Anterior ischemic optic neuropathy

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UNIVERSITY OF ZAGREB
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Anterior Ischemic Optic Neuropathy

GRADUATE THESIS

Zagreb, 2016.

This graduate thesis was made at the department of Neuro-ophthalmology of KBC Retro, mentored by Prof. Dr. sc. Branimir Cerovski and was submitted for evaluation in the academic year 2015 / 2016.

Abbreviations:

AAION: arteritic anterior ischemic optic neuropathy

AION: anterior ischemic optic neuropathy

CRP: C reactive protein

ESR: erythrocyte sedimentation rate

GCA: giant cell arteritis

IOP: intraocular pressure

IV: intra vascular

NAION: non-arteritic anterior ischemic optic neuropathy

OCT: Optic Coherence Tomography

ON: optic neuropathy

PDE5: phophodiesterase type 5

SAS: sleep apnea syndrome

SPCA: short posterior ciliary arteries

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Summary:

Anterior ischemic optic neuropathy- Laurent Martini

AION is a condition that involves the impairment or complete loss of vision due to damage to the optic nerve from insufficient blood supply. By definition, AION involves the first 1mm segment of the optic disc, the optic head. It is very important because it constitutes one of the major causes of blindness or seriously impaired vision among the middle-aged and elderly population, although no age is spared. AION is divided into two main categories according to its etiologies: NAION and AAION. The presentation at clinical examination of the two types of AION is similar, but differences exist. The biomicroscopic exam shows the color, size of cup (cup-to-disc ratio), sharpness of edge, swelling, hemorrhages, notching in the optic disc and any other pathological abnormalities. In the case of AION the optic disc is swollen and pale. Since this presentation is not specific to this condition, further examination methods have to be used like a perimeter to test the visual field of the patient. AAION occurs in aproximately 20% of patients with GCA and constitutes 5 to 10% of all AION.The pathophysiology of NAION remains unknown but several risk factors and conditions have been shown to increase its incidense. NAION is the most frequent kind of AION and no treatment has been proven really effective until now, while AAION is managed with corticosteroids.

Key words: ophthalmology, optic neuropathy, giant cell arteritis

1. Introduction

ON refers to damage to the optic nerve, it is one of the major causes of blindness among the middle-aged and elderly population, but it can affect people of any age. Damage and loss of neurons lead to the characteristic features of ON. Loss of vision is the main symptom, with colors fainting in the affected eye. On medical examination with an ophthalmoscope, the head of the optic nerve can be visualized, a pale disc is characteristic of long-standing optic neuropathy. Most commonly only one eye is affected and it may be unnoticed by patients until they are asked to cover the healthy eye during the medical examination.



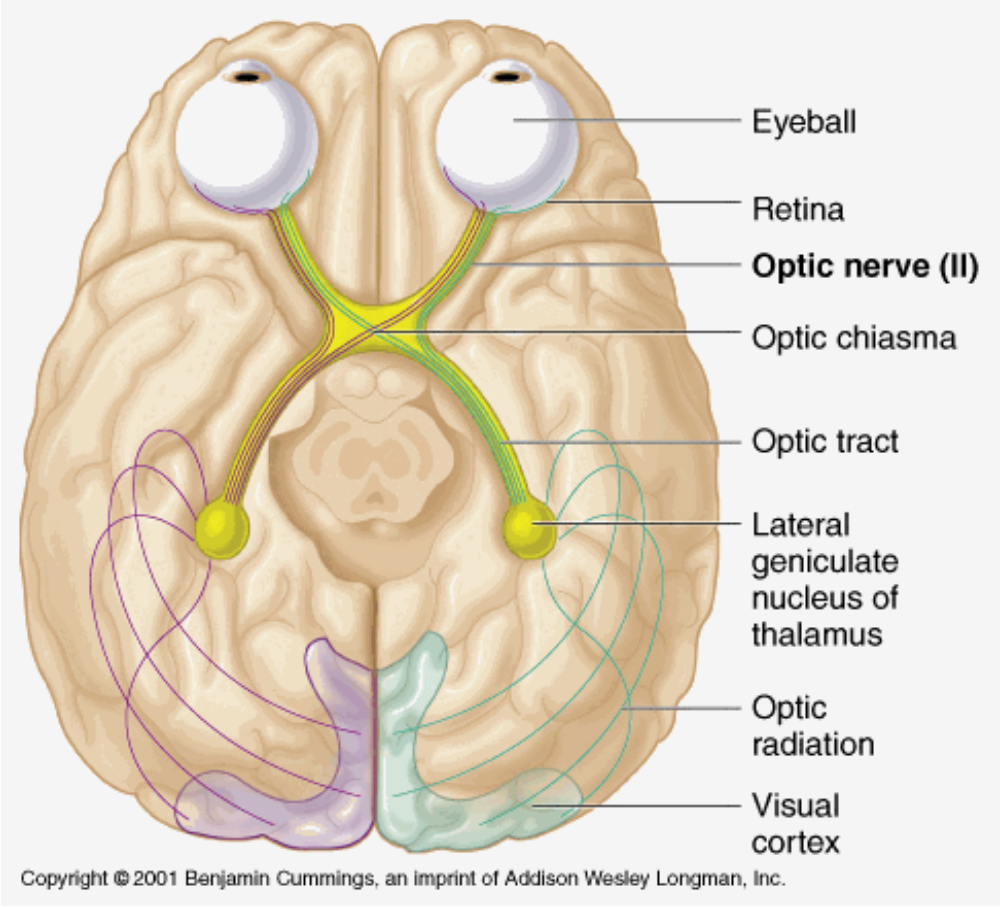
Examination of an eye with an ophthalmoscope

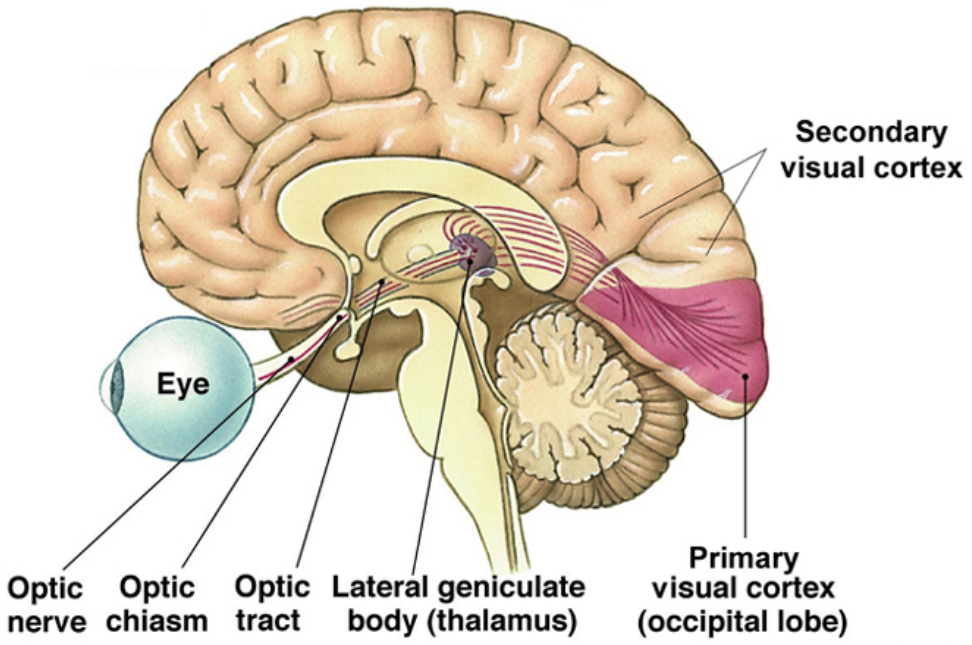
ON is the end result of any disease that damages nerve cells anywhere between the retinal ganglion cells and the lateral geniculate body (anterior visual system).

It is classified as **anterior** (optic nerve head) and **posterior** according to the blood supply of the optic nerve.

The subject of this thesis being AION, we will not talk about the posterior optic neuropathies.

1.1. Anatomy of the Optic Tract:





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Figure 10-29

The optic nerve is the second pair of cranial nerves. It contains axons that exit from the retina, leave the eye at the optic disc and go to the visual cortex where inputs from the eye are processed into vision. There are 1.2 million optic nerve fibers.

AION is a disorder that involves impairment or loss of vision due to damage to the optic nerve from insufficient blood supply. By definition, **AION involves the 1mm segment of the optic nerve head, (the optic disc), and results in visible disc swelling**.

AION is divided into two types: AAION, and NAION, the later being much more frequent. Ischemia of the optic nerve can occur in different anatomical locations and can have many etiologies. It is useful to classify these

syndromes according to their location and etiology since their presenting signs and symptoms as well as treatment and prognosis will depend on that.

The distinction between AAION and NAION was made to highlight the different etiologies of anterior ischemic optic neuropathy. NAION results from the coincidence of cardiovascular risk factors in a patient with "crowded" optic discs. NAION is more common than AAION and usually occurs in a slightly younger group. While only a few cases of NAION result in near total loss of vision, most cases of AAION involve nearly complete vision loss. (1)

In contrast, AAION, is due to giant cell arteritis, an inflammatory disease of medium-sized blood vessels that occurs more often in late middle-aged and elderly people. (2)

Overview table comparing AAION and NAAION (3)

Feature	Arteritic AION	Nonarteritic AION
Age (mean years)	70	60
Sex ratio	Female > male	Male = female
Associated symptoms	Headache, scalp tenderness, jaw claudication	Pain occasionally noted
Visual acuity	Up to 76% < 20/200 (6/60)	Up to 61% > 20/200 (6/60)
Disc	Pale > hyperemic edema Cup normal	Hyperemic > pale edema Cup small
Mean erythrocyte sedimentation rate (mm/hour)	70	20–40
Fluorescein angiogram	Disc and choroid filling delay	Disc filling delay
Natural history	Improvement rare Fellow eye in up to 95%	Improvement in up to 43% Fellow eye in < 30%
Treatment	Corticosteroids	None proved

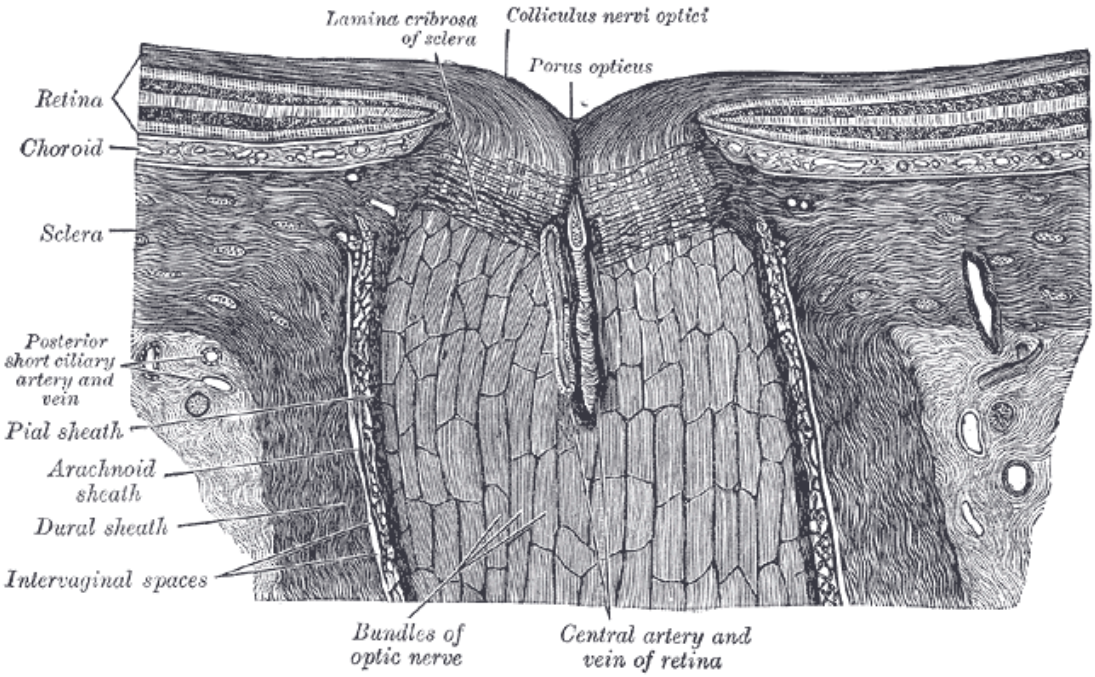
1.2. The optic disc

The **optic disc** (**optic nerve head**) is the place of exit for axons leaving the eye. It corresponds to a small **physiological blind spot** in each eye because there are no rods or cones overlying it.

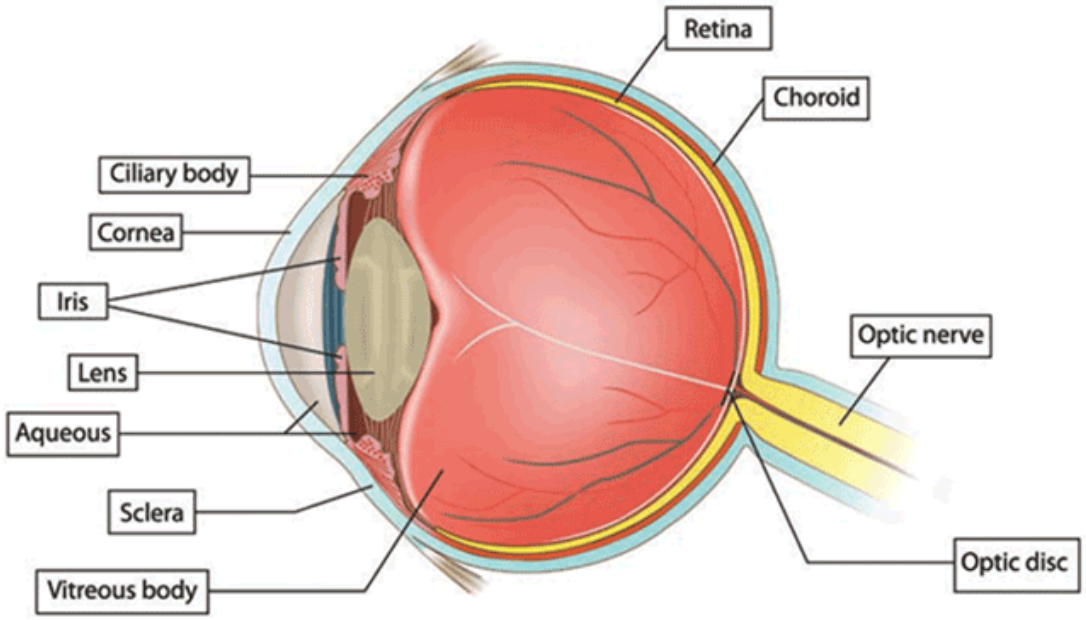
The optic disc is also the entry point for the major blood vessels that supply the retina.

Anatomy:

The **optic disc** is placed 3 to 4 mm to the nasal side of the fovea. It is a vertical oval, with average dimensions of 1.7mm horizontally by 1.9mm vertically. There is a central depression, of variable size, called the **optic cup**.



The terminal portion of the optic nerve and its entrance into the eyeball, in horizontal section.(4)



Schematic diagram of the human eye, with the optic disc, or blind spot, at the bottom.(5)

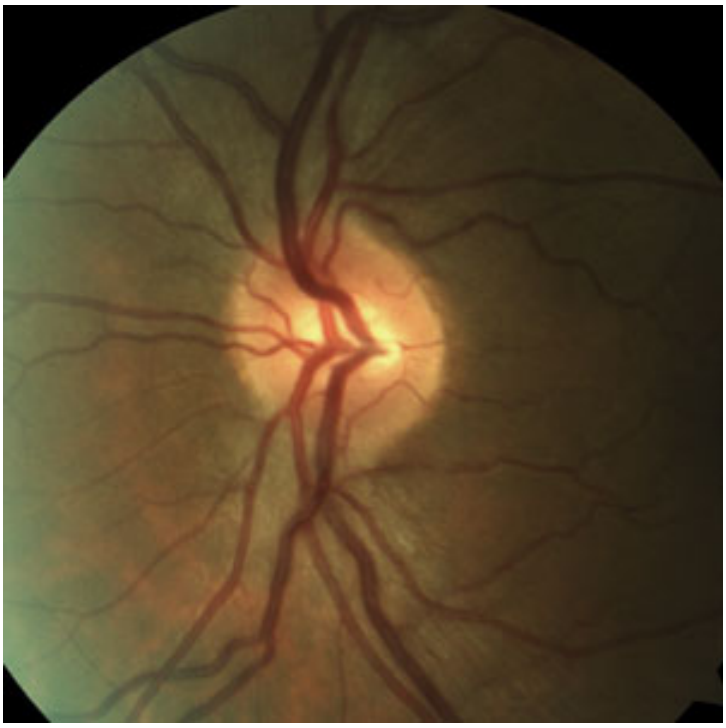
Clinical examination

The eye is unique because of the transparency of its media. Almost all eye structures can be examined with appropriate optical equipment and lenses because of their transparency. With a direct ophthalmoscope we can visualize the optic disc using the principle of reversibility of light. A slit lamp biomicroscopic examination and an appropriate aspheric focusing lens are required for a detailed stereoscopic view of the optic disc.

The health of the optic nerve is given by a biomicroscopic exam. The ophthalmologist notes the color, size of cup (cup-to-disc ratio), sharpness of edge, swelling, hemorrhages, notching in the optic disc and any other pathological abnormalities. It is useful for finding evidence corroborating the diagnosis of anterior optic neuropathy, glaucoma, optic neuritis, papilledema and optic disc drusen.

A normal healthy optic disc is pink or orange. A **pale disc** is an indication of a pathological condition, including anterior ischemic optic neuropathy. (6)

1.3. Imaging of the optic disc

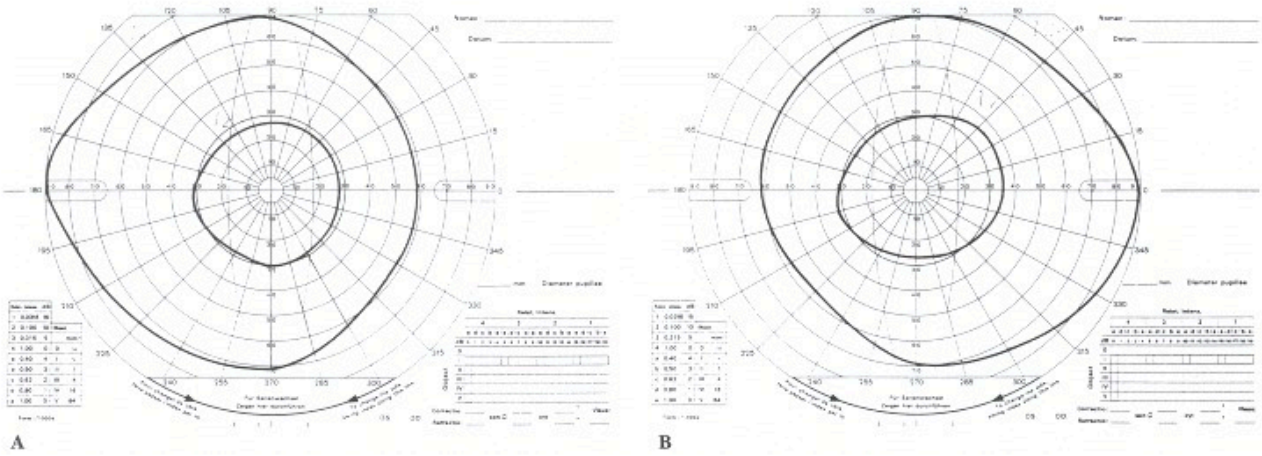


Optic disc showing microvasculature. (7)

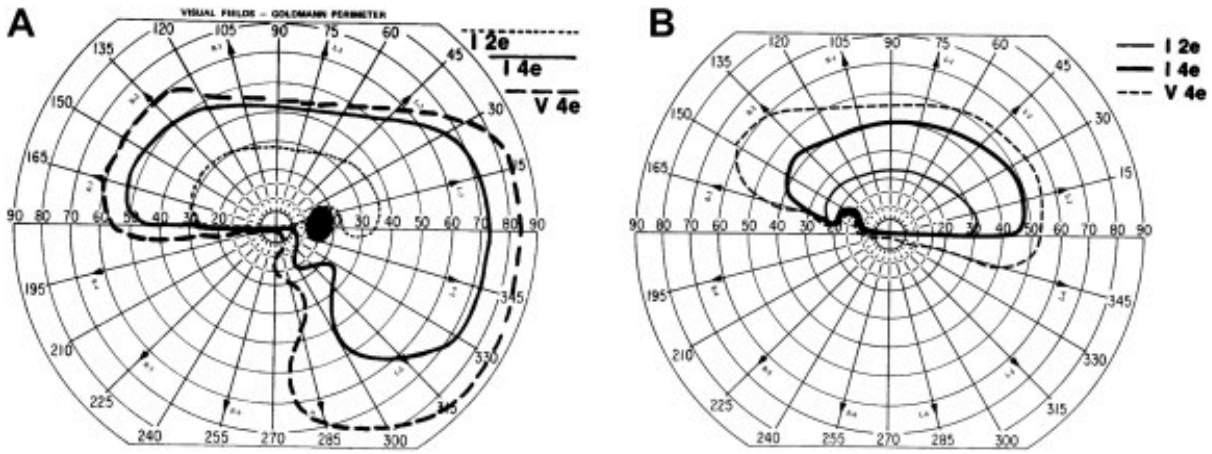
Stereoscopic images are an excellent investigative tool for close follow-up of suspected pathological changes in the eye for an ophthalmologist.

Automated techniques have also been developed to allow more efficient and less expensive imaging. They are useful to monitor any changes in optic disc morphology and appearance. However imaging will not provide conclusive evidence for clinical diagnosis. In order to establish a solid diagnosis other medical tests need to be made to prove the presence of functional changes. Such tests include visual field charting with a perimeter. Final clinical interpretation of the complete eye examination by an eye care physician. (8)

Perimeter results:



Normal visual field. (9)



Visual field defects in a NAION

2. Non arteritic anterior ischemic optic neuropathy

NAION is an isolated white-matter stroke of the optic nerve. NAION is the most common cause of sudden optic nerve-related vision loss, often bilaterally. No clinically effective treatments exist mainly because its pathophysiology remains unknown and there are not enough histopathological studies of this condition. (10)

2.1. Etiology and Risk Factors

Most cases of NAION are idiopathic but NAION has been found in patients suffering from some other conditions although no causal relationship has been proved. They are considered to be risk factors; evidence indicates that **NAION is multifactorial** in nature.

Predisposing risk factors make a person susceptible to develop NAION but do not necessarily produce NAION on their own. These may be *systemic* or *local* in the eye and/or optic nerve head. We can distinguish two categories of risk factors.

a) Systemic risk factors: (11)

- arterial hypertension, nocturnal arterial hypotension,
- diabetes mellitus,
- ischemic heart disease,
- hyperlipidemia,
- atherosclerosis and arteriosclerosis,

- SAS

  It is unclear how SAS can cause NAION but it is hypothesized that apneic spells might result in acute increases in blood pressure, intracranial pressure or nocturnal hypoxemia which could cause optic nerve edema and ischemia.

- arterial hypotension due to a variety of causes,
- malignant arterial hypertension,
- migraine.
- medications

  Sildenafil is a treatment for erectile dysfunction by inhibiting PDE5, an enzyme that regulates blood flow in the penis. At therapeutic doses this medication can cause systemic hypotension. It has been hypothesized that it might exaggerate the physiologic nocturnal hypotension resulting in ischemia to the optic nerve head and compartment syndrome in susceptible patients with small cup to disk ratios. Moreover, it might interfere with the autoregulation of blood flow thereby decreasing perfusion to the optic nerve head. This association remains very controversial.

b) Ocular and optic nerve head risk factors**:**

A significant association of NAION has been seen with a number of ocular and optic nerve head conditions. These include (11)

- small cup in the optic disc,

- angle closure glaucoma or other causes of markedly raised IOP,
- marked optic disc edema due to any cause,
- location of the watershed zone of the posterior ciliary arteries in relation to the optic disc,
- optic disc drusen

  Optic disc drusen might increase the risk of developing NAION by theoretically contributing to the “crowded” optic nerve in discs with small cup to disc ratios. There are anecdotal reports of NAION occurring in patients with optic disc drusen but a causal relationship has not been proved.

- cataract extraction.
- Defective autoregulation of the optic nerve head

2.2. Pathophysiology

The pathophysiology of NAION is still unknown and no mechanism has been definitively accepted. It is supposed to be the consequence of a circulatory insufficiency or infarct within the retrolaminar portion of the optic nerve head that is supplied by the SPCA. Additional fluorescein and indocyanine studies have shown delayed optic disc filling in the prelaminar layers of the optic disc with normal choroidal circulation suggesting that the vasculopathy is located in the para-optic branches of the SPCA after their branching from the choroidal branches rather than in the short ciliary arteries themselves. (12)

The cause of the edema of the optic disc is unclear but it is thought that the final common pathway leads to a compartment syndrome from axonal edema in a structurally crowded optic disc resulting in apoptosis of the retinal ganglion cell. (13)

a) A. Optic Disc Anatomy

Around 97% of patients with NAION have small optic discs with small optic cups. Acutely, it can be difficult to determine the cup/disc ratio because of optic nerve edema and the clinician should note the cup/disc ratio in the other eye. It is typically less than 0.3mm and these discs are referred to as a “disc at risk”. The role of the small cup/disc ratio is unclear but there are probably contributory mechanical effects of the small cup/disc ratio in the pathogenesis of NAION. A crowded disc can exacerbate chronic mechanical obstruction to axoplasmic flow resulting in secondary compression and ischemia. An inhibition in axoplasmic flow can inhibit critical neurotrophins leading to additional ganglion cell death. (14)

b) Autoregulation

The optic nerve head efficiently autoregulates blood flow (15). Flow is normally maintained constant despite variations in perfusion pressure and intraocular pressure under various metabolic conditions and different diseases can impair the optic nerve’s ability to autoregulate its blood flow. Systemic hypertension, arteriosclerosis, vasospasm or medications may reduce the autoregulatory capacity of the optic disc. Vasoactive substances might be

released in. Dr Hayreh has said that the release of endogenous serotonin may contribute to optic nerve ischemia by vasoconstricting arterioles and impairing autoregulation. (16)

c) Nocturnal hypotension

During the night the blood pressure fluctuates and this nocturnal systemic hypotension may be a factor to NAION. Patients who have a chronically altered optic disc autoregulation, from either systemic hypertension and / or atherosclerosis are susceptible to exaggerated decreases in nocturnal blood pressure. This effect might be exacerbated when patients are treated with strong antihypertensive drugs if they take them before going to bed. (17)

d) Venous Insufficiency

NAION might result from venous insufficiency that occurs from closure of tributary venules receiving blood from optic nerve capillaries that drain into the central retinal vein posterior to the optic nerve head (18). This hypothesis comes from the fact that NAION does not have the clinical characteristics of an arterial disease. AAION causes a pallid edema that ultimately resolves leaving significant excavation and atrophy of the disc whereas NAION typically exhibits normal or hyperemic edema that resolves leaving relatively preserved disc substance (19). Disc hemorrhages are seen less commonly in AAION and central retinal artery occlusion but are more common in NAION and central retinal vein occlusion. NAION causes less severe vision loss than AAION. Furthermore, the choroidal circulation is typically affected in AAION due to SPCA occlusion (and sometimes ophthalmic artery) and occlusion of

this artery in the monkey results in choroidal circulation changes (20). The infarct in NAION does not fit the vascular bed of any known artery and fluorescein angiography shows normal choroidal filling and slightly delayed arterial filling of the prelaminar disc.

e) Vasculopathic Risk Factors

NAION is presumed to result from vascular insufficiency but there is no clear association of well-known risk factors for ischemic small vessel disease and NAION. Lipohyalinosis is suspected in the pathogenesis of NAION but no histopathologic confirmation has been demonstrated. Smoking does not seem to be an independent risk factor. (21)

2.3. Symptoms and diagnosis

The typical symptoms of NAION present suddenly and upon awakening. The patient sees poorly in one eye. Vision in that eye is diminished by a dark shadow, usually involving the upper or lower half of the vision field and the area towards the midline, and no pain. Visual acuity improves by at least 3 lines of vision on the Snellen chart in approximately half of the patients in a period of six months. The involvement of the second eye occurs in 15% to 20% of patients within 5 years. Fortunately it may not be devastating as the visual acuity may remain only slightly diminished. Furthermore, in most cases NAION involve the loss of a hemifield, upper or lower half of the visual field. Only a few patients with NAION suffer from an almost total loss of vision. (22)

Since arteritic AION and NAION have an extremely similar presentation, patients over the age of 50 diagnosed with NAION must always be evaluated to exclude AAION (symptoms: painful jaw muscles, tenderness of scalp, weight loss, fatigue, loss of appetite and myalgia, discussed in detail later).

a) Symptoms

The typical description of patients with NAION during acute and painless unilateral vision loss that is often described is a blurring of vision, often inferiorly. The majority of patients do not have accompanying pain, headache or periocular pain is encountered in approximately 10% of patients, which make it difficult to differentiate from ON. Patients with NAION complain of the loss of vision occurring over a few hours, sometimes days. Almost 65% of patients report vision loss upon awakening, which suggests that nocturnal arterial hypotension may be critically involved in the pathophysiology of NAION. (23)

b) Diagnosis

Patients presenting with NAION will typically have several symptoms and signs of an ON including diminished visual acuity, a swollen optic nerve with splinter hemorrhages, dyschromatopsia and a visual field defect. Patients who report the classic history of acute, painless, unilateral vision loss and who have the typical findings on examination of a swollen and hyperemic optic nerve with peripapillary splinter hemorrhages and a small cup to disc ratio, the clinical diagnosis is easily made and no further tests are needed.

1. Visual Acuity

Visual acuity varies widely but no light perception is extremely rare and when it happens, it should make the ophthalmologist suspects AAION. (23)

2. Color Vision

Dyschromatopsia, acquired loss of color vision, is a sign of optic nerve malfunction, also very sensitive. The degree of dyschromatopsia in NAION is proportional to the visual acuity loss, unlike with optic neuritis. However, altitudinal and quadrantic defects are commonly seen in NAION and in these cases color vision is often preserved likely due to sparing of the central fibers involved in the central vision. (24)

3. Pupils

Despite the loss of vision in one eye, the pupils are symmetric and round. There is no anisocoria. A relative afferent pupillary defect will be present as long as the contralateral eye is normal.

4. Visual Fields

Any defect of the visual field in relation to optic nerve damage can occur. Almost one patient over four will have central scotomas but the most of them will have an altitudinal field loss, most commonly at the inferior portion. (25)

5. Optic disc and retinal appearance

The edema of optic disc is always present during the acute phase of NAION and it comes in two different varieties, which are diffuse or segmental.

Segmental (usually altitudinal) is the most frequent but it does not always correspond to the area of visual field loss. The edema is always hyperemic and rarely pallid. Pallid edema is more common in AAION so it should alert the physician to the probability of GCA, as we will see later in the second part of the thesis. Peripapillary splinter hemorrhages are seen in almost 75% of patients and it can sometimes be used to help differentiating NAION from optic neuritis since they will only be present in 10% of patients with optic neuritis. Retinal exudates are uncommon but hard and soft exudates have been reported in up to 5% of patients. (26)

2.4. Causes and risk factors

The pathophysiology of NAION is controversial however most cases involve two main risk factors. The first risk factor is a predisposition of certain optic discs because of their shape and size. The optic nerve goes through the back of the eye and the opening to allow this is 30% larger than the diameter of the nerve. In certain patients the optic nerve is almost as big as the hole in the back of the eye, and as a result the optic disc appears "crowded" when observed by ophthalmoscopy. A crowded disc represents a disc at risk. Even though this represents a risk factor, the large majority of individuals will never experience NAION.

The second important risk factor involves general cardiovascular risk factors. The major ones are high cholesterol levels, diabetes and hypertension. These

conditions predispose a patient to develop NAION, but the most important precipitating factor is a dramatic fall of blood pressure during the night (nocturnal arterial hypotension), this is the reason why the vast majority of patients discover visual loss on waking from sleep. These vascular risk factors predispose to ischemia to the optic disc. As a consequence the disc then swells and this leads to compression and increases ischemia. (27)

Since the shape of both eyes tend to be similar, the clinician needs to look at the healthy eye to assess the anatomical predisposition. The unaffected eye has a 16% risk of NAION within five years.

2.5. Treatment

Once NAION happens, if patients are treated with corticosteroids in large doses during the early stage there is visual acuity improvement in almost three quarters of them. According to Dr. **Sohan Singh Hayreh, from Iowa in his article "Anterior Optic Neuropathy, part II a discution for physicians"** **"***The sooner the treatment is started, the better are the chances of visual improvement. That may be because the shorter the duration of axonal ischemia, the fewer axons are likely to be damaged permanently(...)I have found that the most effective way to use corticosteroid therapy is to hit hard at the beginning and then taper down. The major flaw in the way corticosteroid therapy has been given for NAION in some studies is "too small a dose, for*

too short a period". This timidity has led to the prevailing misconception that corticosteroid therapy does not help NAION". (27)

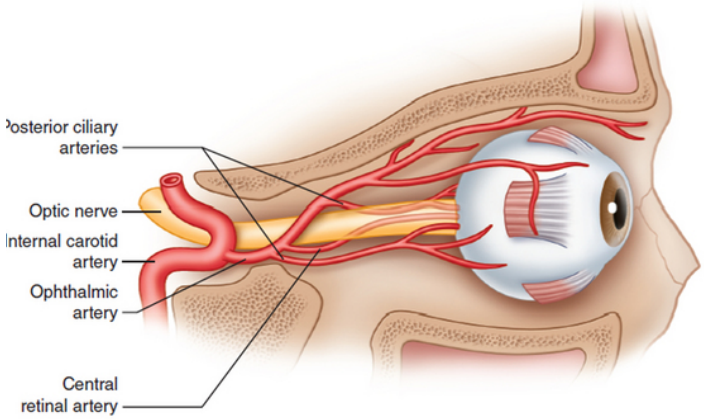
In order to decrease the risk of further visual loss in the other eye or the same eye, it is essential to minimize and control the risk factors. First of all trying to control the cardiovascular risk factors to avoid seeing the same condition happening to the second eye. Sudden vision loss should always lead to an urgent ophthalmological consultation. A neuro-ophthalmologist's consultation should be obtained if NAION is suspected. (28)

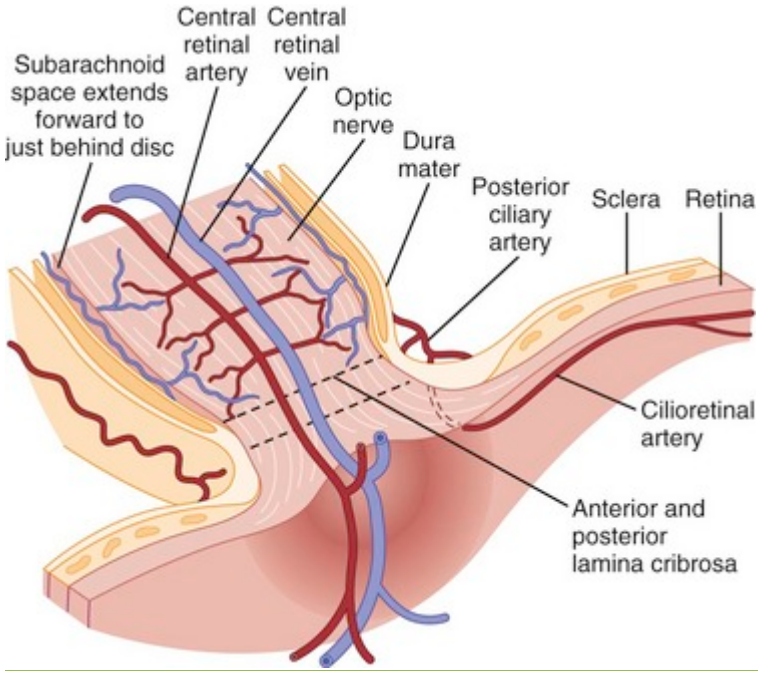
Thrombosis therapy does not reduce the severity of NAION or shorten the visual disturbance.

3. Arteritic anterior ischemic optic neuropathy

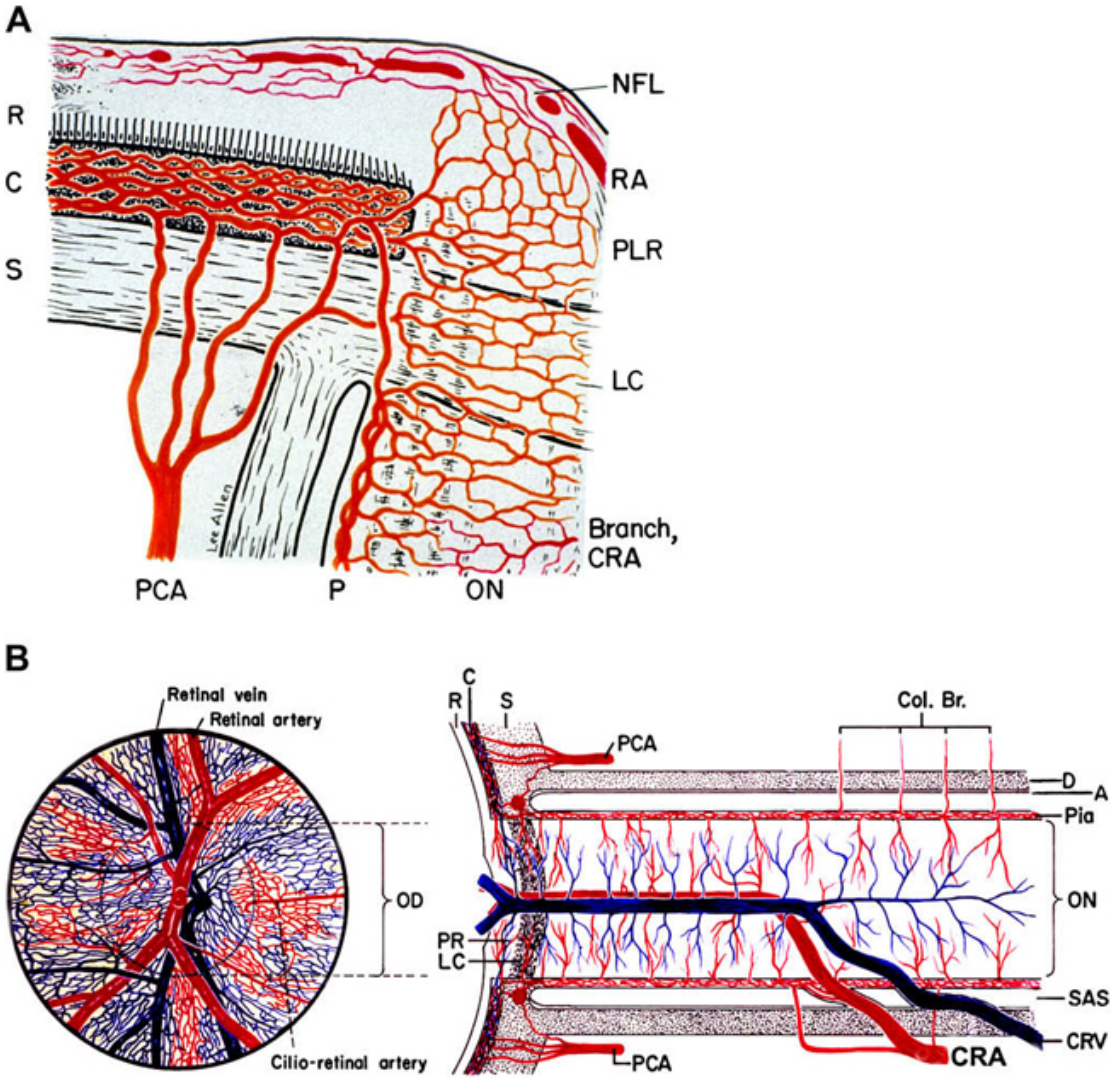
AAION occurs in about 20% of patients with **GCA** also called **temporal arteritis** or **Horton's disease**. GCA is a systemic vasculitis that affects the temporal arteries primarily. In the eye, it involves the posterior ciliary artery leading to occlusion due to thrombosis (29). The result is development of AAION and severe visual loss.

When the blood vessels supplying the optic nerves get damaged, it leads to ischemia of the nerve and optic nerve fiber death if not treated promptly. Most cases of AAION result in nearly complete vision loss to one eye first. If the temporal arteritis is left untreated, the second eye is probably going to suffer vision loss as well in less that two weeks. Ischemia that occurs at the head of the optic nerve impairs perfusion and producing optic disc edema, giving a similar appearance that in NAION on ophthalmoscope. AAION is considered an eye emergency, immediate treatment is essential to rescue remaining vision. This condition is painless and acute, it occurs predominantly in patients over 70 years old; it is three times more common in women than in men. The racial differences suggest a genetic predisposition to giant cell arteritis being more often seen in Caucasian population. (30)





Optic nerve vascularization (31)



Schematic representation of blood supply of: **(A)** the optic nerve head and **(B)** the optic nerve (32)

Abbreviations: **A** = arachnoid; **C** = choroid; **CRA** = central retinal artery; **Col. Br.** = Collateral branches; **CRV** = central retinal vein; **D** = dura; **LC** = lamina cribrosa; **NFL** = surface nerve fiber layer of the disc; **OD** = optic disc; **ON** = optic nerve; **P** = pia; **PCA** = posterior ciliary artery; **PR** and **PLR** = prelaminar region; **R** = retina; **RA** = retinal arteriole; **S** = sclera; **SAS** = subarachnoid space.

3.1. Pathogenesis

It accounts for only 5-10% of AION and inflammation and thrombosis of the SPCA or other arteries supplying the optic nerve head resulting in infarction, optic disc swelling, chronic inflammatory cells infiltration and necrosis of the nerve if left untreated. Extremely poor or absent filling of the choroid has been depicted as a characteristic of AAION.

The pathological mechanism seems to starts when dendritic cells in the vessel wall recruiting T cells and macrophages to form granulomatous infiltrates. There is infiltration of lymphocytes, monocytes and neutophils in the arterial walls, destruction of the muscle cells in the media and fragmentation of the elastic fibers. Cytokines are increased and play a central role in the inflammatory pathogenesis. (33)



Microscopic pathology image showing a normal temporal artery biopsy on an elastic stain performed for a Giant cell temporal arteritis. (34)

3.2. Symptoms

a) General Symptoms:

The symptoms of GCA usually are systemic and not specific, including weight loss, anorexia, scalp tenderness, headache, abnormal temporal artery, myalgia, neck pain, malaise and anemia, and the most characteristic symptom jaw claudication (spasms of the jaw muscle), joint and muscle pain, and ear pain. (35)

b) Ocular Manifestations

AAION may occur as an ocular manifestation of the vasculitis related to GCA in 5-10% of the cases. Rapid onset of painless, unilateral visual loss manifested by decreased visual acuity that is severe in over 70% of the patients, visual field or both. Compared to NAION, the visual defects are much more extensive and severe in AAION (36). A relative afferent pupillary defect is common in unilateral neuropathies. Pallor of the optic disc, which may be severe, chalky-white is the hallmark of AAION, but it’s not uncommon to see hyperemic swelling. The disc most often is swollen diffusely, but a segment of more prominent involvement may be present with flame hemorrhages located adjacent to the disc, and the peripapillary retinal arterioles frequently are narrowed. Choroidal ischemia may be associated with the optic neuropathy and produces peripapillary pallor and edema deep to the retina. The disc of the fellow eye is of normal diameter in AAION, as is the physiologic cup, which is different than in NAION where the cup is smaller.

Occult GCA without overt systemic symptoms happens and it occurs in approximately 20% of patients with AAION. (37)

Besides the several systemic symptoms of GSA that help in diagnosis of AAION such as jaw claudication, scalp tenderness, unintentional weight loss, fatigue, myalgia and loss of appetite there are also elevations in three blood tests that help identify AAION: **ESR**, **CRP** and **platelet count**. A related rheumatic disease called polymyalgia rheumatica has a 15% incidence of GCA. Nevertheless, many cases are asymptomatic.

Early diagnosis is of first importance since the sudden blindness in the affected eye is often followed, within days, by similar symptoms in the second eye. Prompt treatment prevents further damage. Any patient diagnosed with NAION over the age of 50 must be questioned about the general symptoms mentioned earlier. Moreover, AION patients older than 75 should always be blood tested.

3.3. Diagnosis

Measurement of the ESR remains the standard, which usually elevates up too 70-120mm/min in GCA. Serum CRP concentration measurement may help in diagnosis. It has been reported a 97% specificity for temporal arteritis in cases of AION in which both ESR and CRP were elevated. Confirmation of the diagnosis of temporal arteritis by superficial temporal artery biopsy is recommended in cases of AION with clinical suspicion of arteritis. Positive biopsy findings are: intimal thickening, internal limiting lamina fragmentation, and chronic inflammatory infiltrate with giant cells. They are confirmatory for

GCA (38). A negative biopsy doesn't rule out AAION (5% false-negative error rate). OCT is useful in assessing the disc edema, retinal nerve fiber layer thickness, as well as documenting the resolution to a normal or an atrophic optic disc. (39)

3.4. Differential Diagnosis

The differential diagnosis of AION include: idiopathic optic neuritis, optic nerve inflammation related to syphilis or sarcoidosis (because of the granulomatous inflammation), infiltrative optic neuropathies, anterior orbital lesions with optic nerve compression, and diabetic papillopathy. (40)

3.5. Treatment

Corticosteroids are the treament of choice. Typically high-dose **prednisone** (1 mg/kg/day) must be started as soon as possible when the diagnosis of arteritis temporalis is suspected, even before the diagnosis is confirmed by biopsy in order to prevent irreversible blindness secondary to ophthalmic artery occlusion. IV **methylprednisolone** at 1g/day for the first 3 days has been recommended for severe cases. (41)

Steroids do not compromise the diagnosis by biopsy even though some histological changes might be observed after the first week of treatment and are more difficult to identify later. (42)

3.6. Course and Outcome

Without therapy visual loss happens in more than half of the patients typically in 4 to 6 months according to the literature. With corticosteroid treatment the rate of visual loss is reduced to an estimated 15%. Visual recovery of the affected eye that is treated is poor with only a 25% improvement rate, higher with intravenous therapy though. Worsening of visual acuity has been reported in 15% despite the therapy. (43)

4. Differentiation of AAION from NAION

When a patient is diagnosed with AION, the first and critical step in patients older than 50 is to identify as soon as possible whether it is AAION or NAION. Clinical examination and investigation give information helping to differentiate the two types of AION with a certain success.

1. *Systemic symptoms of giant cell arteritis:* however, 20% with *occult GCA do not* have systemic symptoms and visual loss is the only complaint. Patients with never NAION systemic symptoms of giant cell arteritis. So if the systemic symptoms are present we can rule out NAION but if they are absent we can not elliminate AAION of the differential diagnosis.
2. *Visual symptoms:* amaurosis fugax is highly suggestive of AAION and is extremely rare in NAION.
3. *Blood test: hematologic abnormalities.* Immediate evaluation of ESR and CRP is vital in all patients older than 50. Elevated ESR and CRP, particularly CRP, is crucial in the diagnosis of GCA. Patients with NAION do not show those abnormalities, unless in the presence of another disease.
4. *Sudden, acute and important visual loss:* suggestive of AAION. However, the presence of a normal visual acuity does not rule out AAION.

5. *Chalky white optic disc edema: s*een in 70% of AAION eyes and is almost diagnostic. In NAION, chalky white optic disc edema occurs only very rarely with embolic occlusion of the SPCA.
6. *AAION associated with SPCA occlusion: this is in most cases diagnostic of AAION.*
7. *Temporal artery biopsy:* this test finally establishes the diagnosis with certainty.

AION is not one disease but a spectrum of several different types, each with a different etiology, risk factors, pathogenesis, management and treatment. They must be considered a separate clinical entity. Put together they constitute one of the major causes of blindness or severely impaired vision, yet their pathogeneses and management are not well understood and controled.(44)

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Biography

Laurent Antoine Roger Martini was born in Ajaccio in 1985. After graduating from high school in Ajaccio he studied medicine for two years in Montpellier, one of the oldest universities of medicine in the world (13th century). Later he transfered to the University of Zagreb in order to continue his studies in the english program. After completing his medical training in Zagreb, Laurent is going to Switzerland in order to specialize in ophthalmology.