

## Hydrocephalus

Hydrocephalus is an excessive accumulation of cerebrospinal fluid (CSF) within the cranial cavity. CSF is produced mainly by modified ependymal cells, the thin epithelial membrane lining the ventricular system, in the choroid plexus. Thirty to fifty percent of CSF is produced around blood vessels. CSF is produced at a rate of five hundred milliliters per day but the brain only utilizes one hundred and thirty five to one hundred and fifty milliliters. CSF acts as a cushion to the brain as it keeps the brain tissue buoyant, delivers nutrients to the brain, removes wastes, and compensates for any fluctuations of intracranial blood volume.

Hydrocephalus dates back to 5th century B.C., when Hippocrates, the father of medicine, was the first to record cases of hydrocephalus and attempt treatment. About two hundred years later Galen formed his own theory about the cause of the condition, a theory that only led to misdiagnoses and mistreatments. He believed that the brain ventricles were connected by the soul and purified themselves. Vesalius (1514-1564), at the University of Padua, observed that water gathered in the brain ventricles of patients. In line with Galen's theory he believed that CSF was the spirit that gave the body energy.

The first to theorize that CSF was produced in the choroid plexuses was Thomas Willis in 1664. Robert Whytt wrote the *Observations on the Dropsy in the Brain* in which he documented cases of hydrocephalus caused by meningitis thus describing it as a disease.

The accumulation that causes hydrocephalus can be attributed to an imbalance between the production and absorption of CSF or an impediment of the CSF flow through the ventricular system. Unobstructed CSF fluid flows from the choroid plexus in the ventricles, through the inter-ventricular foramina that connects lateral ventricles to the third ventricle, through the cerebral aqueduct connecting to the fourth ventricle, and exits through one median aperture and two lateral apertures. The fluid then flows down the spinal cord, passing over the cerebral hemispheres. A disruption in this normal flow will result in an over-accumulation of CSF fluid in the brain.

Deciphering the circulation of CSF was central to understanding much of the physiology of the disease. Magendie in 1825 wrote a paper describing the cycle of CSF from production to absorption. The introduction of radioactive tracers in the 20th century allowed for a more detailed picture of the circulation of CSF. Milhorat dispelled common belief that it took months for hydrocephalus to develop when his rhesus monkeys developed hydrocephalus within an hour.

Robert Whytt observed that hydrocephalus was an acquired or congenital disease. Congenital cases of hydrocephalus occur three times more often than acquired ones, with three to four cases every one thousand births. Congenital cases can originate from events during fetal development or from genetic abnormalities. Pre-natal cases can occur from cerebral malformations, post infection, vascular issues, cranial deformities, metabolic issues, or mass lesions. Aqueductal stenosis, a cerebral malformation, occurs when the narrow channel that passes through the midbrain and connects two ventricles is blocked. Causes of aqueductal stenosis include congenital, post-infectious, post-hemorrhage, tumor in the midbrain, and unknown causes. Dandy-Walker syndrome, another cerebral

malformation, consists of a cyst in the lower portion of the brain and a deformity in the cerebellum. Arnold-Chiari syndrome, a cerebral malformation, is a defect in the formation of the brainstem and cerebellum, which can impede the flow of CSF from the brain into the spinal canal.

Infections including cytomegalovirus, toxoplasmosis, meningitis, and encephalitis can cause post-infectious hydrocephalus. About one percent of babies born in the US have congenital cytomegalovirus, commonly known as the Human Herpesvirus 5. Vascular causes of hydrocephalus include intrauterine cerebral hemorrhage, which occurs within the brain tissue itself. Cranial deformities that may cause hydrocephalus include osteogenesis imperfecta, achondroplasia, craniofacial dysmorphism, and platybasia. Osteogenesis imperfecta, commonly known as Brittle Bone Disease, is caused by the body's inability to make nondefective connective tissue. Achondroplasia, the cause of dwarfism, is an autosomal dominant genetic disorder that results from a mutation in the fibroblast growth factor receptor on gene 3. Craniofacial dysmorphism is a genetic disorder that causes the premature closing of the skull bones and craniofacial abnormalities. Platybasia is a spinal disease caused by an incorrect formation between the occipital bone and the cervical spine. Mass lesions including tumors and arachnoid cysts can lead to hydrocephalus. Arachnoid cysts are formations of CSF encapsulated by collagen and arachnoidal cells. The cysts generally develop between the brain and the cranial base or on the arachnoid membrane.

Post-natal cases of hydrocephalus most often occur as a result of trauma, intracranial hemorrhage, infection or tumors. Infections including bacterial meningitis, ventriculitis, and cerebral abscess can be causing factors. Bacterial meningitis may cause the brain tissue to swell and in children under the age of two years, this may cause the fontanelles to bulge. The bulging fontanelles, or soft spots, may obstruct the flow of CSF around the brain, causing hydrocephalus. Ventriculitis is an inflammation of the cerebral ventricles caused by group B streptococci. A cerebral abscess is caused by an inflammation and the collection of infected material within the brain tissue. The infected material comes from localized areas, such as an ear infection, sinus infection, epidural abscess or dental abscess or a remote source, such as a heart or kidney problem. The symptoms of a brain abscess are caused by the increased intracranial pressure and the brain tissue damage. Symptoms of the increased pressure present as headache, vomiting, confusion and coma, while the symptoms of brain tissue damage present as hemiparesis and aphasia.

Tumors including glioma, teratoma, and choroid plexus papilloma can also cause postnatal hydrocephalus. A glioma is a cancer that originates from glial cells in the brain or spine. Symptoms of brain gliomas present as headaches, nausea, vomiting, seizures and cranial nerve disorder. Symptoms of spine gliomas present as pain, weakness and numbness in the extremities. Teratoma is a germ cell made up of different types of tissue from one or more of the three germ cell layers. It is rare that a teratoma arises in the head or neck region. When one does arise, it is usually attributed to Rathke's pouch remnants. Choroid plexus papilloma (CPP) are neoplasms, an abnormal mass of tissue, of the choroid plexus. The choroid plexus is a structure made from the tufts of the villi that produce cerebrospinal fluid within the ventricular system. The tumor cells secrete CSF and cause most of the symptoms related to CPP.

Symptoms of hydrocephalus in postnatal babies present as macrocephaly, a condition where the head is abnormally large, dilated scalp veins, bulging anterior fontanelle, vomiting, irritability, variable consciousness, retraction of the head and neck and abnormal skull percussion note. Before making a diagnosis of hydrocephalus, it is important to rule out some other possible causes of increased intracranial pressure in postnatal babies. These include meningitis, cerebral abscess and tumor without hydrocephalus, encephalopathies, and intracranial hematoma. A cranial ultrasound is an efficient diagnostic tool to determine the cause of the raised intracranial pressure.

Adults may experience different symptoms than young children as an adult's skull cannot expand to house the accumulation of CSF. Symptoms may present as an initial headache, vomiting, nausea, papilledema, double vision, balance and coordination problems, urinary incontinence, slowing of developmental progress, lethargy, drowsiness, memory loss and changes in personality.

As the understanding of hydrocephalus grew, so did attempts at viable treatments. Poor understanding of the disease throughout history led to many failed treatments usually resulting in the death of patients. Bloodletting and skull trephination was commonly attempted. Other attempted treatments included lumbar puncture, continuous draining of the ventricles, and perforation of the corpus callosum to drain CSF in subdural spaces. Heile was the first to drain CSF into the urinary system. Most treatments like bilateral choroid plexectomy, which aimed to reduce the amount of CSF produced by the choroid plexus, were largely unsuccessful. Treatments began to focus on diverting the flow of CSF to other parts of the body through the usage of shunts. The most common locations for the shunts to empty out have become the right atrial and peritoneal spaces. CSF drainage is now regulated by a valve system preventing over drainage and regulating CSF flow rates.

There are both non-operative and operative treatments available for hydrocephalus. Non-operative treatments include CSF drainage by drugs, lumbar puncture, and head wrapping. Acetazolamide is a drug used in premature babies with post-hemorrhagic hydrocephalus. It works as a carbonic anhydrase inhibitor with a starting dose of twenty five milligrams two to three times per day. The drug works to delay the time until an operative treatment is necessary. Isosorbide works by reducing the rate of production of CSF via osmotic gradient. It is most successful in patients with congenital hydrocephalus associated with myelomeningocele, a condition where the spinal cord and backbone do not close before birth. Isosorbide has been high ineffective in babies with post-hemorrhagic and post-meningitic hydrocephalus. CSF drainage by lumbar puncture is used along with acetazolamide in post-hemorrhagic hydrocephalus. This procedure is used as an emergency treatment for the rapid decrease of intracranial pressure.

Operative treatments of hydrocephalus include external ventricular drainage, reservoir and endoscopic ventriculostomy, and ventricular shunts. External ventricular drainage is only used when the patient is not a candidate for internal shunt insertion because of other medical conditions including an untreated bacterial infection or extreme contamination of the blood. External ventricular drainage is also useful in treating ventricular shunt infection. Although a reservoir ventriculostomy avoids repeated punctures, it only offers temporary relief of intracranial pressure. The ventriculostomy is usually inserted into the frontal lobe and the CSF is aspirated. Endoscopic

ventriculostomy is a prime contender for the treatment of hydrocephalus for two main reasons. First, forty to sixty percent of hydrocephalus cases can be treated endoscopically. Secondly, the advancement of the endoscope has made endoscopic surgery highly successful. It seems the most promising candidates for the surgery are babies with aqueduct stenosis and babies with arachnoid cysts in their ventricular systems. Approximately forty-eight hours after surgery, a lumbar puncture is performed to encourage CSF flow through the ventriculostomy.

Hydrocephalus is most often treated by inserting a shunt system, which sends CSF fluid to another part of the body for absorption. The risks associated with intravascular shunts too greatly outweigh the rewards and thus this path is no longer in use. The dangers associated with intravascular shunts include pulmonary embolism, perforation of the heart, chronic bacteraemia, septicaemia, shunt nephritis, and superior and inferior cava occlusion. The preferred path is now the ventriculo-peritoneal shunt. Either a frontal or lambdoid (posterior) entry point is used for the shunt. The lambdoid is preferred because the low amount of exposed scalp during the surgery greatly reduces the change of epilepsy. Some complications of ventricular shunting include obstruction, blockage, acute and chronic infection, migration, disconnection, intracranial hemorrhage, epilepsy, slit-ventricle syndrome and trapped ventricles. Slit-ventricle syndrome refers to the very small "slit" like ventricles seen on the MRI scan. Trapped ventricles may require additional shunts and it is advised that a separate system be used rather than trying to combine the new shunt with the old shunt. Shunt infection symptoms present as fever, irritability, inflammation along the line of the catheter, or recurrence of increased intracranial pressure. While disconnected, blocked, and migrated shunts require minor surgery, loose ventricular catheters can be fixed endoscopically.

Another shunting procedure, third ventriculostomy, is used to treat a small number of patients with hydrocephalus. In this procedure, a neuroendoscope allows the surgeon to view the ventricular surface. A tool on the neuroendoscope then makes a tiny hole on the floor of the third ventricle, which allows the CSF to flow around the obstruction to a site of re-absorption.

The prognosis for those with hydrocephalus is difficult to predict, as it depends on the presence of associated disorders, the success of treatment, and the timelines of the diagnosis. It is not well understood the degree to which the decrease of intracranial pressure can reverse the damage to the brain. Many children who have hydrocephalus benefit greatly from rehabilitation therapies. Progressive hydrocephalus left untreated is generally fatal. In the study Clinical relevance of hydrocephalus in bacterial meningitis in adults conducted by Wang and Chang (2004) in Taiwan shows that of the twenty-eight patients with hydrocephalus secondary to bacterial meningitis, only fourteen survived. Research for the prevention, treatment, and a possible cure of hydrocephalus is being conducted at The National Institute of Neurological Disorders and Stroke, NIH sponsored labs, and other prestigious universities and medical centers around the world.