PSEUDOTUMOR CEREBRI

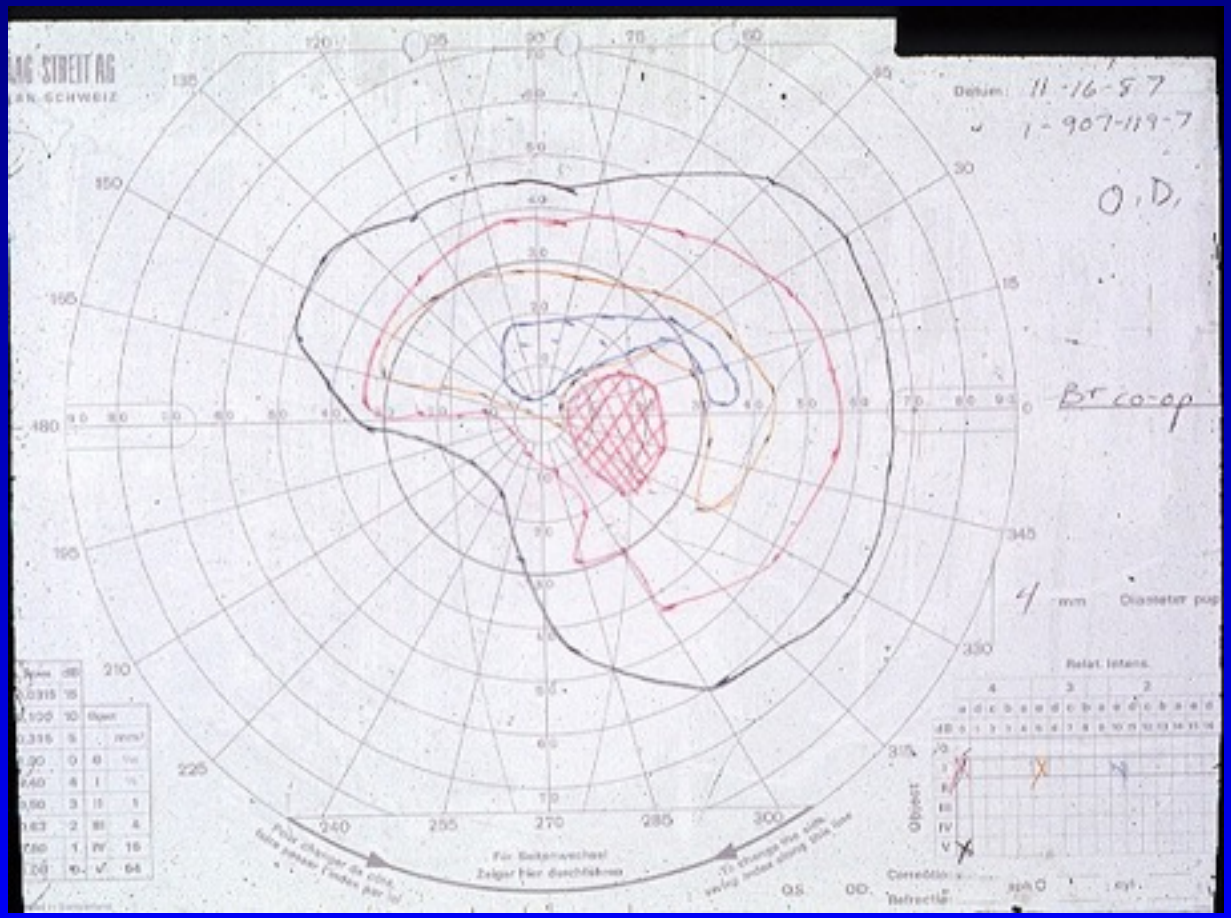
PSEUDOTUMOR CEREBRI

- 11/16/87
  - 31 year old obese Caucasian woman
  - bifrontal, pounding HA's
  - referred to R/O brain tumor

PSEUDOTUMOR CEREBRI

- no diplopia
- hundreds of TOV's per day
- 20/15 OU
- +1 RAPD OD
- GVF's
  - OD-arcuate defect inferiorly
  - OS-enlarged blind spot

PSEUDOTUMOR CEREBRI



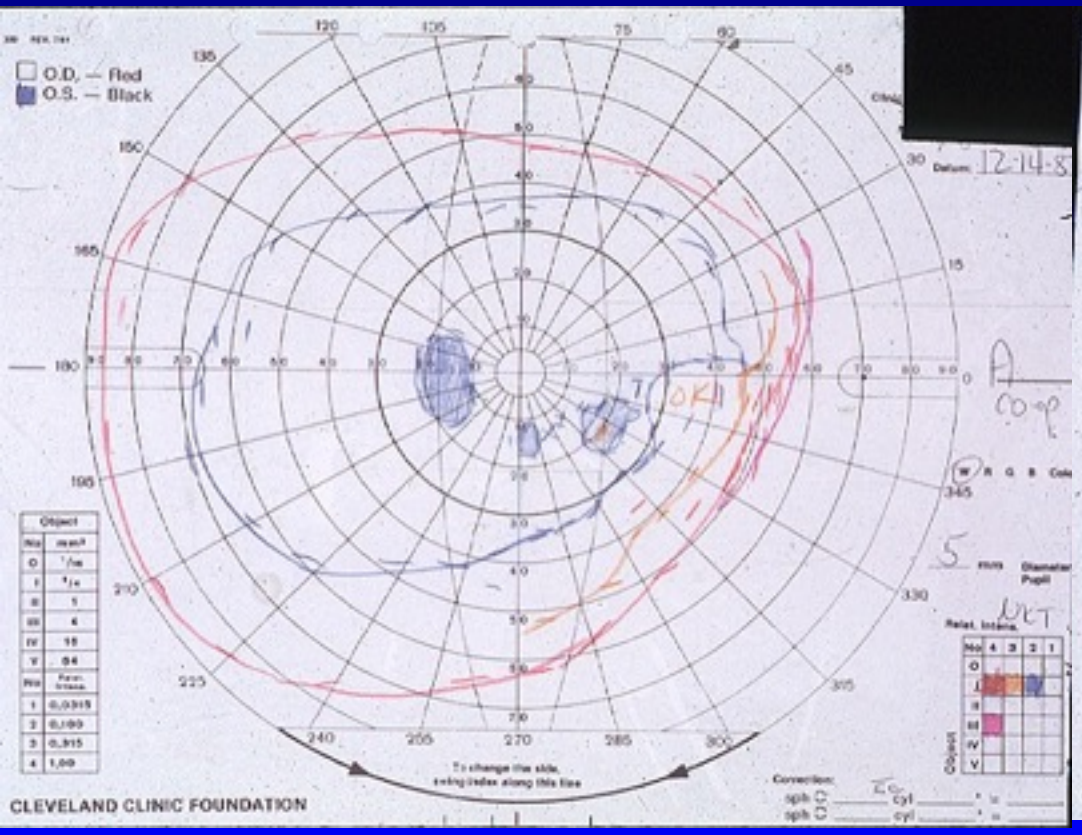
PSEUDOTUMOR CEREBRI

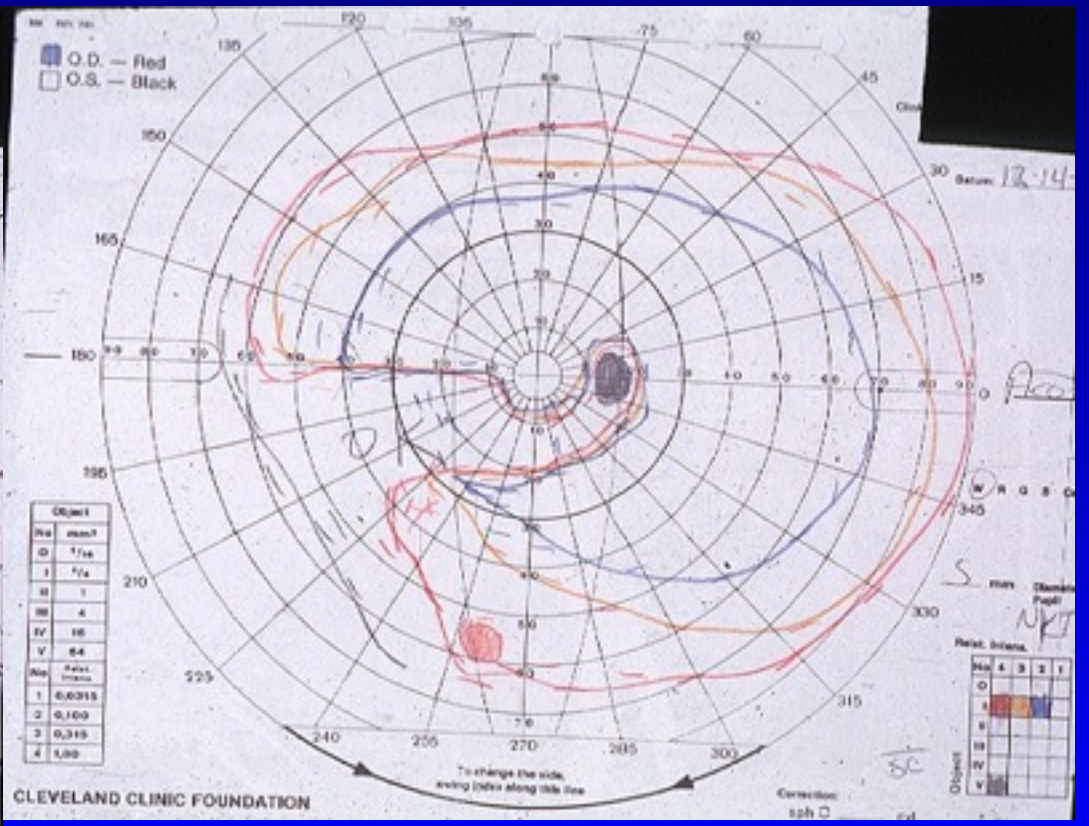
- Imaging
  - CT-nl
  - MR-nl
- LP
  - OP=330 mmH_2O
    - WBC=1
    - RBC=1
    - pro=24
    - glu=61

PSEUDOTUMOR CEREBRI

- 12/14/87
  - "my vision is a little dimmer"
  - 20/15 OU
  - ***NO*** RAPD
  - GVF's
    - bilateral inferior arcuates
  - Rx: Diamox 500mg bid

PSEUDOTUMOR CEREBRI





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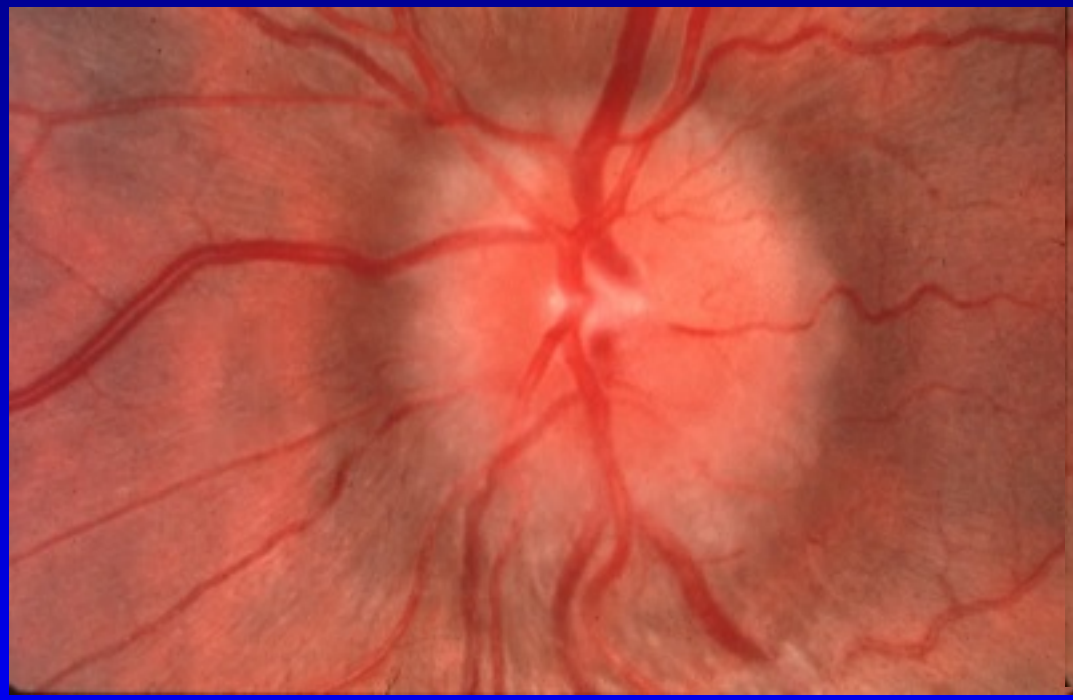
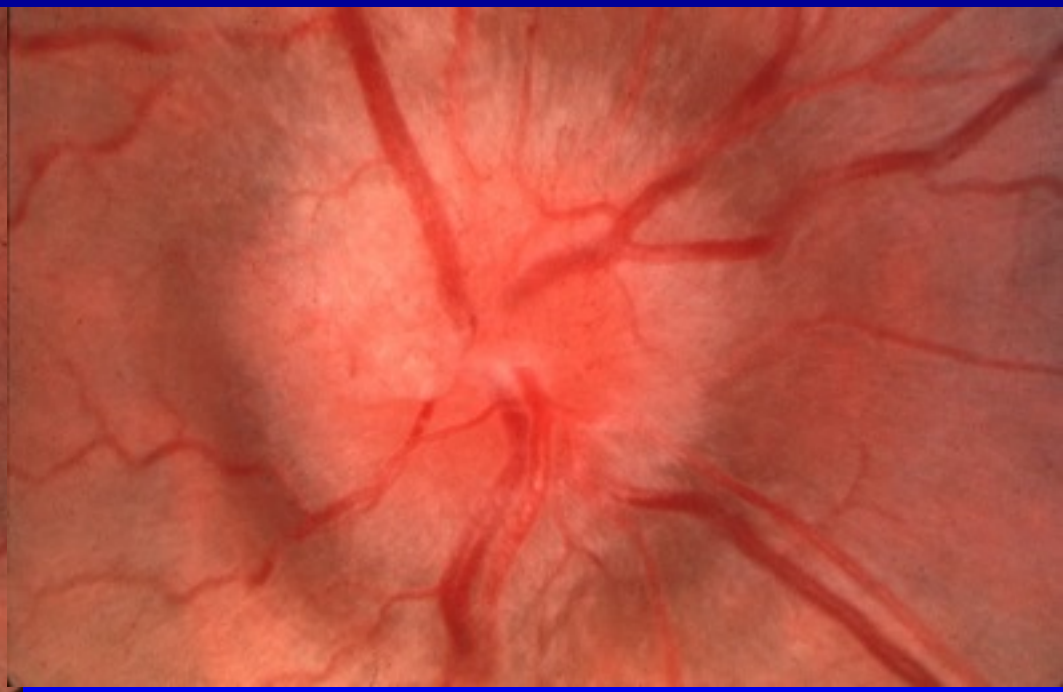
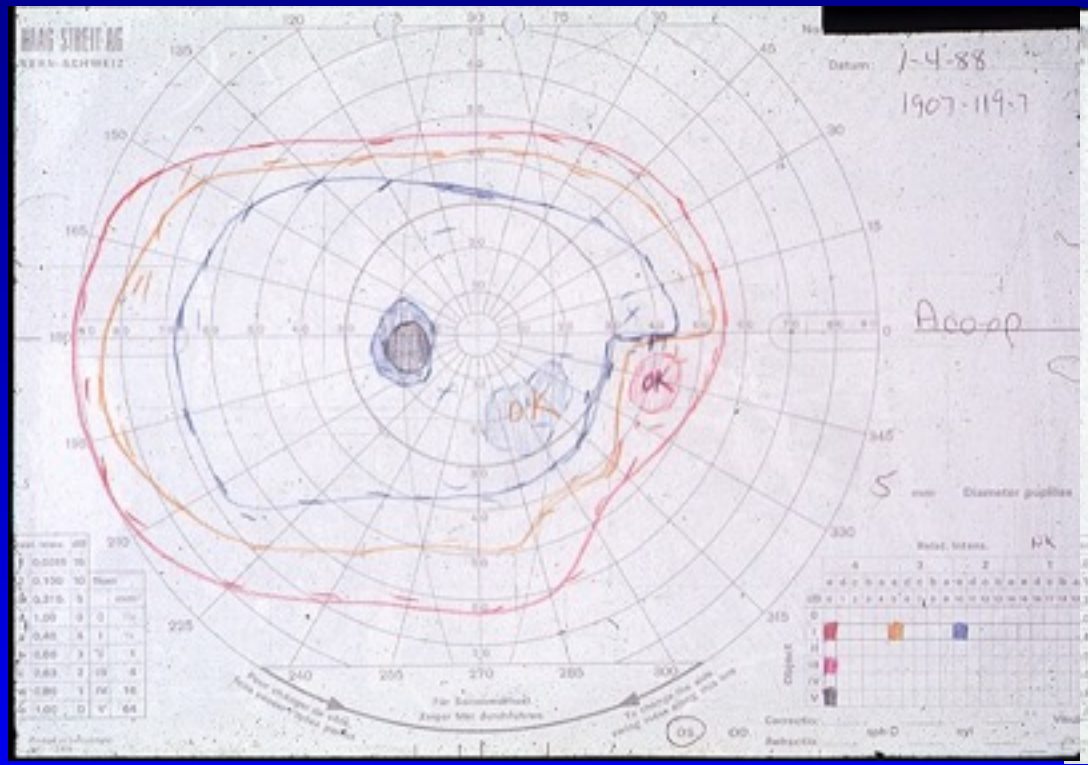


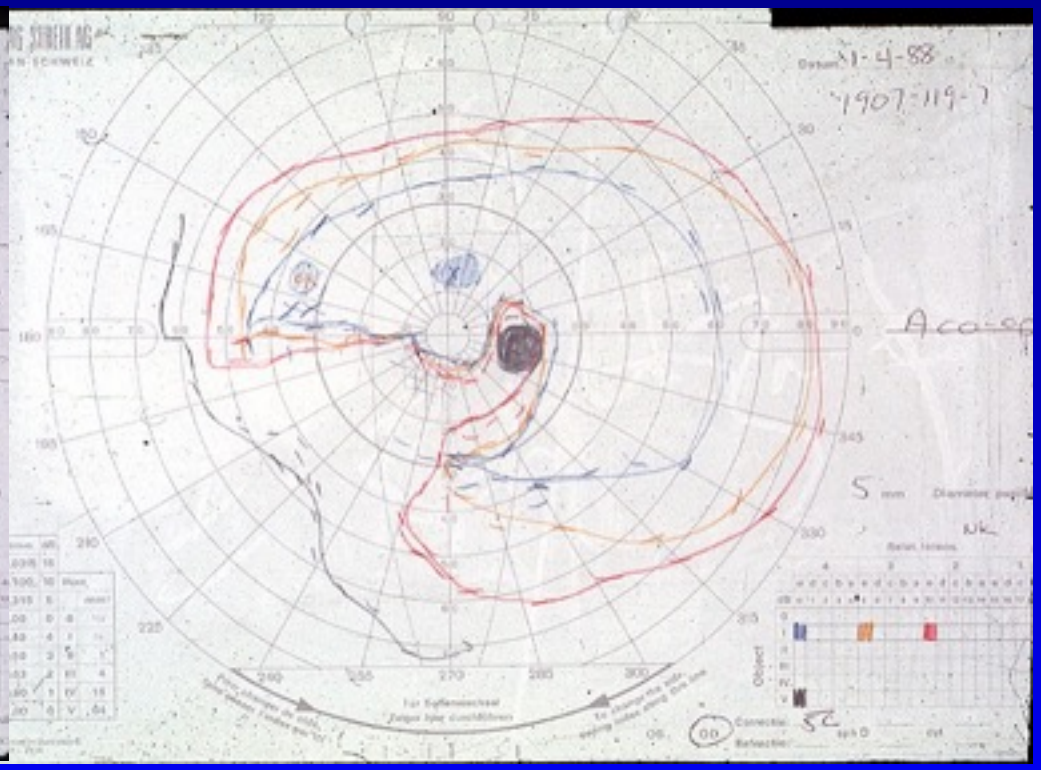


PSEUDOTUMOR CEREBRI

- 1/4/88
  - "there's a lot of pressure in the right eye and the vision is different"
  - 20/15 OU
  - 2+ RAPD OD
- GVF's
  - bilateral inferior arcuate defects

PSEUDOTUMOR CEREBRI



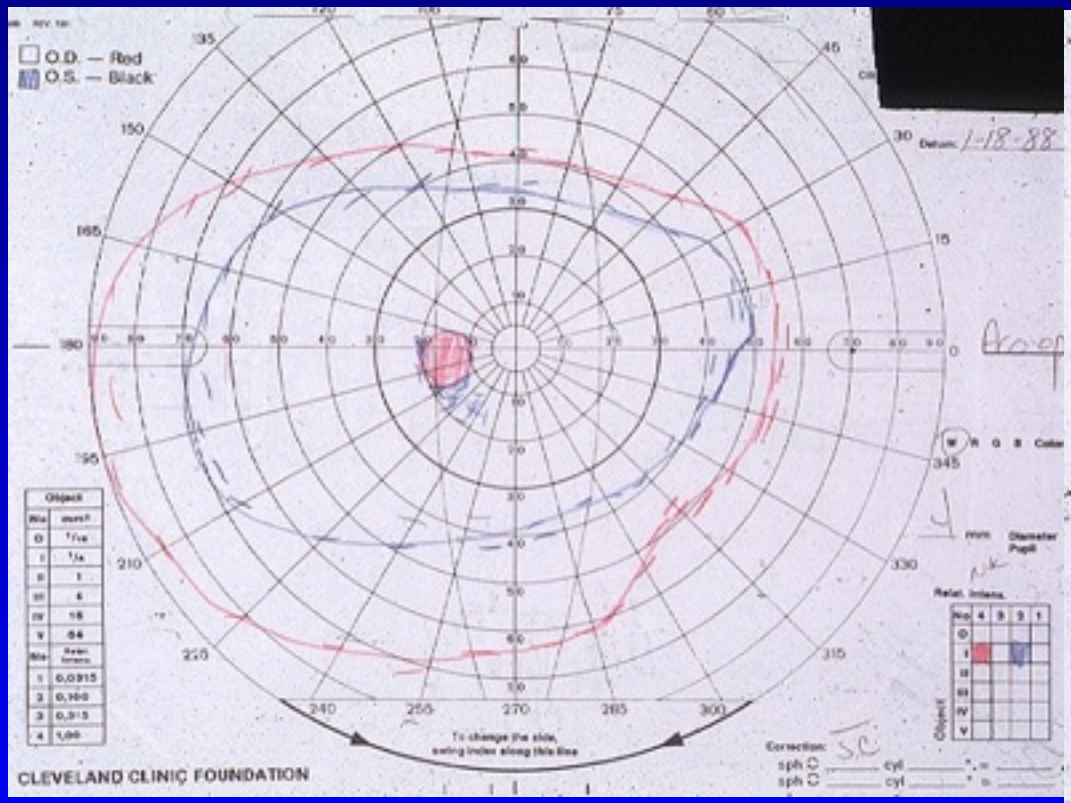


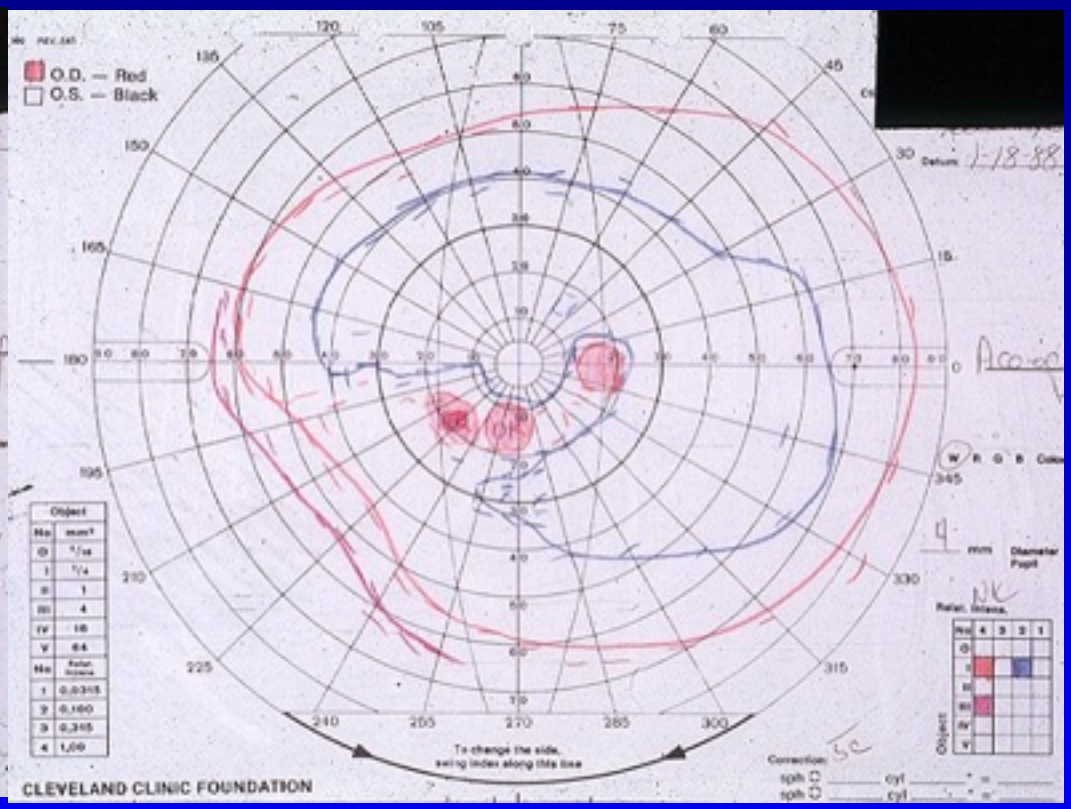
PSEUDOTUMOR CEREBRI

PSEUDOTUMOR CEREBRI

- 1/18/88
  - 20/15 OU
  - GVF's
    - OD-smaller inferior arcuate
    - OS-normal
  - D/C Diamox

PSEUDOTUMOR CEREBRI





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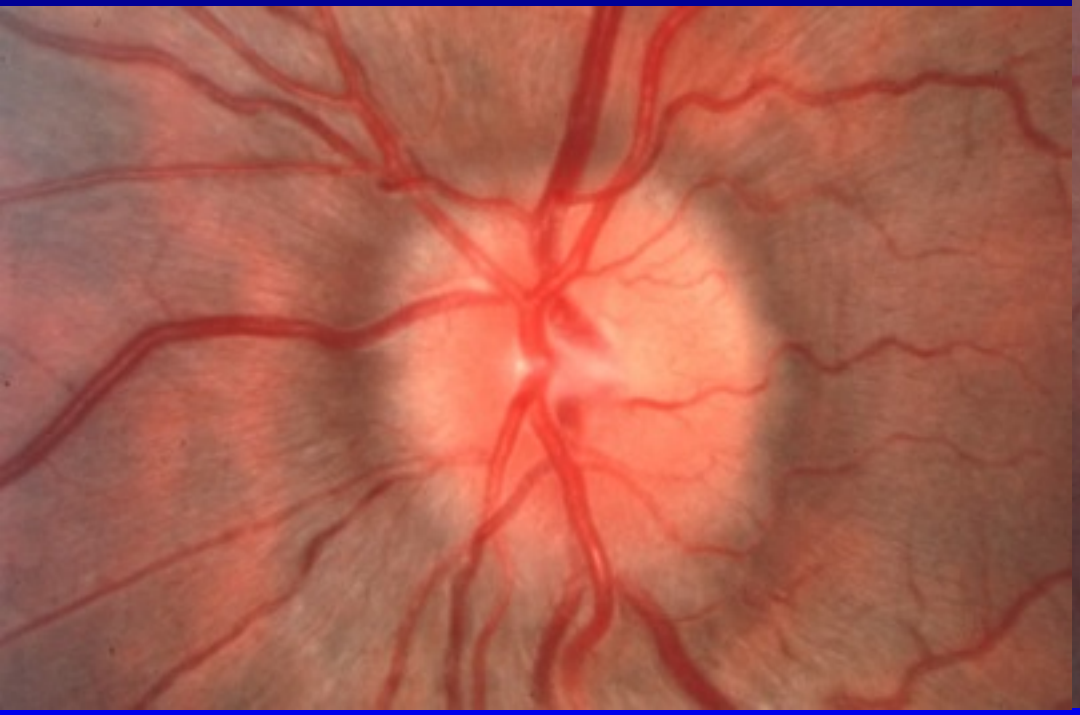
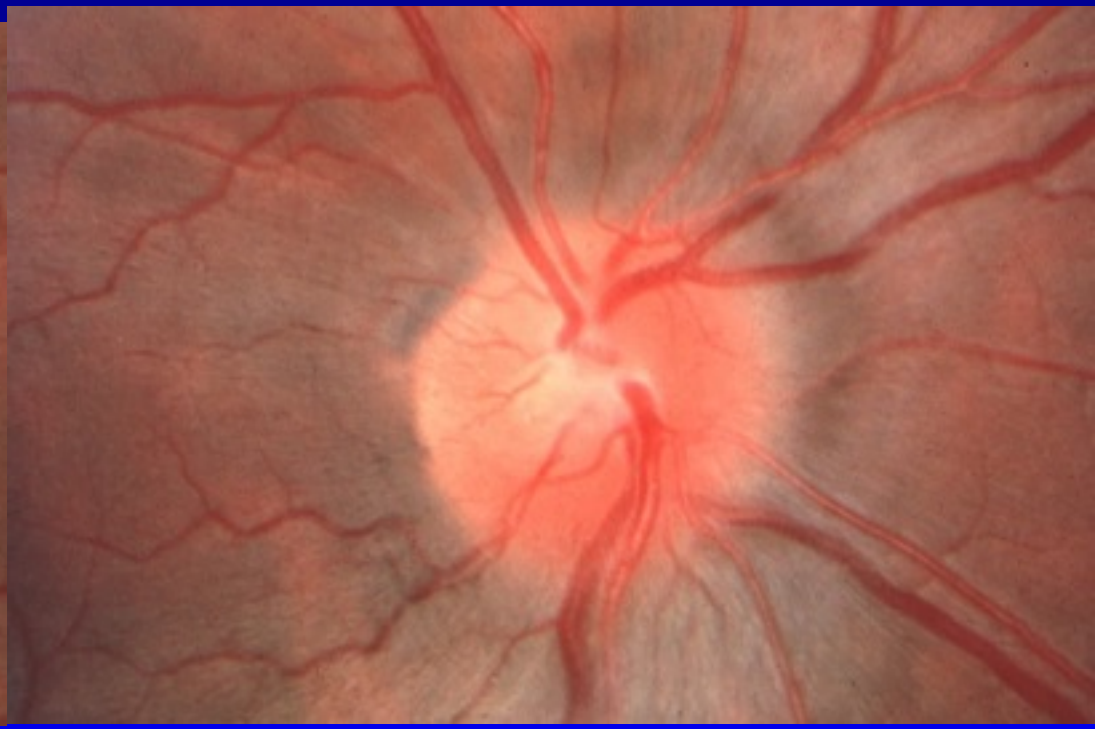




PSEUDOTUMOR CEREBRI

"BENIGN"

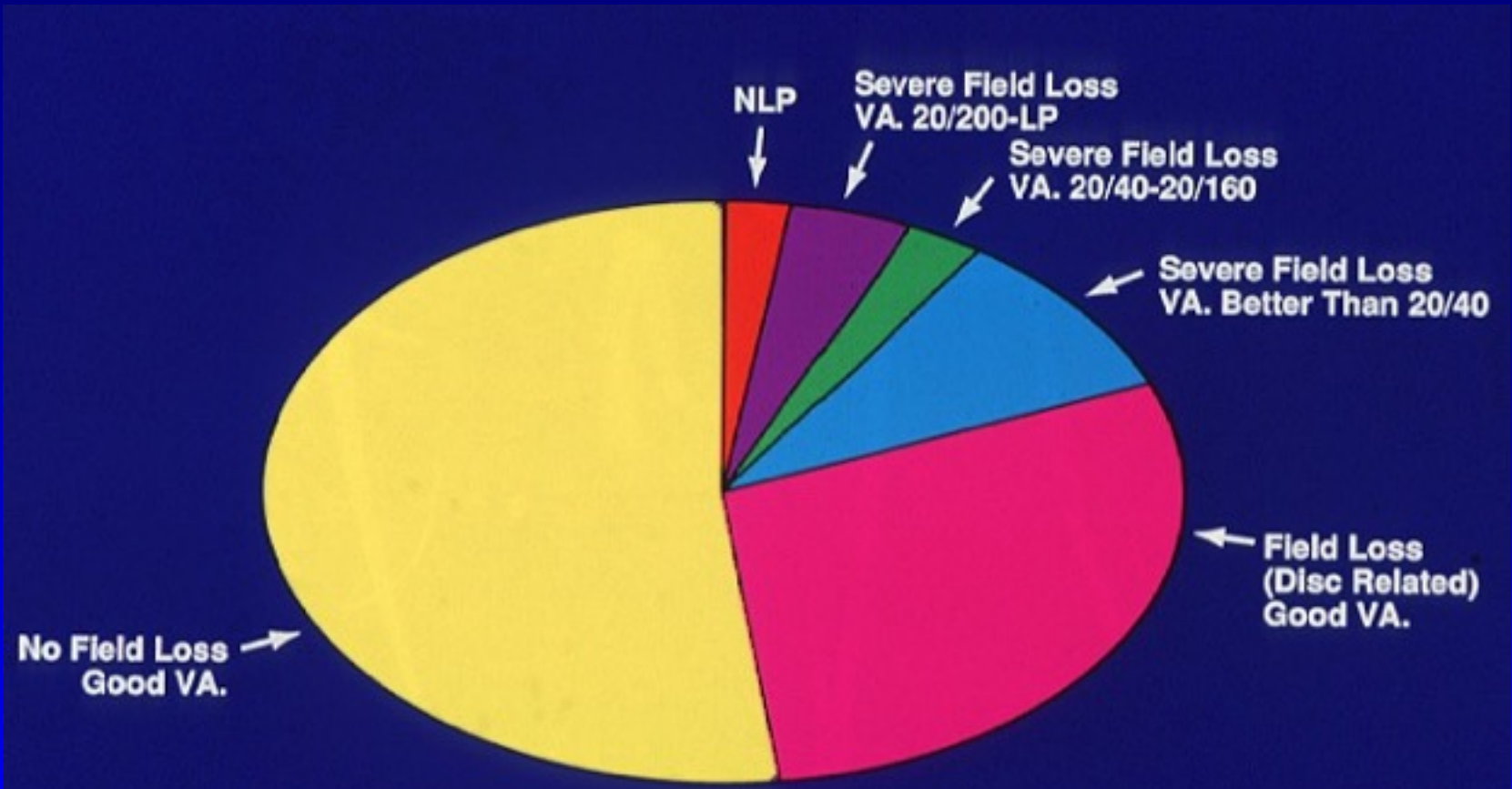
Intracranial Hypertension

PSEUDOTUMOR CEREBRI

PSEUDOTUMOR CEREBRI

NOT a benign disease!

PSEUDOTUMOR CEREBRI



Visual loss in 114 eyes of 57 patients. NLP indicates no light perception; VA, visual acuity; and LP, light perception.

PSEUDOTUMOR CEREBRI

- DEFINITION
  - increased ICP
  - normal or small ventricles
  - normal CSF composition
  - papilledema
- OTHER ASSOCIATIONS
  - empty sella
  - enlarged ON sheaths

PSEUDOTUMOR CEREBRI

History of PTC

- first recognized by Quincke in 1897
- toxic hydrocephalus - McAlpine 1937
- otitic hydrocephalus - Symonds 1931
- hypertensive meningeal hydrops - Davidoff and Dyke 1932
- pseudoabscess - Adson 1924
- intracranial pressure without brain tumor - Dandy 1937
- brain swelling of unknown cause - Saks and Hyndman 1939
- papilledema of indeterminate etiology - Yaskin et al 1949
- pseudotumor cerebri - Warrington 1914
- benign intracranial hypertension - Foley 1955

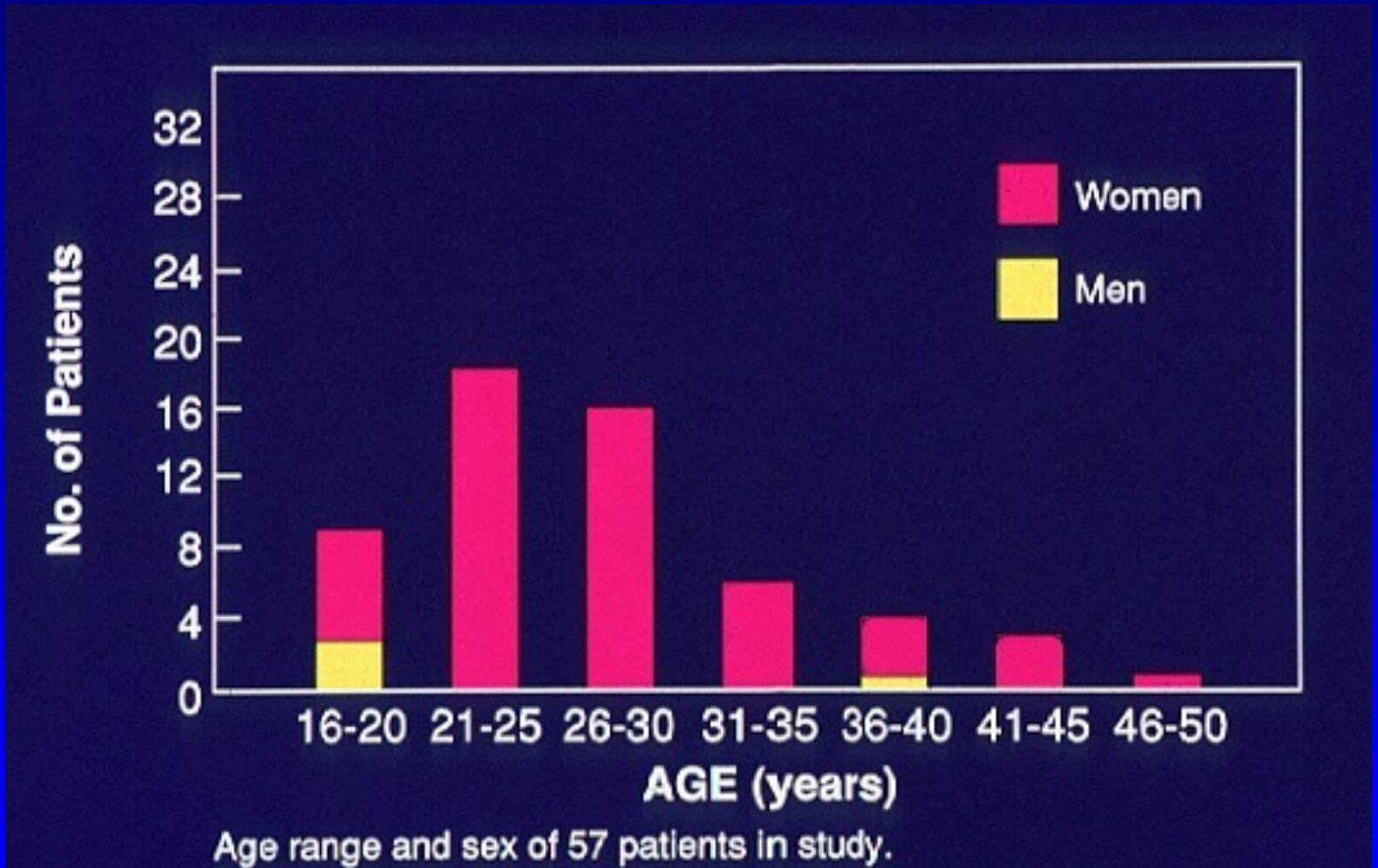
PSEUDOTUMOR CEREBRI

- CLINICAL PROFILE
  - disease of overweight women
  - headache
    - can have morning HA increased by Valsalva
    - non-specific
  - peak incidence in 3rd decade
  - more females

PSEUDOTUMOR CEREBRI

- Female:male ratio is 8:1
- Incidence in general population 0.9/100,000
- Incidence in obese females 13-14/100,000 when 10% over ideal wt and 19.3/100,000 when 20% over ideal wt
- 90% are female
- 90% are obese
- Age range 1-67; mean = 27

PSEUDOTUMOR CEREBRI

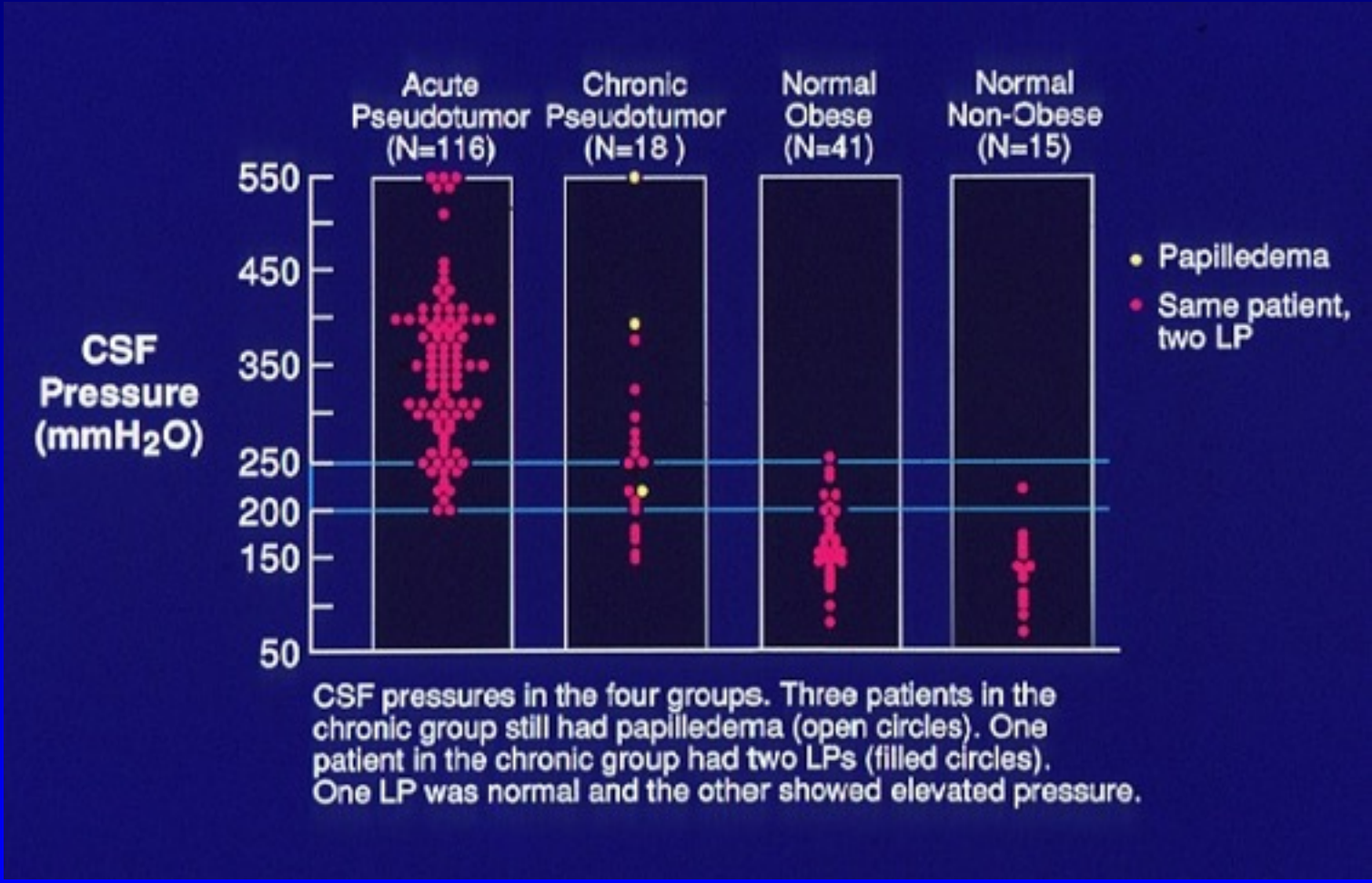


Age range and sex of 57 patients in study.

PSEUDOTUMOR CEREBRI

- MAKING THE DIAGNOSIS
  - MR vs CT
  - LP - mandatory
  - CBC and CMP
  - ? Iron studies

PSEUDOTUMOR CEREBRI



CSF pressures in the four groups. Three patients in the chronic group still had papilledema (open circles). One patient in the chronic group had two LPs (filled circles). One LP was normal and the other showed elevated pressure.

PSEU EBRI

Differential Diagnosis of IIH (Cases Must Meet the Modified Dandy Criteria Except That a Cause Is Found)

HIGHLY LIKELY

- Decreased flow through arachnoid granulations
  - Scarring from previous inflammation, e.g., meningitis, sequel to subarachnoid hemorrhage
- Obstruction to venous drainage
  - Venous sinus thromboses
  - Hypercoaguable states
  - Contiguous infection (e.g., middle ear or mastoid-otitic hydrocephalus)
  - Bilateral radical neck dissection
  - Superior vena cava syndrome
  - Increased right heart pressure
- Endocrine disorders
  - Addison's disease
  - Hypoparathyroidism
  - Obesity
  - Steroid withdrawal
- Nutritional disorders
  - Hypervitaminosis A (vitamin, liver, or isotretinoin intake)
  - Hyperalimentation in deprivation dwarfism
- Arteriovenous malformations

PROBABLE CAUSES

- Anabolic steroids (may cause venous sinus thrombosis)
- Chlordecone (kepone)
- Ketoprofen or indomethacin in Bartter's syndrome
- Systemic lupus erythematosis
- Thyroid replacement therapy in hypothyroid children
- Uremia

POSSIBLE CAUSES

- Amiodarone
- Diphenylhydantoin
- Iron deficiency anemia
- Lithium carbonate
- Nalidixic acid
- Sarcoidosis
- Sulfa antibiotics

CAUSES FREQUENTLY CITED THAT ARE UNPROVED

- Corticosteroid intake
- Hyperthyroidism
- Hypovitaminosis A
- Menarche
- Menstrual irregularities
- Multivitamin intake
- Oral contraceptive use
- Pregnancy
- Tetracycline use

From Wall M: Idiopathic intracranial hypertension. Neurol Clin 9(1):76, 1991

PSEUDOTUMOR CEREBRI

- Recombinat human growth hormone
  - Ophthalmology 1999;106:1186-1190
- Cyclosporine
  - AJO September 1996;436-437
- all transretinoic acid (ATRA)
- Leuprorelin (Lupron)
  - Lancet; March 17th 1990:668
- Beta HCG
  - Neurology 1993:vol 43. 448-449

PSEUDOTUMOR CEREBRI

Prevalence of Symptoms in Cases and Age/Sex-Matched Controls

SYMPTOMS	CASES (%)	CONTROL (%)	P VALUE	ODDS RATIO	LOWER 95% CI
Diplopia	38	0	<0.00001	51.5	6.6
Visual loss	30	0	<0.00001	42.9	5.4
Retrobulbar pain	44	12	<0.00001	5.8	2.5
with eye movement	22	0	<0.00001	28.2	3.5
Shoulder/arm pain	18	2	0.001	21.9	2.7
Dyscoordination	14	0	0.0003	16.3	1.9
Intracranial noises	58	9	<0.00001	14.0	5.8
Decreased smell	12	1	0.0016	13.5	1.6
Numbness	24	3	0.0001	10.2	2.7
Visual obscurations	68	21	<0.00001	8.0	3.7
Headache	94	79	0.03	4.2	1.2
Motor weakness	10	2	0.04	5.4	1.0
Photopsia	54	68	NS*	0.6	0.3

* NS = P value is not significant.
CI = confidence interval.
Modified from Wall M, Giuseffi V, Rojas PB: Symptoms and disease associations in pseudotumor cerebri: A case-control study. Neurology 39(suppl):210, 1989; with permission.

PSEUDOTUMOR CEREBRI

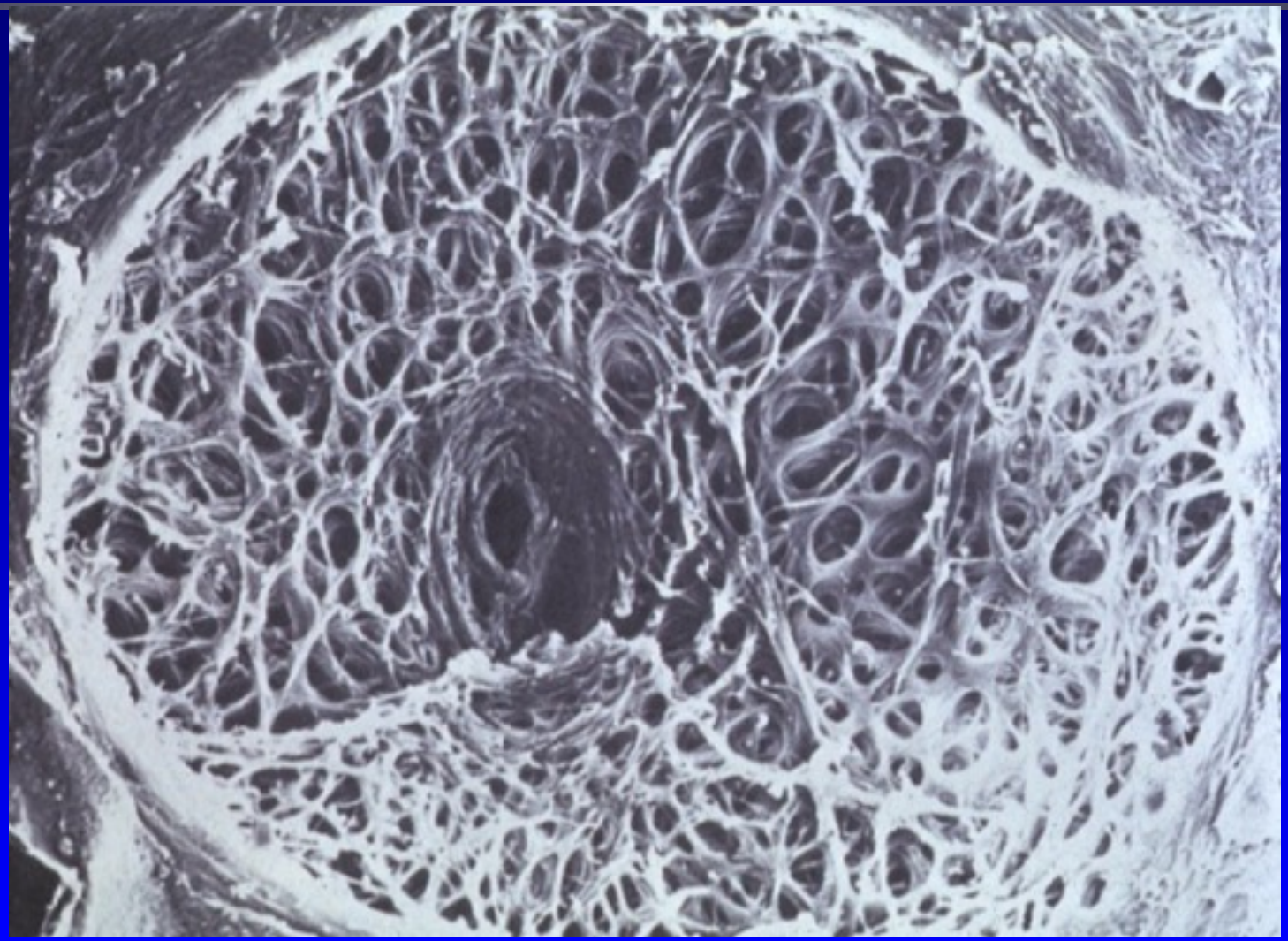
- TOV's
  - very common monocular or binocular
  - usually occur with a postural change
  - perfusion defect in laminar region
  - no relationship to visual loss
    - NO correlation with HA
    - NO correlation with disc pallor

PSEUDOTUMOR CEREBRI

LAMINA CRIBROSA : THE CRITICAL AREA

- disc edema caused by stasis of axonal transport
  - mechanical
  - vascular

PSEUDOTUMOR CEREBRI



PSEUDOTUMOR CEREBRI

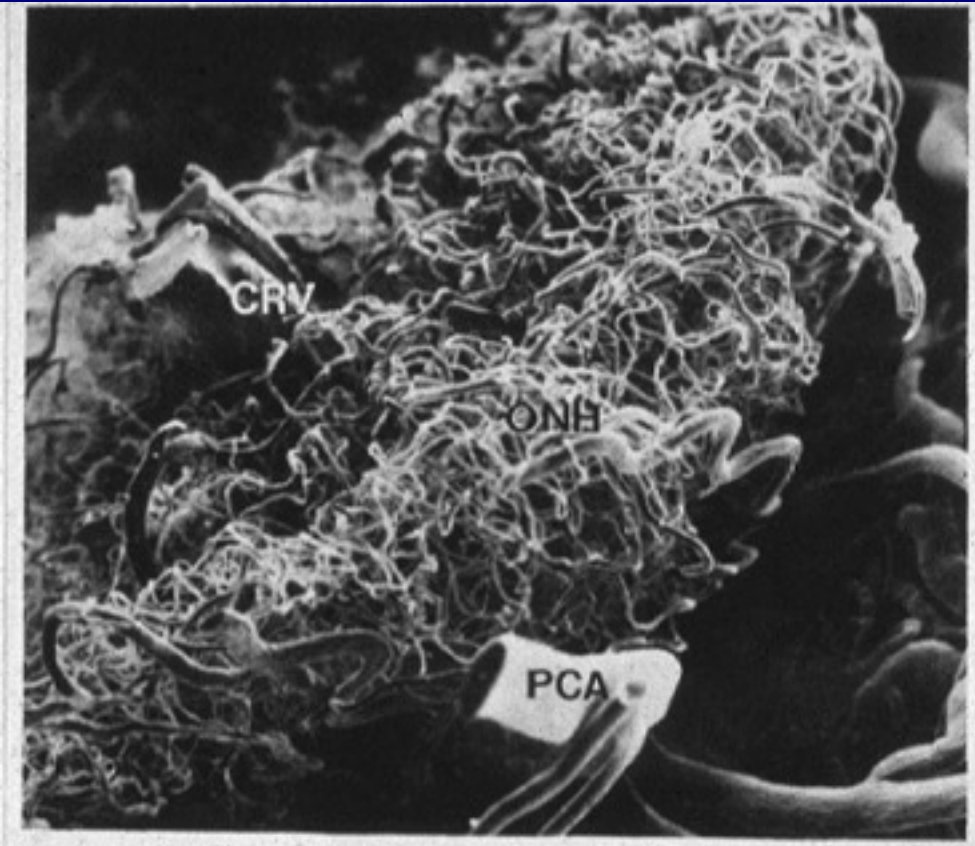
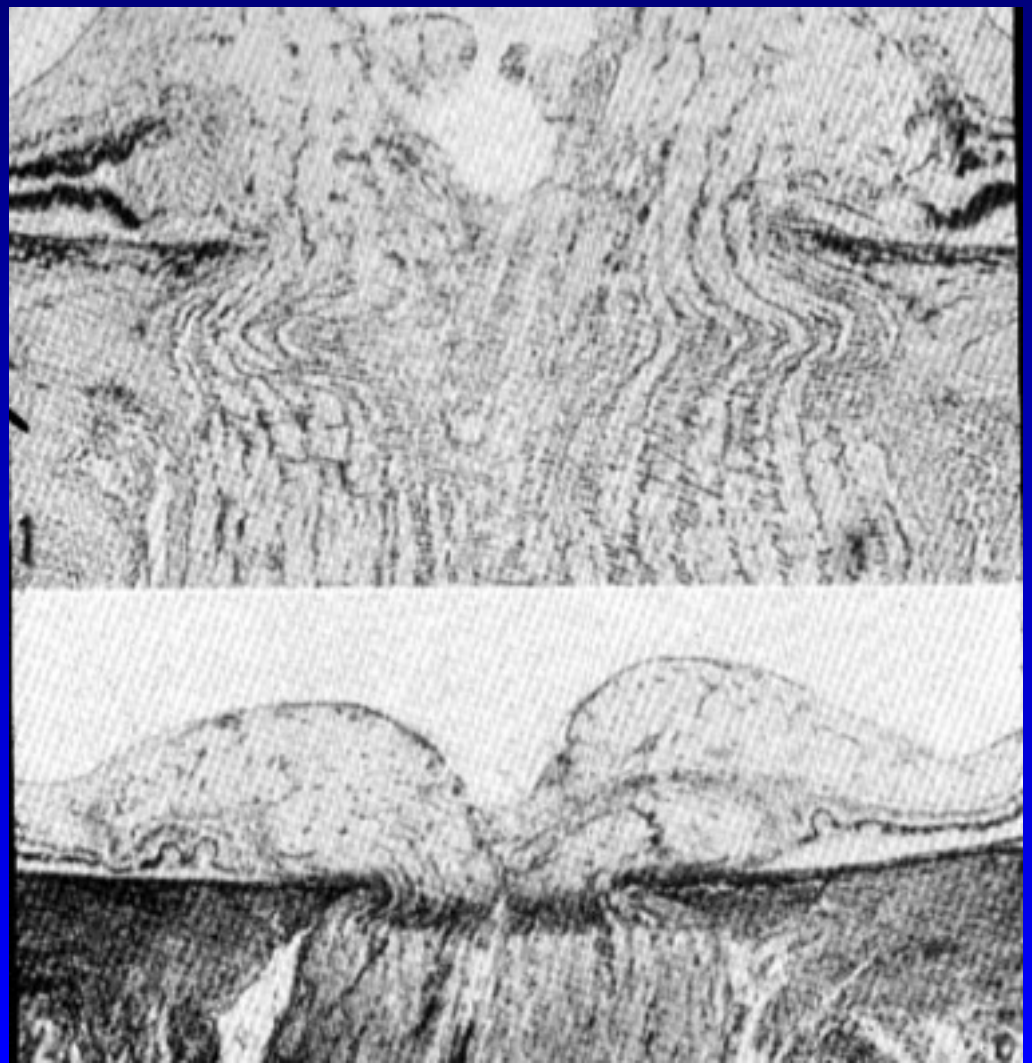


Figure 3.08. Scanning electron micrograph showing extensive vascular structure of the optic nerve head (*ONH*) supplied by the central retinal vessels (*CRV*) and the posterior ciliary arteries (*PCA*). (Courtesy of Dr. H.A. Quigley.)

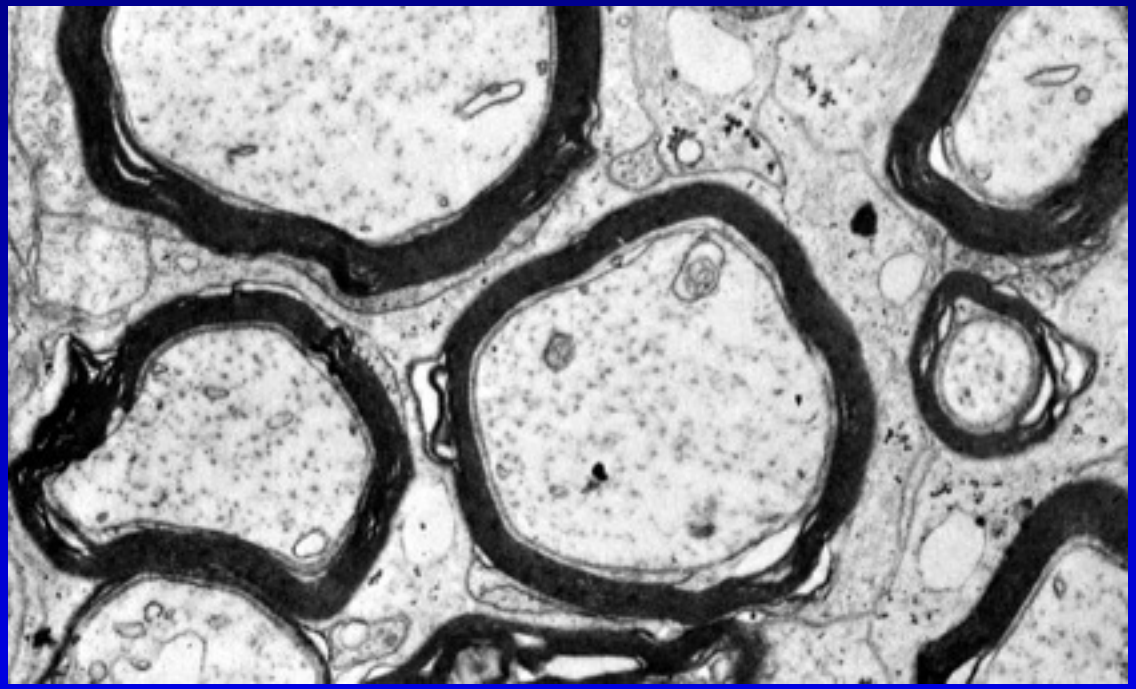
PSEUDOTUMOR CEREBRI

Papilledema

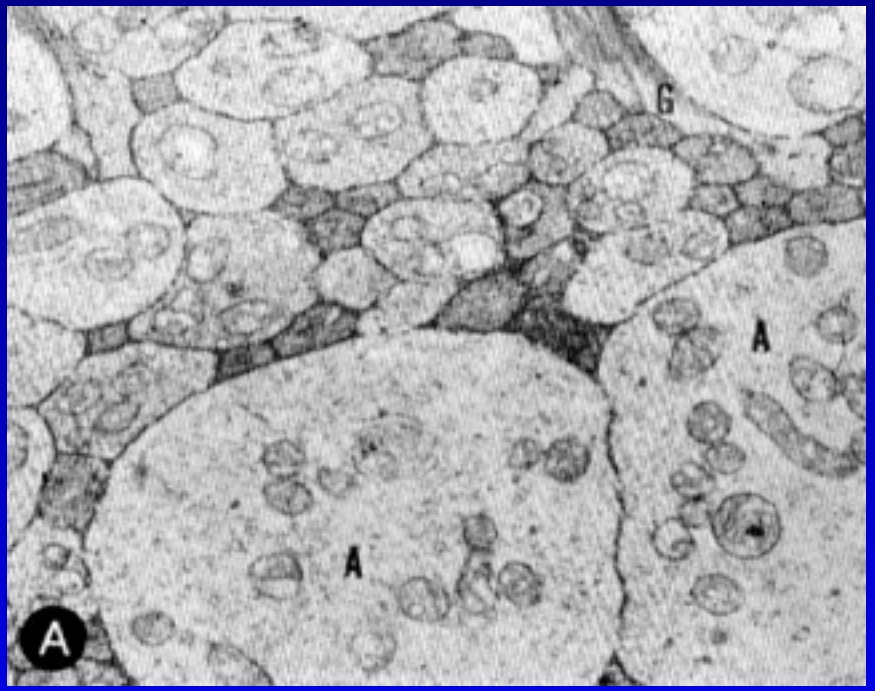
Normal ON



PSEUDOTUMOR CEREBRI



Normal ON



Chronic papilledema

PSEUDOTUMOR CEREBRI

- RISK FACTORS FOR VISUAL LOSS
  - hypertension
  - increased IOP
  - AA male
  - Renal disease

PSEUDOTUMOR CEREBRI

- PATHOPHYSIOLOGY
  - 2 theories
    - abnormal CSF absorption (Johnston and Patterson)
    - cerebral edema (Foley; Reid)

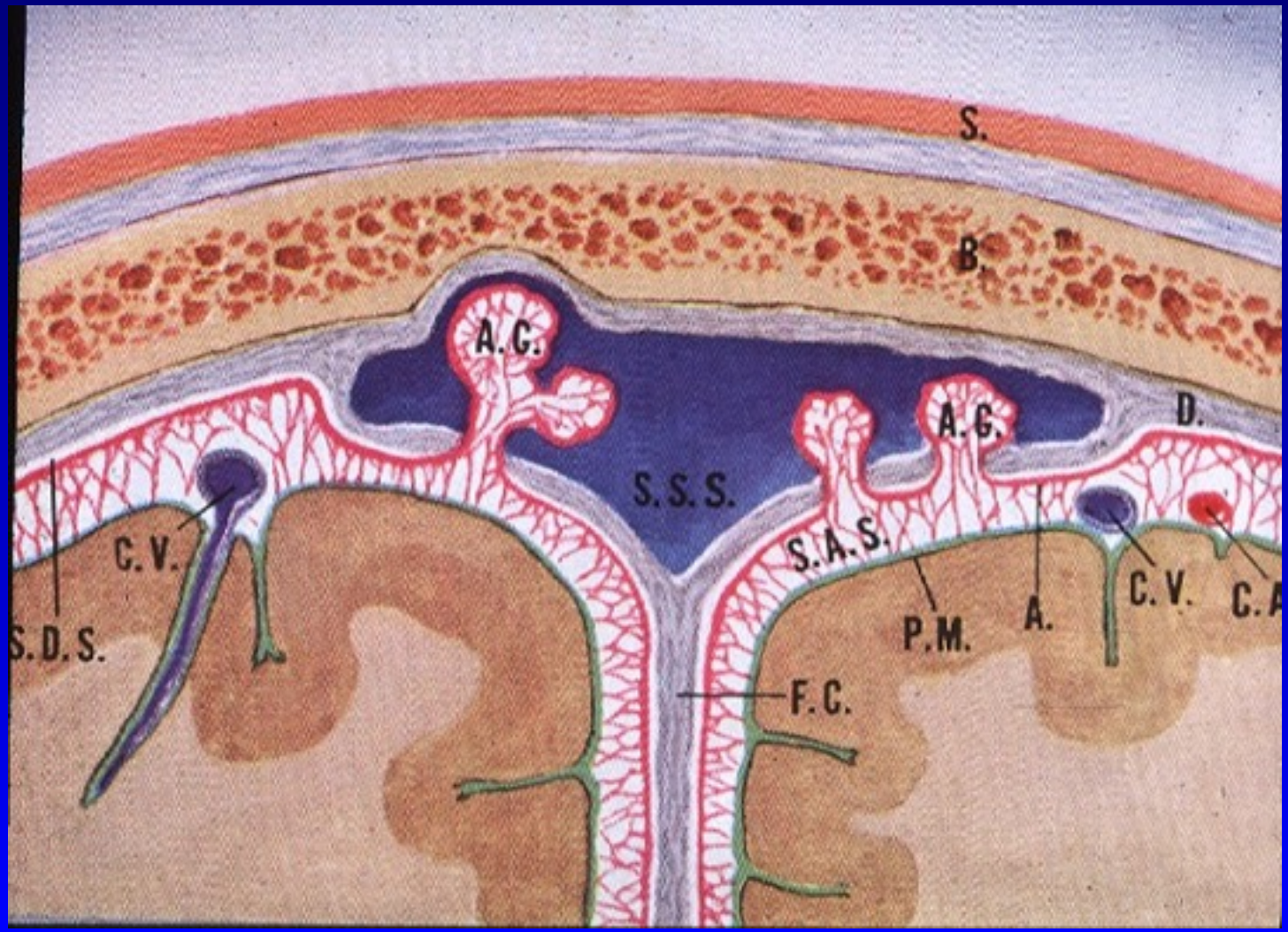
PSEUDOTUMOR CEREBRI

- CEREBRAL EDEMA
  - some of the drugs that cause PTC poison the mitochondria
  - water pores could be affected
    - highly energy dependent
      - microvesicular transport
      - bulk flow

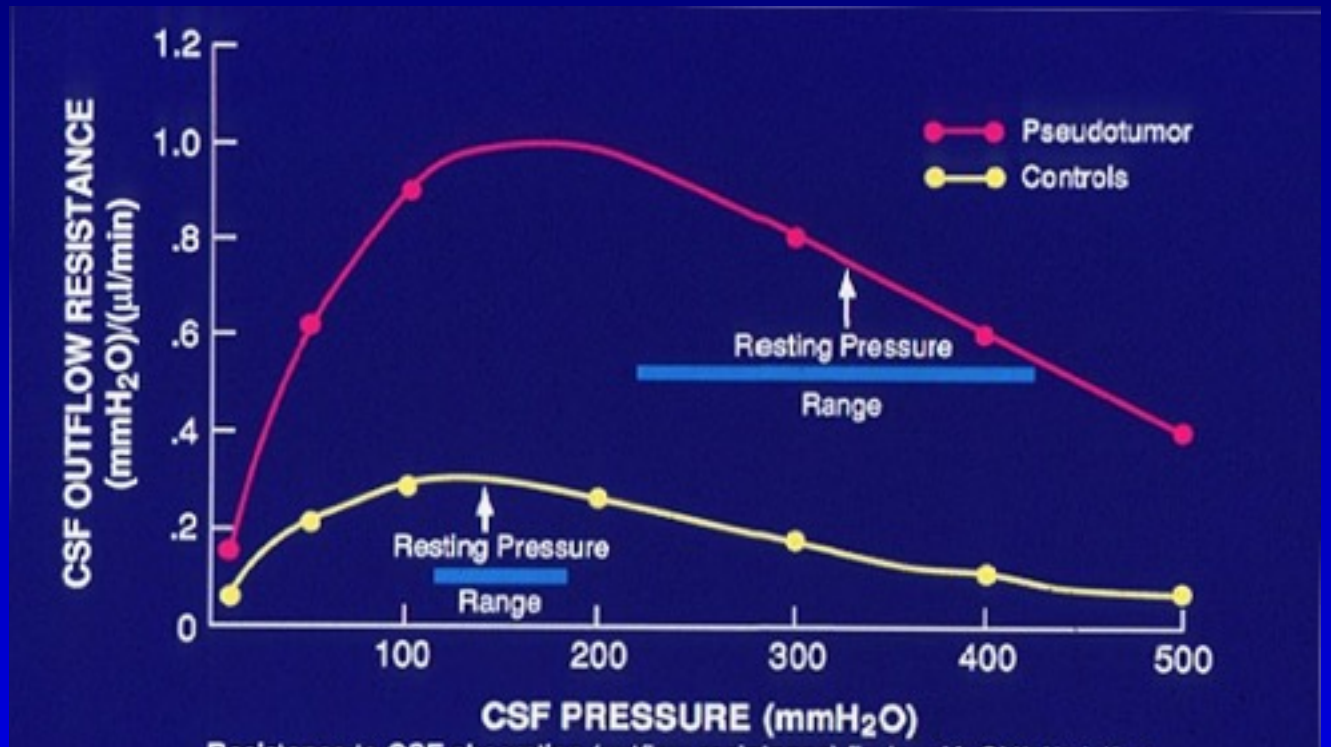
PSEUDOTUMOR CEREBRI

- COAG relationship to PTC
  - both represent disorders of decreased absorption of fluid
  - energy dependent mechanisms are also likely responsible

PSEUDOTUMOR CEREBRI



PSEUDOTUMOR CEREBRI



Resistance to CSF absorption (outflow resistance) [in $(mmH_2O)/(\mu l/min)$] at different CSF pressures in pseudotumor-cerebri and control patients. Mean resting pressure for each group is indicated by arrow, with range of resting pressures denoted by black bar. CSF pressures are those measured under steady-state conditions during constant-rate manometric infusion of artificial CSF into subarachnoid space (SAS). Intracranial pressure (ICP) was significantly increased in pseudotumor-cerebri patients compared to control patients at all flows tested. Linearity of outflow resistance was found in both groups, and resistance to absorption fell over range of pressures and flows tested.

PSEUDOT

Brain Research Reviews
64 (2010) 241-262
The formation of cerebrospinal fluid: nearly a hundred years of interpretations and misinterpretations
D Oreskovic, M Klarica

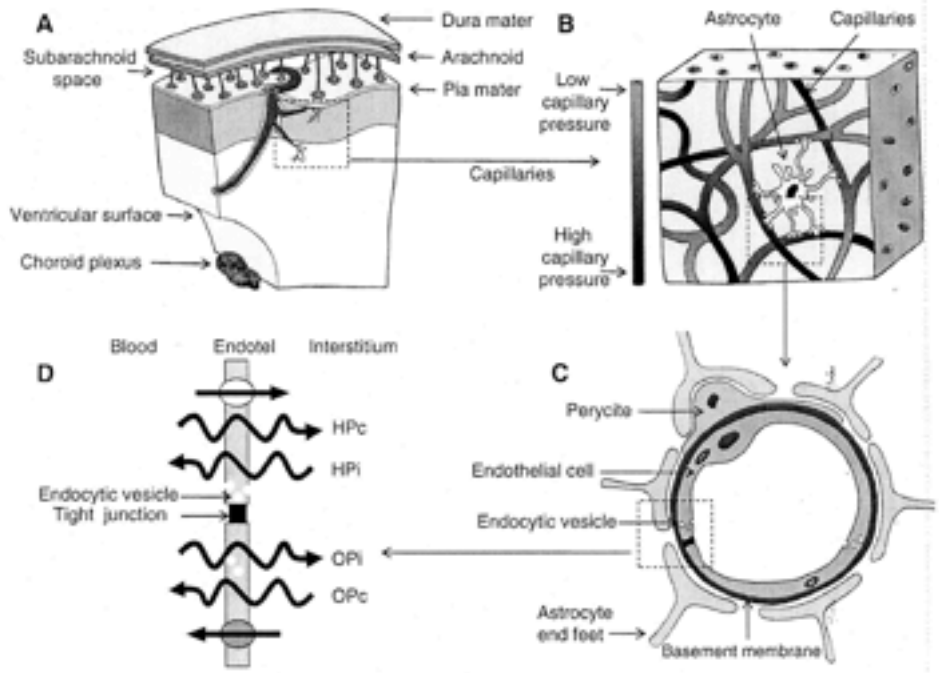
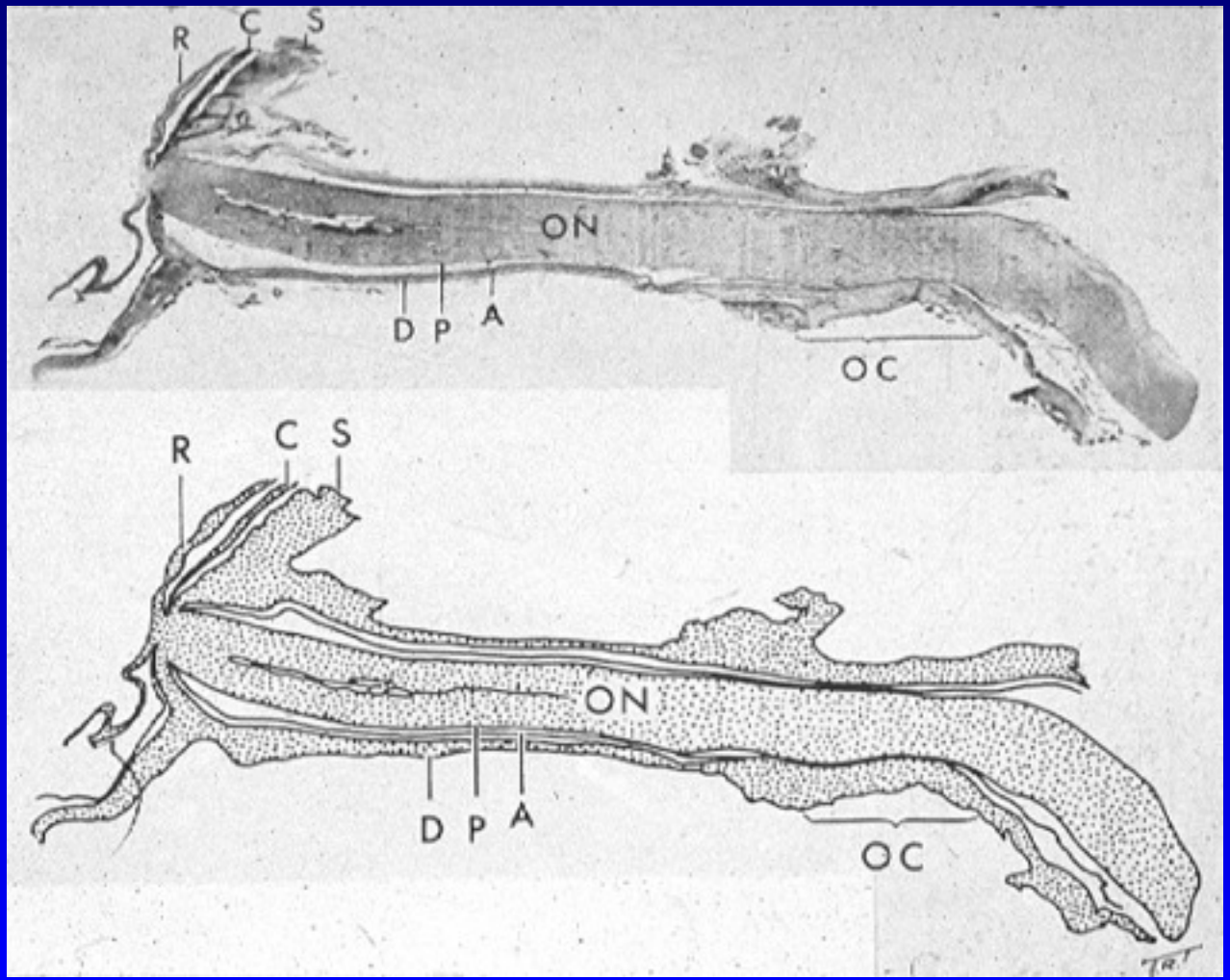


Fig. 8 – A scheme of the interrelation between cerebrospinal fluid (CSF), interstitial fluid (ISF) and cerebral blood vessels, and the exchange of water and substances between the blood and ISF–CSF through the blood–brain barrier. A. Larger blood vessels enter deep into the brain tissue. The substances with large m.w. can, after being applied into the CSF system, rapidly enter deep into the tissue via perivascular spaces and reach the vast capillary net. Due to the slow elimination from ISF–CSF into the blood, those substances should be widely distributed inside the brain parenchyma and along the CSF system. On the other hand, smaller molecules like water can rapidly reach the capillary net situated under the pia mater after application into the CSF, and then they can be removed from the ISF. Similar to that, the molecules of water from the ventricles can rapidly reach the choroid plexus and the capillaries under the ependyma surrounding the ventricles. B. The contact surface of the capillaries inside the brain is vast (250 cm^2/g of the tissue), and it is about 5000 times larger than the surface of the capillaries inside the choroid plexus. Apart from this, the surface of the arachnoid villi and perineural sheaths of the cranial and spinal nerves are not assumed to be higher than 10 cm^2. Filtration of water from the blood to the ISF takes place at the arterial capillaries (high capillary pressure), and absorption is observed at the vessels under low hydrostatic pressure (venous capillaries, postcapillary venules). The rapid turnover of water volume between the cerebral capillaries and ISF–CSF takes place. Due to great differences between the contact surface of capillaries in brain tissue and in the choroid plexus, it should be expected that the volume of CSF–ISF is predominantly regulated inside the brain parenchyma. The differences in hydrostatic pressure inside the capillaries are shown by the intensity of the color gray. C. A scheme of the relationship between a cerebral capillary endothelial cell and the surrounding structures (pericytes, neurons, astrocyte end-feets, and basement membrane) which contribute to the blood–brain barrier function. D. The ways substances pass through the membranes of the cerebral capillaries' endothelial cells. A passive diffusion is highly expressed regarding liposoluble substances, and it is conducted under gradient of concentration. The net transport of water depends on the gradients of hydrostatic (hydrostatic capillary pressure — HPc, and hydrostatic interstitial pressure — HPi) and osmotic (osmotic capillary pressure — Opc, and osmotic interstitial pressure — Opi) pressures. The transport systems enable the entrance of more hydrophilic and larger molecules from the blood to the ISF (influx; the straight arrow at the top of the figure). There are also the transport systems which enable the return of molecules from ISF–CSF into the bloodstream (efflux; the straight arrow at the bottom of the figure). The transport of molecules with large m.w. often occurs via endosomes (the formation of the endocytic vesicles; it can also be receptor-dependent).

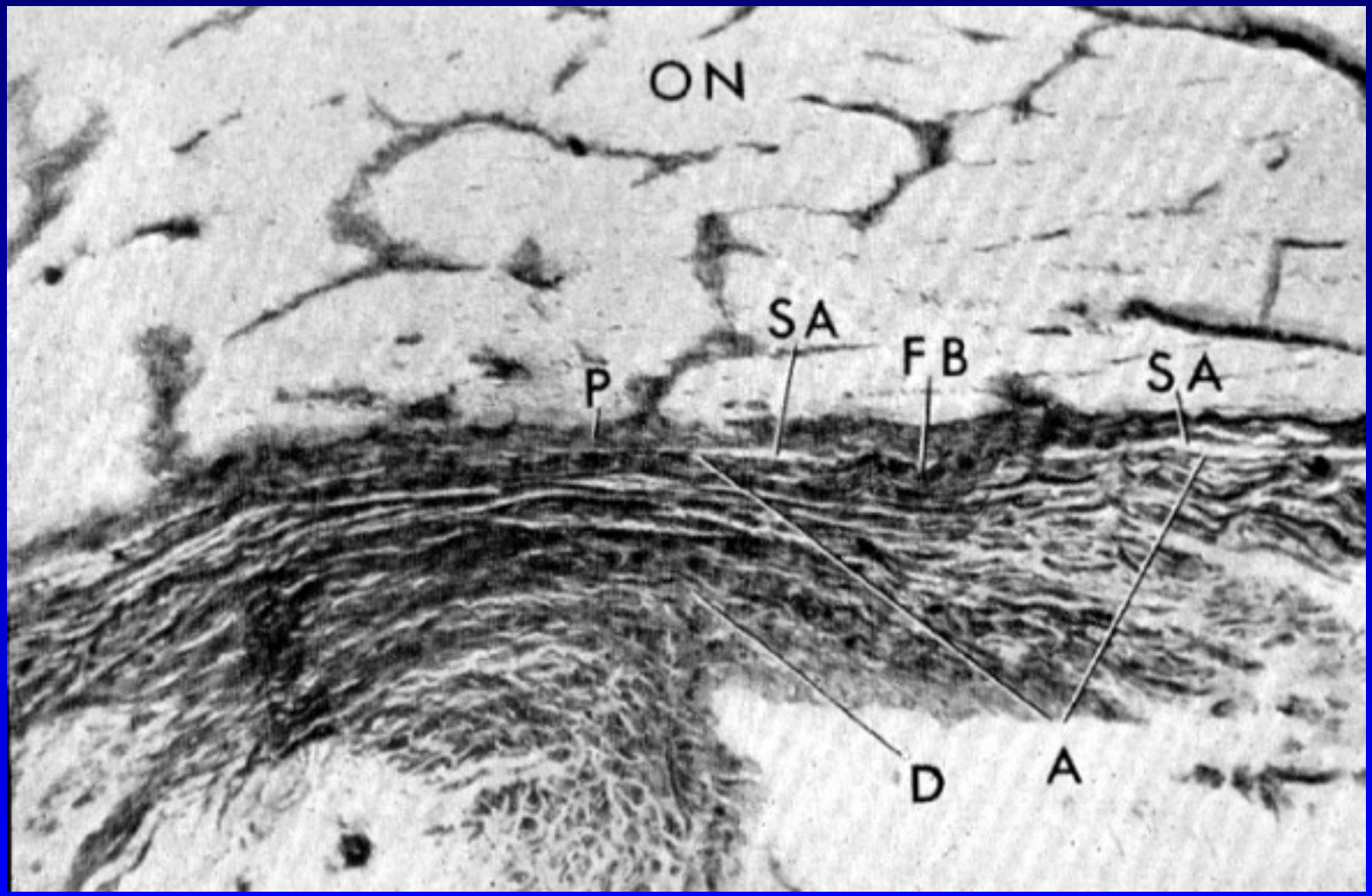
PSEUDOTUMOR CEREBRI

- UNILATERAL OR ASYMMETRIC PAPILLEDEMA
  - some patients have highly asymmetric papilledema
    - differences in the anatomy of the optic canal
  - unilateral edema is unlikely to be true papilledema (usually intraorbital process)
  - atrophic or anomalous disc may not swell

PSEUDOTUMOR CEREBRI



PSEUDOTUMOR CEREBRI



PSEUDOTUMOR CEREBRI

- Objective: To determine whether magnetic resonance (MR) imaging can be used to predict the presence of elevated intracranial pressure.
- Design: Retrospective case series.
- Participants: Twenty patients with pseudotumor cerebri and 20 control subjects.
- Intervention: Magnetic resonance imaging.
- Main Outcome Measures: The presence or absence of the following six neuroirnaging signs was measured: (1) flattening of the posterior sclera; (2) enhancement of the prelaminar optic nerve; (3) distension of the perioptic subarachnoid space; (4) intraocular protrusion of the prelaminar optic nerve; (5) vertical tortuosity of the orbital optic nerve; and (6) empty sella.
- Results: The MR imaging disclosed flattening of the posterior sclera in 80% of patients with pseudotumor cerebri, empty sella in 70%, distension of the perioptic subarachnoid space in 45%, enhancement of the prelaminar optic nerve in 50%, vertical tortuosity of the orbital optic nerve in 40%, and intraocular protrusion of the prelaminar optic nerve in 30%. Each neuroimaging sign was detected in 5% of control subjects, except for enhancement of the prelaminar optic nerve, which was not detected in control subjects. Based on these MR imaging signs, the examiner was able to predict the presence of elevated intracranial pressure in 90% of cases with pseudotumor cerebri and the absence of elevated intracranial pressure in all control subjects.
- Conclusions: Elevated intracranial pressure produces a constellation of MR imaging signs that can assist in establishing the diagnosis of pseudotumor cerebri.
  - Michael C. Brodsk-v, MD, Michael Vaphiades, DO Ophthalmology 1998;105:1686-1693

Magnetic Resonance Imaging in Pseudotumor Cerebri

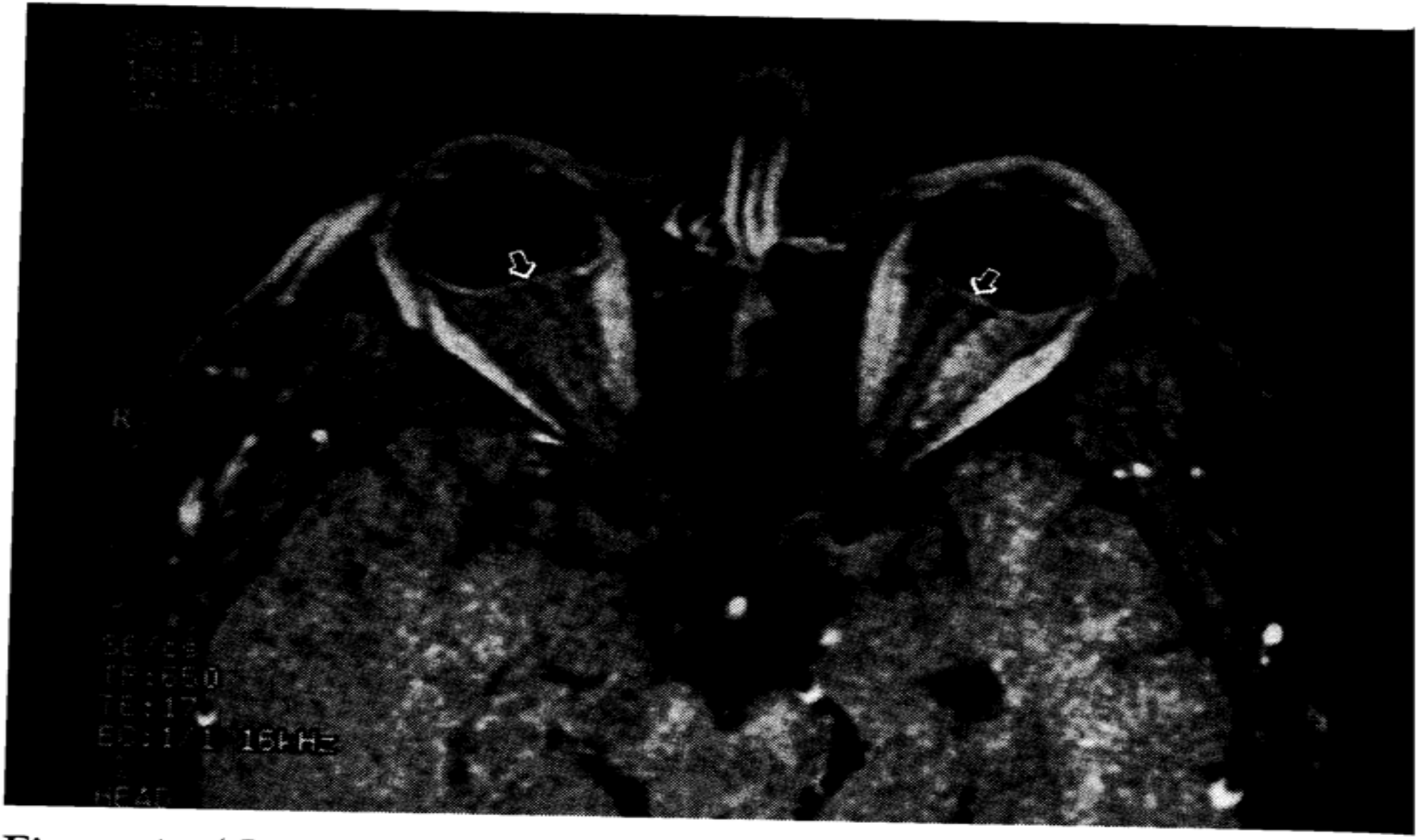
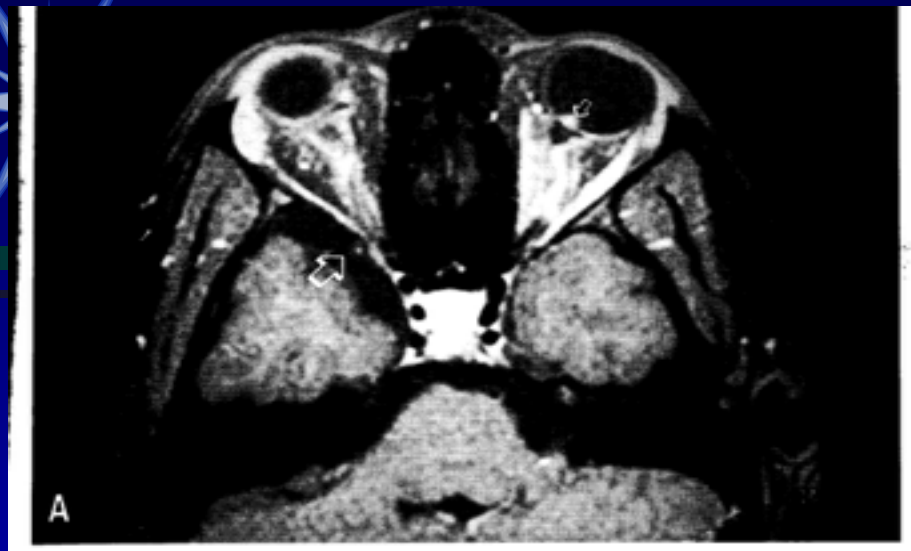
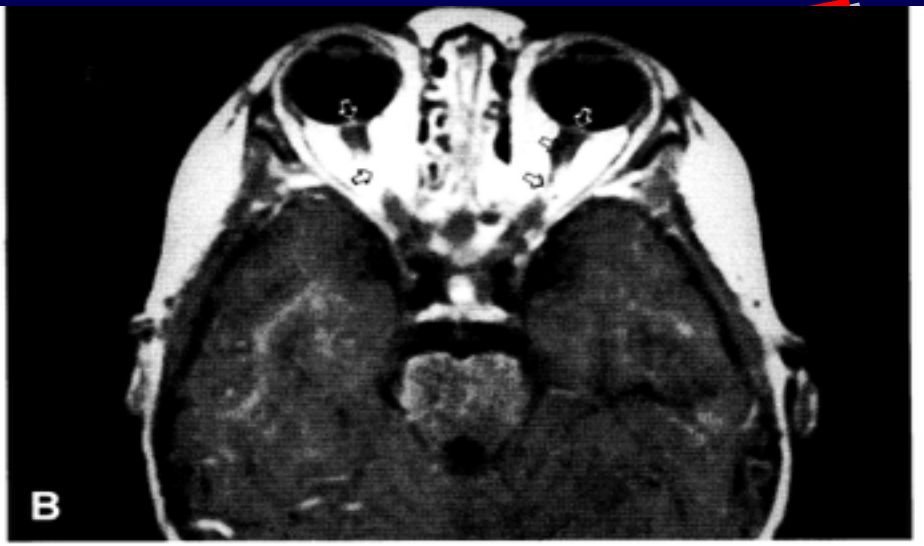


Figure 1. (Case 2) Flattening of posterior sclera. T_1-weighted axial image with fat suppression shows bilateral flattening of the posterior sclera (arrows).





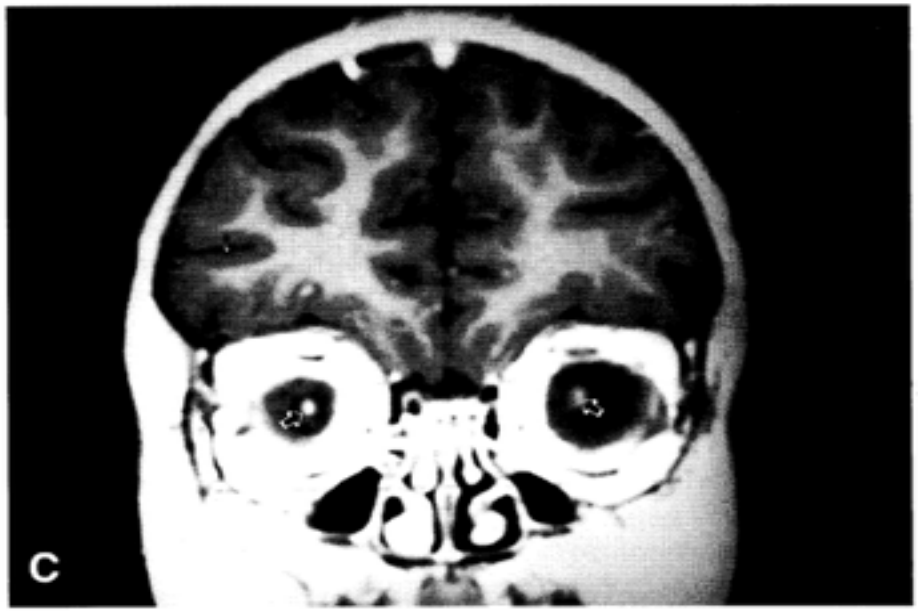


Figure 2. Enhancement of the prelaminar optic nerve. **A,** T_1-weighted axial image (case 1) with fat suppression shows maximal prelaminar enhancement in the left eye (upper arrow). There is a probable arachnoid cyst producing a hypointense signal anterior to the right temporal lobe in the middle fossa (lower arrow). **B,** T_1-weighted axial image (case 3) shows prelaminar enhancement of both optic nerves (upper arrows). Also note prominent perioptic CSF (middle arrow in left orbit) and vertical tortuosity of both optic nerves with "smear sign" (lower arrows in both orbits). **C,** T_1-weighted coronal image showing focal enhancement of the prelaminar optic nerves within the globes (arrows).

PSEUDOTUMOR CEREBRI

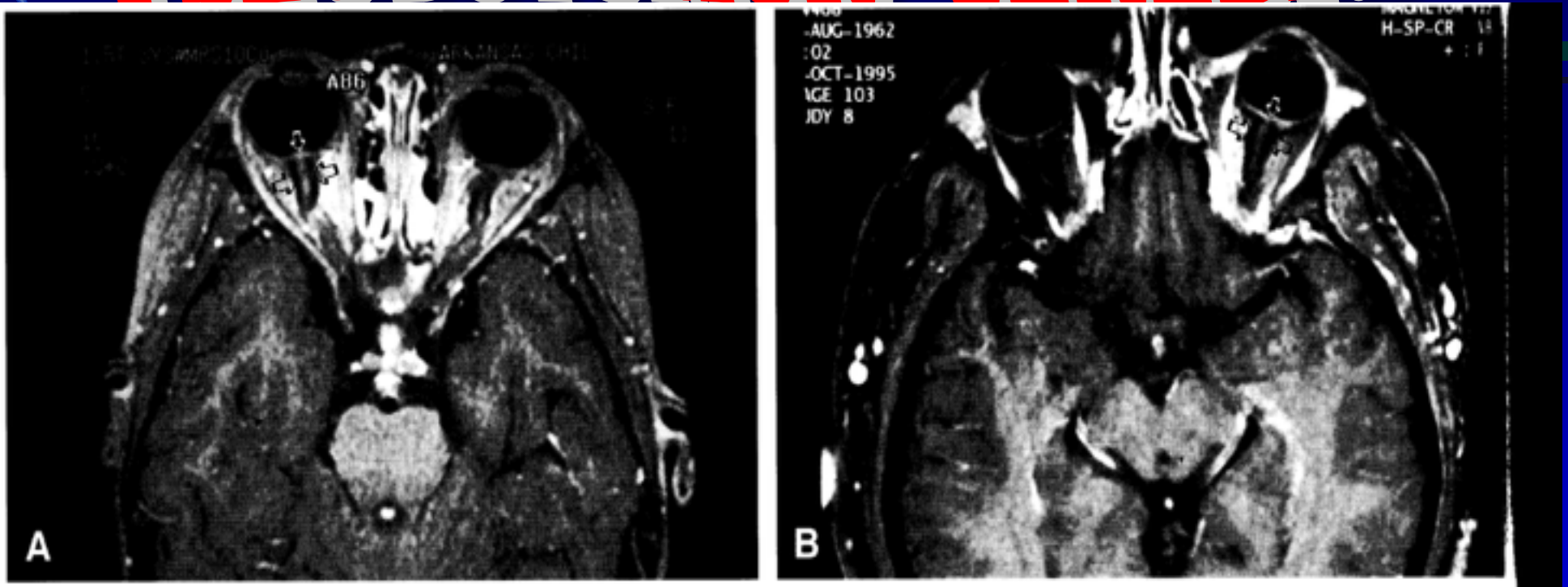
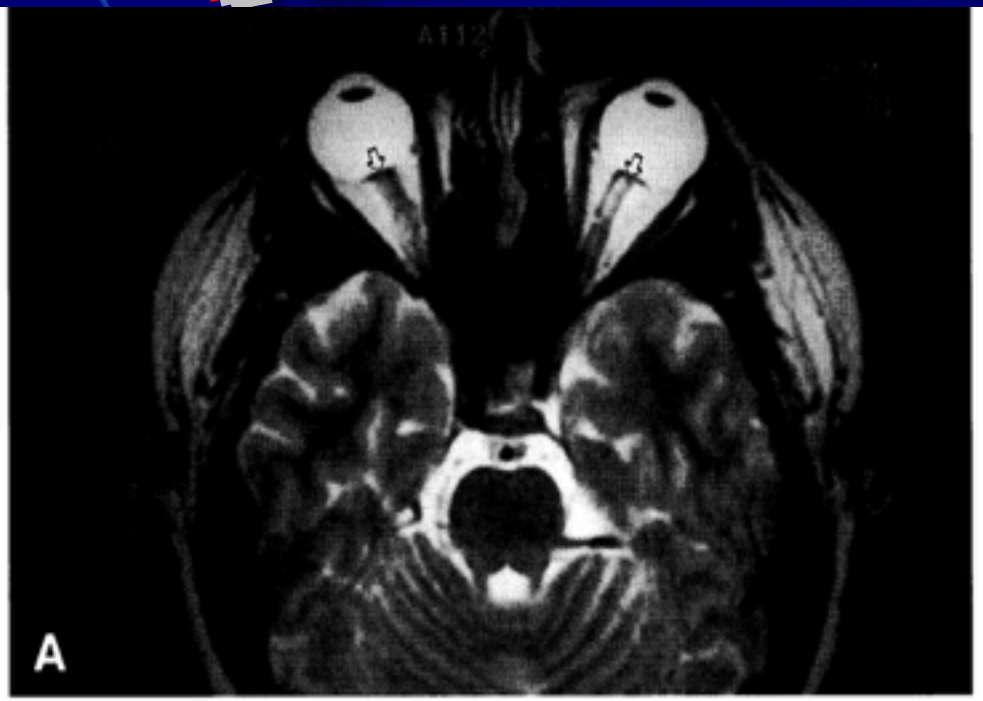


Figure 3. Distension of the perioptic subarachnoid space. **A,** Enhanced T_1-weighted images axial image (case 3) shows bilateral perioptic cerebrospinal fluid (CSF) distension (lower arrows) and vertical tortuosity of the orbital optic nerves. Upper arrow denotes focal prelaminar enhancement of the optic disc. **B,** Enhanced T_1-weighted axial image (case 4) shows flattening of left posterior sclera and widening of the left perioptic CSF signal (lower arrows), which is hypointense to the left optic nerve. The optic nerve sheath diameter also is increased. Upper arrow denotes flattening of posterior sclera.

PSEUDOTUMOR CEREBRI



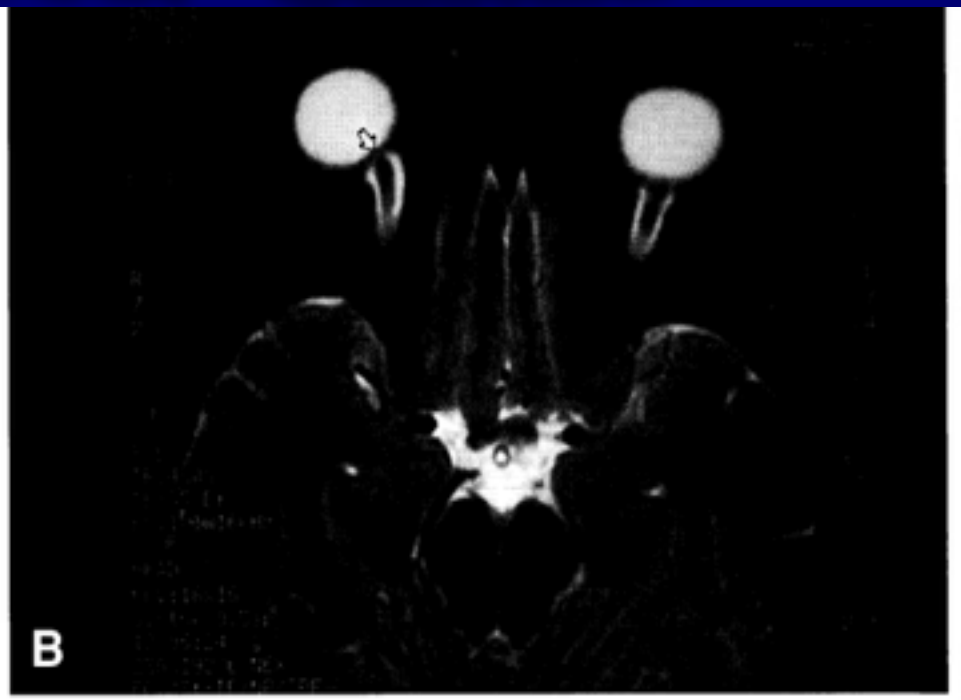
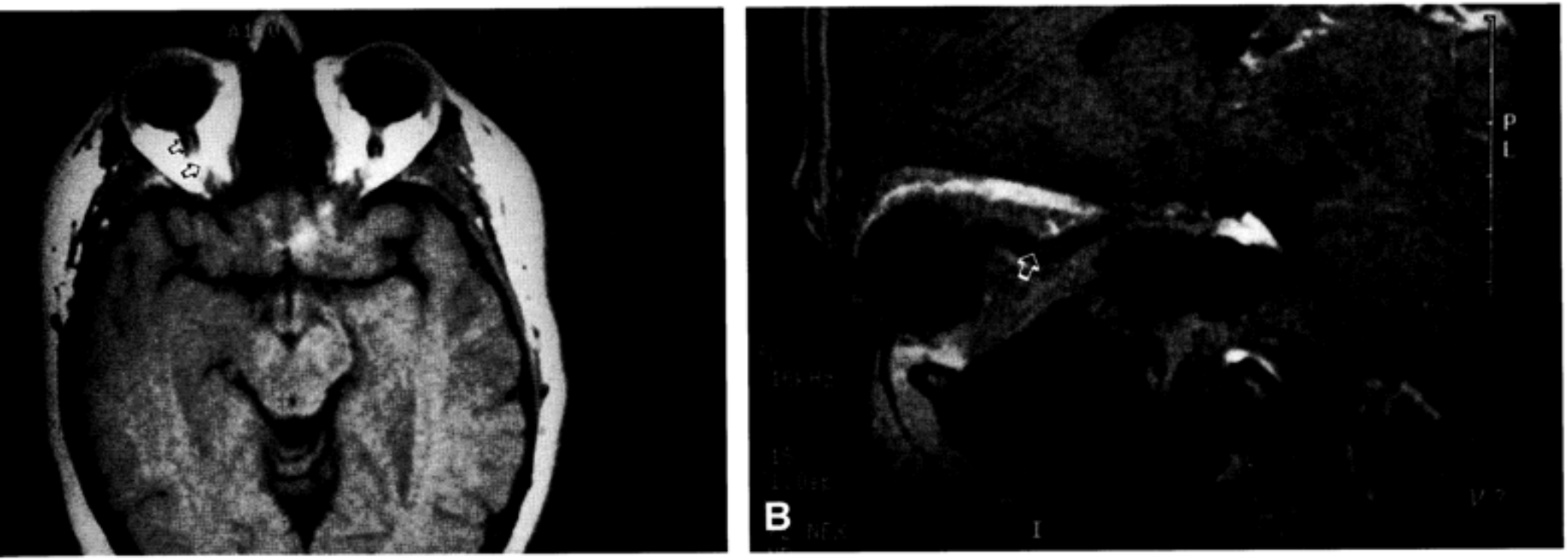


Figure 4. Intraocular protrusion of the swollen optic disc. **A,** T_2-weighted axial magnetic resonance image (case 2) shows discrete signal hypointensities protruding into the posterior vitreous cavity bilaterally (arrows), corresponding to the position of swollen optic discs. **B,** T_2-weighted fast spin-echo axial image with fat suppression (case 8) shows anterior protrusion of the swollen optic disc (arrow) and distended perioptic cerebrospinal fluid space.

PSEUDOTUMOR CEREBRI



5. Vertical tortuosity of the orbital optic nerve. **A,** T_1-weighted axial magnetic resonance (MR) image (case 6) shows vertical tortuosity with sign" (lower arrow) and distension of the perioptic subarachnoid space with "string sign" (upper arrow). This image shows no flattening of the or sclera. **B,** T_1-weighted oblique sagittal MR image with orbital fat suppression (case 8) shows vertical tortuosity, flattening of the posterior sclera, ioptic cerebrospinal fluid distension with string sign (arrow denotes optic nerve within its sheath).

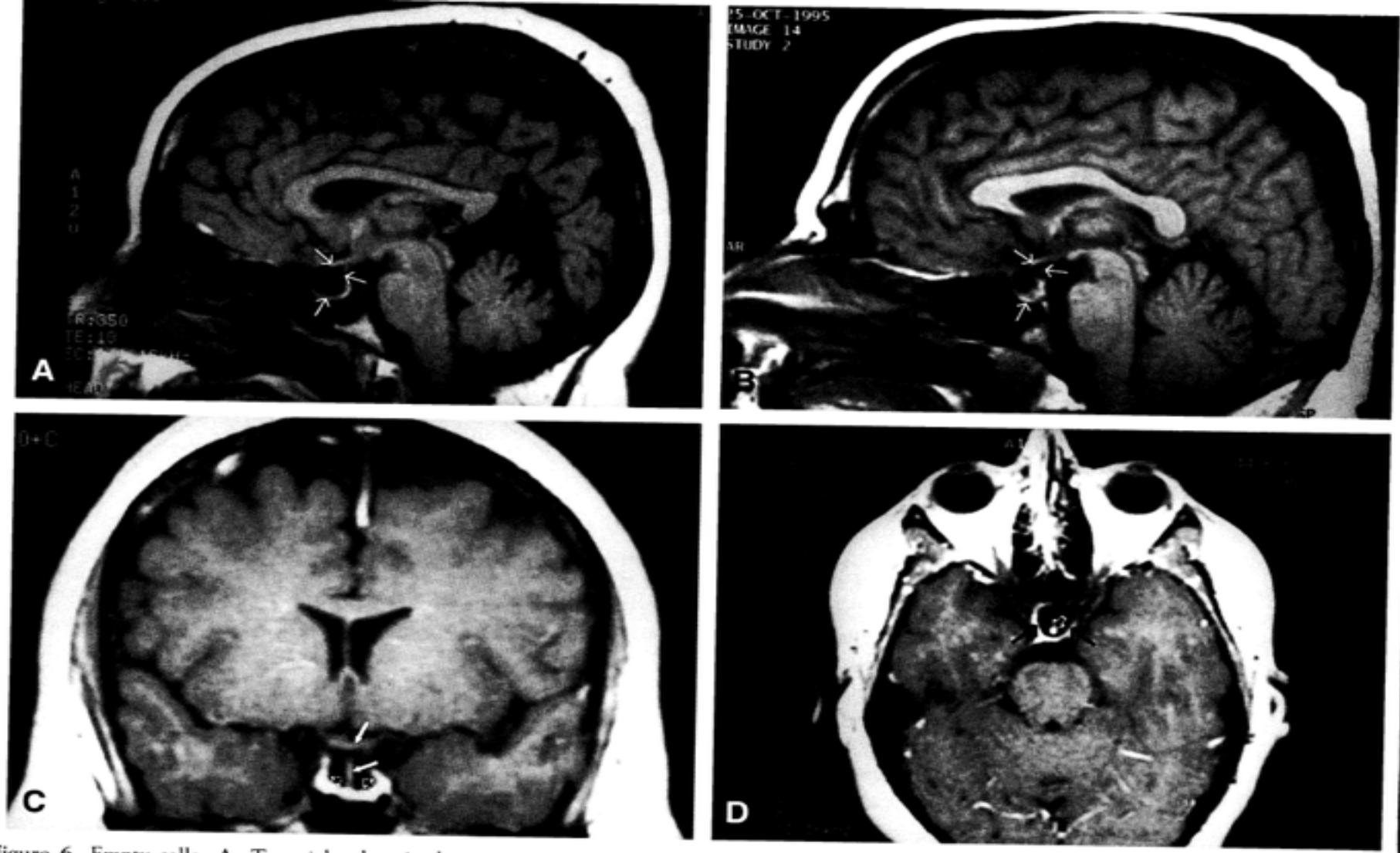


Figure 6. Empty sella. **A,** T_1-weighted sagittal magnetic resonance (MR) image (case 6) shows small inferior crescent with concave upper surface corresponding to compressed pituitary gland (lower arrow). Note posterior displacement of the posterior infundibulum (middle arrow). Upper arrow denotes optic chiasm. Note abnormally prominent extraventricular subarachnoid space that appears hypointense and lies superior to the cerebral hemispheres. **B,** T_1-weighted sagittal MR image shows a partially empty sella (case 4). Note concave upper pituitary surface and posterior displacement of the pituitary infundibulum (middle arrow). Upper arrow denotes optic chiasm, lower arrow denotes sellar floor. **C,** T_1-weighted coronal MR image (case 6) shows no visible pituitary gland within this portion of the sella. Open arrow denotes CSF-filled arachnocele, middle arrow denotes infundibulum, and upper arrow denotes optic chiasm. **D,** Enhanced T_1-weighted axial MR image (case 6) shows a hyperintense ring corresponding to the sella (open dark arrows), which contains a CSF-filled arachnocele. Intrasellar CSF appears as a discrete region of signal hypointensity surrounding a single focus of signal hyperintensity corresponding to a posteriorly displaced pituitary infundibulum (open white arrow).

PSEUDOTUMOR CEREBRI

- IS THE DISEASE CURABLE?
  - many studies have revealed persistent elevations of ICP despite therapy that reduces or eliminates papilledema

PSEUDOTUMOR CEREBRI

- MEDICAL THERAPY
  - weight loss
  - Diamox
  - Lasix
  - steroids
  - repeat LP's

PSEUDOTUMOR CEREBRI

- SURGICAL THERAPY
  - subtemporal decompression
  - LP shunts
  - VP shunts
  - ONSD

PSEUDOTUMOR CEREBRI

- Article abstract–We reviewed the efficacy of CSF diversion for pseudotumor cerebri (PTC) in patients from six different institutions. Thirty seven patients underwent a total of 73 lumboperitoneal shunts and nine ventricular shunts. Only 14 patients remained "cured" after a single surgical procedure. The average time between shunt insertion and shunt replacement was 9 months, although 64% of shunts lasted less than 6 months. Shunt failure (55%) and low–pressure headaches were the most common causes for reoperation. The vision of most patients improved (13) or stabilized (13) postoperatively. However, three who had initially improved subsequently lost vision. Six had a postoperative decrease in vision. Two patients improved in one eye but worsened postoperatively in the other. Four lost vision despite apparently adequate shunt function. Shunt failure with relapse of PTC occurred as late as 7 years after insertion. CSF diversion procedures have a significant failure rate as well as a high frequency of side effects.
  - M.L. Rosenberg. MD; J.J. Corbett, MD; C. Smith, MD; J. Goodwin, MD; R. Sergott, MD; P. Savino, MD; and N. Schatz, MD Neurology 1993;43:1071–1072
- Cerebrospinal fluid diversion procedures in pseudotumor cerebri

PSEUDOTUMOR CEREBRI

- PROBLEMS WITH SURGERY
  - LP shunts
    - low pressure HA's
    - sciatica
    - abdominal abscess
    - meningitis
      - several deaths

PSEUDOTUMOR CEREBRI

- ONSD
  - DeWecker in 1872 (blind procedure)
  - 2 approaches
    - lateral
    - medial

PSEUDOTUMOR CEREBRI

- ONSD has been used for:
  - PTC
  - papilledema
    - tumors
    - trauma
    - meningitis
    - lateral sinus thrombosis
    - craniosynostosis
  - ARN
  - ON meningioma
  - ON cysts/hygromas
  - CRVO

PSEUDOTUMOR CEREBRI

- COMPLICATIONS OF ONSD
  - intra or post op hemorrhage
  - orbital cellulitis
  - diplopia
  - irregular (tonic) pupils
  - blindness
  - doesn't lower ICP
  - papilledema can recur

PSEUDOTUMOR CEREBRI

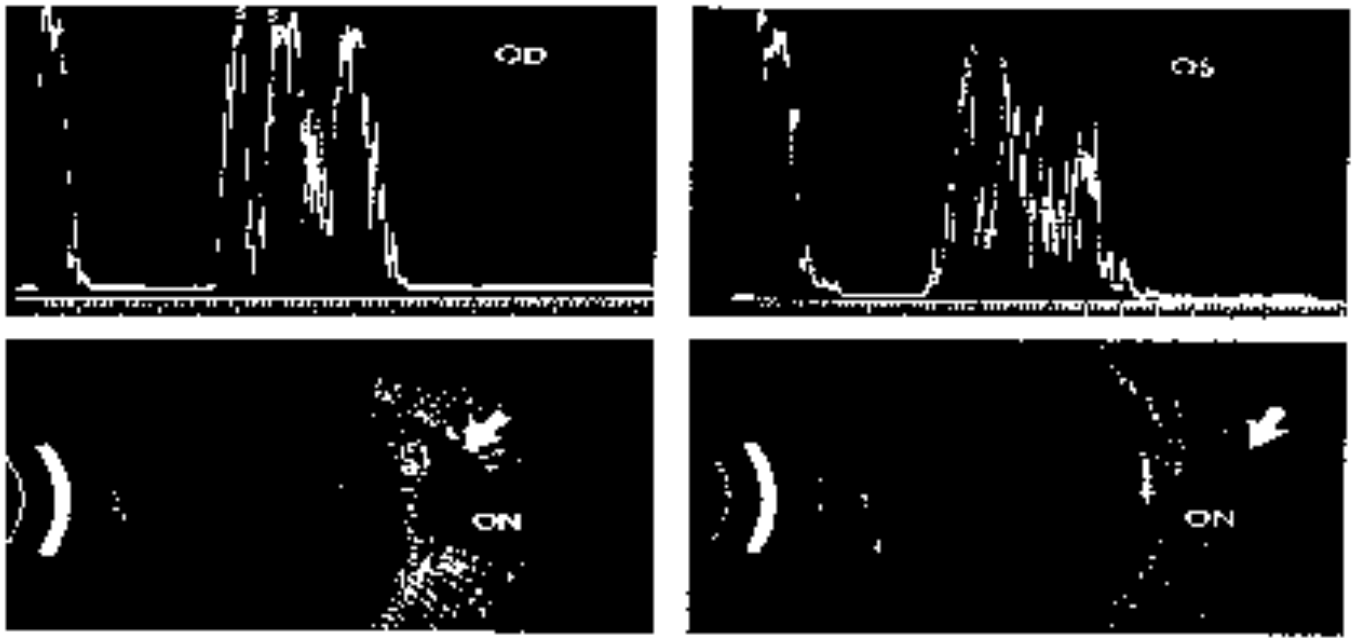
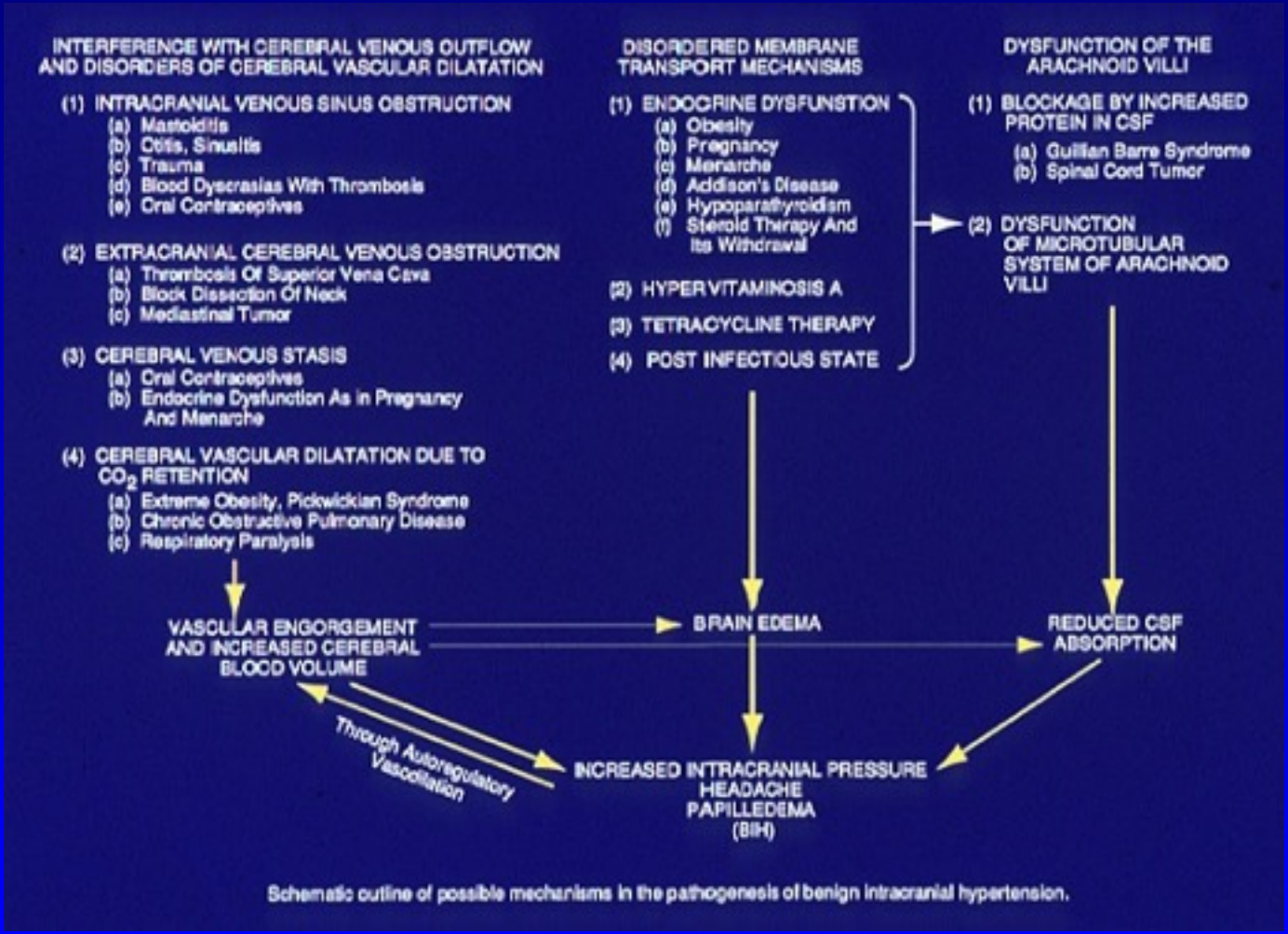


Fig 3. —Case 1. Reevaluation of optic nerves of the right eye 10 days after surgery and of the left eye 7 days after surgery. Top, A standardized A-scan echogram shows normal diameter of arachnoid sheaths (S) in primary position (2.6 mm OD and 2.4 mm OS). Bottom, Vertical B-scan echograms of the optic nerves (ON) show a fluid compartment extending from the optic nerves (arrows) in both nerves. Fluid was located anteriorly (region of fenestration).

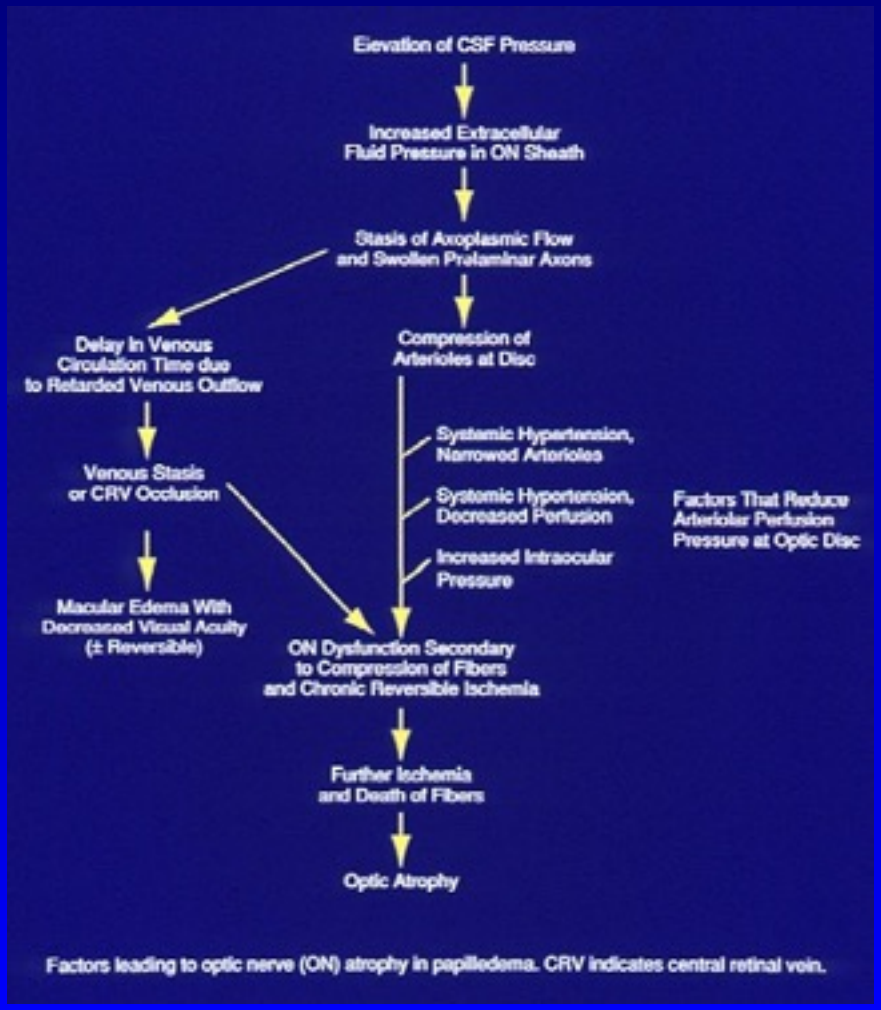
Post ONSD bleb-possible mechanism of surgical effect

PSEUDOTUMOR CEREBRI



Schematic outline of possible mechanisms in the pathogenesis of benign intracranial hypertension.

PSEUDOTUMOR CEREBRI



Factors leading to optic nerve (ON) atrophy in papilledema. CRV indicates central retinal vein.