

Lipids & Eye

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Introduction

- Lipids are classified from a group of hydrophobic or amphiphilic small molecules composed of the carbanion-based condensation of thioester or isoprene groups;
- They include fatty acids, glycerololipids, sphingolipids, and sterols
- Lipids represent the most energetic nutrients, providing 9 kcal per gram
- Lipids execute a variety of biological functions such as
 - cell signaling,
 - energy storage, and
 - maintenance of compartmental boundaries

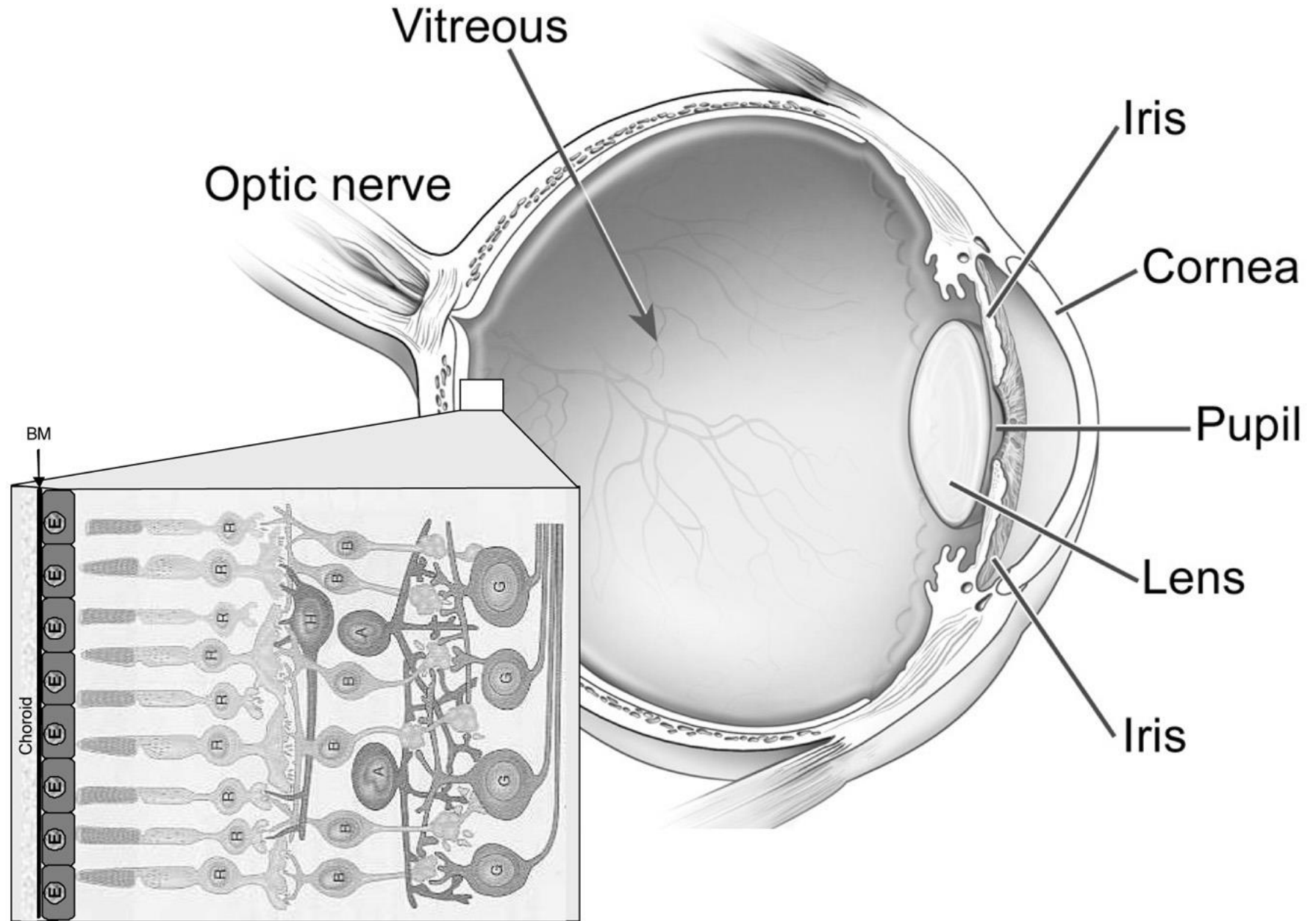
Introduction

- Lipids are nutrients that account quantitatively for an important part of daily energy intake in humans
- In western and developed populations, more than one third of the daily energy intake comes from lipids.
- Lipids are also metabolic substrates and cellular effectors that participate in various cellular mechanisms
- They provide essential fatty acids indispensable in diverse physiological processes.

Introduction....

- Lipids are key components of the retina, and are closely associated with the aging processes.
- Omega-3 fatty acids show protective properties against inflammation and neurodegeneration in retinal aging and the development of AMD
- The eye retina is a part of the central nervous system, together with the brain and the spinal cord and as such is also naturally rich in lipids

- The human eye and retina
- BM, Bruch's membrane; E, retinal pigment epithelium; R, photoreceptor (rods and cones); H, horizontal cell; B, bipolar cell; A, amacrine cell; G, ganglion cell



Lipids as crucial components of the retina

- The retina covers the internal side of the posterior chamber of the eye
- The retina is composed of
 - neurosensory tissue: neuroretina,
 - a pigment epithelium: retinal pigment epithelium (RPE)
- The main function of the neuroretina is to convert the light stimulus into an electrical signal that can be decoded by the brain
- The RPE creates a physical and metabolic barrier between the neuroretina and the choriocapillaris that limits the entry of exogenous compounds in the neuroretina.
- One of the primary function of the RPE is to eliminate the metabolic debris generated by photoreceptors.
- The RPE exhibits an endogenous capacity to synthesize and secrete lipoprotein-like particles
- Low density lipoprotein particles (LDL) participate significantly in retinal lipid supply.

Lipids as crucial components of the retina

- Lipids account for about 25% of the dry matter in the neuroretina.
- Phospholipids are the prominent lipids therein (more than 85%), while cholesterol is present as free cholesterol (10%), and to a lesser extent as cholesteryl esters (less than 2%)
- Phospholipids are present in great quantity in the outer segment of rods and cones.
- Docosahexaenoic acid (DHA) is the main long-chain polyunsaturated fatty acid in the phospholipids of the neuroretina: 12–20% of the fatty acids in human and more than 30% in rodent
- DHA is involved in the phototransduction pathway by enhancing the ability of the photopigment rhodopsin to undergo the transition to the active form.
- Modifying the dietary intake of omega-3 fatty acids may have consequences on the level of DHA in the retina and possibly its functioning

Lipids as crucial components of the retina

- The potential of a diet enriched in DHA and EPA (eicosapentaenoic acid) to increase the level of the longer chain omega-3 fatty acids (EPA; DPA, docosapentaenoic acid; and DHA) in the retina has clearly been demonstrated
- Intervention trials have been conducted in pregnant and lactating women and premature and at-term babies in order to evaluate the efficacy of dietary long chain omega-3 fatty acids to improve vision performance in infants.
- The positive effect of omega-3 fatty acids was obvious only in studies where the intake of DHA was higher than 1g daily

Aging of the retina

- Aging, and to a larger extent AMD, is associated with the accumulation of extracellular lipid particles at the basement of the RPE, within Bruch's membrane
- These lipid particles are called drusen (singular, “druse”).
- Drusen comprise multiple components including lipofuscin, fibrillar and non-fibrillar amyloid, cholesterol, glycoproteins, vitronectin, inhibitors and activators of the extracellular matrix, complement factor H, complement component C3, and zinc.
- Morphologic criteria are used to define drusen as soft or hard: soft drusen appear often liquefied or oily, whereas hard drusen are partially or completely crystallized.
- Hard drusen are the most abundant type throughout the retina.
- Soft drusen appear specifically in the macula and are considered as the most fateful of age-related macular lesions.

Aging of the retina & Lipids

- The “lipid wall”, made of cholesterol, participates in the age associated thickening of Bruch's membrane that increases hydraulic resistance and may reduce the fluxes of nutrients to the retina
- AMD targets a specific area of the retina: the macula.
- High fat intake has been associated with higher risk for AMD.
- Smoking and light exposure are, for instance, recognized as promoting factors

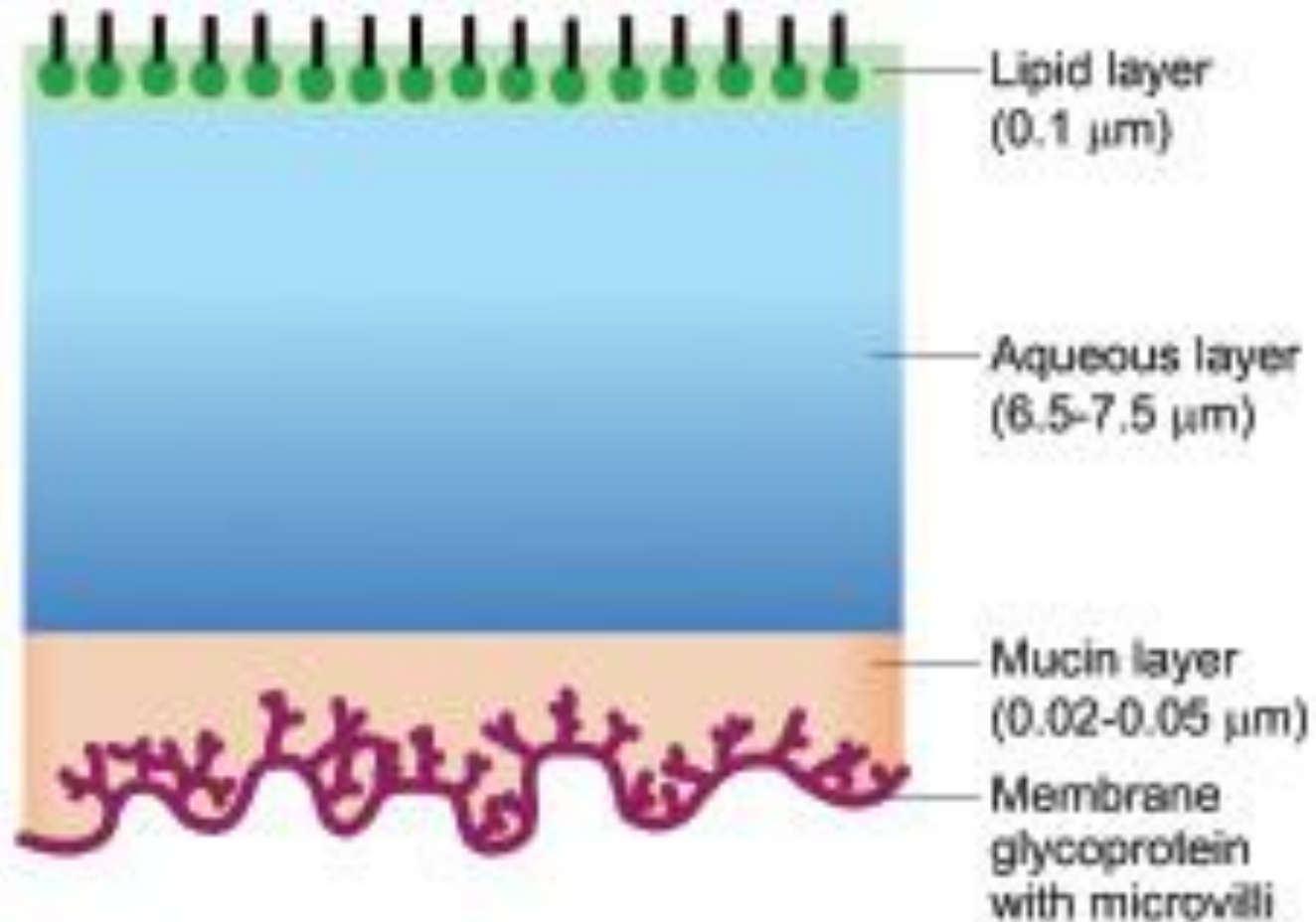
Lipids are powerful factors preventing retinal stress, aging and death

- Glaucoma is characterized by the death of ganglion cells that, in the last stages of the pathology, induces blindness.
- Various factors are associated with glaucoma, including elevated intra-ocular pressure
- A reduced activation of glial cells in the group of rats fed both omega-3 and omega-6 fatty acids was observed, suggesting their potential to prevent retinal stress.
- In a study it was observed that participants who have the highest omega-3 long-chain polyunsaturated fatty acid (EPA and DHA) intake (0.11% of total energy intake) were 30% less likely to develop Geographic atrophy and neovascular AMD than low consumers (0.01% of total energy intake)

Lipids in tears

- Tear film is actually composed of three basic layers: mucin, water and lipids from posterior to anterior.
- ***Lipid or oily layer*** is the outermost layer of tear film formed at air-tear interface from the secretions of Meibomian, Zeis, and Moll glands.
- This layer prevents the overflow of tears, retards their evaporation and lubricates the eyelids as they slide over the surface of the globe.
- Lipids within tears help prevent water evaporation from the ocular surface and protect the eye against infection
- Prolonged dry eyes leads to cloudy cornea, inhibiting self repair of the damaged cornea

Structure of tear film



Eye Diseases linked to lipids

- **Arcus senilis** refers to an annular lipid infiltration of corneal periphery. This is an age-related change occurring bilaterally in 60 percent of patients between 40 and 60 years of age and in nearly all patients over the age of 80.
- **Fatty degeneration (Lipoid keratopathy) of cornea** is characterised by whitish or yellowish deposits. The fat deposits mostly consist of cholesterol and fatty acids
- **Diabetic retinopathy:** hyperlipidemia is a risk factor
- **Seborrhoeic or squamous blepharitis:** glands of Zeis secrete abnormal excessive neutral lipids which are split by *Corynebacterium acne* into irritating free fatty acids

Eye Diseases linked to lipids

- **Xanthelasma:**

- These are creamy-yellow plaque-like lesions which frequently involve the skin of upper and lower lids near the inner canthus.
- Xanthelasma represents lipid deposits in histiocytes in the dermis of the lid.
- These may be associated with diabetes mellitus or high cholesterol levels.

Eye Diseases linked to lipids

- **THE DRY EYE:**

- Lipid deficiency is extremely rare.
- It has only been described in some cases of congenital anhidrotic ectodermal dysplasia along with absence of meibomian glands.
- However, lipid abnormalities are quite common in patients with chronic blepharitis and chronic meibomitis

- Lipid soluble drugs have better permeability in eyes

- ***Asteroid hyalosis.***

- It is characterised by small, white rounded bodies suspended in the vitreous gel.
- These are formed due to accumulation of calcium containing lipids.
- Asteroid hyalosis is a unilateral, asymptomatic condition usually seen in old patients with healthy vitreous.
- There is a genetic relationship between this condition, diabetes and hypercholesterolaemia.
- The genesis is unknown and there is no effective treatment

Eye Diseases linked to lipids

Lipodermoids.

- These are solid tumours usually seen beneath the conjunctiva.
- These are mostly located adjacent to the superior temporal quadrant of the globe.
- These do not require any surgical intervention unless they enlarge significantly



New perspectives in the role of lipid nutrition in eye health

- The role of omega-3 fatty acids in the prevention of neuroretinal cell death has been increasingly appreciated over the last few years.
- It has been demonstrated that they help resolve inflammation and neurodegeneration in response to extracellular stresses, including oxidative stress
- Epidemiological studies consistently support the benefit of consumption of not only fish and marine products rich in omega-3 fatty acids, but also of fruits and vegetables that are rich in carotenoids.
- These dietary recommendations should be considered by clinicians providing care to patients at early stages of AMD in order to prevent the evolution into late stages