

# Diagnosis and Management of the Pseudotumor Cerebri syndrome in Children. A critical review.

Toronto 2014  
Daniel Tibussek, MD



## Disclosures

- none

# Two Germans, Two Revolutions

1891



1851



## Overview

- Nomenclature
- Definition
  - „Normal“ values of CSF opening pressure
  - Other diagnostic difficulties
- Epidemiological and clinical data Germany
  - IIH as an incidental finding
  - IIH without papilledema
- Cases report
  - Diagnostic difficulties
- Concluding thoughts

# Pathophysiologie

Headache  
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## Review Article

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### **Pseudotumor Cerebri Pathophysiology**

Brian E. McGeeney, MD, MPH; Deborah I. Friedman, MD, MPH, FAAN

Headache 2014;54:445-458

# Nomenclature

## What's in a name

- Quincke 1897  
„seroese Meningitis“
- Symonds 1931  
"otitic hydrocephalus"
- Benign Intracranial Hypertension
- Pseudotumor Cerebri
- Idiopathic Intracranial Hypertension
- Pseudotumor cerebri Syndrome/Komplex



Johnston I. Neurosurg Focus 11(2) 2001.

## Nomenclature confusion

“ This variation in nomenclature reflects the continuing uncertainty about the precise nature of the condition...”

“...an uncertainty also quite clearly reflected in the variations in ideas of origin and treatment”

Johnston I. Neurosurg Focus 11(2) 2001.

## Pseudotumor cerebri syndrome/complex

- Takes into account that differences between „idiopathic“ and „secondary“ intracranial hypertension are somewhat arbitrary
- association with underlying illnesses in up to 77.7% of pediatric patients with “idiopathic” PTC

Scott IU, et al. Am J Ophthalmol 1997; 124:253–255  
Youroukos S et al. J Child Neurol 2000; 15:453–457  
Tibussek et al. Childs Nerv Syst 2010;26:313-21

## Associations with intracranial hypertension

### Medical Conditions:

- ▶ Hypothyroidism/hyperthyroidism
- ▶ Cushing's disease/adrenal insufficiency
- ▶ Hypoparathyroidism/hyperparathyroidism
- ▶ Polycystic ovary syndrome
- ▶ Chronic anaemia
- ▶ Vitamin D deficiency
- ▶ Chromosomal abnormalities (Trisomy 21, Turner syndrome)
- ▶ Cystic fibrosis (mainly secondary to associated nutritional problems)
- ▶ Systemic lupus erythematosus

### Drugs:

- ▶ Antibiotics: tetracyclines and related compounds, sulfonamides, nalidixic acid, nitrofurantoin, penicillin
- ▶ Hormones: levothyroxine, growth hormone, oral contraceptive pills
- ▶ Corticosteroids therapy or withdrawal
- ▶ Cyclosporine
- ▶ Amiodarone
- ▶ Phenytoin
- ▶ Lithium
- ▶ Vitamin A analogues and isotretinoin

Babiker MOE, et al. Arch Dis Child Educ Pract Ed 2014;0:1–7.

## Definition

What is Pseudotumor Cerebri in the 21. Century?

### Definition of Pseudotumor cerebri

- A. Papilledema
- B. Normal neurologic examination except for cranial nerve abnormalities
- C. Neuroimaging: Normal brain parenchyma
- D. Normal CSF composition
- E. Elevated lumbar puncture opening pressure

Adapted from: Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*; 2013;81:1159–1165.

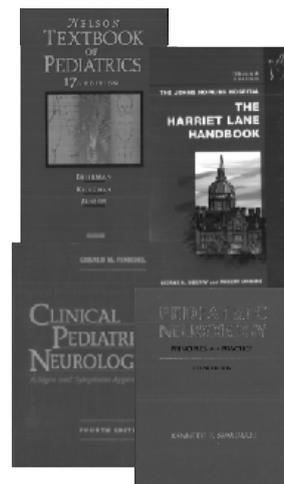
## Definition of Pseudotumor cerebri

- A. Papilledema
- B. Normal neurologic examination except for cranial nerve abnormalities
- C. Neuroimaging: Normal brain parenchyma
- D. Normal CSF composition
- E. Elevated lumbar puncture opening pressure
- BUT: what is elevated opening pressure?

Adapted from: Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*; 2013;81:1159–1165.

## What is the „normal“ CSF opening pressure in childhood?

- Many pediatric textbooks stated an abnormal opening pressure (OP) in children is greater than 20 cm H<sub>2</sub>O
- Often no references or cross-referencing
- No studies had systematically defined the value for an abnormally elevated OP in children



## Reference Range for Cerebrospinal Fluid Opening Pressure in Children

TO THE EDITOR: A reference range for cerebrospinal fluid (CSF) opening pressure in children undergoing diagnostic lumbar puncture has not been established.<sup>1</sup> The influence of age, body-mass index (BMI), and depth of sedation on opening pressure in children is also uncertain.<sup>2</sup>

We conducted a 2-year, single-center prospec-

mined on the basis of the 90th percentile for all patients in the reference population, was 28 cm of water (Fig. 1A). The threshold for an abnormally reduced pressure in the 10th percentile was 11.5 cm of water. Subjects placed under moderate to deep sedation during lumbar puncture had a slightly higher opening pressure, as compared

Avery et al. N Engl J Med 363;891-3

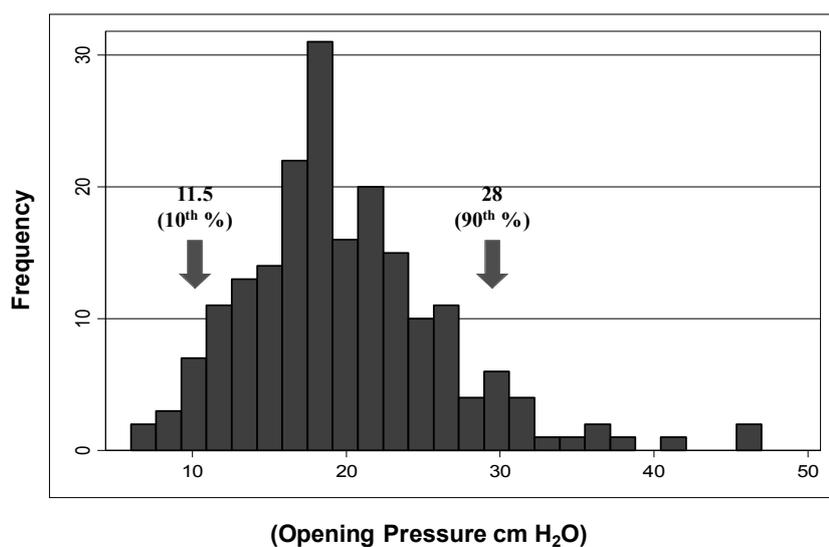
## Methods

- 2 year prospective study at Children's Hospital of Philadelphia
- Patients undergoing LP as part of their routine clinical care were recruited  
Ages  $\geq 1$ -18 years of age

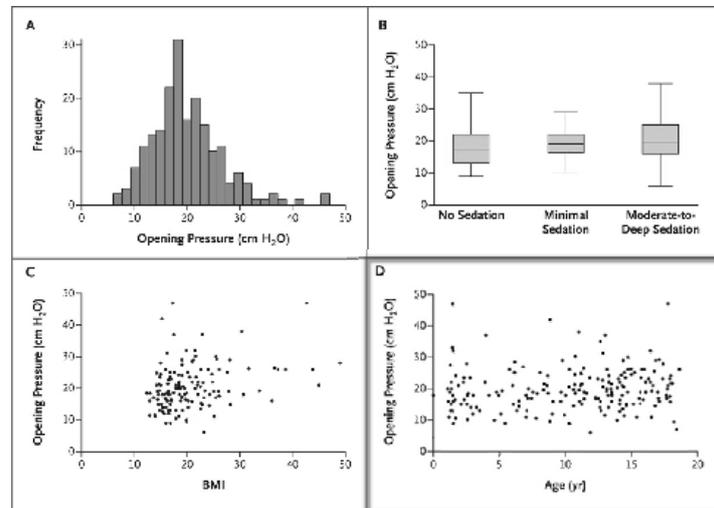
## Outcomes

- Primary Outcome: OP (cm H<sub>2</sub>O)
- Study variables:
  - 1) age
  - 2) BMI
  - 3) depth of sedation
  - 4) sedation medication
  - 5) needle size

### Opening Pressure Distribution (N = 197)



Distribution of CSF Opening Pressure and Effects of Sedation, Body-Mass Index and Age (N=197).



Avery RA et al. N Engl J Med 2010;363:891-893.

## Limitations

- Subjects cannot be considered “normal”
- LPs performed by many different physicians
- Different sedation regimens
- Still: relatively low number of patients
- Pediatric BP percentiles are based on > **80.000** patient visits!!

Table 2 Diagnostic criteria for pseudotumor cerebri syndrome

1. Required for diagnosis of pseudotumor cerebri syndrome\*

- 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

E. Elevated lumbar puncture opening pressure ( $\geq 250$  mm CSF in adults and  $\geq 280$  mm CSF in children

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 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.

Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology; 2013;81:1159–1165.

## Diagnostic Criteria for Pseudotumor Cerebri Syndrome

- Elevated lumbar puncture opening pressure ( $\geq 250$  mm CSF in adults and  $\geq 280$  mm CSF in children)
- **[250 mm CSF if the child is not sedated and not obese]**

Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology; 2013;81:1159–1165.

## Diagnostic Criteria for Pseudotumor Cerebri Syndrome

- Elevated lumbar puncture opening pressure ( $\geq 250$  mm CSF in adults and  $>280$  mm CSF in children)

**CLINICALLY NOT HELPFUL AT ALL.  
VERY POOR SUPPORTIVE EVIDENCE!**

Adapted from: Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*; 2013;81:1159–1165.

## CSF opening pressure measurement

A technique prone to confounders

„normal“ values

**Cerebrospinal Fluid Opening Pressure in Children:  
Experience in a Controlled Setting ?**

Marcus W. Lee MD<sup>\*</sup>, Vettakikoru V. Vedanarayanan MD

*Department of Pediatric Neurology, University of Mississippi Medical Center, Jackson, Mississippi*

- Friedman et al: “in a properly performed lumbar puncture” ?

Lee and Vedanarayanan. Pediatric Neurology 2011; 45:238-240

What is „controlled setting“?



N Engl J Med 2006;355:e12.

# What About Leg Position?

- Numerous textbooks recommend that the legs must be straight to avoid false elevation of OP.

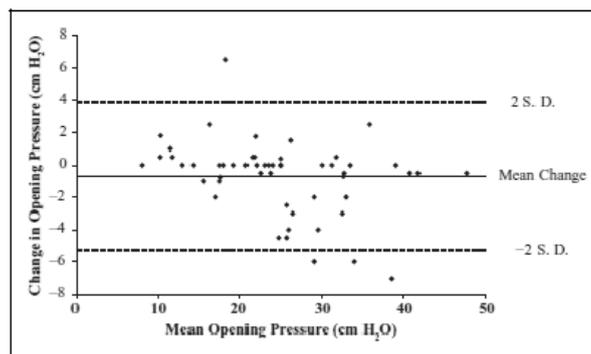
Brief Communication

## Patient Position During Lumbar Puncture Has No Meaningful Effect on Cerebrospinal Fluid Opening Pressure in Children

Robert A. Avery, DO,<sup>1,2,3</sup> Rakesh D. Mistry, MD,<sup>4</sup>  
Samir S. Shah, MD, MSCE,<sup>3,5,6,7</sup> Jan Boswinkel, MD,<sup>5</sup>  
Jimmy W. Huh, MD,<sup>8</sup> Michael D. Ruppe, MD,<sup>8</sup>  
Santiago Borasino, MD,<sup>8</sup> Daniel J. Licht, MD,<sup>1</sup>  
Jeffrey A. Seiden, MD,<sup>4</sup> and Grant T. Liu, MD<sup>2</sup>

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DOI: 10.1177/0885073809359158  
http://jcn.sagepub.com  
SAGE

## OP in Flexed vs. Extended Position

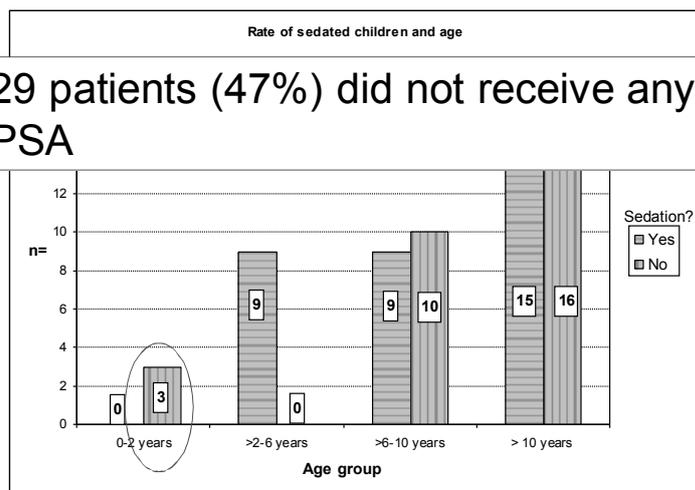


- Flexed 25.1+9.2 cm H<sub>2</sub>O
- Extended 24.4+8.4 cm H<sub>2</sub>O
- In 92.4% opening pressure measurements had less than a 5 cm H<sub>2</sub>O difference

# How about sedation?

## LP in PSA. German data.

29 patients (47%) did not receive any kind of PSA



Tibussek et al. Klin Padiatr 2012; 224: 40-42

Does it matter?

## Advantages of LP in PSA

- Prevents pain (and pain related elevation of pressure)
- Prevents anxiety/panic/trauma (repeated LP likely!)
- Higher success rate!!
- Comparability better if same PSA regime used

## But

- Literally all strategies of sedation/analgesia have the potential to alter the CSF opening pressure!
- The effect is almost unpredictable
- Role of depth of sedation?
- Role of hypercapnia?
- Role of the drugs used?

## Ketamine and OP

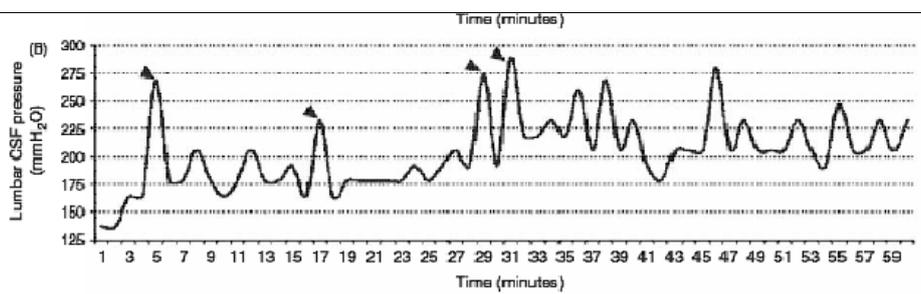
- Ketamine has long been suspected to contribute to a rise in ICP  
Ben Yehuda Y, et al. J Child Neurol 2006;21(6):441–443  
Michalczyk K, et al. Pediatr Crit Care Med 2013;14(3):e149–e155
- Avery et al. found no statistically significant relationship between ketamine use and OP (n=15!)
- Controversy continues among neurointensivists

## LP under sedation

- ...should be standard
  - ...should be standardized
- >> guideline?

In order to get routine, LP pressure measurement should generally be done more often.

## !Pressure variability in 1 h!



- Bilateral transverse sinus stenosis
- Initial LP Opening pressure < 20cm

*Cephalalgia* 2010 30:1419-25

## Remember!

Deborah I Friedman:

„A high opening pressure in and of itself is neither specific nor diagnostic and must be used in context with other data from the history,

examination,

neuroimaging and

laboratory

to arrive at the correct diagnosis“

Cephalgia 2010; 30:1415-16

## Germany-wide Pseudotumor Cerebri Study

## Study details

- Recruiting period: January and December 2008
- Active hospital-based surveillance on paediatric PTC in the German population
- All German pediatric clinics were asked to report all new cases of paediatric IIH to the German ESPED study centre  
*(German Surveillance Unit for Rare Diseases in Childhood)*
- *Questionnaires were sent out to get clinical details*

## Inclusion criteria

- Pseudotumor cerebri was defined as:
  - Age < 18 years
  - Documentation of increased **CSF opening pressure (> 20 cm H<sub>2</sub>O)**
  - Normal CSF composition (cell count, protein, sugar)
  - Normal cerebral imaging (except “empty sella”)
  - Normal neurological exam except for cranial nerves.

## Incidence Germany

- 2008: 61 pediatric cases per year
- **$\approx 0,5/100.000$  children/year**

### Previous data

- Incidence general population:  
Ca. 1 per 100.000 /y
- Incidence ♀ 20-44 yrs:  
19 /100.000 ♀ /y

**ADC**

### UK surveillance of childhood idiopathic intracranial hypertension (IIH)

YY Matthews, F Dean, K Matyka, et al.

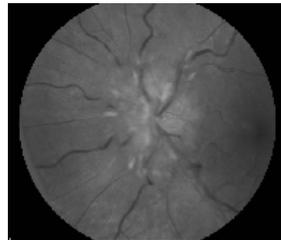
*Arch Dis Child* 2012;97: A6

- Estimated UK annual incidence is 0.8 (1.0 for girls, 0.5 for boys) per 100,000 child population aged 1-16 years.

However...

## Subgroup analysis

- 13 patients had a opening pressure **< 28 cm H<sub>2</sub>O**
- This represents 18% of the total PTC study population
- 11 of these had papilledema



Are these cases  
pseudotumor cerebri???

## After careful review

- 9 out of 11 patients with papilledema and CSF opening pressure < 28 cm H<sub>2</sub>O had additional signs and symptoms to convincingly support the diagnosis of Pseudotumor cerebri
- We suggest to label these patients as „probable PTC“ and treat as PTC
- We believe that in clinical reality there is NO *cutoff value* for normal CSF opening pressure

## The concept of „probable IIH“

- 1) If symptoms present, they may only reflect those of generalized intracranial hypertension or papilledema.
- 2) If signs present, they may only reflect those of generalized intracranial hypertension or papilledema
- 3) **CSF opening pressure may be < 20 cm H<sub>2</sub>O**
- 4) Normal CSF composition
- 5) No evidence of hydrocephalus, mass, structural, or vascular lesion on MRI and/or MR venography
- 6) Exclusion of other causes of intracranial hypertension
- 7) **Clear clinical response to initial pressure release and/or treatment**

Distelmaier F, Mayatepek E, Tibussek D (2008) Probable idiopathic intracranial hypertension in pre-pubertal children. Arch Dis Child 93:356–357

Table 2 Diagnostic criteria for pseudotumor cerebri syndrome

1. Required for diagnosis of pseudotumor cerebri syndrome\*

A. Papilloedema

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

\* 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.

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

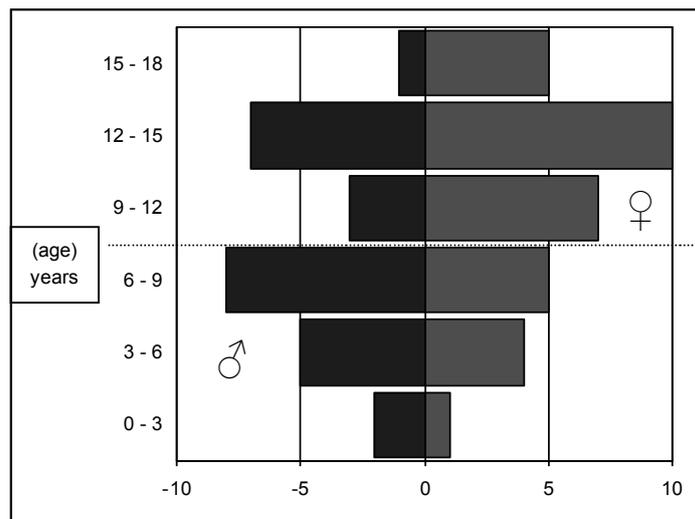
iv. Transverse venous sinus stenosis

\* A 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.

Adapted from: Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology; 2013;81:1159–1165.

# More epidemiology

## Age/Sex

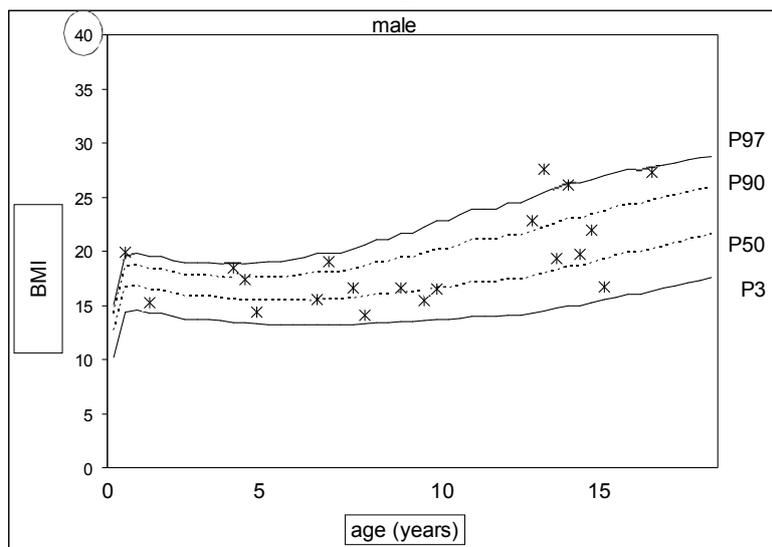


## Female vs Male

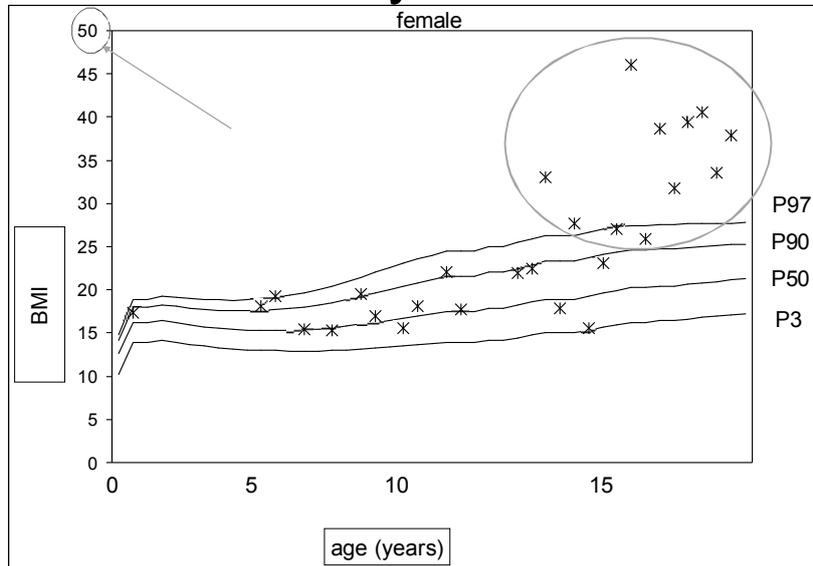
N=61	Female	Male
prepubertal (N=32)	15 (53.1%)	17 (46.9%)
pubertal (N= 29)	20 (68.9%)	9 (31.1%)

In the IIH Treatment Trial (IIHTT) of adult IIH patients, women account for approximately 97% of cases.

## Obesity male



## Obesity female



## Clinical manifestation

- 1) IIH as incidental finding
- 2) Headache
- 3) IIH without papilledema

## IIH as incidental finding

- Germany: 5 von 61 Kinder

„An apparent lack of symptoms does not rule out chronic increased intracranial pressure in young children.“

Tibussek et al. Child Nerv Syst 2010; 26:313-21  
 Lim et al. Arch Dis Child 2005; 90:206–210  
 Bassan et al. Acta Neurol Scand. 2008 Oct;118(4):251-5

## Early eye symptoms

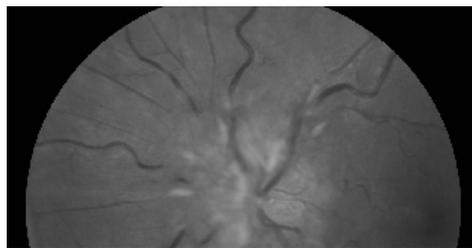
	prepubertal	pubertal
$\Sigma$	32	29
Papilledema	26	24
Abducens nerve palsy	10	9
Visual acuity	7	12
Stereo vision	2	0
Colour vision	2	0
Visual field	1	5
Eye pain	1	6
No papilledema	6	5

Approx.  
20%

Abducens nerve palsy?  
Think Pseudotumor cerebri



Does IIH without Papilledema  
exist?



„idiopathic intracranial hypertension  
(IIH) without Papilloedema“  
(IIHWOP)

PubMed.gov | IHWOP | Search

Display Settings: Summary, 20 per page, Sorted by Recently Added

Results: 10

1 Sinus Venous Thrombosis-Associated Idiopathic Intracranial Hypertension Without Papilloedema as a Powerful Risk Factor for Progression and Refractoriness of Headache

**SHORT REPORT**

**Idiopathic intracranial hypertension: is papilloedema inevitable?**

**E Wraige, C Chandler, K R E Pohl**

*Arch Dis Child* 2002;**87**:223-224

PMID: 1205943 [PubMed] | Indexed by: MEDLINE | Related citations

4. Sinus venous thrombosis-associated idiopathic intracranial hypertension without papilloedema as a risk factor for migraine progression  
De Simone R, Ranieri A, Florio C, Di L, Donzella V.  
*Neurology* 2010 Aug 11;81(4):411-5. Epub 2010 Feb 25. Review.  
PMID: 20182800 [PubMed] | Indexed by: MEDLINE | Related citations

5. Idiopathic intracranial sinus thrombosis and idiopathic intracranial hypertension without papilloedema in chronic tension-type headaches  
Sera F, Messina D, Gibello C, Chiarino D, Bussacchi G, Masera S, Condini F, Mangione I, Meloni G, Fera F, Cardinale A.  
*J Neurol* 2006;253(5):777-82. Epub 2006 May 6.  
PMID: 16759211 [PubMed] | Indexed by: MEDLINE | Related citations

6. Idiopathic intracranial hypertension with and without papilloedema in a consecutive series of patients with chronic migraine  
Viana JSS, Bavaresco MK, Gonçalves AL, Zuberstein L, Senneker-Schneiders CA, Botelho-Ferreira-Filho Mda G, Mendes M.  
*Cephalalgia* 2008 Jun;28(6):695-703. Epub 2008 Mar 11.  
PMID: 18284410 [PubMed] | Indexed by: MEDLINE

Recent activity

Q IHWOP (10)

## Germany-Studie: „IIHWHOP“?

Sex	Age	Opening pressure	Signs and symptoms	Headache	Other
♂	0,6	32	Vomiting, Bulging fontanelle, Sunset phenomenon	-	
♂	4,8	37	Abducens nerve palsy	+	
♂	7,0	?	Abducens nerve palsy, visual loss	+	
♀	7,3	44	Vomiting	-	
♂	9,1	33	?	?	
♀	10,6	25	-	+	
♂	12,0	26	Visual loss	+	
♀	12,2	38	-	+	Path. Sono N. opticus
♂	13,0	39	Visual loss	-	Path. Sono N. opticus
♀	13,1	45 2 d später normal	Eye pain	+	

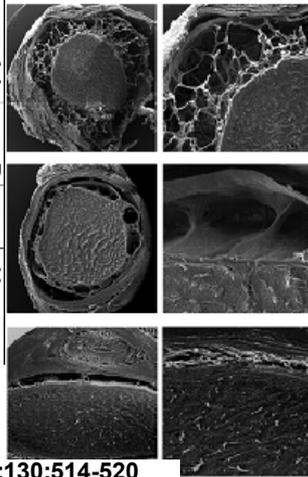
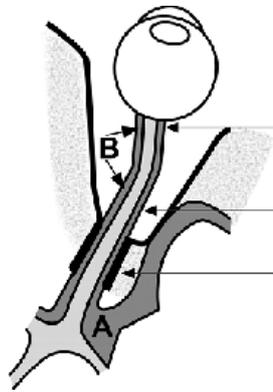
## After critical review

Sex	Age	Opening pressure	Signs and symptoms	Headache	Other	Valide?
♂	0,6	32	Vomiting, Bulging fontanelle, Sunset phenomenon	-		☺
♂	4,8	37	Abducens nerve palsy	+		☺
♂	7,0	?	Abducens nerve palsy, visual loss	+		?
♀	7,3	44	Abducens nerve palsy	-		☺
♂	9,1	33	?	?		?
♀	10,6	25	-	+		?
♂	12,0	26	Visual loss	+		?
♀	12,2	38	-	+	Path. Ultrasound N. opticus	?
♂	13,0	39	Visual loss	-	Path. Ultrasound N. opticus	?
♀	13,1	45 2 d later normal	Eye pain	+		?

**IIH without papilledema does exist even after infancy!**

**However, diagnosis should be critically questioned in these cases!**

## Explanation?



“a multichambered and subdivided tubular system with a blind end (cul de sac) behind the ocular globe.”

Killer H E et al. *Brain* 2007;130:514-520

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**BRAIN** A JOURNAL OF NEUROLOGY

## The Papilledema Problem

## „False diagnosis of papilledema and IIH“

- 18 children referred with disc swelling and **suspected IIH**.
- Following a tertiary ophthalmological review:  
**papilloedema was excluded in 10.**
- In these 10 children, five had a mean opening pressure on lumbar puncture of **27.2cm H<sub>2</sub>O**, range 19–32

Mishra A et al. Eur J Paediatr Neurol 2007 ; 11 : 39 – 42

## „Light at the end of the tunnel of the blind leading the blind?“

„Thus, **for every child that truly has IIH, I typically see four or five other children without IIH**

but with CSF pressure measurement between 17 and 27 cm of CSF“

Colin Kennedy (Editorial) Dev Med Child Neur 2006;48:83-83

## **Idiopathic intracranial hypertension in childhood: pitfalls in diagnosis**

DEEPA KRISHNAKUMAR<sup>1</sup> | JOHN D. PICKARD<sup>2</sup> | ZOFIA CZOSNYKA<sup>2</sup> | LOUISE ALLEN<sup>2</sup> | ALASDAIR PARKER<sup>3</sup>

<sup>1</sup> Department of Paediatric Neurology, Addenbrooke's Hospital, Cambridge; <sup>2</sup> Department of Neurosciences, Addenbrooke's Hospital, Cambridge; <sup>3</sup> Department of Ophthalmology, Addenbrooke's Hospital, Cambridge, UK

Childs Nerv Syst  
DOI 10.1007/s00381-014-2390-y

ORIGINAL PAPER

## **Pseudopapilledema and association with idiopathic intracranial hypertension**

Betty Liu · Rory K. J. Murphy · Deanna Mercer ·  
Lawrence Tyebsen · Matthew D. Smyth

LP pressure measurement and eye  
investigation frequently lead to  
false diagnosis of  
Pseudotumor cerebri

# Role of cerebral imaging

Clinical Radiology 67 (2012) 656–663



Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: [www.clinicalradiologyonline.net](http://www.clinicalradiologyonline.net)



## Accuracy of brain imaging in the diagnosis of idiopathic intracranial hypertension

P.J. Maralani<sup>a</sup>, M. Hassanlou<sup>b</sup>, C. Torres<sup>a</sup>, S. Chakraborty<sup>a</sup>, M. Kingstone<sup>a</sup>, V. Patel<sup>b</sup>, D. Zackon<sup>b</sup>, M. Bussière<sup>a,c,\*</sup>

## Results

- N=43
  1. Partially empty sella  
(specificity 95.3%, p<0.0001)
  2. Flattening of the posterior globes  
(specificity 100%, p<0.0001)
  3. Combined stenosis score CSS<4  
(specificity 100%, p<0.0001)**were highly specific for IIH.**

## Low sensitivity!

- However, absence of these signs did not exclude a diagnosis of IIH.

Clinical Radiology 67 (2012) 656-663

- Needs to be confirmed in pediatric population

Passi N, Degnan AJ, Levy LM. MR Imaging of Papilledema and Visual Pathways: Effects of Increased Intracranial Pressure and Pathophysiologic Mechanisms. AJNR Am J Neuroradiol

Partial empty sella



intraocular protrusion of optic nerve  
optic nerve sheath distension



flattening of posterior globe



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

Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*; 2013;81:1159–1165.

## Optic nerve ultrasound and intracranial pressure



Fig. 1. Example of optic nerve sheath diameter (ONSD) measurement using ocular ultrasonography.

Dubost C Jr, et al. *Anesthesiology* 2012 May;116(5):1066-71  
Lochner et al. *J Neuroimaging* 2013;23:533-534.

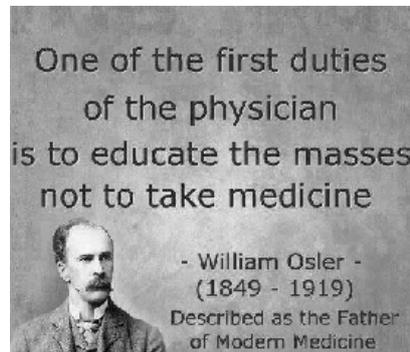
## Therapy and therapy guidance.

How do we decide and why?

### Case: Therapy resistance?

- 7 yrs, boy,
- subjective visual disturbance since 6 wks
- Papilledema (Papille prominent, disc margin blurred, R>L)
- Normal visual acuity, visual fields OK
- OP 37 cm H<sub>2</sub>O
- 4 wks Acetazolamid 10 mg/kg, no adverse effects, BE – 8,4
- **No visual disturbances any more**
  
- after wks: 35 cm H<sub>2</sub>O, eyes did not change
- Plus Furosemid: significant side effects
- E-mail to Dr Tibussek:  
„Doctors talk about VP-shunt“

# Therapy



**Sir William Osler, 1st Baronet** (born July 12, 1849 – December 29, 1919) was a Canadian physician and one of the four founding professors of Johns Hopkins Hospital (Wikipedia).

## Therapy: Controversies

- Medication:  
(when, what, how long?)
  - Monitoring: How? How long?
  - Re-LP to control pressure?
  - What is therapy-resistance?
- {
- When and which invasive therapy?
  - Role of sinus venous stenosis? >> Stent in children?
  - When consider bariatric surgery
- }

# Acetazolamide, the evidence



„Since no trials met the inclusion criteria no studies were assessed for quality, no data were collected and no analysis was undertaken.“

## Acetazolamide. Mechanism of action?

*Effect of acetazolamide (Diamox) on spinal fluid production*

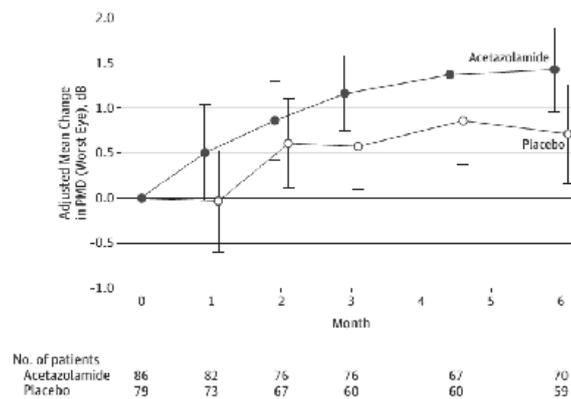
Patient	Expt. No.	Dose	90 Min. Average		% Change	Maximum % change per 15 min. period
			Pre ml./min.	Post ml./min.		
H.W.	2	1.0	0.34	0.27	21 decrease	41 decrease
	4	1.0	0.52	0.60	0	21 decrease
	6	1.0	0.52	0.50	0	35 decrease
	7	1.0	0.40	0.40	0	24 decrease
F.B.	3	1.0	0.30	0.28	6 decrease	10 decrease
	4	1.0	0.27	0.40	48 increase	79 increase
A.M.	3	0.5	0.51	0.22	57 decrease	62 decrease
	4	1.0	0.30	0.25	50 decrease	68 decrease
	8	1.0	0.53	0.26	50 decrease	18 decrease
M.E.	4	0.5	0.47	0.44	6 decrease	25 decrease
A.R.	4	0.5	0.46	0.26	21 decrease	56 decrease

Rubin RC, Henderson ES, Ommaya AK, Walker MD, Raff DP.  
The production of cerebrospinal fluid in man and its modification by acetazolamide. *J Neurosurg.* **1966** Oct;25(4):430-6.

Original Investigation

## Effect of Acetazolamide on Visual Function in Patients With Idiopathic Intracranial Hypertension and Mild Visual Loss The Idiopathic Intracranial Hypertension Treatment Trial

The NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee



JAMA. 2014;311(16):1641-1651

## Conclusion

- In patients with IIH and **mild visual loss**, the use of acetazolamide with a low-sodium weight reduction diet, compared with diet alone, **resulted in modest improvement in visual field function**.
- **No significant treatment effects** were noted with respect to **headache** disability (HIT-6 total score)

## What are our treatment goals?

### 1) Maintain/regain normal visual function

With good interdisciplinary work and good drug adherence realistic goal in > 90% of pediatric patients.  
Level of evidence: German „expert opinion“

### 3) (prevent invasive therapies)

## Step-wise approach

- Step 1: correct potentially causal factors (medication, anaemia, hypothyroidism, ..)
- Step 2: LP with CSF drainage to lower pressure >> measure post punctional pressure („closing pressure“)

## Pressure release as the only therapy

„Interestingly, it is **not uncommon** to observe a lasting clinical remission after a single lumbar puncture in some IIH patients“

### Germany study

- **14/61 Patients** got LP pressure as the only treatment. In 1 case successfully as serial LP.

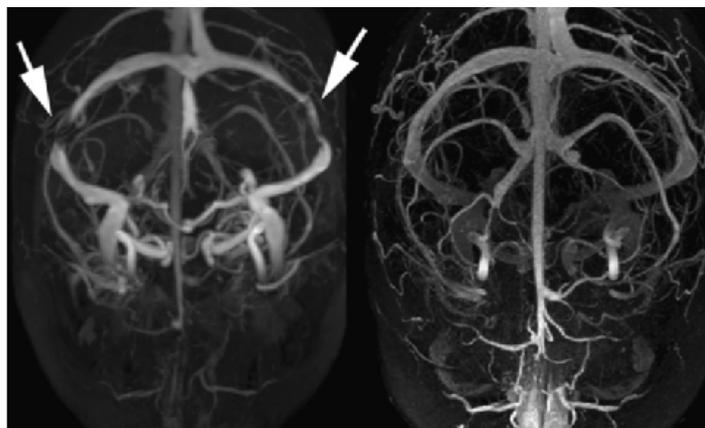
Bruce BB, Biousse V, Newman NJ. Update on Idiopathic Intracranial Hypertension. Am J Ophthalmol 2011;152:163-169

## Sinus venous stenosis

Before

After

LP



Biousse V et al. J Neurol Neurosurg Psychiatry (2012, online first).  
Stienen et al. European Journal of Neurology 2008, 15: 1416–1418

## Therapy-Escalation: When and Why?

„Corbett and Thompson have emphasized that treatment decisions should **not** rest on ... the severity of papilledema, or CSF opening or closing pressure.“

„Instead, the modern management of pseudotumor cerebri is **based largely upon the level of visual loss.**“

Aus: Liu et al.: Neuro-Ophthalmology. Diagnosis and Management. Second edition. 2010

## Headache as criteria for success?

„Many IIH patients have persistent headaches, **even after normalization of the intracranial pressure**“

„Patients with IIH frequently have headaches **not necessarily related to increased intracranial pressure**“

Bruce BB, Biousse V, Newman NJ. Am J Ophthalmol 2011;152:163-169  
Friedman DI, Rausch A. Neurology 2002; 58:1551-1553

## Step-wise approach

Step 3: No visual loss:

- Symptomatic headache (migraine) therapy
- Weight reduction, correct other secondary causes
- **If necessary Acetazolamide**

Step 4: Mild visual loss:

- Acetazolamide
- Furosemide
- (Topiramate)
- Weight reduction, if necessary

Liu et al. 2011 in: Neuro-Ophthalmology, Diagnosis and Management, Saunders, Elsevier

## Invasive therapy

- Step 5: Severe, or progression of visual

**Always critically question your diagnosis before even considering!**

- High-dose IV steroids and acetazolamide
- Lumboperitoneal shunt for failed ONSD or intractable headache
- Bariatric surgery

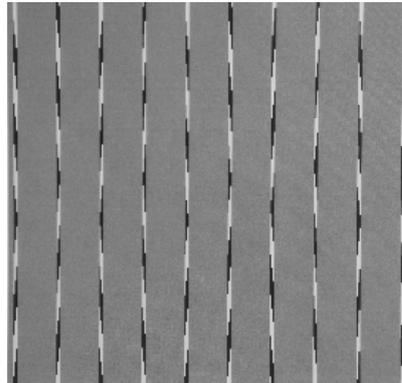
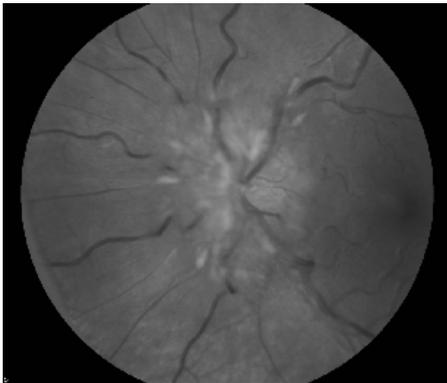
## Back to the case...

8 months later:

„The eye doctor now questions the diagnosis of PTC. Ultrasound suggests drusen.“ Fluorecence confirmed it

This child did NOT have PTC!

Beware: Our eyes are „subjective“



## Neuroophthalmology

- Papilledema: Photo-documentation!
- Visual field (how?)
- Optical Coherence Tomography
- Colour vision
- Contrast sensitivity
- Ultrasound (Drusen)
- ...

### The so called „therapy resistance“

Without visual disturbances no  
escalation of therapy!

*Exception: worsening papilledema*

**LP control: do not do routinely!**  
**Often unreliable in children!**

Mathews et al. Curr Opin Ophthalmol 2003; 14:364-370

## Non-Compliance

- Düsseldorf:  
2 Patients with **Non-Compliance**  
1 x optical atrophy (adolescent)  
1 x VP-Shunt
- Israel:  
„visual outcome was **less favorable in  
pubertal patients**“  
due to drug adherence problems?

Stiebel-Kalish et al. Puberty as a risk factor for less favorable visual outcome in idiopathic intracranial hypertension. Am J Ophthalmol 2006; 142:279–283.

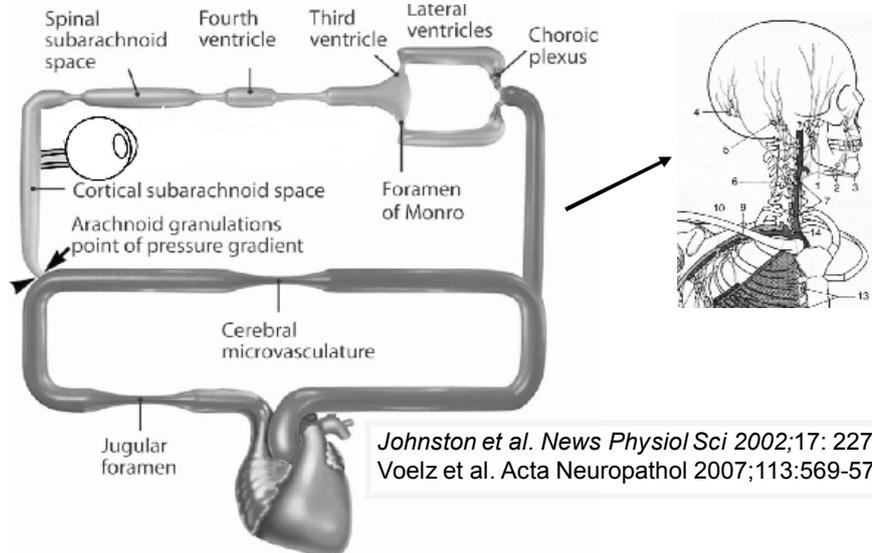
## Therapy resistance? CAVE: Think of the unlikely!



Spinal Arachnoidal Cyst

N Engl J Med 2009;361:2367-78.

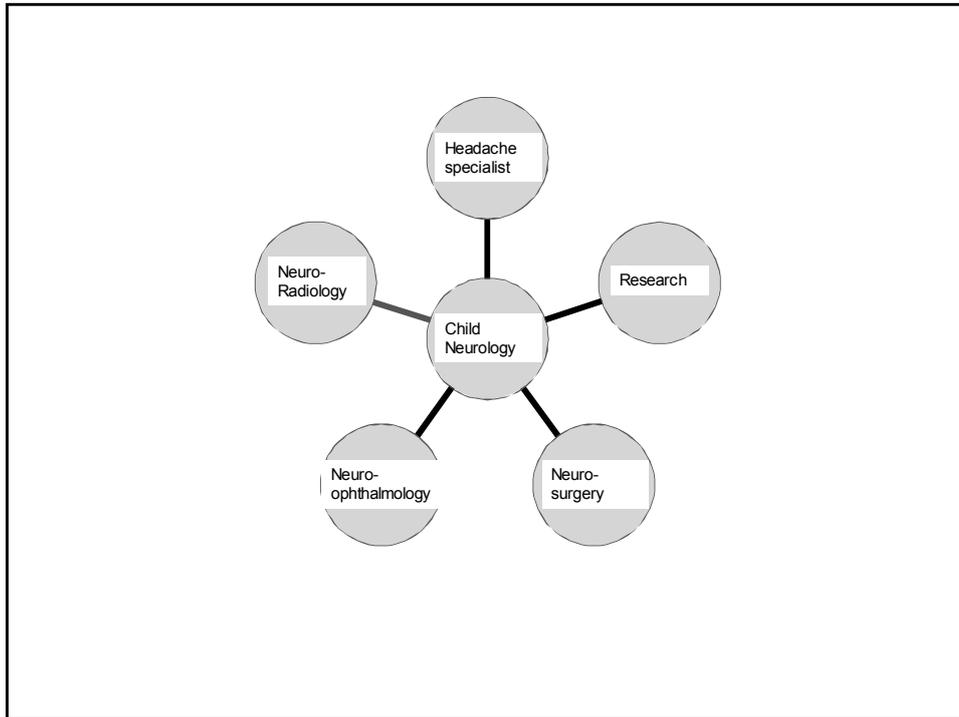
## The complex mechanisms of CSF circulation



Adapted from: Grzybowski and Lubow. In: Ocular disease. Mechanisms and Management. 2010

### C) Invasive Therapy

- FIRST:  
DO NO HARM!
- SECOND:  
WHAT IS YOUR TREATMENT GOAL?



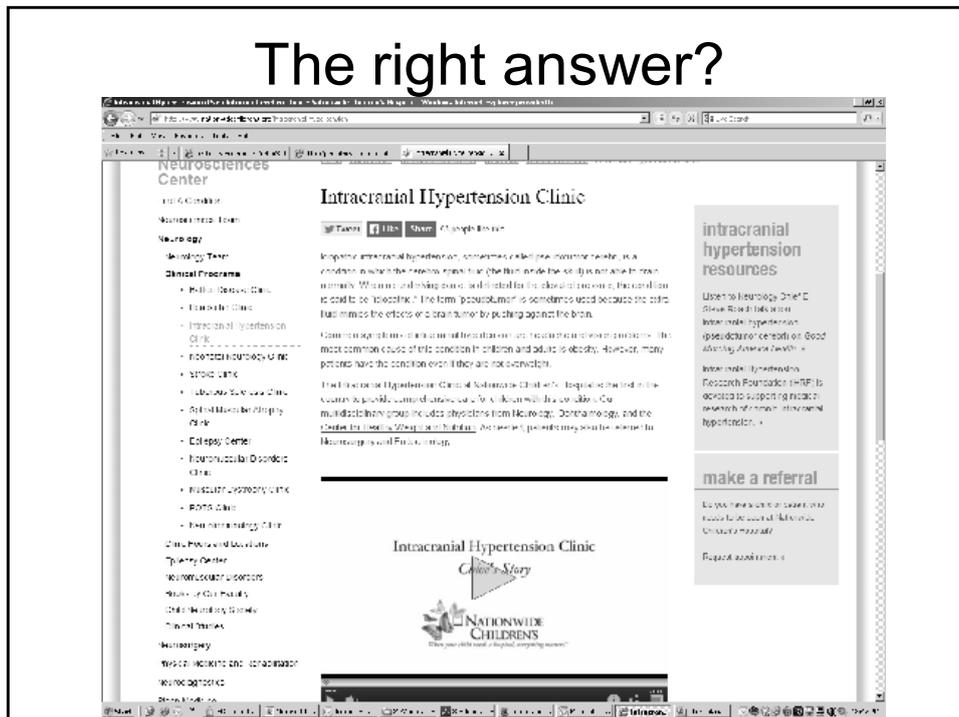
## Interdisziplinäre decision!

- Optimal management of IIH requires good communications between specialties to protect the patient from unnecessary lumbar punctures and CSF diversion surgery on the one hand and avoidable visual loss on the other.

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Standridge SM. Idiopathic intracranial hypertension in children: A review and algorithm. *Pediatr Neurol* 2010;43:377-390.

# The right answer?



## Take Home Messages

- The doubtless diagnosis of PTC is difficult!
- Therapy escalation follows visual function monitoring.
- Critically question whether invasive procedure is really unpreventable.
- Critically question diagnosis in any atypical case.
- Interdisciplinary approach!
- Many open questions!
- Do research!