matter can be demonstrated. Agenesis of the corpus callosum is commonly associated with mental retardation but may occur in clinically normal individuals. It can be present in isolation or associated with a wide range of other malformations.

Posterior Fossa Anomalies

A distinct set of malformations primarily affect the brainstem and the cerebellum, which often show dramatic changes in size and shape. These may be accompanied by morphologic changes in other regions of the brain.

- *Arnold-Chiari malformation* (Chiari type II malformation) consists of a small posterior fossa, a misshapen midline cerebellum with downward extension of vermis through the foramen magnum (Fig. 28-7), and, almost invariably, hydrocephalus and a lumbar myelomeningocele. Other associated changes may include caudal displacement of the medulla, malformation of the tectum, aqueductal stenosis, cerebral heterotopias, and hydromyelia (see later).
- *Chiari type I malformation* is a less severe disorder in which low-lying cerebellar tonsils extend down into the vertebral canal. This may be a silent abnormality or may become symptomatic because of impaired CSF flow and medullary compression; if present, these symptoms can usually be corrected by neurosurgical intervention.
- *Dandy-Walker malformation* is characterized by an enlarged posterior fossa. The cerebellar vermis is absent or present only in rudimentary form in its anterior portion. In its place is a large midline cyst that is lined by ependyma and is contiguous with leptomeninges on its outer surface. This cyst represents the expanded, roofless fourth ventricle in the absence of a normally formed vermis. Dysplasias of brainstem nuclei are commonly found in association with Dandy-Walker malformation.

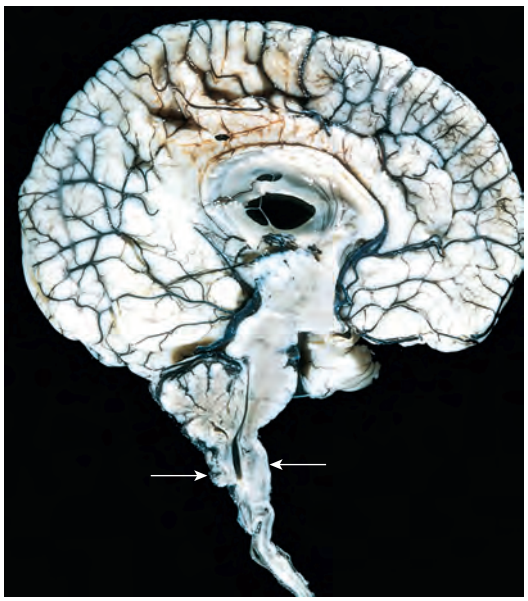

Figure 28-7 Arnold-Chiari malformation. Midsagittal section showing small posterior fossa contents, downward displacement of the cerebellar vermis, and deformity of the medulla (*arrows* indicate the approximate level of the foramen magnum).

- *Joubert syndrome*, and its related disorders, share hypoplasia of the cerebellar vermis with apparent elongation of the superior cerebellar peduncles and an altered shape of the brainstem; together these changes give rise to the 'molar tooth sign' on imaging. This group of malformations has been found to be caused by diverse mutations affecting genes that encode components of the primary (non-motile) cilium.

Syringomyelia and Hydromyelia

These are disorders characterized by expansion of the ependyma-lined central canal of the cord *(hydromyelia)* or by the formation of a fluid-filled cleft-like cavity in the inner portion of the cord *(syringomyelia, syrinx)* that may extend into the brainstem *(syringobulbia)*.

Syringomyelia may be associated with the Chiari malformations; it may also occur in association with intraspinal tumors or following traumatic injury. In general, the histologic appearance is similar in all these conditions, with destruction of the adjacent gray and white matter, surrounded by a dense feltwork of reactive gliosis. The disease generally becomes manifest in the second or third decade of life. The distinctive symptoms and signs of a syrinx are the isolated loss of pain and temperature sensation in the upper extremities because of the predilection for early involvement of the crossing anterior spinal commissural fibers of the spinal cord.

KEY CONCEPTS

Malformations and Developmental Disorders

- Malformations may be associated with single gene mutations, larger scale genetic alterations, or exogenous factors.
- Overall, the earlier in development a malformation occurs, the more severe the morphologic and functional phenotype.
- Neural tube defects are associated with failure to close or inappropriate reopening of the developing neural tube; these range from incidental findings to severe manifestations.
- Cortical development depends on proper orchestration of progenitor cell proliferation in the germinal matrix and migration of progenitors upwards into the developing cortex. Disruption of these processes can alter the size, shape, and organization of the brain.
- Malformations involving the posterior fossa are typically distinct from those which affect the cerebral hemispheres.

Perinatal Brain Injury

Brain injury occurring in the perinatal period is an important cause of childhood-onset neurologic disability. Injuries that occur early in gestation may destroy brain tissue without eliciting the reactive changes observed in adult brain and, therefore, may be difficult to distinguish from malformations.

The term *cerebral palsy* refers to a nonprogressive neurologic motor deficit characterized by combinations of