DRY EYE DISEASE. **MYTHS & FACTS**

Prof. José Manuel Benítez del Castillo

DRY EYE
DISEASE

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MYTHS & FACTS

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Design and layout: aQuatinta Comunicació gràfica

Printed by: Gràfiques Cuscó (Barcelona)

ISBN: 978-84-121817-5-3

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Prologue

Constant dryness of the eye surface affecting the conjunctiva and cornea is what define xerophthalmia, a term that was coined in the 5th century BC by Hippocrates. The word xerophthalmia comes from Greek and means dryness *xerós* and eye *ophthalmos*. In his definition, Hippocrates wrote that xerophthalmia was an eye pathology with dryness of the conjunctiva and complete corneal opacity, and he recommended treatment *with water and olive oil*.

Dry eye can be considered to be a pathology as old as the history of medicine. Therefore, it is not difficult to find references to this disease in the annals of history. It is well worth taking a short look at how the remedies that were used over time sought a main objective: to modify the tear, both in terms of its amount as well as its composition.

Dioscorides, based on Pliny the Elder's *Naturalis Historia*, recommended bathing the eye with olive oil. In the 2nd century, Galen, a pharmacist and doctor, based on scientific concepts, extoled an ointment with a complex composition as a treatment for dry eye: a carrier based on vaseline which was impregnated with myrrh, saffron, pepper and wine. It was called *eristatus*. Galen's arguments to justify the therapeutic effect of this ointment were in no way exempt from fundamental, logical deductions. Vaseline offered a protective and, at the same time, lubricating effect on the corneal epithelium; pepper stimulated the secretion of tears due to its irritant properties; saffron gave aroma and colour to the preparation and myrrh, as a gum resin, helped increase viscosity and gave greater permanence to the eye surface. Wine, thanks to its

composition, would have had an acidifying and lubricating action, while increasing the viscosity of the tear through the presence of tannins and mineral salts.

It is likely that the reason for the low beneficial efficacy for this pathology lay in the difficulties in preparing and dosing it for the laboratories of those times. In the 7th century, Paul of Aegina recommended a simple remedy: lubrication with oil and warm water using sponges soaked in it and placed on the back of the conjunctival fornix.

During the 12th and 13th centuries, soldiers in the wars at these times were advised to use compounds with a mixture of lead oxide and zinc in a carrier that could be goose fat. We can read how, in the 16th century, Vesalius proposed a similar therapy to that prescribed by Galen centuries earlier, while years later, Boerhaave, in *De Morbis Oculorum*, considered the beneficial effect of the combination of vinegar, butter and oil in the form of drops applied to the eyes. Hadden (1888) pointed out the association between a deficit of tears and a hypofunction of the salivary glands and Fuchs (1919), in his compendium of ocular pathology, referred to a clinical case with lacrimal hypersecretion and filamentary keratitis in a 54-year-old woman who also had alterations of her salivary glands and vaginal dryness, attributing the cause to a hormonal disorder brought on during the menopause.

I am providing these historic references to point out how, over the centuries, dry eye disease was considered to be an isolated eye affection and that it was probably Henrick Sjögren (1933) who contributed most to the conceptual change by highlighting three joint symptoms: dry eye, dry mouth and joint pain. The term dry eye was coined by him and research started to open the way towards finding the causes that would clarify the mechanisms to be able to produce and establish specific therapies.

The population prevalence of dry eye makes this the most frequent pathology in our speciality, although the intensity of its symptoms and, therefore, the discomfort that it causes varies notably from mild cases to very serious developed forms. A prevalence of 10 to 15% in the adult population is considered and it is more frequently found in women of a certain age with hormonal disorders due to the menopause.

In view of the high prevalence of this pathology and the incognito that there still is regarding its cause and the limited efficacy of treatments, we are indebted to this book which continues the endless search to broaden knowledge through a path that represents an enormous daily effort by the author, working with the backing of his great experience. By reading this book, we can adapt the scientific story to what the patient needs to know, in their own words, what is known and what is not yet known about the disease, how to distinguish it from other eye pathologies, what treatments exist and where the research is heading. It is all very practical and up-to-date.

We would like to congratulate the author and thank him for his hours of work and effort that are shared in this book that enables us to get to know the disease in question. Something which many colleagues minimise but which ruins the quality of life of those suffering from it.

José Luis Encinas Martín
Former President
Sociedad Española de Oftalmología

Preface

I was invited to introduce this magnificent book for patients with dry eye disease, an invitation which I was delighted to accept for several reasons, which crowd into my brain. I will not give a detailed list of all of them, but I cannot resist highlighting a few of them.

I will start by defining what, in my opinion, is the scenario in which humans who are dedicated to taking care of patients move. You will agree with me that the speed of innovation is extraordinary, due to the confluence of artificial intelligence, the Internet of things and robotics, driven by the computational capacity of the cloud, nanotechnology and sensors. Their use drives innovation in medicine, biotechnology and neurosciences. This enables us to conceive that all medical problems have a short or long-term solution. Nevertheless, we must admit that there are still a series of medical processes, such as dry eye disease, that have not yet been effectively solved.

I am addressing you by means of a common tool for everyday use, my computer, to transmit the message which, in a brilliant way, is expressed in this magnificent book. The new technologies (Internet, mobile phones, laptops and tablets, virtual reality goggles, smart devices for the home, etc.) are having a direct impact on our lives and their effects on health are inevitable. In this point, Professor Benítez del Castillo argues that man is not designed to carry out activities in which blinking is inhibited, as happens with the use of the new technologies.

This book offers, in a pioneering way, one of the most pragmatic and advanced visions to deal with this chronic process. It aims to offer the human beings suffering from it the necessary information to get to know the causes of this disease affecting them and conditioning their quality of life. Thanks to the handling of the information generated by the big data, offered by Professor José Manuel Benítez del Castillo in an accessible, enjoyable way, by reading it the person who suffers from this affliction is empowered to be able to understand how they can live with it, in this transition until a cure is found for it.

Neither the public administrations nor work centres have a suitable understanding of this problem. Lifestyles, our nutrition and the control of chronic stress are the pillars of a healthy life to achieve the happiness we yearn for so much. In this book, readers find advice about how to avoid eye dryness which they probably suffer from due to a translocation-error produced in the words that are written in the story of our life, and that lead us to suffer from unpleasant discomfort that is not completely resolved by the replacement therapy, which is the ongoing use of artificial tears.

I like this book and I hope that you will enjoy it as the author has written it with a very clear intention. Life is a science which we are not given in an innate way but which we must learn. The maestro Benítez del Castillo is able to write, in colloquial, everyday language, this excellent text that I have the honour and privilege of introducing.

My professional and personal relationship with Professor Benítez del Castillo has enriched me intellectually and enables me to defend what this book offers by transmitting to patients what lifestyles and everyday customs mean to control their dry eye disease. Let me express the hope that the research that he carries out in this field, as the unarguable expert, provides the results that enable us to announce a revolution in the treatment of dry eye disease. In the meantime, dear readers, I recommend you to follow his advice.

Arturo Fernández-Cruz
Full Professor in Medicine
President of the Fundación Fernández-Cruz

Introduction

In recent years, dry eye has become one of the most frequent reasons for appointments with ophthalmologists. It is calculated that it affects one in every ten Spanish adults aged over 40, although other figures raise the prevalence to between 15 and 30% of the entire population. A Spanish study, carried out in 2008, in the Galician region of O Salnés (Pontevedra), calculated that it affected 11% of the population.

It is envisaged that these prevalence rates will rise. There are diverse reasons for this: our lifestyle (with many hours at the computer or tablet), our nutrition or everyday activities such as driving, reading or sewing. Central heating, air conditioning, pollution and the use of certain medications, among other factors, also play a relevant role.

The name “dry eye” has been maintained due to it being deeply rooted amongst the population, instead of using its scientific name of Keratoconjunctivitis Sicca. Nevertheless, this popularity has led to contempt to what dry eye represents. Patients with dry eye suffer; in many cases, their quality of life is very poor. On occasions, they are disdained by specialists who do not understand that it is a chronic condition. They are misunderstood at work, where they are considered to be people who exaggerate and who do not want to work when the fact is that they cannot spend hours in front of a computer. They are misunderstood by their families and are not taken care of by the health authorities who oblige them to pay for the great majority of their treatments themselves. This is why I, and many other experts, believe that it should be called dry eye disease.

Unfortunately, to date there is no cure for dry eye disease; but there are various solutions and preventative measures as well as changes in our diet that can help gain a better quality of life. All these actions are dealt with in detail in the book you are holding, a book that we have taken great care of in terms of design and layout, using the ideal typefaces recommended by the Spanish organisation for blind people, the ONCE, to make it as easy as possible to read.

It is, in part, a self-help book based on the knowledge that I have acquired over the years with my patients, as they have taught me what I know and I want to transmit this to those who need it. Therefore, some concepts may seem to be repeated. This is my intention: that certain ideas should become totally clear, and this is achieved through repetition.

Last, but not least, I would like to express my deep thanks to Thea for their decisive, altruistic and enthusiastic support for this health publication initiative and for having made this book possible, the main objective of which is, and this is our shared wish, to contribute towards better care of our patients.

José Manuel Benítez del Castillo

01

What is dry eye disease?

Dry eye disease is due to a lack of tears. This shortage can be due to there not being enough tears or to the excessive evaporation of tears. Another reason can be that the tear is poor quality and that it cannot spread over the eye surface, for diverse dysfunctional reasons that we will look at.

Dry eye is due to different factors and is a complex, chronic disease. It causes discomfort as well as problems with sight and, in some cases, damages to parts of the eye such as the cornea and the conjunctiva and, despite its name, it is much more than simply not having tears.

The eye is the result of the evolution of species. As human beings, we do not have an eye that is designed to see close up: the eye was used by hominids, millions of years ago, to make out enemies and threats in the distance while they were searching for berries, fruit or roots or while they were looking for carrion that a larger predator than them had left in the savannah.

When we blink, we lubricate our eyes. When we are looking into the distance, we blink about 17 times a minute and when we stare, we

blink less than five times a minute, which is why the eye dries. Let us imagine this on a “normal” work day, driving, using the computer, filling things in on the tablet and the mobile phone, and watching the television or reading. How many hours does this take up?

All of us, at some time in our life, have dry eyes. For example, if we go on holiday to the Caribbean and we go by plane, we will probably watch films until we reach our longed-for destination. It is likely that when we get there, our eyes will have dried up.

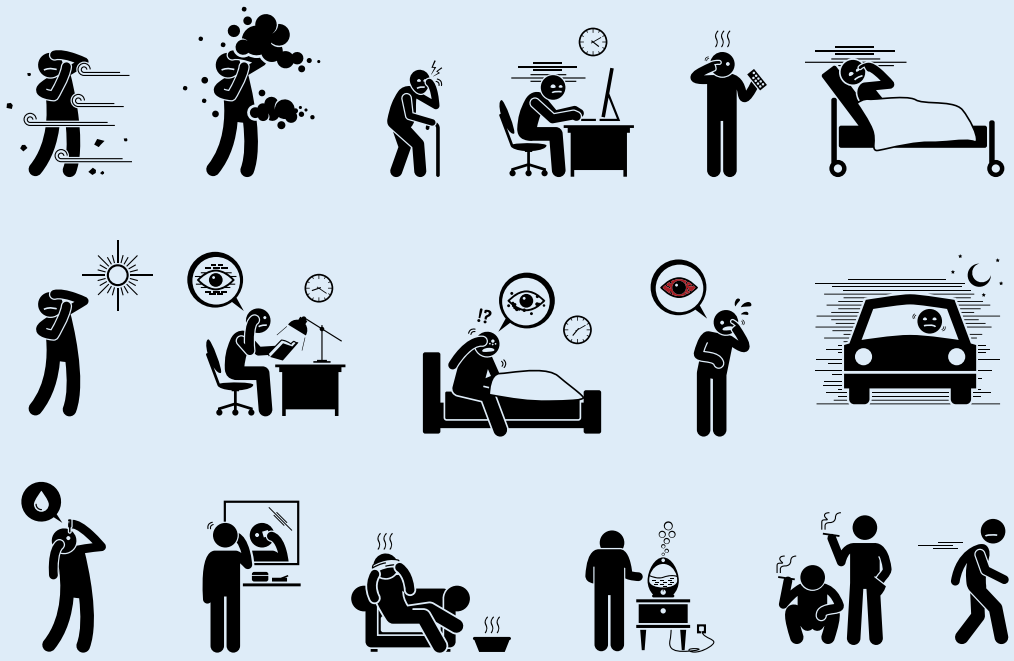


Figure 1. Many situations in our everyday lives can produce dry eye.

Why is there more dry eye now?

Why have figures for dry eye shot up so much? The answer can be found in the computers, devices and tablets that we use during marathon workdays. Or in the television screens on which we watch our favourite series. Or when we drive, sew or write.

In all these situations, when we concentrate in front of the screen or on the road, as I have already said, we stop blinking. And as we do not blink, we do not secrete tears. If we add to this the dry environments in which we live due to air-conditioning or central heating, the evaporation of tears is even greater.

As I have already mentioned, when we look into the distance, we blink about 17 times a minute. When we stare, the number of blinks drops to below five. If the activity we are carrying out is more interesting or stressful, we blink even less. The few blinks that we make are incomplete or partial, meaning that they are less effective and leave the lower part of the eye exposed.

The situation is such that ophthalmologists are increasingly coming across children with dry eye disease because they spend hours watching videos on YouTube on their tablet or playing video games in front of the television, or because their school encourages them to use electronic devices instead of textbooks.

Strangely, studies carried out in Japan have shown that a laptop causes less dry eye than a tabletop computer. The reason is that with laptops, we open our eyes less as we are looking down. Therefore, there is less evaporation surface for the tear and less dry eye. Another Japanese study also shows that the more stressful —or interesting— our work is, the less we blink.

All these situations mean that we are hearing more and more about dry eye. But is there anything more? Yes, because it affects the quality of life of those who suffer from it. We should not forget that now we complain more and we want a perfect life with zero tolerance to negative aspects of our lives.

The vicious circle of dry eye disease

Activities in which blinking decreases cause dry eye. However, at the same time, as we do not have tears, the cornea is exposed and we cannot see as we need tears to be able to see well. It is a vicious circle: tears are necessary so that the cornea becomes a perfect optical quality lens. Without tears, we see badly and we need to blink to be able to see correctly again. Therefore, people who see poorly and whose sight improves when they blink have dry eye disease.

Do you think you have dry eye disease? Before you continue reading this book I encourage you to answer the attached dry eye disease symptom questionnaire (1).

Dry eye symptom questionnaire
Each of the symptoms in the attached list are classified according to their severity during the last week, in keeping with the following scale:
0: you did not have this symptom
1: you had this symptom a few times, but it did not annoy you
2: you had this symptom sometimes, it annoyed you, but it did not interfere with your activities
3: you frequently had this symptom, it annoyed you, but it did not interfere with your activities
4: you frequently had this symptom, it annoyed you, and it interfered with your activities

Dry eye symptoms questionnaire	
Red eye	Burning sensation
Red around the eyelids	Itching
Inflamed eyelids	Eye discomfort
Scales or scabs on the eyelids	Pain (prickling sensation in the eyes)
Froth on the edges of the eyelids	Tearful eyes
Sticky eyes on waking up	Watery eyes
Secretions	Sensitivity to light (photophobia)
Dryness	Transitory blurry sight
Sensation of grit	Tired eyes and eyelids
Sensation of a foreign body	Heavy feeling

Give a score to each of these symptoms from 0 to 4. Now add them up.

Have you finished?

If you got a score of more than 13, you have dry eye!

So I recommend you continue reading this book.

(1) Donate J, Benítez del Castillo JM, Fernández C, García Sánchez J. Validation of a questionnaire for the diagnosis of dry eye. Arch Soc Esp Oftalmol. 2002;77(9):493-500.

How does dry eye affect quality of life?

There are numerous studies that quantify the impact of dry eye disease on people's quality of life, such as the one carried out by Dr. Schiffman on 56 patients in 2003. Although it is difficult to quantify, there are different methods, questionnaires and techniques that enable us to get an idea of how dry eye disease affects patients in their everyday lives. Unfortunately, as indicated by Dr. Ridder in 2011, there is no simple test that can be used to assess the loss of vision caused by dry eye disease.

One of the most relevant studies carried out in this field was done in Beijing and published in 2013. This work showed the relationship between dry eye disease and depression: in 2006, almost 2,000 patients were chosen at random to participate in a piece of research called the Beijing Eye Study. The patients were given tests and answered a questionnaire. Five years later, in 2011, the depression in 1,456 of these patients was assessed. The results showed that, particularly in the elderly population, depression was associated to dry eye and, particularly, to its symptoms.

Another Chinese study, carried out in 2012 on 229 people, confirmed that the pain, the discomfort and the impact on mental health are the main repercussions of dry eye.

The work carried out by Professor Vehof, published in 2015, looked in detail at the clinical characteristics of dry eye in patients with depression. Another interesting study is the one that was headed by Masahiko Ayaki in Japan in 2015, with 1,000 volunteers and 730 patients, and which showed that patients with dry eye have more problems with sleep and with their mood. A year later, Professor Yeom confirmed these results among the rural Korean population.

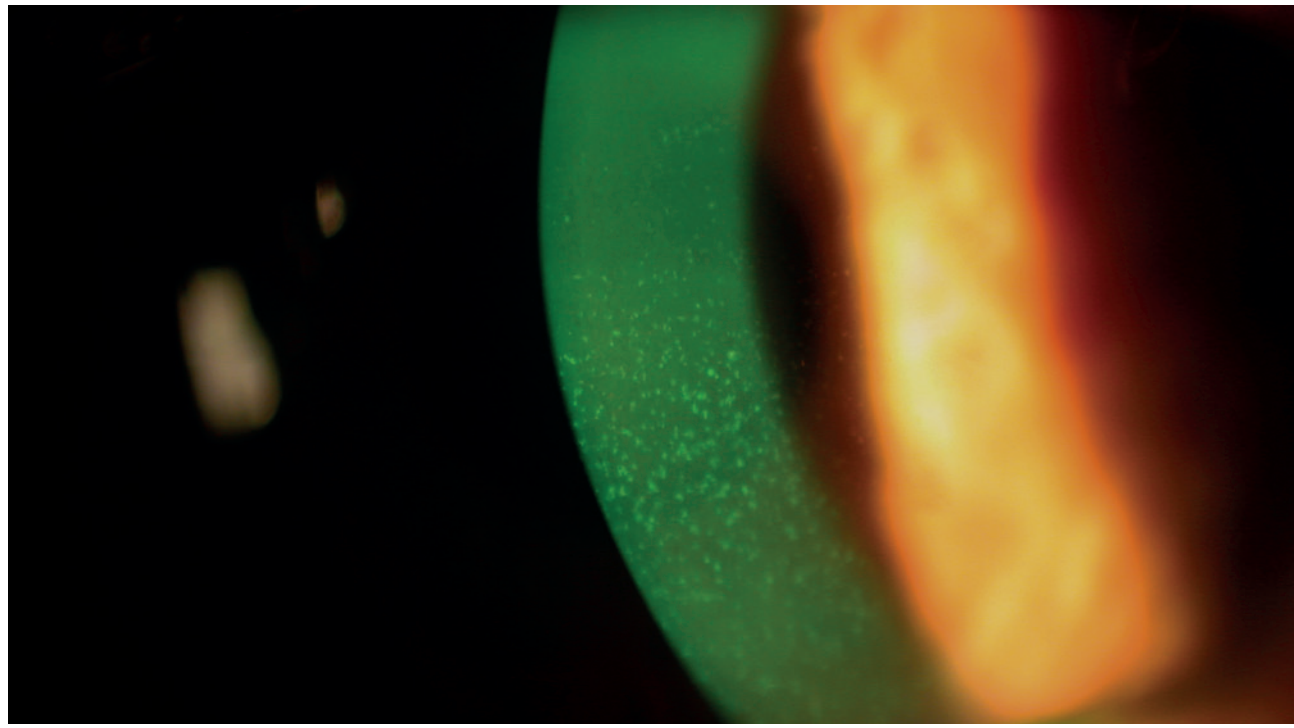
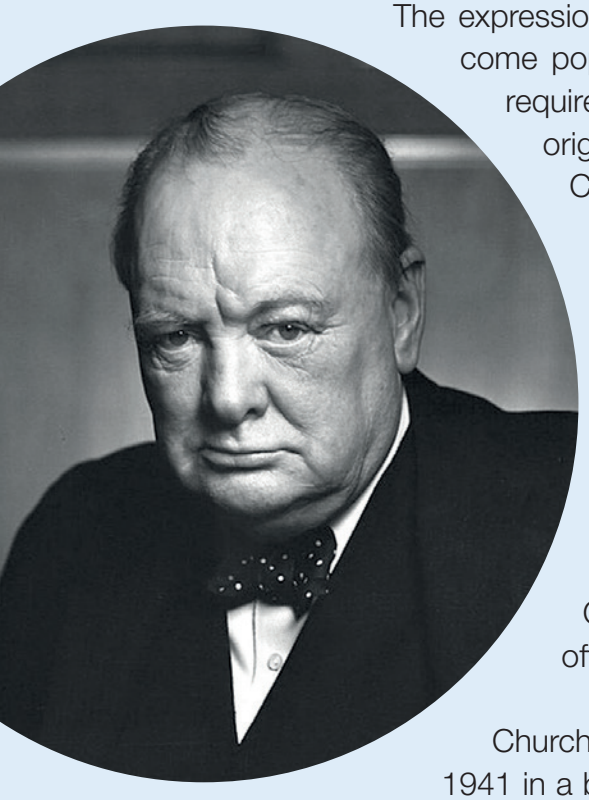


Figure 2. Image of keratitis (wounds on the cornea) due to dry eye.

One of the aspects that most catches my attention is the lack of empathy given to patients with dry eye disease: they are not well understood by their doctors (or their ophthalmologists), their families, their bosses or work colleagues. And, even more seriously, neither are they understood by the health authorities because nearly all the treatments and costs have to be met by the patients themselves.

How strange!

Churchill never said «blood, sweat and tears»



The expression “blood, sweat and tears” has become popular as a simile for something that requires a lot of effort to be achieved. The original phrase is attributed to Winston Churchill. However, strangely, that is not the original sentence and he was not the original author.

The sentence was spoken in the British Parliament on 13th May 1940, when Churchill substituted Neville Chamberlain as Prime Minister. The British Army was suffering ongoing defeats in France and Churchill confessed “I have nothing to offer but blood, toil, tears and sweat.”

Churchill himself compiled his speeches in 1941 in a book called *Blood, Sweat and Tears*, which contributed to popularising the expression. The original quote has been attributed to authors such as Henry James and to politicians such as Theodore Roosevelt, but the first person to use it was Lord Byron in 1815, in his poem *The Age of Bronze*.

02 Anatomy and parts of the eye

The human body is a fascinating structure. And the eye is one of the most developed and complex organs. Millions of years ago, hominids developed excellent distance vision, which enabled them to get away from other predators. Throughout our lives, our eyes do not stop processing information about everything we see and transmitting it to the brain. In parallel, they do not stop adjusting the amount of light that enters the eye and focusing so that we can see nearby and distant objects clearly.

However, the brilliant design of the eye has its Achilles tendon: each component is essential for the overall functioning and the slightest fault or destabilisation can alter the production of tears, as well as the efficacy of blinking and impair the health of our eye or the quality of our sight.

Let us take a look at all the parts of the eye, one by one:

- The eye is housed in the **orbit**, a set of bones that are also home to the muscles, the ocular nerves, the blood vessels and the lacrimal gland.

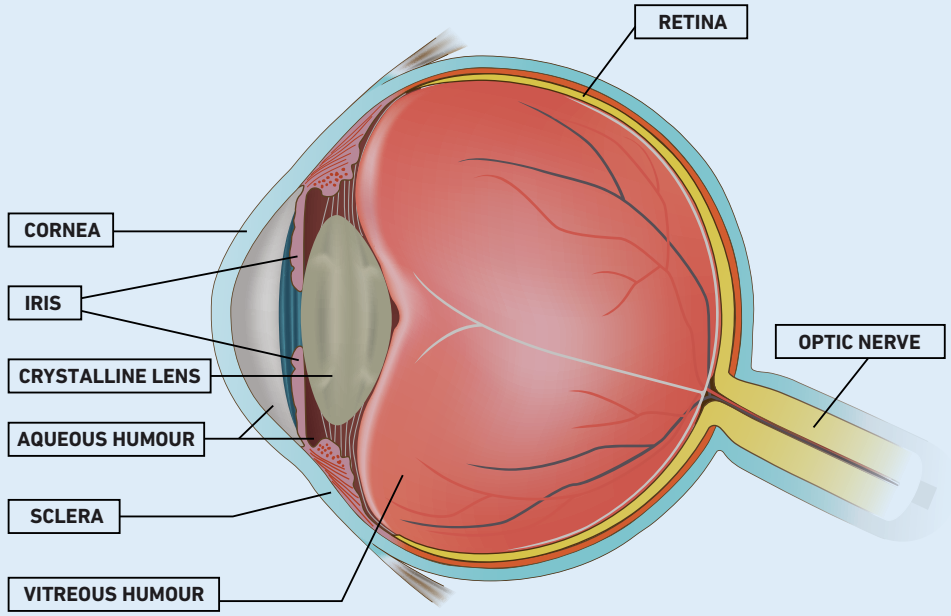


Figure 3. Main parts of the eye.

- The external part of the eyeball is white and hard and is called the **sclera**.
- The sclera is covered, in the area protected by the eyelids, by the **conjunctiva**. This fine, transparent layer of the eye, full of blood vessels, goes out to the edge of the cornea and also lines the damp surface behind the eyelids.
- The **cornea** is the transparent, curved layer that is found in front of the iris and pupil. Light comes in through it and is concentrated on the retina. It also protects the front of the eye. It has no blood vessels (which is why it is transparent) and has the greatest concentration of nerves in the entire human body. This is why our eyes are so sensitive to any stimulus.
- Light goes through the cornea and the pupil, the black point in the centre of the eye. Around this is the **iris**, the pigmented area which can be brown, blue or green and which dilates or contracts the pupil

to let more or less light in. The colour of the iris depends on the concentration of melanin and genetic factors.

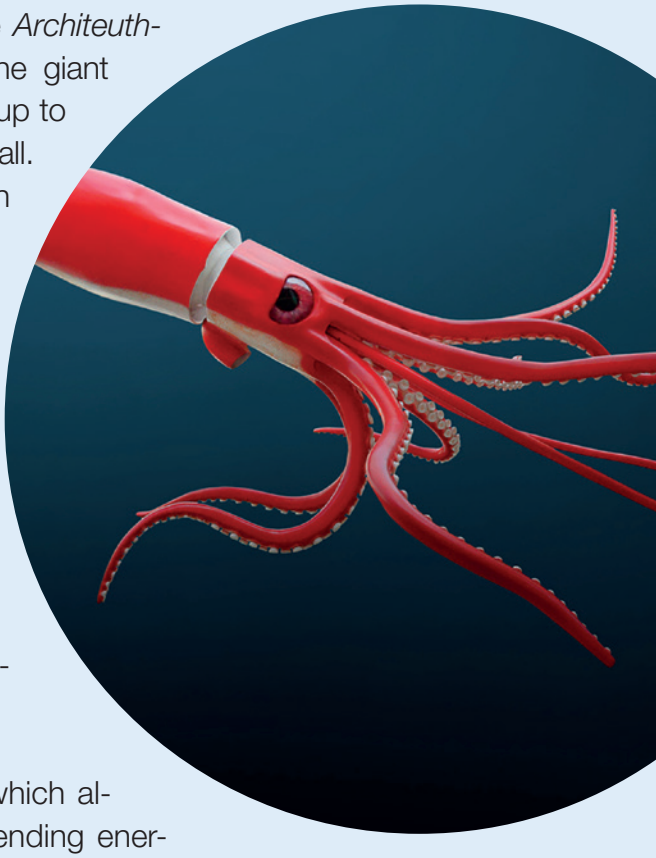
- The **pupil** works in the same way as the diaphragm of old cameras. When we go into a dark room, it gets larger so that we can see better. And the opposite happens when there is too much light. The muscles responsible for this action are the pupillary sphincter muscle and the dilator muscle, both of which are in the iris.
- Behind the iris, there is the **crystalline lens**, our eye's natural lens. It is transparent and elastic and does not have blood vessels or nerves. Thanks to the ciliary muscle, it thickens to see nearby objects or narrows to see distant objects. This change of shape is called accommodation and is similar to the zoom in a camera. As we age, the crystalline lens stops being transparent and becomes opaque, which is known as a cataract. In addition, and also with age, this change in the shape of the crystalline lens becomes more difficult, which is why we have to move objects further away from us. This is what is known as presbyopia or eyestrain. It should be taken into account that, although the term eyestrain in Spain is synonymous with presbyopia (lack of accommodation), this is not the case in the rest of the world. Doctors in other places interpret eyestrain as visual fatigue or the need to close our eyes, which is a symptom of dry eyes.
- The **retina** is the innermost layer of the eye that contains the photoreceptors, which are the cells that perceive light, and the blood vessels that feed them. This is the layer in which light is transformed into nerve impulses that are sent to the brain by the optic nerve.
- Inside the retina, we find the **macula**, the area with the best vision of the entire eye, thanks to the fact that it contains millions of cells known as cones, which are a type of photoreceptor. An anomaly in the cones can produce colour blindness, which is more frequent in males. The macula can become damaged with age and macular degeneration can appear. Some elderly people have to say that they have "macula", when what they mean is macular degeneration, as we all have macula. The name comes from Latin. Ancient anato-

mists, on studying the retina, observed a darker area, with more pigment, and called it the *macula* of the retina, the stain on the retina.

- In the **peripheral retina** we find another type of photoreceptor, the rods which are responsible for night vision and produce black and white vision.
- The **aqueous humour** and the **vitreous humour** are found in the middle of all these structures and play a fundamental role. The aqueous humour is a transparent liquid that feeds and oxygenates the cornea and the crystalline lens. An accumulated excess of the aqueous humour in the eye causes glaucoma. The vitreous humour is transparent and has a gelatinous consistency. It occupies two thirds of the eye, it supports the eyeball and protect the retina from possible impacts. Its alteration is responsible for "floaters", those small, moving dark points that move when we look at a white background or when there is a lot of light. They occur when the vitreous humour comes away from the retina and they are annoying, but they are not serious as long as an ophthalmologist rules out that when the vitreous humour comes away there has been no tear to the retina.
- Finally, in the next chapter we will talk in depth about the **lacrimal apparatus** and **tears**, which play a fundamental role in dry eye disease.

Which is the largest eye that can be found in nature?

How strange!



This honour corresponds to the *Architeuthis dux*, commonly known as the giant squid. Its eye has a diameter of up to 30 cm, larger than a basketball ball. Specimens have been found with a length of more than 20 metres and a weight of almost 300 kilos. They live in the open sea, at a depth of between 300 and 1,500 metres, where light does not reach and where their eyes enable them to make out predators and prey.

Asturias is one of the areas where there has been the greatest number of sightings.

Their flesh is full of ammonia, which allows them to float without expending energy, but makes them inedible for humans. However, they are one of the favourite dishes of sperm whales, which descend more than a thousand metres to hunt them. The giant squid's diet is based on fish such as blue whiting and other small crustaceans.

03
Tears

Tears are produced permanently and their function is to keep the eye surface clean and hydrated. They also feed the external part of the cornea and act as a lubricant to facilitate the movement of the eyelids.

Their production increases when we are subject to external aggressions such as brusque changes in temperature, when a foreign object gets into our eye, such as a speck of dust, pollen or an insect, or due to psychological reasons, such as seeing a film that makes us cry or suffering from the loss of a loved one.

Tears consist of three layers. The main one, 90% of the entire tear, is the aqueous layer, made by the lacrimal gland and which is located between the other two, to be mentioned below.

	Tears	Plasma
Total proteins	7.37 g/L	68-82 g/L
Lysozyme	2.4 g/L	4-15 g/L
Lactoferrin	1.5 g/L	ND
Albumin	54 mg/L	35-55 g/L
IgA	411 mg/L	0.9-4.5 g/L
EGF	1.66 mg/ml	0.72 mg/ml
Vitamin A	16 mg/ml	883 mg/ml
Vitamin C	117 µg/ml	7-20 µg/ml
TGFß	247 (M) and 180 (F) pg/ml	147 pg/ml
Na^+	145 mEq/L	135-146 mEq/L
K^+	24.1 mEq/L	3.5-5.0 mEq/L
Ca^{2+}	1.5 mm	1.1 mm
Cl^-	128 mm	96-108 mm
HCO_3^-	26 mm	21-29 mm

Table 1. Composition of tears and of plasma, from which tears derive. In the table, you can see the complex composition of a tear and this only shows the most important components. In the right-hand column, you can see the composition of the plasma. Its similarity means that it is used for treatment in serious cases, as we will see later.
IgA: Immunoglobulin A; EGF: Epidermal growth factor; TGFß: Transforming growth factor beta; M: in men; F: in women; ND: undetermined.

Our lacrimal apparatus is made up of the secreting system, the lacrimal gland, in which the tear is produced, as already mentioned, and the excretory —or output— system, from where the tear is eliminated as far as the nostril. The excretory system is made up of several structures including (see figure):

- **The lacrimal puncta:** found on the inner corner of the upper and lower eyelid. They collect the tears produced by the lacrimal gland.

- **Lacrimal canaliculi:** they carry the tears to the nasolacrimal duct.
- **Lacrimal sac:** it connects the lacrimal canaliculi with the nasolacrimal ducts and pumps tears to the nostrils.
- **Nasolacrimal duct:** it carries tears to the nose and from there to the throat, so that they are eliminated by it. This is why, when we cry because of sadness, we often have to blow our nose. When any of the parts of this excretory system are blocked, we also constantly shed tears. In this case, we do not have dry eye, in other words, we produce plenty of tears. This situation is known as epiphora, a Greek word that literally means “overflow”. Its name comes from the fact that the tear, after gradually accumulating in the lower eyelid, ends up spilling or overflowing over the edge.

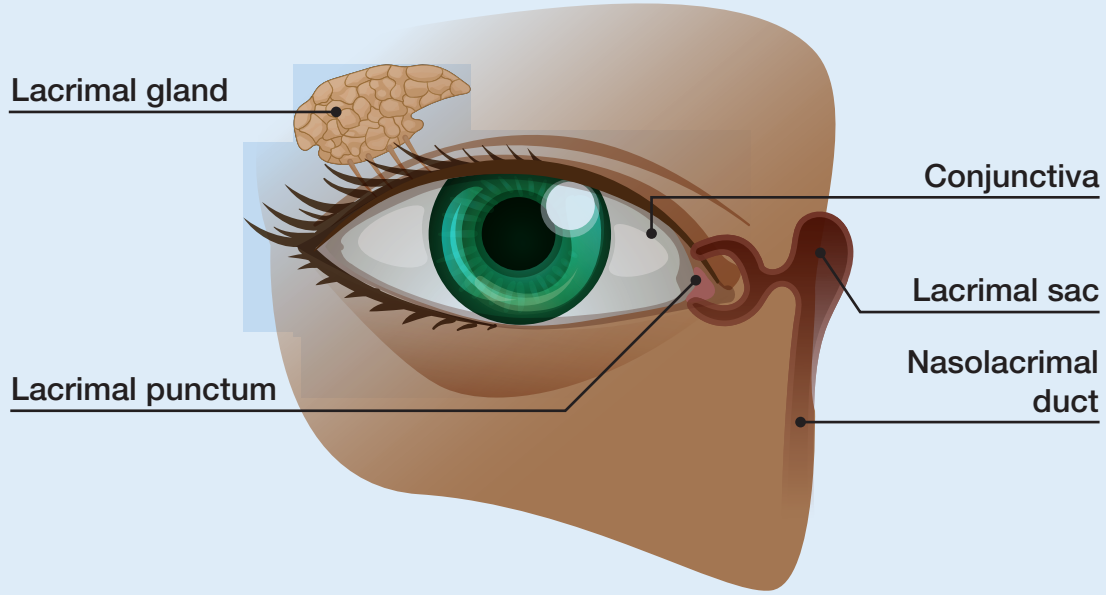


Figure 4. Diagram of the lacrimal apparatus of the eye.

Our lacrimal apparatus, as we have already said, connects to the throat via the nose. Therefore, when we use certain eyedrops, we can taste them.

However, in addition to the aqueous layer, there are another two layers in a tear which are no less important: the mucin layer (the deepest layer in contact with the corneal and conjunctival cells) and the oily layer (the external layer in contact with the air).

The mucin in the tear is produced by the goblet cells of the conjunctiva. Rheum or sleep is the excess mucin that is produced by the goblet cells —which get their name because they are shaped like a chalice— when there is infectious or allergic conjunctivitis.

Figure 5. In the image, you can observe some yellowish points on the edge of the eyelid behind the eyelashes. These are the Meibomian glands obstructed with solid oil due to inflammation.

The surface layer of oil in the tear, which prevents the evaporation of the water, is produced by the Meibomian glands in the eyelid, sebaceous glands that we have in the upper eyelid (about 50 of them), as well as in the lower eyelid (about 25 of them). They were given this name after the 17th-century German Dr. Heinrich Meibom who described them for the first time.

When these glands are inflamed, the oil becomes solid and the glands become blocked. When this oil is missing, the water evaporates sooner and evaporative dry eye occurs. It is a situation similar to putting two glasses of water in the sun: if you drizzle some oil into one of them, the water in this glass will take longer to evaporate. In blepharitis (a situation in which the Meibomian glands inflame and become obstructed), it is as if they were missing the oil. Situations that cause evaporation, such as low humidity in cities such as Madrid or draughts (such as those caused by central heating and air conditioning) make evaporative dry eye worse. On the contrary, if we go to the beach, we will improve our evaporative dry eye as we take a break from the computer and the environment is damper.

What happens every time we blink?

Every time we blink, we produce tears, we reduce their evaporation and we spread them over the eye surface. This is why blinking is so important: when we blink less, when driving or using computers or as a result of diseases such as Parkinson's, our eyes dry up.

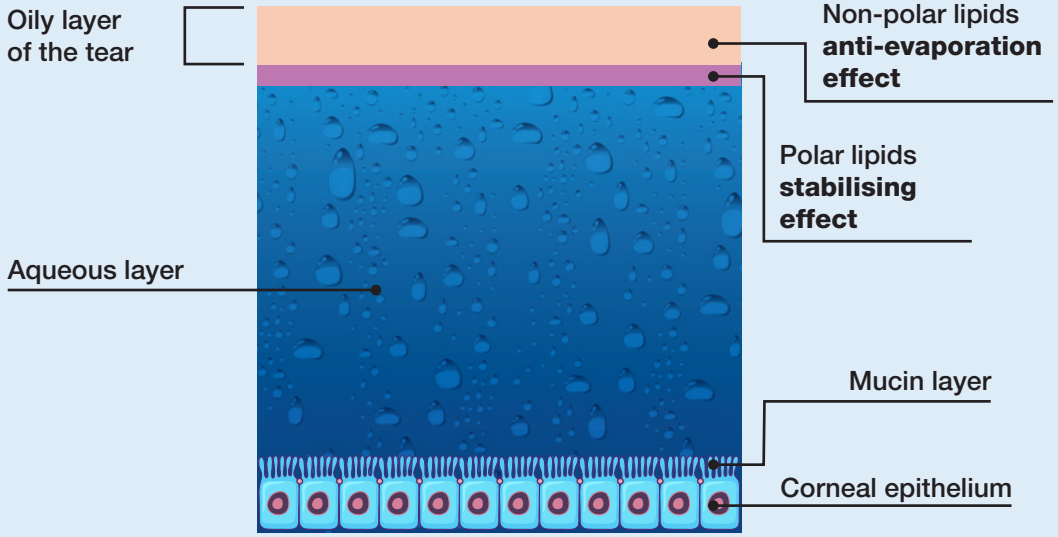
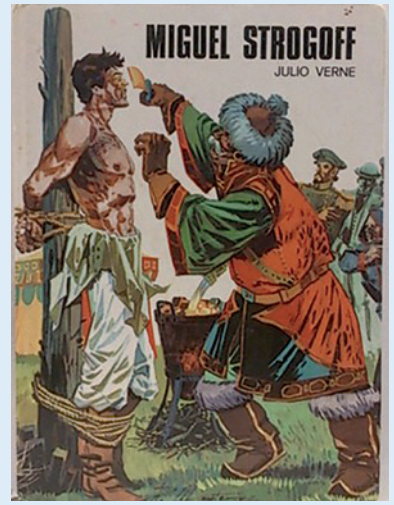


Figure 6. Diagram of the layers of the tear film.

Michel Strogoff's tears

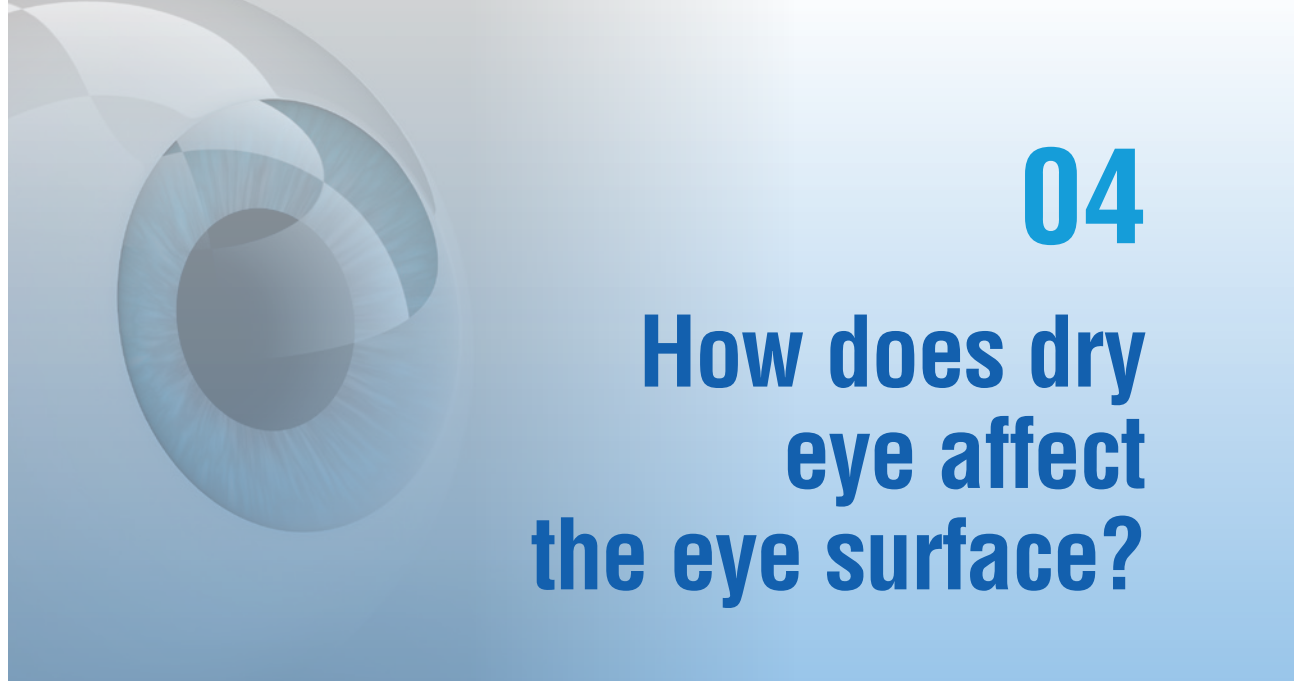
How strange!

Jules Verne achieved great popularity during his lifetime but above all, he has gone down in history as advancing inventions such as submarines and moon rockets in his novels. Strangely, his two best sellers are adventure stories: Around the World in Eighty Days and Michel Strogoff. The latter, published in 1876, tells the adventures of one of the Czar's couriers who had to cross Siberia to warn the sovereign's brother about the treason of the evil Ogareff.



The culminating moment of the story (warning: spoiler) happens when the courier is captured and punished by being blinded with a red-hot blade. However, just before he is blinded, he sees his mother and starts to weep. In Jules Verne's imagination, Strogoff's tears save his sight, although he feigned blindness to finish his adventure.

In fact, tears have a temperature close to that of the human body meaning that, even had he cried a great deal, his tears, which have a temperature of about 25°C, would have evaporated immediately in the presence of the glowing hot blade, which would have been close to one thousand degrees centigrade.



04

How does dry eye affect the eye surface?

The scientific name for dry eye disease is Keratoconjunctivitis sicca. In other words, conjunctivitis appears, which is the inflammation of the conjunctiva, the fine, transparent membrane that covers the inside of the eyelid and the white part of the eye.

As its name indicates, along with conjunctivitis, there is keratitis, which is the main problem. The dryness causes erosions (small wounds) in the epithelium (the layer of the cornea nearest to the surface), making sight difficult and producing significant annoyance. We should remember that the cornea is the part of our body that has the most sensitive nerve endings.

Therefore, a patient with mild dry eye disease will have, as a minimum, conjunctival alteration, with discomfort, particularly at times of stress, whilst a patient with serious dry eye disease will have a significant conjunctival and corneal lesion, with continuous discomfort.

One significant aspect is that today, dry eye disease is considered to be an inflammatory disease. But usually red eye is associated with inflam-

mation and although patients with dry eye disease show inflammation, their eye is completely white or only slightly red. Therefore, it is fundamental to know that an inflamed eye does not always go red.

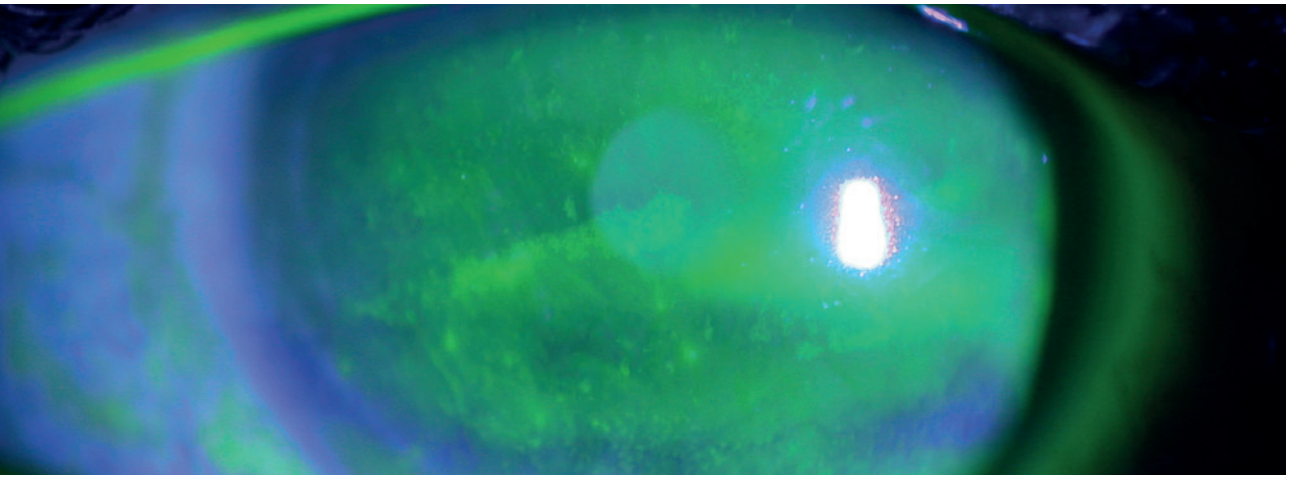


Figure 7. Keratitis due to dry eye disease (fluorescein stain).

The symptoms of dry eye disease are eye discomfort, in other words, the sensation of grit, burning, stinging, eye fatigue, the need to close your eyes, and so on. However, if your eyes are itching and you feel the need to rub them, it is much more likely that this is due to an allergy and not to dry eye disease (although they can sometimes go together). Poor sight is another of the consequences of dry eye disease, particularly if your poor sight improves when you blink. When you concentrate, reading on the computer or on another device, you stop blinking and secreting tears. The result is that the cornea remains unprotected, even though it may not have keratitis, because the epithelium, although it is transparent, has microvilli meaning that the cornea without tears becomes irregular and rough, which is bad from the point of view of your sight. This is why tears are fundamental, they regularise the surface of the cells, converting the cornea into a smooth surface which guarantees good sight.

Transitory, occasional dry eye is not a progressive disease. But it can become so if it becomes chronic, if the environmental conditions persist or it is not given suitable treatment. It is a controversial subject, but most professionals believe that it is progressive, at least in a significant percentage of cases. Therefore we recommend early treatment and not waiting until the problem has become irreversible. One of the most frequent causes of dry eye disease, blepharitis or dysfunction of the Meibomian glands is progressive if it is not treated. In our everyday practice, we see how the Meibomian glands become atrophied if not correctly treated.

It should be pointed out that dry eye, as of today, has no cure, but that there are solutions to deal with it. I tell my patients that it is similar to if I were to get high blood pressure or high cholesterol: I will always have to take a pill, but I will be able to improve my clinical picture and my quality of life.

Figure 8. Anterior blepharitis can be seen (scabs on the eyelashes) and posterior

blepharitis or dysfunction of the Meibomian glands (blockages in their openings).

Therefore, treatments are chronic and maintenance measures must be started. As we will explain later, in blepharitis you must clean the glands regularly at home and at the ophthalmologist's, in the same way that you brush your teeth and periodically go for a professional mouth cleaning at the dentist.

Can dry eye disease be prevented?

There are not enough studies, but evidence suggests that it can. Also, with certain attitudes and treatments, we can slow down its progression. Adopting a healthy diet, a judicious use of screens by taking periodical breaks from them, using wrap-around glasses that prevent the tears from evaporating, avoiding or restricting certain medications and being careful about the cosmetics that are used in and around the eye, such as eyeliners or mascara, among other actions, are effective. Regarding periodical breaks from the screen, I recommend the 20-20-20 rule, in other words, every twenty minutes working at the computer, take a twenty-second break while looking at something about 20 feet (6 metres) away. In other words, looking into the distance to increase the frequency of your blinking and to refresh your eye to thereby improve your productivity.

One of the most notable things is that there are more women than men with dry eye disease. The explanation is due to the androgens (male hormones) which protect men, whereas oestrogens (female hormones) favour inflammation. This is why women also have more rheumatoid arthritis, lupus and Sjögren's disease, which are all diseases related to dry eye disease. It has been shown that the daily use of cosmetics, particularly applying products behind the eyelash

(waterlining), favours evaporative dry eye disease as waterproof products, which contain tar pitch and waxes, block the openings of the Meibomian glands thereby reducing the oily layer of the tear.

Classically, the disease was usually found in people aged over sixty, but we are now seeing it at any age. And as it is chronic, the total number of patients is increasing enormously. There are also more cases due to the increase in life expectancy, as the dysfunction of the Meibomian glands is part of our ageing process.

Figure 9. Dry eye produces discomfort, inconvenience and even pain in the eyes.

Dry eye does not often hurt, it is more uncomfortable than painful. But the fact that it is chronic makes life difficult, both for those who suffer from it as well as the people nearest to them. If it really hurts, we would consider a complication known as neuropathic pain, in which the eye hurts, even though the nerve endings are not being stimulated. In this

case, the nerves, despite there being no stimulus, spontaneously send pain signals to the brain. These are people who feel pain from minor stimuli or stimuli that would not cause pain to other people. There are many causes of neuropathic pain, one of them is dry eye disease. This neuropathic pain can be peripheral or central and has a specific treatment.

Symptoms

Although I have already mentioned it, I would like to insist that usually visual symptoms are not associated with dry eye disease either by patients or by doctors.

- Most symptoms caused discomfort (like the sensation of grit or something in your eye, burning, stinging, the need to keep your eyes closed, and so on). These symptoms are worse in the evening and on waking, as the production of tears decreases as the day advances and we do not secrete tears at night.
- The other group of symptoms are visual problems, such as poor eyesight, photosensitivity and visual fatigue which appear when we do not blink and that temporarily improve on blinking, but which repeat cyclically, making visual work or leisure activities impossible and having a negative effect on the quality of life.

Una furtiva lagrima

How strange!

The aria *Una furtiva lagrima* is the most famous one in Gaetano Donizetti's opera *L'elisir d'amore*. This comic opera was premiered almost 200 years ago, in 1832, and continues to be one of the most performed operas even today.

Set in the French Basque country, Donizetti had barely two weeks in which to write this opera. The reason was that the entrepreneur at the Teatro della Cannobiana in Milan had no repertory to premier due to a failed commission to another composer. The rapture of inspiration Donizetti had has allowed many of the best tenors in history to triumph in the best opera houses in the world.

The romanza "Una furtiva lagrima" is the best-known piece of this opera in which the protagonist, Nemorino, a shy peasant in love with the rich landowner, Adina, talks about a furtive tear that he saw in his loved one's eyes which was, for him, the unmistakable sign of love.

05

Causes of dry eye

There are many occasions in our everyday lives that can favour dry eye disease, even though there is no recognised cause. Its prevalence increases with age and is more frequently found in menopausal women due to hormonal changes. Breastfeeding can also cause it to dry due to the hormone prolactin as our water is destined to creating breastmilk.

Certain allergies constitute a significant factor, as dry eye favours allergens and allergies favour dry eyes. Another reason is the use of contact lenses. These, in particular the soft ones, cause dry eye disease in the long term, and when their users decide to have their sight operated on, the intervention worsens the symptoms (we should remember that eye surgery can cause dry eye disease). It should be taken into account that all eye surgeries dry the eye meaning that it is important for a pre-operatory dry eye study to be carried out.

Dry eye disease, as already indicated, can be due to the continuous use of computer, tablet, mobile phone and television screens. In many of these devices, the preventative use of blue filters has become fashionable, but to date, it has not been shown that blue light damages

human eyes. It is said that it produces macular degeneration and other eye diseases, but it has not been proven that it protects from dry eye disease.

However, it should be taken into account that a screen which, for example, receives reflections from a window can cause us to see poorly, which will increase blinking even more by trying to improve our attention to the screen. The solution is to avoid these reflections by changing the position of the screen and adjusting the brilliance and contrast, meaning that you can save yourself from acquiring these filters.

Another cause is the medication that we take orally and others that we apply to the eyes:

- Oral antihistamines.
- Antihypertensive medication, such as beta-blockers and diuretics.
- Medication for Parkinson's disease.
- Cough mixtures.
- 13-cis-retinoic acid: this is a notable case, because people who use medication with this compound are usually young people with acne who develop serious dry eye and blepharitis with atrophying of the Meibomian glands.
- Chemotherapy.
- Anticholinergics.
- Opiates.
- Psychotropic drugs, such as benzodiazepines and tricyclic antidepressants.

Should you be taking any of these medicines, please consult your ophthalmologist.

Eyedrops such as Gentamicin, anaesthetics, antiviral drugs, medications for glaucoma and vasoconstrictors can also produce dry eye disease. It

is even worse if the eyedrops have preserving agents, as these are very often a cause of dry eye. One special group is patients with glaucoma, as the pharmacological treatments with preserving agents that control intraocular pressure produce dry eye and blepharitis. Very often, patients put up with these pathologies thinking that the most important thing is not to lose their sight. However, eye pressure can be controlled with drugs without preserving agents, improving the surface area of the eye and even complying with the therapy for the glaucoma.

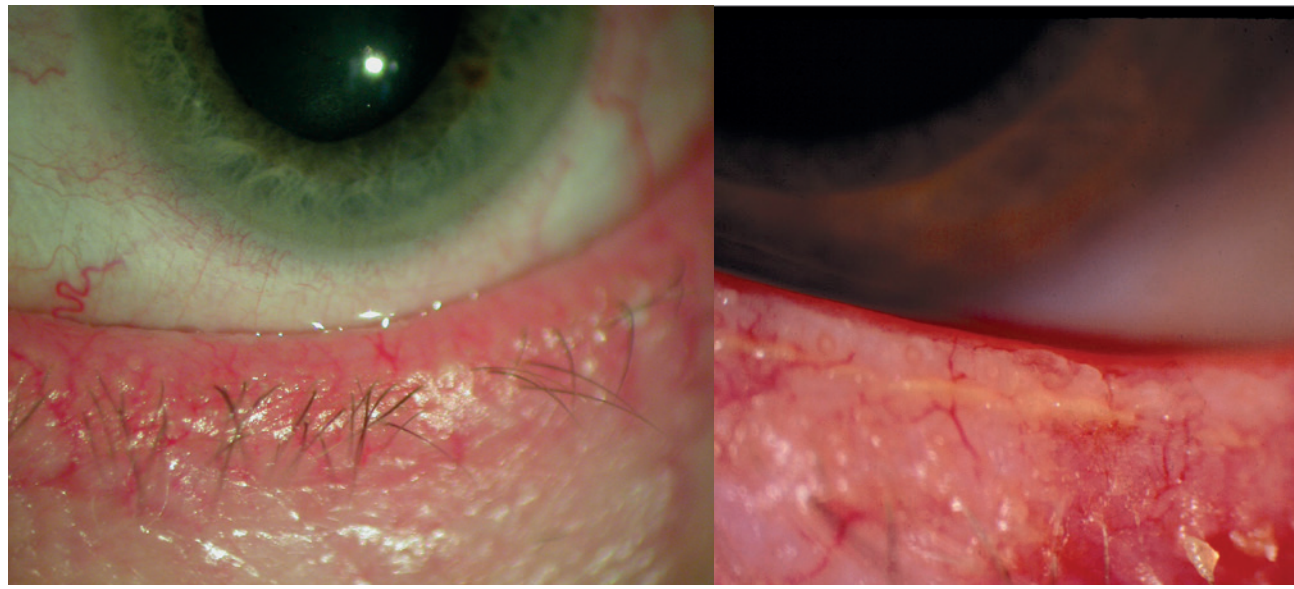


Figure 10. Two images of blepharitis. You can observe redness around the edge of the eyelids with dilated veins called telangiectasias. In some cases, patients lose their eyelashes.

As it is a silent disease, initially, patients do not attach any importance to dry eye. They think that it is normal to have tired or red eyes, or to have the sensation of having something in their eye and that, with a bit of rest, these sensations will disappear. This is why it is essential to start treating it as early as possible because, although it has no cure, there are numer-

ous treatment options that will improve the quality of life and prevent any possible progression.

How does dry eye happen? It is mainly due to two reasons: either an increase in the evaporation rate of the tear film or a decrease in its production. As I have already mentioned, any dysfunction in this extraordinary piece of machinery that is known as the eye produces problems. Recently, another subgroup of dry eye disease has been described, that of low humidity (when the goblet cells do not produce mucin and the water in the tear cannot spread over the eye surface). In other cases, there are problems of the eye surface, such as conjunctivochalasis and pinguecula, which prevent the tear film from spreading adequately.

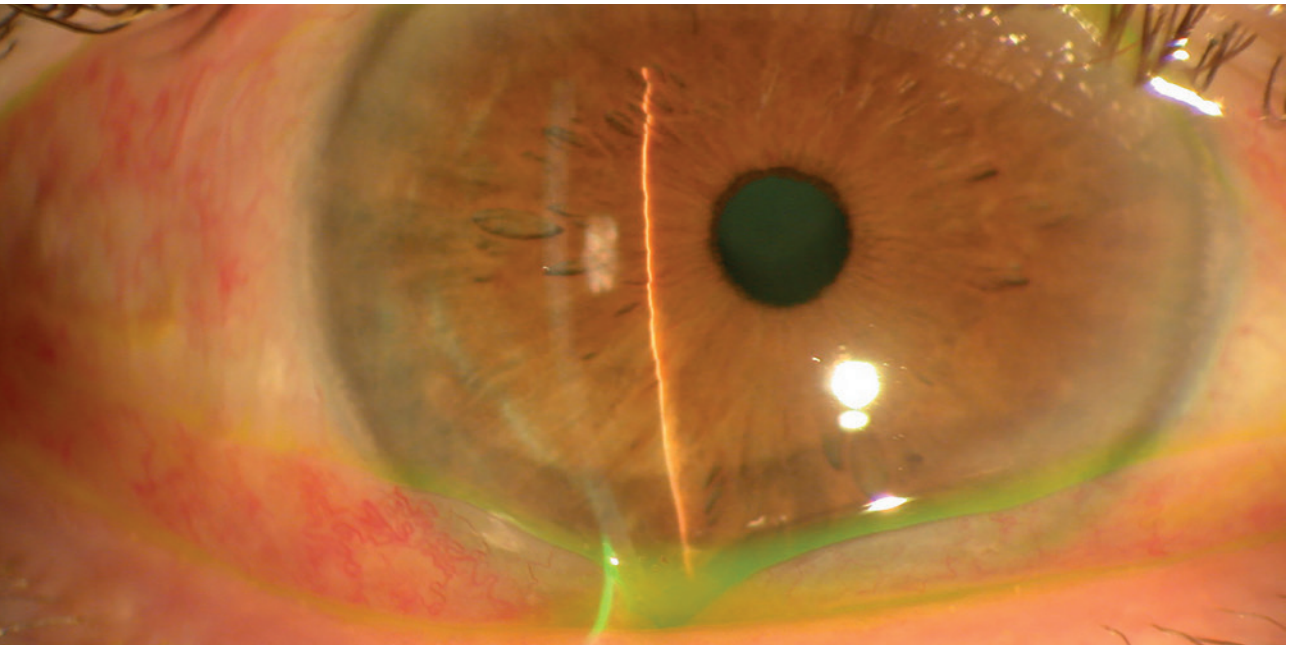


Figure 11. Image of a case of severe conjunctivochalasis. You can see folds in the conjunctiva on the lower eyelid.

The increase in the evaporation can be due to the poor functioning or dysfunction of the Meibomian glands (blepharitis, which is inflammation of the eyelid: blepharon means eyelid in Greek). Therefore, any narrowing or qualitative alteration of this oily film increases the evaporation and spoils the entire functioning mechanism of the eye.

Strangely, one of the main causes for the dysfunction of these glands is a dermatological disease: rosacea. This chronic inflammatory disease affects the blood vessels and is characterised by redness frequently on the face, particularly the cheeks, nose and space between the eyebrows. In these cases, it is essential that the dermatologist treats the rosacea in collaboration with the ophthalmologist. It should be taken into account that, on many occasions, a rosacea that does not seem to have much dermatological significance can affect the eye severely.

Evaporation can also increase due to a fault in the blinking mechanism: Although the frequency varies from one person to another, it is essential that the eyelids close completely. Statistics show that, under normal circumstances, we blink approximately every four seconds. Therefore, if we are awake for 16 hours a day, we blink more than 14,000 times a day (and more than five million times a year). The problem with the use of screens is not only that we blink less but that these blinks are partial or incomplete, meaning they are less effective, and the lower part of the eye, which is not lubricated, becomes dry.

Diseases such as diabetes, herpes zoster or simplex, or having undergone cataract surgery or laser surgery using the corneal refractive technique may be reasons for blinking less. Diabetic patients must be particularly careful as they do not usually show symptoms through having lower sensitivity, as well as patients with Parkinson's and other neurological diseases.

If blinking is partial, this can be due to thyroid diseases in which the eyes stand out of the eyeball more than is normal, to paralysis of the facial muscles due to a CN VII lesion, to Parkinson's (not only do they blink less, but their blinks are partial) or to the eyeball being so big that the eyelid does not completely cover it (high myopia). It can also be due to the use of computers because, as I have already mentioned, when we use them we blink less and the blinks are partial or incomplete. Another possible cause are patients who have undergone plastic surgery such as blepharoplasty.

In this case, where blinking is partial, it is common for the patient to sleep with their eyes open, which increases the dryness of the eye and makes them feel so tired and upset when they get up in the morning. This is known as lagophthalmos, which means hare's eye, due to the belief in ancient times that these animals slept with their eyes open to be alert to any possible threat. Often, placing a humidifier in the bedroom can contribute to decreasing the symptoms. You can also talk to your ophthalmologist about the possibility of sleeping with an eye mask on. Another aspect to be taken into account is that patients with insomnia or those who use a CPAP machine (which enables them to sleep despite having sleep apnoea) also suffer from dry eye disease. In the case of a CPAP, the air can escape towards the eyes and, if they are minimally open, the eye surface is dried by the draught.

Finally, having a job that obliges you to focus your sight for a long time can also mean that the blinking mechanism is affected. An example of this is people who work with monitors at night, as at night, tears are not secreted and this is why we usually sleep with our eyes closed.

One cause of a decrease in the amount of the tear could be Sjögren's disease. This is an autoimmune disease, in other words, the body itself mistakenly attacks the glands that produce tears and saliva, among other parts of the body. It mainly affects women and is diagnosed by looking at their clinical history, a physical examination at an appointment, several tests on their eyes and mouth, a blood test, a gallium scan or biopsy of the accessory salivary glands. It can cause severe dry eye disease, meaning that patients who suffer from it must be treated with anti-inflammatory medications for life.

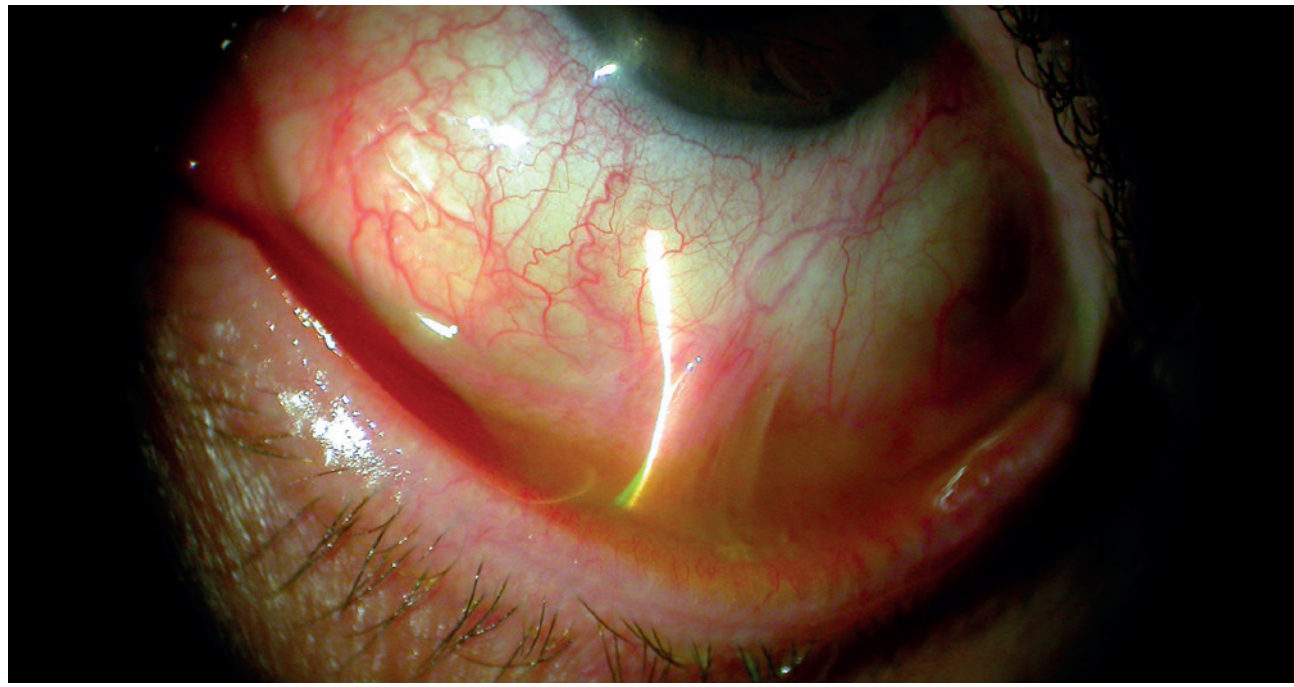


Figure 12. Pemphigoid is an autoimmune condition that causes dry eye disease and in which symblepharon can be observed (conjunctival bridges).

There are many other reasons why tears are produced in lesser quantities than required and that lead to dry eye disease, such as virus infections like hepatitis C, mononucleosis, HIV or adenovirus conjunctivitis. It is highly frequent that after dealing with adenovirus conjunctivitis, there is residual dry eye disease, sometimes for ever more. Trachoma, an in-

fection caused by chlamydia, also causes it, as do allergic reactions to drugs or ocular pemphigoid, an autoimmune disease of the skin. It is interesting to point out that an ophthalmologist may easily diagnose this disease by observing how the dry eye is accompanied by scars on the conjunctiva of the lower eyelid. Even the lymphoma and the radiotherapy and chemotherapy that are used to treat many kinds of cancer decrease tear production.

As far as systemic and local drugs are concerned, as we have already mentioned, there are many medications that produce dry eye. Therefore, it is essential to ask your family doctor and your specialist which alternative drugs can be used to prevent dry eyes.

For example, if you are hypertensive and need hypertensive medication, you could ask your doctor to prescribe drugs that are not diuretics. If you sleep badly and you have been prescribed benzodiazepines, you could ask your doctor about the possibility of taking melatonin. You should always remember that any change must be supervised by your family doctor or relevant specialist.

In addition to any medications that you may take orally, you should also take care, as I have already mentioned, with topical or local medications (which are those that are applied directly to the eye) such as eyedrops, which may contain preserving agents and active ingredients that give rise to dry eye (see page 48).

Convection currents and damp

It is becoming increasingly more frequent to work and live in closed environments with air conditioning. In fact, the battle to adjust the air conditioning in offices is one of the most frequent causes for arguments at

work. In comparison with the exterior, in the summer they are too cold and in the winter they are too hot.

These differences of temperature between the inside and the outside cause draughts that dry the eye surface very quickly. The solution lies in preventing the air-conditioning from reaching your eyes by feeling it on the nape of your neck. But be careful about getting a stiff neck if the draught is constant!

Once again, having a humidifier nearby may help the eye surface stay hydrated for longer. To a lesser degree, indoor plants can also contribute towards this. The use of glasses while you are working can also help, but they must wrap round as much as possible to prevent draughts circulating between the glasses and the eye.

Another aspect to be taken into account is that sleeping near a radiator can also contribute to drying the eye surface, meaning that it might be necessary to change the layout of the bedroom furniture. It is also useful to place recipients with water in on top of the radiators.

It is important to bear in mind that means of transport such as the car, train, aeroplane or bus on long-distance journeys mean that we are closed in with air that circulates in a single direction. If possible, try to redirect the focus of the air-conditioning so that it does not go straight into your eyes. If you are driving, it is a very good idea to make periodical stops to give your sight a break, as well as the rest of your body. When our eyes dry we have a tendency to close them and this causes sleepiness, meaning we are more likely to have an accident. Once again, wrap-around glasses may help. If you are a passenger, close your eyes for a few seconds to help hydrate the eye surface or use eye drops.

How strange!

Why do we usually have sleep in our eyes when we wake up?

Rheum or sleep is the secretion of the goblet cells in the eye, made up of a mixture of mucus, oil, skin cells and other waste. When we sleep, the temperature of our body tends to drop and therefore the mucin produced by the cells becomes hard faster and accumulates. In addition, the relaxation of the muscles and the lack of blinking when we sleep means that less of it comes out of our eyes. In the same way, unlike during the daytime, at night, the lacrimal glands do not secrete aqueous tears to clean the eye surface.

In Spain and in Latin America there are several words for rheum or what is commonly known as “sleep” in the eyes. These words appear in several traditional sayings, giving an idea of how common it is. Here are three examples translated into English: “There are eyes that fall in love with sleep”. Or “God gives sleep to those who do not have eyelashes”. “They even stole the sleep from his eyes”. And this other highly illustrative one: “Although they might not have sleep in them, eyes sometimes deceive”.

How strange!

Boabdil was never told:

«Weep like a woman for what you could not defend as a man»

One of the most repeated historic lies in the history of Spain concerns the last sultan of Granada, Boabdil “el Chico”. Supposedly his mother, the sultana Aixa, told him this highly repeated sentence when he surrendered the city on 2nd January 1492 and handed over the keys of the Alhambra to the Catholic monarchs.

But the sentence is not true, it was invented by an author, Padre Juan de Echevarría, in a book he wrote in the form of dialogues called *Paseos por Granada y sus contornos o descripción de sus antigüedades*, published in 1764. This sentence allowed Padre Echevarría to question the personality of the Emir Boabdil, who frequently varied his alliances so as not to lose his power in the Nasrid kingdom of Granada, and even swore vassalage and the handing over of the city to the kingdom of Castile in exchange for his freedom when he was taken prisoner in 1481, a promise that was not kept as he was released in 1483.

By handing over Granada, the Catholic monarchs terminated the *Reconquista*. Boabdil went into exile in Las Alpujarras, and died in Morocco in 1527.

06

Nutrition: truth and hoaxes

We spend our lives surrounded by information. All we have to do is turn on our telephone, our tablet, our television or our computer to be able to obtain an amount of information that was unimaginable by the generations before ours.

Unfortunately, much of this news is false. It is the so-called fake news that is put out to get more hits on websites or, far worse, to con patients by taking advantage of the vulnerability caused by their illness.

Most people would think it was absurd for someone to advise people with dry eye disease to wash their eyes with their urine, but I have real patients who have done this!

The problem arises in severe cases when the patient has tried treatments that have not worked. The patients' desperation and need to have a good quality of life mean that some of them will try treatments without any scientific evidence. This is why it is essential to ask your ophthalmologist if you have any doubt, however absurd it may seem.

In fact, some products you can buy in the herbalist that are not controlled can be counter-productive for dry eye.

Focusing on the subject, the general recommendations for a healthy life are the same for patients with dry eye: eating in moderation, in particular fruit and vegetables; sleeping for seven or eight hours a night; avoiding a sedentary lifestyle and doing regular exercise; not smoking, as tobacco contains substances that irritate the eyes; not drinking alcohol or, if you do so, in small doses, because it contributes to dehydration; not getting stressed (stress and depression cause dry eye disease) and relaxing your sight from time to time.

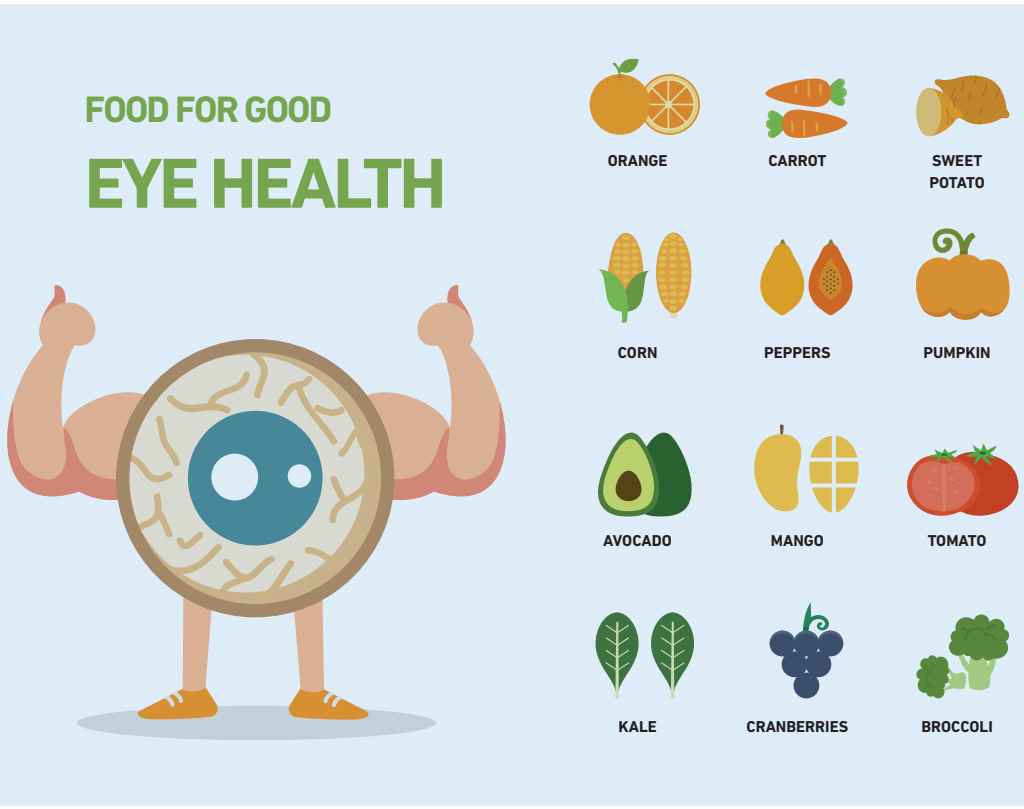


Figure 13. There are many foods that are beneficial for eye health.

If you drink tea, choose green tea; as far as coffee is concerned, caffeine is good as it stimulates the lacrimal gland, but the problem is that it is also a diuretic and therefore dehydrates you. If you like coffee, have a glass of water to compensate for each cup you have.

As I have already indicated, when talking about how it affects the eye surface in dry eye, the key lies in inflammation. This natural process, which defends us when we have wounds or when we have an infection, is exacerbated with age due to processes that we do not yet fully understand, but which affect the quality and the function of the tear. Although it sounds easy to say, the way to improve dry eye symptoms is to avoid actions that favour inflammation and to opt for those that prevent it.

The importance of omega-3

Therefore, in addition to avoiding alcohol and tobacco, the consumption of foods that contain omega-3 is highly recommended. This fatty acid is found, among others, in fish such as sardines, anchovies, salmon, mackerel and tuna fish, as well as in walnuts. It can also be taken as a supplement, but it is important that you acquire them from a chemist.

There are many other beneficial contents, such as vitamin B12 which are found in mackerel, salmon and sardines. Oily fish (salmon, tuna fish, bonito, mackerel, anchovies, herrings, and so on) are also rich in choline, phosphatidylcholine and lecithin, as are walnuts, almonds, scallops, cod, Brussels sprouts, broccoli, spinach, cauliflower, asparagus and plain chocolate.

Other useful trace minerals are polyphenols which are found in virgin olive oil, avocados and walnuts. Tomatoes and kale contain lycopene and

zeaxanthin. If you are a post-menopausal woman, take pumpkin seeds which are rich in zinc and phytoestrogen. All of these are good for eye health.

Figure 14. Walnuts are an important source of omega-3 fatty acids and of polyphenols.

What type of food should you avoid?

There are numerous foods and substances that favour dry eye, therefore you are recommended to take them in moderation or to eliminate them from your diet.

For example, you should limit your intake of arachidonic acid, which is found in egg yolks, red meat, wheat germ and peanuts.

It is also essential to keep your cholesterol level under control. There are many foods that raise it: egg yolks, seafood or dairy derivatives such as

butter, cheese, ice cream and yoghurt. One alternative to dairy products is almond milk.

Another substance to be avoided, although we do not consciously ingest it or it enters our organism through other channels, is phthalates, as they interfere with hormonal production. They are found in plastic bottles, perfumes, nail varnish and in children's toys. As they can be found in plastic, it is best not to heat up recipients made of this material in microwaves.

Finally, it is not advisable to ingest bisphenol A, which is found in the inner lining of food and drink cans. It is better to use glass jars than cans or plastic bottles.

How to keep hydrated

As far as hydration is concerned, the simplest way is to drink the recommended amount of water, which is around two litres a day, depending on your age and physical constitution. In most Spanish homes the quality of tap water is excellent. If, as is the case in some places, the water has a bad taste, a lot of limescale or is not transparent, the best option is mineral water. It is best to avoid soft drinks and cartons of juice due to the amount of sugar they contain.

Finally, vitamin and mineral supplements have been found to be useful in dry eye disease. A lack of vitamin A has been described as a cause of dry eye in developing countries, but any healthy diet we consume in Spain, which includes carrots or spinach, has enough of it that we need not worry. If you have any doubts, you may occasionally use food supplements with vitamins and minerals.

How strange!

Why do we cry when we chop onions?

When we chop onions, the knife breaks the cells and the liquid inside them is released, transforming cellular amino acids into other products. During the process, a volatile substance called syn-propanethial-S-oxide is produced, which is rich in sulphur. This substance combines with the water of tears and sulphuric acid is produced.

Sulphuric acid is an irritant and the eyes defend themselves from it by adding more water, in other words, by crying. To avoid onions from releasing these substances, it is advisable to freeze them to make it more difficult for this gas to be produced.

This physical event associated to chopping onions has also been used by authors, such as Günter Grass who called his memoirs *Peeling the Onion*, and said about them “Memories are like an onion, layer after layer has to be peeled to reach inside our memory and, as happens when peeling an onion, tears are inevitable.”

07 Contact lenses

Contact lenses cause dry eye, so when they are used, great care must be taken. The liquids that are used to clean them also cause dry eye.

In fact, contact lenses are one of the main causes of dry eyes, by decreasing corneal sensitivity and favouring the evaporation of tears. If you have used them, you will remember the difficulties they caused you the first time and that they probably made you cry. Over time, this discomfort when putting them in probably disappears. The corneal nerve density decreases as well the sensitivity of the eye surface.

However, thanks to having sensitivity in our eyes, we secrete tears. Therefore, if any particle or an eyelash gets into our eyes, it will start to blink and cry until it has been removed, due to eye sensitivity and its nerves.

The same happens with tear secretion: when a tear evaporates, it stimulates the numerous nerves in the eye. The cornea is the human tissue with most nerve endings, between 20 and 40 times more than tooth pulp and 300 times more than the skin. The process continues when

the nerves send information to the brain to create more tears. By using contact lenses and having less sensitivity, you secrete fewer tears.

In addition, if the lens you use is soft, it will absorb water because it needs to hydrate itself to maintain its shape. It does so at the expense of the tear, as no residual tear remains to separate the lens from the eye meaning that, when you blink, the contact lens traumatises the eye surface.

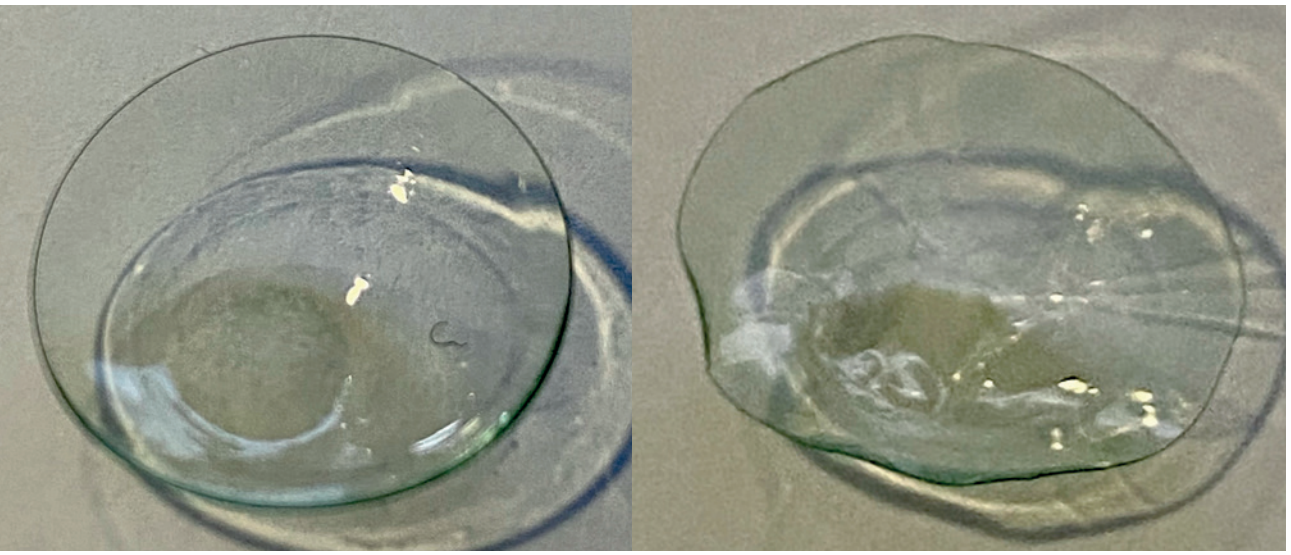


Figure 15. Image of a hydrated lens (left) next to a dry one (right).

Best contact lenses for everyday use

Therefore, you must be careful with the kind of contact lens you use: the greater its content in water, the worse it is for the eye. And if you use them and start to feel that your eye is dry, the best thing to do is to alternate glasses and contact lens and, if they are soft ones, ensure that they

are made of a material called silicone hydrogel. This material requires fewer tears than classical hydrogel. In short, the less amount of water the lens contains, the better it is for the eye.

Another very important aspect is that the lens should be for daily use. Why? Because lens cleaning liquids are toxic to germs to guarantee hygiene, but some may adhere to the lens and this is also dangerous to human cells. Therefore it is best to have new contact lenses every day.

Take great care with the tinted lenses that have become fashionable for celebrations such as Halloween. If you want to use them, you should first ask your ophthalmologist if you are a good candidate for them.

How strange!

How do actors cry in the movies?

Actors have many tricks to make them cry: from remembering places from their childhood to objects with which they have a special link or to thinking about a family member who is no longer with them. One common technique is not blinking: focusing your gaze on a bright light until you feel that your eyes are starting to become moist and entering onto the scene. The negative part is that sometimes the weeping does not seem credible.

If the actor does not manage to produce tears, which is what usually happens, the magic of the movies comes into play: a technician, outside the shot, throws drops of glycerine with long straws so that they appear in the actor's eyes. The effect is very real.

08 Allergies

Allergic reactions can affect and produce dry eye and, in fact, both of them, allergies and dry eye, occur together frequently making it difficult to diagnose them. Therefore, ophthalmologists often refer their patients to the allergy specialist.

There are two main groups of allergies: those that affect the conjunctiva and those that affect the skin of the eyelids. The former are caused by pollen, animal hair and dust mites and the latter, known as contact dermatitis, are due to hypersensitivity to eyedrops or to cosmetics that the patient may use.

There is one hypersensitive reaction which, without being specifically an allergy, is a serious immunological disease and is known as the Stevens-Johnson disease. This can be devastating and affect the production of tears for life. Its name comes from the two North American paediatricians Albert Mason Stevens and Frank Chambliss Johnson, who gave it this name in 1922.

The allergy specialist will carry out various tests to check whether the patient is allergic to any kind of substance such as dust mite, animal hairs (for example dogs and cats), mildew or pollen. The allergy specialist will diagnose the type of allergy by initially asking the patient about their family background, the environment in which they live and work, the months in which it appears and other factors that trigger the symptoms. They will then apply substances that can cause allergies to the arm and observe whether they react. They can also be determined by means of a blood test or a provocation test, which is particularly useful in the case of allergies to medications, additives and foods.

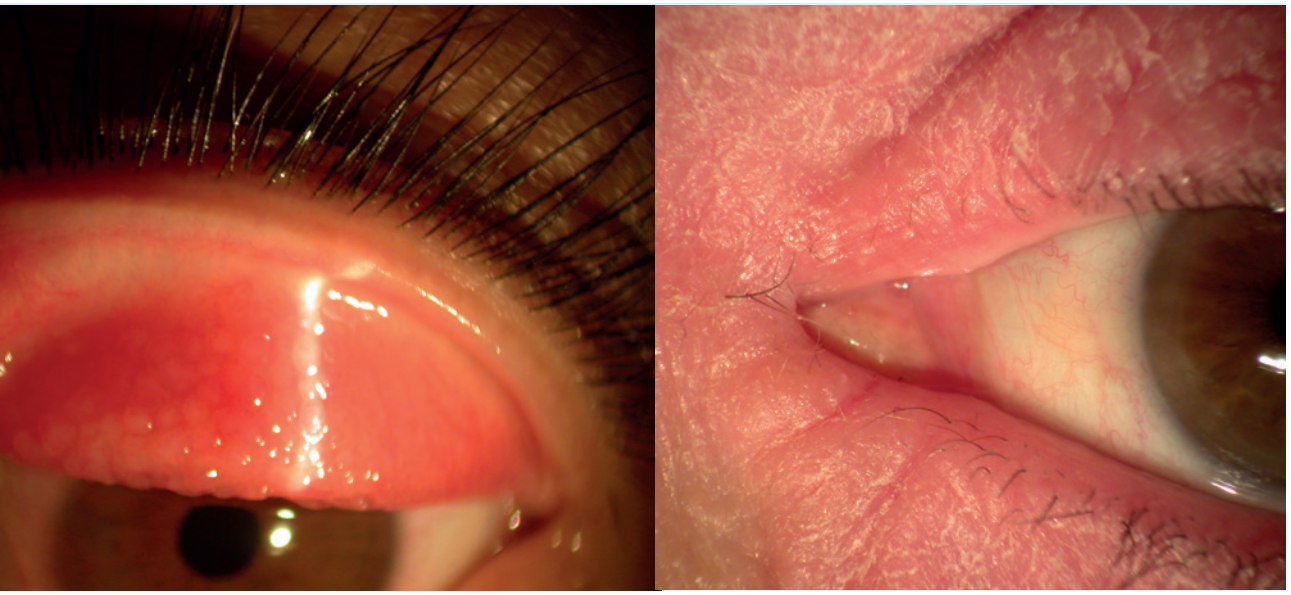


Figure 16. Allergic conjunctivitis (left) and dermatitis around the eye (right).

It should be noted that the treatment for allergic conjunctivitis can make dry eye disease worse, meaning that it is essential to take it into account when offering treatment. You should remember that oral antihistamines decrease tear production.

One good option to minimise the symptoms of the allergy could be to install an air purifier next to where you work, in the bedroom or in the place of the house where you spend most time. And do not forget to wear glasses, preferably wrap-around ones, when you go outside.

ADVICE FOR PEOPLE WITH ALLERGIES
If your allergen is seasonal, it is recommendable to stay inside the home as long as possible.
Keep doors and windows closed during pollination time (dawn and dusk).
Change your clothes and have a shower, and even wash your hair, when you get home.
Refresh the ambience with air conditioning and clean the filters.
When the allergen is inside the house (dust mite) you should change your pillows and mattresses frequently.
Clean domestic items such as furniture, rugs, cushions, and so on regularly.
Hoover up dust frequently.
Get rid of mildew, damp and sources of fungi.
Remove any pets from the home if they are the source of the allergen.
Avoid rubbing your eyes so that the physical trauma of pressing with your hands does not make things worse.

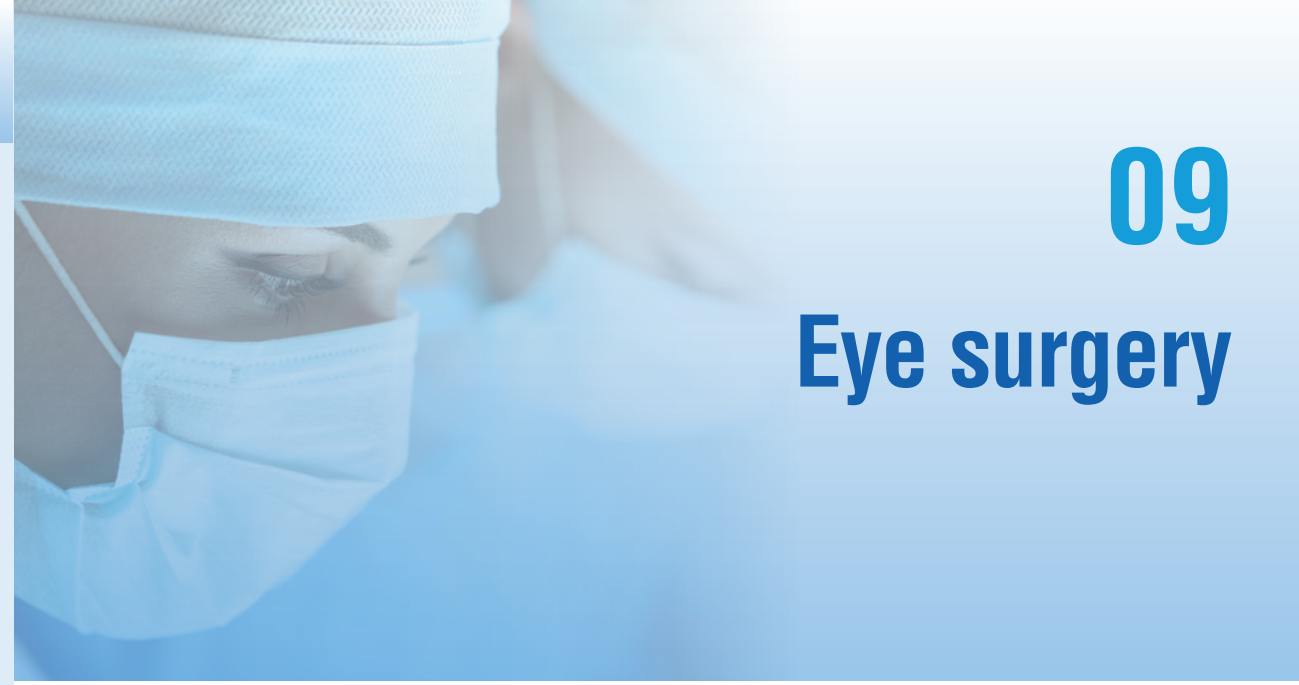
How strange!

The origin of the word allergy

Although allergy is a Greek word and one could imagine that it is thousands of years old, it was coined little more than a century ago, in 1906, by the Austrian paediatrician and immunologist Clemens von Pirquet who talked about allergy for the first time in a short article that he wrote for a scientific journal, with the Hungarian paediatrician Bela Schick.

Literally, it means “the work of others” and it defines a special type of immunological or defensive reaction of the organism against a substance that does not normally produce reactions in most people. Therefore, the origin of an allergic reaction is not in the agent that produces it, but in the individual themself.

In addition to its use in medicine and physiology, the word allergy also defines extreme, contrary sensitivity (rejection) towards certain subjects, people or things.



09 Eye surgery

Refractive corneal surgery is used to correct refractive errors in the eyes such as myopia, farsightedness and astigmatism. It can be done using LASIK (laser-assisted in situ keratomileusis), PRK (photorefractive keratectomy), LASEK (laser-assisted sub-epithelial keratectomy) or SMILE (small incision lenticule extraction). They are very safe interventions, with good optical results and few adverse effects. However, if you suffer from dry eye, it can be aggravated, meaning you would not be the best candidate for the surgeries.

As in all surgeries, there may be complications, although the rate is very low, calculated to be below 1%. After the surgery, dry eye may appear in almost half the patients, and usually disappears in the first weeks after the intervention, although there have been cases in which the discomfort becomes chronic. On rare occasions, neuropathic pain can appear due to an abnormal regeneration of the nerves after the intervention. It is fundamental to follow the indications of your ophthalmologist, who will most likely prescribe artificial tears without preserving agents after the operation.

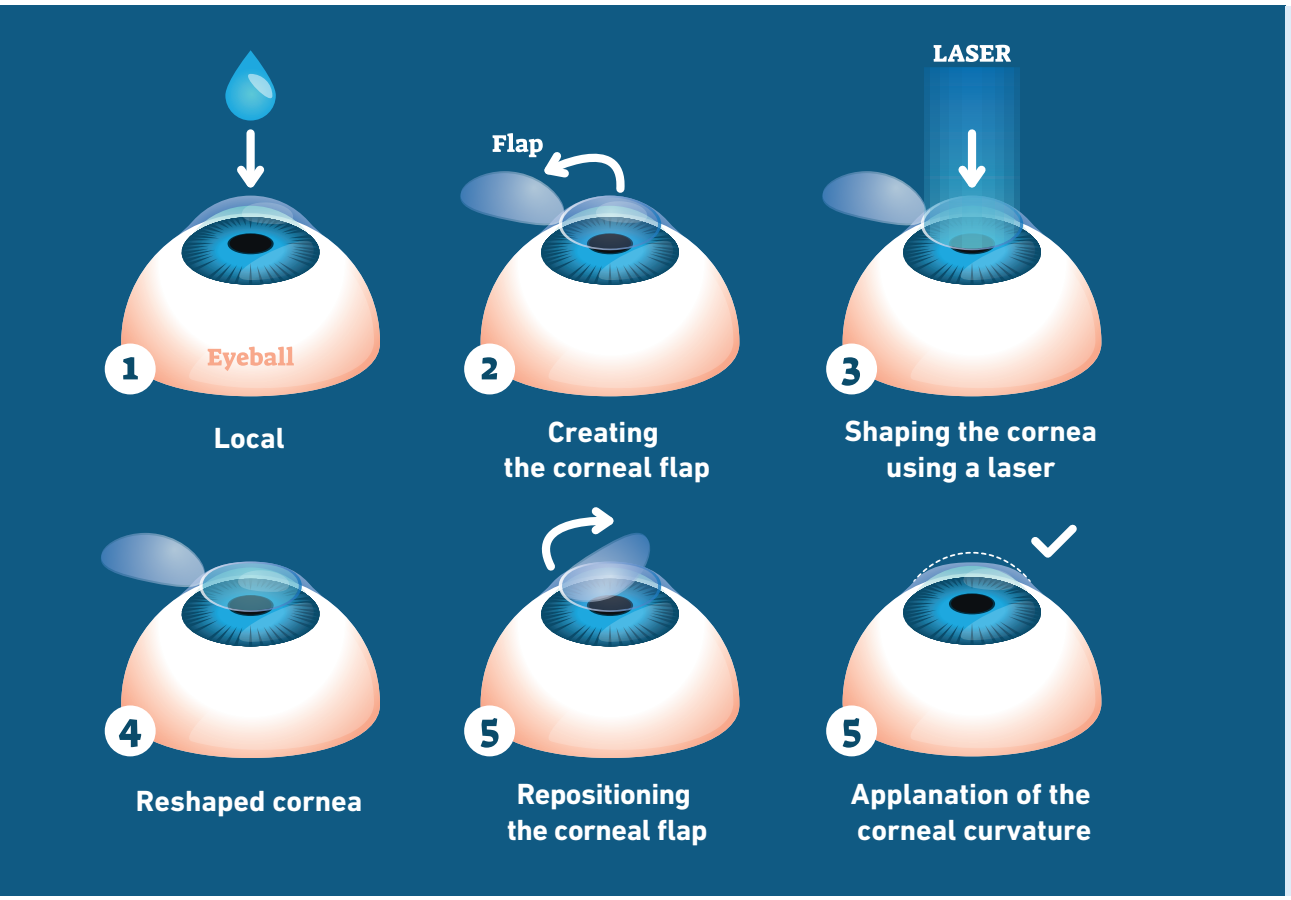


Figure 17. Phases of LASIK refractive corneal surgery (reduction of myopia).

After cataract surgery, dry eye symptoms can also appear. As is the case for corneal refractive surgery, they usually gradually decrease. It should be taken into account that cataracts appear with age, as does dry eye.

Other surgeries, such as operations on the retina, glaucoma and blepharoplasty are associated to dry eye. In most surgeries, dry eye is produced on cutting the nerves when operating. And in the case of blepharoplasty, on altering the normal blinking function.

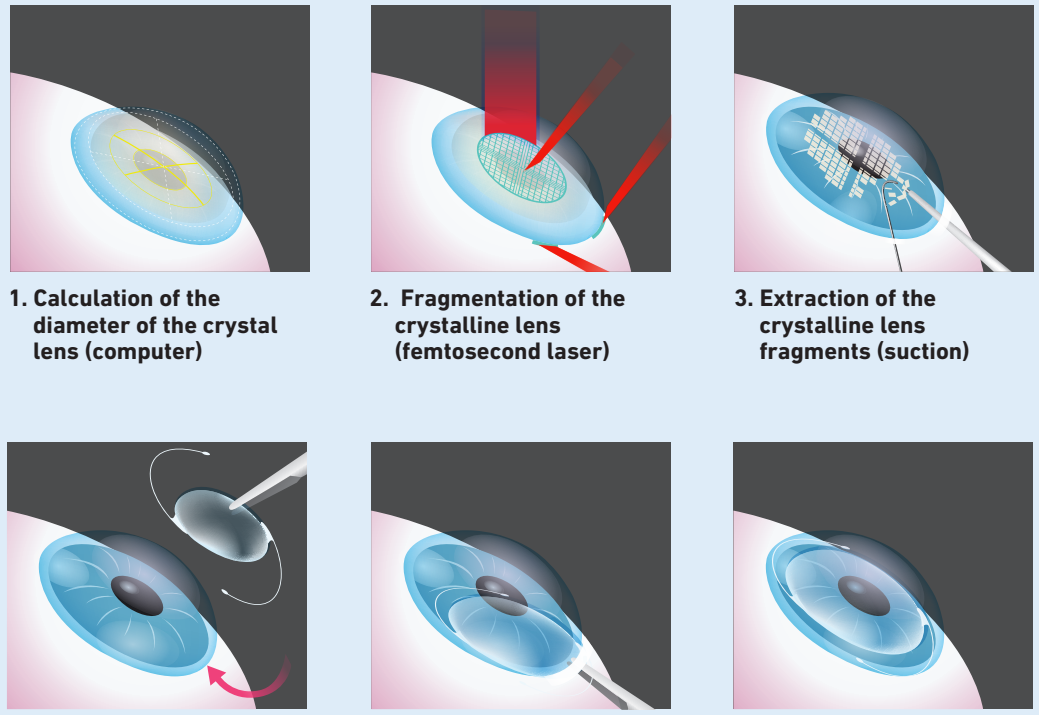
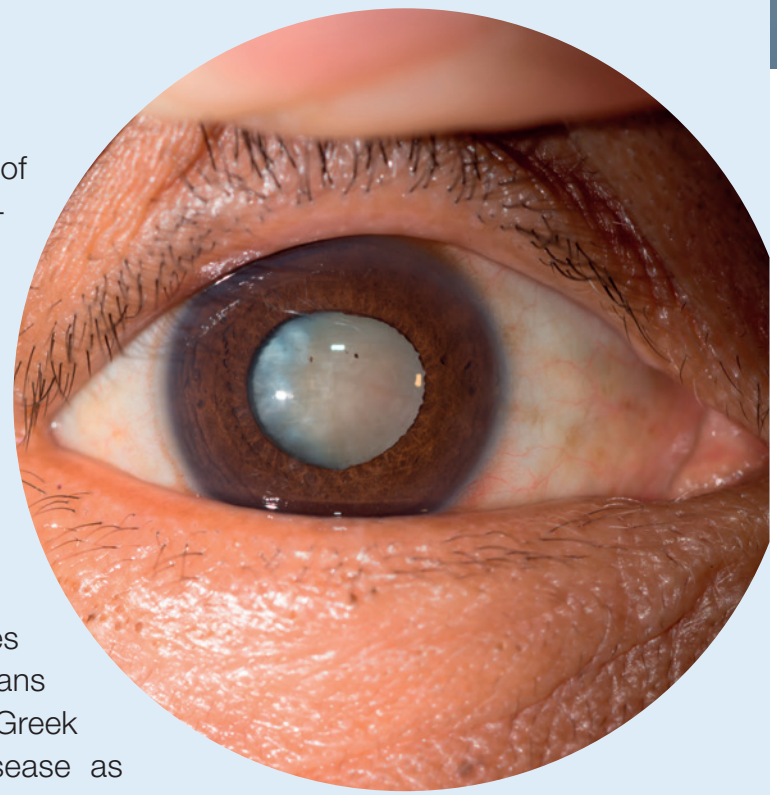


Figure 18. Phases of cataract surgery with laser.

How strange!

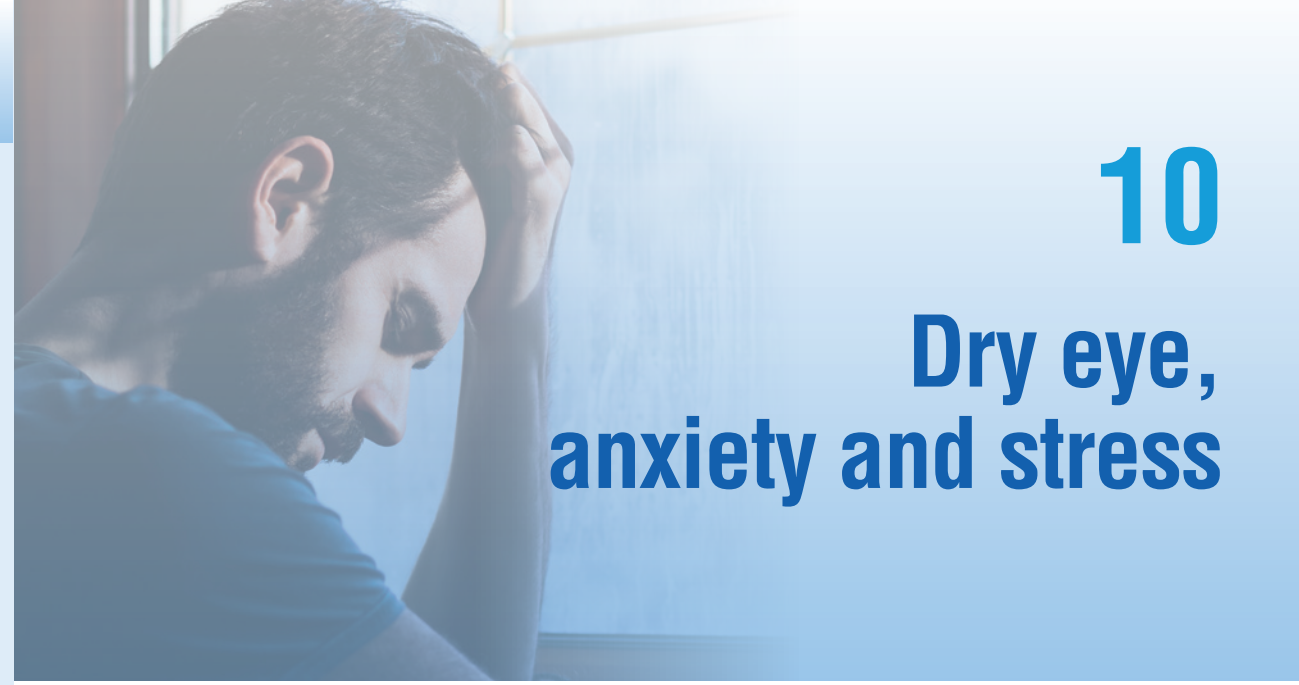
Be careful with cataracts!



A cataract is the opacity of the eye's lens, the crystalline lens, which prevents rays of light getting in and leads to a gradual loss of sight and to blindness (it is the number one cause of blindness in the world and affects more than 50% of people aged over 65).

The word cataract comes from Greek and literally means to pour down. However, Greek doctors referred to the disease as *hipókima*, meaning "descending flow".

The Romans translated *hypochima* as *suffusio*; the Arabs called it "waterfall" which translated back into Latin as *gutta opacta* or cataract. Spanish was the first modern language to adapt it and its existence has been documented since 1250.



10

Dry eye, anxiety and stress

Stress has enabled us to evolve as a race, warning us about the dangers our predecessors faced on the African savannah. Today, we know that excessive stress leads to various health problems such as migraines, muscular tension, rosacea, high blood pressure, alterations to the appetite and even pain.

But stress can also mean that we blink less, that we sleep less and that we eat unhealthy food because we do not have time to sit down and prepare a salad or grilled fish. And it is precisely eating junk food, not sleeping enough and blinking less than we should that are the circumstances that encourage the inflammation that causes dry eye.

Therefore, although it may be complicated, we must reduce our level of anxiety, putting aside time for ourselves, enjoying our favourite activity, finding time to go for a walk or to go to a museum and spending time with our family or friends. Even smiling is useful as it reduces the exposure of the eye surface and hydrates it.

Figure 19. Depression and dry eye disease, a possible combination.

This aspect must be particularly taken into account in patients with depression, as depression produces dry eye disease and, at the same time, dry eye disease produces depression.

In short, dry eye disease can be a cause of frustration for people suffering from it, as it directly affects them being able to carry out their everyday life activities, in other words it affects their quality of life.

Why do we cry

when we see romantic movies or get sad?

How strange!

The response is simply biological: stress causes us to accumulate hormones such as adrenaline and oxytocin. By crying, we hydrate our eyes and release them, alleviating tension and achieving a natural calming effect. Various questionnaires show that 92% of the world population have cried at some time in their life watching part of a film.

The so-called psychic tear, the result of sobbing, comes about from different emotions, ranging from sadness to joy, and is a challenge for scientific researchers. The other tears are basal tears that keep the eye lubricated and clean and there are also reflex tears, which are the result of an irritant, such as when chopping onions.

11

What makes you suspect you have dry eye?

As we have already mentioned, everyday activities such as driving, watching television, reading, working at the computer, travelling in an aeroplane, sewing or writing can favour the appearance of dry eye.

External agents such as very pungent smells, smoke or very powerful perfumes can affect the eye surface and start off the process that ends up as dry eye disease. It has been shown that people who work in perfumeries have more dry eye, as the volatile chemicals destroy the oily layer of the tear, increasing its evaporation.

The main cause of dry eye is not blinking. This is due to the fact that we do not replace the tear film and the existing one evaporates. Recently, it has been observed that, on closing your eye while blinking, if you do so completely, you squeeze the Meibomian glands that secrete oil. The more oil secreted, the more we reduce the evaporation. If we do not blink, the oil becomes locked up in the glands and they inflame. Over time they can atrophy which is then irreversible.

Therefore, if for work or leisure time reasons we carry out activities that do not let us blink, we are favouring its appearance.

We blink thousands of times a day, and we do so without realising it. But in the same way, we are not aware if we are not blinking. Spending several hours a day in front of the computer screen or unwinding by looking at the social networks or watching a film on the television or playing a video game is the most usual way to not blink enough and end up with tired eyes.

Figure 20. The use of wrap-around glasses, ergonomics in the workplace and humidification of the ambience are three important resources to combat dry eye.

As I have already mentioned, one key aspect is whether we close our eyes completely. Ask your ophthalmologist what your blinking is like: if you do so incompletely, it is advisable to do blinking exercises. If you spend many hours in front of the computer or monitor it is essential to look at the screen from above: if the screen is at the same height as your eyes you open them completely, and more of your eye surface is exposed. Therefore, it is best to sit in front of the computer

or in front of the television in a fairly high chair or to place the screen slightly lower. Placing a humidifier next to where you are, can help to minimise the symptoms.

If you live in a place with a dry climate, there are many more possibilities for your eyes to become dry. Therefore, out of doors, the use of glasses is compulsory, and if they are wrap-overs, all the better.

As I have already mentioned, closed spaces such as cars, aeroplanes or trains dry the eye surface a great deal. Therefore, the use of wrap-around glasses is also highly recommended, as well as placing the jet of the air-conditioning so that it is not aimed straight at your eyes. And do not forget to use glasses if you do outdoor sport or any kind of physical exercise as, in this case, in addition to limiting evaporation, you will protect them from injuries.

Side effects of medications

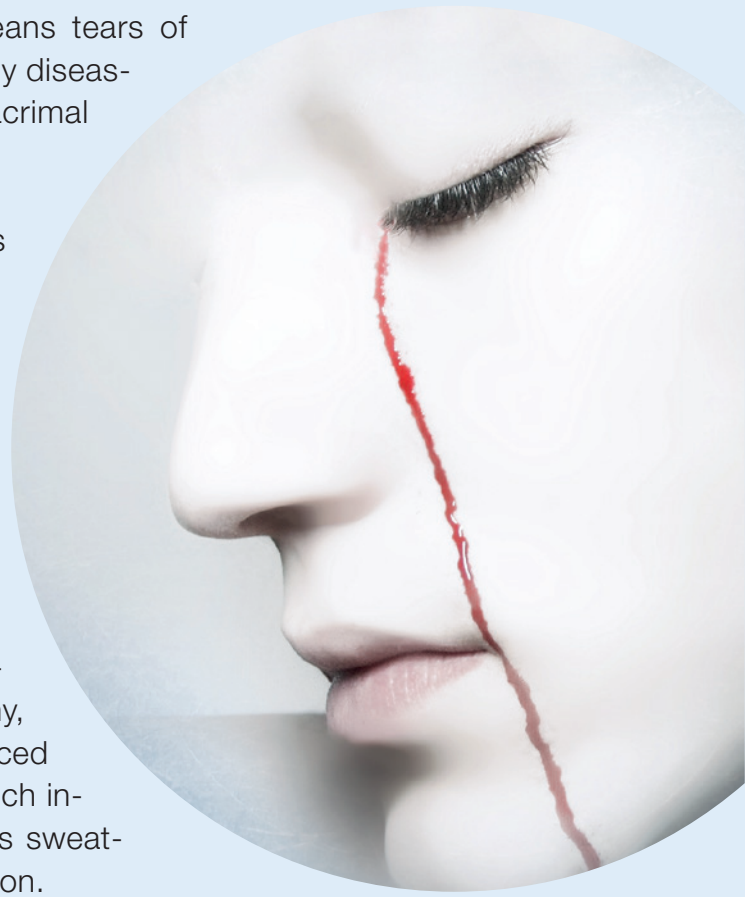
Some medications for other diseases can cause dry eye as a side effect. It is essential that you tell your ophthalmologist about any medication you are taking and the reasons why you are taking it. This should be particularly taken into account if you take any of the medications mentioned on page 48. You should also tell your doctor if you take any over-the-counter medications or you use creams or remedies from a herbalist as their composition could contain ingredients that may damage your eyes.

I have mentioned that many of the eyedrops we use, particularly to control glaucoma, produce dry eye (ask your doctor if there are any without preserving agents!). Take care with drops that whiten your eyes; most of them produce dry eye or even greater problems.

How strange!

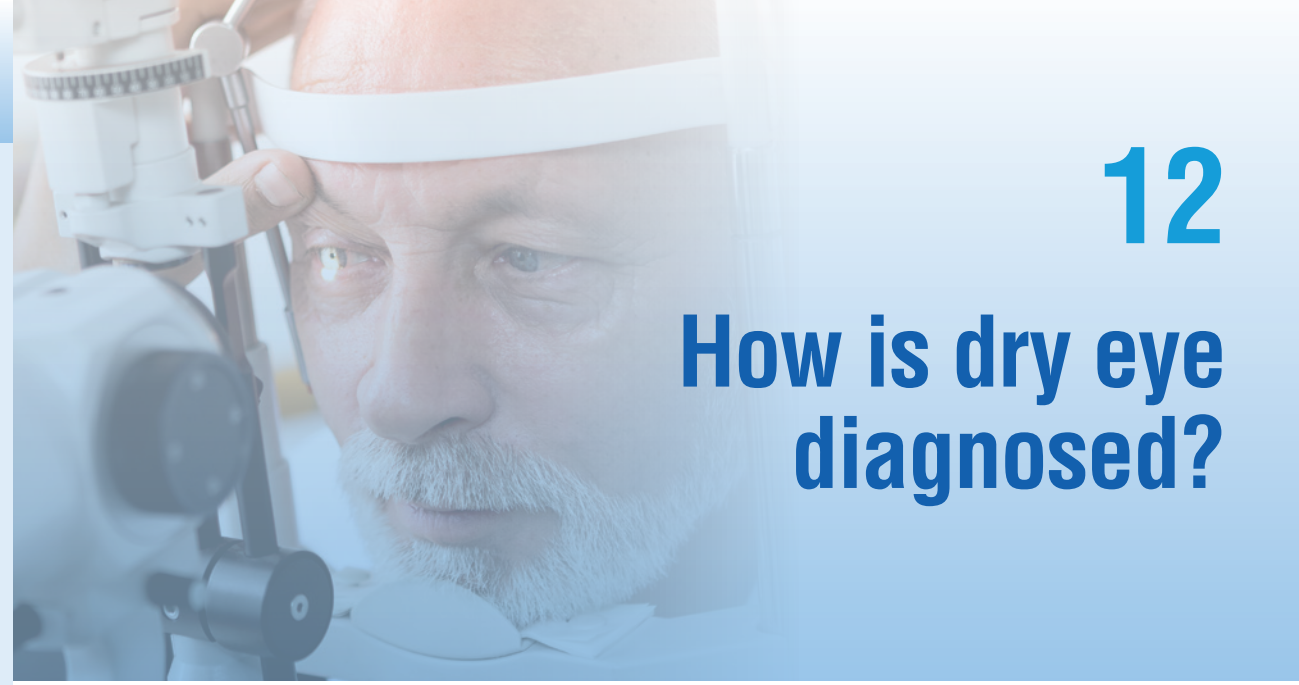
Can we cry blood?

The answer is yes, although it is not frequent. This phenomenon is called haemolacria, a word that comes from Greek and which literally means tears of blood. It is a symptom of many diseases, such as tumours in the lacrimal apparatus.



It can also be due to serious conjunctivitis or wounds.

Traditionally, haemolacria, crying tears of blood, has been linked to certain supernatural phenomena as well as to miracles. One very well-known case is that of Teresa Neumann, a peasant from the village of Konnersreuth in Bavaria, Germany, who in the 1950s experienced alleged mystical episodes which included haemolacria as well as sweating drops of blood and levitation.



12 How is dry eye diagnosed?

If you suspect you have dry eye, it would be a good idea to see your family doctor. It can also be useful and interesting to check websites on the Internet to inform yourself, but only consult those which contain accredited sources (such as those given on page 119 of this book) because, as I mentioned in the section on nutrition, you can frequently find pages full of hoaxes and incorrect information.

Once you have asked for an appointment with your ophthalmologist, make sure you take your clinical history and a list of any medications you are taking and eyedrops that you have used unsuccessfully. This will help get a more accurate diagnosis. You should also tell your doctor if there are any circumstances that are notable, such as symptoms that worry you, if there are times of the day when it is better or worse, if there are any foods or circumstances that improve or worsen its condition. Remember that you will also be asked if you have or have had any allergies and if you have undergone any eye surgery.

The ophthalmologist will carry out an initial exploration of your eyes and will probably ask you many of these questions. They will then look at

your eyes using a slit lamp, an instrument that emits a highly intense light that allows them to analyse the eye. The ophthalmologist (the word comes from Greek) or oculist (a synonym, but the word comes from Latin) will assess your rate of blinking, whether your blinking is complete and whether your eyes close fully or not completely.

Figure 21. When you go to your ophthalmologist's appointment you should go with a clean, unmade-up eye.

Another test you will probably be given is one of visual acuity. I am sure you will have seen those posters on which the letters get increasingly smaller. The ophthalmologist will ask you to read the different rows. The usual study of visual acuity does not reflect the visual problems that patients with dry eye experience, and this is one problem of the poor sight in patients with dry eye which cannot be objectified with the apparatus that exists in a normal surgery, as the patient blinks when they want and restores their vision.

There are tools that determine sight in a dynamic way, asking the patient not to blink (which happens when we read, we watch a series or we are working at a computer). In this way, it can be seen that in people with dry

eye disease, visual acuity drops rapidly until the next blink and does not remain intact as would happen in a normal person.

Questionnaires are also useful tools, although they are mostly used for studies. One of the most commonly used ones is available on the first pages of this book and, by answering the questions in it, it is possible to make an initial determination as to whether a person is a possible candidate to suffer from dry eye.

The OSDI, SANDE and DEQ-5 are other questionnaires that are frequently used. They are useful, but they may not be necessary. It is usually sufficient for your doctor to ask certain questions.

Ophthalmologists also have other kinds of tests that enable them to be more precise about the diagnosis. One of the most habitual ones uses fluorescein, a yellowy-orangish coloured stain that allows the structures of the eye to be analysed.

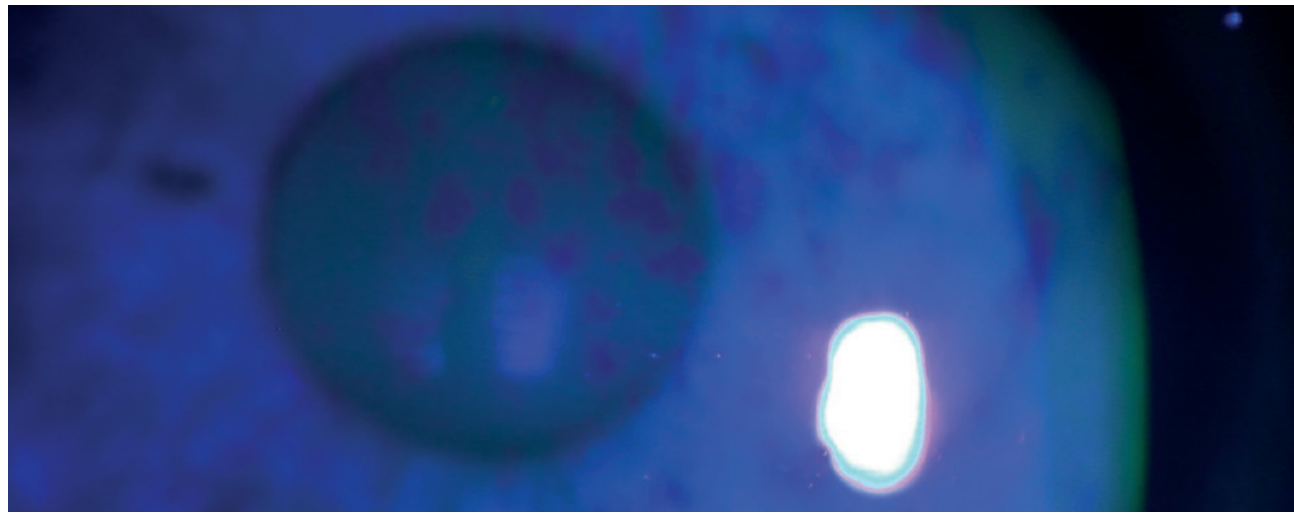


Figure 22. The TBUT (tear breakup time) test evaluates the stability of the tear film.

Thanks to this, we are able to see, by applying the drop, if there are “wounds” in the eye as a result of the disease known as keratitis. To analyse the stability of the tear film, we can also use what is usually known as the TBUT or tear breakup time test. The patient will be asked not to blink and we count the seconds the tear takes to break after the eye opens. Usually, it takes about 10 seconds. Should it appear sooner, it is evidence that there is a problem with dryness.

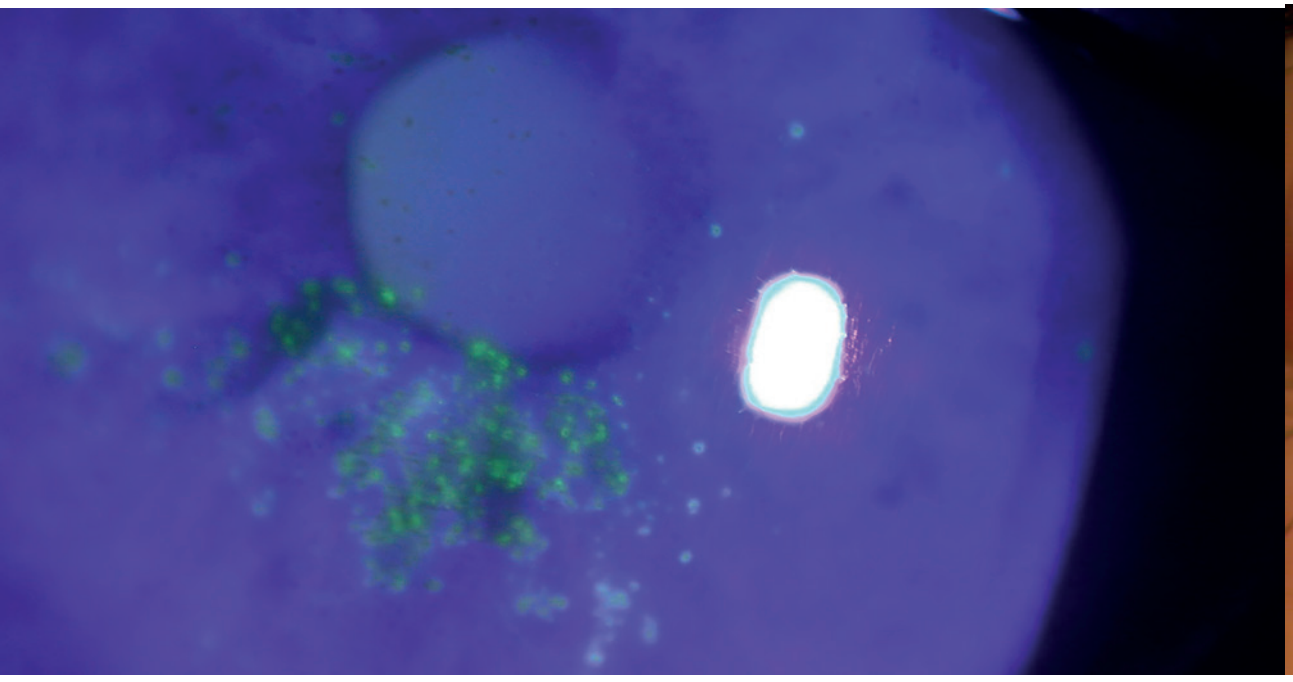


Figure 23. Fluorescein is a stain that is key to diagnosing dry eye (in the image, keratitis caused by dry eye). The green points are the “wounds” captured by the fluorescein, which turn blue with blue light.

Fluorescein is also useful for measuring the so-called tear clearance rate, in other words, how long the eye takes to eliminate tears through the excretory lacrimal channels. These tests can also be carried out using other stains such as rose bengal or lissamine green. Both of

them allow other alterations that cannot be seen with fluorescein, and if necessary, the ophthalmologist can combine them.

Schirmer’s test is used to measure the volume or amount of tear that we have. A strip of paper is placed on the conjunctiva of the lower eyelid for five minutes and the eye is kept closed. If it is only slightly damp, the existence of dry eye is highly possible. It usually collects at least 10 millimetres.

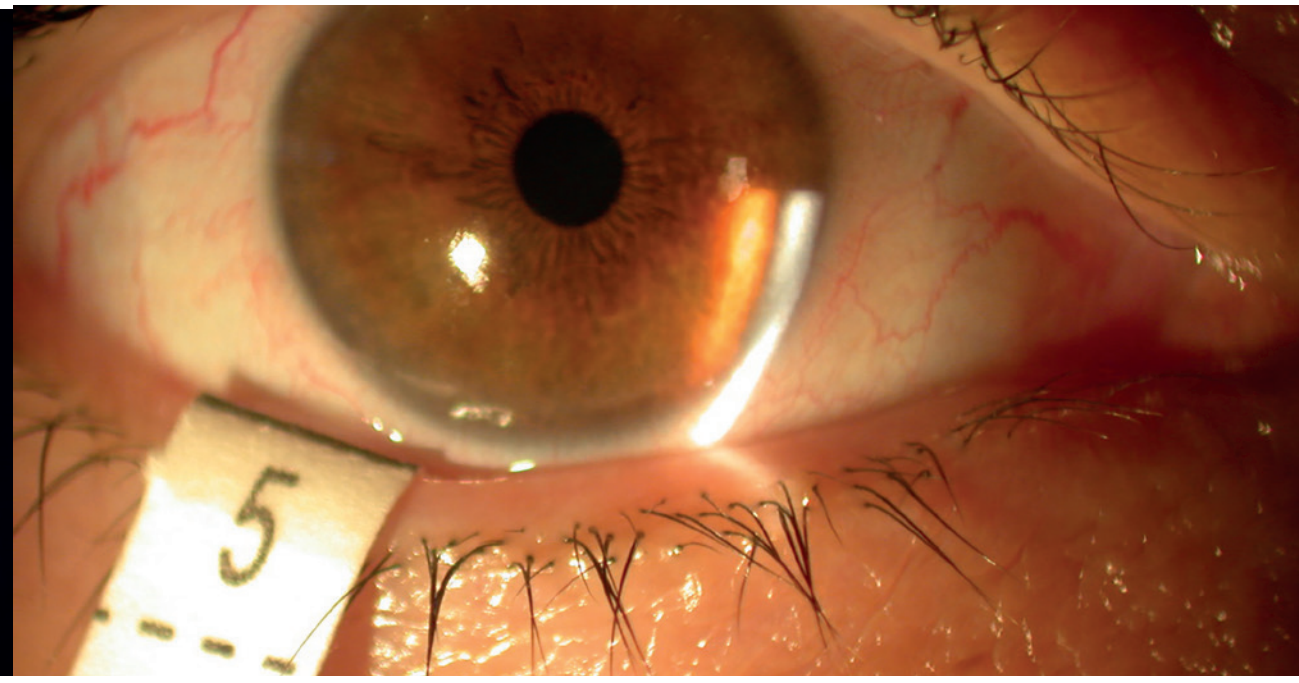


Figure 24. Schirmer’s test is used to measure the volume or amount of tear.

Other ways of measuring tear volume are meniscometry and OCT (optical coherence tomography). These tests quantify the tear volume that is supported on the edge of the lower eyelid, which gives us an idea about the tear volume. Abnormal values in Schirmer’s test, meniscometry and OCT indicate the existence of aqueous deficiency dry eye, in other words, due to a shortage of tear production by the gland.

To measure the quality of the tear film the tear osmolarity is determined, which is the concentration of salt found in it. In dry eye, this concentration increases both due to excessive evaporation as well as low production of water, and the tear becomes more concentrated, in other words, its osmolarity increases. The ophthalmologist will take a small sample of tear, which is analysed by an instrument (osmometer) which indicates whether it contains a greater or lesser amount of salt. A high amount is a clear indicator of the presence of dry eye.

The levels of proteins such as lactoferrin can also be measured, as well as inflammatory enzymes such as matrix metallopeptidase 9 (MMP-9). Lactoferrin is found in the tear film and usually decreases with age. Depending on the amount of it, it can be established whether the patient has dry eye. The same thing occurs with MMP-9, which is measured with a sample of tear and with a similar test to a pregnancy one (with a yes or no response). MMP-9 is a protein that increases in the tear when the eye dries.

Measuring the thickness of the oily film of the tear using interferometry also allows the presence of evaporative dry eye to be found. The thinner it is, the greater the dryness, as it increases the evaporation.

There are instruments that measure the sensitivity of the eye surface, which are known as esthesiometers. The ophthalmologist will use a cotton or nylon thread with which they will touch several parts of the eye. In most cases, the patient will notice it. But in the case of people with diabetes and herpes, this will not happen. And because they do not have sensitivity, their eyes do not send messages to their brain saying that the eye is dry so the brain, in turn, can send messages to the muscles in the eyelids to blink and to the lacrimal gland to start to produce tears.

In these cases, treatment should start immediately, as patients cannot detect the symptoms and need greater protection of their eye surface. We have recently designed a more precise esthesiometer without contact that sends pulses of air onto the cornea.

Finally, a blood test may be necessary to detect the disease causing dry eye, such as lupus, rheumatoid arthritis or Sjögren's disease. Sometimes studies are requested on sexual hormones, thyroids or vitamins A, B and D. Another test is to calculate the number of goblet cells on the eye surface. To do this, a membrane of a material called nitrocellulose is rubbed onto the conjunctiva, the membrane is stained and the number of goblet cells are counted using a microscope. If there are not very many of them, the patient probably has dry eye.

In short, there are numerous tests that can help ophthalmologists to diagnose dry eye. You might ask yourself: Why so many tests if, for example, by just measuring my blood sugar they know if I am a diabetic or not? The answer is that dry eye is a very complex disease and there are many types of it.

In addition, our organism tries to compensate for alterations (which it can do in mild cases), meaning that on some occasions the tests can be normal, therefore several of them need to be done. Finally, these tests are useful to find out what type of dry eye you have, so as to be able to provide you with a customised treatment.

How strange!

Do crocodiles really cry?

The myth that crocodiles cry when they devour their prey is a very old one. The first references can be found in the 12th century. Although these reptiles have lacrimal glands and cry to hydrate their eyes when they come out of the aquatic environment to hunt, they do not do so while they eat. In other words, they do not cry out of sorrow from eating another animal.

One scientific explanation would be the fact that the salivary glands and the lacrimal glands of crocodiles are very close to each other. When they eat, the two glands are activated at the same time, and this would produce the constant weeping we refer to as crocodiles tears.

Strangely, crocodile tears can occur in humans. As a result of a facial trauma, there can be an aberrant nerve regeneration that makes us cry when we chew.

13 Treatment

The ideal treatment for dry eye is, unfortunately, difficult to apply. The ideal scenario would be that the patient should move to the tropics to live in a damp climate, that they should stop using their computer, tablet and mobile phone, that they should follow a healthy diet mainly consisting of fresh fruit and vegetables and that they should live in an environment that does not cause them stress. We would all like to get to reorganise our lives to live like that but unfortunately, our everyday lives take us along another route.

The most common thing when facing a health problem is that we go to the nearest chemist. There are numerous treatments available in these health establishments, in the form of drops, ointments or sprays, the latter of which, by the way, are of questionable effectiveness. Most of them provide momentary relief, but do not get to the root of the problem. In any case, you must ask your ophthalmologist how useful they are.

Artificial tears

The first treatment option, in the immense majority of cases, is artificial tears, also popularly known as eyedrops, although to be precise, an eye drop is any medication that is diluted in water or in oil and that is placed into the eye in the form of drops.

Artificial tears come in different viscosities meaning that the more fluid ones will hydrate the eye better and offer greater relief to symptoms, but will not last for long on the eye surface. Therefore, we recommend applying gels in the afternoon and ointments or creams at night, as the eye also dries more throughout the day. Among other reasons, as already mentioned, we sleep with our eyes closed to protect them as we do not produce tears during the night.

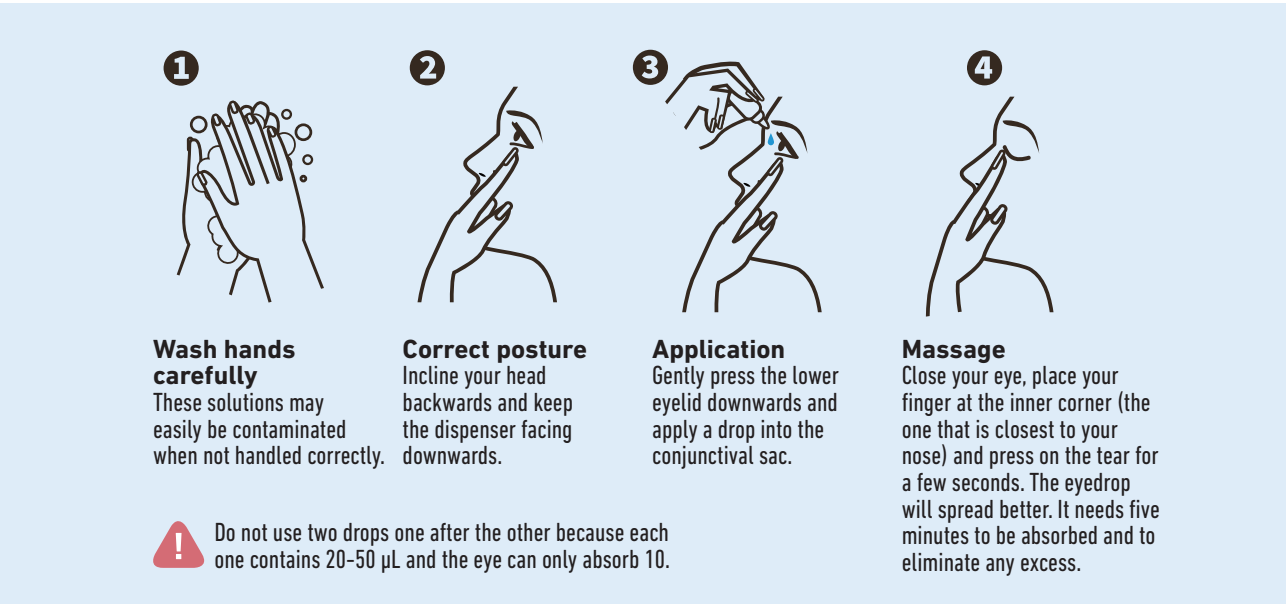


Figure 25. Correct application of eyedrops.

Many artificial tears contain preserving agents to prevent bacteria and fungi from contaminating the product. However, these preserving agents can favour the eye becoming inflamed and may be allergens for some patients and, long term, can even do irreversible damage to the eye surface. Therefore, you should choose artificial tears that have been recently developed and that do not contain preserving agents or phosphates in their formula. They are available in single doses and in special flasks that incorporate a physical system that prevents the inside of the bottle from becoming contaminated. We also recommend that these tears should have low osmolarity to compensate for the excess of salts in tears in dry eye. Nowadays, there are also tears with oil for patients with evaporative dry eye disease.

There are hundreds of artificial tears and therefore the best thing to do is to ask your family doctor which is the one that best suits your needs. One point to be made is that it is not clear whether an excess of tears inhibits the production of natural tears. However, this excess will bathe or eliminate the few natural tears that you produce and artificial ones are not as good as natural ones. Therefore, if you need more than one artificial tear every two hours, you should look at other kinds of therapy.

Treatment with medication

Regarding treatment with medication, whether topical or systemic (oral), remember to tell your ophthalmologist what you are taking in case it could interact and cause a side effect. Do not forget to mention any remedies from the herbalist, vitamin supplements or creams. they can interact, so you must not forget.

Anti-inflammatories are the first choice of drug for dry eye. Corticoids are a magnificent choice for short-term treatment, although you must watch

out for the possible appearance of cataracts and eye pressure (with mild corticoids such as hydrocortisone for short periods, these complications are unlikely, although you must take care).

Figure 26. Tell your ophthalmologist about all the medications that you are taking in case they interact and cause any side effect.

Cyclosporine ophthalmic is the drug that is used for treating chronic dry eye disease as it does not have any general side-effects. Until some years ago, in Spain we could only use it in magisterial formulations, but it is now available in chemists. Bear in mind the fact that once treatment with this drug is started, it may take a month or a month and a half before any improvement is noticed. In fact, the initial results, before the treatment for dry eye starts to take effect, may be a sensation of burning and redness. Therefore, the ophthalmologist should warn the patient that this is possible. If I were a patient and I was not told that it would sting when I used it and, after 15 days, I did not notice any improvement, I would give up on the treatment. It is not an artificial tear, it is something different, an anti-inflammatory, that treats the root cause of dry eye.

Antibiotics such as tetracycline, azithromycin and erythromycin in children can be useful. It is best not to use non-steroidal anti-inflammatory drugs as they decrease sensitivity and therefore cause dry eye.

There are also new drugs, such as lifitegrast that may become available for patients in Europe in the near future.

Other treatment options are medications to reduce the inflammation of the eyelids, those that stimulate tear production —oral secretagogues, such as pilocarpine. In Europe we do not have topical secretagogue such as diquafosol or rebamipide which exist in Japan— and ocular inserts, which are devices similar to a transparent grain of rice that are placed between the eyelid and the eyeball and that release artificial tears, such as Lacrisert.

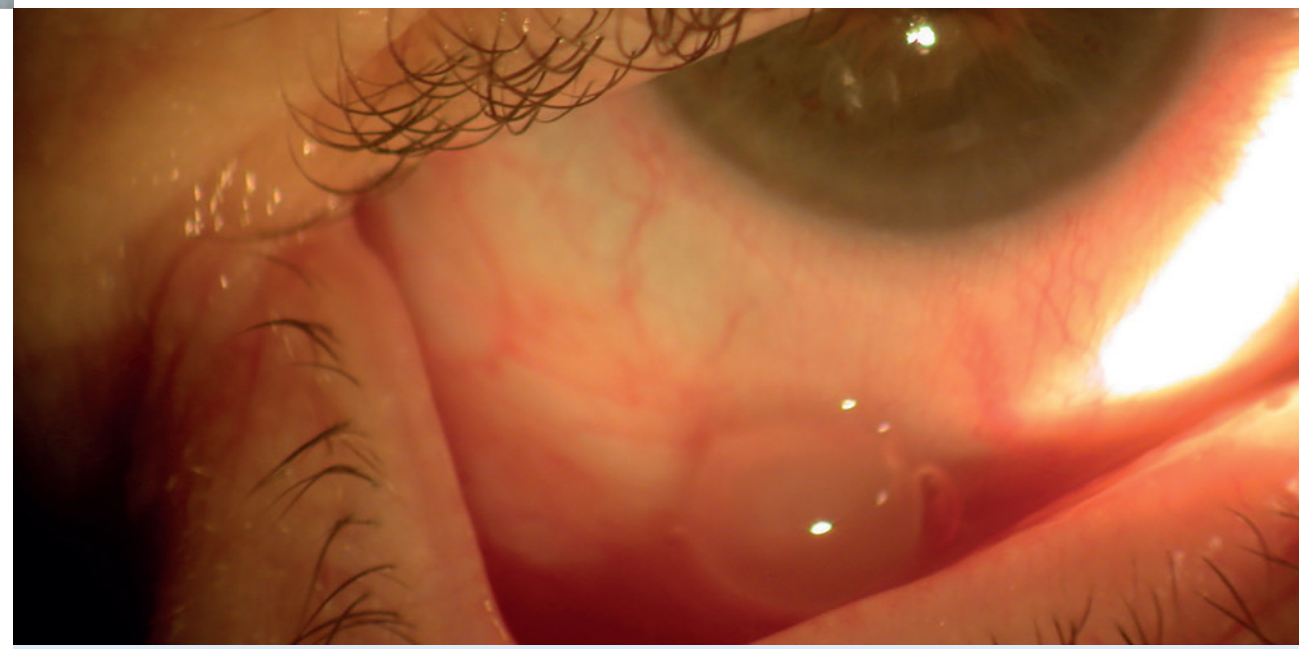


Figure 27. In the image, you can observe an ocular insert in the bag of the conjunctival sac.

There is even the option of using ophthalmology eyedrops made using your own blood, called PRGF, meaning Plasma Rich in Growth Factors.

These are reserved for those who have serious symptoms that do not respond to other treatments. It is the most similar thing to a natural tear. It will be extracted from your blood approximately every three months and, from the sample, the red corpuscles will be removed, to later mix the remaining plasma with the saline solution for the serum or to break up the platelets for the PRGF. The product must be kept refrigerated and sterile in the fridge and freezer. These blood derivatives have been found to have an anti-inflammatory and neuroprotective effect.

Plugs and surgery

Sometimes, ophthalmologists close the lacrimal puncta with plugs in a reversible way; in this way, the tear does not leave the eye and increases its volume and lubrication. It is important to take into account that we must first remove the inflammation from the eye, otherwise the plugs will only make all the inflammatory substances stay on the eye, which will make things worse.

This surgery is usually only used when no previous treatment has worked. There are different techniques, based on the alteration of the eyelids and the tear secretory glands.

The 20-20-20 rule

Apart from the existing treatments, North American ophthalmologists, as I have already mentioned, have developed a mnemonic rule that could be useful. It is the 20-20-20 rule. It consists of stopping for 20 seconds every 20 minutes of intense work in front of the computer (or reading from a screen or a book or watching television) and looking at a distance of 20 feet, which represents some six metres in the metric system. This makes us blink more frequently and helps our eye surface to recover. It is sufficient to look at a far-away wall or to look at the window. Various studies have shown that the 20-20-20 strategy allows for much more productive work days than concentrating in front of the screen for hours on end. Relaxing your sight like this is the best way to deal with dry eye and it is even better if you have a humidifier in the room and redirect the direction of the air conditioning, as I have already mentioned.

Figure 28. Closing the lacrimal punctum with a plug.

The use of glasses is also fundamental, as I have reiterated several times. Wearing normal glasses represents 40% less tear evaporation than in people who do not wear them. The reason for this is that it prevents air coming in, which is what evaporates the tear. In fact, the more the glasses wrap around the eyes, the better.

It is well-known that the consumption of tobacco and alcohol are not advised under any circumstances, and this is also the case if you have dry eye, as they contribute to increasing the evaporation of the tear.

New techniques

There are also many new techniques that can be useful, such as Lipiflow, MiBoFlo and IPL (Intense Pulsed Light), BlephEx and Maskin's Meibomian Gland Probing. The first consists of an automatic system that preheats the internal part of the Meibomian glands to 42.5°C. Later, the system starts to give pressure pulses for 12 minutes. A device is used to open the eyelids, without damaging the eyeball, and to drain the content of the Meibomian glands by means of pneumatic chambers. The beneficial effects last for approximately 12 months.

Figure 29. From left to right, system for micro-exfoliation, IPL machine and thermal pressure machine.

MiBoFlo is a device that uses a thermoelectric heat pump and that enables treatment to be customised thanks to its adjustable timer. In this case, the heat is supplied from the outside and the pressure is applied by the ophthalmologist.

IPL is a special kind of lamp that acts directly on the skin of the cheek, temple, nose and eyelid, improving the symptoms of blepharitis. It has been found that it has an anti-inflammatory effect and stimulates the nerves of the Meibomian glands. It is particularly useful in patients with rosacea, but also in other forms of blepharitis. It is usually applied in four separate sessions with a two-week gap between each of them. As it is a chronic pathology, one or two isolated sessions must be applied yearly for maintenance purposes.

As far as BlephEx is concerned, it involves micro-exfoliation that is carried out with a tiny sponge. In about eight minutes and in a precise way, it removes flaky cells and the remains of bacteria, dust mite and solidified oil that accumulate on the edges of the eyelids. These substances cause inflammation and other eye discomfort, such as blepharitis. BlephEx reduces itching, weeping eyes, stinging and the sensation the patient has of having a foreign body in their eye. It is the "professional" cleaning of the edge of the eyelid and manages to do what the patient cannot achieve using wipes.

Finally, Meibomian gland probing developed by Dr. Maskin achieves a reduction in the tension of the eyelids of approximately 90%. It is used in extreme cases for inflamed, puffy eyelids.

These techniques are complementary and are indicated in blepharitis or a dysfunction of the Meibomian glands. In a professional way, we carry out the different forms of care that patients should do at home (heat and hygiene). I tell my patients that it is like cleaning their teeth

on a daily basis and going to the dentist — in this case the ophthalmologist— for deep cleansing.

What more can be done?

In addition to the numerous options we have mentioned, a simple solution that can be carried out at home is that of using a wipe or compress that you have heated with steam or hot water. Wait until it reaches a temperature that does not hurt your skin and place it on your eyelids while lying on your bed or relaxing on the sofa. Three minutes will be sufficient to dissolve the solidified oil of the Meibomian glands and increase the thickness of the oily film. The heat can also be dry, by using masks containing gel or seeds that are introduced into the microwave and then placed on top of a mask.

Another option consists of showering under hot water. The shower will have the same effect as the wipe or compress although it is never so effective. After this, wash your face with cold water to stimulate the circulation of the blood vessels in your face. Do not over massage the eyeball or the eyelid as this could be counter-productive. Bear in mind that the application of heat in the shower can, in some patients, cause redness in the eyes. Many patients doubt about using heat or cold. Heat deals with the problem, making the oil that obstructs the inflamed Meibomian glands more liquid, whilst cold is a symptomatic treatment that relieves discomfort without treating the root of the problem.

Take care with the use of cosmetics, as some make up removers, eyeliners, mascaras and other similar products may alter tear production and irritate, as many of these products contain tar or wax that may block the Meibomian gland drainage holes. Anti-ageing

creams mostly contain retinoids and these substances inflame the Meibomian glands. Once again, should you have any doubts, ask your ophthalmologist and remember not to wear make up to the appointment, as it can interfere with any examination and tests to be carried out

Figure 30. Heat from gel masks is useful to dissolve the solidified oil of the Meibomian glands.

Finally, take care when using home-made remedies such as placing slices of cucumber on your face because, although they may refresh your face and alleviate the inflammation, they could also make your case worse. Once again, if you have any doubts, ask your ophthalmologist.

The present and future of research

To date, dry eye does not have a cure, although it does have treatments. I will now mention some of the existing lines of research.

Cellular therapy consists of the introduction of new cells into tissue to treat the disease of the organ. The injection of healthy tear cells into the lacrimal gland or substances that heal these cells is promising, although tests on animals are being started.

Another line of work is immunotherapy, which consist of stimulating the patient's immune system itself so that their own defences fight the disease. The advances in this field are based on cancer and on the so-called "bubble boy disease". In the future, these advances could benefit patients with autoimmune diseases, such as those suffering from Sjögren's disease.

One very promising channel is the study of microbiota, the millions of bacteria we have in our body. The ones that are most talked about are the ones in our guts, but they are all over our body and, therefore, also in our eyes. In our eyes, these bacteria are protected with a film known as biofilm.

The main characteristic is that there are no two people in the world with the same microflora. As we have already commented, the incidence of some diseases or others and the effect on them is completely different, causing greater or lesser inflammation. Research could modify the way in which diseases as different as rheumatoid arthritis, multiple sclerosis, depression and dry eye are dealt with.

One promising line in this field —although it is still in the preclinical research phase— is faecal transplant, which consists of the oral or anal

administering of the stool of a healthy person. The gut bacteria of the dry eye receptor will previously have been given an aggressive antibiotic treatment to eliminate them and the new bacteria will help to improve diseases in which inflammation plays a key role.

Figure 31. The study of microbiota would seem to be a promising line of research in dealing with dry eye.

Another possible challenge focuses on finding which genes are responsible for dry eye and, if possible, modifying them with genetic therapy. Or modulating them with changes in diet or modifying aspects of the patient's life. However, dry eye is multifactorial meaning that it is produced by different diseases, each one with its own genetic involvement.

Exploration of the hormonal channel (oestrogens and androgens which, respectively, stimulate and suppress inflammation) is also rather promising.

The expectation is that the changes in dealing with the disease will be ongoing in forthcoming years. Do not hesitate to ask your ophthalmologist about the new therapeutic options as they appear.

Next, we will show you those products in experimental phase that are currently being studied. Note that the majority of them are anti-inflammatory (see table).

Product	Mechanism of action	Develop. phase
NM-133	Nano-enabled form of cyclosporine A	2
ALG-1007	Local anti-integrin	2
EBI-005	IL-1 inhibitor local protein	2
ESBA-105	Antibody fragment against TNF-alpha	2
OCS-02 (LME-636 or ESBA-1622)	Local antibody against TNF-alpha	2
ISV-101 (ISV-303, BromSight)	Bromfenac at low doses 0.075%	2
BOL-303242-X	Selective glucocorticoid receptor agonist	2
Cis-Urocanic	Anti-inflammation through JNK inhibition	2
R-348	JAK/SYK inhibitor	2
XG-102 and XG-104	D-amino-acids peptide, highly selective, non-competitive, long-acting inhibitor of JNK	2
Tofacitinib (CP-690,550)	JNK inhibitor	2
ST-266	Proteins from amniotic cell cultures that modulate inflammation	2
SA-001 oral (SJP-002 local)	Increase in the volume of tears and anti-inflammatory	2
DA-6034	MMP-9 and mucin secretagogue inhibitor	2
RX-10045	An RvE1 mimetic	2
SDP-4	Silk protein, inhibition of inflammation	2
CyclASol	New cyclosporine (0.05% and 0.1%)	3
Seciera	Nano-cellular formation of cyclosporin	3
OCU-310	Combination of brimondine and steroids	3
EGP-437	Iontophoretic delivery of dexamethasone phosphate	3
KPI-121 0.25%	Particle penetrating in mucus to favour the release of Loteprednol etabonate	3
HL036337	Local TNF-alpha blocker	3
TOP-1630	Narrow spectrum kinase inhibitors	3
MIM-D3 (Tavilermide)	Partial NTRK1 inhibitor	3
RGN-259	Tβ4 promotes cellular migration and reduces apoptosis and inflammation	3
ADX-102 or Reproxalap	Malondialdehyde inhibitor	3

Table 2. Novelties in research into dry eye treatment.

Glossary

Accommodation: a change in the shape of the crystalline lens that enables us to see nearby objects, when the lens thickens, and distant objects when it narrows.

Androgens: hormones that promote the development of male characteristics.

Antihistamine: a drug that prevents or antagonises the effects of histamine, a substance that plays an important role in all allergic processes.

Aqueous humour: a transparent liquid that feeds and oxygenates the cornea and the crystalline lens. An accumulated excess of it causes glaucoma.

Artificial tears: see eyedrops.

Autologous serum drops/PRGF: eye drops made with the patient's own blood. PRGF is the acronym for Plasma Rich in Growth Factors.

Blepharitis: an inflammation of the edge of the eyelid, usually caused by a bacteria.

Blepharoplasty: plastic surgery on the eyelids.

Cataract: opacification of the lens, usually due to age.

Colour blindness: a congenital dysfunction that affects the viewing of certain colours (usually red and green) which are often confused.

Cones: a kind of photoreceptor cell in the retina which is light sensitive.

Conjunctiva: a fine, transparent layer of the eye. It is full of veins and goes out to the edge of the cornea. It also lines the damp surface behind the eyelids.

Conjunctivitis: an inflammation of the conjunctiva, the transparent layer that covers the inside of the eyelid and the white part of the eye, which turns red. It is usually associated to an infection or allergy. Dry eye also causes conjunctivitis.

Contact dermatitis: an allergy caused by hypersensitivity to eyedrops or cosmetics.

Cornea: one of the parts of the eye that is transparent and free from veins, It looks like a convex disk and is in front of the iris.

Crystalline lens: our eye's natural lens, which is transparent and elastic. It has no nerves or veins. When it enlarges, we see nearby objects and when it narrows, we see distant ones.

DEQ-5: a questionnaire that is usually used to diagnose dry eye.

Dust mite: a microscopic arachnid animal that feeds on dust and can cause allergies.

Epiphora: constant overflow of tears due to lack of drainage.

Epithelium: tissue formed by closely connected cells that covers the external surface of the cornea and the conjunctiva.

Esthesiometer: an instrument that measures the sensitivity of the eye surface.

Eyedrops: any drug that is diluted in water or in oil and that is instilled in the eye in drop form, such as artificial tears.

Eyestrain: a synonym for presbyopia. A problem with one's sight due to the natural ageing of the eye. It is due to a lack of accommodation and therefore people have problems seeing close up.

Fluorescein: a yellowy-orangish coloured stain that is used to diagnose eye diseases. It enables the structure of the eye to be analysed.

Glaucoma: an increase in the pressure inside the eye due to the accumulation of the aqueous humour. Left untreated, it can cause blindness.

Goblet cell: goblet-shaped cells that are found in the conjunctiva. They produce a type of mucus, an excess of which causes rheum (sleep).

Interferometry: a test that measures the amount of lipid in a tear.

Intraocular pressure: pressure that occurs in the eye. An excess of it, due to an accumulation of aqueous humour, causes glaucoma.

Iris: pigmented area in the centre of the eye which can be brown, blue or green and which dilates and contracts the pupil to allow a greater or lesser amount of light in.

Keratitis: inflammation of the cornea which can compromise one's sight. When there are lesions on the epithelium, it is known as superficial or punctate keratitis, and it is the characteristic of dry eye.

Keratoconjunctivitis sicca: the scientific name for dry eye.

Lacrimal canaliculi: small channels that carry tears from the lacrimal puncta to the lacrimal sac.

Lacrimal gland: a gland in the eye that produces tears. It is in the upper, external part of the orbit.

Lacrimal puncta: part of the eye in the inner corner of the upper and lower eyelids which collects the tears produced by the lacrimal gland.

Lacrimal sac: the structure of the eye that connects the lacrimal canaliculi with the nasolacrimal ducts and pumps tears to the nostrils.

Lactoferrin: a protein found in the tear film that usually decreases with age. Depending on the amount of it, it can be decided whether or not a patient has dry eye.

Lagophthalmos: the inability to close the eye when sleeping. It causes dryness in the eye and means that the person suffering from it awakens feeling tired.

LASEK: a laser technique that is usually used to correct refractive errors in the eye, such as myopia, farsightedness and astigmatism to be able to do away with spectacles. The acronym LASEK stands for Laser Assisted Sub-Epithelial Keratectomy.

LASIK: a laser technique that is usually used to correct refractive errors in the eye, such as myopia, farsightedness and astigmatism to be able to do away with spectacles. The acronym LASIK stands for Laser Assisted In Situ Keratomileusis.

Macula: the area in the eye with the best vision due to the presence of millions of cones, a kind of photoreceptor. Its deterioration, due to age, causes macular degeneration.

Macular degeneration: a disease which frequently appears in elderly people. It slowly destroys the central vision, which can end up causing blindness.

Meibomian glands: glands that we have in the eye and that produce oil that forms the surface layer of the tear. We have around 50 in the upper eyelid and 25 in the lower one.

Melanin: a pigment that determines the colours of the eyes. The more there is, the darker the eyes. Blue, green and grey eyes have little melanin.

Meniscometry: a test used to measure the tear volume.

MMP-9: a protein found in the tear and that increases when the eye dries.

Mucus: the deepest layer of the tear, it is in contact with the corneal and conjunctival cells.

Nasolacrimal duct: a structure in the eye that carries tears to the nose and, from there, to the throat.

Neuropathic pain: pain caused by damage or disease affecting the structures of the nervous system, If it occurs in the nerves, it is called peripheral neuropathic pain and if it occurs due to damage to the spinal cord or the brain, it is called central neuropathic pain.

OCT: the acronym for Optical Coherence Tomography which is a test that allows the amount of tear to be quantified.

Oculist: a word that comes from Latin, which means the same as ophthalmologist (which comes from Greek), and is currently in disuse.

Oestrogens: hormones that promote the development of female characteristics.

Oily layer: the surface layer of the tear, made up of oil which prevents the tear from evaporating. It is one of the three layers of the tear film,

along with the intermediate, watery layer and the internal, mucous layer.

Omega 3 acids: fatty acids found in numerous fish and in food like walnuts. It plays a fundamental role in vision as well as other body functions.

Optic nerve: the nerve that transmits visual information from the retina to the brain.

Orbit: the set of bones that house the eye and the muscles that move it, the ocular nerves, the blood vessels that feed it and the lacrimal gland.

Photoreceptors: cells in the eye responsible for perceiving light.

Photosensitivity: an exaggerated response by the nervous system to light stimulation.

Plasma: a substrate that the lacrimal gland uses to make tears.

Presbyopia: a visual problem due to the natural ageing process of the eye. It can cause symptoms such as watering eyes, blurred vision, itching, eye redness and headaches.

Prevalence: the proportion among the number of cases of a disease, whether new or old cases, and the total number of subjects at risk.

PRK: a laser technique that is usually used to correct refractive errors in the eye, such as myopia, farsightedness and astigmatism to be able to do away with spectacles. The acronym PRK stands for Photorefractive Keratectomy.

Pupil: the black point in the centre of the eye, surrounded by the iris.

Red eye: an inflammation of the conjunctiva, the transparent layer that covers the inside of the eyelid and the white part of the eye, which turns red. It is usually associated to an infection or allergy. It is also usually known as conjunctivitis.

Retina: the innermost layer of the eye which contains the photoreceptors (the cells that perceive light) and the blood vessels that feed them.

Rheum: a very thick or solidified ocular secretion.

Rods: photoreceptor cells in the retina which, as their name indicates, are rod-shaped. They are responsible for what we see at night.

Rosacea: an inflammatory, chronic skin condition that affects the blood vessels and is characterised by redness frequently on the face, particularly the cheeks, nose and space between the eyebrows.

Sclera: the external part of the eyeball which is white and hard.

Schirmer's test: a test that measures the volume or amount of tears.

Sjögren's disease: an autoimmune disease in which the body mistakenly attacks the glands that produce tears and saliva, among other parts of the body.

Slit lamp: an instrument that emits a highly intense light that allows the ophthalmologist to analyse the patient's eye.

SMILE: a laser technique that is usually used to correct refractive errors in the eye, such as myopia, farsightedness and astigmatism to be able to do away with spectacles. The acronym SMILE stands for Small Incision Lenticule Extraction.

Stevens-Johnson disease: a serious immunological disease that is characterised by a hypersensitive reaction. It is not an allergy.

Systemic treatment: treatment for the entire body, not just for one part or one organ.

TBUT: a test that measures the stability of the tear film, counting the seconds the tear takes to break up. The acronym TBUT stands for Tear Break-Up Time.

Tear film: a set of three layers that cover the eye and protect it from external agents. The outer layer is oily, the other two layers are the middle, watery layer and the inner, mucous layer.

Tear film osmolarity: a concentration of salts in the tear.

Visual acuity: the ability of our visual system to discriminate details of objects depending on the lighting or the distance.

Visual fatigue: tired eyes caused by intensive use, such as driving for a long time or looking at a screen or mobile phone for too long. It is also known as eyestrain.

Vitreous humour: a transparent, gelatinous liquid that occupies two thirds of the eye and protects the retina from possible impacts.

Xerophthalmia: a synonym for dry eye; constant dryness of the eye surface.

Further information

Sociedad Española de Oftalmología (in Spanish)
https://www.oftalmoseo.com/patologias-frecuentes-2/ojo-seco/

Asociación Española del Síndrome de Sjögren (in Spanish)
www.aesjogren.org

Free Stop Ojo Seco App (in Spanish)
https://stop-ojos-secos.com/

Sociedad Española de Superficie Ocular y Córnea (SESOC) (in Spanish)
www.lasuperficieocular.com

Sociedad Española de Cirugía Ocular Implanto-Refractiva (SECOIR (in Spanish))
www.secoir.org

The Dry Eye Zone
www.dryeyezone.com

EuDES European Dry Eye Society
www.dryeye-society.com

TFOS Tear Film and Ocular Surface Society
www.tearfilm.org