Pediatric Hydrocephalus; A Statistical and Historical Approach

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Results: The presence of congenital malformations at hospital admission was the strongest predictor of hydrocephalus followed by intracerebral tumor. The most affected children were still in neonatal period.

Conclusion: using clinical data and empirical modelling strategy, we were able to categorize and analyse the most common background diseases which cause hydrocephalus.

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I. ANATOMICAL ASPECTS

a) Anatomy: Ventricular system of the Brain

The ventricular system of the brain consists of a continuous communicating system of five fluid-filled cavities whose inner walls are lined with ependymal cells. Each ventricle possesses a choroid plexus. CSF is produced by modified ependymal cells of the choroid plexus found in all components of the ventricular system except for the cerebral aqueduct and the occipital and frontal horns of the lateral ventricle. The cavities are numbered and comprise the cerebral aqueduct, the unpaired 3rd and 4th ventricles and paired lateral ventricles.

The 4th ventricle is a roughly pyramid-shaped cavity that is bounded ventrally by the medulla and pons and its floor is called the rhomboid fossa. The roof of the ventricle is incomplete and is formed from the anterior medullary velum and the posterior medullary velum. The apex passes upward into the cerebellum at a point called the apex or fagtigium. Cerebrospinal fluid (CSF) can flow from the 4th ventricle into the subarachnoidal space through two apertures. The foramen of Luschka is an opening of the lateral recess into the subarachnoidal space in the region of cerebellar flocculus. There is a more important aperture, the foramen of Magendie, which lies caudally in the ventricular roof. Most of CSF outflow from the ventricle occurs via this aperture.

From the 4th ventricle a narrow channel called the cerebral aqueduct runs into the 3rd ventricle. This is a relatively narrow channel that runs between the two medial walls of the diencephalon. The roof of the ventricle consists of a tela choroidea and a lining of ependyma and pial cells, from which a choroid plexus protrudes into the cavity of the ventricle. The medial walls of the paired thalami from the most of the walls of the 3rd ventricle, and the hypothalamus supplies the floor and the basal part of the lateral walls. Rostrally, the boundary of the 3rd ventricle defined by the lamina terminalis and the anterior comissure. At the rostral end there is a small extension of the ventricle called the optic recess, and there is a small downward extension called the infundibular recess where the infundibulum extends downwards towards the pituitary gland.

The 3rd ventricle communicates with the lateral ventricles through two interventricular foramina, or foramina of Monro. These are apertures between the anterior end of the thalamus and the column of the fornix. The lateral ventricles are the largest of the ventricles, and have a pared, irregular appearance. On each side there are anterior and posterior horns and a central body. The roof of the anterior horns is formed by the corpus callosum and its medial wall by the septum pellucidum. Each lateral wall and the floor is supplied by the head of the caudate nucleus. The body extends rostrally from the interventricular foramina to the splenium of the corpus callosum. The corpus callosum forms the roof of the body portion, and the floor is contributed to by a number of structures, these being from lateral to medial the caudate nucleus, vena terminalis, stria terminalis, thalamus, choroid plexus and fornix. The posterior horn extends caudally into the occipital lobe; its roof is formed by part of corpus callosum.

b) Physiology of Cerebrospinal Fluid

Cerebrospinal fluid (CSF) appears in response to degeneration of primitive mesenchyme (meninx primitive) that surrounds the brain. Though the exact

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timing of CSF formation is not understood, CSF circulation from the ventricles to the subarachnoid space does not occur until after formation of the 4th ventricle outlet foramina at the 9th to 10 th week of gestation.

c) Flow of Cerebrospinal Fluid

Approximately 60% of CSF is produced by the choroid plexus. The rate of the CSF volume in a neonate is approximately 50 ml.

The cerebrospinal fluid (CSF) is an ultrafiltrate of plasma actively secreted into the cerebral ventricles by the choroid plexus, a highly vascularised and perfused lining of the ventricles. Average blood flow through the cerebral circulation is about 0.5 ml/min/g of brain tissue, and flow to the choroid plexus is about ten times higher. The choroid plexus supplies at least 75% of the CSF, which is also derived from the interstitial fluid (ISF), which is produced by the endothelial cells of the blood-brain barrier in the choroid plexus. The transformed ISF is pumped into the subarachnoid space as CSF across the pial-glial membranes. CSF passes through the ventricles and into the subarachnoid space through the foramina of Magendie and Luschka. A 3rd source of water for CSF is provided by the complete oxidation of glucose by brain parenchymal cells. The subarachnoid space is a cavity between the arachnoid membrane and pia mater surrounding the brain and spinal cord. CSF flows through the cisternae and trabeculae of the subarachnoid space, which, when filled with CSF, provides buoyancy for the brain, effectively reducing its weight from around 1400 g to about 45 g when it is suspended in CSF. The trabeculae are delicate columns of tissue bridges tethered to the arachnoid mater, which strengthen the subarachnoid space and this provide stable support for the brain within its fluid cushion of CSF.

CSF flows into the ventricles and through the subarachnoid space, driven by two forces. There is (i) the gradient set up between the point of secretion of CSF into the ventricles from the choroid plexus to the point where CSF drains through the arachnoid villi into the venous sinuses, and (ii) the mechanical propulsion provided by the pulsing of the cerebral arteries in the subarachnoid space and the movement of the trabecular tethers. CSF is propelled through the choroid plexus into the ventricles with a driving pressure of about 15 cm of water. CSF exits the subarachnoid space back into the venous system through the arachnoid villi by means of a hydrostatic pressure-dependent mechanism.

The sites of CSF absorption remain controversial. It is widely accepted that arachnoid villi are the major sites of absorption. Various studies have also suggested that a portion of CSF drains through the perivascular and perineural spaces into the lymphatics or through the capillaries of the brain and the spinal cord.

The flow of CSF must be regulated to prevent the build-up of excess pressure on brain tissue. This is achieved through the regulation of water flow across the blood-brain barrier, both at the level of the ISF and the level of glial and neuronal and intracellular fluid. ISF constitutes about 15-20% of the total tissue weight, and is the principal source of extracellular fluid in the brain. Cerebral capillary walls are less permeable than those of peripheral capillaries, and the flow across into the CSF is balanced by the return of CSF to the plasma compartment. CSF flows through the ventricles and the subarachnoid space at the rate of about 0.3 ml per minute. Neurons and glia contribute to the maintenance of normal hydrostatic pressures through the activity of their membrane ion transporters. CSF flow is turned over about three times in 24 hours. CSF provides not only a buffering and cushioning system for brain, but also carries many substances such as trophic factors and nutrients.

d) Blood-Brain Barrier

The Blood-brain barrier is a collective term referring to a complex system of metabolic, physical, and transport filters or barriers that control access of blood-borne chemicals to the brain. These barriers maintain an optimal and stable physico-chemical environment within which the CNS can operate. The blood-brain barrier consists, broadly, of two main compartments: the choroid plexus, and the CNS capillary bed.

The choroid plexus serves as a blood-CSF barrier through the specialized structure of ependymal cell lining of the plexus. The endothelial cells are bonded by thight junctions that bar the passage of high molecular weight substances. This is what is generally meant by the blood-brain barrier. Unlike the capillaries of the general circulation, choroid plexus cells have no intercellular pores and fenestrations. Instead, there are numerous microvilli, and the cells contain several enzymes that transport ions, such as NA+ and K+, and metabolites, such as glucose.

The endothelial cells of brain capillaries lie on a basement membrane, which is surrounded by end feet of the astrocytes. Endothelial cells, like those of the choroid plexus, are joined by tight junctions and possess the same ion and metabolite transport systems. There are very few pinocytotic ventricles in these cells. And no fenestrations. The brain capillary bed is enormous, and has been estimated to cover the area of a tennis court. The CNS capillary bed is also sometimes referred to as the blood-ECF (extracellular fluid) barrier, while the choroidal plexus is the blood-CSF barrier.

The tight junctions may break down or be breached under certain pathological conditions. Tumor

development may be accompanied by the formation of new capillaries at the site of lesion. These capillaries are not closely apposed to astrocytes, and they have intercellular pores and fenestrations that permit substances to pass through that are not normally allowed. This is of diagnostic value; if a tumor is suspected, the patient is injected with an amino acid that penetrates to the tumor and can be visualized there by scanning technics. Thight junctions may be forced open in patients with hypertension, leading to cerebral edema and headaches, and, in severe cases coma.

The brain is not uniformly impermeable to blood-borne components. Circulating macromolecules can breach the blood-brain barrier at the circumventricular organs. These are seven areas at the ependymal border of the 3rd and 4th ventricles, where hydrophilic solutes can pass through capillaries. The pineal body makes melatonin, and is thought to be involved in certain brain rhythms. The area postrema, which lies at the caudal end of the 4th ventricle, is in close contact with the nucleus of the tractus solitarius. This site allows passage of chemical stimuli that trigger, for example, the vomiting reflex. The organum vasculosum of the lamina terminalis lies in the wall of the 3rd ventricle, and seems to mediate water balance through vasopressin. The subfornical organ in the dorsal wall of the 3rd ventricle mediates drinking behaviour via angiotensins signals.

II. Embryology

The structures of the ventricular system embryologically deriver from the centre of the neural tube (the neural canal), between the 4th and 8th weeks. Within each of the brain vesicles the neural canal expands into a cavity termed the primitive ventricle. In the rhombencephalon this will become the 4th ventricle and in the mesencephalic cavity becomes the cerebral aqueduct (aqueduct of sylvius). The 3rd ventricle forms within the diencephalon, while paired lateral ventricles form within the cerebral hemispheres.

III. Hydrocephalus; Definition and Background

The term hydrocephalus has a Greek origin and literally means 'water on the brain'. Hydrocephalus is one of the most common sequelae of any insult to a child's CNS. It occurs almost in 1 in 2000 live births, and is associated with one third of all CNS malformations.

IV. Historical Sketch of Brain Architecture

The 160- year history of research on the brain cortex has been well described by several authors (Soury 1899, Scarff 1940, Rasmussen 1947, Lorente de No` 1949, Walker 1957, Creuzfeld 1983,…). According to Clarke and Dewhurst 'The story of discovery of cerebral architecture is of particular fascination and relevance because it not only reveals a sequence of intriguing notions, but also contributes to our understanding and appreciation of the modern view' (fig. 1).

V. Historical Approach

Increased intracerebral pressure and its manifestation in children was already known in ancient time and can lead to a fatal course which has been described as early as more than 4000 years ago. Richard (16) studied the published literature about pathologic findings in skeletons dating 2500 BC, finds numerous hydrocephalic skulls. The most famous of these is may be that of Pharaoh Ikhnaton (13).

The first scientific description of hydrocephalus is assigned to Hippocrates. He describes hydrocephalus symptoms as headache, visual disturbance and nausea and explains the situation as a liquefaction of the brain caused by epileptic insults.

The first precise anatomic detail of cerebrospinal fluid and especially of the median aperture of the fourth ventricle had been described by Claudius Galen of Pergamon (130-200 AD), using animal models. Since the seminal work of Galen of Pergamum, cerebral liquor dynamics have been object to concentrated medical research [2]. According to Galen theory the CSF wouldn't flow through the pituitary or cribriform plate into the oral or nasal cavity.

The first anatomical-pathological classification of intracerebral fluid collections is performed by Galen:

"There are four kinds of hydrocephalus: between the brain and the meninges, between the meninges and the bone, between the bone and pericranium, and between the bone and the skin. We treat hydrocephalus between the skin and the pericranium with two or three free incisions; that between the meninges and the brain is incurable" (translated by Quin 1814)(17).

Later on, during the Renaissance was the dissection of human body for the first time allowed and this led to applying and observating anatomy and of course opened a new perspective to pathological anatomy of human being.

The first illustration and 3D model of the ventricular system drawn from a dissected human brain appeared in 1505-1510 by Leonardo da Vinci. Leonardo, like all physicians until the nineteenth century, had no knowledge of the outlets of the fourth ventricle.

Vesalius's epochal achievement came in 1551 with the first scientific description of hydrocephalus based on a human necropsy (second edition of *De Humani Corporis Fabrica Libri Septem,* 1555): "I observed [a disease] in Augsburg in a 2-year-old girl whose head had grown in 7 months more or less to a

size that was not surpassed in bulk by any man's head I ever saw. This disease was what ancients called *hydrocephalus*, from water which is stored in the head and gradually collects. In this girl's case, however, the water had not collected between the skull and its outer, surrounding membrane or the skin, where doctors' books teach that water is deposited in other cases, but in the right and left ventricles of the cavity of the brain itself. The breadth of these cavities had so increased and the brain itself was so distended that they contained about 9 pounds of water, or 3 Augsburg wine measures, so help me God (17)... Just as the brain itself at the vertex was membrane-like in thinness, indistinguishable from its own membranous covering, so was the skull membranous" (15).

"... the base of the skull was in correct proportion to that of the young child before her head took on abnormal proportions. Nevertheless, the cerebellum and entire base of the skull were in their natural state; and so also were the extensions of the nerves". "...found no water in any other places but the ventricles of the brain, which were enlarged to the extent that I have stated" [17]. These experiments ended the more than 2000-year-old misinterpretation of hydrocephalus as a collection of fluid outside the brain and made the way free for further observation of the circulation of the CSF and its pathophysiology.

Vesalius examined the patient while she was still alive and, was surprised to observe "that the girl had full use of all her senses," and that "such a great force of water had been accumulated for so long in the ventricles of the brain without more extensive symptoms" [18].

Pacchioni (1665–1726) described in 1701 the arachnoid granulations, but still assumed they were a site of CSF secretion. As for the resorption of CSF, he supposed that the brain was surrounded by a rhythmically contracting muscle propelling the "lymph" of the brain into the venous sinuses by way of "lymph nodes" [12]. Fantoni discovered the resorptive function of Pacchionian granulations and the Flow of CSF the venous sinuses in 1738.

On the basis of autopsy observations published Giovanni Battista Morgagni (1682–1771) several cases of hydrocephalus. In one case he described low lying cerebellar tonsils, what we know as Arnold-Chiari malformation.

Albrecht von Haller (1708–1777) discovered the foramina of Luschka and, published in 1747, was the first to present as a hypothesis the modern theory of CSF circulation [17, 18].

Appearing in 1842, Francois Magendie's (1783–1855) anatomical studies of the pachymeninges in the posterior fossa and spinal canal contained a new description of the caudal opening of the fourth ventricle, which had been discovered by Galen but later went unrecognized by Vesalius, Willis, and others. He proposed a "reverse theory" of CSF circulation in which fluid was produced at the brain surface, flowed into the ventricles through the foramen of Magendie, and was resorbed by the choroid plexus. Modern medical-historical research thus tends to regard him as an obstacle to progress rather than a contributor [18]. Nonetheless, it is to him that we owe the hypothesis that occluded CSF pathways can cause hydrocephalus [19], which was definitively proven by Hilten in 1879. He was also, in 1841, the first to measure CSF pressure, employing suboccipital puncture in a dog.

Robert Whytt of Edinburgh (1714-1766) was the first who performed systematic, clinical neurological experiments on hydrocephalus patients. In 1768 he described differences in the clinical course of the disease that depend on whether the infant patient had open or closed sutures. Diaphany, the transillumination of a fluid-filled skull when the cortical mantle is extremely attenuated, was discovered by Bright in 1831 [34], and the "cracked pot sound" by Macewen in 1893 [1]. Many early reports of ventricular puncture contained rough estimates of CSF pressure, but Quincke was the first to measure it precisely in 1891 with a water column manometer in both the ventricle and the spinal sac [14]. Walter Dandy and Kenneth Blackfan of the Johns Hopkins Hospital (Baltimore) presented the first animal model of hydrocephalus in 1913 [11] by blocking the aqueducts of dogs with small pieces of cotton. They went on to occlude selectively the right and left foramina of Monro. Dandy also demonstrated that animals subjected to such occlusions would not develop hydrocephalus if the choroid plexus had been excised [10]. Further experimental landmark studies were made by Weed in the 1920s and by Bering, Sato, Davson, Pappenheimer, Rubin, Welch, Milhorat, and Raimondi in the 1960s and 1970s.

By 1970, various linear measures have been used; however these often did not correlate well with changes in volume [3, 4]. Modern volumetric methods based on computed tomography emerged with a series of publications in 1978 [5–7]. At the same time, mathematical models of the cerebrospinal fluid system have been developed to study intracranial liquor kinetics [8]. In the late 1980s, first quantitative studies based on magnetic resonance imaging (MRI) were published. An elegant method to derive separate measures for intracranial and ventricular CSF volumes from two sagittal MR projection images was proposed by Grant et al. [2, 9].

VI. Mechanisms of Hydrocephalus

1. *Classic Bulk Flow Theory*

According to this model, hydrocephalus occurs as a result of imbalance between the production and absorption of CSF. It can result from increase in CSF flow or decreased CSF uptake.

2. *Hemodynamic Model For CSF Circulation*

Greitz et al have proposed a hemodynamic model for CSF circulation and a new view on the pathogenesis of hydrocephalus. The model is based on the concept that the absorption of CSF occurs through the capillaries in the CNS rather than arachnoid granulations and villi. They postulated that, in systole, there is expansion of the intracranial arteries, which increases ICP. In diastole, there is inflow of CSF from the spinal canal, causing elevation of pressure in the subarachnoidal space. Therefore, there is increased pressure in the CSF spaces during the entire cardiac cycle, which in turn compresses the venous outlets, causing increase in outlet resistance and venous counter pressure. This pressure is necessary to keep the intracerebral veins sufficiently distended to accommodate the normal cerebral flow.

The traditional communicating hydrocephalus is renamed restricted arterial pressure hydrocephalus in the Greitz model. Obstructive hydrocephalus has been termed venous congestion hydrocephalus.

Classification of Hydrocephalus in Newborns and Infants:

Infants with ventriculomegaly typically present with macrocephaly. It is critical and often difficult to differentiate between ventriculomegaly caused by communicating hydrocephalus, which requires shunting, and ventriculomegaly related to benign extra-axial fluid of infancy, which does not require intervention. These babies should therefore be assessed clinically for other signs of elevated ICP, such as bulging fontanelles and sutural diastasis. Infants with macrocephaly should be evaluated with imaging to assess for ventricular dilatation.

Because of the inability of the cranium to expand as quickly as in infants, older children with hydrocephalus have a more acute presentation. They may have the classical triad of headache, vomiting, and lethargy. Children developing chronic hydrocephalus as a result of slowly expanding lesions typically present with persistent morning headache, and intermittent vomiting. Papilledema is often observed. Pyramidal tract sign, more severe in lower extremities, are encountered. In general hydrocephalus can be divided into two main functional groups:

1. obstructive (non-communicating): block proximal to the arachnoid granulations. On CT or MR shows a enlargement of ventricles proximal to block.
2. commuicating (non-obstructive): CSF circulation blocked at level of arachnoid granulations.
3. *Hydrocephalus ex vacuo* Ventriculomegaly associated with increased ICP is termed hydrocephalus. It is crucial to differentiate it from ventriculomegaly due to loss of cerebral tissue (cerebral atrophy), accelerated by certain disease processes. It is not really true hydrocephalus.

4. *CT/ MR criteria of hydrocephalus* Computer tomography, and nowadays increasingly MR, are primary modalities to quantitatively define hydrocephalus. Some are presented here.

VII. Hydrostatic Hydrocephalus

Hydrostatic hydrocephalus is suggested when either (2)

A. the size of both temporal horns is $>= 2mm$ in width, and the sylvian and interhemispheric fissures and cerebral sulci are not visible

or

B. both TH are $>= 2mm$, and the ratio FH/ID > 0.5 (where FH is the largest width of the frontal horns, and ID is the internal diameter from inner-table to inner-table at this level).

Other features suggestive of hydrostatic hydrocephalus are:

1. periventricular low density on CT, or periventricular high intensity signal on T2 W on MR suggesting transependymal absorption or migration of CSF
2. ballooning of frontal horns of lateral ventricles ("Mickey Mouse" ventricles) and 3rd ventricle
3. used alone, the ratio FH/ID:

   < 40%   normal
   40-50%   borderline
   >50%   suggests hydrocephalus

4. Evan's ratio: ratio of FH to maximal biparietal diameter > 30%
5. sagittal MR may show upward bowing of the corpus callosum

VIII. Hydranencephaly

A post-neurulation defect. Total or near-total absence of the cerebrum, with intact cranial vault and meninges, the intracranial cavity being filled with CSF. There is usually progressive macrocrania, but head size may be normal specially at birth, occasionally microcephaly may occur. Facial dysmorphism is rare.

May be due to a variety of causes, the most commonly cited is bilateral internal carotid artery infarcts (which results in absence of brain tissue supplied by the anterior and middle cerebral arteries with preservation in the distribution of the posterior cerebral artery). May also be due to infection (congenital or neonatal herpes, toxoplasmosis, equine virus).

Less affected infants may appear normal at birth, but are often hyper irritable and retain primitive reflexes (Moro, grasp, and stepping reflex) beyond 6 month.

Progressive enlargement of CSF spaces may occur which can mimic severe hydrocephalus. It is critical to differentiate the two since hydrocephalus may be treated by shunting which may produce some re-expansion of the cortical mantle. In case of Hydranencephaly shunting my be performed to control head size, but unlike the case with maximal

hydrocephalus, there is no restitution of the cerebral mantle.

IX. External Hydrocephalus

Key features are

- enlarged subarachnoid spaces over the frontal poles in the first year of life
- may be distinguished from SDH by the "cortical vein sign"
- ventricles are normal or minimally enlarged
- usually resolves spontaneously by 2 years of age

Enlarged subarachnoid space seen in infancy (primarily in the first year of life) usually accompanied by abnormally increasing head size with normal or mildly dilated ventricles. There are often enlarged basal cisterns and widening of the anterior interhemispheric fissure. No other symptoms or signs should be present. Etiology is unclear, but a defect in CSF resorption is postulated. External hydrocephalus may be a variant of communicating hydrocephalus. No predisposing factor may be found in some cases, although may be associated with some craniosynostoses (especially plagiocephaly) or it may follow interventricular hemorrhage or superior vena cava obstruction.

X. Arrested Hydrocephalus

Most clinicians use these terms to refer to a situation where there is no progression deleterious sequelae due to hydrocephalus that would require the presence of a CSF shunt. Patients and families should be advised to seek medical attention if they develop symptoms of intracranial hypertension.
Arrested hydrocephalus satisfies the following criteria in the absence of a CSF shunt:
1. near normal ventricular size
2. normal head growth curve
3. continued psychomotor development

a) Entrapped fourth ventricle

Isolated or entrapped fourth ventricle, as the name implies, is a 4th ventricle that neither communicates with the 3rd ventricle (through the sylvian aqueduct) nor with the basal cisterns (through the foramina of Luschka or Magendie). Usually seen with chronic shunting of the lateral ventricles, especially with post-infectious hydrocephalus or in those with repeated shunt infections. Possibly as a result of adhesions forming from prolonged apposition of the ependymal lining of the aqueduct due to the diversion of CSF through the shunt. The choroid plexus of the 4th ventricle continues to produce CSF which enlarges the ventricle when there is 4th ventricular outlet obstruction at the level of the arachnoid granulations.

XI. Etiologies of Hydrocephalus

Hydrocephalus is either due to subnormal CSF reabsorption, or rarely to CSF overproduction (as with some choroid plexus papillomas; even here, reabsorption is probably defective in some as normal individuals could probably tolerate the slightly elevated CSF production rate of the tumor).

*congenital

- Chiari Type 1 malformation: hydrocephalus may occur with 4th ventricle outlet obstruction
- Chiari Type 2 malformation and/or myelomeningocele
- Primary or secondary aqueductal stenosis
- Dandy-Walker malformation: atresia of foramina of Luschka and Magendie
- Associate with spinal malformation (e.g. spina bifida)

*acquired

- post-hemorrhagic
- Infectious
- secondary to mass: neoplastic and non-neoplastic
- neurosarcoidosis
- constitutional ventriculomegaly: asymptomatic, needs no treatment
- associate with spinal tumors

a) Signs and symptoms of Hydrocephalus in children
1. irritability, headache, nausea and vomiting
2. cranium size enlarges at a rate more than facial growth
3. fontanelle bulging
4. enlargement and engorgement of scalp veins: due to reversal of flow from intracerebral sinuses due to increased intracranial pressure
5. Macewen's sign: cracked pot sound on percussing over dilated ventricles
6. 6th nerve (abducens) palsy: the long intracranial course is postulated to render this nerve very sensitive to pressure
7. "setting sun sign"(upward gaze palsy): parinaud's syndrome from pressure on region of suprapineal recess
8. hyperactive reflexes
9. splaying of cranial sutures
10. papilledema
11. gate changes

b) Occipital-frontal circumference (OFC)
The OFC should be followed in every growing child. Generally, the OFC of a healthy infant should equal the distance from crown to rump.

Normal head growth: Any of the following may signify treatable conditions such as Hydrocephalus and should

prompt an evaluation of the intracranial contents (e.g. CT, ultrasound, MR, ...):

1. upward deviations (crossing curves)
2. continued head growth of more than 1.25 cm/wk
3. OFC approaching 2 standard deviations above normal
4. head circumference out of proportion to body length or weight, even if within normal limits for age.

These conditions may also be seen in the "catch-up phase"of brain growth in premature infants after they recover from their acute medical illnesses.

XII. Patients and Methods

a) Study Design

The study design, selection of the patients and clinical grouping classification have been described previously. The patients younger than 18 years at the time of the first registration in the university hospital Homburg with a confirmed diagnosis of hydrocephalus due to radiological and/or clinical examination were eligible for study. All of the select patients have at least one cranial MRT with special T2 sequence and/or phase contrast sequence (CSF flow measurement).

Clinical group assignment was based upon type of pathogenesis (Table 1). The submitting institutions classified patients into one of the seven groups at the time of registration or diagnosis. Within each clinical group, patients were classified in different subgroups.

b) MRT Data Analysis

Hypotheses of the pathogenesis of diseases associated with abnormal cerebrospinal flow dynamics often concentrate only on the bulk flow of the cerebrospinal fluid.

With the introduction of modern software's of magnetic resonance imaging (MRI) a new era of brain research was heralded and new neuroradiological developments became possible. In order to gain further knowledge about the dynamics in the ventricular system, detailed models of the ventricular system and flow simulations including pulsatile information are needed. Characterization of subject-specific flow patterns is highly desired.

All examinations were performed on a 1.5-T scanner (Magnetom Vision; Siemens Medical Systems, Erlangen, Germany). Beside other standard sequences, a fast MR sequence based on the RARE allows the determination of cerebrospinal fluid flow with a flow sensitivity below 1 mm/sec. The noninvasivity and the very short acquisition time make this sequence a attractive tool for a variety of CSF-flow dependent disorders like the determination of different types of hydrocephalus.

193 patients 83girls, 110 boys, 0 to 18 years old at the time of the first diagnosis, there were 18 patients who was not exactly obvious when the first hydrocephalus diagnosis occurred, patients who referred to our clinic from other hospitals) with already known or suspected diagnosis at the registration time with MR imaging are included in our study, as well the patients with special features of hydrocephalus, e.g. hydrocephalus ex vacuo, Hydranencephaly, etc. All images were reported by at least two neuroradiologists at the time of examination. The MR images were not retrospectively reviewed.

XIII. Results

a) Group Characteristics

A total of 193 patients were enrolled. Most of the patients were younger than 1 year (129pt., 67%), a total of 152 patients (78.8%) were younger than 4 years. The first diagnostic age of 18 patients (9%) were unknown. A total of 83 patients were female (43%), and 110 patients (57%) were male (fig. 2).

We classified the patients into the one of the six clinical groups depend on pathogenesis of hydrocephalus at the time of diagnosis regardless of initial diagnosis.

Within each clinical group, patients were divided in different subgroups, as a direct cause of hydrocephalus.

The distribution of patient characteristics for all eligible patients and each clinical group is given in Table 1. The percentages of patients by clinical groups I, II, III, IV, V, VI und VII were, respectively, intracerebral mass 16%(31), skull trauma 1.5% (3), congenital malformations 51.3% (99), premature (defined as younger than 36 weeks of age) 14.5% (28), ex vacuo 6.2% (12), intracerebral hematoma 5.2% (10) and post infection 5.2% (10) .

i. *Group I: Intracerebral Mass*

The age of patients ranged from 0 to 18 years, 15 male and 16 female. The most frequent primary tumor were low grade astrocytom 29% (9), glioma 16% (5), meduloblastoma 12.9% (4) and hemangioma 9.65 (3). Kelloid cyst and plexus papilloma had 6.5% (2) each, ependymoma, craniopharyngeoma, epidermoid and cavum vergae cyst 3.2% (1) each. (Fig. 3).

ii. *Group II: Skull Trauma*

3 patients in this group (0, 2 and 11 years old, 1 male and 2 female) are characterized by post traumatic brain damage, one patient with suspected shaken baby syndrome. The other patient experienced asphyxia (hypoxic brain damage) after bathing accident (almost drowning). The third patient had an auto accident with consequently intracerebral hematoma.

iii. *Group III: Congenital Malformation*

Table 2 gives the distribution of patients according to different congenital malformations. As you see congenital malformation is the most populated clinical group with the most subgroup components.

Noticeably are the majority of patients, almost 74% (73) prenatal or immediately postnatal at the first year after birth have developed hydrocephalus. 16 Infants (16%) have hydrocephalus unclear genesis, 26 of patients (26%) suffered under multiple morbidity, most of them (88%,23) combination of Chiari malformation and spina bifida. 10 patients (10%) had aqueduct stenosis. 9 patients isolated spina bifida and 5 patients isolated Chiari malformation.

In addition there were 14% (14 patients) premature children.

iv.   *Group IV: Premature*

25 patients (89.2%) developed a rapid secondary hydrocephalus after intracerebral bleeding, 3 infants (10.8%) had a primary not bleeding-associated intracerebral pressure of unknown origin.

v.   *Group V: Ex Vacuo*

Patients in group V have actually no intracerebral pressure sign or symptoms, nevertheless they show typical hydrocephalus morphology. We consider these patients as a separate group. This category counts 12 patients (6.2%), 8 male and 4 female, most of them (8 pt., 66.7%) are still in their first year of life, 2 patients younger than 2 years old.

vi.   *Group VI: Intracerebral Bleeding*

Some of the children who are classified into group II and IV show intracerebral bleeding (especially premature children) as a result of trauma or prematurely birth.

There were no direct radiological evidence of pathological back ground (of hematoma). To homogenize our groups we decided to add a separate class of patients who had secondary intracranial hematoma not as a result of traumatic accident or prematurely birth.

A total of 10 patients (5.2%), 5 male and 5 female were registered in this group, most of them younger than 1 year (7 pt., 70%), 40% (4 pt.) had a bleeding unknown origin. Aneurysma, angioma, subdural hematoma and AVM counts 40% of the patients (4 pt.).

vii.   *Group VII: Post Infection*

A total of 10 patients (5.2%), 7 male and 3 female developed hydrocephalus due to a CNS infection. Most of the patients were in first year of their life (6 pt., 60%), 2 patients younger than 3 years, 1 child was 5 and another one 8 years old. The most cause of CNS infection was Toxoplasmosis (4 pt., 40%) and second place meningitis tuberculosa (3 pt., 30%). Furthermore one case of CMV infection, one case of E-coli infection and one patient with meningitis unclear genesis is observed in this population.

b)   *Analysis and Discussion*

The central clinical concern of hydrocephalus is not with the abnormal size of the ventricles but the deformity of the brain tissue and its consequences. Large pressure differences are not needed to cause communicating hydrocephalus; small gradients in pressure can slowly enlarge the ventricles with little ICP elevation.

Periventricular areas are the most stretched and deformed, and the blood vessels are elongated and compressed, resulting in ischemia. The tissue away from the ventricular surfaces can be compressed by displacing extracellular fluid and is, at least initially, spared from neuropathological changes.

A high-quality MRI of a subject displaying the relevant brain anatomy (white matter, gray matter, ventricular spaces) is obtained. Phase contrast sequences and reconstruction tools are applied and images are produced to show CSF flow.

Several important clinically relevant deductions can be reached from this analysis. First of all, most of the children with different form of hydrocephalus are born or develop this during the first year of the life. Unregard to 9% unknown first diagnostic age, we had about 67% of all pediatric hydrocephalus whom were younger than one year. On the other side there is a gender related distribution of hydrocephalus in infants (43% female, 57% male)

A related point is that 51, 3% of high ICP was a consequence of congenital malformations. This can explain the high incidence of hydrocephalic situation acutely after birth. The common etiologies for malformation associated ventriculomegaly are listed in Table 2.

As you see Chiari malformation associated or not associated with spina bifida is a major cause of hydrocephalus (about 30%). It consists of protrusion of the cerebellar tonsils and adjacent parts of the inferior cerebellum through the foramen magnum into the upper cervical canal with obliteration of the cisterna magnum. It is not considered an abnormality of closure of the neural tube but rather a dysplasia of the base of the calvarum and cervical vertebrae. Development of a Chiari I anomaly in patients who are initially normal during infancy has been observed.

Evaluation of the groups shows that the second populated group (intracerebral tumor) is mostly inhomogeneous what age the patients concerned and reaches its first peak (19,4%) among the younger than one year old babies. Astrocytoma and glioma with respectively 29% and 16% are the common causes of Hydrocephalus in this group. Astrocytoma, the second most common posterior fossa neoplasm is the first most observed cause of hydrocephalus. These children present with signs of raised intracranial pressure secondary to hydrocephalus resulting from compression of the fourth ventricle by the neoplasm. Eightyfive percent of cerebellar astrocytomas are pylocytic, and 15% are fibrillary type.

The distribution of patients in post traumatic and post infectious hydrocephalus is Shows the least population, respectively, 1,5% (3 patients) and 5,2% (10 patients). These two groups have also a wide pattern age distribution.

Toxoplasmosis is produced by a coccidian parasitic protozoan (Toxoplasma gondii). The typical triad of findings in infants with congenital toxoplasmosis meningoencephalitis is hydrocephalus, chorioretinitis and gliosis in the region of the aqueduct of sylvius.

Tuberculous meningitis the second major cause of hydrocephalus occurs when tuberculosis bacteria (Mycobacterium tuberculosis) invade the CNS. The infection usually begins elsewhere in the body, usually in the lungs, and then travels through the bloodstream to the meninges where small abcesses (called microtubercles) are formed. When these abcesses burst, TB meningitis is the result. Infants and previously unvaccinated children whose parents or grandparents were born in a country with a TB incidence have a higher chance of infection.

Non traumatic ICB is a significant cause of hydrocephalus in infants and children. The common causes are mostly unknown (40%). For a 1.5 –T MRI scanner, the appearance of hemorhage is as follows:

- A hyperacute hemorrhage in the biochemical form of oxyhemoglobin is isointense or hypointense on T1-weighted and hyperintense on T2-weighted images.
- An acute hemorrhage (7 hours to 3 days old), is in the deoxyhemoglobin form and is isointense or hypointense on T1-weighted and hypointense on T2-weighted images.
- The subacute stage (1 week old) is in an intracellular methemoglobin form and demonstrates hyperintensity on T1-weighted and hypointensity on T2-weighted images.

The most common intracranial abnormality in preterm infants is ICH. Primary germinal matrix hemorrhage is probably caused by fluctuations in cerebral blood flow. Intraventricular bleeding is most often preceded by germinal matrix hemorrhage. Some believe increased venous pressure may play a role in the pathophysiology of intraventricular hemorrhage. An important complication of intraventricular hemorrhage is posthemorrhagic hydrocephalus. This occurs because of the following:

- The clot obstructs the ventricular system, most often at the aqueduct or at the foramina of Luschka or Magendie.
- Obliterative arachnoiditis. This occurs most often in the posterior fossa.
- Reactive changes such as resorption or secretive malfunction of the subarachnoid pacchionian granulation occur.

There are about 11% premature infants with hydrocephalus without an ICB or other defined genesis of high ICP.

References Références Referencias

1. Caffey's Pediatric Diagnostic Imaging, Tenth Edition, Volume 1, Jerald P. Kuhn, Thomas L. Slovis, Jack O. Haller MRI Based Volumetry of Intra- and Extracerebral CSF Spaces H. K. Hahna, M. G. Lentschigb, M. Deimlingc, B. Terweyb, and H.-O. Peitgena a MeVis
2. J.-P. Changeux. Neuronal Man – The Biology of Mind. Princeton Univ Pr, 1985.
3. M.S. van der Knaap, C.J. Bakker, J. A. J. Faber et al. Comparison of Skull Circumference and Linear Measurements with CSF Volume MR Measurements in Hydrocephalus. J Comp Assist Tomogr 16(5): 737–743, Sept/Oct 1992.
4. R. Kikinis, M.E. Shenton, G. Gerig et al. Routine Quantitative Analysis of Brain and Cerebrospinal Fluid Spaces with MR Imaging. J Magn Res Imaging 2: 619–629, 1992.
5. H.T. Thaler et al. A Statistical Method for Determining the Proportions of Gray Matter, White Matter, and CSF Using Computed Tomography. Neuroradiol 16: 133–135, 1978.
6. W.D. Sager, G. Gell, G. Ladurner et al. Calculation of Cerebral Tissue and Cerebrospinal
7. Fluid Space Volumes from Computer Tomograms. Neuroradiol 16: 176–178, 1978.
8. H. Hacker et al. The Calculation of CSF Spaces in CT. Neuroradiol 16: 190–192, 1978.
9. A. Marmarou, K. Shulman, and R. M. Rosende. A Nonlinear Analysis of the Cerebrospinal Fluid System and Intracranial Pressure Dynamics. J Neurosurg 48: 332–344, 1978.
10. G.M. Teasdale, B. Grant, B. Condon et al. Intracranial CSF Volumes: Natural Variations and Physiological Changes Measured by MRI. Acta Neurochir, Suppl. 42: 230–235, 1988.
11. Dandy WE (1919) Experimental hydrocephalus. Ann Surg 37:129–142
12. Dandy WE, Blackfan KD (1913) An experimental and clinical study of internal hydrocephalus. J Am Med Assoc 61: 2216–2217
13. De Lange SA (1977a) Progressive hydrocephalus. In: Vinken PJ, Bruyn GW, Myrianthopoulos NC (eds) Congenital malformations of the brain and skull, part I. North-Holland, Amsterdam, pp 525–563 (Handbook of clinical neurology, vol 30)
14. Gjerris F, Snorrason E (1992) The history of hydrocephalus. J Hist Neurosci 1:285–312
15. Payr E (1919) Elfjähriger Dauererfolg einer Ventrikeldrainage bei Hydrocephalus. Med Klin 49:1247–1251

16. Raimondi AJ (1987) Hydrocephalus. In: Raimondi AJ (ed) Pediatric Neurosurgery, Springer, New York Berlin Heidelberg, pp 453–491

17. Richards GD, Anton SC (1991) Craniofacial configuration and postcranial development of a hydrocephalic child (ca 2500 BC–500 AD): with a review of cases and comments on diagnostic criteria. Am J Phys Anthropol 85:185–200

18. Torack RM (1982a) Historical aspects of normal and abnormal brain fluids. I. Cerebrospinal fluid. Arch Neurol 39:197–201

19. Torack RM (1982b) Historical aspects of normal and abnormal brain fluids. II. Hydrocephalus. Arch Neurol 39: 276–279

20. Voth D, Henn M (1983) Historischer Überblick über die Behandlungsverfahren des Hydrocephalus internus im Kindesalter. In: Voth D, Gutjahr P, Glees P (eds) Hydrocephalus im frühen Kindesalter. Enke, Stuttgart, pp 168–180

21. 20.Richard D. Penn, Andreas Linninger, The Physics of Hydrocephalus; pediatric neurosurgery, Vol.45, No.3, 2009

22. Alexander E, Davis CH (1987) Macewen's sign – "the cracked pot sound". Surg Neurol 27:519–522