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North-Western State Medical
University after I.I. Mechnikov

Physiological characteristics diffusion of fluid in the Lens and Vitreous Chamber of rabbits

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Krasnoyarsk, St. Petersburg, Russia 2018

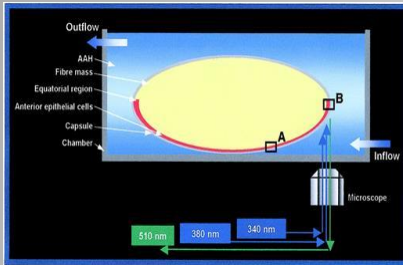
The functioning of the eye in norm and in pathology ensures the constancy of water exchange in its structures



<http://benefitspecialists.biz/blog/2012/10/when-should-your-child-receive-their-first-vision-test/>



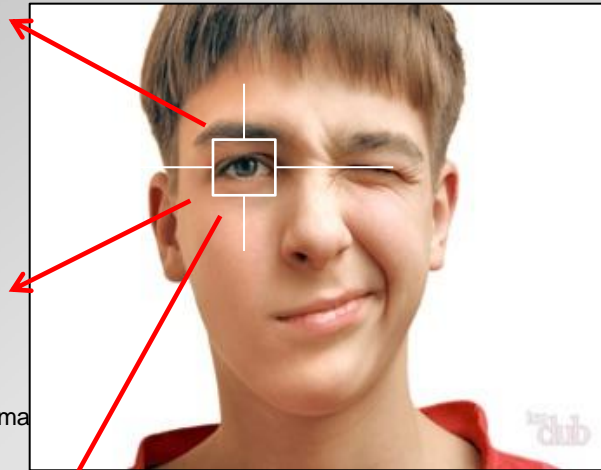
However, current studies of the movement of aqueous humor in the structures of the eye do not give a clear and unambiguous picture of the water exchange in the eye



<https://www.diabetesselfmanagement.com/managing-diabetes/complications-prevention/keeping-your-eyes-healthy/>



<http://www.ambu03.ru/sovremennye-klassifikaciya-i-farmakoterapiya-sindroma-suxogo-glaza/>

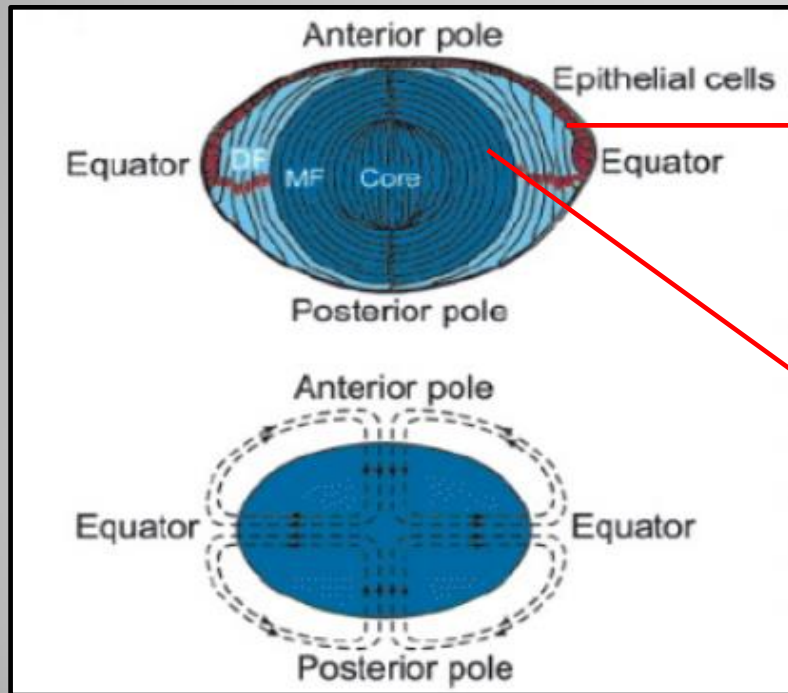


<http://www.wzglyad.ru/services/lazernaja-korrekcija-zrenija-u-detej/>



<https://www.daedalus.co.in/8-vital-career-questions-millennials/millennial-question/>

Traditional ideas about the movement of aqueous humor in the lens suggest its movement inside and out of the lens equally through the anterior or posterior capsule
 (Mathias R.T. et. al.,1997; Gao J. et. al., 2000; Ehsan Vaghefi et. al.,2012)
 and its surface distribution in the lens mass
 (Rae J. L. et. al., 1996; Buzhynskyy N. et. al., 2011)



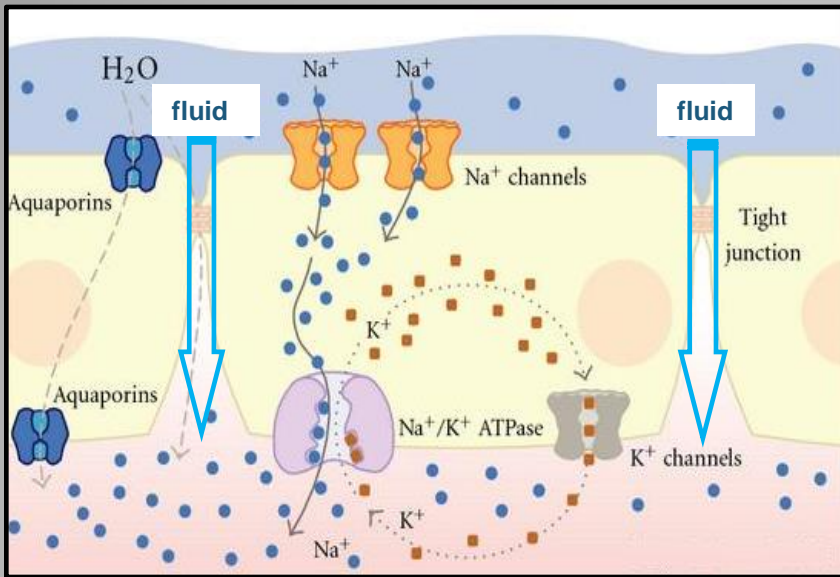
!?! not taken into account



physiological features of the epithelium of the anterior capsule - **transport properties**

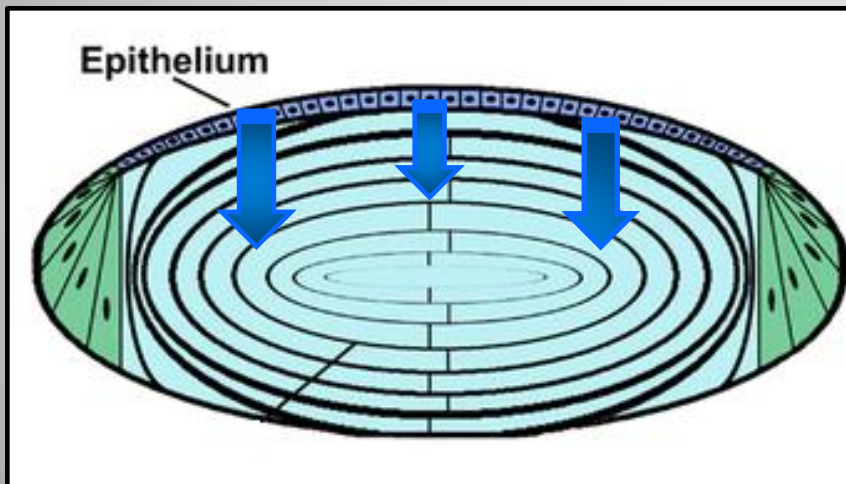
Rae J. L. et. al., 1996;
 Buzhynskyy N. et. al., 2011

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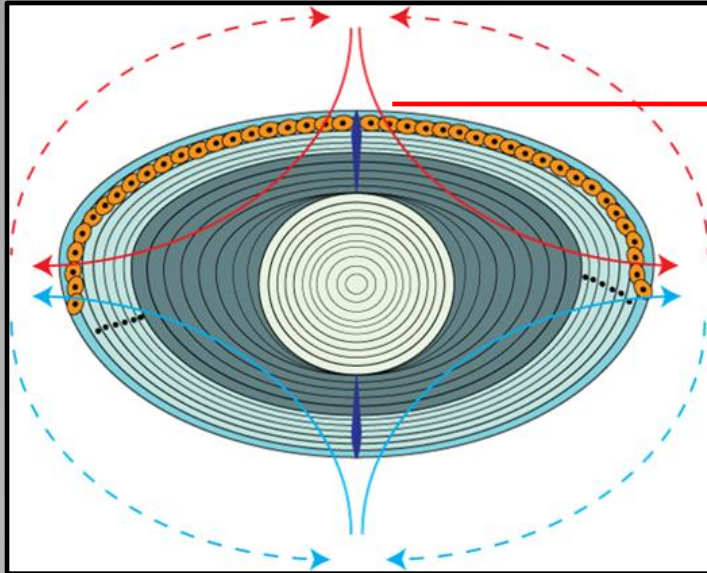
<https://basicmedicalkey.com/nutrition-digestion-absorption/>

Epithelial cells contain an ion exchange system Na^+ , K^+ -ATPase that due to active ion transport, creates their difference in concentration in the outer and inner space, increased osmolarity promotes fluid pumping (Bessonov B.I. et. al., 1997)



↓ - fluid pumping

https://www.researchgate.net/publication/236225664_Connexin_Mutants_and_Cataracts

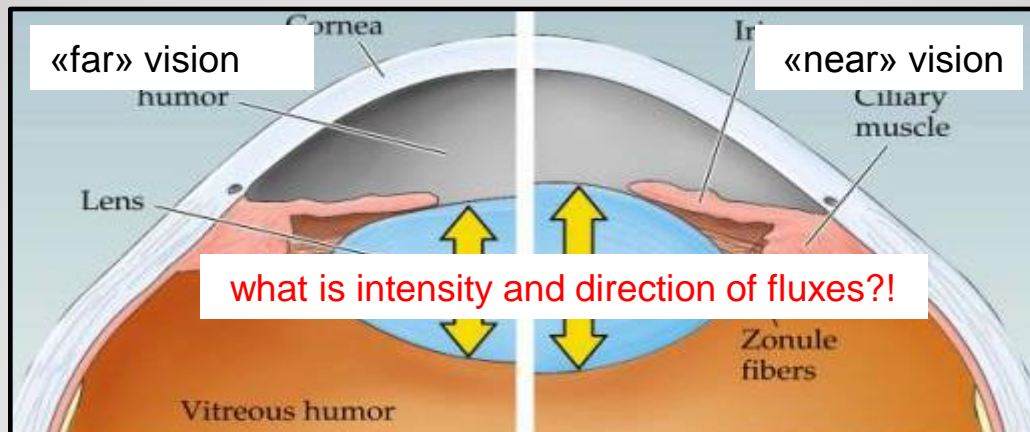


Ho-Ting D. Wu, L. A. Howse; E. Vaghefi, 2017

!?! not taken into account

the influence of a change in the pressure within the lens in different accommodation phases on the intensity or direction of water exchange

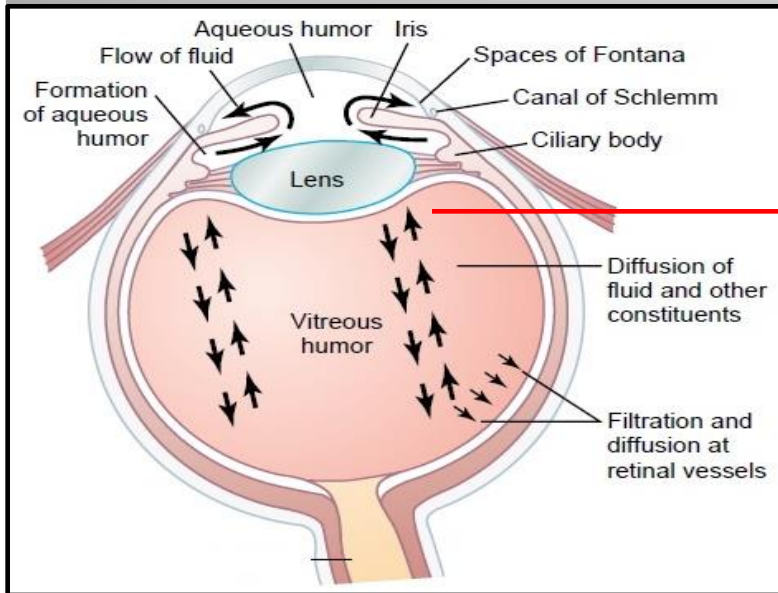
(Koschitc I.N. et.al., 2002, 2014, 2016, 2017; Svetlova O.V. et.al., 2016)



http://www.rci.rutgers.edu/~uzwiak/AnatPhys/Sensory_Systems.html

It is argued that aqueous humor can slowly diffuse in vitreous chamber, but little fluid outflow

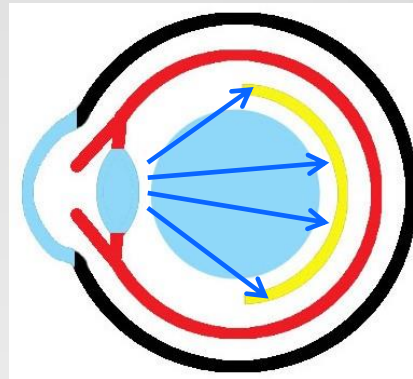
(Shilova O.G. et. al. 2012; Arthur C. Guyton et.al. 2017)



Arthur C. Guyton et.al. 2017

!?! not taken into account

the oncotic pressure created by the blood plasma in the vascular system of the eye is higher than in the vitreous chamber



the movement of aqueous humor in the vitreous chamber can occur only in the direction of the posterior eye through the gradient of the oncotic pressure **7**

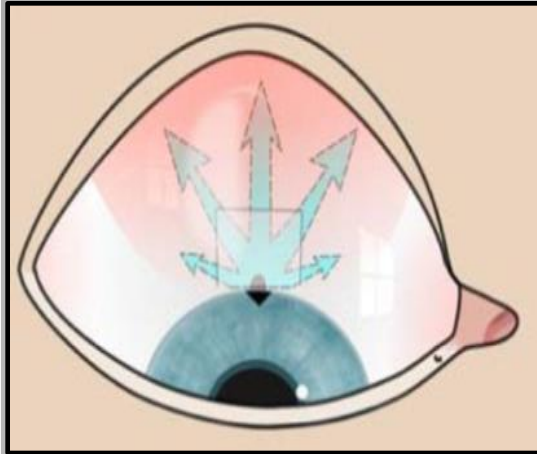
<http://bio-faq.ru/zubr/zubr040.html>

ophthalmology/eye clinic



Representations of water metabolism in the eye structures require adjustment.

This will allow a deeper understanding of the physiological features of the circulation of aqueous humor in the eye and the conditions for the development of eye diseases



<http://migs.org/wp-content/uploads/2016/07/how-it-works.png>

The purpose of the study:
to determine the mechanisms
of the water exchange processes
in the lens and the vitreous chamber
of the eye of a rabbit

Material of experimental research

N=88



- the breed "Soviet Chinchilla"
- weight 1.5-3.0 kg
- age 3-7 months
- both sexes
- without signs of pathology on the part of the eyeball
- kept in standard conditions in the vivarium

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The processes of water exchange in the eye were examined

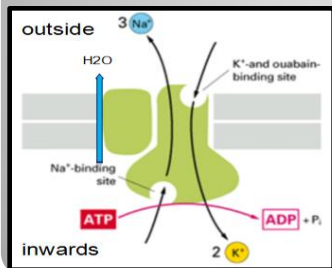
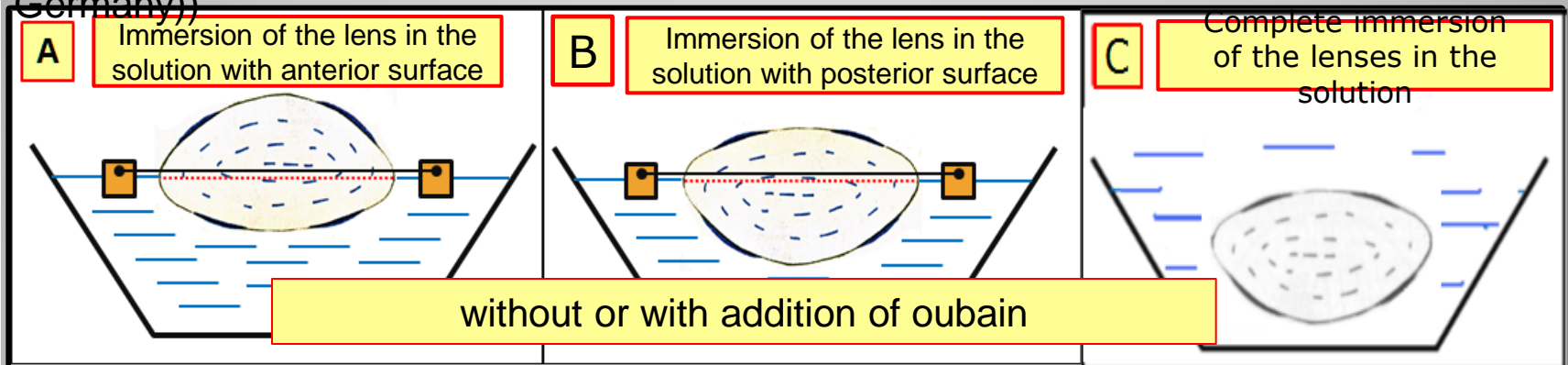
in vitro -
the state of the
accommodation phase
is «near» vision

in vivo -
the state of the
accommodation
phase is «far» *vision*

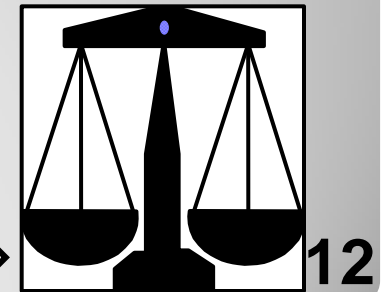
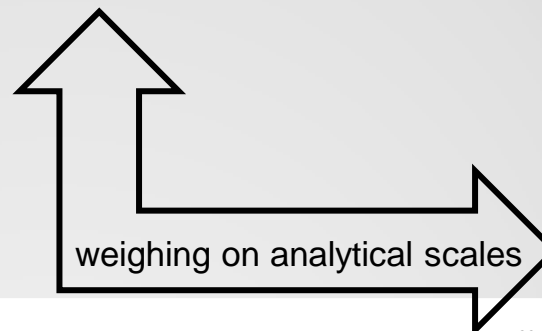
The processes of water transport in the lens were investigated *in vitro* by the change the mass of the lense

A , B - the incubation solutions are represented by a solution identical in ionic composition to moisture content in the anterior chamber (aqueous humor) or vitreous humor

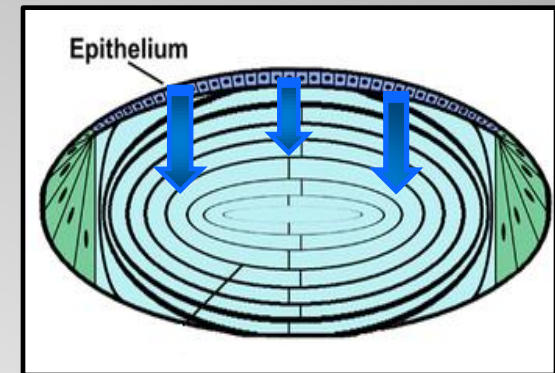
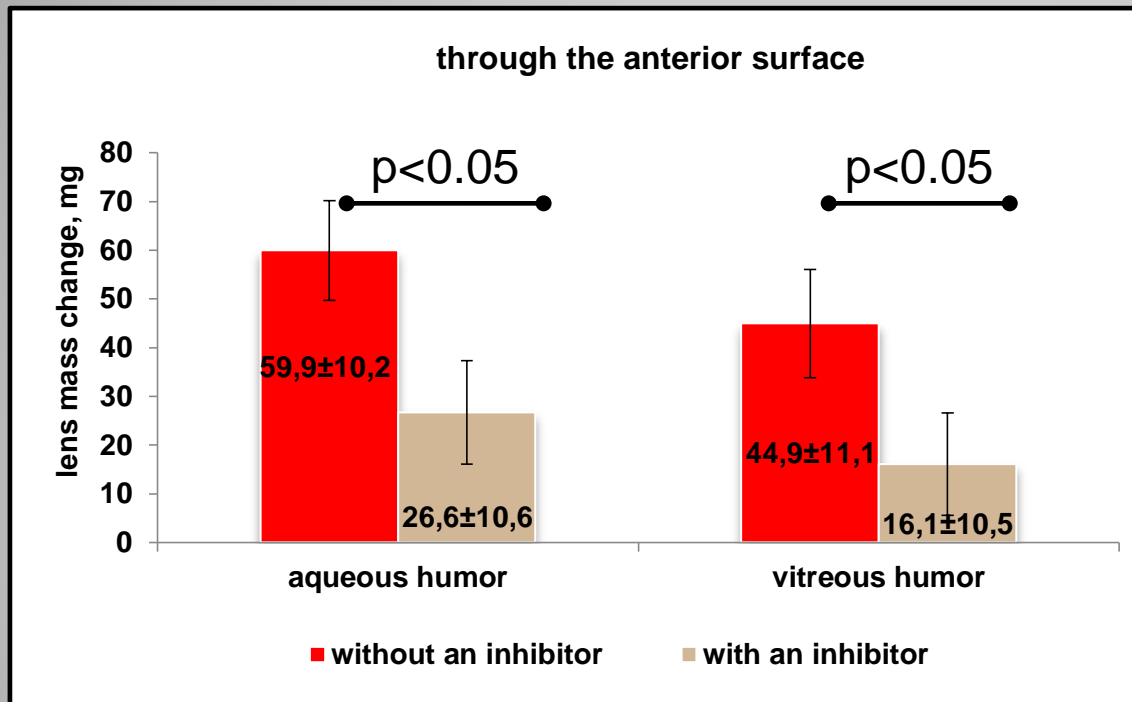
C - the osmotic pressure in the solution (aqueous humor) varied from 22 to 60 mm Hg, when a high-molecular substance is added (Polyvinylpyrrolidone, 60 kDa (BASF, Germany))



Oubain is an inhibitor of active transport system Na⁺, K⁺-ATPase



The work of the active transport system of Na⁺, K⁺-ATPase promotes the osmotic transfer of fluid inside the lens



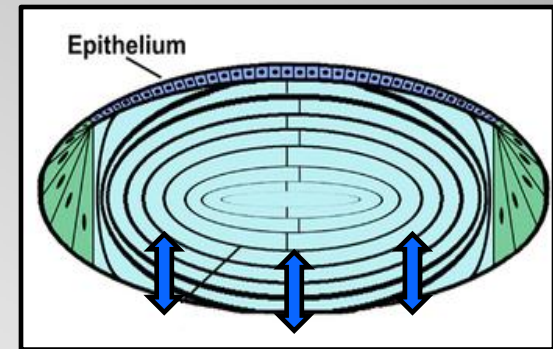
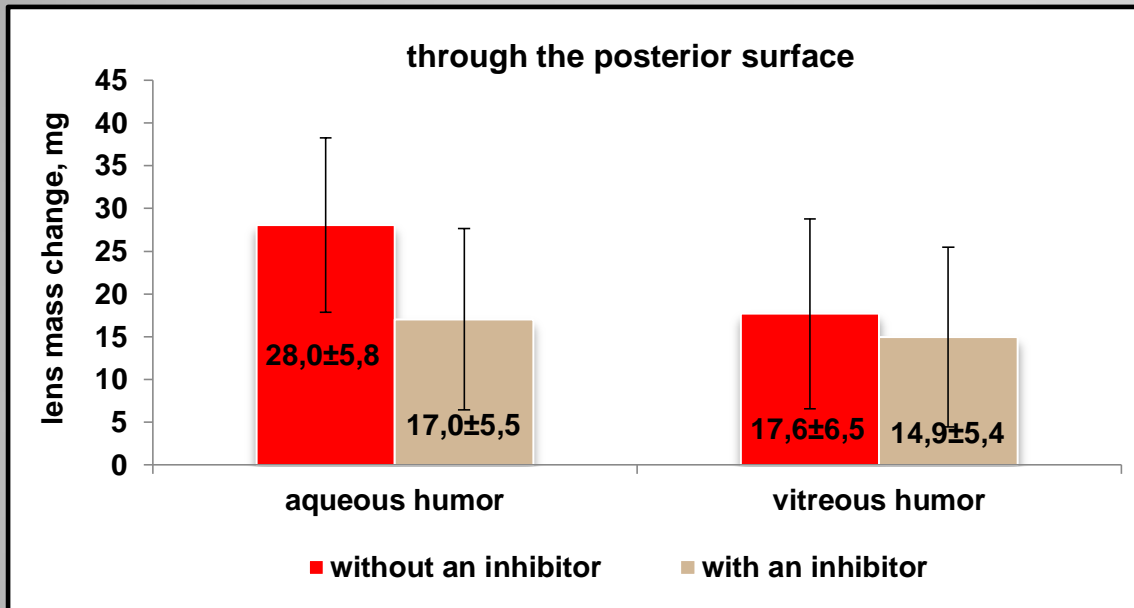
↓ - fluid pumping

https://www.researchgate.net/publication/236225664_Connexin_Mutants_and_Cataracts

Figure 1 - Change in the mass of the lenses when they are immersed in the incubation solutions with the anterior surface

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The inhibitor of Na⁺, K⁺-ATPase did not affect the flow of fluid through the posterior surface of the lens.
Transport of fluid through the posterior surface of the lens capsule occurs through diffusion



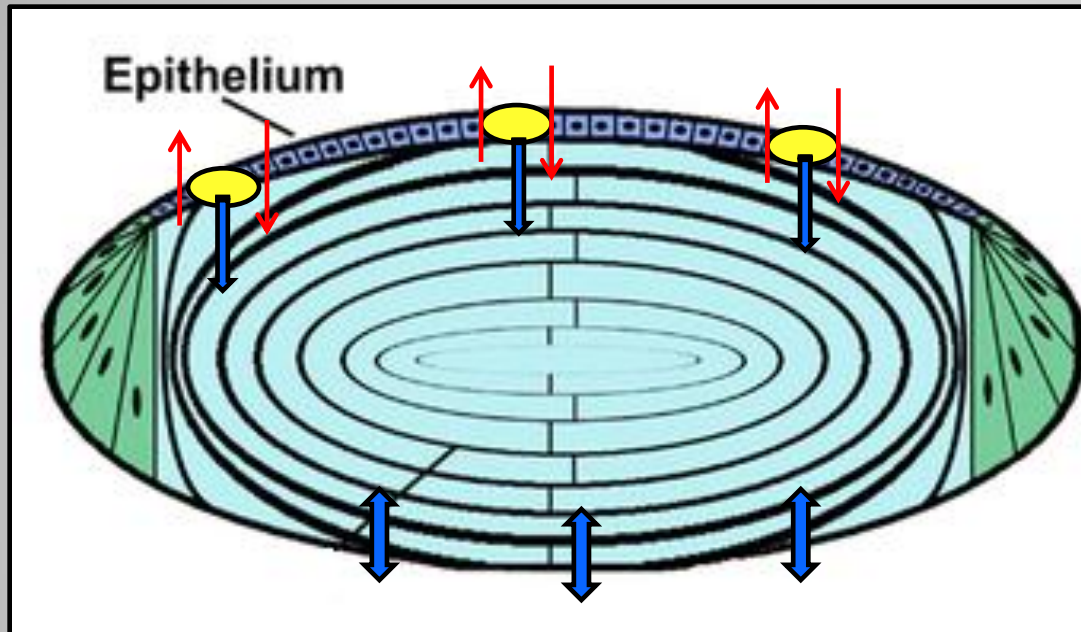
↕ - fluid diffusion

https://www.researchgate.net/publication/236225664_Connexin_Mutants_and_Cataracts

Figure 2 - Change in the mass of the lenses when they are immersed in the incubation solutions with the posterior surface

The anterior surface of the capsule of the lens is represented by a monolayer of epithelial cells. The epithelium of the anterior surface of the lens participates in the transport of aqueous humor inside the lens

anterior surface



posterior surface

- Na⁺, K⁺ -ATPase
- fluid diffusion
- fluid pumping

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https://www.researchgate.net/publication/236225664_Connexin_Mutants_and_Cataracts

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The process of water exchange in the lens occurs with the participation of the active transport system $\text{Na}^+, \text{K}^+ \text{-ATPase}$

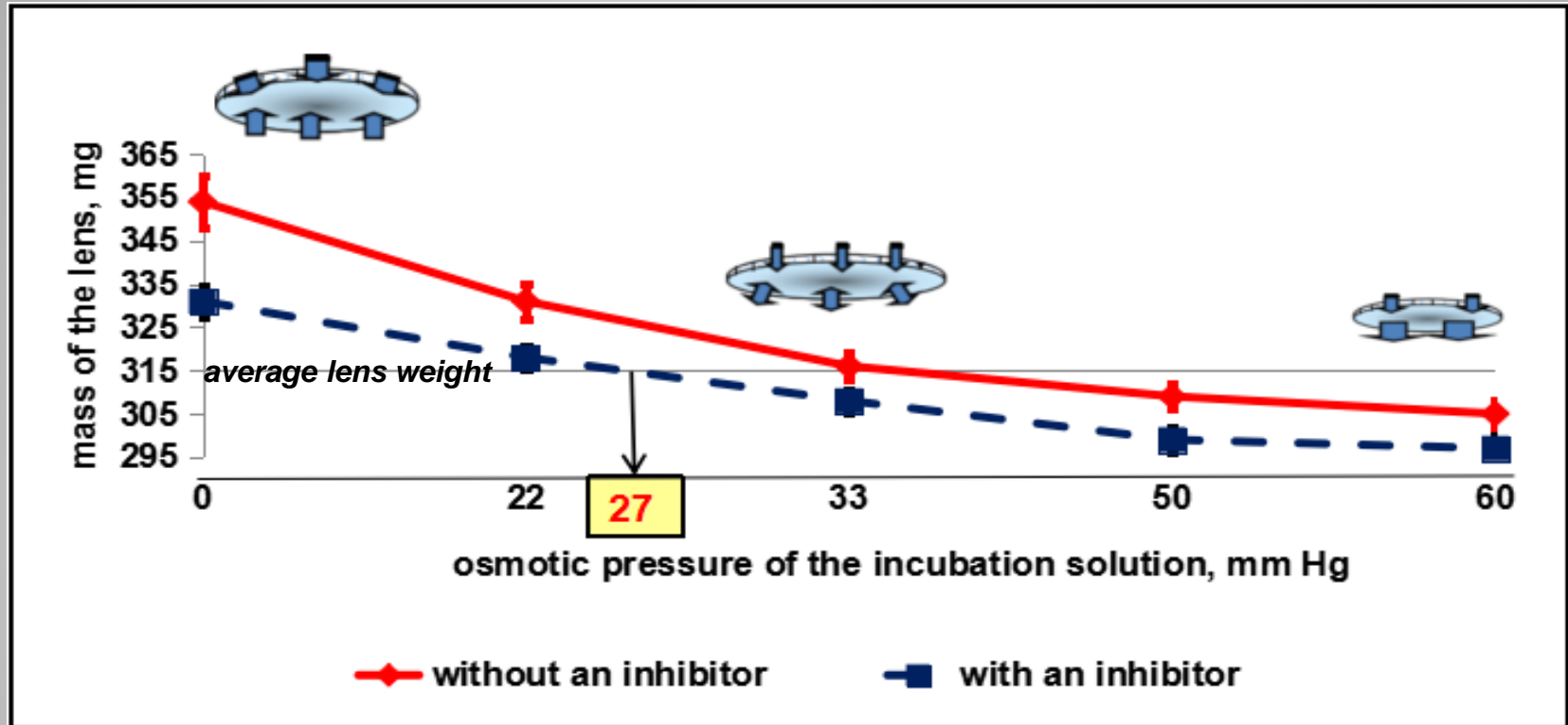
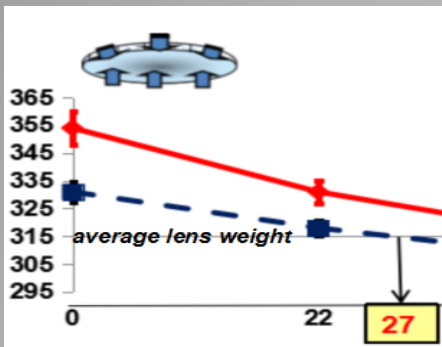
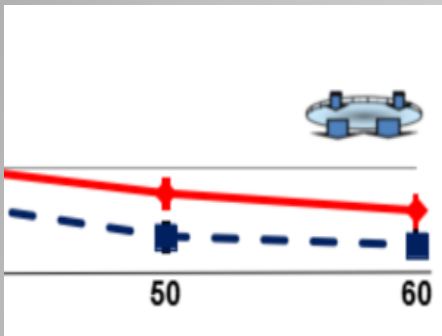


Figure 3 - The change in the mass of the lens in the incubation solution with different by osmotic pressures (Arrows indicate the priority directions of fluid movement)

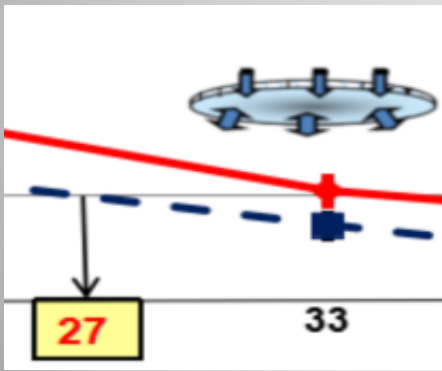
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- the osmotic pressure in solution 0 - 27 mm Hg - intensive flow of aqueous humor into the lens through the epithelium by means of osmosis

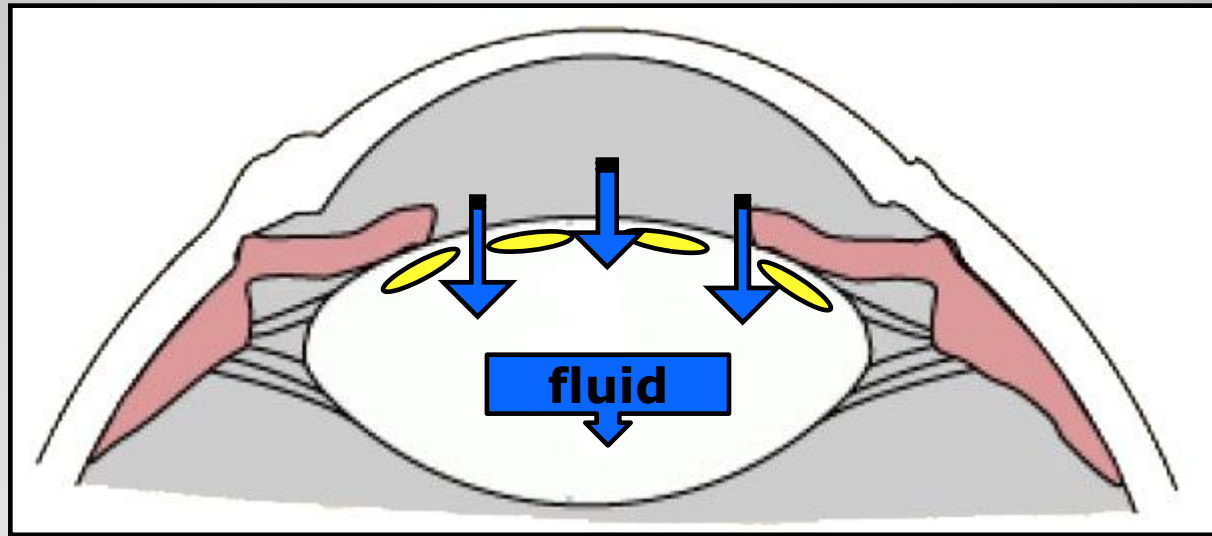



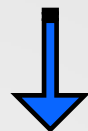
- the osmotic pressure in solution 33 - 60 mm Hg - the lens partially lost its free fluid due to the difference in pressure



- the osmotic pressure in solution 33 mm Hg - this pressure in the lens, when the oncotic pressure in it is balanced by the transport system. The oncotic pressure of the lens is 27 mm Hg produced by proteins. The difference in the values of the osmotic and oncotic pressures is 6 mm Hg determines the efficiency of Na^+, K^+ -ATPase

The active transport system (Na^+ , K^+ -ATPase) in the epithelium pumps the fluid inside the native lens and can promote directional diffusion movement of the fluid outward with additional help from the lens capsule, which compresses its lens mass



 - Na^+ , K^+ -ATPase  - fluid

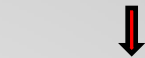
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The intraocular fluid movement in the lens was studied *in vivo* by the "stopped diffusion" method

10% fluorescein solution



intravital dye introduction into the lens and into the vitreous chamber



enucleated



froze with liquid nitrogen



dissected on microtome
(Slide 2002 Compact, Germany)



photographed
(Olympus Camedia C-50, China)

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Intravital distribution of fluorescein in the lens

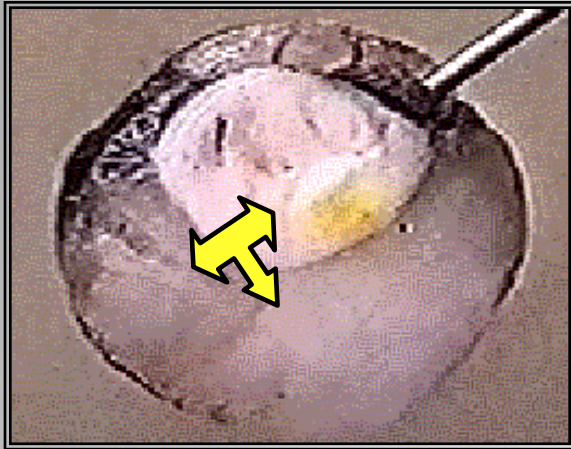


Figure 4 - 10-15 min after dye introduction

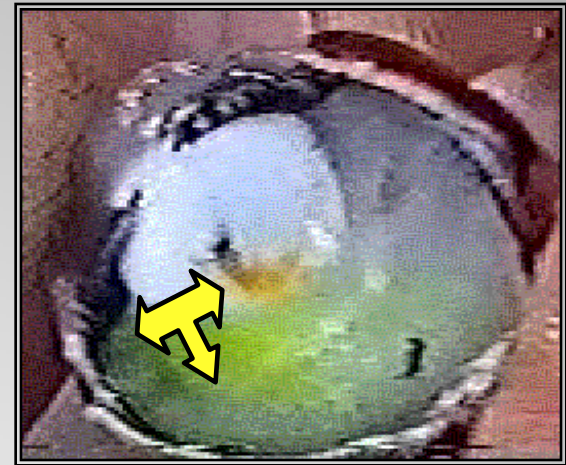


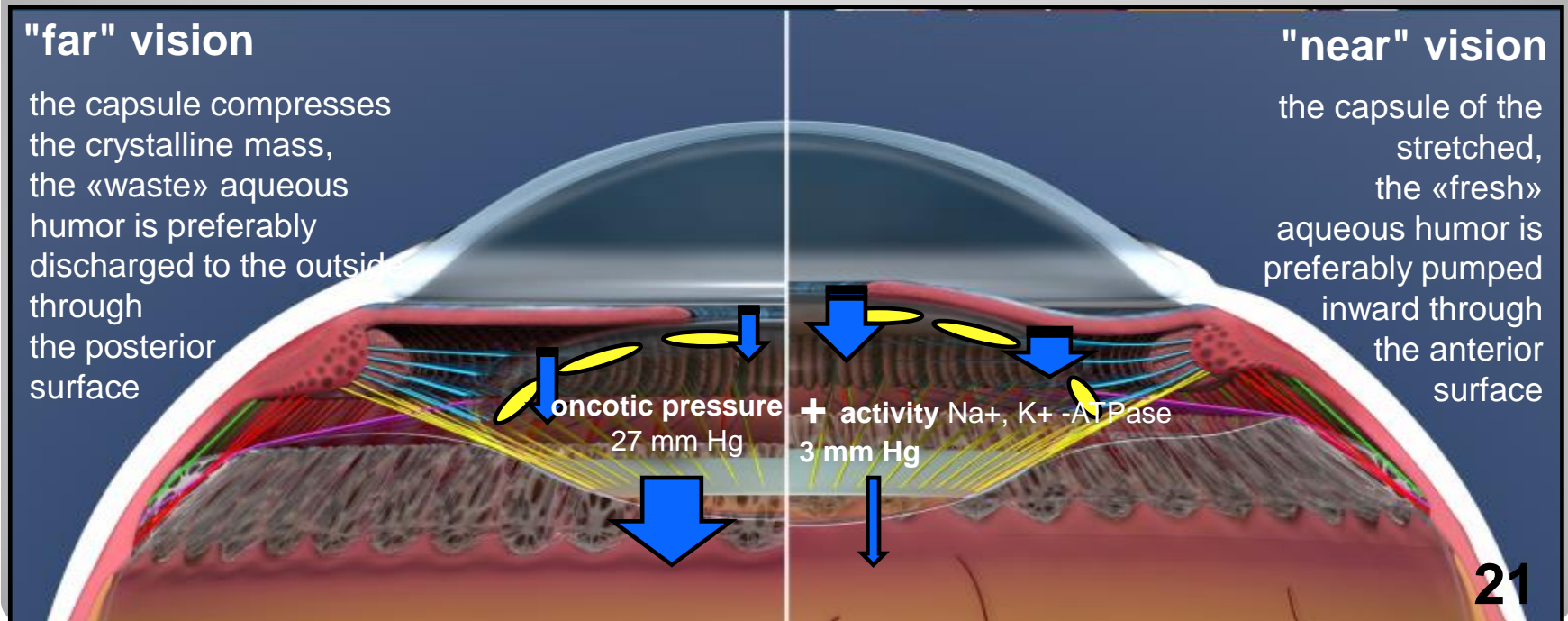
Figure 5 - 25-30 min after dye introduction

The spread of the dye in the lens occurred in the direction from the anterior surface of the lens to its posterior surface

In the unfrozen enucleated eye, the distribution of the dye was observed both towards the anterior surface of the lens and into the vitreous chamber of the eye

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The directional movement of fluid from the anterior to posterior surface of the lens is formed by the transport system of Na^+ , K^+ - ATPase, which is localized in the lens epithelium (the determining mechanism) and the pressure inside the lens in different accommodation phases (an additional mechanism)



Intravital distribution of fluorescein in the vitreous chamber

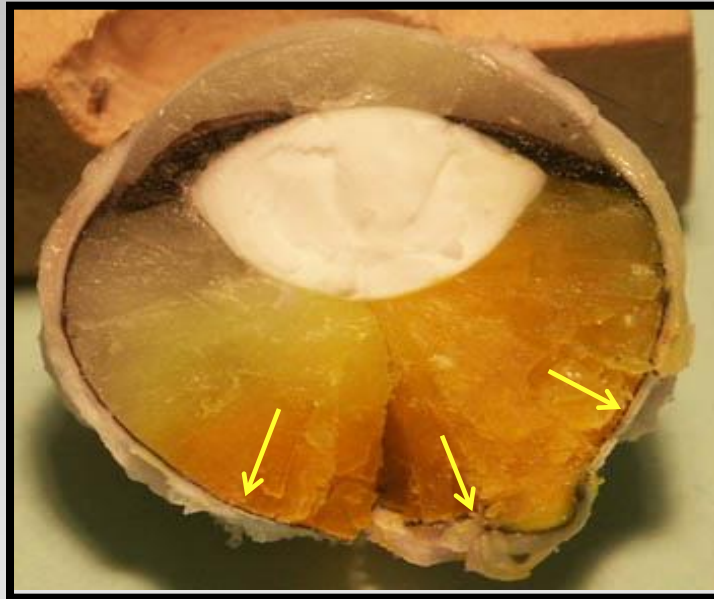
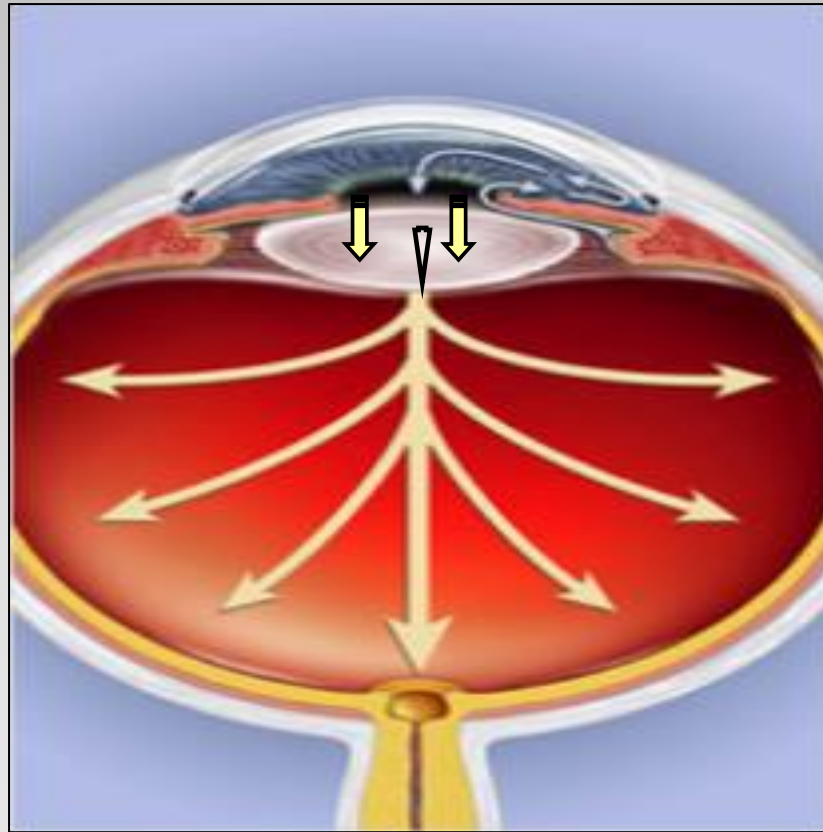


Figure 6 - Distribution of fluorescein in a vitreous chamber

The spread of the dye in the vitreous chamber occurred in the direction toward the posterior part of the eye, movement to the anterior part of the eye did not occur

The movement of fluid in the eye is directional and occurs from the lens to the vitreous chamber, followed by movement to the posterior part of the eye

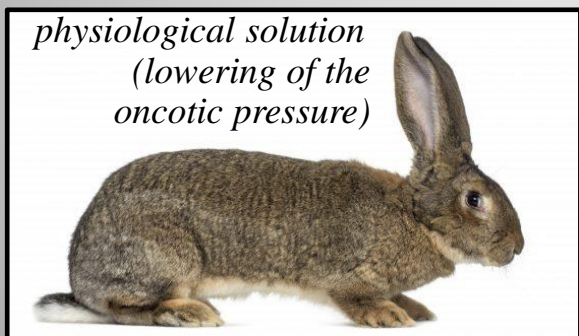
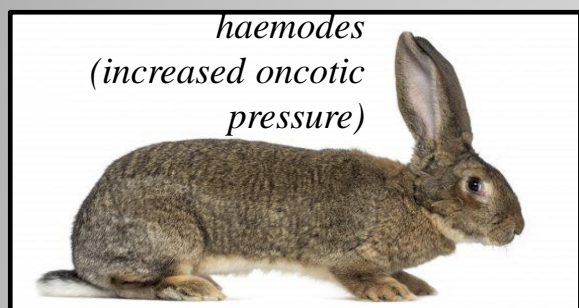


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The removal of the fluid from the vitreous chamber was determined by the fluorescence method, fixing the accumulation of the dye in the vascular system with different oncotic pressure

intravenous injection

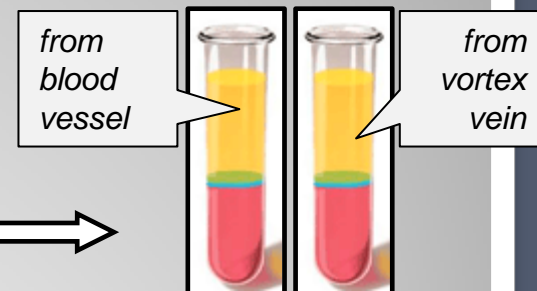


10% fluorescein solution



intravitreal injected into the vitreous chamber

blood plasma



fluorescent spectrometer
(Thermo Spectronic, USA) **24**

The fluorescein concentration is greatest in the hydrous veins of the eye, the veins of the circulatory system are smaller

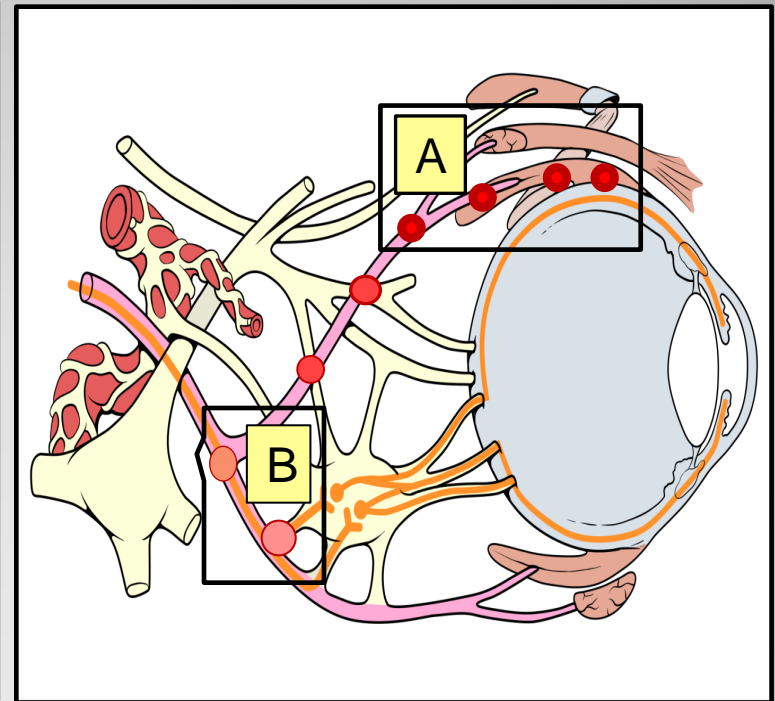
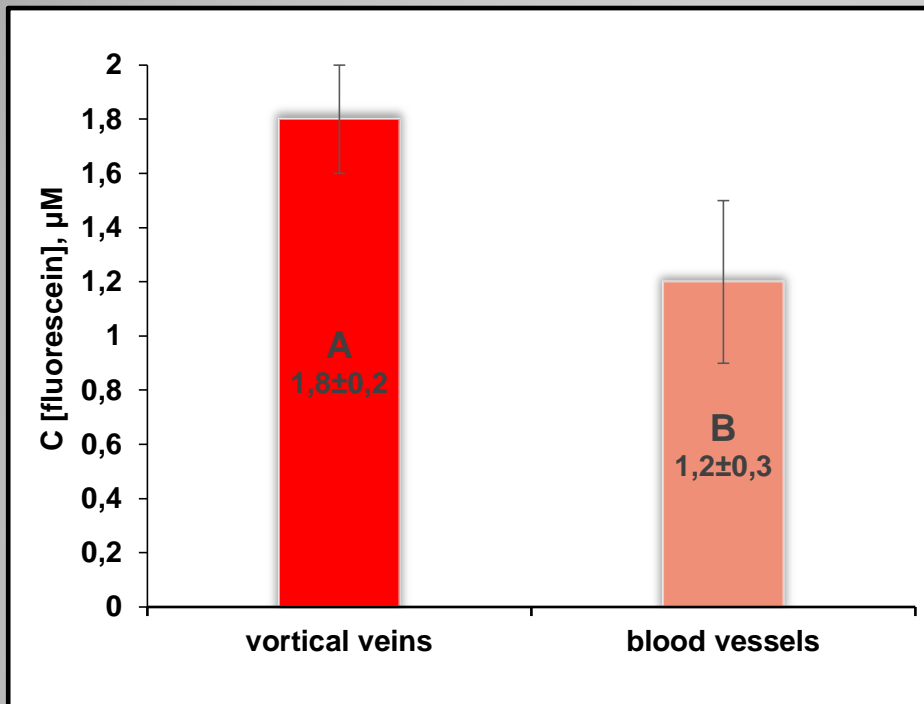


Figure 7 - Concentration of fluorescein in the circulatory system https://commons.wikimedia.org/wiki/File:Eye_nerves_diagram.svg

Increased oncotic pressure in the vascular system increases the outflow of intraocular fluid, a decrease - slows its outflow from the eye

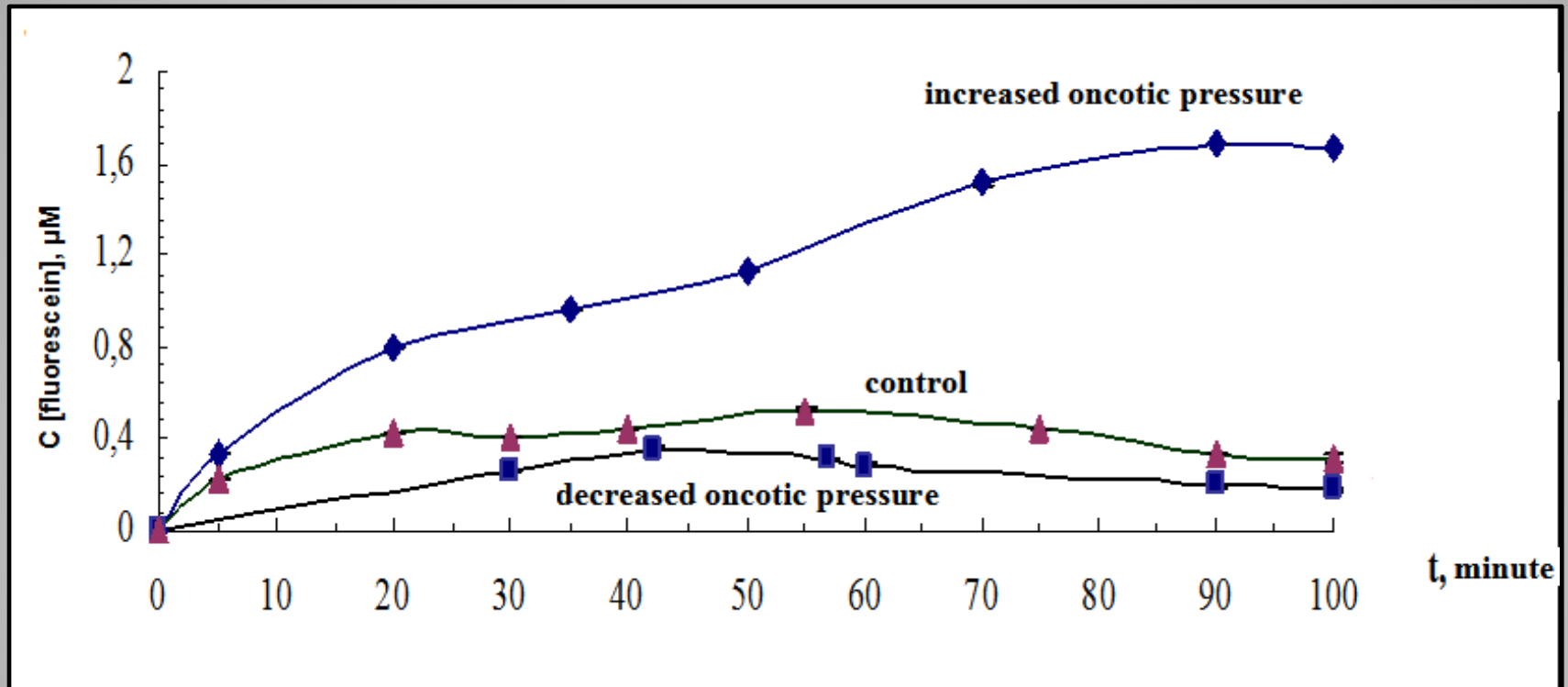
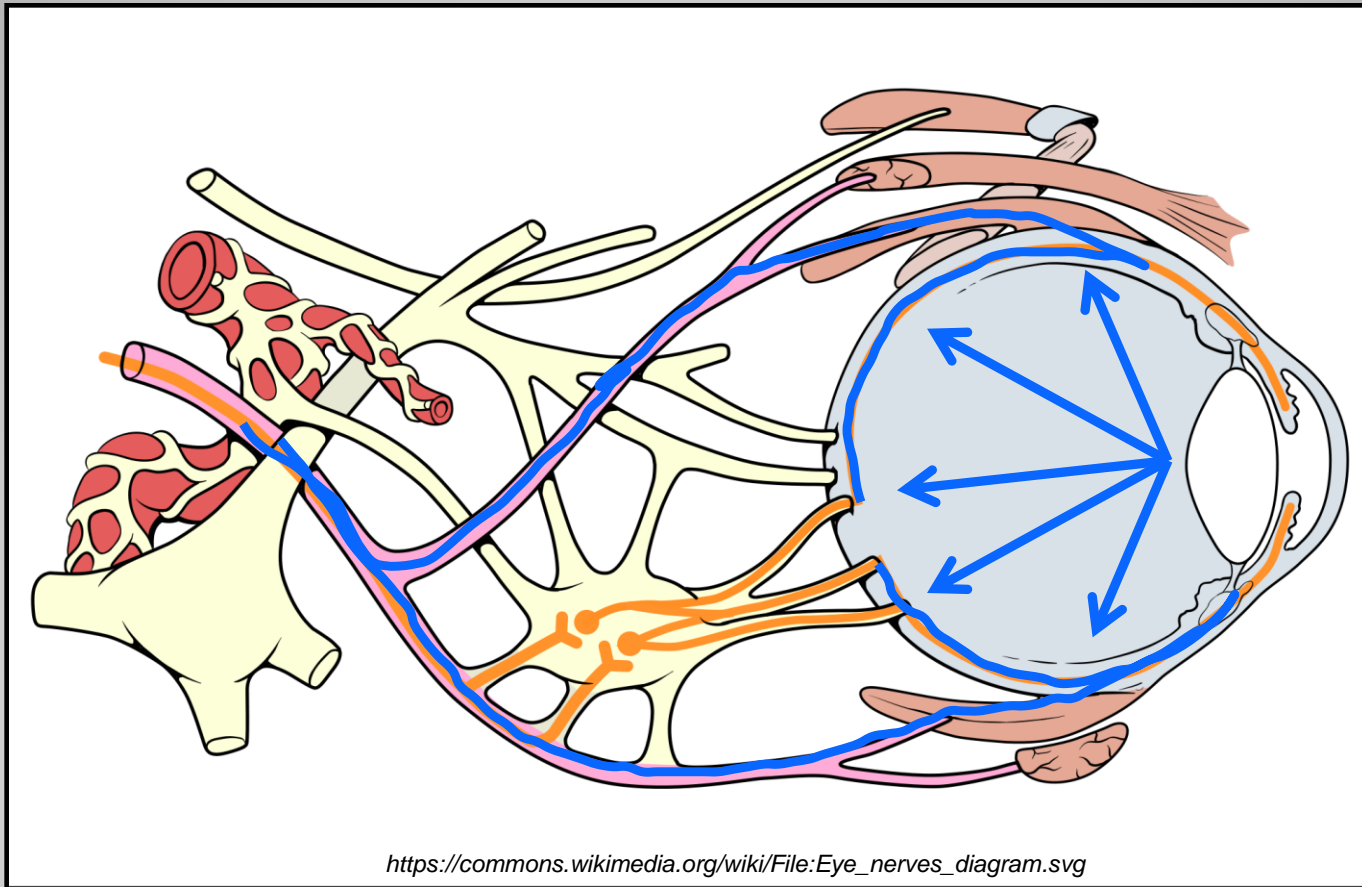


Figure 8 - Accumulation of fluorescein in blood plasma with increased or decreased oncotic pressure in the circulatory system

Aqueous humor from the vitreous chamber is diverted into the veins of the vascular system of the eye and discharged into the circulatory system



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Conclusion

- ① The determining mechanism that provides normal feeding of the lens with "fresh" aqueous humor is active ion transport with the participation of Na^+ , K^+ -ATPase, which is located in the epithelium of the anterior capsule of the lens
- ② An additional mechanism that helps to remove the "spent" aqueous humor from the lens is a change in the amount of pressure inside the lens in different phases of accommodation
- ③ Osmotic pressure in the environment of the lens should be above 30 mm Hg in order to maintain a constant volume of aqueous humor in the lens, i.e., incoming watery moisture inside the lens due to osmosis was compensated by outgoing aqueous humor outwards due to diffusion

Conclusion

- ④ The lifelong movement of aqueous humor in the eye occurs in the direction from its anterior surface of the lens to the posterior and then exits into the vitreous chamber, where it is retracted through the retina into the vortex veins of the vascular system and discharged into the circulatory system. The rate of excretion of aqueous humor depends on the oncotic pressure in the circulatory system.
- ⑤ A possible way to successfully combat initial cataract and presbyopia is to ensure the normalization of metabolic processes by excluding the maximum rounding of the lens with prolonged comfortable work in the vicinity with the help of rational correction

Conclusion

- ⑥ Irrational correction can contribute to the accelerated development of cataracts, especially in glaucoma eyes in combination with myopia, as the flattened state of the lens reduces the effectiveness of the actuators removing the "spent" aqueous humor

- ⑦ Accelerated development of cataracts in the glaucamatus myopic eye with prolonged use of antihypertensive drugs is due to the thickened state of the lens, which has a delayed or switched off mechanism for throwing out "spent" aqueous humor

Thank you for attention!



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