Neuro-Ophthalmology Study Guide

High Yield Review For Ophthalmology Exams

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Ophthalmology Review

First Edition

Introduction

How To Read This Book

Hello! This is the stand-alone version of the neuro-ophthalmology section to my upcoming review book, Last Minute Ophthalmology. As I write each chapter, I plan to release them as individual review books, and compile every topic into one complete book (with a few minor differences between them, such as section introductions and descriptions). I have designed the entire book to be a last-minute reference in the preparation for taking ophthalmology examinations. As such, this not meant to be a comprehensive text on the entirety of ophthalmology.

There are various methods I envision this book will be read - as a pure reference by using the table of contents and index to find specific topics, perhaps as a part of a study plan to help review the salient points after finishing a deeper review, or as a last minute read-through right before a test. Or, perhaps there is some other application that would be more useful for your study plan. In any case, I hope that the information that is presented will be useful and not anything too similar to other review texts already available on the market.

Disclaimers and Acknowledgements

Obviously, there are far more topics beyond the scope of this book. Additionally, the information I've culled for this book is not guaranteed to show up on any test, so if you find that there is a lot of extraneous information, please let me know! Additionally, I am not reproducing test questions from any of the exams I've previously taken; it's been far too long since I've taken the OKAP, Written Qualifying Exam, and Oral Board Exam anyways that I wouldn't be able to accurately recall any of that information.

I had to make the difficult choice of leaving out direct citations within the text as well; as a review book, this just did not seem to flow very well, but while I do claim this work as entirely original (from the standpoint of how I'm writing it and presenting it), obviously the content itself is not original to me and is the organized collection of my notes from studying the many tomes of ophthalmology that we've all used to learn the subject matter. The references I list at the end of this introduction comprise the majority of the sources I used to create this outlined resource.

I ended up creating many mnemonics to help me remember differentials and other pertinent information; however, there were many mnemonics I learned from my peers, review courses, and books. Out of respect to these other individuals since I was unable to get permission to publish their mnemonics, I did not include any unoriginal mnemonics in this guide. As such, you may see specific topics that I've highlighted as sets of lists to memorize. Just because I did not include a mnemonic does not diminish the importance of the subject in any way, and perhaps it will encourage you to find your own ways to help remember the information.

How This Section Is Organized

Neuro-ophthalmology is generally very difficult to organize in some ways, because some of the topics are very diverse. In general, neuro-ophthalmologists organize neuro-ophthalmology into the context of afferent disease (that is, disorders affecting visual input), and efferent disease (disorders that affect eye movement, pupil function, etc.). There are also other categories, such as disorders of CN 5 and CN 7, that don't fit into a neat category, so they're listed as separate sections.

The book itself is formatted as an outline, with the goal of highlighting the essential details about each topic. The assumption is that this information is a review, rather than a detailed explanation of the minutiae. If you are looking for a detailed, nuanced discussion of the topics, I am always working on articles on Ophthalmology Review, or you can check out the references I've listed.

This book is one of the many resources I plan to provide through Ophthalmology Review. As such, you'll probably find that the formatting and organization of information in this book is similar to what you'll find on the website.

Happy studies!

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Sourced References and Suggested Reading

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9. Beck RW, Gal RL. Treatment of Acute Optic Neuritis: A Summary of Findings From the Optic Neuritis Treatment Trial. *Arch Ophthalmol* 2008;126(7):994-995. doi: 10.1001/archopht.126.7.994. PMID 18625951.

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Optic Neuropathies

Optic Neuropathies Presenting As Optic Nerve Swelling

Optic Nerve Swelling with Normal or Near-Normal Vision

Pseudopapilledema

Optic Disc Drusen

- Refractile, **calcified** nodules within the ON head (visible on **ultrasound** or **CT**); bilateral (80%)
- **VF loss** (75%): arcuate, enlarged blind spot, depression; field loss **may mimic glaucoma**
- **Histopathology:** basophilic deposits stains positive for **calcium** (alizarin red, von Kossa), mucopolysaccharides (Alcian blue)
- **Associations: RP**, **angioid streaks** (non-PXE), **pseudoxanthoma elasticum**

Pseudopapilledema

- Optic disc drusen
- Myelinated NFL
- Astrocytic hamartoma
- Physiologic crowding

Papilledema/Intracranial Hypertension

- Optic nerve swelling specifically in the context of **increased ICP**
- **Clinical presentation**
  - Symptoms: TVOs/↓ VA, diplopia (usu. CN VI); HA, pulsatile tinnitus
  - VA, color vision, and pupils initially normal, permanent visual loss late
  - **Acute:** hyperemia, telangiectasis, blurred margins, NFL edema/heme, cotton-wool spots, choroidal folds, **hyperopic shift**
  - **Chronic:** pale, loss of central cup, NFL gliosis, optociliary shunt vessels, refractile bodies, subretinal neovascularization
  - **VF loss like glaucoma:** enlarged blind spot, nasal step, arcuate defects, generalized peripheral depression, central loss
- **Causes: IIH**, tumor, hydrocephalus, craniosynostoses (Crouson & Apert), meningitis, demyelinating polyneuropathies, POEMS syndrome (**p**olyneuropathy, **o**rganomegaly, **e**ndocrinopathy, **m**onoclonal gammopathy, **s**kin Δs), **cerebral venous thrombosis**

Medications Associated With Pseudotumor Cerebri: "SANTA C"

- **S**teroid (withdrawal)
- **A**ccutane
- **N**alidixic acid
- **T**etracyclines (minocycline, doxycycline)
- Vitamin **A**
- **C**yclosporine

Oral contraceptives have been implicated but link to PTC is controversial

Idiopathic Intracranial Hypertension (IIH, Pseudotumor Cerebri [PTC])

- **Diagnostic criteria:** (a) signs/symptoms solely attributable to ↑ ICP; (b) ↑ ICP; (c) normal CSF composition; (d) normal neuroimaging studies; (e) no other etiology identified (diagnosis of exclusion)
- **Mandatory studies:** MRI ± MRV w/contrast; LP (lateral decubitus) w/opening pressure; CSF cytology/culture, medication history
- **Medical treatment:** weight loss, Diamox, Topamax, Lasix
- **Surgical treatment:** VP/LP shunt, ON sheath fenestration/decompression

Optic Nerve Swelling with Decreased Vision

Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION)

- **Most common acute optic neuropathy in patients > 50 yo**
- **Risk factors:** small C/D ratio ("disc at risk"), hypertension, diabetes; smoking, hyperlipidemia, hypotension, sleep apnea
  - Medications: interferon-alfa, **sildenafil**, **amiodarone** (mimics NAION)
- **Clinical presentation:** acute painless monocular visual loss, altitudinal VF defect (usually inferior), sectoral hyperemic edema
- **Clinical course:** typically stable, may worsen while edema present; fellow eye involved in ~15%
- **Management:** systemic risk factor optimization, ASA for vasculopathic risk factors, sleep study, no proven treatment

Idiopathic Intracranial Hypertension Treatment Trial (IIHTT) - 2010-2012

- **Acetazolamide** (start 250 mg BID, titrating to max tolerated or 4 g/day) **+ weight loss** vs. **placebo + weight loss** in IIH patients with **mild visual loss** (mean deviation average on 2 VFs on same day between -2 dB and -7 dB), **starting treatment at diagnosis**
  - **Definition of IIH:** modified Dandy criteria or, if ICP was 200-250 mmCSF, did not have pseudopapilledema and had either CN6 palsy, pulse-synchronous tinnitus, > grade 2 papilledema, or transverse sinus stenosis/collapse on MRI
  - **Weight loss:** telephone-based low-sodium weight loss program with **goal of losing >6% body weight within 6 months**
- **Primary outcome:** mean deviation in worse eye
- **Conclusions on visual acuity**
  - **No significant difference in visual acuity between groups** (71% of worse eyes & 77% of better eyes > 20/20 at baseline)
- **Conclusions on visual fields**
  - **Arcuate field loss was most common visual field abnormality** (inferior > superior)
  - **Improvement of mean deviation significantly greater in acetazoalmide group vs. placebo**, both had improvement
  - **"Performance failure": 25% of patients had worsening VF on one follow-up test,** but **only 17% of those patients (4% of total patients) had confirmed worsening** (2nd VF 1 hour to 4 days later) - **don't determine worsening on only one VF!**
- **Conclusions on Frisén grade**
  - **Treatment effect greater in patients with higher papilledema grade at diagnosis**
  - Initial CSF opening pressure correlated with Frisén grade (**> 35 cmCSF more commonly had Frisén grade IV or V**)
  - **Strong correlation between Frisén grade and OCT measurements** up to 6 months
- **Conclusions on OCT measurements**
  - **Initial CSF opening pressure correlated with OCT** (ONH volume, RNFL thickness, and total retinal thickness (TRT))
  - **Acetazolamide more significantly reduced OCT values** (ONH volume, RNFL thickness, and TRT) compared to placebo
- **Conclusions on CSF pressure**
  - Only 52% had a follow-up LP at 6 months
  - Of that subset, **acetazolamide had statistically significant reduction of ICP** compared to placebo
- **Conclusions on Quality of Life**
  - Most frequently reported symptom was **headache** (84%)
  - Patients with IIH have decreased quality of life unrelated to obesity and comorbid conditions
  - **Acetazolamide significantly improved quality of life** in areas of subjective cognitive dysfunction, dizziness/vertigo, and transient visual obscurations
  - **Acetazolamide did not demonstrate any benefit on headache severity** compared to placebo
- **Conclusions on the safety and tolerability of acetazolamide**
  - **Acetazolamide is safe and tolerated at doses up to 4 g/day**, acetazolamide had more side effects and abnormal lab values (↑ liver transaminases); no blood dycrasias or hypokalemia (**lab monitoring not necessary on routine basis if Diamox solo tx**)
  - **Side effects of acetazolamide did not increase with dose**, resolved after discontinuation without permanent disability
  - **Provided Level Ib evidence for the safe use of acetazolamide up to 4 g/day**

Ischemic Optic Neuropathy Decompression Trial (IONDT) - 1992-1994

- **Optic nerve sheath decompression** vs. **observation** in patients with **acute NAION** (onset of symptoms within previous 14 days), visual acuity between 20/64 and light perception, age ≥ 50 yo, no other visual condition that could affect visual acuity ≥ 3 lines
- **Definition of NAION:** 1) sudden onset of visual symptoms, 2) RAPD, 3) swollen optic disc, 4) visual field defect
- **Primary outcome:** change in ≥ 3 lines of visual acuity at 6 months
- **Conclusions on optic nerve sheath decompression for acute NAION: not effective and may be harmful**
- **Demographics:** M (62%) > F, predominantly white (95%), HTN in 47%, DM in 24%
- **Natural history of NAION:** symptoms within first 2 hours of waking (42%), **NAION in fellow eye in 14.7% over 5 years** (risk factors for worsening include DM, initial VA of ≤ 20/200 in first eye), **42.7% had improvement of ≥ 3 lines at 6 months**

Arteritic Anterior Ischemic Optic Neuropathy (AAION)/Giant Cell Arteritis (GCA)

- **Most common cause of visual loss in giant cell arteritis**
- **Clinical presentation:** acute painless severe monocular visual loss (may have amaurosis-like episodes leading up to event)
  - **Systemic symptoms:** headache (most common), jaw claudication (most specific), scalp tenderness, diplopia, malaise, anorexia, myalgia, fever, arthralgias
  - **Exam:** "pallid" disc edema (chalky white disc), non-crowded optic nerve in unaffected eye, multiple cotton-wool spots
- **Clinical course:** rarely improves, up to 95% involve fellow eye within days-weeks if no treatment; non-glaucomatous cupping
- **Histopathology: granulomatous** inflammation of the **short posterior ciliary arteries** resulting in liquefactive necrosis of ON
  - Concentric intimal hyperplasia, **diffuse loss of internal elastic lamina** (highlighted by **Verhoeff van Gieson stain**), transmural granulomatous inflammation with multinucleated giant cells (transmural scarring is a sign of previous GCA)
- **Workup:** ESR, CRP, CBC (↑ platelets); temporal artery biopsy (start steroids after labs if high suspicion prior to biopsy)
  - Skip lesions in 5%; must get ≥ 2 cm of artery for best results
- **Management:** steroids (slow taper, follow ESR/CRP), toclizumab (follow with rheumatology)

Neuroretinitis

- **Causative organisms:** ***Bartonella henselae*** **(most common)**, **post-viral**, syphilis (2° and 3°), Lyme, leptospirosis, DUSN
- **Clinical presentation:** acute monocular visual loss ± pain; color vision much worse than visual acuity
  - **Macular star:** lipid precipitate (hard exudate) in **outer plexiform layer** (Henle); typically presents days/weeks later
  - **Visual field loss:** cecocentral scotoma (most common)
  - NOT associated with multiple sclerosis
- **Clinical course:** self-limited, good visual prognosis; rarely recurs or affects other eye
  - ON swelling resolves over 6-8 weeks (normal/pale), macular exudates resolves over 6-12 months

Differential Diagnosis of Optic Nerve Edema + Macular Star

- Acute hypertensive emergency (malignant/accelerated HTN)
- Anterior ischemic optic neuropathy (NAION, less likely AAION)
- Bartonella
- Diabetes mellitus
- Diffuse unilateral subacute neuroretinitis (DUSN)
- Herpes simplex virus
- Leukemic infiltration of optic nerve
- Lyme disease
- Leptospirosis
- Pseudotumor cerebri/IIH
- Recurrent idiopathic neuroretinitis
- Salmonella
- Sarcoidosis
- Syphilis
- Tuberculosis
- Toxoplasmosis
- Toxocariasis
- Varicella

Atypical Optic Neuritis

Differential Diagnosis of Atypical Optic Neuritis

- Autoimmune
  - Sarcoidosis (ON involvement may have necrosis)
  - Lupus
  - Vasculitis
  - Chronic Relapsing Inflammatory Optic Neuritis
  - Autoimmune Retinopathy and Optic Neuropathy
- Post-vaccination
- Parainfectious and infectious
  - Coccidiomycosis
  - Cryptococcus (capsule stains with mucicarmine)
  - HIV and AIDS
  - Lyme
  - Sinus disease
  - Syphilis

Optic Neuropathies Presenting As Normal Optic Nerves

Retrobulbar Optic Neuritis

Acute Demyelinating Optic Neuritis

- Most common type of optic neuritis; **most frequent cause of optic nerve dysfunction in young adults**
- **Clinical presentation:** subacute monocular visual loss, **pain with eye movement**, photopsias, **dyschromatopsia** (worse than VA), visual field defects (diffuse loss most common), retinal vein sheathing, **normal optic nerve** (65%)
  - **Uhthoff phenomenon:** blurring/photopsias/decreased vision with ↑ body temp or exercise after previous optic neuritis
  - **Pulfrich phenomenon:** elliptical motion seen on a pendulum (demyelination decreases axonal conduction in affected eye)
  - **Lhermitte phenomenon:** shock-like sensation with neck flexion in MS
- **Clinical course:** improvement over 4-6 weeks; most have good vision but had persistent abnormalities (contrast sensitivity, color vision, visual field, etc.); steroids speed recovery but does not affect final visual outcome
- **Systemic associations: multiple sclerosis**, **neuromyelitis optica** (**anti-aquaporin-4** disease, aggressive (often bilateral) optic neuritis + transverse myelitis), anti-myelin oligodendrocyte glycoprotein (anti-MOG)
- **Management:** MRI brain with and without contrast to assess risk for developing MS, IV steroids if 1 or more lesions (can also offer to speed up recovery), neurology referral

Optic Neuritis Treatment Trial (ONTT) - 1988-2006

- **Observation** (placebo) vs. **PO prednisone** (1 mg/kg/day for 14 days) vs. **IV methylprednisolone** (250 mg Q 6 hours x 3 days) + prednisone (1 mg/kg/day for 11 days) in patients with first time, untreated, acute unilateral optic neuritis with visual symptoms ≤ 8 days
- 50% of patients with optic neuritis developed MS in 15 years
- For typical retrobulbar optic neuritis, the **only diagnostic test required is an MRI brain w/wo contrast** to stratify MS risk
  - **0 lesions:** 25% risk of MS at 5 years, 22% at 10 years
  - **≥ 1 lesion:** 72% risk of MS at 5 years, 56% at 10 years
  - **No lesions on MRI after 10 years:** 2% risk of MS by year 15
- **Recurrence of optic neuritis:** 28% at 5 years, 35% at 10 years, 50% in MS
- **Oral steroids alone dramatically increase the rate of recurrence of optic neuritis**
- **IV steroids sped up visual improvement but did not improve final visual acuity**
- **IV steroids decreased risk of MS from 36% to 16% over the next 2 years** if ≥ 2 lesions on MRI

Traumatic Optic Neuropathy

Direct Traumatic Optic Neuropathy

- Avulsion of nerve or laceration by bone fragments or other foreign bodies

Indirect Traumatic Optic Neuropathy

- Most common form of traumatic optic neuropathy
- **Pathophysiology:** shear forces on nerve/vascular supply at the tethered intracanalicular optic nerve
- **Clinical presentation: immediate** visual loss after closed head injury, RAPD with normal DFE (optic atrophy after 4-8 weeks)
- **Clinical course:** poor prognosis; spontaneous recovery of visual function possible
- **Management:** observation, may consider surgical decompression; IV steroids not proven to help (may worsen mortality)