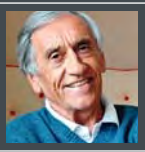
THE EFFECTS OF AGEING ON THE VISUAL SYSTEM



YVES POULIQUEN
of the Académie française
member of the Academy of medicine
France

__ **THERE IS A TERRIBLE DEFINITION OF OLD AGE**, given to us at the very end of the 16th century by Shakespeare in his own way in As You Like It, "Last scene of all… is second childishness and mere oblivion, sans teeth, sans eyes, sans taste, sans everything." and this was at a time when great age could be seen as a blessing! This is truly an atrocious image that he introduces into the script of a comedy, an image where eyes play their part. The literary genius has nonetheless, and paradoxically, extended to the majority of men and women the unavoidable fate of Man, this fatal stage in their ageing process. Up until recent times, in fact, most people living never even reached the age of presbyopia. Life expectancy at birth, and life expectancy at the age of 65 have, we can happily say, considerably increased. Infant mortality, horrifying in the past,

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and seen as an inevitability, decreased in remarkable proportions over the past century, and for the past thirty years the improvements in hygiene conditions and medical progress have led to an impressive reduction in morbidity amongst elderly people, many of whom now live without any major incapacity to over 80 years and beyond. Of course ageing is still inevitable but it has become partially influenceable, even though the biological evolutions that govern it still retain numerous unknowns. Why do we age?
The important question that we all ask ourselves still remains, when our past abilities are substituted by new and increasing inabilities that mark every stage on our final journey.

What we do know is "Ageing follows a period of growth and reproduction. Death may occur when the immortality of the germinal line has been ensured. In other cases it results from gradual cellular deterioration."[1] Experimental studies on the *C. elegans* worm, the *D. melanogaster* fly (fruit fly) and mice have been used to demonstrate four routes that are involved in senescence:
• Inhibition of the Insulin/IGF-1 pathway,
• The production of reactive oxygen species,
• Telomere shortening,
• Lysosomal autophagia.
Not to mention genetic factors which also play their part in ageing. So our various organs age in their own specific ways: blood vessels lose their suppleness, the heart is invaded by fibrosis, the brain by neurofibrillar degeneration and the appearance of senile plate, the kidney function declines, immune defences are down and the frequency of cancer increases with age.

The eye itself evolves in its own way. The first obvious signs of its ageing are the appearance of a difficultly in reading close up, which is known as presbyopia. In reality this is merely the revelation of a long process that affects the accommodative power of the crystalline lens. If one compares this power, at the age of 20, with that of a four year-old child, it is already clear that a large part of the accommodative power has already been considerably reduced. But at that time it is still of no consequence. It is only around the age of forty-five that someone with emmetropia[2] begins to experience some difficulties with reading, which will only increase with age and which requires optical assistance. The causes of presbyopia are due to structural changes in the crystalline lens and the ciliary muscles which are responsible for modifying the curves of the lens.
Up until the thirteenth century this was a major handicap for intellectuals and was resolved only by the introduction of magnifying lenses. Today we can consider that presbyopia has found its remedy in the remarkable solutions provided by designers of corrective lenses and, in a word, progressive lenses have now almost completely removed this first and inevitable consequence of ageing.
Indeed, presbyopia is so painfully perceived by some that, today, it has resulted in the use of surgical techniques to avoid the wearing of spectacles, which show one's age.

Everyone knows that primitive form cataract[3] occurs with age. It is the main cause of changes to vision after the age of sixty-five. This gradual change in the crystalline lens, which leads to modifications in its transparency results in a range of visual effects, such as reduced acuity, glare or an alteration in contrast, which become increasingly debilitating and lead to surgery which,

[1] Biologie du vieillissement Jean-Yves Le Gall et Raymond Ardaillou. Rapport à l'Académie Nationale de Médecine du 3 février 2009.
[2] A person with normal refraction.
[3] As opposed to cataracts that are secondary to various pathologies.

Our various organs age in their own specific ways.

FIG. 1 | Giovanni Serodine (1594-1630), "Ritratto del padre" (Portrait of the artist's father), 1624. Oil on Canvas, 152 x 98 cm. Lugano, Museo Civico d'Arte Lugano.
Photo: akg-images / André Held

in our times and thanks to remarkable technical developments, is now a precise, short, out-patient procedure which restores normal vision. This condition, which has been recognised since antiquity, but whose nature was not specified before the start of the 18th century, was previously treated by lowering the crystalline lens[4]. It was Jacques Daviel[5] who proposed, in around 1760, substitution of this lowering by extraction of the crystalline lens, thus opening the way to a surgical technique that has been gradually perfected to reach current practice.

It is in the retina that the signs of ageing are the most harmful to vision and the origin of major visual handicaps. Age-related macular degeneration (AMD) is the most common of these handicaps and is, understandably, feared amongst the ageing population. With age the retina regularly loses photo-receptor cells (cone and rods) but without affecting vision, since 30% of them are enough to maintain what we consider to be normal vision. On the other hand, AMD affects around 25 to 30% of men and women aged over 80. It is the consequence of a degenerative alteration of the retina, which is expressed in an impact to central vision, vision which is used for reading and seeing colours, whereas peripheral vision is maintained. It can occur from the age of around sixty, but only in a very low percentage of cases. This percentage increases regularly with age. AMD is expressed in two ways: the most common is a slow-progression, dry form, characterised by the presence of lipid deposits or "drusen" on the macula and, to a lesser extent, a fast-progressing exudative or "wet" form, characterised by major vascular proliferation. It is in this second form that injections of anti-vascular proliferation factors into the vitreous humour permit clear but fragile stabilisation of macular alterations. Dry forms of AMD do not require this treatment, which is the first real treatment available for the wet forms of AMD. We now know what drusen are made of and we know in part the reasons for their formation. It has been clearly established that high-risk factors encourage the appearance of AMD (age, tobacco, oxidative) but also that major genetic factors are involved and these are beginning to be identified with precision. The result of all these causes being the alteration of microglial cells which contribute to the formation of "drusen" and crucial modifications to the cells in the pigmentary epithelium which we know to play an essential role in the biology of photoreceptors.

Although AMD is the major retinal complication during the ageing process, added to it are slow degenerative modifications to the retinal periphery or the role of degeneration of the vitreous humour which, since they cause the separation of its intimate relations with the retina, may be the cause of retinal tears which are themselves responsible for retinal detachment. There is a particularly large incidence of these cases in myopics over the age of fifty. Is it incongruous to attribute to ageing the aggravation of the lesions of a pigmentary retinopathy which, whilst compatible with a normal life up until middle age lead, over the last years, to total blindness?

It is often during an examination by the ophthalmologist that a patient is found to have ocular hypertension and glaucoma. Patients are usually unaware that they are suffering from this terrible disease since at the outset it is entirely without symptoms. Without treatment we know that it leads to optic atrophy. Although genetic factors now appear to be responsible for some of these cases of glaucoma, it is nonetheless true that it is modifications to the trabecular space which are responsible for the failure in excretion from the aqueous humour, which conditions ocular hypertony. These alterations are conditioned, more or less, by age which, in any case, will intervene in late failure of the optic nerve, due to associated vascular factors. Although open angle glaucoma, to which we have just referred, is influenced by age, there is another condition that is totally linked to it: closed angle glaucoma[6], which is acute sudden-onset glaucoma, causing terrible eye pain and vomiting, and requiring emergency treatment. It is caused by the narrowness of the iris-corneal angle, which has remained sufficiently open for most of the patient's life but which suddenly closes for a variety

[4] The eye and the crystalline lens were transfixed with a thorn or needle; it was detached and lowered into the vitreous body where it remained and was more or less well tolerated.
[5] *Jacques Daviel, Un oculiste au siècle des lumières*, Yves Pouliquen, Odile Jacob, 1999.
[6] The angle is the narrow area between the root of the iris and the posterior side of the prelimbic cornea. It is where the aqueous humour is filtered, which being secreted by the ciliary body comes out of the eye through the intermediary of this filter. Its obstruction is responsible for chronic hypertony of open angle glaucoma and acute closed angle glaucoma.

FIG. 2 | Jean Fouquet (1420-1481), "Portrait of the Ferrara Court Jester Gonella", 1442. Vienna, Austria.

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of reasons, either due to drugs making the dilated iris responsible for obstruction of this narrow angle, or due to swelling of the crystalline lens with cataract, encouraging occlusion of the angle under the effect of an associated cause. A simple iridotomy[7] by laser can now avoid it when observation of the anterior segment shows that it may occur.

Although expressions of ageing on the eye mainly affect the clinical forms previously mentioned, there are many other signs. We have all noticed the changes that affect the eyes with age. Those eyes that were so fascinating lose their sparkle and those previously highly colourful irises have now become dull. De-pigmentation of the iris is the cause of this, the pupil that was previously so black turns greyish in colour and the cornea that was so transparent often bears at its periphery a white ring, known as arcus senilis. The conjunctiva itself becomes dull and its pingueculas look more yellowish. And what about the eyelids that crease due to alterations to the conjunctive tissue that filled them out? The folds that occur cause many patients to contact a plastic surgeon. Distortion, with their eversion position in the ectropion, bearing witness to very great age, require surgical treatment in order to avoid corneal-conjunctival complications. And what to think about the "bags" that hang over or underline the eyelids and which are linked to the failing of an orbital septum, itself the victim of tissular degeneration? And why do old people so often have watery eyes?
A condition that causes eyelid distortion and, above all, late onset obliteration of the tear ducts. This is an extremely common and unpleasant handicap but to a lesser extent than the reverse, the constitution of ocular dryness, which is responsible for chronic keratitis and the need to humidify the eye several times a day…
All small ailments in the face of other more major disorders. Those we have taken a look at and also those which no doubt find their most painful expression in lesions to the optic pathways which can be caused by ageing. Factors which are for the most part of vascular origin – linked to atheroma, hypertension, diabetes – are responsible for serious and often irreversible visual disorders in the retina: obliteration of the central artery, thrombosis of the central vein, in the optic nerve, acute ischemic optic nevritis of the retrochiasmatic visual pathways, with the consequence, most often, of homonymous lateral hemianopsia or even cortical blindness. Stable hemianopsia, which should not be confused with hemianopsic scotoma, which rapidly resolves the ophthalmic migraine that is so frequently encountered after the age of seventy, is entirely benign.

Will we be able to write another story one day? The story of humans who could live up to the limits estimated by science, at least thirty years longer than our current averages, without any expression of ageing, where one can imagine how difficult it would be to have to die, without understanding the reason. •

[7] Perforation of the iris at its root.