

DIFFERENT TYPES OF OPTIC NEUROPATHY

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Summary: Any damage to the optic nerve is termed as optic neuropathy. Depending upon the causative agents involved, and the effects produced, different types of optic neuropathies are observed.

What is Optic Neuropathy?

Damage to the optic nerve arising out of any cause is termed as optic neuropathy.¹ This damage can also manifest itself as swelling of the optic neurons termed as optic neuritis.²

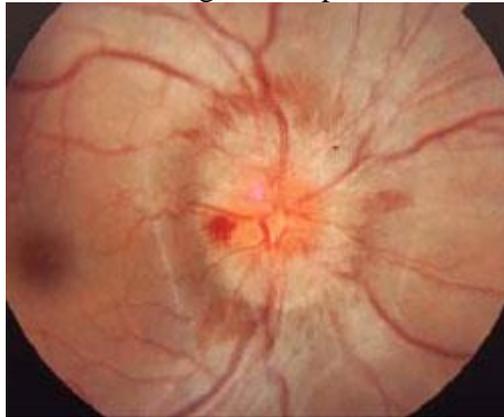


Fig. 1 Optic nerve swelling in a patient with optic neuritis.

3

Optic neuropathy is suspected by the ophthalmologist when the patient reports the following warning signs –⁴

- Visual field defect – Any type of visual field defect is seen. Initially, loss of vision occurs in a small area in the centre of visual field, slowly progressing to complete blindness.⁵
- Dyschromatopsia – Colour vision is negatively affected. Additionally, deficits are detected in light contrast, brightness, sensitivity to colours, etc. For instance, red colour may be viewed as a lighter shade, or another colour similar to red in a patient shows signs of optical neuropathy.⁶
- Abnormal pupillary response – The pupil helps the eye to adjust to varied levels of light brightness as well as contrast. This is a reflex action controlled by the optic nerve as well as the oculomotor nerve.⁷

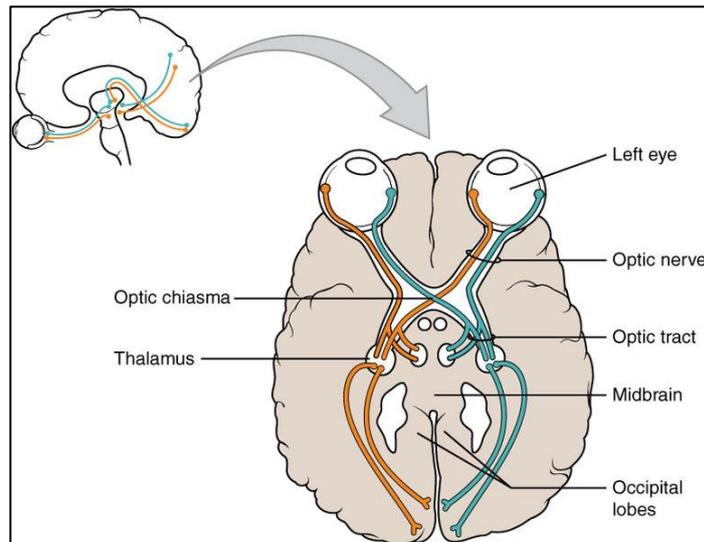
In young patients -

- Eye pain during eye movement – This is a mild to severe pain⁸ surrounding the eyeball (periocular) which worsens during eye movement.⁹
- Limb weakness – Spastic paraplegia is seen, in addition to other conditions such as optic atrophy, cognitive decline, etc.¹⁰
- Ataxia – Mitochondrial diseases are characterized by association of optical neuropathy alongwith cerebellar ataxia as a result of a missense variation in the mitochondrial DNA (valine replaced by alanine).¹¹

In older individuals –

- Loss of vision – Autoimmune disorders such as Systemic Lupus Erythematosus (SLE) can result in autoimmune attacks to the optic region, leading to loss of vision.¹² This vision loss can occur in one eye, and it worsens with increase in body temperature. Most cases of optic neuritis take twelve months to achieve full visual recovery after completing treatment.¹³
- Fatigue – Fatigue in vision is observed in patients suffering from optic neuritis, for which tinted lenses may be prescribed.¹⁴
- Myalgias – Presence of muscular dysfunction (pain / spasm) alongwith optical atrophy is a sign of Arteritic Ischaemic Optic Neuropathy.¹⁵

Structure of Optic Nerve



16

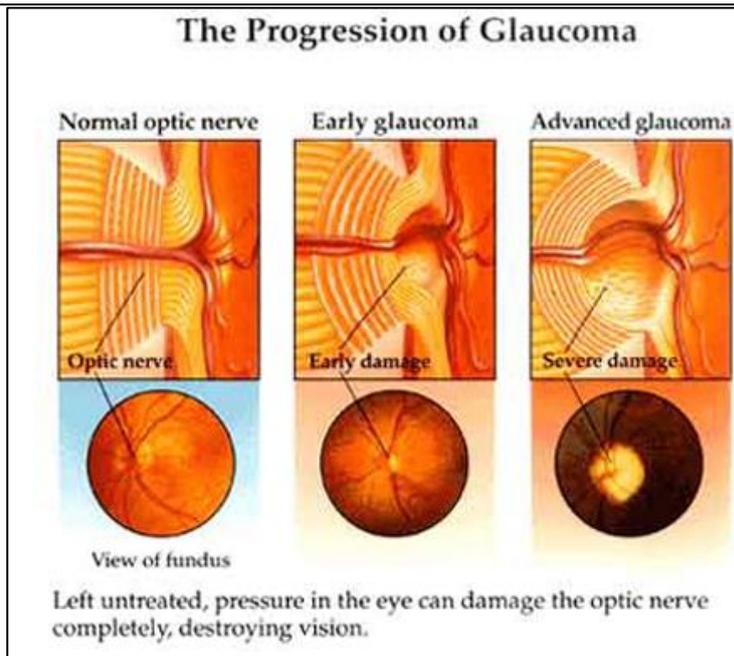
Types of Optic Neuropathy

The most common form and well-known form of optic neuropathy is glaucoma. This is also known as Glaucomatous Optic Neuropathy. All other forms are classified as non-Glaucomatous Optic Neuropathy.

1. Glaucomatous Optic Neuropathy –

Cupping of the optic nerve head is the characteristic form of glaucomatous optic neuropathy. This occurs due to nerve fibre loss.⁵⁵ Early glaucomatous cupping comprises of the loss of nerve fibres and other parts of the optic neuron.⁵⁶

Degeneration of nerve fibres occurs due to oxidative stress and unstable blood flow. Oxygen free radicals superoxide, nitric oxide, etc. combine together forming peroxynitrite. This induces apoptosis in neurons and necrosis of neuronal tissue. The optic neuronal head comprises of nitric oxide synthetase. This induces production of nitric oxide on a large scale, damaging the axons.^{57,58}



59

2. Non-Glaucomatous Optic Neuropathy can be further classified as follows – ^{17,18}

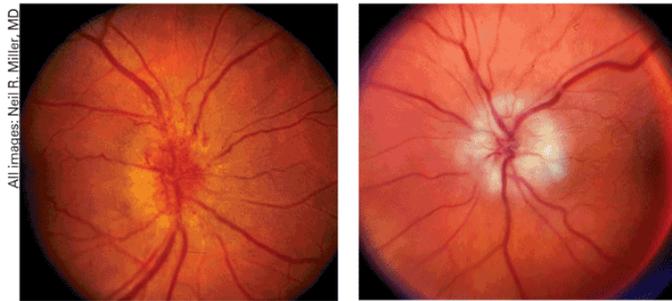
Ischaemic Optic Neuropathy	Optic Neuritis
- Anterior (AION)	- Ophthalmoscopic
- Posterior (PION)	➤ Retrobulbar Neuritis
Compressive Optic Neuropathy	➤ Papillitis
Infiltrative Optic Neuropathy	➤ Neuroretinitis
Traumatic Optic Neuropathy	- Etiologic
Mitochondrial Optic Neuropathies	➤ Demyelinating
- Nutritional Optic Neuropathy	➤ Parainfective
- Toxic Optic Neuropathy	➤ Infective
- Hereditary Optic Neuropathy	➤ Autoimmune

This classification is based on the causative agent(s) involved as well as the effects produced. Ischaemic Optic Neuropathy – Decreased blood supply to any part of the body is termed as ischaemia. This leads to reduced oxygen supply, hampering tissue metabolism and functioning. ¹⁹ Similarly, the eye is directly dependent on blood circulation for oxygen supply. Therefore, any damage to the optic blood vessels leads to interrupted blood supply and decreased oxygen. This affects optic nerve functioning, slowly progressing to loss of vision. ²⁰

Ischaemic Optic Neuropathy is of two types –

- Anterior Ischaemic Optic Neuropathy (AION) – This affects the head of the optic neuron (anterior part of optic nerve) ²¹, leading to optic disc inflammation. There are two types of AION –
 - Arteritic AION – Arteritis implies inflammation of the arteries. A condition known as Giant Cell Arteritis (GCA) leads to inflammation of the arteries in the temporal region, which in turn affects the optic arteries. ²² Vision loss accompanied with physical illness is observed in 80% individuals. If AION is detected, temporal arterial biopsies should be performed to check for GCA. ²³

- Non-arteritic AION – Direct inflammation of optic arteries does not take place. However, certain conditions occur which may be found to be associated with optic arterial inflammation, such as – Sleep Apnea Syndrome (SAS), side-effects of medication, lipid deposits under retina (optic drusen)²⁴, insufficient circulation, anaemia, nocturnal hypotension, metabolic disorders, etc.²⁵ This is the more common of the two AIONs.²³



Left: Nonarteritic anterior ischemic optic neuropathy. Note the hyperemic swelling of the optic disc associated with the flame-shaped peripapillary hemorrhage. Right: Arteritic anterior ischemic optic neuropathy. Note the pallid swelling of the optic disc and a peripapillary cotton-wool spot.

26

- Posterior Ischaemic Optic Neuropathy (PION) – This affects the retrobulbar (posterior) part of optic nerve resulting in nerve damage, but with a normal optic neuron head.²⁷ This may cause acute, painless blindness in one eye or both eyes. PION may be classified as –^{28,29}
 - Arteritic PION – This occurs due to Giant Cell Arteritis (GCA)²⁹
 - Non-Arteritic PION – Idiopathic causes which may involve sudden vision loss along with metabolic disorders such as hypercholesterolemia, arterial hypertension, sleep apnea, etc.²⁹
 - Peri-Operative PION – PION occurring as a result of post-surgical complications, such as arterial hypotension due to blood loss, haemodilution due to excessive intravenous fluids, etc. this can cause permanent blindness in both eyes.²⁹



Peri-Operative PION²⁸

Compressive Optic Neuropathy – Any injury caused to the optic neuron by an external lesion, which affects the bunch of nerve fibres extending from optic globe to the optic chiasm, is known as Compressive Optic Neuropathy. The injury is ‘compressive’ as the nerve fibres are located to a bone segment hence compressed or confined.³⁰



CT scan of left optic nerve compression ³¹

Infiltrative Optic Neuropathy – Infiltration of the optic nerve and nerve fibres occurring due to infection (microbial infection), inflammation (sarcoidosis), metastasis, carcinomas, etc. ^{32,33} Trauma is detected by neuroimaging. ³³



15. Early (left) and late (right) optic neuritis due to presumed neurosarcoidosis.

Infiltrative Optic Neuropathy due to infection ³³

Traumatic Optic Neuropathy (TON) – Any injury to the optic nerve leads to trauma. This results in partial or complete loss of vision. ³⁴ Injury can also take place by cranial bones coming in contact with the optic nerve fibres and rupturing them. This happens as the optic nerve dura mater is in constant contact with the orbital periosteum, which can cause nerve trauma. ³⁵ TON can also occur due to head trauma. TON is of two types – ³⁶

- Direct TON – Trauma to optic nerve which penetrates it. Can lead to permanent blindness with minimal recovery. ³⁶

Types of direct injury – ³⁷

- Nerve transection – Fracture of orbital bone leads to nerve trauma
 - Nerve sheath haemorrhage – Hematoma in nerve sheath
 - Orbital haemorrhage – Retrobulbar injury leads to orbital fracture and haemorrhage
 - Orbital emphysema – Fractures in bone lining orbital region lead to swelling of orbital walls in paranasal sinuses
- Indirect TON – Acceleratory forces cause blunt trauma to optic neuron (dura mater being in contact with periosteum) which results in apoptosis of injured neuron. ³⁶

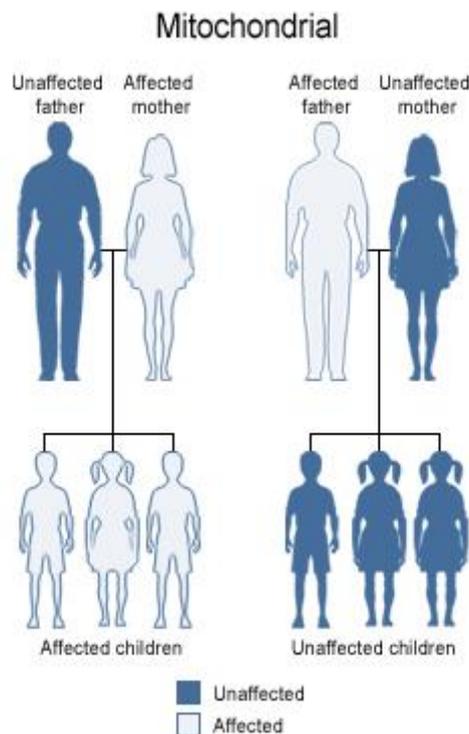


Traumatic Optic Neuropathy³⁴

Mitochondrial Optic Neuropathies – The central nervous system (CNS) has an extremely high rate of metabolism, requiring 20% of inhaled oxygen. ATP energy required for neurons is derived from oxidative metabolism. Thus, neuronal mitochondria require high amount of energy for functional purposes - nerve transmission by exciting cell membranes, communicating nerve signals, and carrying out neurotransmission.³⁸

Proper mitochondrial functioning is extremely critical as far as neuronal energy demands are concerned. Different parts of neurons (axons, dendrites, synapses, etc.) have varied energy requirements. Also, the structure and functioning of neurons is completely dependent on proper mitochondrial functioning. Consequently, any mitochondrial dysfunction has a serious impact on neuronal survival.³⁸

Trauma affecting mitochondria include exposure to mutagens resulting in mitochondrial DNA mutations, consumption of alcohol, drug abuse, etc. This has an adverse impact on the effective functioning of mitochondria of the optic nerves, resulting in mitochondrial optic neuropathy.



Hereditary pattern of Mitochondrial Optic Neuropathies³⁹

There are three types of mitochondrial optic neuropathies –⁴⁰

- Nutritional Optic Neuropathies – Optic nerve damage occurring as a result of nutritional deficiencies is termed as nutritional optic neuropathy.

The nutrients whose deficiency can result in nutritional optic neuropathy include the B-complex vitamins (thiamine, riboflavin, niacin, folic acid, cyanocobalamin) as well as copper.

Vitamin B12 is responsible for the formation of the myelin sheath covering the neurons.⁴⁰

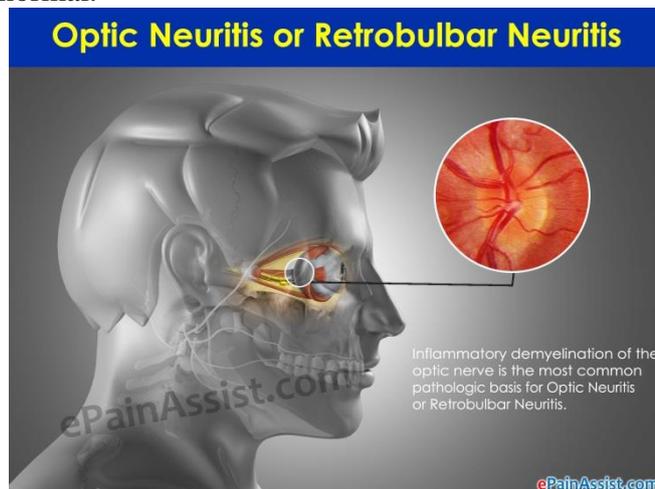
- Toxic Optic Neuropathies – Optic neuronal toxicity can occur due to drug toxicity, methanol toxicity, and tobacco toxicity.⁴⁰
- Hereditary Optic Neuropathies – Optic neuron damage is permanent. Heritable mutations in the optic mitochondrial DNA in neurons are known as heritable optic neuropathies.⁴⁰

3. Optic Neuritis –

Any damage to the optic nerve that can result in inflammation of the optic neurons is termed as optic neuritis.

Optic Neuritis can be classified as –¹⁸

- Ophthalmoscopic – Direct examination by an ophthalmologist. Three types –
 - Retrobulbar neuritis – The posterior part of the optic neuron in contact with the eyeball undergoes inflammation. However, the optic disc remains structurally normal.¹⁸

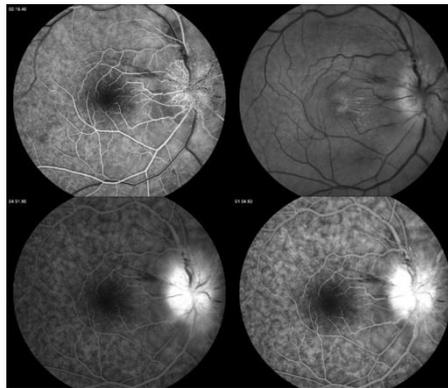


- Papillitis – Inflammation and deterioration of optic neuronal head (blind spot). Loss of vision may occur within hours of onset of inflammation.⁴²



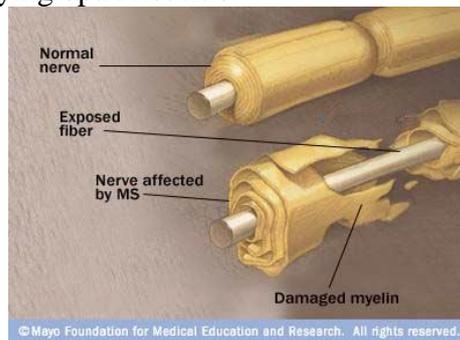
Papillitis⁴³

- Neuroretinitis – Inflammation of retina as well as the optic neuron associated with it, accompanied with star-shaped hard exudates near the cone cells of the retina.⁴⁴



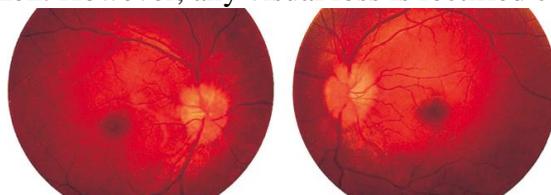
Neuroretinitis⁴⁵

- Etiologic – Causal consequence for optic neuritis –
 - Demyelinating – Removal of myelin sheath disrupts the process of neurotransmission which affects optic nerve function. For instance, multiple sclerosis accompanying optic neuritis.⁴⁶



47

- Parainfective – This manifests as bilateral visual loss, and is more commonly seen in children as compared to adults. This condition is known as parainfective as it occurs as a consequence of a viral infection (such as mumps, glandular fever, whooping cough, etc.). The optic disc may be found to be swollen. However, any visual loss is rectified completely.⁴⁸



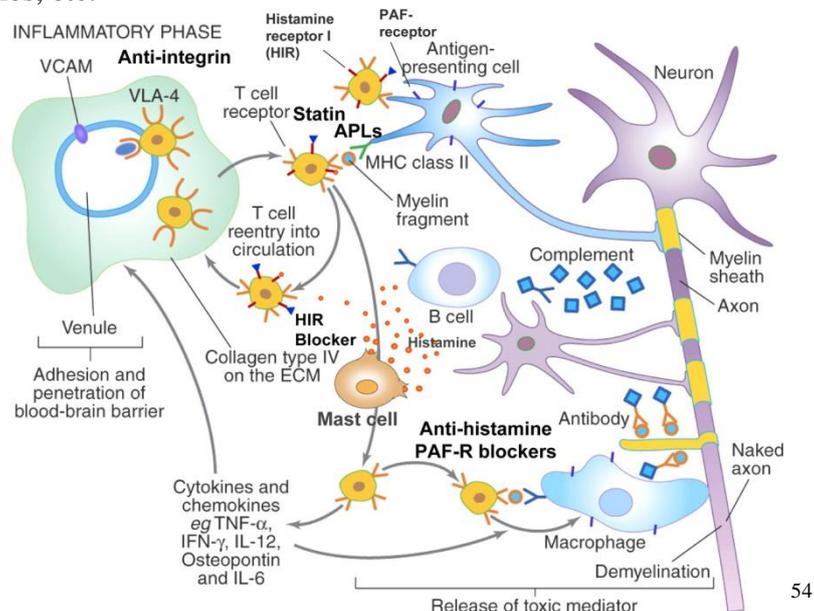
Parainfectious Optic Neuritis⁴⁹

- Infective – Infections directly resulting in inflammation of the optic neuron.⁴⁸
 - Varicella zoster virus (causing chicken pox) – Optic neuritis occurs if immunocompromised or retinal infection
 - Sinus infection – Direct spread of infection through sphenoid-ethmoid sinus
 - Cat scratch disease – Lymphadenopathy can cause inflammation of optic neuron in severe cases.⁵⁰ Visual recoveries take place 1-4 weeks after initiation of therapy.
 - Lyme Disease – A link between Lyme disease and optic neuritis is yet to be established. Yet, rare instances occur when optic neuritis is observed in individuals suffering from Lyme Disease.⁵¹
 - Syphilis – Optic Neuritis has been observed in advancing stages of infection



Optic neuritis due to Lyme borreliosis⁵²

- Autoimmune – This is distinct as compared to other forms of optic neuritis as it involves the study of a patient's clinical history along with other pathological testing. In this disorder, progressive vision loss is seen along with the pathological confirmation of the presence of an autoimmune disorder through suitable markers such as antinuclear antibodies, skin biopsies, anticardiolipin antibodies, etc.⁵³



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