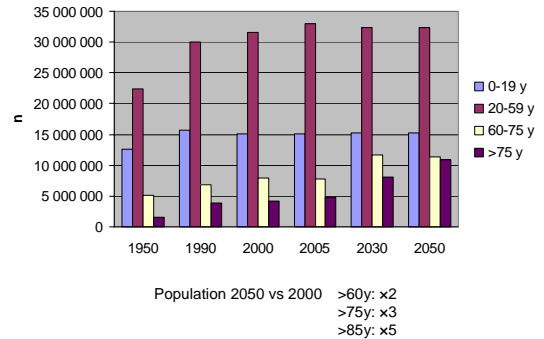


Nutrition and prevention of aging and pathology of the retina

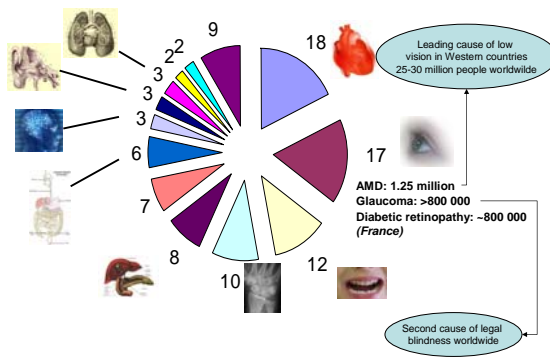
From concept to clinical application



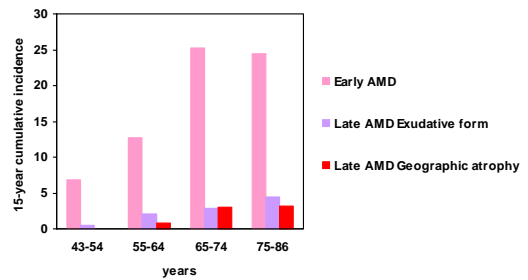
Demographic data in France



Prevalence of pathologies after 65 years of age

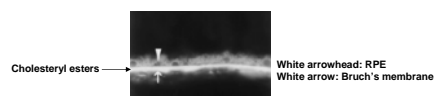
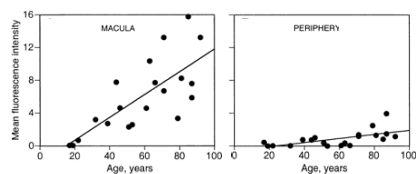


Aging is the main risk factor for AMD



Data from the Beaver Dam Eye Study
Klein et al. 2007 *Ophthalmology*

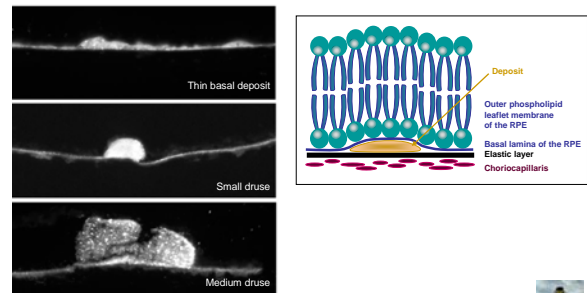
Accumulation of cholesteryl esters, cellular debris, lipofuscin is characteristic to normal aging of the retina



Section of human eye labelled with filipin to reveal cholesteryl esters after extraction of free cholesterol and hydrolysis of the fatty acid residue from CE (fluorescence imaging: excitation 346nm, barrier 460nm)

Curcio et al. 2001 *Invest. Ophthalmol. Vis. Sci.* 42:265-74

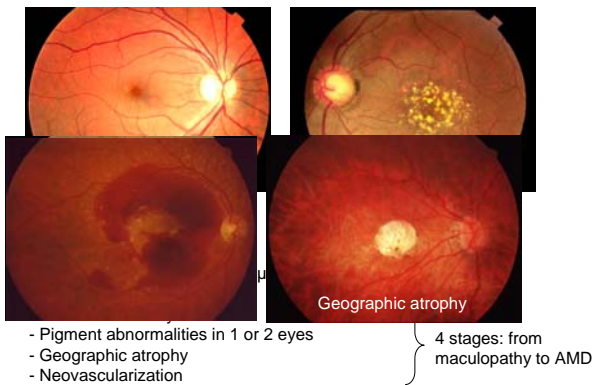
and age-related maculopathies



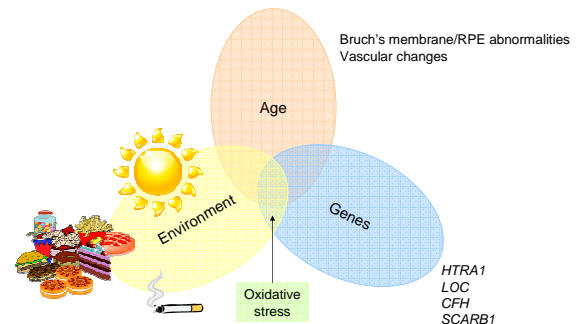
Sections of human eyes labelled with filipin to reveal cholesteryl esters after extraction of free cholesterol and hydrolysis of the fatty acid residue from CE (fluorescence imaging: excitation 346nm, barrier 460nm)

Malek et al. 2003 *Am. J. Pathol.* 162:413-25

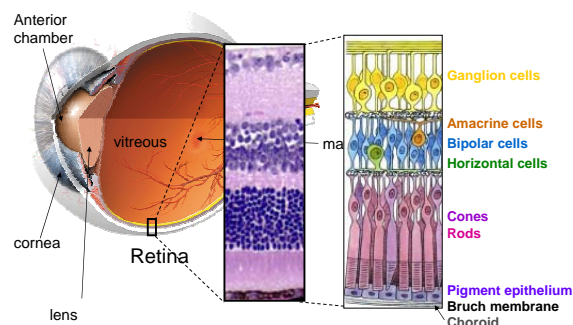
From age-related maculopathies to severe forms of AMD



AMD: a multifactorial aging disease



Structural organization of the retina



The retina: an ideal environment for oxidative stress

- O_2 consumption by the retina is much greater than by any other tissue,
- The retina is subject to high levels of cumulative irradiation,
- Photoreceptor outer segment membranes are rich in polyunsaturated fatty acids, which are readily oxidized and which can initiate cytotoxic chain-reactions,
- The retina and RPE contain photosensitizers (rhodopsin, lipofuscin),
- The process of phagocytosis by the RPE is itself an oxidative stress and results in the generation of reactive oxygen species.

May dietary compounds prevent the retina from aging and the development of AMD ?

Anti-oxidants (vit C, vit E, β -carotene) do not prevent from AMD, but do in combination with Zinc

Treatment	Participants in AMD Categories 2, 3, and 4 (n = 3609)		Participants in AMD Categories 3 and 4 (n = 2556)	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Antioxidants vs no antioxidants	0.87 (0.70-1.09)	.22	0.83 (0.66-1.06)	.01
Zinc vs no zinc	0.82 (0.66-1.03)	.02	0.79 (0.62-0.99)	.009
Antioxidants vs placebo	0.80 (0.59-1.09)	.07	0.76 (0.55-1.05)	.03
Adjusted	0.77 (0.56-1.07)	.03 ^a	0.76 (0.54-1.05)	.03 ^a
Zinc vs placebo	0.75 (0.51-1.03)	.02	0.71 (0.52-0.99)	.008
Adjusted	0.71 (0.51-0.98)	.005 ^a	0.70 (0.50-0.97)	.005 ^a
Antioxidants + zinc vs placebo	0.72 (0.52-0.98)	.007	0.66 (0.47-0.91)	.001
Adjusted	0.68 (0.48-0.93)	.002 ^a	0.66 (0.47-0.93)	.001 ^a
Total No. of participants with events	803		775	

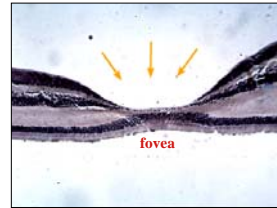
^a Adjusted for age, sex, race, AMD category, and baseline smoking status.

Age-Related Eye Disease Study Research Group. 2001. Arch Ophthalmol 119:1417-36.

Omega-3: protective factors

		Early AMD	Late AMD
		Odd-ratio	
Lipids		1.54	2.90
Omega 6	Linoleic acid (LA)	1.49	2.00
Omega 3	Total omega 3		0.61
	Linolenic acid		0.61 (low LA)
	EPA		0.44 (Geogr. atrophy)
	EPA+DHA		0.45 (Geogr. atrophy)
	DHA	0.70	0.54
	Tuna fish		0.48
	Fish oil	0.65	0.36 (low LA) 0.60 (low LA)

The macula: a specific area of the retina rich in carotenoids



Characteristics

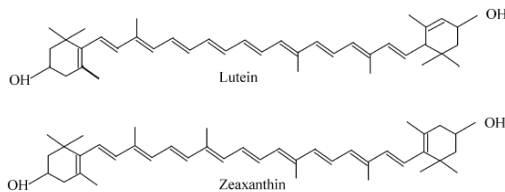
Cone-rich
(≈ 6 millions)

(vs **Rods**, ≈ 120 millions,
not specific to the macula)



Rich in lutein

Carotenoids



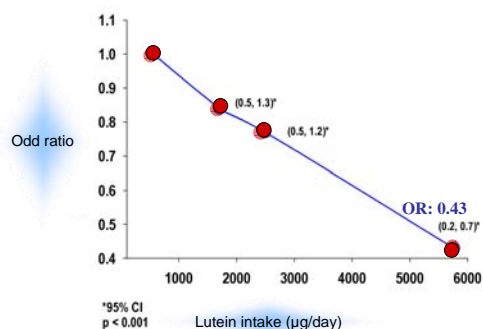
Agrumes, green leaves, vegetables

Variables associated with the macular pigment

	Nature of the association
Age	Ø
Sex	Ø, H>F
Right/left eye	Ø
Iris color	Ø, light<dark
Smoking habits	Smoker<Non-smoker
Obesity	High BMI – low macular pigment
Dietary intake	>0
Plasma levels	>0

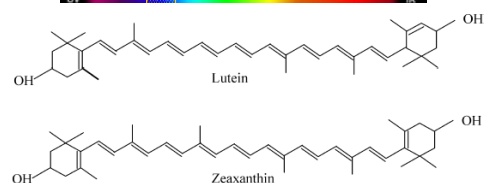
Carpentier et al. 2009 Crit Rev Food Sci Nutr

Lutein intake reduces the risk for AMD



The mechanisms of prevention by carotenoids

1. Carotenoids absorb the most energetic and deleterious wavelengths of the light spectrum
2. Carotenoids are anti-oxidant molecules thanks to the



Clinical trial

AREDS-2 (Age-Related Eye Disease Study-2)

- 11 centers in USA
- randomized clinical trial
- 4000 participants during 5 years
- dietary supplementation with:
 - EPA (650mg/d) + DHA (350mg/d)
 - and/or lutein (10mg/d) + zeaxanthin (2 mg/d)
- Criteria: progression of AMD into late stages

Conclusion

- Oxidative stress is an intimate mechanism of aging of the retina and tightly associated with the development of AMD
- Compounds with anti-oxidant properties may be beneficial in the prevention of oxidative stress-mediated cell dysfunctions