Hydrocephalus is one of the most common CNS developmental disorders. The incidence of congenital hydrocephalus is estimated as 3 per 1000 live births. Hydrocephalus is defined as an increase in the cerebral spinal fluid (CSF) volume within the ventricular system independent of the actual head circumference.

GENETICS/BASIC DEFECTS

1. Physiology of CSF production and absorption
   a. Production of CSF: by choroid plexus of lateral ventricles
   b. Pathway of CSF flow
      i. From lateral ventricles to third ventricle through foramen of Monro
      ii. From third ventricle to fourth ventricle through aqueduct of Sylvius
      iii. Out of the ventricular system: from fourth ventricle to spinal subarachnoid spaces through foramen of Magendie or to the basal cisterns through two lateral foramina of Luschka
   c. Site of CSF resorption into venous system: primarily through superior sagittal sinus via arachnoid granulations

2. Types and causes of hydrocephalus
   a. Overproduction of CSF: usually caused by choroid plexus tumors (very rare)
   b. Noncommunicating hydrocephalus
      i. Mechanical obstruction within the ventricular system causing impaired CSF absorption
         a) Foramen of Monro
         b) Aqueduct of Sylvius
         c) The fourth ventricle and its outlet channels
      ii. Causes
         a) Tumors
         b) Cysts
         c) Inflammatory scarring
         d) Intraventricular hemorrhage
         e) Rarely genetic disorders
   c. Communicating hydrocephalus
      i. Obstruction distally at the arachnoid granulations causing impaired absorption into blood stream
      ii. Causes
         a) Meningitis
         b) Trauma
         c) Intraventricular hemorrhage
   3. Etiology of congenital hydrocephalus
      a. Tumors blocking CSF pathway
         i. Benign tumors such as choroid plexus papilloma
         ii. Malignant tumors
      b. CNS malformations/syndromes
         i. Congenital atresia of the foramina of Monro, Magendie or Luschka
         ii. Dandy-Walker syndrome
         iii. X-linked hydrocephalus: Bickers-Adams syndrome characterized by:
             a) Stenosis of the aqueduct of Sylvius
             b) Severe mental retardation
             c) An adduction-flexion deformity of the thumb
      v. Chiari II malformation
      vi. Cerebellar agenesis
      vii. Neural tube defects
          a) Meningomyelocele
          b) Encephalocele
      viii. Other Mendelian conditions with congenital hydrocephalus
          a) Walker-Warburg syndrome
          b) Hydroethalus syndrome
          c) Meckel syndrome
          d) Smith-Lemli-Opitz syndrome
   c. Chromosome abnormalities
      i. Trisomy 13
      ii. Trisomy 18
      iii. Trisomy 9 and 9p (mosaic)
      iv. Triploidy
      v. Other aneuploidies
   d. Skeletal dysplasias
      i. Achondroplasia
      ii. Craniosynostosis syndromes such as Crouzon syndrome or Apert syndrome
      iii. Fanconi anemia
      iv. Hurler or Hunter syndromes
   e. Infections
      i. Congenital CMV infection
      ii. Congenital toxoplasmosis
      iii. Congenital rubella infections
      iv. Congenital syphilis
      v. Meningitis
      vi. Ventriculitis
      vii. Abscess
   f. Vascular malformation
   g. In utero intraventricular hemorrhage
   h. Birth trauma
      i. Destructive lesions
         i. Hydranencephaly
         ii. Porencephaly
         iii. Perinatal leukomalacia
   4. Familial (X-linked) aqueductal stenosis (HSAS: hydrocephalus-stenosis of the aqueduct of Sylvius sequence)
      a. X-linked recessive inheritance
      b. Linked to chromosome Xq28
c. Mutations in *LI-CAM*, the major gene for X-linked hydrocephalus (accounting for 7–27% of all male cases)

d. *LI-CAM*, a neuronal surface glycoprotein, has been implicated in neuronal migration and axon fasciculation

5. Traits known to be due to allelic mutations of *LI-CAM*

a. HSAS

b. MASA
   i. Mental retardation
   ii. Aphasia
   iii. Shuffling gait
   iv. Adducted thumbs

c. SP1 (complicated spastic paraparesis, type 1)

d. MR-CT (mental retardation-clasped thumbs)

e. ACC-DCC (agenesis or dysgenesis of the corpus callosum)

6. Pathogenesis of hydrocephalus-induced brain dysfunction: complex
   a. Chronic ischemia in white matter related to changes in intracranial pressure and in the vasculature
   b. Physical damage to periventricular axons with disconnection of neurons
   c. Alterations in the extracellular chemical environment of neurons

**CLINICAL FEATURES**

1. Children <2 years
   a. Relatively benign course because infants can expand their cranium
   b. Early signs
      i. Increased head circumference (macrocephaly)
      ii. Full anterior fontanelle
      iii. Split cranial sutures
      iv. Prominent scalp veins
      v. Poor feeding
      vi. Vomiting
      vii. Irritability
      viii. Reduced activity
      ix. Delay or loss of developmental milestones
      x. Hypertonia
      xi. Hyperreflexia
   c. Late signs
      i. Lethargy
      ii. Sixth cranial nerve palsy
      iii. Limitation of upgaze resulting in a chronic downward deviation of the eyes (sunsetting sign)

2. Children >2 years
   a. Symptoms and signs more related to increased intracranial pressure due to inability of cranium to expand sufficiently to offset the mounting volume of CSF
   b. Headaches
   c. Nausea
   d. Vomiting
   e. Lethargy
   f. Loss of milestones
   g. School performance and behavioral change
   h. Sunsetting of the eyes
   i. Sixth cranial nerve palsy
   j. Papilledema

3. Natural history of untreated childhood hydrocephalus: poor. Handicaps resulting directly from hydrocephalus include the following:
   a. Disturbances in motor abilities, particularly gait
   b. Impaired cognitive development
   c. Hypothalamic dysfunction with delayed growth and short stature

4. X-linked neurological syndromes
   a. HSAS (hydrocephalus-agenesis of the aqueduct of Sylvius sequence)
      i. Hydrocephalus
      ii. Macrocephaly
      iii. Adducted thumbs
      iv. Spasticity
      v. Agenesis of the corpus callosum
      vi. Mental retardation
   b. MASA syndrome
      i. Mental retardation
      ii. Aphasia
      iii. Shuffling gait
      iv. Adducted thumbs
      v. Hydrocephalus

**DIAGNOSTIC INVESTIGATIONS**

1. Fundoscopic examination
   a. Bilateral papilledema secondary to high intracranial pressure
   b. Normal finding in some cases of acute hydrocephalus

2. Lumbar puncture for measuring intracranial pressure
   a. Avoid if an increase in intracranial pressure is suspected due to obstruction since relief of pressure may cause herniation of the brainstem
   b. Perform only after imaging studies ruling out an obstruction

3. TORCH titers on the infant and mother if intrauterine infection is suspected

4. Chromosome analysis in cases of associated multiple congenital anomalies

5. Cranial sonography (provided anterior fontanelle is still open)
   a. Ventriculomegaly
   b. Intraventricular hemorrhage

6. CT scans
   a. Ventriculomegaly
   b. Cerebral edema
   c. Mass lesions
      i. Colloid cyst of the third ventricle
      ii. Thalamic tumor
      iii. Pontine tumor

7. MRI
   a. Ventriculomegaly
   b. Mass lesions
   c. Associated brain anomalies
      i. Agenesis of the corpus callosum
      ii. Chiari malformations
      iii. Disorders of neuronal migration
      iv. Vascular malformations

8. Molecular genetic diagnosis to identify *LICAM* mutations, identified in 22.4% (15/67) of sporadic cases of clinically or prenatally suspected L1-disease
GENETIC COUNSELING

1. Recurrence risk
   a. Patient’s sib
      i. Sporadic: low (4%)  
      ii. Multifactorial trait (e.g., neural tube defect or in female infants with congenital hydrocephalus due to stenosis of the aqueduct of Sylvius): low recurrence risk (5%) for subsequent sibling; 10% risk if there are two affected siblings  
      iii. Autosomal recessive traits (e.g., Dandy-Walker syndrome): 25% affected; 50% carriers; 25% normal  
      iv. X-linked hydrocephalus: 50% of brothers affected and 50% of sisters carriers if the mother is a carrier; negligible in males with “sporadic” hydrocephalus representing a new X-linked mutation  
   b. Patient’s offspring  
      i. Sporadic: low (4%)  
      ii. Multifactorial trait: 3–4.5% recurrence risk  
      iii. Autosomal recessive traits: not increased unless the spouse is a carrier or affected  
      iv. X-linked hydrocephalus: all daughters will be carriers in case of an affected father

2. Prenatal diagnosis
   a. Ultrasoundography  
      i. Fetal ventriculomegaly  
      ii. Additional CNS malformations  
      iii. Extracerebral malformations  
   b. Sonographic findings in HSAS or MASA syndromes  
      i. Male fetus  
      ii. Hydrocephalus  
      iii. Hypoplasia or agenesis of the corpus callosum  
      iv. Bilateral adducted thumbs  
   c. Amniocentesis  
      i. α-fetoprotein and cholinesterase determination from amniotic fluid for neural tube defects  
      ii. Chromosome analysis for suspected chromosomal disorder  
   d. Molecular genetic diagnosis  
      i. DNA diagnosis often requested in families with ‘isolated’ hydrocephalus case due to high rate of de novo mutations, small family size, and the improved sensitivity of prenatal ultrasound scanning  
      ii. Molecular diagnosis of prenatally suspected L1 spectrum disorders, even in cases without positive family history

3. Management
   a. Folic acid intake before and during the first trimester reduces the incidence of neural tube defects, thereby reducing the incidence of hydrocephalus  
   b. Shunting CSF from the ventricles  
      i. Ventriculoperitoneal shunting (VP) devices with pressure-controlled valves under the scalp close to the burr hole  
      ii. Ventriculopleural shunt  
      iii. Ventriculoatrial shunt  
      iv. Frontal or parietal ventriculostomy  
      v. Does not completely reverse the pathologic alterations in the brain and, unfortunately, treatment by shunting is associated with frequent complications  
   c. Major complication associated with shunt treatment: 81% of children with shunts suffer at least one and usually several malfunctions necessitating hospitalization  
      i. Shunt obstruction  
      ii. Valve malfunction  
      iii. Disconnection  
      iv. Hematoma  
      v. Overdrainage  
      vi. Outgrown shunt  
      vii. Shunt fracture  
      viii. Shunt-related infections, most often caused by staphylococcus aureus, with unexplained fever or frank meningitis  
      ix. Signs of increased intracranial pressure with headache, lethargy, and vomiting  
   x. Abdominal complications  
      a) Peritonitis  
      b) Perforation of an abdominal organ  
      c) Peritoneal cysts  
      d) Development of hydroceles in boys  
   xi. Seizures  
   xii. Allergic reaction to material

REFERENCES

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Pudenz RH: The surgical treatment of hydrocephalus—an historical review.
**Fig. 1.** A child with hydrocephalus which was shunted.

**Fig. 2.** An adult with severe congenital hydrocephalus and mental retardation.

**Fig. 3.** Prenatal ultrasound at 33 weeks showing markedly dilated lateral ventricles

**Fig. 4.** CT scan of the head of a patient showing ventriculomegaly with congenital hydrocephalus.

**Fig. 5.** CT scan of the head of a patient after ventriculoperitoneal shunt.
Fig. 6. MRI of the brain of a patient showing hydrocephalus due to aqueduct stenosis.

Fig. 7. CT scans of the brain of a patient showing dilatation of the lateral ventricles with stretching of corpus callosum and cortical atrophy.