestation but peaks from 2 to 4 months. In the case of lissencephaly and pachygyria, the brain appearance is smoother because there are fewer convolutions of the cortical surface. In polymicrogyria syndromes, the brain is more irregular in appearance due to an increased number of abnormally small gyri. In schizencephaly, clefts form from the surface of the brain to the lateral ventricle; the clefts are often lined by polymicrogyri.

Clinical Presentation
Lissencephaly has a severe presentation with marked motor disability and seizures. Polymicrogyria and schizencephaly, depending on the extent and location, often result in less severe developmental disabilities. All neuronal migration disorders are associated with high risk of seizures.

Diagnosis/Differential
Neuroimaging is the primary method of diagnosing the neuronal migration disorders. Further diagnostic evaluation is often done because these disorders are heterogeneous in etiology and may be associated with other genetic syndromes or environmental factors, such as teratogens or intrauterine infections. Single gene mutations are responsible for many malformation syndromes and identification of these genes can aid in counseling and prognosis.

Treatment
The most common medical issue in this population is intractable epilepsy which is treated with medications and possibly by surgical resection of the abnormal epileptogenic cortex. In the case of severe neurologic impairment, a number of medical complications can arise: orthopedic complications from immobility and spasticity; failure to thrive and aspiration from poor oromotor coordination; vulnerability to pulmonary infections; and complications due to respiratory insufficiency.

Prognosis
Long-term outcome depends on the degree of neurologic impairment and, to a lesser extent, the etiology of the migration disorder. Genetic evaluation is useful for prognostic counseling and management.

Chiari Malformation, Type 1 (CMI)

Definition/Epidemiology
Chiari malformation, type 1 (CMI) is cerebellar tonsillar ectopia with displacement of the cerebellar tonsils more than 5 mm below the foramen magnum, usually accompanied by deformity of tonsils and evidence of altered CSF flow (indicated by loss of peritonsillar CSF space or impaired CSF flow dynamics.) It is common, likely occurring in 0.5 % of the population.

Pathology
The cerebellar tonsils are inferiorly displaced, elongated, and compressed by the foramen magnum. This displacement can cause increased intracranial pressure and change CSF flow dynamics, leading to development of syringomyelia.

Clinical Presentation
In CM1 cases with severe displacement, there may be lower cranial neuropathies, disordered sleep, headaches, and vertigo, among other symptoms. If there is an associated syringomyelia, this may also result in symptoms (see discussion of syringomyelia.) Rarely, patients may experience difficulty with balance and gait.

Diagnosis/Differential
MRI is most useful for making the diagnosis. CSF flow studies may be helpful to establish clinical significance of the Chiari malformation. Since any cause of increased intracranial pressure can lead to tonsillar herniation, it is important to exclude idiopathic intracranial hypertension and CNS mass lesions.

Treatment
Surgical decompression by removing suboccipital bone and posterior C1 vertebrae may be necessary when the symptoms are severe and when syringomyelia is present, symptomatic, and worsening. Otherwise, conservative management is sufficient.

Prognosis
CM1 is generally not disabling. Surgical decompression is generally effective and prognosis is good.

Spinal Cord Malformations

Spina Bifida

Definition/Epidemiology
Failure to completely close the neural tube during the 24th to 26th days post conception can result from defects anywhere along the neuroaxis. These abnormalities are termed neural tube defects (NTDs), the most common of which occur caudally, and are collectively termed spina bifida. Spina bifida occurs in about 1 in 2800 births in the United States. The prevalence of NTDs varies by geography and is influenced by genetic and environmental factors. Use of folic acid at the time of conception and during pregnancy can significantly reduce NTD rates.

Pathology
The neural plate folds and seals itself to form the neural tube in a process, called neurulation, from gestation day 18 to 28. The central portion of the neural tube closes first, then the cranial and caudal portions. Abnormal caudal closure can be associated with overlying bony and skin defects, leading to "open" NTDs, such as myelomeningocele (MMC). The severe neuropathology seen in MMC may not be due only to the lack of caudal tube closure, but also to exposure of neural tube contents to amniotic fluid, trauma, and the leakage of CSF leading to downward herniation of the cerebellum. In cases of "closed" spina bifida where the abnormal caudal cord tissue is covered by fat or skin, neurologic function is less impaired.

Clinical Presentation
The more severe and disabling the defect, the earlier it will present. A large MMC is clinically obvious at birth. MMC can be diagnosed prenatally as well. MMC causes severe distal spinal cord dysfunction, including paralysis and sensory loss in the