Cerebrospinal space
Brain ‘lump in a box’? Compensatory role of lumbar space

Thanks to Dr.O.Baledent
Anatomy of cranial CSF spaces

- Lateral ventricle
- Foramen of Monro
- Third ventricle
- Aqueduct of Sylvius
- Foramen of Luschka
- Arachnoidal villi
- Choroid plexuses
- Tentorium cerebelli
- Fourth ventricle
- Foramen of Magendie
Volume of CSF in ventricles may change

Ventricular volume 25 ml

Ventricular volume 127 ml
Volume of brain = 1400 ml

Volume of CSF = 150 ml

CSF in ventricles around 25 ml

Volume of blood = 150 ml

Brain does not ‘float’ in CSF
Role of CSF: ‘mechanistic’ - cancelling pressure gradients
: ‘metabolic’ ???

Total volume of cerebrospinal fluid (infant) = 50 ml
Turnover of entire volume of cerebrospinal fluid = 3 to 4 times per day
Rate of production of CSF = 0.35 ml/min (500 ml/day)
pH of cerebrospinal fluid = 7.33 (from Kandel et al., 2000, p. 1296)
Specific gravity of cerebrospinal fluid = 1.007
Colour of normal CSF = clear and colourless
Sites of choroid plexi: pink- lateral ventricles, green- 3rd and 4th ventricles; red- chorid plexi
Cerebrospinal fluid (CSF) is secreted by the epithelial cells of the choroid plexuses. These cells like those of other secretory epithelia are polarised so that the properties of their apical membrane (ventricle facing) differ from those of the basolateral membrane (blood facing). Both membranes have a greatly expanded area (apical membrane is made up of numerous microvilli, and the basolateral membrane has many infoldings), so that the total area available for transport is similar to that of the blood-brain barrier.
CSFprod = Infusion (Ci-Co)/Co
Figure 3.13 The resistance of the CSF outflow is the sum of total resistances, which include at the foramina of Munro, the aqueduct, the foramen of Luschke and magendie, the subarachnoid spaces of the infra- and supratentorial regions, the tentorial notch, and the arachnoid granulations of the venous sinuses. Multiple resistances at the various regions of the CSF pathway may cause hydrocephalus. In addition, the degree and the location of a resistance increase may determine the treatments associated with the different types of hydrocephalus.83
Disproportionately Enlarged Subarachnoid-space Hydrocephalus

Diagnosis of idiopathic normal pressure hydrocephalus is supported by MRI-based scheme: a prospective cohort study

Hashimoto et al.

Figure 1 Typical iNPH findings on MRI. Illustrative coronal sections of coronal T1-weighted images selected from an included patient showing enlarged ventricles (*), tight high-convexity and medial surface subarachnoid spaces (oval ring), and expanded Sylvian fissures (arrow).
CSF flow in lumbar space
Constant versus pulsatile CSF flow

Intracranial
Subarachnoid spaces

Ventricles
Arteries
Veins
Lumbar subarachnoid space
compliant dural Sac

Young brain
agging brain

Thanks to Dr. O. Baledent
The heart, origin of the Cerebral hydrodynamic

Monro-Kellie relation: the volume inside the cranium is CONSTANT.

Thanks to Dr. O. Baledent
MATERIAL AND METHODS

Data Acquisition

Scanner: 1.5 Tesla General Electric Healthcare
Sequence: Retrospectively-gated Cine phase-contrast
Cardiac synchronization with peripheral gating
TR: 30 ms  TE: 12-17 ms
FOV: 160x120 mm
Matrix: 256x128
Section thickness: 5 mm
Flip angle: 30°
Acquisition of 32 cardiac phases

The acquisitions parameters result of a compromise between time acquisition, Signal Noise Ratio and spatial and temporal resolution.

Aqueductal CSF flow level:
Velocity encoding: 10 cm/sec

Cervical blood flow level:
Velocity encoding: 80 cm/sec

Cervical CSF flow level:
Velocity encoding: 5 cm/sec

Thanks to Dr. O. Baledent
METHODS

Data Analysis

Cervical CSF flow levels:
- Velocity encoding: 5 cm/sec
- Dynamic flow images were analyzed on dedicated software, developed on site, based on an automatic segmentation algorithm of region of interest.
- The algorithm uses the temporal evolution of the intensities to extract those which correspond to the cardiac frequency. **Balédent et al. Investigative Radiology 2001**

Thanks to Dr. O. Baledent
**Cranial flow**

- **Flush peak flow**
- **CSF flow at C2-C3 level**

**Caudal flow**

- **Flush peak flow**
- **Fill peak flow**

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**Stroke volume (μl/cc)**

<table>
<thead>
<tr>
<th>Examen</th>
<th>656</th>
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<tbody>
<tr>
<td>Serie</td>
<td>4</td>
</tr>
<tr>
<td>Level</td>
<td>C2_C3</td>
</tr>
</tbody>
</table>

- **BPM** 61
- **Peak flush V(mm/sec)** 43
- **Tflush (%) of cc** 25
- **Tflush (ms)** 252
- **Peak fill V (mm/sec)** -37
- **Tfill (%)** 80
- **Tfill(ms)** 794
- **Peak-flush-F (mm3/s)** 3065
- **TD_flush (%)** 25
- **TD_flush (ms)** 252
- **Peak-fill F (mm3/s)** -1231
- **TD_flush (%)** 80
- **TD_flush (ms)** 794

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The software was developed with *Interactive Data Language (IDL)*

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Thanks to Dr. O. Baledent
Aqueductal CSF curve flow

Thanks to Dr. O. Baledent
Blood and CSF flows
Mean and standard deviation from 44 healthy volunteers

Cerebral blood flow: 633 ± 126 ml/min

Thanks to Dr. O. Baledent
Population studies
• 44 Healthy volunteers

Arterial peak flow propagation
5% of cardiac cycle (cc) later 10-20% of cc later 25-35% of cc later

Arterial Peak flow
16 ml/sec

Cervical CSF peak flush
2.5 ml/sec

Jugular blood Peak flush
13 ml/sec

Ventricular CSF Peak flush
0.2 ml/sec

Brain Equilibrium Pressure

Ventricular CSF flow represents only 11% of cervical CSF flow less than 2% of arterial flow

Thanks to Dr. O.Baledent
Absorption of CSF into sagittal sinus
CSF hydrodynamic studies in man

2 Normal hydrodynamic variables related to CSF pressure and flow

JAN EKSTEDT

From Department of Neurology, Uppsala University, and Department of Neurology, Umeå University, Umeå, Sweden

SUMMARY With the patient in the supine position, the subarachnoidal space was infused with artificial CSF at several constant pressure levels. The resulting flow of liquid was recorded. By draining CSF at a low pressure the CSF production rate was determined. Normal values are given and discussed for (1) the resting pressure, (2) the conductance of the CSF outflow pathways, (3) the formation rate of CSF, (4) the pressure difference across the CSF outflow pathways, and (5) the sagittal sinus pressure. None of the variables showed any age dependence, nor was there any sex difference.
Davson’s equation

CSF pressure = $p_{ss} + R_{csf} \times I_{formation}$

Rcsf - resistance to CSF outflow; units mmHg/(ml/min)

Normal resistance 4-10 mmHg/(ml/min)

In hydrocephalus, resistance is increased to > 13 mmHg/(ml/min)

Is it always constant?

Fig. 6 Curves for the intracranial pressure and external flow describing the constant pressure method. The left graph shows typical $P_{IC}$ data and accumulated infused volume versus time. The right graph is calculated from the time series to the left and shows points for mean pressure and flow determined for each steady state level. Outflow resistance is determined with linear regression and interpreted as the inverse of the slope.
CSF hydrodynamic studies in man

Normal hydrodynamic variables related to CSF pressure and flow

JAN EKSTEDT

From Department of Neurology, Uppsala University, and Department of Neurology, Umeå University, Umeå, Sweden
Age dependence of cerebrospinal pressure–volume compensation in patients with hydrocephalus

MAREK CZOSNYKA, PH.D., D.SC., ZOFIA H. CZOSNYKA, M.SC.,
PETER C. WHITFIELD, PH.D., F.R.C.S., TIM DONOVAN, B.SC.,
AND JOHN D. PICKARD, M.CHIR., F.MED.SCI.

Academic Neurosurgical Unit and Wolfson Brain Imaging Centre, Addenbrooke’s Hospital, Cambridge, United Kingdom

Fig. 3. Graph showing the relationship between CSF production and patient age. In hydrocephalic patients, the estimated CSF production rate is inversely proportional to age.

Fig. 1. Graph demonstrating the relationship between Rcsf and age in patients presenting with symptoms of hydrocephalus. The best-fit model is inverse: $y = 1/(a - bx)$. 
Arterial hypotension decreases RCSF (17% per 50 mm Hg)

Vascular components of cerebrospinal fluid compensation


Medical Research Council Cambridge Centre for Brain Repair and Academic Neurosurgical Unit, Addenbrooke’s Hospital, Cambridge, United Kingdom
Early experimental works- rabbits-Rcsf increases with hypercapnia (27-48 mm Hg; 18%)

Possible intraparenchymal CSF absorption

CSF

- Disrupted ependyma
- Entry to parenchyma
- Mixing with extracellular fluid
- Flow in perivascular spaces
- Lymphatic nodes- extracranial
Lymphatic drainage of the brain and the pathophysiology of neurological disease

Roy O. Weller · EYe Djuanda · Hong-Yeen Yow · Roxana O. Carare

Fig. 6 Diagram of the proposed route for lymphatic drainage of the brain. Interstitial fluid and solutes drain from the brain parenchyma into the basement membranes of capillaries and then along the basement membranes between smooth muscle cells in the tunica media of arteries. ISF and solutes then enter the adventitia around leptomeningeal arteries and continue through the base of the skull along the carotid artery (and probably the vertebral artery) to cervical lymph nodes. A layer of pia-arachnoid separates the adventitia of the leptomeningeal arteries from the CSF in the subarachnoid space (SAS).
CSF pressure dynamics

Professor Anthony Marmarou
Sagittal Sinus Pressure (3-8 mm Hg). Is it always coupled to CVP?

Vascular component = F1(arterial inflow) + F2(venous outflow)

**TABLE 6**

Contribution of CSF and Pv to raised ICP in head-injured patients compared with independent measures of If, Ro, and Pv*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Mean ICP (mm Hg)</th>
<th>If (ml/min)</th>
<th>Ro (mm Hg/ml/min)</th>
<th>Pv (mm Hg)</th>
<th>If x Ro (mm Hg)</th>
<th>% ICP Rise Due to:</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CSF</td>
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<tr>
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</tbody>
</table>

*CSF = cerebrospinal fluid; ICP = intracranial pressure; If = CSF formation rate; Ro = outflow resistance; Pv = vascular component; SD = standard deviation; SEM = standard error of the mean.
Idiopathic intracranial hypertension: Simultaneous measurement of ICP and pressure in venous sinuses
A nonlinear analysis of the cerebrospinal fluid system and intracranial pressure dynamics

Anthony Marmarou, Ph.D., Kenneth Shulman, M.D., and Roberto M. Rosende, M.D.
The Leo M. Davidoff Department of Neurological Surgery, Albert Einstein College of Medicine, Bronx, New York

A mathematical model of the cerebrospinal fluid (CSF) system was developed to help clarify the kinetics of the intracranial pressure (ICP). A general equation predicting the time course of pressure was derived in terms of four parameters: the intracranial compliance, dural sinus pressure, resistance to absorption, and CSF formation. These parameters were measured in the adult cat, and the equation was tested by comparing experimental and calculated values of the time course of pressure in response to volume changes. The theoretical and experimental results were in close agreement, and the role of each parameter in governing the dynamic equilibrium of the ICP was determined. From this analysis, dynamic tests were developed for rapid measurement of CSF formation, absorption resistance, and the bulk intracranial compliance. These techniques are applicable to clinical settings, providing data that are useful in characterizing the physiological mechanisms responsible for raised ICP and assessing changes induced by therapy.

Key Words: intracranial pressure, compliance, mathematical model, cerebrospinal fluid system

Fig. 1. The CSF system was depicted by an equivalent electrical circuit that distributed the CSF parameters among three fundamental mechanisms: formation, represented by a constant current generator; storage, represented by a nonlinear capacitance (C); and absorption represented by resistance element (R). The venous outflow site (dural sinus) was represented by a constant pressure source P_d. The system equations were derived from this configuration.
Intracranial pressure-volume compensation:

MONRO-KELLY DOCTRINE


$V_{\text{brain}} + V_{\text{blood}} + V_{\text{csf}} = \text{const}$
Message to take home:

- CSF Formation = Absorption + Storage
- Sagittal sinus pressure is not necessarily constant
- CSF flow: DC and AC components
- CSF pressure = $R_{out} \times CSF_{formation} + P_{ss} + \text{Vascular component?}$
- Brain does not float in CSF (Volume Brain:CSF = 10:1)
- CSF equalizes pressure in brain compartments