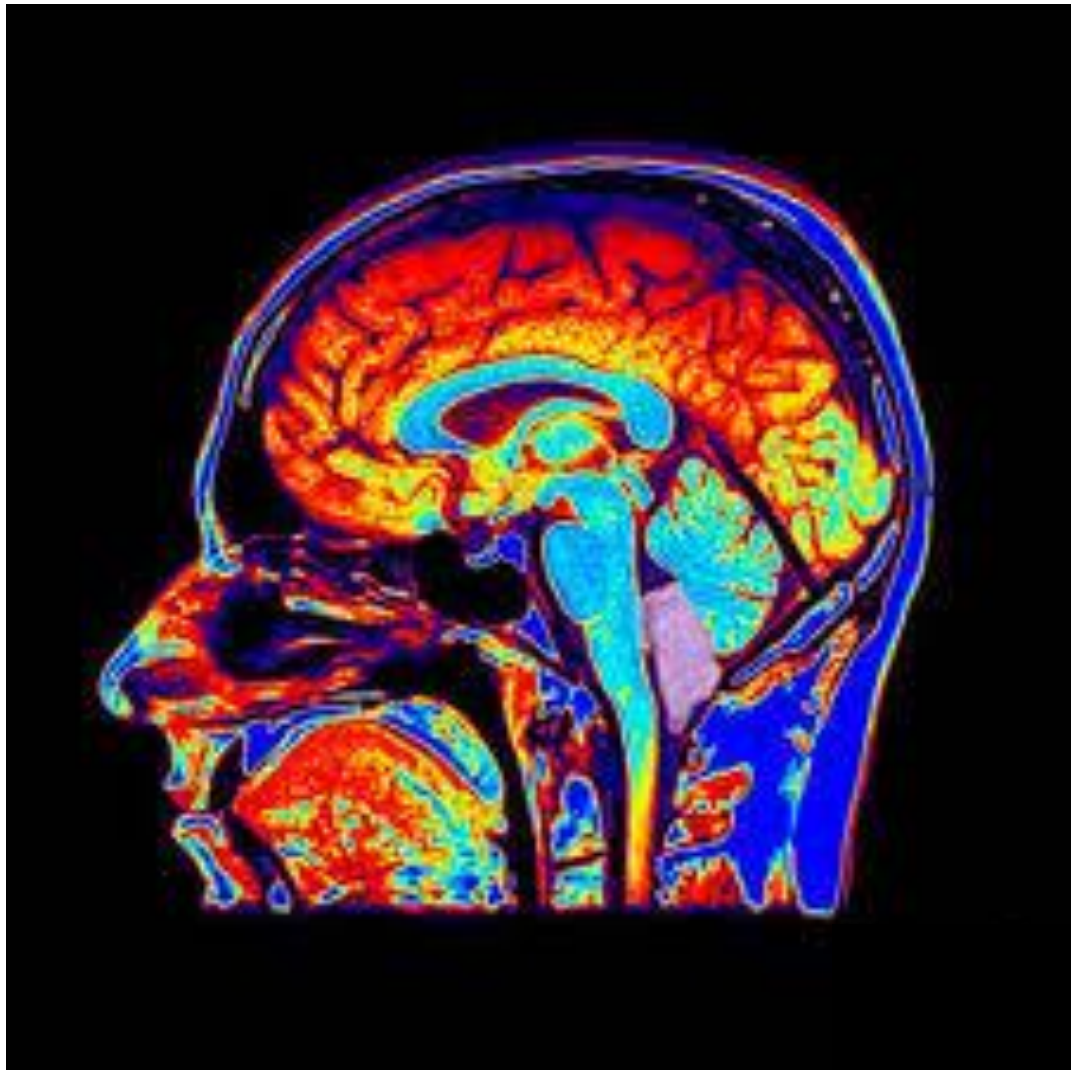

MALFORMAZIONE DI CHIARI E SIRINGOMIELIA
diagnosi, trattamento, vita quotidiana

AISMAC
ASSOCIAZIONE ITALIANA SIRINGOMIELIA E ARNOLD CHIARI

Corso di formazione ECM

Roma, 10-11 aprile 2026

Consorzio Interregionale Siringomielia-Sindrome di Chiari

Diagnosi differenziale: altre patologie neurologiche

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OSPEDALI DEI COLLI
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Monaldi - Cotugno - C.T.O.

Cerebellar Tonsillar Ectopia (CTE)

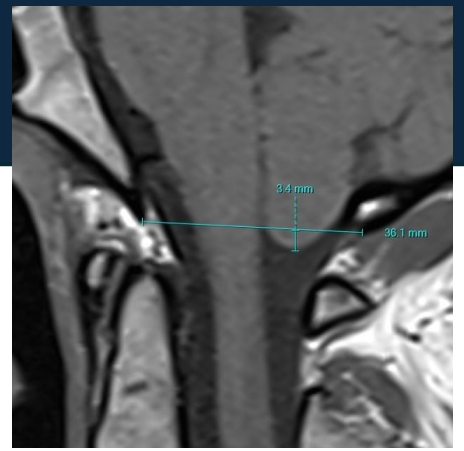


TABLE 1

SNNOOP10 red flags for secondary headache disorder[8]

CM1

Systemic symptoms including fever

Neoplasm in history

Neurologic deficit or dysfunction (including decreased consciousness)

Onset of headache is sudden or abrupt

Older age (> 65 years)

Pattern change or recent onset of headache

Positional headache

Precipitated by sneezing, coughing, or exercise

Papilledema

Progressive headache and atypical presentations

Pregnancy or puerperium

Painful eye with autonomic features

Posttraumatic onset of headache

Pathology of the immune system such as HIV

Painkiller overuse or new drug at onset of headache

Red flags

- New-onset CTE
- CTE<5 mm
- Normal tonsillar morphology
- No associated malformations
- Rarer syringomyelia
- Adjunctive neuroradiological signs
- Symptoms atypical for CM1

\+

- **Visual and Oto/vestibular signs**
- **Focal neurological signs**
- **Additional neuroimaging signs**

Incidental finding

Mild Ectopia (3–5 mm) is described in up to **5-14%** of otherwise healthy individuals

AGENDA

Cerebellar Tonsillar Ectopia (CTE) +/- Syringomyelia

Disorders of intracranial pressure

Secondary/acquired

- Brain tumors or cysts
- Brain oedema
- Hydrocephalus
- Vascular disorders (arterial, venous)
- Endocrine disorders
- Traumatic brain injury
- Infections and abscesses
- Iatrogenic/post-surgical

Acquired syringomyelia:

- Trauma
- Canal Stenosis
- Post-Inflammatory
- Vascular
- Spinal cord tumor

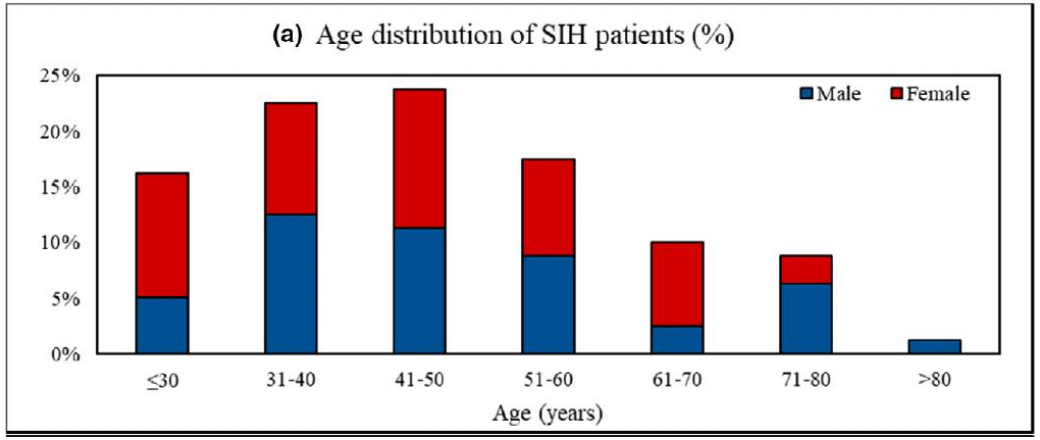
- **Spontaneous Intracranial Hypotension (SIH)**
- **Idiopathic Intracranial Hypertension (IIH)**

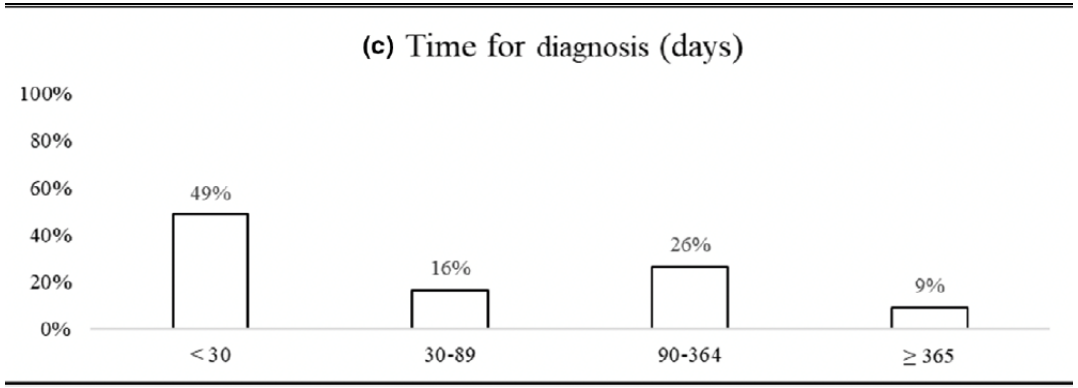
- **Epidemiology**
- **Classification/diagnostic criteria**
- **Clinic, red flags and diagnostic pitfalls**
- **Diagnosis**
- **Neuroimaging**
- **Therapy**
- **Complications and emergencies**

SPONTANEOUS INTRACRANIAL HYPOTENSION (SIH): Background

Epidemiology

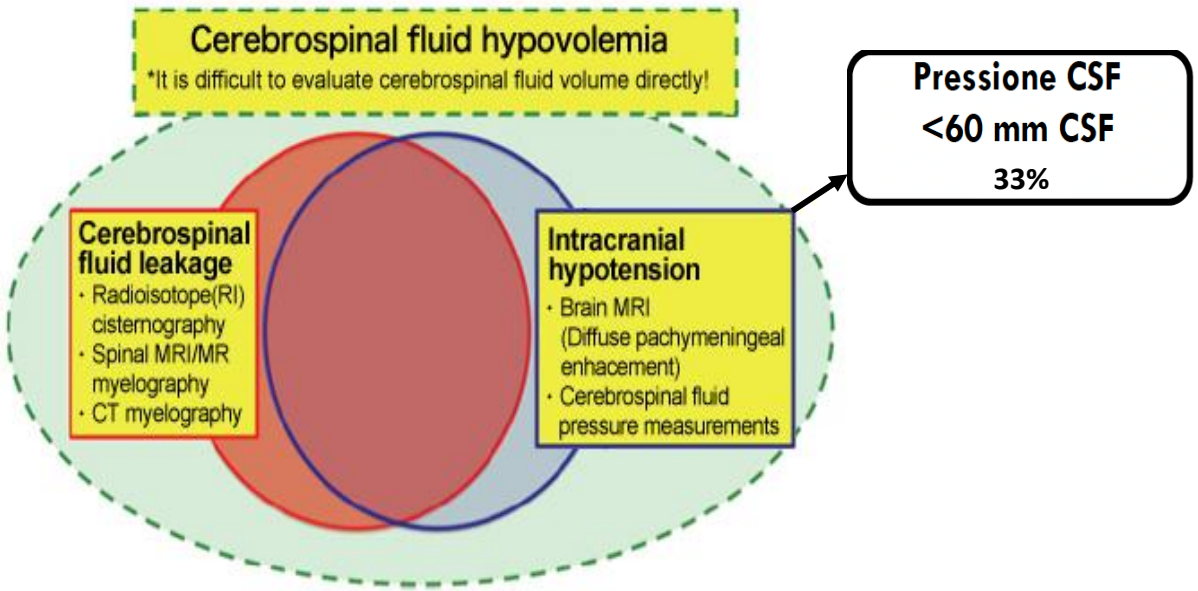
- Can appear at any age
- F>M, >35 yrs
- Incidence rate: 3.7-5/100000/yr
- Probably underestimated





Etiopathogenesis

- CSF hypovolemia due to CSF loss in one or more sites
- Greater CSF venous clearance
- Impaired glymphatic influx
- Abnormal cranio-spinal compliance
- **Progressive sagging of brain structures**



Schievink WI et al. J Headache Pain. 2007;8(6):325—8; Schievink WI et al. Cephalalgia. 2022;42:312—6; García-Ull J et al. Neurologia (Engl Ed). 2025 Jan-Feb;40(1):118-137. doi: 10.1016/j.nrleng.2024.02.009. PMID: 38431253; Dalby SW et al. Eur J Neurol. 2025. doi: 10.1111/ene.16579.; Eide PK et al. Fluids Barriers CNS. 2025 Jul 1;22(1):65. doi: 10.1186/s12987-025-00679-0. PMID: 40597337.

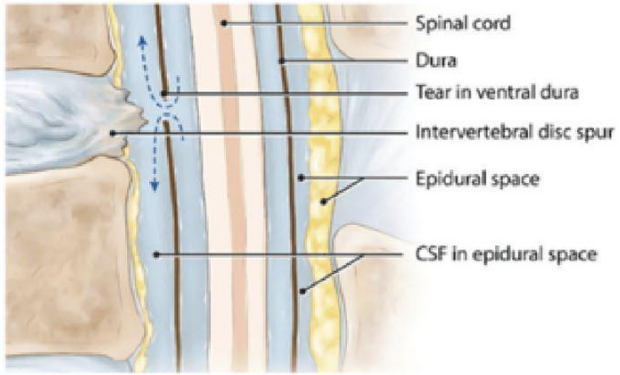
Table 12 Farb radiological classification of cerebrospinal fluid leaks.

Type 1 (48–60%). Ventral dural tear associated with degenerative disc disease and, occasionally, bone spurs. Accompanied by EFC
Type 2 (13–20%). Lateral proximal nerve root sleeve dural tear. Not associated with degenerative disc disease but typically presents with EFC
Type 3 (20%). CSF-venous fistula. Associated with meningeal diverticulum (actually, an embryonic pseudomeningocele). Not associated with EFC
Type 4. Distal nerve root sheath leak. Not associated with EFC. This is the rarest type.

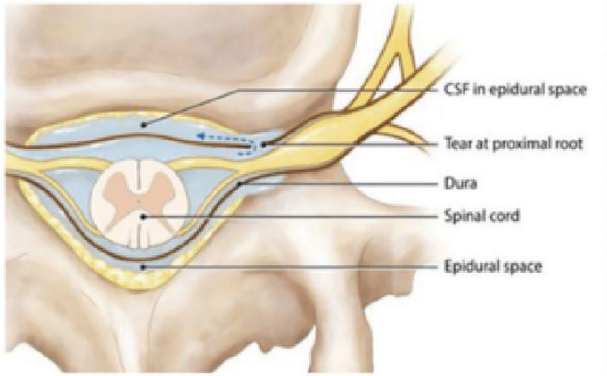
CSF: cerebrospinal fluid; EFC: extradural fluid collection.

Farb Classification of CSF leaks

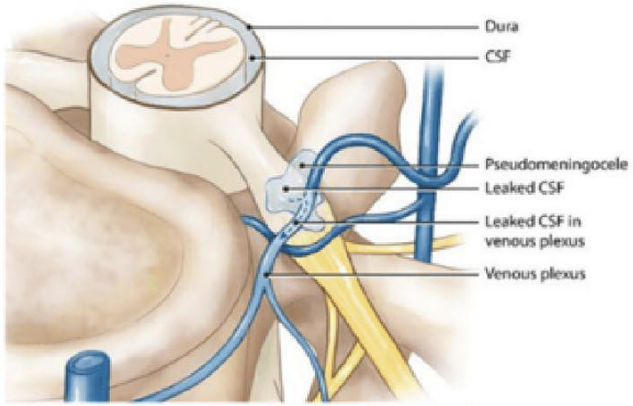
SLEC: Spinal longitudinal epidural CSF collection



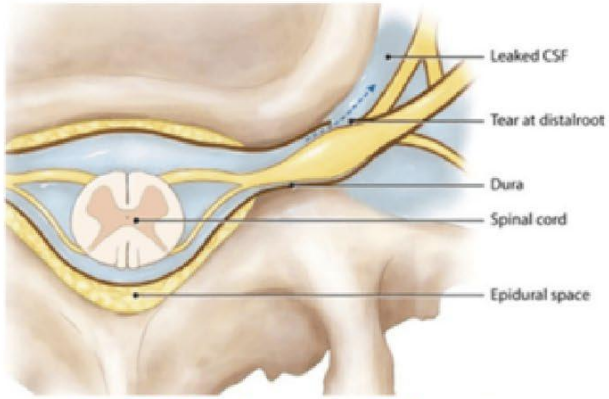
Type 1: Ventral dural tear



Type 2: Lateral dural tear



Type 3: CSF-venous fistula



Type 4: Distal nerve root sleeve tear

1) **Type 1→Dural tears**
   - Ventral
   - **>** thoracic or lower cervical spine
   - Rapid CSF leakage→ **SLEC +**

2) **Type 2→Meningeal diverticula**
   - Lateral
   - Thoracic, lumbar
   - Intermittent flow, also rapid and severe→ **SLEC +**

3) **Type 3→ CSF-venous fistulae**
   - > Thoracic
   - Associated perineural diverticula: 80%
   - **SLEC -**

4) **Undetermined cause: 28%**

doi: 10.1055/s-0043-1774301; https://doi.org/10.1007/s11547-025-02116-6

Spontaneous Intracranial Hypotension Without CSF Leakage—Concept of a Pathological Cranial to Spinal Fluid Shift

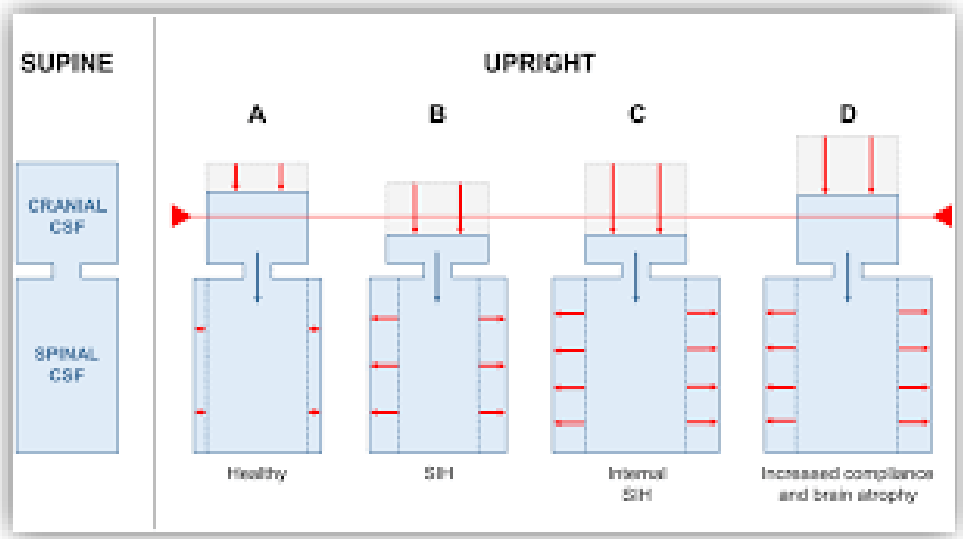
Johannes Goldberg[1†], Levin Häni[1†], Christopher Marvin Jesse[1], Irena Zubak[1], Eike I. Piechowiak[2], Jan Gralla[2], Tomas Dobrocky[2], Jürgen Beck[3] and Andreas Raabe[1]*

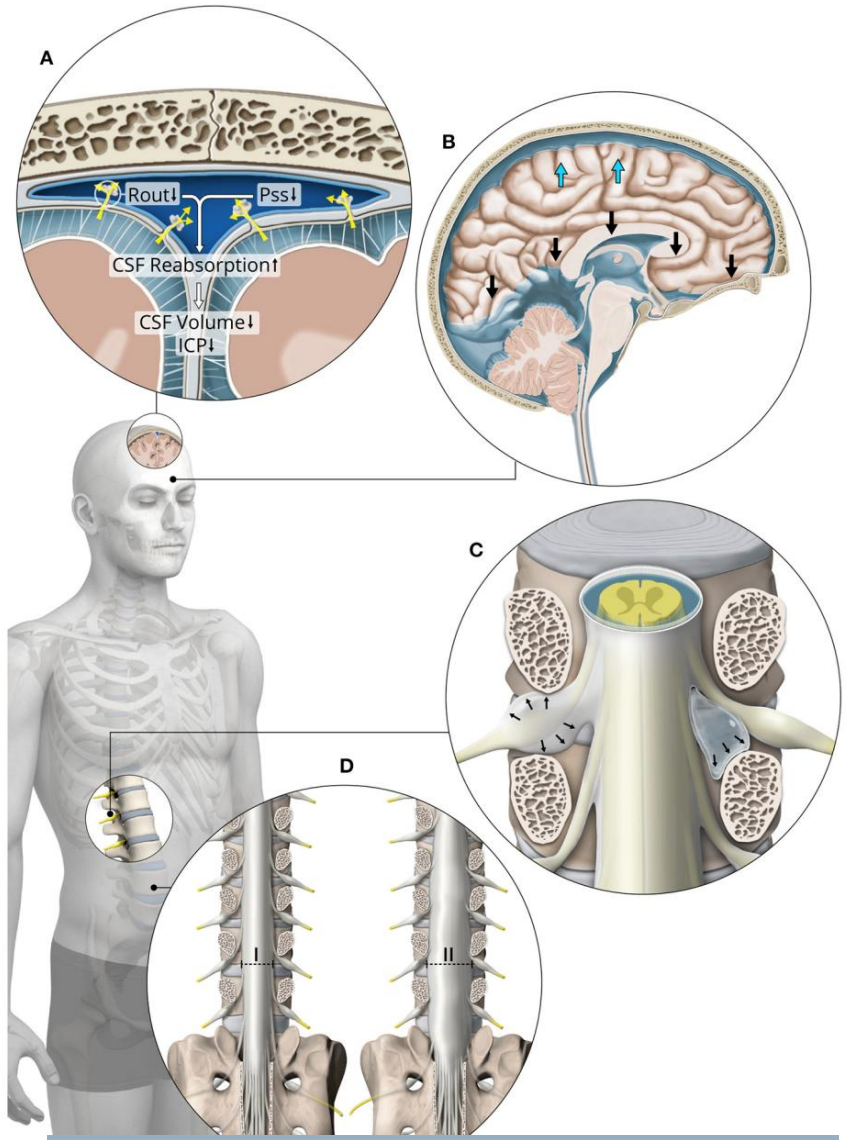
frontiers in Neurology

published: 01 November 2021
doi: 10.3389/fneur.2021.760081

- **CSF leakage can be absent**

- **Suggested physiopathological mechanisms:**
  - Increased cranio-spinal compliance
  - Decreased intracranial CSF volume
  - Low CSF outflow resistance





Orthostatic cranial-to-spinal CSF shift

FIGURE 4 | Overview of factors contributing to internal SIH. Predisposing factors are **(A)** low CSF outflow resistance (Rout), low intracranial venous pressure (Pss) and **(B)** low intracranial CSF volume. The main pathophysiological factor is increased spinal compliance due to **(C)** meningeal diverticula, dural tears with prolapsing arachnoid around meningeal diverticula or **(D)** increased distensibility of the dura mater (I = normal distensibility, II = increased distensibility). A combination of these factors can lead to a pathological cranial-to-spinal CSF shift causing brain sagging **(B)** and orthostatic symptoms without CSF leakage.

Causes and Predisposing Factors for Spontaneous Intracranial Hypotension Syndrome[a]

Connective Tissue Matrix Disorders

- Marfan syndrome
- Ehlers-Danlos syndrome type II
- Autosomal dominant polycystic kidney disease
- Joint hypermobility: hyperflexibility, "party tricks," naturally good at gymnastics, dance, or yoga (inquire about flexibility in childhood)
- Retinal detachment at a young age
- Personal or family history of arterial dissection, aneurysms, nonrheumatic valvular heart disease
- Secondary to unrecognized intracranial hypertension

Trauma

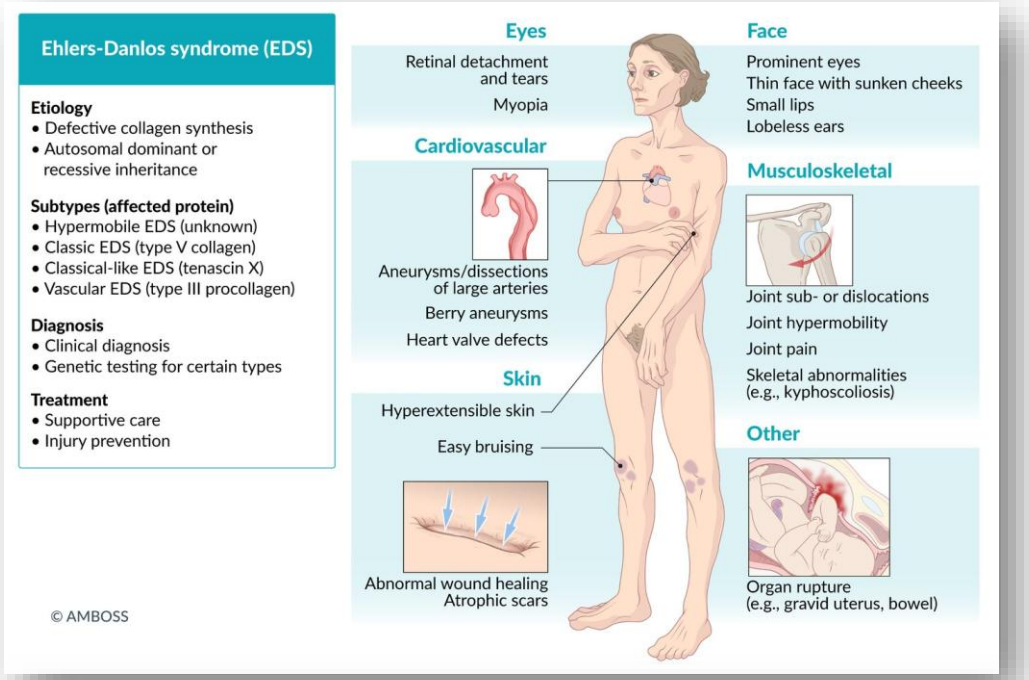
- Previous spine surgery
- History of lumbar puncture
- Nerve root sleeve tears or avulsions
- Previous spinal or epidural anesthesia
- Trivial trauma
  - Valsalva related: heavy lifting, coughing, straining
  - Repetitive truncal torsion: tennis, golf, yoga, kayaking, canoeing
- Impact: motor vehicle accident, whiplash, sports injury

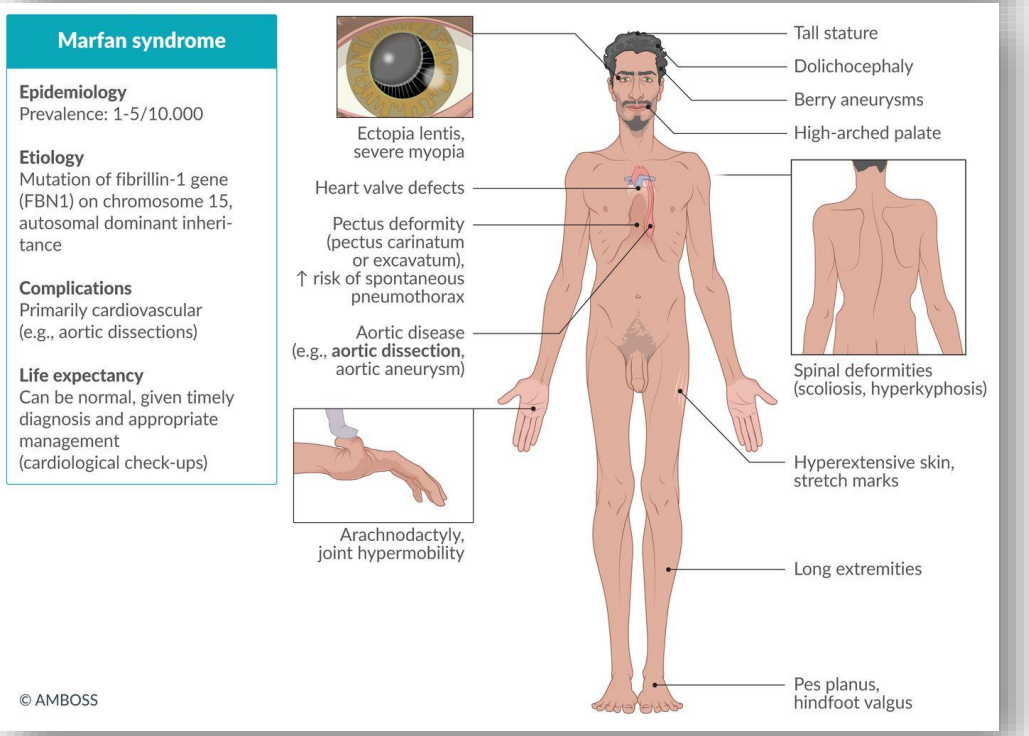
Spine Disorders

- Calcified herniated disks
- Osteophytes and spondylotic spurs
- CSF venous fistula

Bariatric Surgery[7]

Unknown

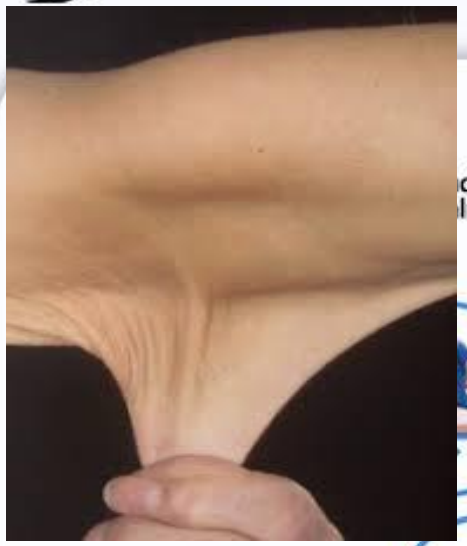




The Ehlers Danlos Society

THE BEIGHTON SC

Measuring joint hypermobili



d and
lm side

B. THUMBS

Test **both sides:** Wit
out straight, the pal
down, and the wrist
bent downward, car
thumb be pushed ba
touch the forearm?

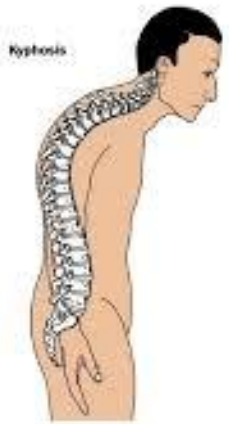
If yes, add **one point** for each thumb.

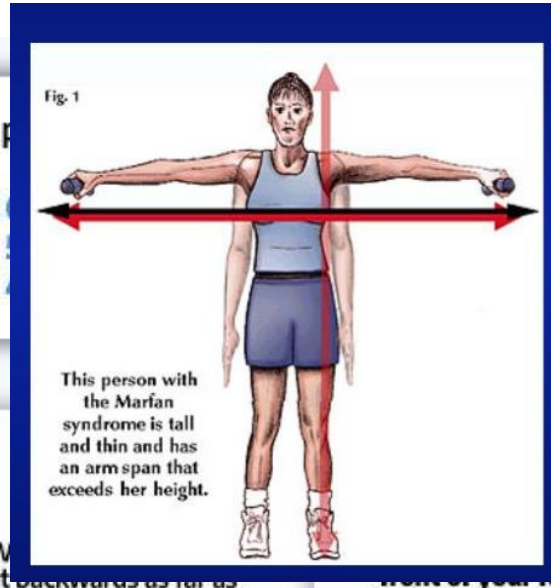
1

C. ELBOWS

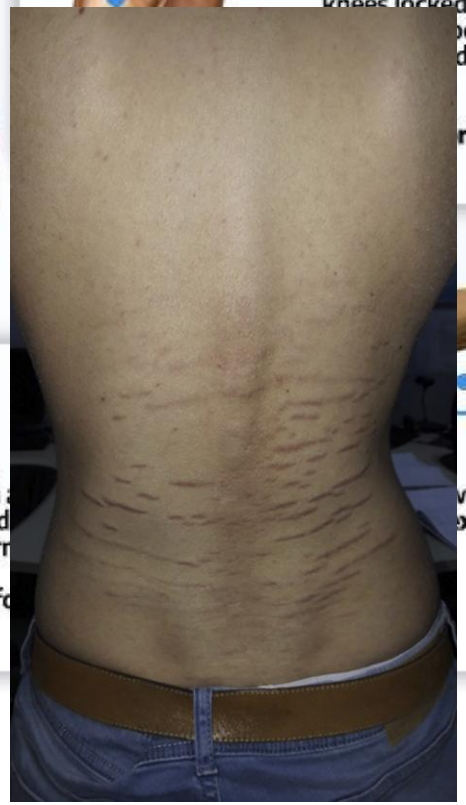
Test **both sides:** With
does the elbow extend
degrees beyond a norm

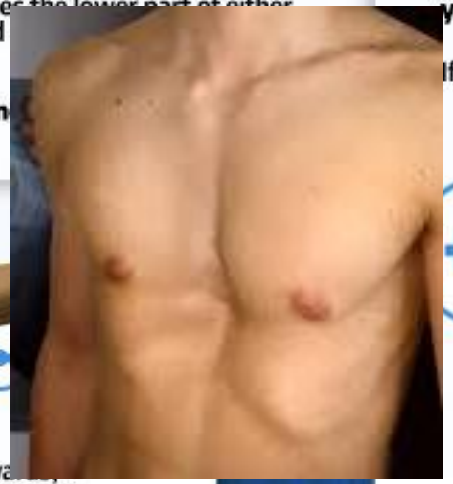
If yes, add **one point** fo

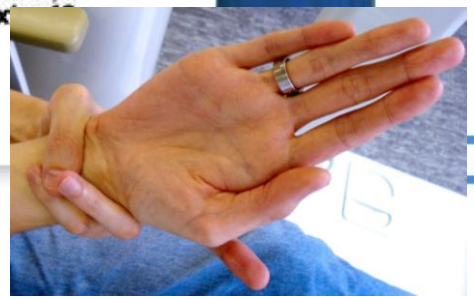




Arm span exceeding height ratio >1.05







SIH: Clinical manifestations 1

Cefalea
Occipito-nucale (28%)
Olocranica (31%)
Frontale (23%)

Disturbi Vestibolari
Vertigini/Capogiri (14%)

Nausea/Vomito (50 %)

Cefalea Ortostatica (92 %)

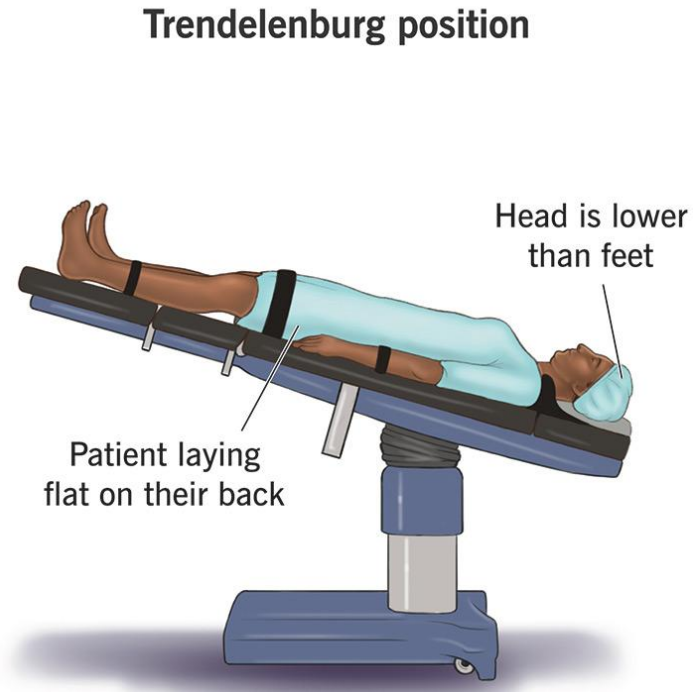
Disturbi Cocleari
Tinnitus (19 %)

Disturbi cognitivi (2.6 %)
Disordini del movimento (1.2 %)

Dolore Cervicale
Rigidità nucale (33%)

Worsened by orthostatic position and Valsalva

- **Baseline severity:** NRS ≤3
- **Onset-time when upright:** ≤4.5 h
- **Time to peak severity:** ≤ 7.5 h
- **Time to baseline severity:** 1.5 h



Adapted from meta-analysis by D'Antona et al. 2021

The headache spectrum

- ✓ Not all headaches are orthostatic
- ✓ The orthostatic component is lost with time
- ✓ OH is clinically heterogeneous
- ✓ OH is not pathognomonic for SIH

Table 4. Orthostatic headache quality and location.

Headache quality		Headache location	
Description	Frequency	Region	Frequency
Throbbing	48 (46.2%)	Occipital	78 (75.0%)
Dull ache	29 (27.9%)	Frontal	61 (58.7%)
Pressing	27 (26.0%)	Peri-orbital	40 (38.5%)
Sharp	16 (15.4%)	Vertex	37 (35.6%)
Pressure	15 (14.4%)	Temporal	33 (31.7%)
Heaviness	6 (5.8%)	Parietal	21 (20.2%)
Pulling	5 (4.8%)	Holocranial	12 (11.5%)
Tightening	4 (3.8%)	Jaw	5 (4.8%)
Stabbing	2 (1.9%)	Nose	8 (7.7%)
Burning	2 (1.9%)	Ear	3 (2.9%)
Other	7 (6.7%)	Cheek	3 (2.9%)

«Atypical» headaches in SIH

- Cervical or interscapular pain (coat-hunger)
- Acute thunderclap-like onset
- “Second-half of the day” headache
- New daily persistent headache
- Morning headache
- Intermittent headache
- Exertional headache

No headache 3%

Mehta D et al. Cephalalgia. 2025 doi:10.1177/03331024241308154.

SIH: Rare atypical manifestations

- **Cranial nerve palsies (VI nc)**
- **Hemifacial spasms**
- **Severe dysphagia**
- **Movement Disorders:** parkinsonism, ataxia, postural tremor, chorea
- Fronto-temporal brain sagging syndrome **(FTD-like syndrome)**
- **Cerebral vasoconstriction syndrome**
- **Nonconvulsive status epilepticus (NCSE)**

→ **Brain sagging**

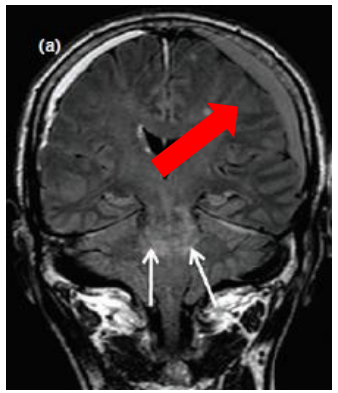
- **Galactorrhea**

→ **Hypothalamus-pituitary axis dislocation**

- **Radiculopathy, myelopathy**
- **Bibrachial amyotrophy** (hanging arm syndrome, bilateral hand muscle weakness and atrophy) mimicking MND
- **Bowel and bladder dysfunction**
- **Spinal pain** (sometimes orthostatic)
- **Torticollis**

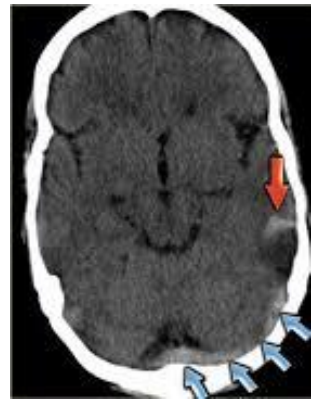
→ **SLEC**

SIH: Severe complications and emergencies



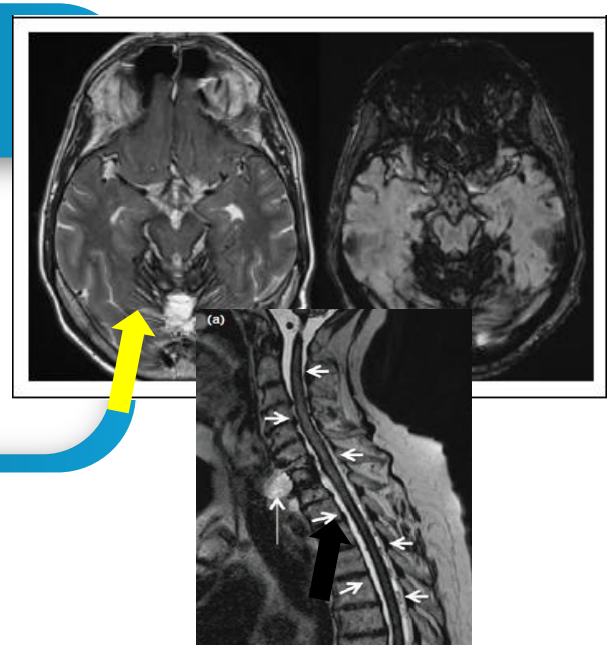
- Non-traumatic subdural hematoma (SDH)
  16-57%

- Cerebral venous thrombosis (CVT)
  1-2%



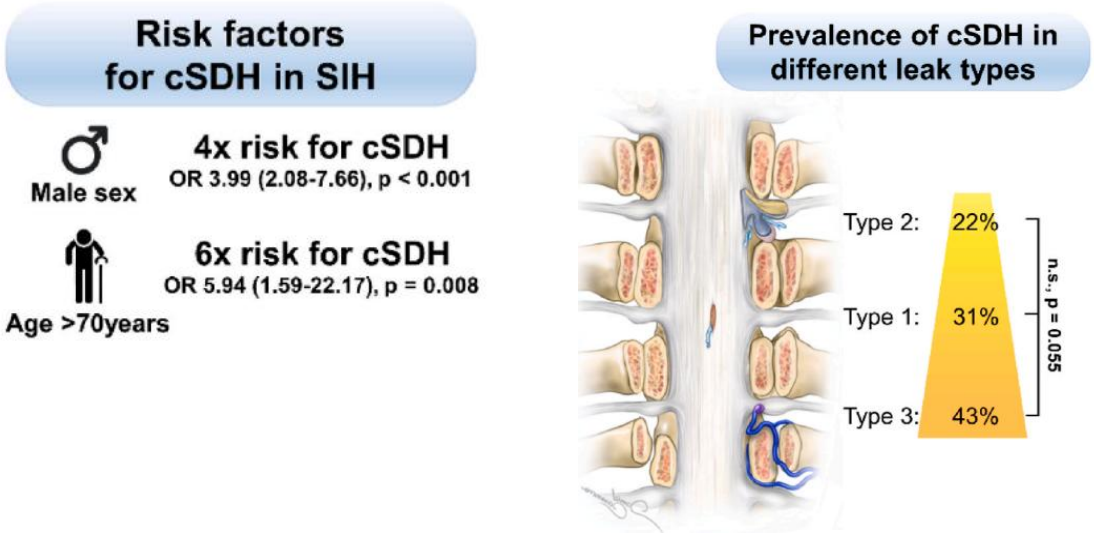
- Coma
  0.5-2.6%

- Leptomeningeal hemosiderosis
  3.6-10%



Management of chronic subdural hematoma in spontaneous intracranial hypotension

Manou Overstijns [a], Amir El Rahal [a], Katharina Wolf [a], Niklas Lützen [b], Urs Würtemberger [b], Lucas Becker [b], Horst Urbach [b], Daniel Casanova Martinez [c], Jürgen Beck [a,*], Florian Vol Brain and Spine 5 (2025) 104320



SDH/CVT due to SIH red flags:

- bilateral (88%)
- young age
- no hemorragic/thrombotic risk factors
- no history of trauma
- frequent recurrence

Coma

A serious complication of spontaneous intracranial hypotension Neurology

Table 1 Patient demographics and clinical data

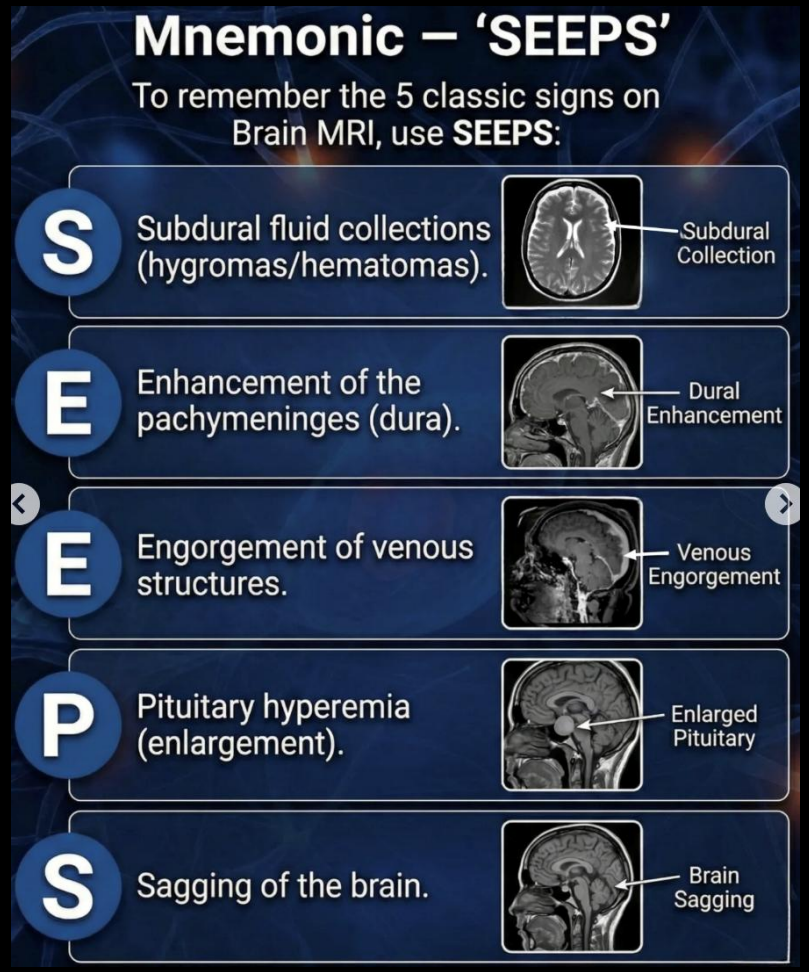
	All patients	Coma		p Value
		Yes	No	
Patients, n (%)	583	15 (2.6)	568 (97.4)	
CSF leak type, n (%)[a]				0.4799
1A	148 (25.4)	6 (40.0)	142 (25.0)	
1B	6 (1.0)	0 (0)	6 (1.1)	
2A	219 (37.6)	6 (40.0)	213 (37.5)	
2B	22 (3.8)	1 (6.7)	21 (3.7)	
3	14 (2.4)	0 (0)	14 (2.5)	
4	174 (29.9)	2 (13.3)	172 (30.3)	
Age at symptom onset, y				0.0073
Mean (SD)	45.9 (14.9)	55.9 (12.7)	45.7 (14.8)	
Median (IQR)	46 (37–56)	57 (43–68)	46 (37–55)	
Range, minimum–maximum	2–88	33–72	2–88	
Sex, n (%)				0.0003
Male	207 (35.5)	12 (80.0)	195 (34.3)	
Female	376 (64.5)	3 (20.0)	373 (65.7)	
Surgery, n (%)				0.0766
Yes	296 (50.8)	11 (73.3)	285 (50.2)	
No	287 (49.2)	4 (26.7)	283 (49.8)	
Extradural CSF				0.7885
Positive	291 (49.9)	8 (53.3)	283 (49.8)	
Negative	292 (50.1)	7 (46.7)	285 (50.2)	

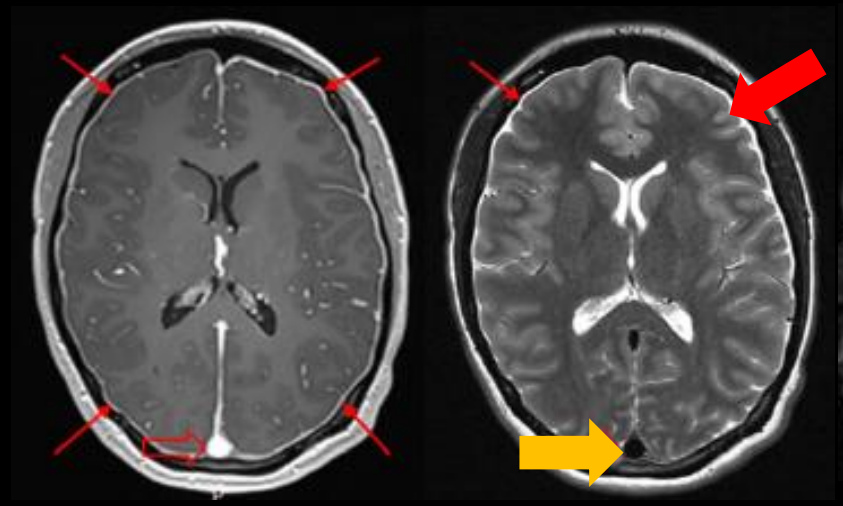
SIH: Diagnostic protocol

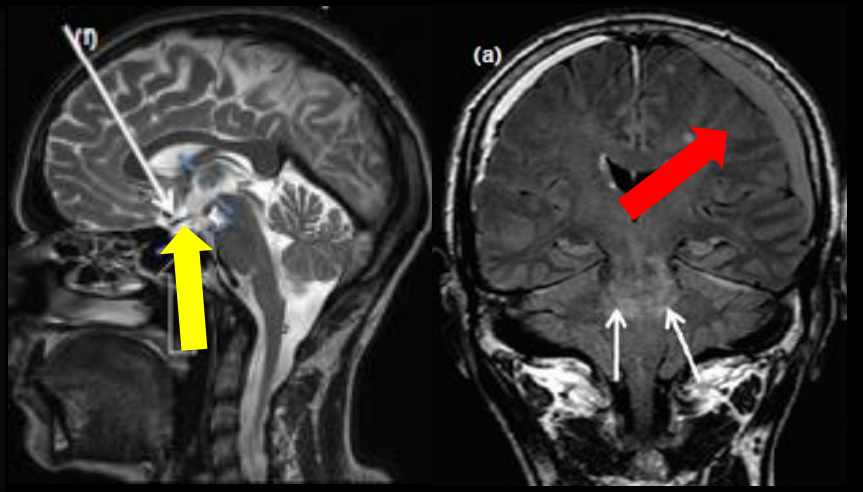
- Diagnosis is based on **compatible symptoms** + **indirect radiological signs** +/- **CSF leaks identification**

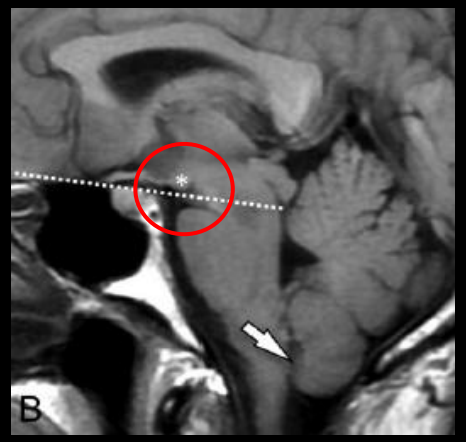
- **Lumbar puncture is not necessary and can exacerbate symptoms**
- **CSF normal opening pressure do not exclude diagnosis (60%)**
- **Invasive intracranial pressure monitoring is not recommended in standard of care**

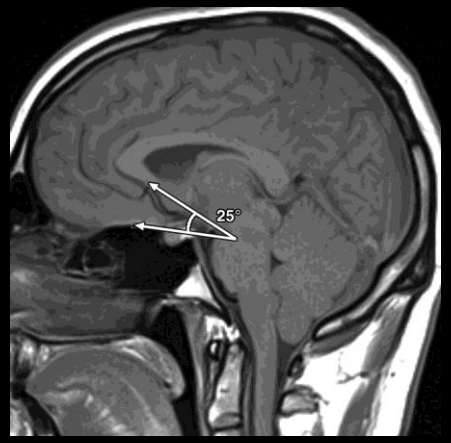
SIH: Neuroimaging

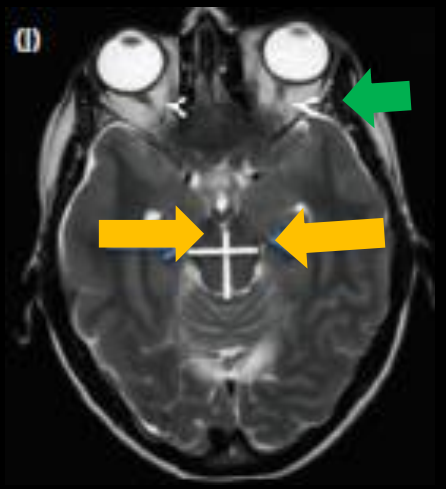










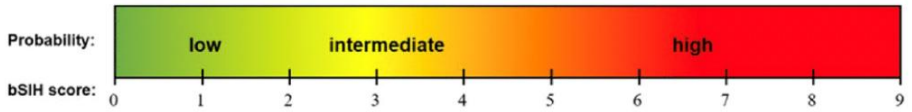


- Cerebellar tonsillar ectopia
- Reduced prepontine cistern < 5mm and suprasellar cistern <4 mm
- Reduced mammillary bodies – pons distance (<6.5 mm)
- Reduced P-M angle (<45°)
- Longer AP mesencephalic diameter ('Sag ratio')
- Pendent optic nerves

Critical Reappraisal and Validation of the Bern Score System for Diagnosing Spontaneous Intracranial Hypotension

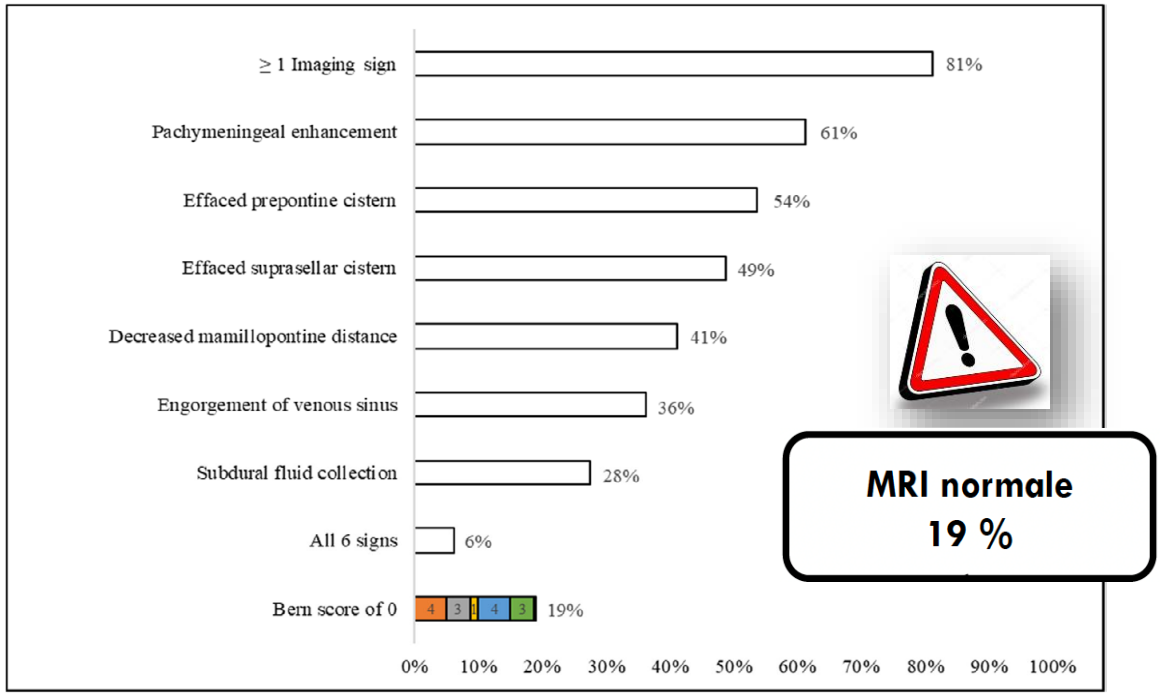
J Clin Neurol 2025;21(6):557-564

		Score
Major	Engorgement venous sinus	2
	Pachymeningeal enhancement	2
	Suprasellar cistern (≤ 4 mm)	2
Minor	Subdural fluid collection	1
	Prepontine cistern (≤ 5 mm)	1
	Mamillopontine distance (≤ 6.5 mm)	1



- **Score of ≤ 2→LOW probability** of SIH due to CSF leaks
- **Score 3–4→INTERMEDIATE probability**
- **Score ≥ 5 →HIGH probability**

Conclusions The Bern score showed high specificity but limited sensitivity in our cohort, indicating it should not be used alone as a screening tool. A lower cutoff may improve its diagnostic performance, and timing from symptom onset should be considered when interpreting the score.



MRI normale 19 %

Se si riscontra valori BERN SCORE (bSIH score) maggiori/uguali a 2 inviare il paz in centro HUB per eventuale approfondimento diagnostico invasivo e percorso terapeutico

https://doi.org/10.3988/jcn.2025.0154; Dalby SW et al. Eur J Neurol. 2025. doi: 10.1111/ene.16579.

AJNR AMERICAN JOURNAL OF NEURORADIOLOGY

Consensus Guidelines on Diagnostic Brain and Spine Imaging of Spontaneous Intracranial Hypotension

Peter G. Kranz, Timothy J. Amrhein, Waleed Brinjikji, Andrew L. Callen, Ian Carroll, J. Levi Chazen, Jeremy Cutsforth-Gregory, Deborah I. Friedman, Troy A. Hutchins,

Brain sequences (4–5 mm thickness or 3D sequences if available)
T2W axial 3D—Look for subdural collections/venous sinuses, look for sagging of brainstem& SICH scoring
Flair axial/3D sagittal—Look for collection/ venous sinuses
SWI—To look for hemorrhage including CVST and its complications if any
T1W pre- and post-contrast—To look for pachymeningeal thickening and enhancement
Spine sequences (3–4 mm thickness)
T2W sagittal (with and without fat suppression)Whole spine screening - to look for epidural collection
T2W axial—in the region of epidural collection
3D heavily T2W (FIESTA/CISS)—To look for meningeal diverticula, dural tear and extent of epidural collection

AINR Associazione Italiana di Neuroradiologia Diagnostica e Interventistica

Ipotensione Liquorale/Ipertensione endocranica: proposta di standard minimi per esami Neuroradiologici

1. In caso di sospetta Ipotensione Liquorale Spontanea (SIH)

RM ENCEFALO

- Volumetrica 3D T1 pre e post mdc
- Volumetrica FLAIR T2-w (da preferire con soppressione del segnale del grasso)
- Sequenze ad alta suscettibilità magnetica (da preferire le Susceptibility Weighted Imaging – SWI)

Se si riscontra valori BERN SCORE (bSIH score) maggiori/uguali a 2 inviare il paz in centro HUB per eventuale approfondimento diagnostico invasivo e percorso terapeutico

RACHIDE

- La valutazione morfologica deve comprendere il rachide in toto (cervicale, dorsale e lombare)
- Studio T2-w ad alta risoluzione (inferiore a 2 mm di spessore) volumetrico da completare con ricostruzioni multiplanari sui tre piani dello spazio
- Studio Mielografico
- Non è mandatario il completamento con mdc

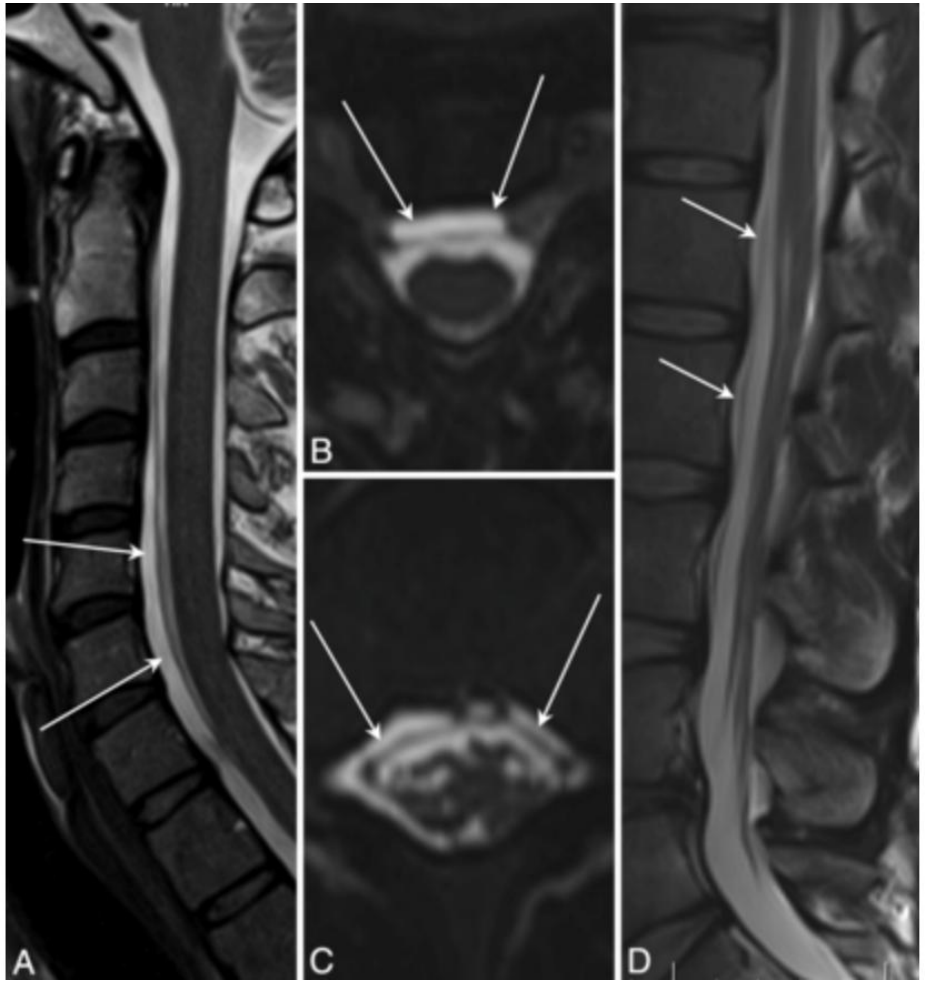
Se si riscontrano SLEC inviare il paz in centro HUB per approfondimento diagnostico invasivo ed adeguato percorso terapeutico

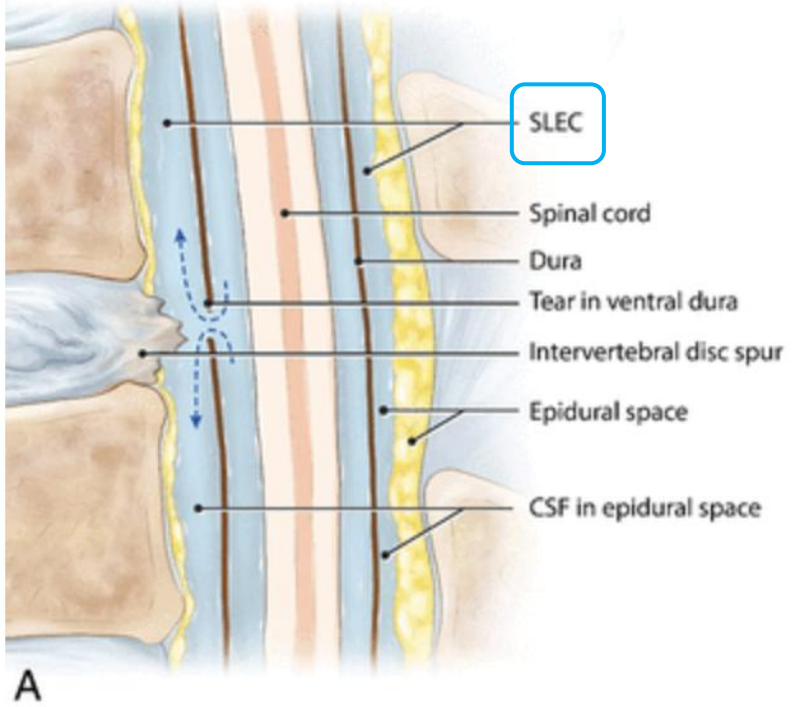
CSF leaks identification

Spinal MRI (fat-suppression) + Gd

SLEC + **SLEC -**

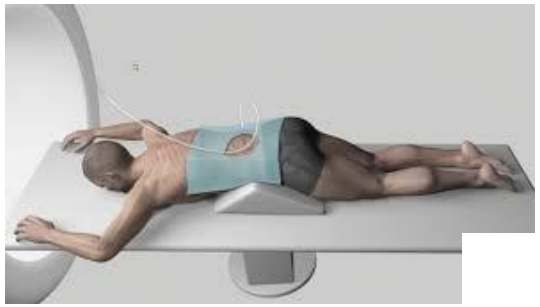
SLEC: Spinal longitudinal extradural CSF collection

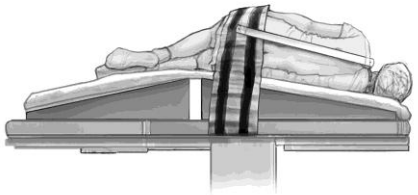


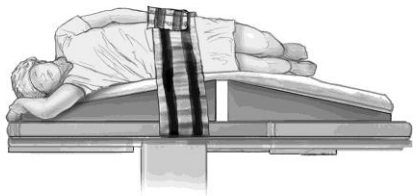


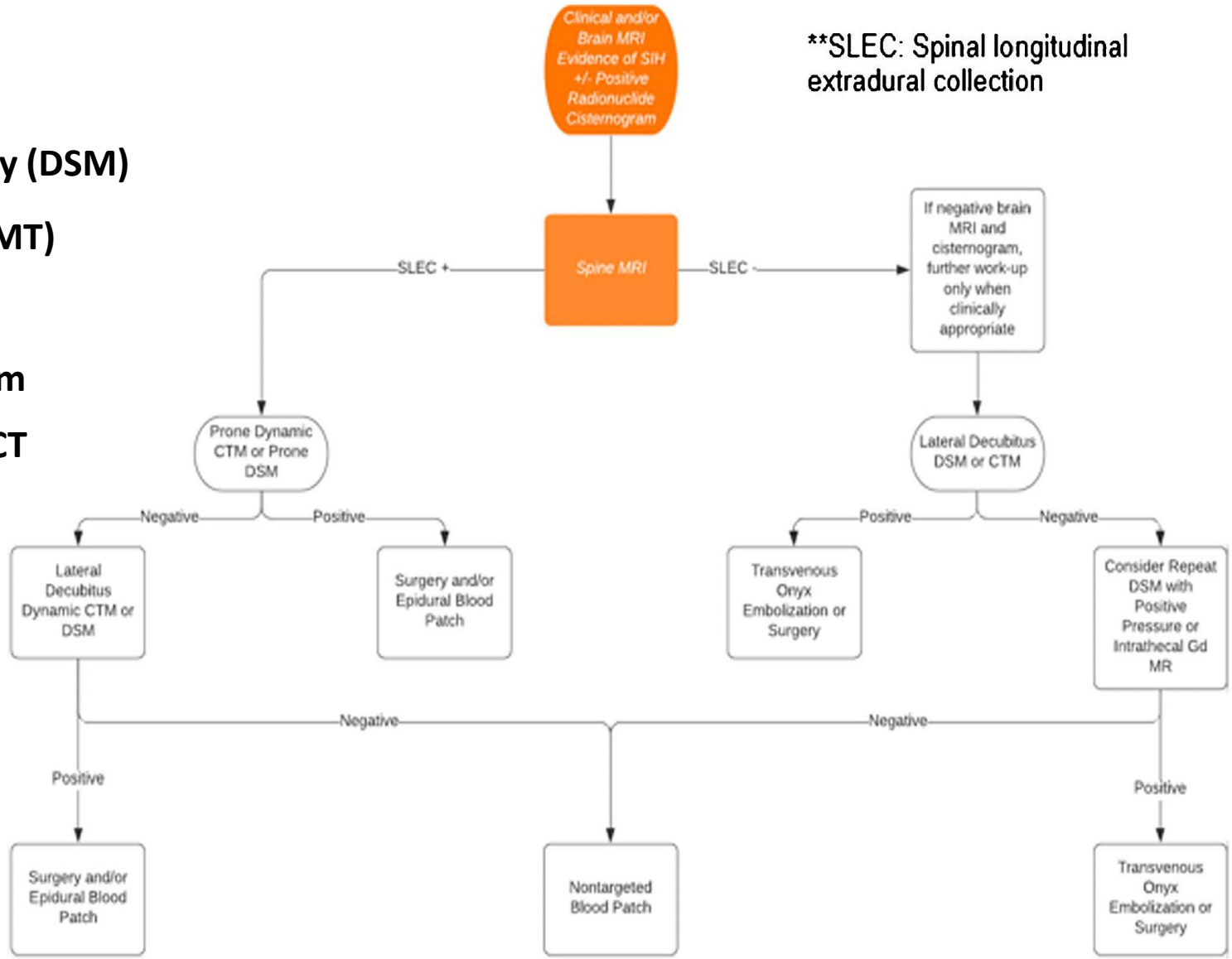
Second-line imaging techniques

- Isotope cisternography
- Conventional digital subtraction myelography (DSM)
- CT myelography with intrathecal contrast (CMT)
- MRI myelography with IV gadolinium
- MRI myelography with intrathecal gadolinium
- CT myelography with flat panel cone-beam CT









https://doi.org/10.1007/s00234-022-03079-5; DOI: https://doi.org/10.3174/ajnr.A6016; Fichtner J et al. J Neurol Neurosurg Psychiatry. 2016;87(6):650—5.

Diagnosis and treatment of disorders of intracranial pressure: consensus statement of the Spanish Society of Neurology's Headache Study Group

J. García-Ull[a,*], N. González-García[b], M. Torres-Ferrús[c], D. García-Azorín[d],

Neurología 40 (2025) 118—137

Multidisciplinary consensus guideline for the diagnosis and management of spontaneous intracranial hypotension

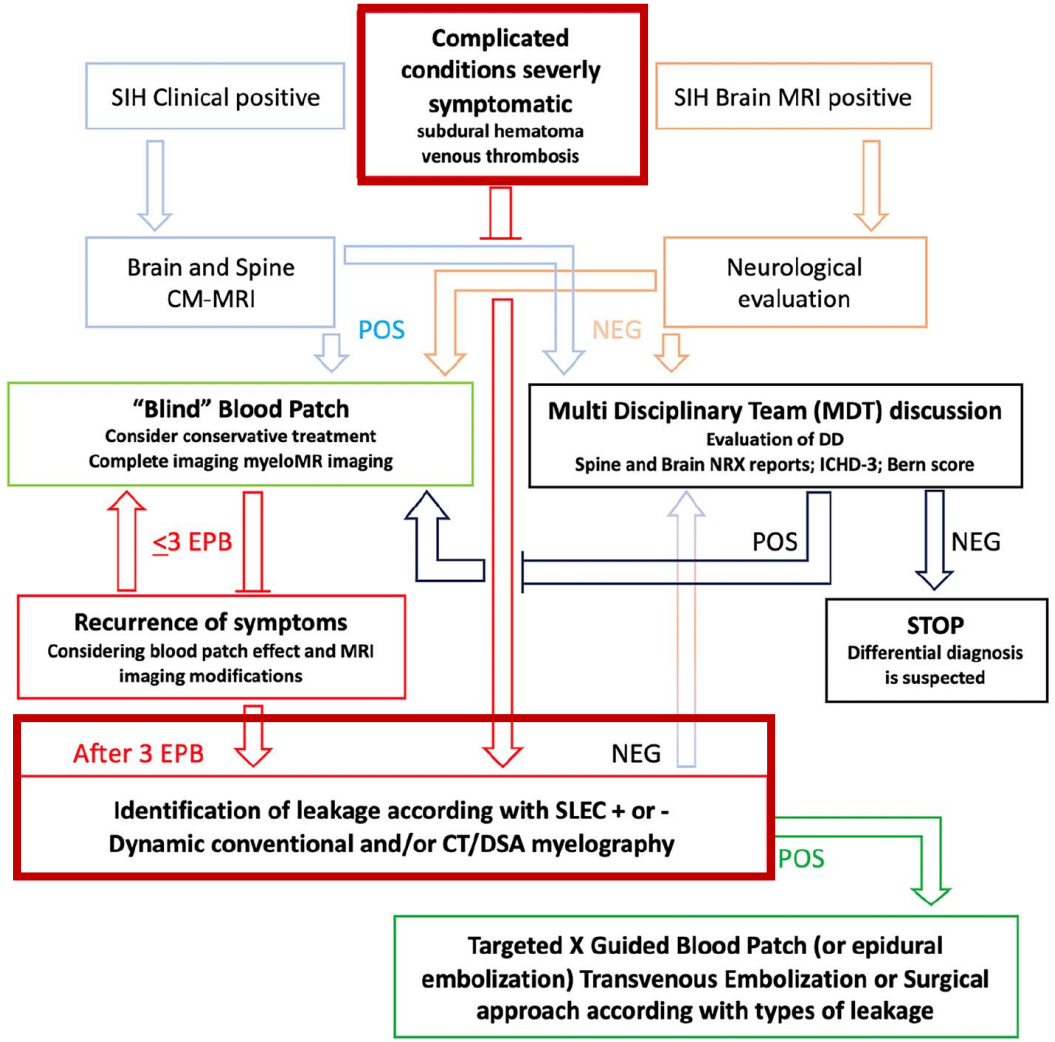
Sanjay Cheema ,[1,2] Jane Anderson,[3] Heather Angus-Leppan ,[4] Pau Cheema S, *et al*. *J Neurol Neurosurg Psychiatry* 2023;

Second-line imaging techniques are reserved to a minority of patients who do not respond to first-line therapy

- MRI suggestive of SIH, no/temporary benefit from >1 blind EBPs
- Normal MRI, SLEC negative, no/temporary benefit from 1 or > blind EBPs
- Normal MRI, high clinical suspicion and myelography recommended after MDT discussion
- MDT decision for myelography based on individual factors
- Emergency complications of SIH requiring «leak-first» strategy

Recommendations for the diagnosis and treatment of spontaneous intracranial hypotension La radiologia medica 2025

Elisa Francesca Maria Ciceri[1] · Luigi Cirillo[7,8] · Francesco Causin[2] · Ferdinando Caranci[3] · Alessandra Splendiani[4] · Mario Muto[5] · Mauro Bergui[6]



SIH: Therapy and management

CONSENSUS STATEMENT

Diagnosis and treatment of disorders of intracranial pressure: consensus statement of the Spanish Society of Neurology's Headache Study Group

J. García-Ull[a,*], N. González-García[b], M. Torres-Ferrús[c], D. García-Azorín[d],
Neurología 40 (2025) 118—137

01

CONSERVATIVE THERAPY

- Bed rest
- Hydration
- Abdominal binders
- No Valsalva
- Caffeine

02

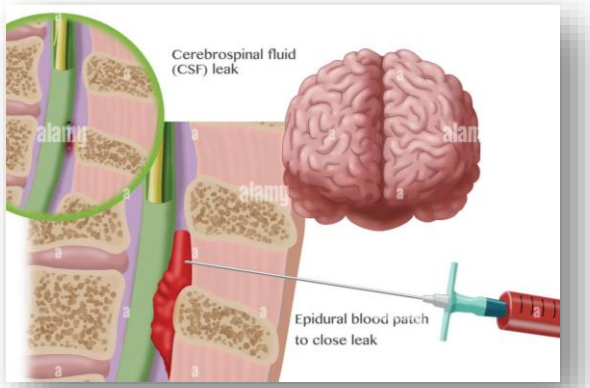
CHECK RESPONSE

2 weeks follow-up

03

NON-TARGETED EBP

20-40 ml



04

CHECK RESPONSE AND COMPLICATIONS

2-4 wks follow-up

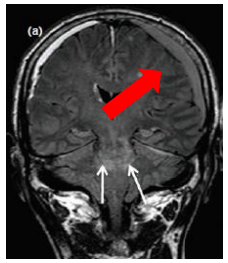
05

REPEAT NT-EBP OR EVALUATE TARGETED EPB

Multidisciplinary team

Seek urgent medical attention if:

- ✓ New-onset severe back or leg pain
- ✓ Lower limb weakness or sensory disturbance
- ✓ Urinary or faecal incontinence or retention
- ✓ Perineal sensory disturbance
- ✓ Nausea and vomiting
- ✓ Rebound headache



Management of chronic subdural hematoma in spontaneous intracranial hypotension

Manou Overstijns[a], Amir El Rahal[a], Katharina Wolf[a], Niklas Lützen[b], Urs Würtemberger[b], Lucas Becker[b], Horst Urbach[b], Daniel Casanova Martinez[c] Jürgen Beck[a,*], Florian Volz[a]

Brain and Spine 5 (2025) 104320

Leak-first strategy

- Asymptomatic cSDH
- cSDH ≤10 mm

Subdural-first strategy

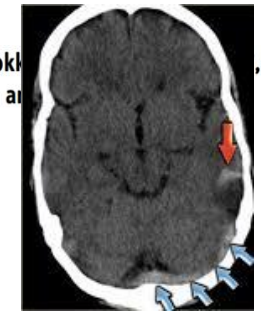
- Symptomatic cSDH
- cSDH >10 mm
- Mid-line shift
- Brain compression
- Rapid clinical deterioration

Mechanical thrombectomy

SDH embolization

Prevalence, clinical presentation, and treatment-management of cerebral venous thrombosis associated with spontaneous intracranial hypotension: A combined case-series and systematic literature review approach 2024

Gaetano Risi[1], Anne Ducros[2], Liesjet van Dokk
Nicola Marchi[4], Max Villain[5], Vincent Costalat[1] a

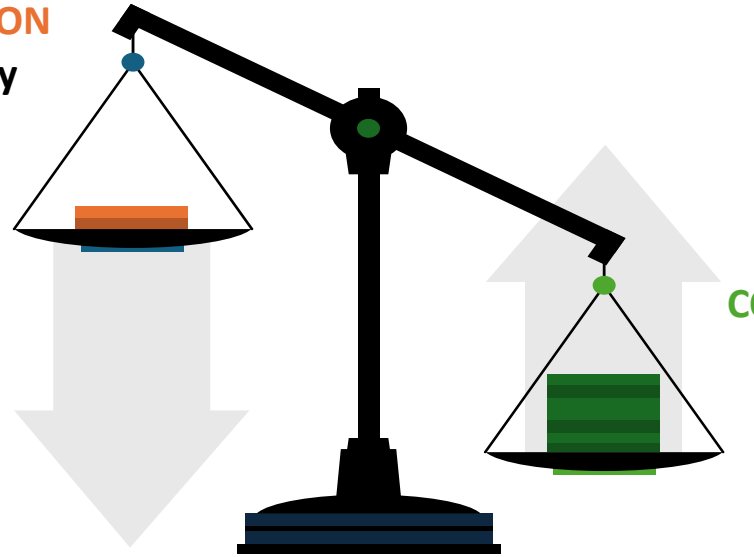


INCOMPLETE RESOLUTION

Non-combined strategy

EBP alone

Anticoagulation alone



COMPLETE RESOLUTION

Combined strategy

EPB+Anticoagulation (EBP before AC)

SIH: Surgical procedures

Table 17 Surgical procedures in the treatment of spontaneous intracranial hypotension.

Intraoperative neurophysiological monitoring is required.

Procedures:

- Direct repair of the dural tear (closure by suturing)
- Duroplasty (''patch'' made of biological or synthetic dura substitute, or muscle, to reinforce the closure, or if the edges cannot be accessed)
- Alternative to duroplasty: fibrin glue
- Resection of bone spurs causing anterior ruptures
- Surgical ligation of CSF-venous fistulae
- Alternative for CSF-venous fistulae: fibrin glue
- Surgical ligation or clipping of meningeal diverticula or (less frequently) cysts
- Dural reduction surgery: proposed by Schievink in 2009, not performed in any of the articles included in the meta-analysis by D'Antona et al.[48]

NOTES:

With current microsurgical techniques, both ventral and lateral tears (e.g., in diverticula) and CSF-venous fistulae (generally also lateral) may be treated with a minimally invasive procedure, generally following a dorsal approach via hemilaminectomy or interlaminar fenestration.

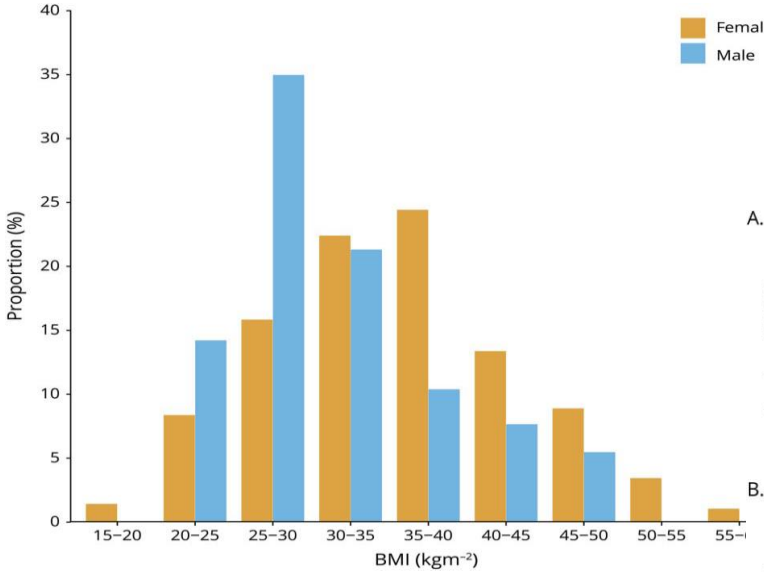
Ventral dural tears require a transdural approach with separation of the denticulate ligaments, enabling mobilisation of the spinal cord outside the surgical field.

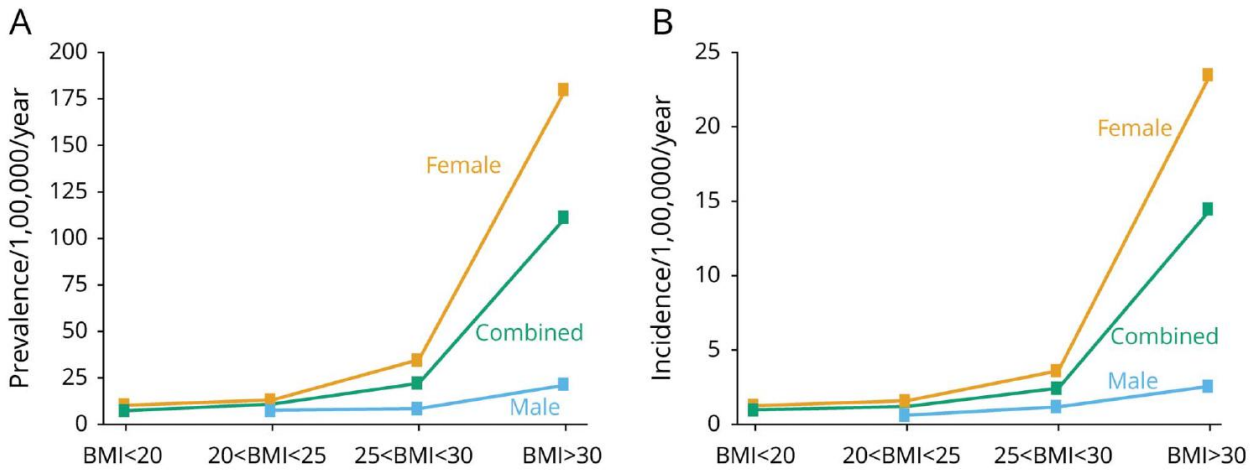
If surgical and endovascular options are not possible or are ineffective, targeted EBP may be repeated.

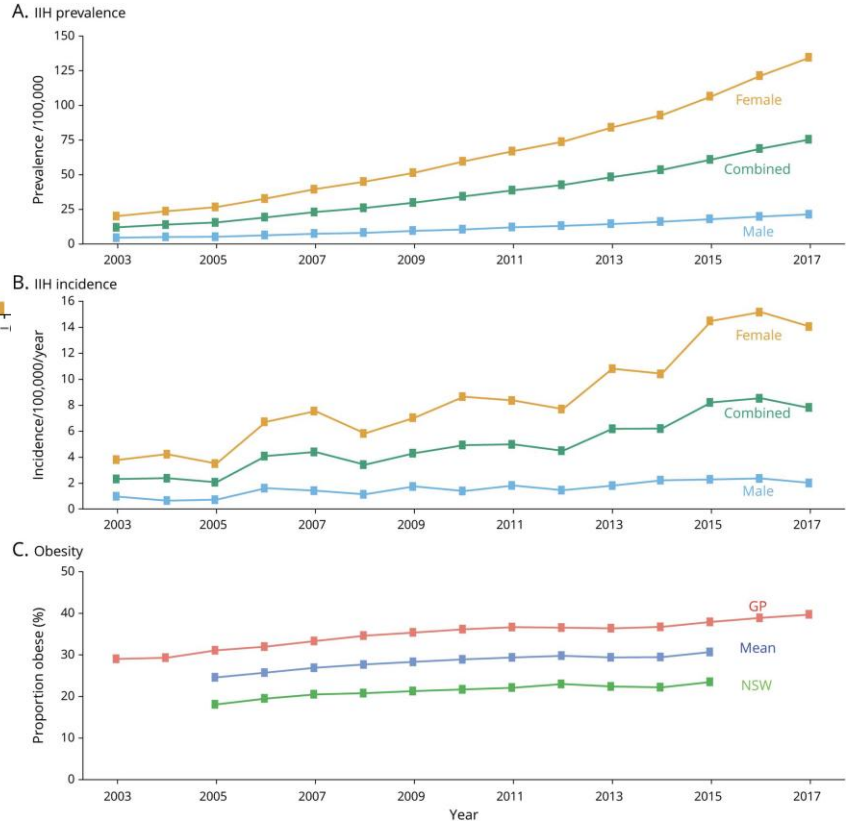
CSF: cerebrospinal fluid; EBP: epidural blood patch.

IDIOPATHIC INTRACRANIAL HYPERTENSION (IIH): Background

- **Condition characterized by signs and symptoms due to elevated intracranial pressure without identifiable causes**
- **With or without papilledema**
- **Epidemiology**
  - Prevalence 76/100000 (2017)
  - Incidence 7.8/100000/y (2017)
  - 3.3-28/100000 (2025)
  - F>>M; 85% females
  - > high BMI



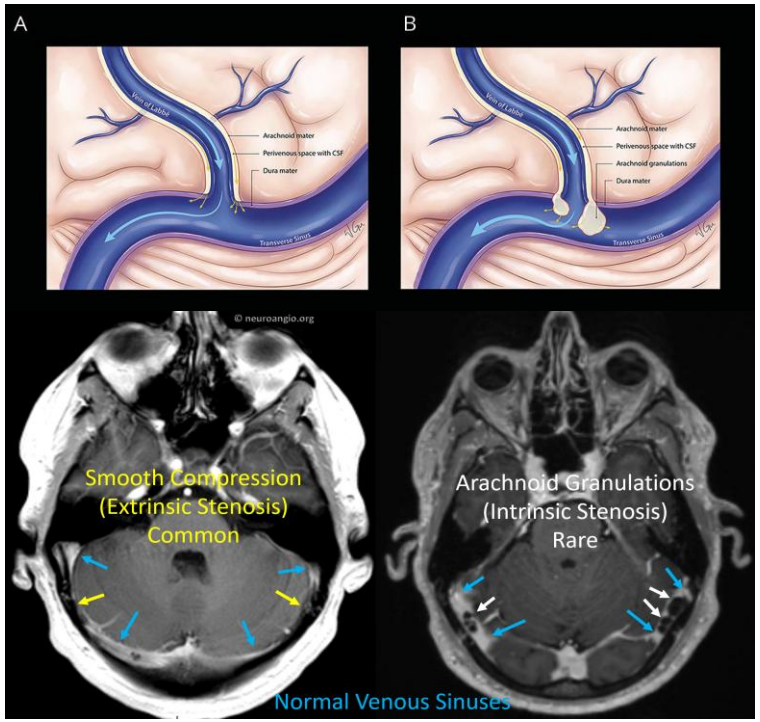


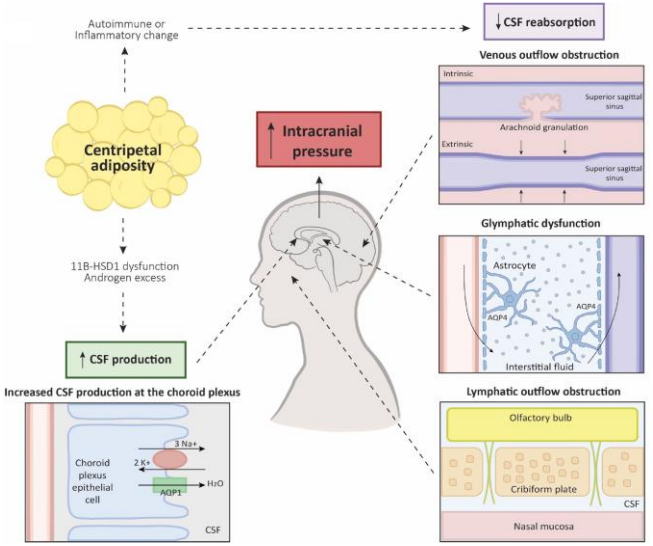


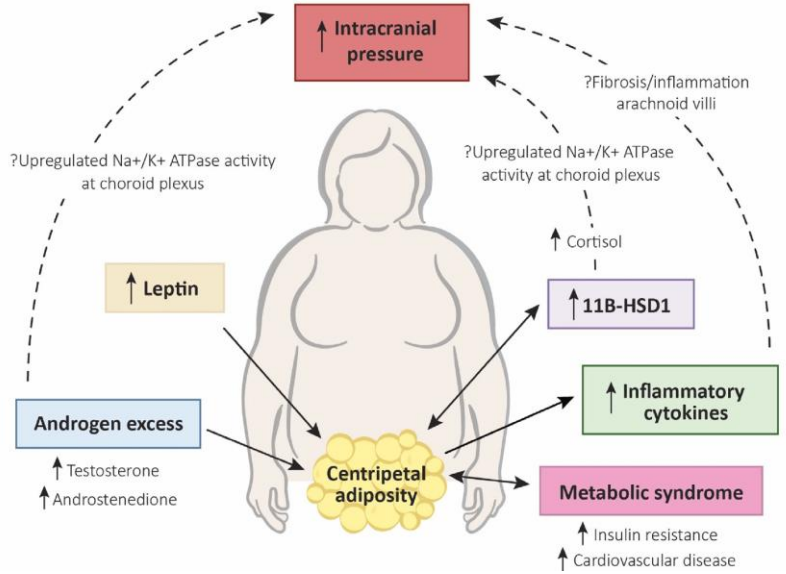
doi:10.1212/WNL.0000000000011463; DOI: 10.1016/j.ophtha.2024.10.031

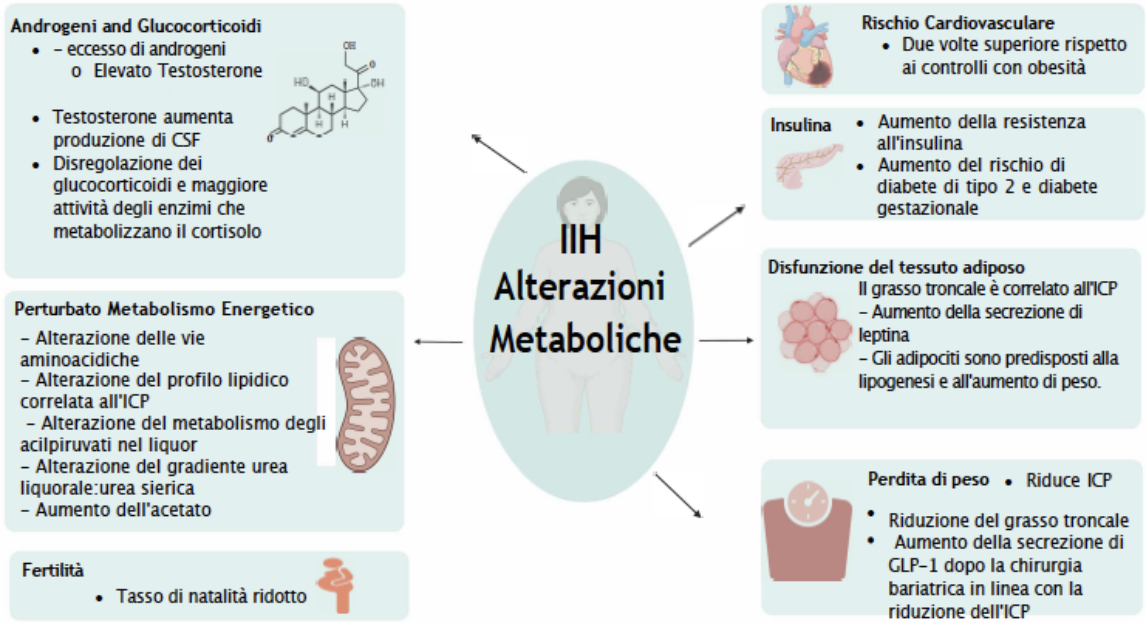
IIH as a systemic metabolic-neuroinflammatory syndrome

↑ CSF production + ↓ CSF reabsorption









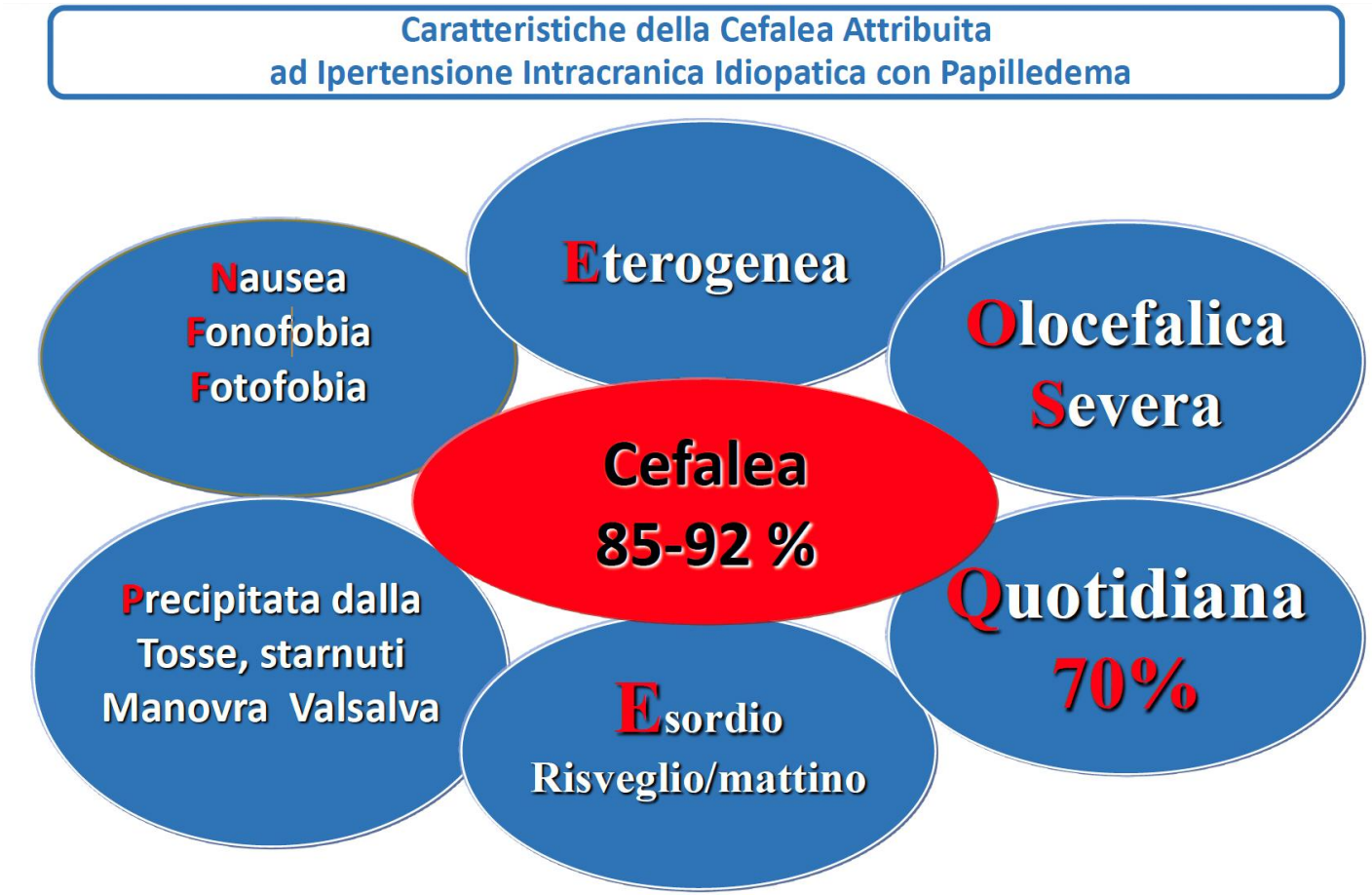
J Neurol Neurosurg Psychiatry 2024;

Understanding the pathophysiology of idiopathic intracranial hypertension (IIH): a review of recent developments

Blake D Colman ,[1,2] Frederique Boonstra,[1] Minh NL Nguyen,[1,2]

doi:10.1136/jnnp-2023-332222; doi:10.1212/WNL.0000000000006166; https://doi.org/10.1038/s41582-023-00893-0

IIH: Clinical manifestations 1



Auditory and vestibular
- Vertigo
- Tinnitus (>50%)
- Auricular fullness

Cranial nerves dysfunction
- VI cn palsy: 30%
- Olfactory dysfunction: 80%

Other symptoms
- Facial palsy
- Neck/Lower back pain
- Cognitive dysfunction
- Anxiety, Depression

Headache is persistent in 60% of pts despite normalisation of ICP

D'amico D. et al. Neurol Sci 2013; Wall M. et al. Jama Neurol 2014; Yri. et al. Eur J Neurol 2014

IIH: Clinical manifestations 2

Ophtalmic features

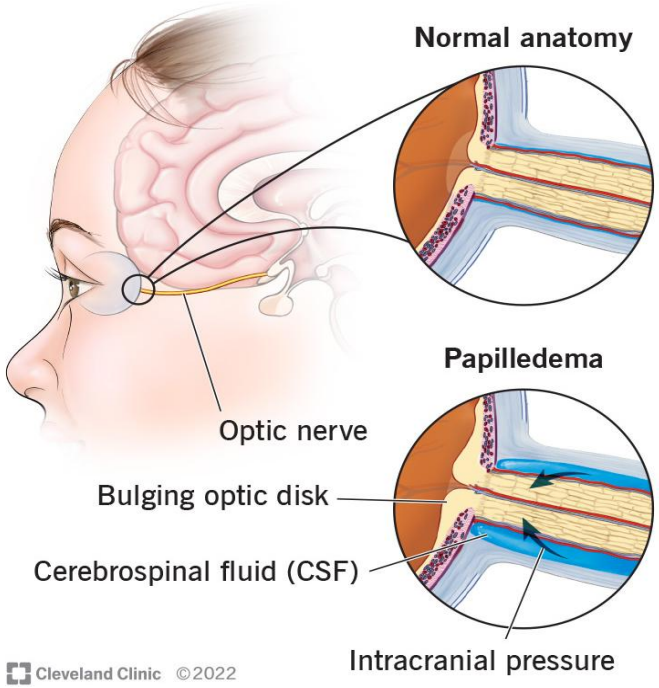
- **Papilloedema (70%)**
- Transient visual obscurations
- Visual blurring
- Photopsia

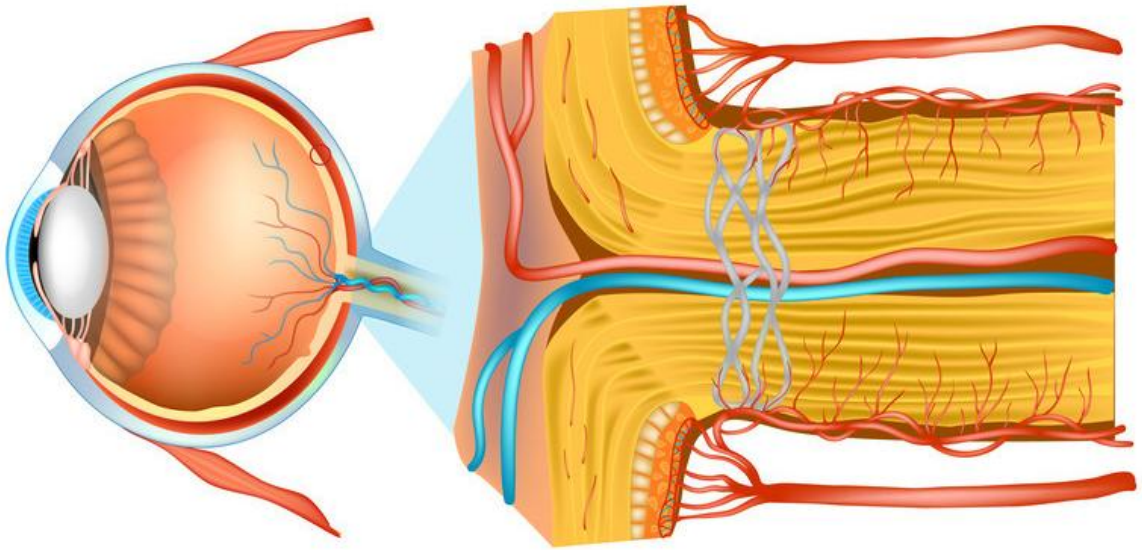
Triggered by:

- Postural changes
- Valsalva manoeuvre
- Exposure to intense light
- Eye movements

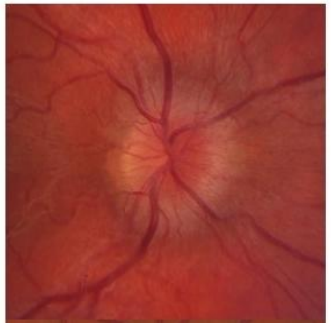
Peripheral vision loss (40%)

Transient ischaemia of the optic nerve



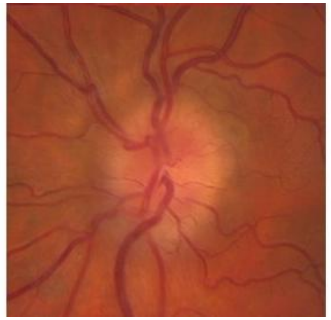


Frisen grading scale



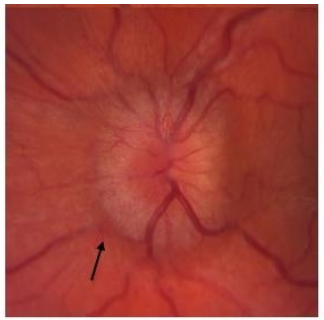
Grade 1

- Grayish C-shaped halo surrounding the disc*
- Sparing of the temporal disc margin
- Radial nerve fiber striation disruption



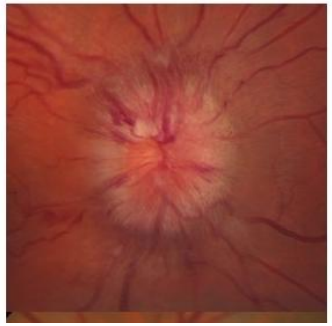
Grade 2

- Halo becomes circumferential*
- Nasal border elevation
- No major vessel obscuration



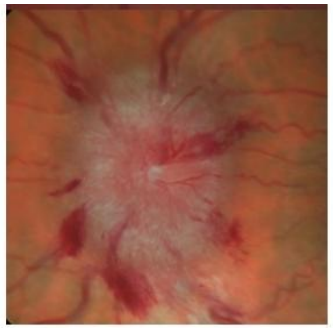
Grade 3

- Obscuration of at least one vessel *leaving the disc** (arrow)
- Elevation of all borders
- Circumferential halo



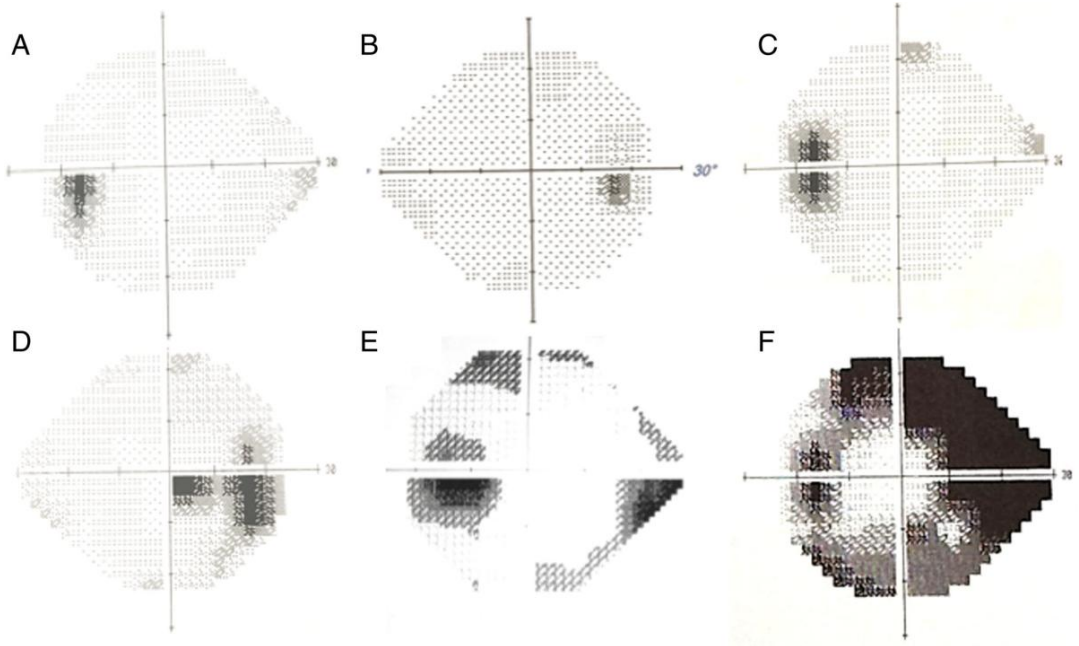
Grade 4

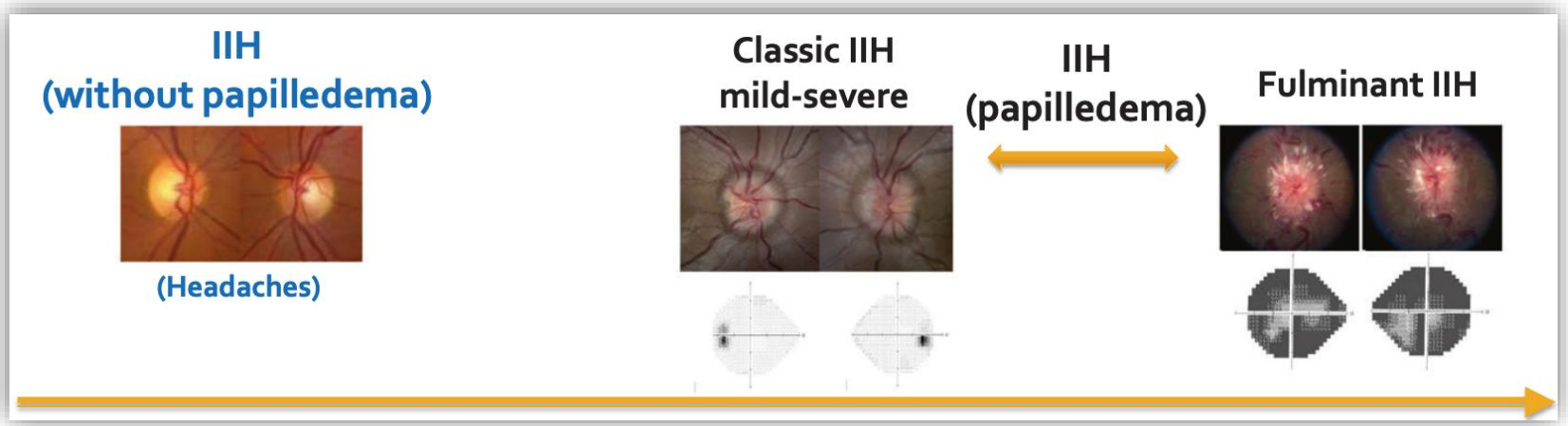
- Obscuration of a major vessel *on the disc**
- Complete elevation including the cup
- Circumferential halo



Grade 5

- Obscuration of all vessels on the disc *and* leaving the disc*
- All features of Grade 4

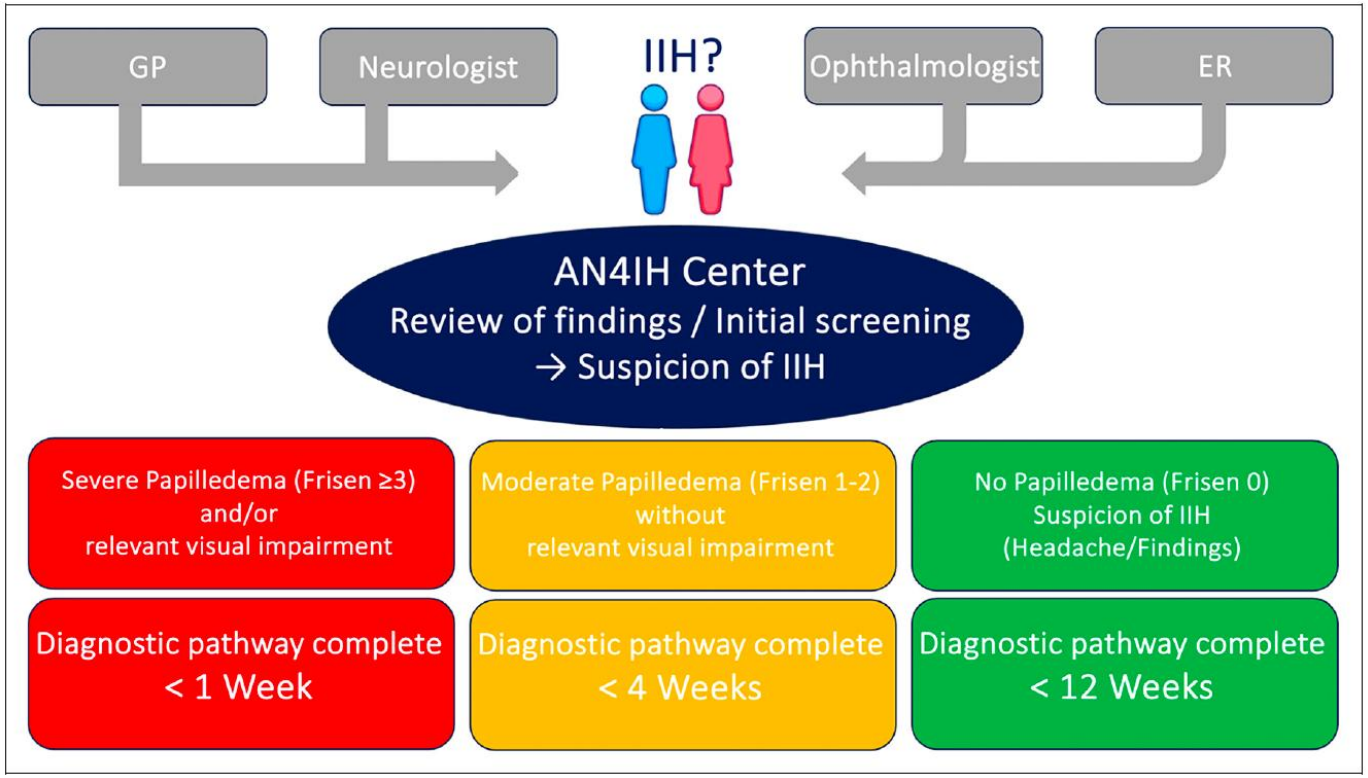




Biousse, V et al. *Eye* **37**, 2361–2364 (2023). https://doi.org/10.1038/s41433-022-02361-3

Diagnosis, treatment and monitoring of idiopathic intracranial hypertension: Consensus recommendations of the Austrian IIH network (AN4IH)

Cephalalgia
2025, Vol. 45(11) 1–13



Pseudopapilloedema causes

- Intraocular hypotony
- Small hypermetropic discs
- Tilted myopic discs
- Vitreous traction
- Disc drusen

Table 4 Secondary causes of idiopathic intracranial hypertension.

Differential diagnosis of IIH with papilloedema
1. Obstruction of venous flow
Venous sinus thrombosis
Jugular vein thrombosis
2. Space-occupying lesions
3. Secondary to decrease in CSF reabsorption
Subarachnoid haemorrhage
CNS infections
4. Increased CSF production

CNS: central nervous system; CSF: cerebrospinal fluid; IIH: idiopathic intracranial hypertension.

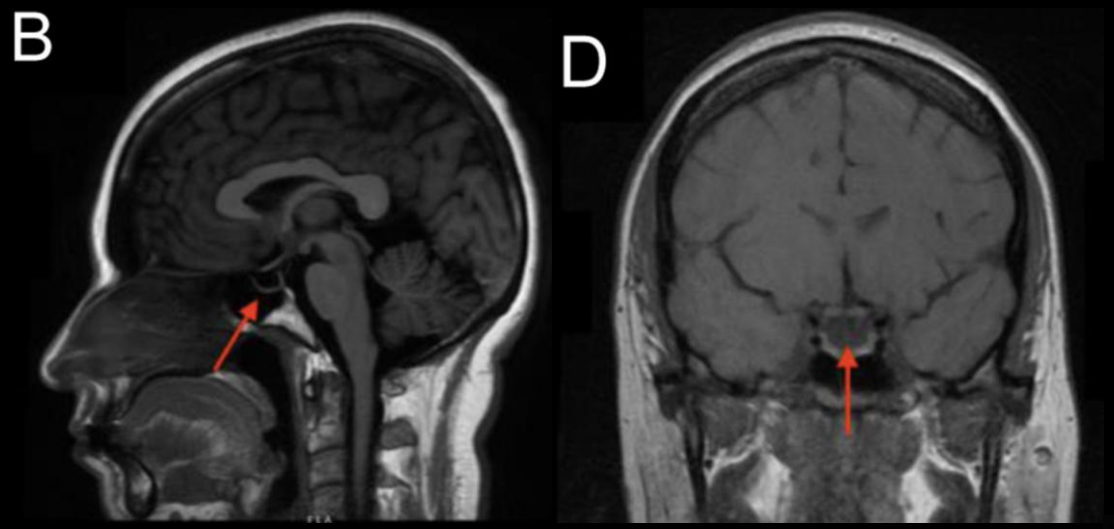
Table 5 Drugs and conditions that may increase intracranial pressure.

Drugs:
Tetracyclines
Retinoids (all-trans retinoic acid and derivatives)
Vitamin A
Lithium
Growth hormone
Corticosteroid withdrawal
Kidney failure
Hypercapnia
Malignant arterial hypertension

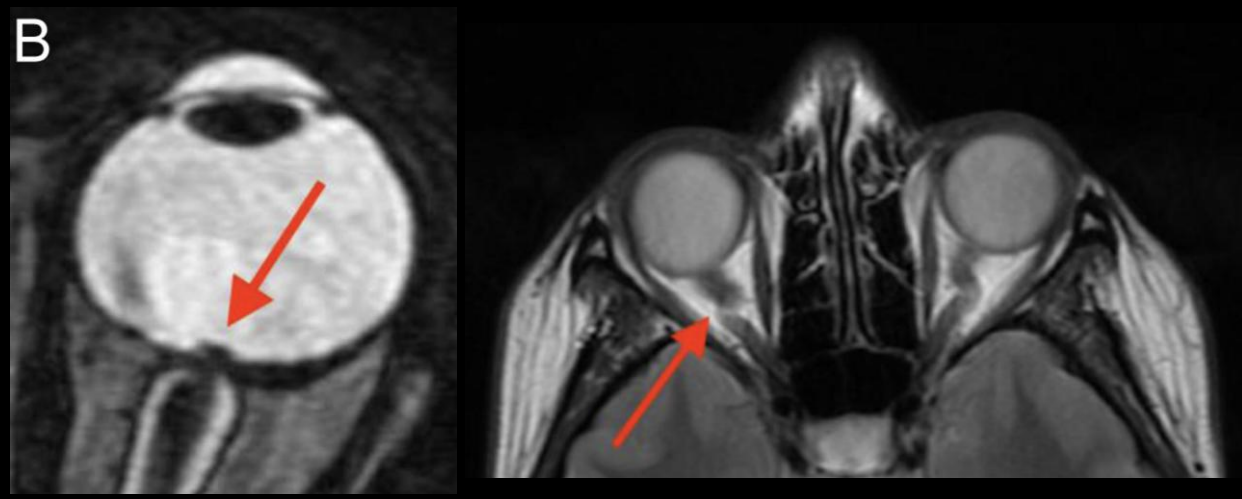
Biousse, V et al. *Eye* **37**, 2361–2364 (2023). https://doi.org/10.1038/s41433-022-02361-3

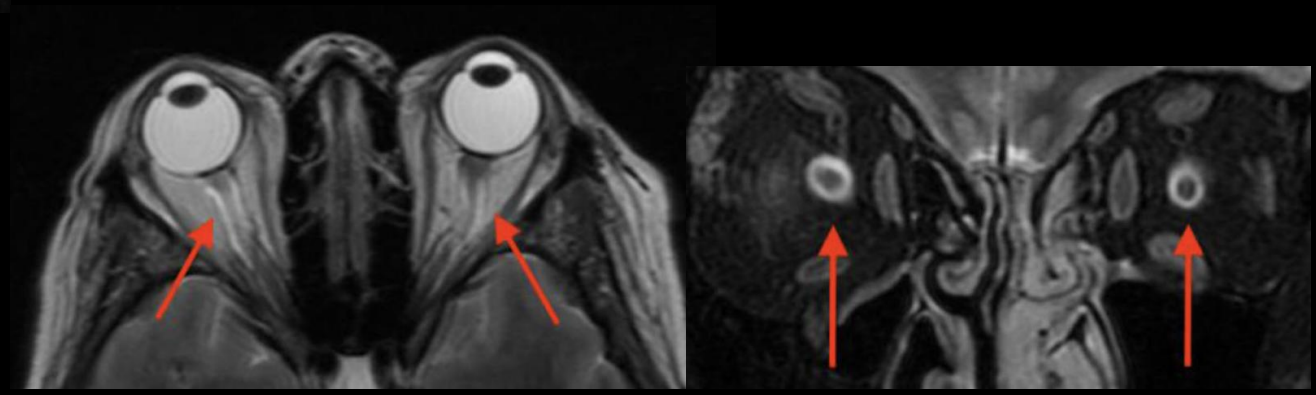
IIH: Neuroimaging

Empty Sella

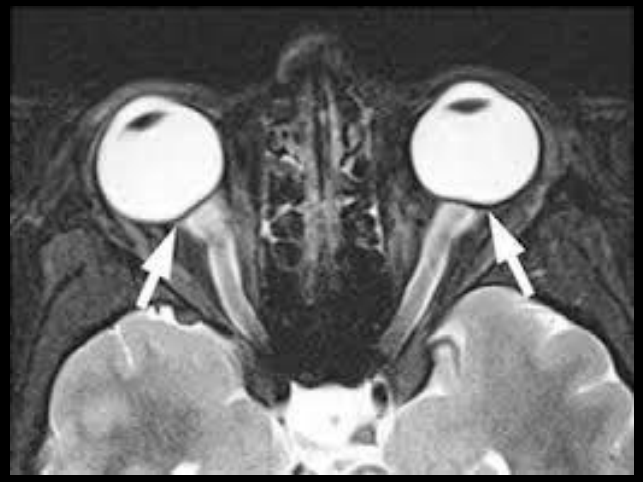


Optic nerve protrusion, tortuosity and sheath distension



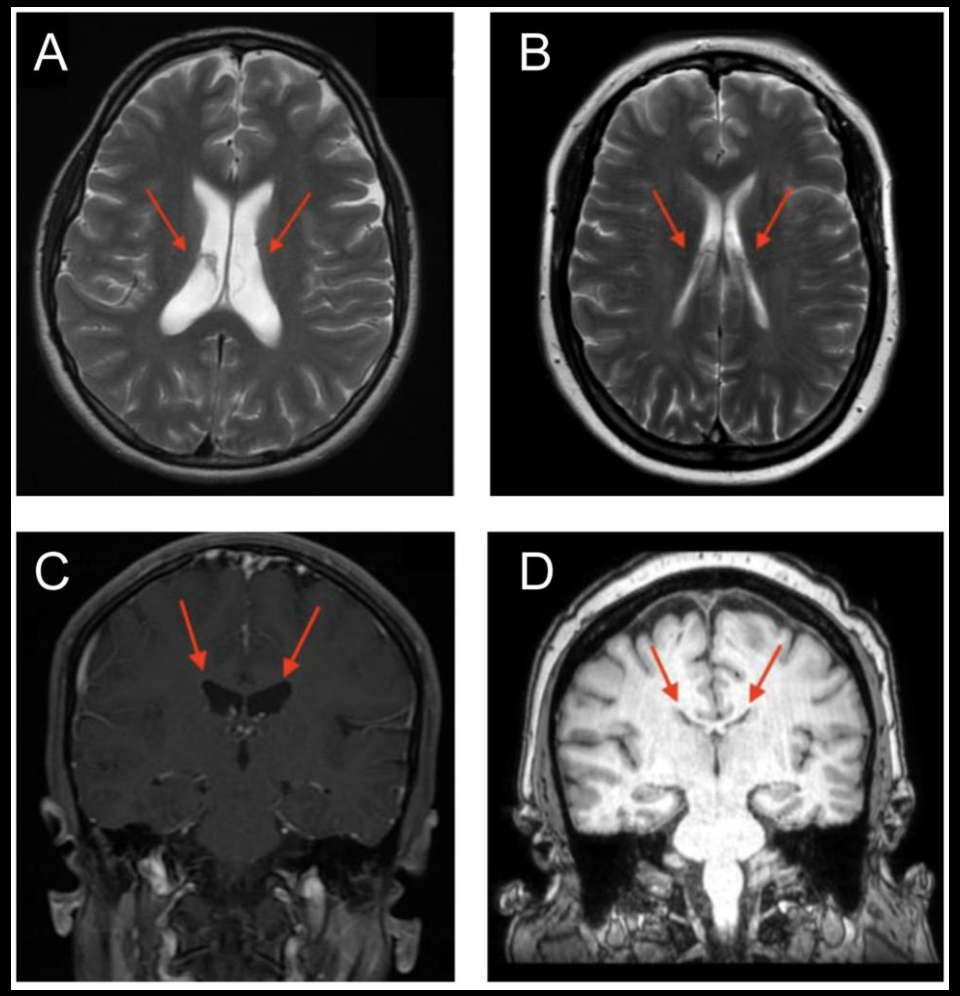


Posterior Globe Flattening

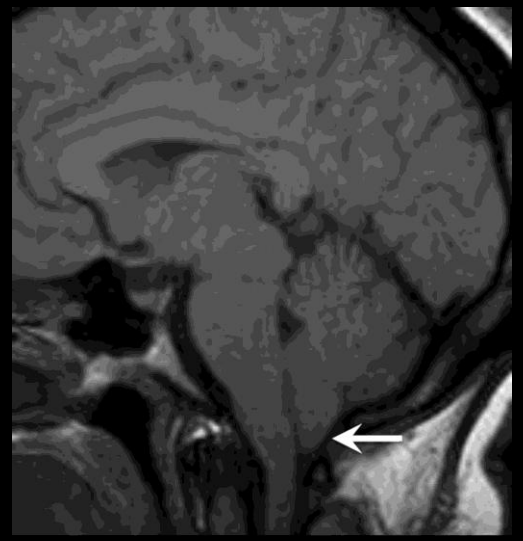


IIH: Neuroimaging

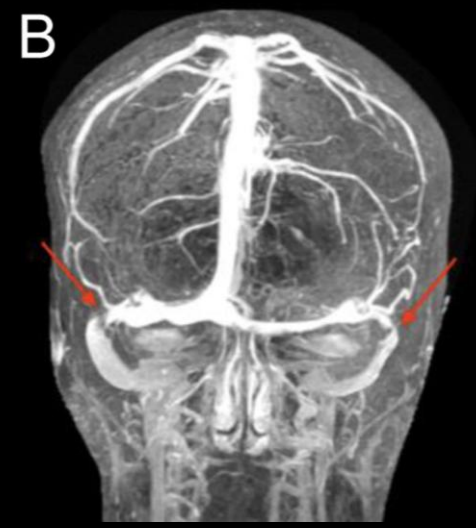
Split-like Lateral Ventricles



Cerebellar tonsillar ectopia



Transverse Venous Sinus Stenosis



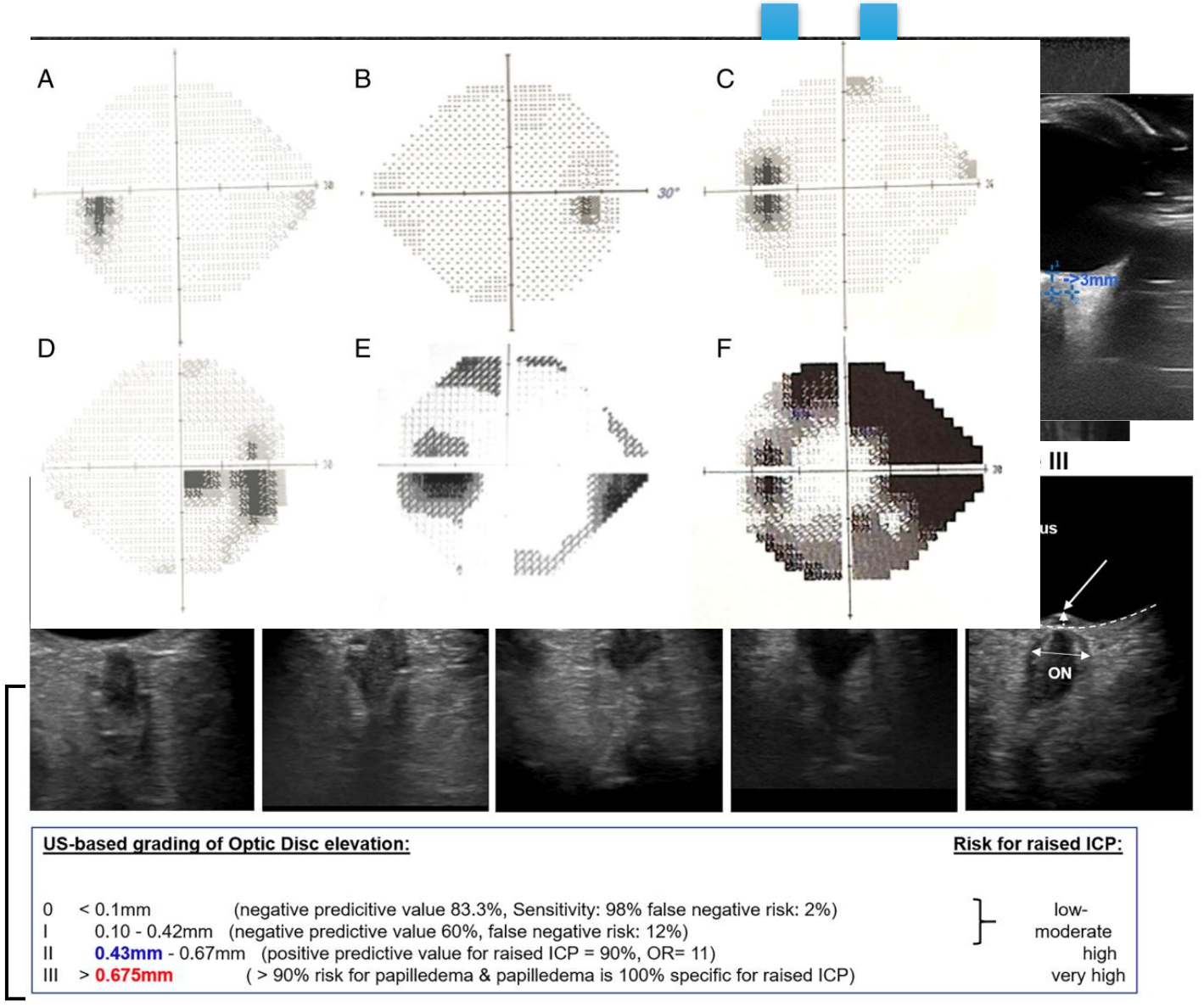
Index of Transverse Sinus Stenosis (ITSS)
0: Normal
1: Stenosis <33%
2: Stenosis 33-66%
3: Stenosis >66%
4: Hypoplasia or Agenesis
Formula: Right TSgrade x LeftTS grade

ITSS value>o=4: high sensitivity (94.7%) and specificity (93.5%) for IIH

Ophtalmological examination

- **Fundoscopy with graded Frisen Scale**
- **Visual acuity**
- **Visual field testing (CVC, perimetry)**

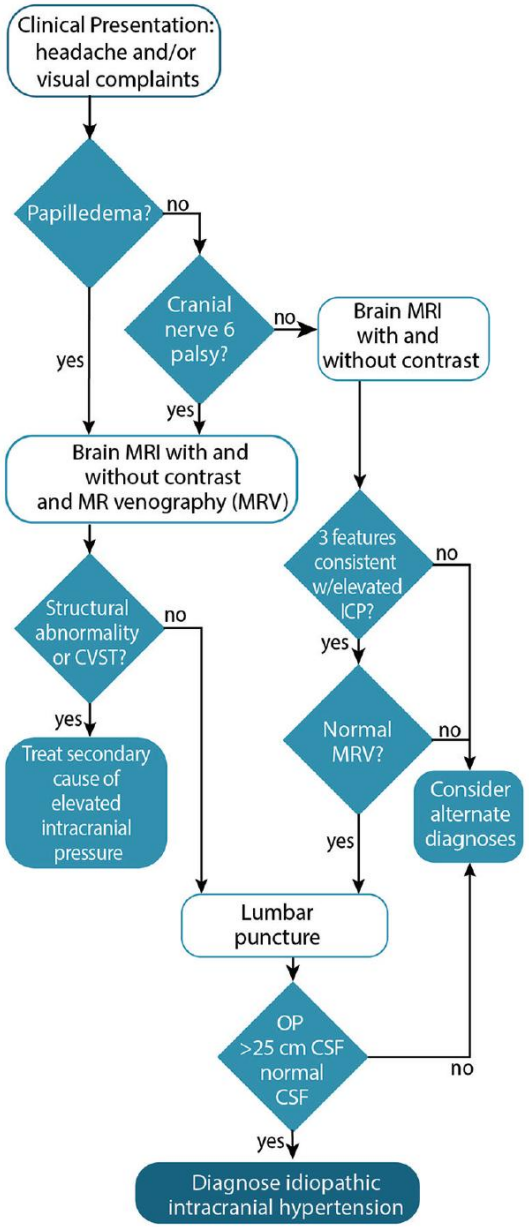
- **Ultrasound of the optic nerve**
- **Quantitative assessment of the optic nerve sheath diameter (ONSD)**
  - ✓ ONSD ≥5.0 mm → high ICP
  - ✓ ONSD <4.5 mm: normal in adults
  - ✓ A ≥10% reduction in ONSD during abduction (30° test) supports high ICP
- **Optical coherence tomography (OCT)**

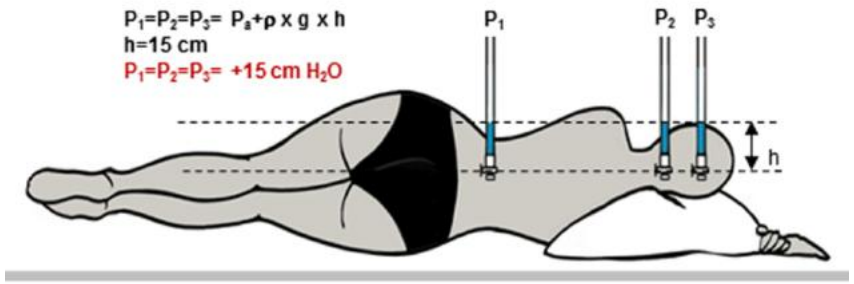


US-based grading of Optic Disc elevation: — **Risk for raised ICP:**

0	< 0.1mm	(negative predicitive value 83.3%, Sensitivity: 98% false negative risk: 2%)	low-moderate
I	0.10 - 0.42mm	(negative predictive value 60%, false negative risk: 12%)	
II	**0.43mm** - 0.67mm	(positive predictive value for raised ICP = 90%, OR= 11)	high
III	> **0.675mm**	(> 90% risk for papilledema & papilledema is 100% specific for raised ICP)	very high

Measurement of CSF Opening Pressure





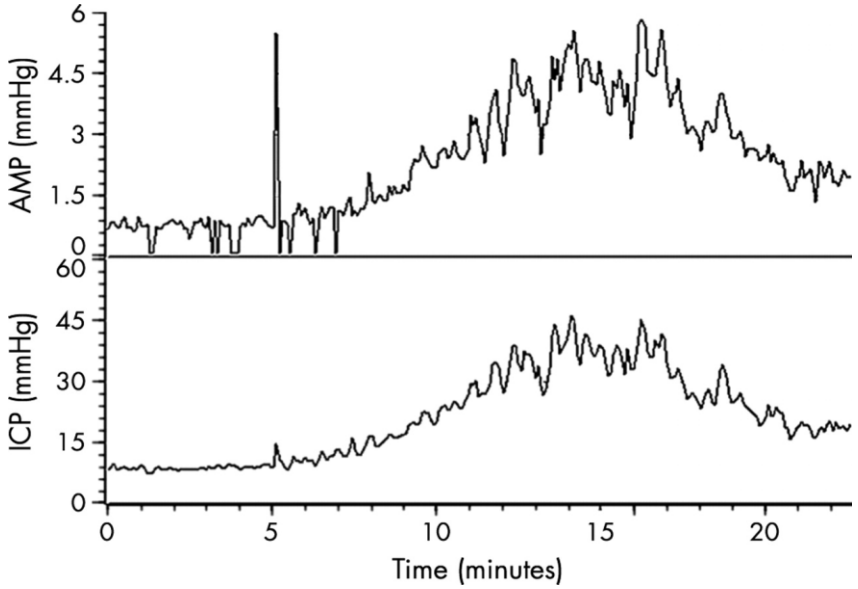
Lumbar Puncture Opening Pressure			
	Normal (cm H_20)	Mean (cm H_20)	Abnormal (cm H_20)
Adult	6-25	18	>25

* In pediatric patients, > 28 cm H_20 is considered abnormal; Values between 20-28 should be interpreted in the appropriate clinical context.

If CSF-OP >=25 cmH2O and/or papilloedema a therapeutic dreinage is necessary:

- ✓ Target CSF-CP 10-15 cmH2O
- ✓ Papilloedema reduction to Frisén grade ≤2
- ✓ Max dreinage 50 ml

ICP monitoring



- **Diagnostic clarification**
- **IIH-WOP (without papilloedema)**
- **Pts with borderline CSF-OP**
- **Monitoring disease activity and guiding surgery**
- **Evaluation in pts with persistent symptoms**
- **Preventing unnecessary procedures**

IIH: Diagnostic criteria

Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children

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Table 2 Diagnostic criteria for pseudotumor cerebri syndrome

1. Required for diagnosis of pseudotumor cerebri syndrome[a]
A. Papilledema
B. Normal neurologic examination except for cranial nerve abnormalities
C. Neuroimaging: Normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion and no abnormal meningeal enhancement on MRI, with and without gadolinium, for typical patients (female and obese), and MRI, with and without gadolinium, and magnetic resonance venography for others; if MRI is unavailable or contraindicated, contrast-enhanced CT may be used
D. Normal CSF composition
E. Elevated lumbar puncture opening pressure (≥250 mm CSF in adults and ≥280 mm CSF in children [250 mm CSF if the child is not sedated and not obese]) in a properly performed lumbar puncture
2. Diagnosis of pseudotumor cerebri syndrome without papilledema
In the absence of papilledema, a diagnosis of pseudotumor cerebri syndrome can be made if B-E from above are satisfied, and in addition the patient has a unilateral or bilateral abducens nerve palsy
In the absence of papilledema or sixth nerve palsy, a diagnosis of pseudotumor cerebri syndrome can be suggested but not made if B-E from above are satisfied and in addition at least 3 of the following neuroimaging criteria are satisfied:
i. Empty sella
ii. Flattening of the posterior aspect of the globe
iii. Distention of the perioptic subarachnoid space with or without a tortuous optic nerve
iv. Transverse venous sinus stenosis

[a] A diagnosis of pseudotumor cerebri syndrome is definite if the patient fulfills criteria A-E. The diagnosis is considered probable if criteria A-D are met but the measured CSF pressure is lower than specified for a definite diagnosis.

Diagnosis of idiopathic intracranial hypertension: A proposal for evidence-based diagnostic criteria

Cephalalgia 2023, Vol. 43(3) 1–10

Table 4. Suggested update to the revised Friedman criteria for diagnosis of idiopathic intracranial hypertension.

A. Presence of at least 2 of 3 signs of elevated intracranial pressure[1]
   1.) Papilledema[2]
   2.) Elevated lumbar puncture opening pressure ≥25 cm CSF in adults measured before withdrawal of CSF in a relaxed patient placed in left, lateral decubitus position with neck and legs extended.
   3.) Presence of ≥3 neuroimaging signs (cerebral MRI and MRI- or CT venography described by a neuroradiologist)[3]
      a. Partial empty sella (≥grade 3)
      b. Uni- or bilateral flattening of the posterior aspect of the globe
      c. Uni- or bilateral distension of the perioptic subarachnoid space
      d. Bilateral sinus venous stenoses (ITSS score ≥4)

B. Normal neurological examination except for cranial nerve abnormalities.

C. Cerebral MRI and venography (MRI/CT) without hydrocephalus, structural lesions or venous sinus thrombosis.

D. Normal CSF composition.

E. No secondary cause of elevated ICP. Secondary ICP-elevation, satisfying A–D, is referred to as secondary pseudotumor cerebri syndrome[4].

Therapy and management: a multi-modal severity-guided approach

Weight loss

(LE I, GR A)

- Diet, bariatric surgery **(IIH Weight Trial-NCT02124486)**

Reduction of intracranial pressure

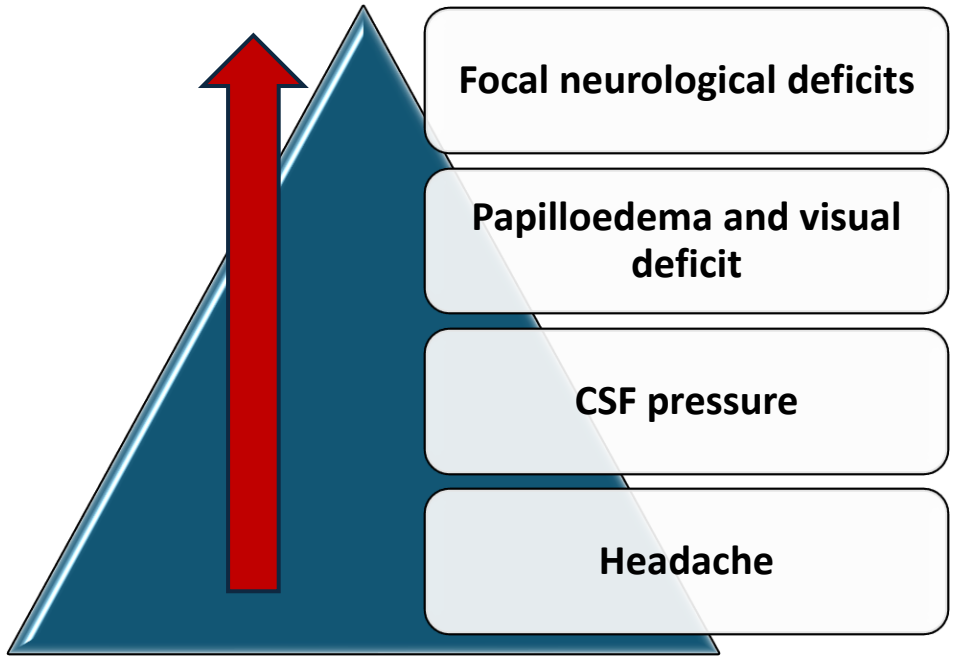
- **New treatments**
  - GLP-1 agonists (exenatide, tirzepatide, semaglutide)→ **TIIHT Trial, IIH Pressure Trial**
  - 11-beta hydroxysteroid dehydrogenase type 1 inhibitors
- **Medical treatments**
  - **Acetazolamide** 250 mg
  - **Topiramate** 25-50 mg →
  - **Furosemide:** not recom
  - **Mannitol bolus 18%** 0.5
  - Acute and prophylactic t

Headache treatment and prophylaxis

- **Repeated Lumbar puncture:** g
- **CSF shunting techniques** (LE II
- **Transverse sinus stenting (VSS** venous blood pressure at the S

Visual function preservation

- **Optic nerve sheath fenestrati**



Stage 0

Headache
No papilloedema
No visual deficit
No neurological deficits

- **Therapeutic LP** (diagnostic setting)
- **Non-pharmacological weight loss strategies** (BMI>=25)
- **Pharmachological weight loss** add-on (BMI>27)
- **Bariatric surgery** (selected cases)
- **Headache treatment:** *«Treat the phenotype approach»*

Stage 1

Headache
Papilloedema (Frisén grade ≤2)
No visual deficit
No neurological deficits

- **Therapeutic LP**
- **Pharmacological ICP lowering**
  - Acetazolamide 250–1000 mg/day **+/-**
  - Topiramate 25–50 mg/day
  - Furosemide40–80 mg/day
- **Weight loss strategies**
- **Headache treatment:** *«Treat the phenotype approach»*

Stage 2

Headache
Papilloedema (Frisén grade ≥3)
Visual deficit and/or neurological deficits

- **Therapeutic LP**
- **Pharmacological ICP lowering**
  - Acetazolamide 1000–4000 mg/day + Topiramate 25–100 mg/day
  - Additive as needed: Furosemide 40–160 mg/day; Mannitol
- **According to response:**
  - Repeat therapeutic LP (target <10 cmCSF)
  - ONS fenestration
  - CSF shunts
  - VSS
- **Weight loss strategies (pharmachological/bariatric>diet /lifestyle)**
- **Headache treatment**

Stage 3

Headache
Papilloedema (Frisén grade ≥3)
Progressive visual deficit and/or neurological deficits

- **Therapeutic LP**
- **Aggressive pharmacological ICP lowering**
  - Acetazolamide 1500–4000 mg/day
  - Topiramate 100–200 mg/day
  - Furosemide 80–320 mg/day; Mannitol
- **Evaluate:**
  - ONS fenestration
  - CSF shunts
  - VSS

After stabilization:
- **Weight loss strategies**
- **Headache treatment**

- ✓ **Target weight loss >10%**
- ✓ **Target CSF-OP 10-15 cmH2O**
- ✓ **Papilloedema <2 or regression of visual deficits**

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TAKE-HOME MESSAGES

- Disorders of intracranial pressure are the main mimics of CM1
- Clinical and radiological features can help in differential diagnosis
- Disorders of intracranial pressure are frequently unrecognized (maintain high clinical suspicion)
- Disorders of intracranial pressure carry risk of emergency complications and impair quality of life
- Improper CM1-mimics surgical treatment carry risk of complications and long-term impairment
- **A multidisciplinary approach is mandatory** especially for uncertain or complex cases