Cerebrospinal fluid production

CSF is produced primarily by the choroid plexuses in the lateral, third, and fourth ventricles of the brain. The choroid plexus consists of specialized epithelial cells that filter blood plasma to create CSF. Ventricular System:

Once produced, CSF flows from the lateral ventricles into the third ventricle through the interventricular foramina (also known as the foramen of Monro). From the third ventricle, it flows through the cerebral aqueduct (also known as the aqueduct of Sylvius) into the fourth ventricle. Subarachnoid Space:

From the fourth ventricle, CSF exits into the subarachnoid space through three small openings: the median aperture (foramen of Magendie) and the two lateral apertures (foramina of Luschka). This space surrounds the brain and spinal cord. Flow Around the Brain and Spinal Cord:

CSF circulates in the subarachnoid space, bathing the brain and spinal cord, providing buoyancy that reduces the effective weight of the brain and protects it from mechanical injury.

In 1664, Thomas Willis first postulated that cerebrospinal fluid production came from the choroid plexuses and that the fluid was contained within the ventricles [1)]

The brain produces roughly 500 mL of cerebrospinal fluid per day. This fluid is constantly reabsorbed, so that only 100-160 mL is present at any one time.

Ependymal cells of the choroid plexus produce more than two thirds of CSF. The remainder of the CSF is produced by the surfaces of the ventricles and by the lining surrounding the subarachnoid space.

Ependymal cells actively secrete sodium into the lateral ventricles. This creates osmotic pressure and draws water into the CSF space. Chloride, with a negative charge, moves with the positively charged sodium and a neutral charge is maintained. As a result, CSF contains a higher concentration of sodium and chloride than blood plasma, but less potassium, calcium and glucose and protein.

Cerebrospinal fluid circulation

The cerebrospinal fluid (CSF) production rate in humans is not clearly defined but is estimated to be 18-24 ml/h (Trevisi et al Croat Med J 55(4):377-387 (24); Casey and Vries Childs Nerv Syst 5(5):332-334 (8)). A frequent clinical observation is that patients often drain higher volumes of CSF than can be explained by the assumed 'normal' CSF production rate (PRcsf). In the National Hospital for Neurology and Neurosurgery PRcsf was recorded in a variety of common neurosurgical pathologies using LiquoGuard7, an automated peristaltic pump that accurately controls CSF drainage and maintains a pre-set CSF pressure.

Methods: A prospective observational study was performed from September 2021 onwards, on all patients in the National Hospital for Neurology and Neurosurgery who required CSF drainage as part

of their ongoing treatment. The external drain was connected to a LiquoGuard7 pump (Möller Medical GmbH, Fulda, Germany), and the internal software of LiquoGuard7 was used to measure PRcsf. Statistical analysis used SPSS (version 25.0, IBM) by paired t test, comparing measured rates to hypothetical 'normal' CSF production rates calculated and published by Ekstedt (16-34ml/h) (Ekstedt J Neurol Neurosurg Psychiatry 41(4):345-353 (14)), assuming a similar distribution.

Results: PRcsf was calculated in 164 patients. Suspected normal pressure hydrocephalus (n=41): PRcsf of 79ml/h±20SD ($p<0.0001$). Post-surgical CSF leak (n=26): PRcsf of 90ml/h±20SD ($p<0.0001$). Subarachnoid haemorrhage (n=34): PRcsf of 143ml/h±9SD ($p<0.0001$). Intracerebral haemorrhage (n=22): PRcsf of 137ml/h±20SD ($p<0.0001$). Spinal lesions (n=7): PRcsf of 130ml/h±20SD ($p<0.0032$). Pituitary adenomas (n=10): PRcsf of 29 ml/h±9SD ($p<0.049$). Idiopathic intracranial hypertension (n=15): PRcsf of 86ml/h±10SD ($p<0.0001$). Decompensated long-standing overt ventriculomegaly (n=4): PRcsf of 65ml/h±10SD ($p<0.0001$). Cerebral infection (n=5): PRcsf of 90ml/h±20SD ($p<0.0001$).

Net CSF production rate may be higher than expected in many conditions, as measured with new device LiquoGuard7 through the study of net flow rate, which may have implications for clinical decisions on CSF diversion. The conventional understanding of CSF production and circulation does not explain the findings of this study. More extensive studies are needed to validate this technique [2].

1)
Rengachary SS, Ellenbogen RG: Principles of Neurosurgery, ed 2. Edinburgh: Elsevier Mosby, 2005
2)
Tariq K, Toma A, Khawari S, Amarouche M, Elborady MA, Thorne L, Watkins L. Cerebrospinal fluid production rate in various pathological conditions: a preliminary study. Acta Neurochir (Wien). 2023 Jun 24. doi: 10.1007/s00701-023-05650-2. Epub ahead of print. PMID: 37354286.