Lipids & Eye
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

Lipid layer (0.1 \(\mu\)m)

Aqueous layer (6.5-7.5 \(\mu\)m)

Mucin layer (0.02-0.05 \(\mu\)m)

Membrane glycoprotein with microvilli
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.