BRIEF REVIEW

Aging and the lacrimal system

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The lacrimal system consists of the lacrimal glands, the tear film in contact with the conjunctiva and cornea, and the lacrimal drainage system through the nasolacrimal duct to the nose. In this review the age related changes in this system will be given, including tear chemistry of the tear film. Certain aspects of tear physiology change with age, such as reflex secretion by the lacrimal gland, tear volume, and tear film stability, whereas others remain more or less unchanged, such as basal tear production.

The reflex secretion of tears, as measured by Schirmer's I method (without anaesthesia), decreases significantly with increasing age as already was observed by Schirmer[1] in 1903 and by many others thereafter.[2–20] The age groups investigated mostly cover the 20–80 age range and the reduction in Schirmer values from the youngest to the oldest age group is about 70%. In contrast with these findings Xu and Tsubota[21] and Nava *et al*[22] failed to demonstrate the decline of the Schirmer I value with age although in both studies the numbers of subjects were large. This discrepancy is probably attributable to the acknowledged variability in the performance of the Schirmer test—that is, in the latter studies the patients were asked to blink normally after placing the Schirmer strip. It is conceivable that blinking causes an extra irritation, which in elderly people may increase reflex tearing compared with a closed eye condition, such as is employed mostly. Newborn babies secrete tears in the first 24 hours of life.[23] Premature infants may fail to secrete tears at birth, depending on the degree of prematurity.[24] A negligible number of tears are formed during sleep,[1 25 26] in the course of which the protein pattern is also altered dramatically.[27] The basal tear production, as measured by fluorophotometry from the decay of fluorescence after instillation of fluorescein solution in the eye, was found to decrease with age,[28 29] to increase,[26] or to show no significant correlation[20 30–33] in the age range between 10 and 90 years. The volume of tears present on the surface of the eye declines with increasing age.[7 20 29 34] Wide discrepancies in the absolute values of tear flow and tear volume were found, although the investigators used the same method of fluorescein dilution. Probably the difficulty in avoiding stimulation during testing is the primary reason. Therefore, a standardised protocol for the measurement of tear turnover by fluorophotometry has been drawn up in cooperation with experts in different countries of the European Union.[31] Disappearance of fluorescein from the tear film after application of fluorescein in an eyedrop was found to be slower in the age group of 20–30 years compared with a group of 50–65 year olds,[35] which was ascribed to slower drainage and tear production in the older age group resulting in longer corneal contact time of the eyedrop. The increase in corneal penetration of fluorescein with advancing age[36 37] seems to be the result of a greater corneal contact time rather than a rise in epithelial permeability.

The lacrimal transit time through the nasolacrimal duct, measured with a modified Jones test by the time of appearance of fluorescein on a cotton applicator in the nose, slows with age.[38] Also a decreased lacrimal drainage capacity was found with increasing age when measured by the drop test.[33] In the drop test the disappearance of fluorescein is measured after repeated instillation of drops of 10 µl of lukewarm saline solution into the conjunctival sac over 3 minutes. The volume of saline solution drained by the lacrimal passage can thus be calculated.

The tear evaporation rate has not been found to be correlated with age.[39 40] The evaporation is primarily controlled by the lipid layer of the tear film and lipid layer thickness appears to be constant for different age groups.[41]

The tear film stability, as measured in seconds by the tear break up time (BUT, the time needed after blinking of the fluorescein treated eye for the appearance of dark spots in the fluorescence of the tear film) is independent of the patient's age according to Norn[42] and Lemp and Hamil,[43] who introduced this method for clinical use. More recent studies report an increase with age in the number of BUT values of less than 10 seconds.[44–46]

Various morphological changes increasing with age were observed in the lacrimal gland, especially periductal fibrosis, which is speculated to be related to the decrease in tear outflow with age and interlobal ductal dilatation, which may be caused by stenosis of the excretory duct in the fornix of the conjunctiva.[47] Magnetic resonance imaging showed sex related influences on the lacrimal gland structure during aging. The thickness and area of the lacrimal gland decreased with age in women, but not in men. Furthermore, the signal intensity of magnetic resonance increased with age only in women.[48] The goblet cells of the conjunctival epithelium produce the mucous component of the tears, which enables tears to stick to the corneal surface. Reports on goblet cell counts in the conjunctiva in relation to age show discrepancies. Abnormal goblet cells, containing a high proportion of neutral rather than acidic mucopolysaccharides, and occlusion of goblet cells with retention of their contents were reported to increase with age.[49] Reduction in the goblet cell population was observed in subjects over 60 years of age[50] and in another study in those over 80 years.[51] In the latter this was sometimes associated with the presence of 'hyaline bodies', which are periodic acid Schiff positive and possibly represent a degenerative form of goblet cells. In a more recent study, using conjunctival impression cytology, in 73 healthy volunteers no correlation between age and goblet cell count could be demonstrated[46]; also by studying peroperative conjunctival biopsies from 54 patients with primary open angle glaucoma undergoing filtering surgery, no statistically significant difference was observed across three age groups between 40 and over 75 years.[52]

Normally the decreased reflex tear secretion capacity in the older eye may be compensated by a reduced lacrimal drainage.[40] The condition of 'dry eye' with subjective symptoms including burning, itching, sticking, dryness, mucus discharge, and foreign body sensation, occurring with increasing frequency in older patients may be caused by an imbalance due to abnormal low tear production or a

high evaporation rate. The lids may become less taut with age and this interferes with normal blinking function, causing a higher evaporation because the tear film is not properly restored over the ocular surface. In some cases the 'dry eye' is associated with defective mucus secretion or the presence of particulate matter in the tear film, which usually consists of mucus that is not remaining in solution because of moderately depleted tear flow. In other cases the tear production is still normal, and this defect in mucus secretion with its secondary irritation may lead to overproduction of the aqueous part of the tear film. This aggravates the condition and may confuse the clinical picture.[53]

The composition of tears is rather complex and varies over a broad range of normal levels for the different components.[54] Moreover, the method of tear collection may influence the composition. Stimulation of tear flow may result in lower values if the component under investigation is derived from the cornea or conjunctiva. Microtrauma caused by Schirmer test paper or cellulose sponges in the conjunctiva may increase leakage of plasma components and tissue cell content into the collected tears. Furthermore, diurnal variation in the concentration may contribute to variation in test results, such as has been described for lysozyme.[55]

Conflicting reports exist as to the effect of age on IgA levels, some reporting a slight decrease with age[56] while others give a gradual increase[57] or no difference.[58] Tears collected with capillaries[57] showed lower mean values of about 300 mg/l compared with the samples collected with filter paper[56] and sponge,[58] with mean values of about 600 mg/l. At birth no IgA is detected in children's tears but within 2 weeks it had risen to a level of 20 mg/l.[59] Adult values were found at about 4–8 years of age.[59 60] Fluorescent antibody staining of IgA in plasma cells in biopsies of accessory lacrimal glands of the conjunctiva showed no trend with age.[61] Some authors found organised mucosa associated lymphoid tissue (MALT) in the normal human conjunctiva,[62–64] others found it only in 31% of cases and suggest that MALT is acquired during life in a proportion of apparently asymptomatic individuals.[65]

Under physiological conditions levels of albumin, IgG, and caeruloplasmin in tears of adults remain low and static until an apparent increase after the fifth decade.[58] At birth IgG and albumin are about threefold higher than adult levels, probably reflecting a propensity for transudation from the plasma, but by 2–3 months they drop to near adult levels.[59] Age increased leakage of conjunctival vessels[66] and conjunctival hyperaemia[67] might be held responsible for the elevated levels of these plasma derived proteins at older age. In pathological conditions local production of IgG by conjunctival tissues has been suggested.[68 69]

The lacrimal gland proteins lysozyme[56 70–73] and lactoferrin[56 74] decline linearly and progressively with age in adults with a reduction of about 35% over the range 20–80 years. Lysozyme is not detected in children's tears at birth but within 2 weeks attains a level of 170 mg/l.[59] Adult values are found at about 4–8 years of age.[59 60]

Osmolality in tears of normal eyes generally remains within the limits of 280–330 mOsm/l and reportedly is not significantly affected by age[75–77] except in one study,[20] where over an age range of 10–85 years a significant increase in osmolality was found.

A variety of medications for various conditions, mostly outside the field of ophthalmology, are known to be inhibitory to tear production.[78 79] These drugs comprise β blockers, ganglion blockers, hypnotics, and sedatives such as phenobarbitone and benzodiazepines, neuroleptics such as phenothiazines, tranquillisers such as diazepam, and antidepressives such as dibenzazepines and monoamine oxidase inhibitors. Even aspirin exerts an inhibitory effect on the tear production[80] and a change in the composition of tears.[81] Therefore it is conceivable that in control people, considered to be normal or healthy, a diminished tear production is measured which is caused by these drugs. Moreover, if the consumption of these drugs is related to age then it is possible that in some studies the changes observed in several variables of lacrimal gland function are drug induced rather than age related.

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