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CLINICAL GUIDELINE FOR FINNISH OPTOMETRISTS – PATIENT HISTORY, CREATING A PATIENT HISTORY QUESTIONNAIRE

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ABSTRACT

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Purpose: The purpose of this project was to produce evidence-based patient history guidelines for the Finnish Ethical Board of Optometry (OEN).

Methods: This innovation project was performed as a literature review analysis-based research project for The Finnish Ethical Board of Optometry between fall 2021 and fall 2022. The project consisted of three phases. The first phase included the search and selection of existing guidelines and evidence-based literature on patient history. The selection of the guidelines was based on geographical and competence viewpoints. Next, an extensive literature search was performed using PubMed, articles in medical journals, information prepared by official health organizations, and textbooks relevant in this field. The second phase included a critical analysis of the selected literature to determine and describe the key elements of patient history. The key elements included in the updated guidelines were such that were found repeatedly in the existing guidelines. These elements were further refined and described after analyzing the selected literature. The third phase consisted of defining the content and structure of the patient history guideline. The content of the guideline was obtained from the previous phases of the work. The selection of the final format of the guideline (a questionnaire) was based on ensuring its usability. This same viewpoint supported the selection of the question types used in the guideline.

Results: As the first result of this project four guidelines on patient history were identified for further analysis. As the second result seven key elements of the patient history were defined as follows: patient information, including demographics; chief complaint, symptoms interview, and history of present illness; ocular status and ocular history; general health status and history; family ocular and medical history; medications and drug allergies; and social history. The third result was the division of these elements into more detailed sub-elements. The fourth result was a narrative literature review that describes in depth the key elements and their sub-elements. The fifth result was the patient history guideline, implemented as a questionnaire.

Conclusions: The results of this project confirmed that the current guidelines need an update because, as such, they do not meet the requirements of a thorough patient history.

Keywords: patient history, optometry, guidelines, questionnaire, clinical work

CONTENT

1 INTRODUCTION

Due to the aging population in Finland, there has been an increase in age-related eye diseases such as cataracts and glaucoma. This, in turn, has increased the need for eye care professionals in Finland. There are not enough ophthalmologists for the number of patients. There is a need to find solutions on how to care for all these patients, and optometrists can play an important role in filling this gap. This, however, creates a need to further educate the optometrists in Finland and to standardize and improve the practice of optometry. To support the need for unifying the practice of optometry, detailed guidelines on standard practices are necessary.

The patient history is the foundation of the eye examination. A thorough patient history will benefit both the patient and the optometrist. Without going through the patient history systematically with the patient, some elements of the examination might be missed or done unnecessarily.

The Finnish Ethical Board of Optometry (OEN) has emphasized that taking the patient history should always be the first part of the eye examination and guide the optometrist's work. The OEN has approached Oulu University of Applied Sciences as they have seen a need to create more detailed guidelines concerning patient history for the use of Finnish optometrists.

This innovation project´s purpose is to answer this requirement and create a uniform guideline on patient history taking.

The optometrists need further education so that they will be able to collect and interpret relevant information required by the more detailed guidelines. The literature review created in this project can also help in this need.

2 THEORETICAL BACKGROUND

2.1 General

2.1.1 The Framework for Optometrists

There are laws, regulations, and recommendations that guide the everyday work of Finnish optometrists and need to be considered when creating new guidelines. Therefore, these laws, regulations and recommendations are briefly introduced in the following chapter.

Laws, regulations, and recommendations for optometrists in Finland

According to the *law on healthcare professionals*, *559/1994, 2 §,* optometrists and opticians are licensed health care professionals ((Laki terveydenhuollon ammattihenkilöistä 559/1994 - Ajantasainen lainsäädäntö - FINLEX ® s.a.). The education of optometrists is broader and allows the use of diagnostic medications. Health care professionals should apply generally accepted and evidence-based procedures in their work. They are also required to participate in continuing education programs.

Regulation on health care professionals (564/1994, 16 §) states that optometrists and opticians are not allowed to independently prescribe glasses to:

1) a child under the age of eight
2) a person who has previously had eye surgery on the eyeball
3) a person who appears to have an eye disease
4) a person whose visual acuity will not become normal with eyeglasses

Contact lenses may be prescribed and fitted by an optometrist or optician who has completed additional training for such qualification. In addition, the optometrist or optician must ensure that there is nothing to prevent the use of contact lenses. (Asetus terveydenhuollon ammattihenkilöistä 564/1994 – Ajantasainen lainsäädäntö – FINLEX ® s.a.).

According to the *law on the rights and status of the patient* (785/192, 5 §), optometrists have an obligation to inform the patient about their findings and conclusions (Laki potilaan asemasta ja oikeuksista 785/1992 - Ajantasainen lainsäädäntö - FINLEX ® s.a.).

The Finnish Ethical Board of Optometry (OEN) has created recommendations for Finnish optometrists on good examination methodology in the field of optometry. The good examination methodology covers patient history, vision examination, contact lens fitting and health assessment of the eye. (Hyvä optometristin tutkimuskäytäntö-ohjeistus 2019).

2.1.2 Creating Guidelines

"Clinical guidelines are statements that include recommendations intended to optimise patient care that are informed by systematic review of evidence and an assessment of the benefits and harms of alternative care options" (National Academies Press 2011).

There are good professional practices on how to create guidelines. Next, two guideline development processes are briefly introduced. According to the American Optometric Association Clinical Guideline Coordinating Committee (Weaver 2006), their guideline development process should contain the following components:

- The Committee chooses a topic of interest
- The Committee chooses a principal author and consensus panel (experts on the subject of the matter)
- Experts transfer the latest scientific evidence into a form of a guideline
- After publication, the guidelines are reviewed on regular basis

The Current Care Guidelines used in Finland (Current Care Guidelines, 2020) are created based on a similar development process:

- The Current Care Board selects a topic based on the suggestion made by a specialist association
- An experienced information specialist performs a systematic literature search
- Current Care working groups produce guidelines in cooperation with Current Care editors

- The guidelines are written based on existing evidence and the most important recommendations are justified with evidence summaries

In the scope of this thesis, a lighter version of guideline development was applied. This innovation project produced a literature review analysis-based patient history guideline for The Finnish Ethical Board of Optometry (OEN). The OEN reserves the right to make changes to the content of the work for the purpose of finalising the guidelines for the use of Finnish optometrists.

2.2 The Role and Components of the Patient History

The patient history is the foundation of an eye examination. Its purpose is to create a relationship with the patient and gather information about the patient`s chief complaint, visual status and needs, ocular and systemic health, risk factors, and way of life. The information gathered should be used as a guide to create a step-by-step approach for the examination. A good patient history helps the optometrist focus the examination and determine the necessary tests. (Carlson & Kurtz 2016, 5).

Pre-existing guidelines on patient history were reviewed, and an extensive literature search concerning patient history was performed as described in chapter 3.5.1. Based on this work, it was found that a thorough patient history contains key elements which further divide into sub-elements.

The key elements are:

- Patient information, including demographics
- Chief complaint, symptoms interview, and history of present illness
- Ocular status and ocular history
- General health status and history
- Family ocular and medical history
- Medications and drug allergies
- Social history

These key elements and their sub-elements are discussed in more detail in the following literature review chapters.

2.3 Patient Information Including Demographics

In some guidelines collecting patient information precedes the taking of the patient history (Evidence-Based Clinical Practice Guideline, Comprehensive Adult Eye and Vision Examination 2015). In this literature review, a decision was made to include the patient information and demographics in the patient history.

Patients need to be identified reliably. The basic information of new patients should be recorded and verified whenever possible. The basic information consists of the patient`s identification and contact information. This information is needed for identifying purposes and communicating with the patient. (Potilastiedon kirjaamisen yleisopas - v 5.0, 2022).

The Patient Document Regulation states that the minimum identification information should contain the patient`s name, date of birth, personal identification number, and gender. The minimum requirement for contact information is the municipality of residence and contact details such as phone number, email, or fax number. Additional contact information may include native language, business language, occupation, possible need for an interpreter, and citizenship. (Potilastiedon kirjaamisen yleisopas – v 5.0, 2022).

Other information gathered consists of insurance information, legal representative or guardian, possible safety ban, and information about recent updates on basic information (Potilastiedon kirjaamisen yleisopas - v 5.0, 2022).

The demographic information that might be important for optometrists includes the patient`s age, gender, ethnic background, and occupation (avocational visual requirements should as well be asked about as mentioned in chapter 2.9.1). This can give important information on the factors influencing the susceptibility to certain systemic and ocular diseases. (Muchnik 2007, 3–4).

Eye pathologies are often **age** dependent. Congenital and hereditary pathologies are often diagnosed in early childhood, whereas middle-aged patients are susceptible to cardiovascular disease and diabetes mellitus type II. (Muchnik 2007, 4). Glaucoma, cataracts, and age-related macular degeneration develop in older age (Vision and Aging Resources | National Eye Institute 2021).

When examining and interviewing the patient, the optometrist should consider the **ethnic background** related risks and susceptibilities to various diseases. For example, different types of glaucoma are more common in different ethnic groups. Primary open-angle glaucoma shows more prevalence among African Americans compared to those of European or Asian origin, whereas Scandinavians are more prone to developing pseudo-exfoliative glaucoma. One common eye disease that varies in ethnical prevalence is age-related macular degeneration. It is more common among White population compared with African Americans. The ocular structures also vary in different ethnic groups. (Chou 2022).The study by Nousome et al. (2021) found that clinically significant differences in the retinal nerve fiber layer thickness are present in healthy adults from different racial and ethnic groups of the same age (Nousome & al. 2021). This racial difference is taken into account when using optical coherence tomography. The system settings require the examiner to select the patient´s ethnicity so that the correct normative data of the eyes is used.

Gender increases the risk for certain systemic diseases with eye manifestations like hypertension. Hypertension is more prevalent among men than women until after menopause. (Reckelhoff 2018). Regarding eye diseases, women are more susceptible to lens opacities than men. Still, the data for other major eye diseases like age-related macular degeneration, glaucoma and diabetic retinopathy is not conclusive (Zetterberg 2016).

Occupation has a strong association with eye diseases and injuries. Chemical and toxic agents, radiation, projectiles, and blood borne pathogens might put the patient´s eyes at risk of injury. When it comes to computer work, the patient might be suffering from computer vision syndrome. (Kulshrestha and Mishra, 2021).

2.4 Chief Complaint, Symptoms Interview, and History of Present Illness

There is always a reason why the patient is attending an eye exam and this reason may vary from a routine check-up to a more specific problem (Franklin and Harvey, 2005). A chief complaint is the reason for the visit given by the patient. It is recorded using free writing. The health care professional´s assessment of the reason for the visit is then recorded in a structured way using the ICD classification. (Potilastiedon kirjaamisen yleisopas v 5.0 2022). Determine the chief complaint by asking open ended questions like “What brought you in today?” or “What kind of problems do you have with your eyes or with your vision?” (Carlson & Kurtz 2016, 5).

To further investigate the symptoms of the patient, the questions might include the following:

“Do you experience any…?” Headaches, blurred vision, distorted vision, double vision, eye pain, floaters, flashes of light, itching, redness, irritation, foreign body sensation and tearing. (Franklin and Harvey, 2005).

The above clarifying questions are commonly used in optometry practice.

Next follows a brief introduction to the most common eye and vision related symptoms and their possible indications.

Headache might be caused by numerous reasons. In optometry practice, a typical cause for a headache could be a refractive error, eye strain, or perhaps problems with binocular vision. Headaches can also be caused by different headache disorders (see chapter 2.6.13). Sometimes the reason might be more severe such as intracranial hypertension, angle closure glaucoma (see chapter 2.5.9), giant cell arthritis (see chapter 2.6.6) or even a benign pituitary tumor and it is therefore essential to investigate the cause carefully. (Salmon 2020, 374, 760, 767, 788).

Blurred vision is often caused by uncorrected vision or cataracts (see chapter 2.5.9). Another typical reason for blurry vision is dry eyes (see chapter 2.5.7). If accompanied by other symptoms such as pain or discomfort or sensitivity to light. it might be due to more severe causes such as keratitis (see chapter 2.5.7) or angle closure glaucoma (see chapter 2.5.9) (Holopainen & al. 2018, 12, 15).

Distorted vision indicates that there is something affecting the area of the macula. Typical reasons for distorted vision include age-related macular degeneration (see chapter 2.5.9), macular pucker, cystoid macular edema, and central serous chorioretinopathy (see chapter 2.8.2) to mention a few. (Salmon 2020, 557,578, 592, 598, 604).

Double vision can be monocular or binocular. Monocular diplopia can be caused by light diffraction due to high refractive errors, irregular astigmatism, corneal opacities, cataract, or tear film abnormalities. Another cause of monocular double vision can be maculopathy. (Tan & Faridah 2010). An easy way to test if the problem occurs in the retina is to perform a pinhole test. Visual

acuity does not improve if it is a case of maculopathy. Binocular double vision is an often-encountered symptom in the optometry practice. It is typically caused by misalignment of the eyes (Salmon 2020, 698). Patients with sudden onset of double vision especially accompanied by a headache or abnormal pupil involvement should be immediately referred for further examinations (Jain 2022).

Causes for **eye pain** are numerous, including acute angle closure attack, eye infection, dry eyes, and uveitis (see chapters 2.5.9, and 2.5.7) (Holopainen & al. 2018, 13, 159).

Most often **flashes and floaters** are caused by posterior vitreous detachment (PVD). Floaters are tiny collagen fibers in the vitreous that cluster together causing shadows to the retina which are seen as small dark floating shapes across the vision. In PVD, floaters are usually accompanied by flashes due to the stimulation of the photoreceptor cells in the retina by the pulling vitreous. PVD typically affects patients that are over the age of fifty and is more common in myopic eyes. Although it can be harmless, every patient experiencing floaters and flashes of lights should be examined by the ophthalmologist within a week in case of a retinal tear which can lead to retinal detachment. (Bergstrom & Czyz 2022). Patients with certain symptoms should be examined within 24 hours. These symptoms include soot rain, decreased vision and/or a shadow in the visual field. (Talvensaari & Uusitalo 2015).

Itching, redness, irritation, foreign body sensation and tearing are a list of symptoms that can appear separately or simultaneously. Itching is typically associated with allergic conjunctivitis and dry eyes (see chapter 2.5.8 and 2.5.7) (Rouen & White 2018; Holopainen & al. 2018, 57). Redness and irritation can be associated with the above and with conjunctivitis, keratitis, iritis and episcleritis (see chapte 2.3.7) (Holopainen & al. 2018, 13; Salmon 2020, 292). Foreign body sensation and tearing are typically associated with dry eyes and might also be present in conjunctivitis and keratitis (see chapter 2.5.7) (Holopainen & al. 2018, 14).

For each complaint, ask further information using modifying questions. This will help to identify the root cause of the problem. It might be helpful to use mnemonics such as **FOLDARQ** which stands for: Frequency, Onset, Location, Duration, Associated factors, Relief and Quality. (Carlson and Kurtz, 2016, 6–7). Frequency tells the clinician if the patient has experienced this problem before and if there is a history of similar problems. Onset indicates the time when the problem began and with location the clinician determines if the problem is in the left or right eye, or whether the patient

experiences problems with the distance or near vision. Duration informs about the length of the symptoms and by associated factors the clinician can get more details about other possible symptoms occurring with this problem. Relief implies whether there is anything that helps with the symptoms. Quality is the patient`s own estimation of the severity of the symptoms. (Carlson and Kurtz, 2016, 6–7). Another example of a widely used mnemonic is **OLD CARTS** (**O**nset**, L**ocation, **D**uration**, C**haracter, **A**ggravating factors, **R**elief, **T**iming, **S**everity) (Goldberg n.d.).

2.5 Ocular Status and Ocular History

Current visual efficiency and optical correction should be asked about if they are not present in the chief complaint. The ocular history should contain information about current optical correction and status of the vision, information about previous visits, history of amblyopia and strabismus, and history of any eye surgeries or ocular trauma. It is also important to ask about any chronic eye diseases like cataracts and glaucoma and ask about any acute or recurrent ocular problems. (Muchnik 2007, 6).

2.5.1 Optical Correction and Visual Efficiency

Details about the patient`s vision and optical correction should be further asked about after determining the chief complaint. A basic list of questions concerning visual efficiency and optical correction might consist of the following:

- "How would you describe your vision, both near and distant?" Or you can use more detailed questioning like

- "How is your vision for driving?" or "How is your vision when reading a book or a tablet?"

- "Do you wear glasses?" (Record when renewed, how long the patient has been wearing glasses and what type of glasses)

- "Do you wear contact lenses?" (Monthly or daily, how often do you use them, any problems with the lenses). (Franklin & Harvey 2005).

While gaining important information about the status of the vision and optical correction, the optometrist also gains information about the patient´s refractive error. This information is important for the optometrist since refractive errors can cause various ocular and visual problems. High myopia is characterized by elongated axial length, increasing the risk for glaucoma, cataracts, retinal tears, retinal detachment, and myopic maculopathy. (Williams & Hammond 2019). A higher degree of hyperopia in young children increases the risk for developing amblyopia, strabismus and eye strain (Majumdar & Tripathy 2022).

The use of contact lenses should always be investigated. The history taking for the contact lenses follows the same framework as the general patient history discussed above. The examiner can start by inquiring about the reason for the visit and continue to further investigate if the patient is experiencing any problems with contact lenses. More detailed questioning should follow to investigate the type and material of the lenses, wearing time, care and compliance and any history of contact lens related problems. (Franklin & Harvey 2005, 390). The examiner should be familiar with the most common problems associated with contact lenses. Although generally contact lenses are well tolerated, they might cause discomfort, dry eyes, corneal staining, giant papillary conjunctivitis (discussed in chapter 2.5.8) contact lens induced peripheral ulcer (CLPU), and microbial keratitis (Alipour & al. 2017).

2.5.2 Previous Visit

Any previous visit should always be inquired about and recorded. Anyone who is at least forty years old is recommended an eye health assessment by an ophthalmologist. After that, a follow-up visit should be arranged every three years, or more often if there are eye findings or a positive family history of eye disease. (Holopainen et al., 2018, 24).

2.5.3 Lazy Eye/Amblyopia

Any history of amblyopia should be reported. According to Birch (2012), amblyopia is the commonest cause of monocular vision loss in children. Amblyopia is decreased vision in one eye that results from abnormal visual development in childhood. The most typical causes of amblyopia are strabismus and anisometropia. Even though the treatment options are effective, sometimes the eye is left with decreased visual acuity and ocular motor defects. (Birch 2012).

2.5.4 Strabismus

Strabismus is a misalignment of the eyes. It usually occurs in early childhood. If strabismus is left untreated, it can cause permanent problems with the vision. These include amblyopia, reduced stereo vision, double vision, asthenopia, and abnormal head posture. In children, strabismus can be caused by refractive errors or an imbalance of ocular muscles. In adults, the cause is typically neurological. The prognosis of strabismus is good if it is treated early. Treatment options include eyeglasses, orthoptics, eye patches, topical medications, and muscle surgery. (Kanukollu & Sood 2022).

2.5.5 Eye Surgery

Ocular history should include information about any eye surgery (Franklin & Harvey 2005). According to the *Regulation on health care professionals* (564/1994, 16 §), optometrists in Finland are not allowed to independently prescribe eyeglasses to a person who has overgone eye surgery. Optometrists are however allowed to examine these patients and prescribe eyeglasses to patients who have permission from an ophthalmologist.

Patients might also be unaware of the regulations concerning optometrists in Finland. Therefore, optometrists should always ask about performed eye surgeries before starting the eye examination. It is however a good practice for the optometrist to examine the eyes even though the patient must be referred to an ophthalmologist for the prescription.

On many occasions, eyes that have gone through eye surgery are encountered in optometrists' everyday practice. It is important to be familiar with the common complications or visual problems related to the most common eye surgeries. It is common to encounter patients that have had cataract surgery, refractive error surgery or strabismus surgery which is usually performed in early childhood.

The most common form of eye surgery in Finland is *cataract surgery,* performed approximately 50000-60000 times a year. Typical complications of cataract surgery are posterior capsule opacification and cystic macular edema. (Tarnanen, Välimäki & Komulainen 2019).

Refractive surgeries include laser refractive surgeries and intraocular refractive surgeries. Over ten thousand laser refractive surgeries are carried out yearly in Finland (Holopainen et al. 2013). There are many techniques to perform laser refractive surgery such as LASIK (laser in situ keratomileuses), SMILE (small incision lenticule extraction) and PRK (photorefractive keratectomy). (Holopainen et al., 2018, 370–371). Laser refractive surgery is generally a safe procedure and complications are rare. After a laser refractive surgery patients might experience complications such as dry eyes, halos, increased glare, remaining refractive error, corneal scarring, and in rare occasions corneal ectasia (Kim et al., 2019).

Strabismus surgeries are relatively safe and the prognosis for vision is good if strabismus is treated early on. Sometimes the result of the surgery is under-, or overcorrection and the patient might be left with strabismus to some degree. (Kanukollu & Sood 2022).

2.5.6 Ocular Trauma

Ocular trauma can lead to ocular complications even years after the trauma. Therefore, it is important to ask the patient about any history of trauma. (Kent, 2008). There are several types of ocular trauma, including eyelid trauma, orbital trauma, trauma of the globe, or chemical injuries (Bowling and Kanski, 2015). Patients with a history of ocular trauma are at increased risk of angle recession glaucoma, retinal tears, and cataract (Kent 2008).

2.5.7 Acute and/or Recurrent Eye Diseases

The patient might be experiencing some ocular problems that are recurrent. Sometimes there might be an underlying systemic condition that is causing these problems. This might require some further examination by a physician or an ophthalmologist, but sometimes the situation might be less severe. Next, we will go through some commonly encountered recurrent ocular problems or conditions in optometric practice.

Conjunctivitis (Pink eye) is typically caused by a virus or bacteria or can be allergic by origin (see chapter 2.5.8). The inflammation of the conjunctiva causes swelling, redness, ocular discharge, and irritation. Careful history should be taken of these patients to determine it from more serious causes of red eye, even for the purposes of referring the patient onwards. For the history of the

present complaint, it is good to use **FOLDARQ**. To further investigate the complaint, the following should be included in the history: the presence of ocular itch (typical for allergic conjunctivitis), decrease in visual acuity (not usually affected), history of contact lens wear, previous respiratory tract infection or sinusitis, swollen lymph nodes, allergies or medications, exposure to toxins. (A. Azari & Arabi 2020).

Next follows a brief introduction to the most common types of conjunctivitis.

Viral conjunctivitis is the commonest type of conjunctivitis and is most often caused by an adenovirus (see chapter 2.6.4). It might present with mild or more severe symptoms. The history usually reveals contact with someone with acute conjunctivitis. (Salmon 2020, 177–178).

Signs and symptoms include:

- conjunctival redness
- watery discharge
- tiny freckle hemorrhages may occur in the conjunctiva
- pseudo and/or true membrane might be present (seen in severe adenoviral conjunctivitis)
- follicles might be present
- lymphadenopathy usually present
- subepithelial infiltrates are typically seen in EKC (epidemic keratoconjunctivitis)

(Salmon 2020, 168-170,178).

Acute Bacterial conjunctivitis is typically caused by the bacterium Streptococcus pneumonia, Staphylococcus aureus, Hemophilus influenzae or Moraxella catarrhalis. Conjunctivitis caused by C. trachomatis or Neisseria gonorrhea is introduced in chapter 2.6.4. Acute bacterial conjunctivitis is typically bilateral, but one eye can get affected 24-48 hours before the other. It is more common among children than adults. (Salmon 2020, 171; A. Azari & Arabi 2020).

Signs and symptoms include:

- acute onset of irritation and ocular burn
- mucopurulent or moderately purulent discharge
- sticky eyelashes upon awakening
- diffuse, beefy-red colour conjunctival redness that is more severe away from the limbus
- membranes (both pseudo and true) might be present

- papillae might be present
- superficial punctate epithelial erosions are common
- lymphadenopathy is not usually present

(Salmon 2020, 168–169, 170–171).

Allergic conjunctivitis is introduced in chapter 2.5.8.

Infective keratitis refers to corneal inflammation that can be caused by bacteria, viruses, fungi, or protozoan. Fungal keratitis is relatively rare in cold climate countries such as Finland and therefore will not be discussed further. (Castano, Elnahry & Mada 2022).

Bacterial Keratitis is typically caused by the bacterium Staphylococcus aureus and Pseudomonas Aeruginosa. Usually, bacteria cannot penetrate the healthy cornea and therefore risk factors for bacterial keratitis include the use of contact lenses, eye trauma and chronic ocular surface diseases such as dry eye. Immunosuppressed people are also more susceptible to bacterial keratitis.

Signs and symptoms include:

- watery eye, with mucopurulent or purulent discharge
- conjunctival hyperemia
- pain and irritation in the eye
- light sensitivity
- blurred/decreased vision
- large infiltrate (epithelial defect)
- corneal edema

(Holopainen & al. 2018, 68; Salmon 2020, 210–211).

Clinical features vary depending on the causative agent. For optometrists, it is important to know that Pseudomonas Aeruginosa is the commonest causative agent for bacterial keratitis among contact lens users. (Salmon 2020, 209; Holopainen & al. 2018, 68).

Protozoan keratitis caused by Acanthamoeba (AK) will be discussed briefly since contact lens use increases the risk of this type of keratitis. Although relatively rare, early diagnosis of AK is important to prevent severe vision loss. Risk factors for AK include contact lens wear, eye trauma, and

swimming in infected water while wearing contact lenses. Also, cleaning and storing contact lenses in tap water might cause exposure. (Zimmerman & al. 2016).

Signs and symptoms include:

- decreased vision
- photophobia
- ocular pain
- conjunctival hyperemia
- pseudodendrites and subepithelial infiltrates, perineural infiltrates (can mimic other types of keratitis)
- later, a typical ring infiltrate

(Zimmerman & al. 2016).

Uveitis is an inflammation in one or more parts of the uveal tract. The uveal tract includes the iris, ciliary body, vitreous, retina, and choroid. Symptoms and outcomes can vary from pain and conjunctival injection to total vision loss. There are multiple causes for uveitis. Most commonly, the pathogenesis is immunologic. Other causes include infections, trauma, or it can be idiopathic. (Duplechain, Conrady, Patel & Baker 2021). Uveitis can be classified by anatomy, duration, or etiology (Table 1.1- 1.3). (Holopainen et al., 2018, 149; Jabs et al., 2005).

Table 1.1 Classification by anatomy

Type	**Primary side of Inflammation**	**Includes**
Anterior uveitis	Anterior chamber	Iritis, iridocyclitis, anterior cyclitis
Intermediate uveitis	Vitreous	Pars planitis, posterior cyclitis, hylalitis
Posterior uveitis	Retina and choroid	Choroiditis, chorioretinitis, retinochoroiditis, retinitis, neuroretinitis
Panuveitis	Anterior chamber, vitreous, and retina or choroid	

(Adapted from Holopainen et al., 2018, 148).

Table 1.2 Classification by duration

Category	Description	Comments
Onset	Sudden, insidious	
Duration	Limited Persistent	duration < 3 months duration > 3 months
Course	Acute Recurrent Chronic	sudden onset, duration < 3 months Recurrent episodes separated by phases of inactivity without treatment > 3 months Persistent inflammation with relapse in < 3 months after discontinuing treatment

(Jabs & al. 2005).

Table 1.3 Classification by etiology

Ethology	Causative Agent	Examples
Infectious	Bacteria	Borrelia, mycobacterium
	Virus	Herpes simplex virus, varicella zoster virus, cytomegalovirus
	Fungi	Candida albicans
	Parasite	Toxoplasma gondii
Non-infectious	Secondary to systemic disease	Seronegative spondyloarthropathies (HLA-27), sarcoidosis, MS-disease, Bechet´s disease, juvenile idiopathic arthritis
	Not related to any known systemic disease	Idiopathic
Masquerade	Neoplastic	Lymphoma, leukaemia
	Non-neoplastic	Ischemic ocular syndrome, retinitis pigmentosa

(Adapted from Holopainen & al. 2018, 148).

Anterior uveitis covers around 90 percent of all cases of uveitis. The main site of inflammation is in the anterior part of the eye, and it is usually further classified into iritis or iridocyclitis. The cause of anterior uveitis is idiopathic in 50 percent of the cases. (Holopainen et al., 2018, 159). HLA-B27 positive uveitis is common. It is associated with spondylarthritis and around 15 percent of the population in Finland carries the HLA-B27 gene. (Spondylartropatia: Reumaliitto 2016). In acute anterior uveitis symptoms include acute onset of unilateral pain, redness, photophobia, watery discharge, slight ocular discomforts a few days before onset, and blurring of the vision. The chronic

form of anterior uveitis is often asymptomatic, and the blurring of the vision might be the only symptom. (Bowling and Kanski, 2015, 397; Holopainen et al., 2018, 158–159).

Intermediate uveitis presentation is usually bilateral, and in most cases idiopathic. Other causes are infectious and non-infectious diseases and systemic diseases. (Ness et al., 2017). Vitreous is predominantly involved, so the symptoms are usually vitreous floaters and blurred vision. Pain and photophobia are not usually present. (Holopainen et al., 2018, 161).

Posterior uveitis involves inflammation of the choroid and retina. Symptoms vary from floaters and minimal blurring of the vision to loss of central vision (Kanski, 2003, 274). The commonest cause of posterior uveitis is ocular toxoplasmosis (Ganesh and Biswas, 2010).

Panuveitis is the inflammation of the whole uveal tract, vitreous and retina or choroid. It is commonly caused by tuberculosis, sarcoidosis, Vogt-Koyanagi-Harada syndrome, and Bechet`s disease but many of the cases are idiopathic. (Bansal et al., 2010). Symptoms include red, painful eye, floaters, and a severe decrease in vision (Duplechain et al., 2021).

Uveitis can cause complications like cataracts, posterior synechiae, glaucoma, hypotony, cystoid macular edema (CME), epiretinal membrane (ERM), band keratopathy and optic nerve edema (Duplechain et al., 2021).

Herpes simplex virus type 1 ocular infection

Herpes simplex virus type 1 (HSV-1) is a common reason for recurrent ocular infection. Herpes simplex virus is introduced in chapter 2.6.4. We will focus on recurrent ocular infection in this chapter. Different stressors like stress, exposure to UV light or topical corticosteroids can cause the virus to reactivate. Ocular infection is caused by the reactivation of the virus. (Lobo et al., 2019). Ocular infection by HSV-1 can manifest as herpes simplex keratitis, herpes simplex uveitis or herpes simplex retinitis (Anahita et al., 2020). By estimation, over 10 million people worldwide might have an eye disease caused by the herpes virus (Ahmad and Patel, 2021).

Herpes simplex keratitis might have some severe complications like corneal scarring, glaucoma, or cataracts (Ahmad & Patel 2021). Uveitis caused by HSV-1 accounts for 5-10% of all cases of uveitis. It manifests as unilateral anterior uveitis and is characterized by raised intraocular pressure,

keratic precipitates and iris atrophy. Retinitis caused by HSV-1 is rare and usually seen in immunocompromised patients. If left untreated it can cause permanent loss of vision. (Anahita et al., 2020).

Herpes simplex keratitis can be divided into epithelial, disciform, or stromal keratitis, and neurotrophic keratopathy (Anahita et al., 2020). The prevalence of recurrent keratitis infection is estimated to be 50 percent in five years and over 60 percent in twenty years (Lobo et al., 2018).

- Epithelial keratitis is also known as dendritic keratitis, and it is characterized by branch like epithelial lesions with terminal bulbs. These lesions might merge forming geographic ulcers. Initial symptoms include eye pain, tearing, redness and foreign body sensation. (Lobo et al., 2018).
- Disciform keratitis (also called as immune stromal keratitis) presents with corneal stromal edema, which may be associated with keratic precipitates and folds in the Descemet's membrane and no epithelial defect. After healing the lesions appear as a faint ring like scars. Symptoms include slow onset of painless blurred vision that might be accompanied by halos. (Anahita et al., 2020).
- Stromal necrotizing keratitis is rare and manifests as severe stromal infiltration with or without epithelial ulceration. Patients are at risk of stromal necrosis and melting (Lobo et al., 2018).
- Neurotrophic keratopathy is a progressive corneal disease with reduced or total loss of corneal sensation which leads to epithelial breakdown, improper healing of the cornea, and eventually corneal melting and perforation (Versura, Giannaccare, Pellegrini, Sebastiani & Campos 2018).

Recurrent corneal erosion is a quite common disorder that causes ocular pain, photophobia, tearing, and blurred vision. Symptoms typically occur upon awakening. Past trauma, ocular surgery, contact lens use, corneal dystrophy, dry eyes, and diabetes can cause recurrent corneal erosions. (Nanba & al. 2019).

Dry eye disease (DED) is common and often chronic in nature. It is defined as a multifactorial condition that affects the ocular surface by the loss of the tear film's homeostasis accompanied by symptoms like discomfort and visual disturbance. DED can be classified to Aqueous-deficient dry eye (ADDE), evaporative dry eye (EDE), or a mixed type. (Craig & al. 2017). Risk factors for DED

include age, female gender, Asian ethnicity, contact lens use, environmental factors, certain autoimmune and other systemic diseases, allergies, medications, and eye surgeries. Patients might report some of the following symptoms: irritated, gritty, or itchy eyes, blurry vision, redness, excess tearing and sensitivity to light, increased blinking, and contact lens intolerance. (Rouen & White 2018).

Episcleritis is a recurrent inflammatory condition affecting the tissue between the conjunctiva and sclera (episcleral tissue). Episcleritis is usually idiopathic but has been linked with dry eyes and contact lens use. Episcleritis is more common among females and typically occurs in middle aged patients. Associated systemic diseases include rheumatoid arthritis, gout, systemic lupus erythematosus, ulcerative colitis, Chron`s disease and others. Episcleritis is usually harmless and self-limiting, lasting from a few days to a few weeks. Episcleritis typically manifests as a sectoral or diffuse red eye with no other symptoms or mild discomfort. The inflammation might be nodular in 15-30 percent of the cases. (Melton & Thomas 2022; Salmon 2020, 292).

2.5.8 Allergic Eye Diseases

Allergic conjunctivitis is a commonly encountered ocular problem that affects around 20 percent of the population (Hazarika & Singh 2015). Allergic conjunctivitis often presents simultaneously with seasonal allergy symptoms or exposure to allergens; therefore, recurrence is common (Baad, Le & Kinzer 2021). The various forms of this disease include seasonal/perennial allergic conjunctivitis, giant papillary conjunctivitis, contact allergic blepharoconjunctivitis, vernal keratoconjunctivitis and atopic keratoconjunctivitis (Villegas, Manuel Benitez-Del-Castillo, Clinico & Carlos De Madrid 2021). This bilateral disease rarely affects vision but there are a lot of ocular symptoms and signs like itching, watery eyes, conjunctival hyperemia and chemosis, serous or mucous discharge and photophobia. (Holopainen et al., 2018, 57; Villegas et al., 2021).

Seasonal/Perennial Allergic conjunctivitis is the most typical form of allergic conjunctivitis. Seasonal allergic conjunctivitis is an acute condition typically caused by outdoor allergens, whereas perennial allergic conjunctivitis is usually caused by indoor allergens and tends to be less severe but prolonged. Immunoglobulin E (IgE) antibodies cause an allergic reaction in both forms. In this reaction, mast cells degranulate and release histamine and other inflammatory mediators. Primary ocular symptoms are itching, tearing, redness and edema. (Villegas et al., 2021).

Vernal keratoconjunctivitis (VKC) is a chronic allergic eye disease typically affecting young boys. It is mostly seen in hot climate countries, and the prevalence in Europe is relatively low. VKC affects the upper tarsal or limbal area. Typical clinical findings include giant papillae in the upper tarsal conjunctiva and round nodes at the limbus (Horner-Trantas dots). Patients experience itching, tearing, redness and watery or mucoid discharge; also, photophobia might be present. The symptoms might be throughout the year but usually worsen during the summer months. VKC can be initiated by IgE mediated or non-IgE mediated processes. (Villegas et al., 2021).

Atopic keratoconjunctivitis (AKC) is a long-term inflammatory disease. It involves the ocular surface and the eyelids. Since AKC can cause scarring, it is the most severe type of allergic conjunctivitis. Risk factors include male gender, personal or family history of atopic dermatitis or other allergic diseases like asthma. Atopic keratoconjunctivitis is considered an ocular form of atopic eczema. It typically presents with eyelid eczema, chemosis, and redness of the conjunctiva. Papillae of the inferior tarsal conjunctiva might be present. Symptoms are like in other ocular allergies, but the itching is usually more severe during the winter months. The mechanism behind the allergic reaction can be both IgE mediated and non-IgE mediated. (Villegas & al. 2021).

Giant papillary conjunctivitis (GPC) is caused by either a mechanical irritation or an immune mechanism. Mechanical irritation is usually caused by contact lenses. Other causes of mechanical irritation include exposed sutures, scleral buckles, and filtering blebs. Immune reaction is believed to be caused by an immunological reaction to the proteins on the surface of the contact lens. The characteristic finding for GPC is giant papillae in the superior tarsal conjunctiva, usually with no corneal involvement. Symptoms include itching, foreign body sensation, watery or mucoid discharge and mild redness. Removal of the stimuli resolves the changes in the tarsal conjunctiva. (Villegas & al. 2021).

Contact blepharoconjunctivitis causes delayed allergic reaction after a direct exposure to an allergen such as nickel. It includes the eyelids, conjunctiva, and periorbital skin. Symptoms include itching, burning, redness and tearing. (Villegas et al., 2021).

Allergic rhinitis (hay fever) is a relatively common disorder, affecting around 10-20 percent of the population. It is an allergic reaction affecting the nasal mucosa, typically caused by allergens such as pollen or dust. It is thought that allergic rhinitis in not only limited to the nose but also affects the

lower respiratory tract. There is a strong association with asthma and allergic rhinitis. Typical symptoms include sneezing, nasal itch, stuffy and runny nose. (Small, Keith & Kim 2018). Ocular symptoms such as itchy, red, and watery eyes often affect patients with allergic rhinitis. Allergic conjunctivitis and allergic rhinitis have a strong association and are often present simultaneously. (Lordache & al. 2022).

2.5.9 Chronic Eye Diseases

Before starting an eye examination, the optometrist should ask the patient about a history of any chronic eye diseases. The optometrist needs to recognize a healthy eye and the signs and symptoms of the most prevalent eye diseases. According to Prokofyeva and Zrenner (2012), the leading causes of European visual impairment include age-related macular degeneration, glaucoma, and diabetic retinopathy (Prokofyeva & Zrenner 2012). Cataract is the main cause of visual impairment worldwide but rarely causes visual impairment in developed counties. (Bourne & al. 2021). Diabetic retinopathy will be discussed later so it is not introduced in this chapter.

Glaucoma is among the main causes of permanent vision loss globally (Nuzzi, Marolo & Nuzzi 2021). In Finland, approximately 90 000 people are diagnosed with glaucoma (Seppänen, 2021). Glaucoma includes a varied group of disorders. All types of glaucoma are characterized by progressive damage to the optic nerve and subsequent visual field defects. (Bowling and Kanski, 2015, 307). Glaucoma can be congenital or acquired. The acquired form can be further subdivided by the mechanism of how the aqueous outflow is compromised. Glaucoma can also be categorized as primary or secondary glaucoma. (Bowling and Kanski, 2015, 307). A thorough investigation of the patient history can reveal findings that suggest a possibility of developing glaucoma even before any clinical findings and can also guide the examiner in choosing the range of testing needed in the eye examination (McMonnies 2017a).

Primary open-angle glaucoma (POAG) is the most frequent type of glaucoma. It is characterized by an open iridocorneal angle, intraocular pressure (IOP) higher than 21 at some point of the disease, and an optic nerve head that appears glaucomatous with corresponding progressive loss of vision. (Bowling and Kanski, 2015). The disease is slowly progressive and often presents with no symptoms until the damage to the optic nerve is severe. It can stay undetected for a long time, and it is usually an incidental finding in a routine eye examination. (Dietze et al., 2022). Risk factors

for developing POAG include high IOP, age, male gender, genetics and family history, black race, myopia, hypertension, diabetes, migraine, long term use of contraceptive pills, steroids, and ocular perfusion pressure (Bowling and Kanski, 2015, 349–350; McMonnies, 2017).

Normal tension glaucoma (NTG) can be seen as a form of POAG. The disease shows optic nerve damage and progressive visual field defects, but the intraocular pressure remains normal (under 21 mmHg). There are a few theories behind normal tension glaucoma. It might be related to a more pressure sensitive optic nerve or insufficient blood flow to the optic nerve. (Dietze et al., 2022). Risk factors include age, female gender, Japanese race, thin corneal central thickness, positive family history, systemic hypotension, obstructive sleep apnea, and migraine (Bowling and Kanski, 2015, p. 358).

Angle closure is caused by an obstruction of the trabecular meshwork preventing the aqueous humour outflow resulting in a rise in the IOP. Angle closure can be further classified by the phases of the disease. (Bowling and Kanski, 2015, 360).

- In *Primary angle closure suspect (PACS),* the IOP, visual fields and the optic disc appear normal. Angle closure is not detected but gonioscopy reveals iris-trabecular contact in three or more quadrants but no peripheral anterior synechiae. The risk of developing an angle closure glaucoma in a five-year time is estimated to be thirty percent. (Bowling and Kanski, 2015).

- *Primary angle closure* shows elevated IOP, iris-trabecular contact in three or more quadrants and/or angle closure. There are no defects in visual fields and the optic nerve head appears normal. (Bowling and Kanski, 2015).

- In *primary angle closure glaucoma*, there is damage to the optic nerve caused by the attacks of IOP elevation. Most patients with angle closure are asymptomatic or might experience mild symptoms such as blurred vision and halos. (Bowling and Kanski, 2015, 363). In acute angle closure, the symptoms tend to be more severe including eye pain, headaches, nausea and vomiting. (Bowling and Kanski, 2015, 360; Dietze et al., 2022). Risk factors for primary angle closure glaucoma include age, female gender, Far Eastern and Indian Asian race, short axial length, hyperopia, family history and genetics (Bowling and Kanski, 2015, 362).

Secondary glaucoma is always a consequence of another condition or trauma. There are several types of secondary glaucoma, and they can be either open angle type glaucoma or angle closure type glaucoma. (Dietze & al. 2022).

- *Pseudo exfoliation syndrome* is the most common cause of secondary open angle glaucoma. It is a systematic disease with predominantly ocular expression. Protein like material is deposited in ocular tissues causing the trabecular meshwork to be obstructed decreasing the aqueous outflow and increasing the IOP. Not all patients with pseudo exfoliation syndrome develop pseudo exfoliation glaucoma but the incidence of glaucoma is 15-30 percent of the cases. Slit lamp examination reveals most of the cases. A clearly noticeable sign of pseudo exfoliation is white flaky material in the pupillary border or on the anterior surface of the lens (Challa and Majka, 2006). Risk factors include age over fifty, female gender and the disease is especially common in Scandinavia (Bowling & Kanski 2015).

- *Pigmentary dispersion syndrome (PDS)* is a common cause of secondary glaucoma. In this condition pigment crumbs are released from the iris and deposited in the anterior part of the eye. The shedding of the pigment is caused by mechanical rubbing of the iris against the lens zonules. (Bowling and Kanski, 2015, 368). Pigment accumulates in the trabecular meshwork and decreases the aqueous outflow often resulting in elevated IOP. Secondary glaucoma can develop due to increased IOP. Signs include dust like formation in the endothelium (Krukenberg´s spindle), increased pigment in the trabecular meshwork and iris transillumination defects. (Scuderi et al., 2019). Most patients are asymptomatic, but the IOP spikes can cause blurry vision and halos (Porter 2021). Pigmentary glaucoma is more common in males especially in myopic individuals in their second or third decade (Bowling and Kanski, 2015, 368).

- *Neovascular glaucoma* is secondary glaucoma, where new blood vessels grow into the iris and the iridocorneal angle. When new vessels grow in the iridocorneal angle the aqueous outflow is compromised. Neovascularization is often accompanied by a fibrous membrane which later contracts causing angle synechiae. Typical causes for neovascular glaucoma are ischemic central retinal vein occlusion, diabetes mellitus, intraocular tumors, and longstanding intraocular inflammation. Symptoms include pain, reduced vision,

photophobia, and redness. The IOP might be normal in the early phase of the disease. (Bowling & Kanski 2015, 371-372).

Early recognition of the disease gives a better prognosis for the vision. The patient´s medical history should give a high indication of suspicion if there is a positive history of the causative diseases present. (Singh Hayreh, 2007).

Cataract is the main cause of blindness globally, although in developed countries it rarely causes permanent vision loss (Hashemi & al. 2020). With cataract the lens of the eye becomes cloudy resulting in unsharp vision. (Cataract (acquired): Current Care Guidelines Abstract, 2019). Cataract is considered an age-related disease. However, there are some other known risk factors like genetics, ultraviolet radiation, smoking, diabetes mellitus II, uveitis, trauma, steroid use, eye surgeries, and certain occupations that can increase the risk of developing cataract. (Hashemi et al., 2020). Cataract can be classified into many different types (Cataract (acquired): Current Care Guidelines Abstract, 2019).

Congenital cataract is a rare eye disease but is nevertheless one of the major causes of curable vision loss in children (Bremond-Gignac et al., 2020, 1). The most common cause of congenital cataract is autosomal dominant inheritance. Other causes include chromosomal defects like Down syndrome, intrauterine infections such as toxoplasmosis, varicella and rubella and metabolic disorders such as Fabry disease. (Bowling and Kanski, 2015, 297).

Acquired Cataract can be divided into three subtypes:

- *Nuclear cataract* occurs in the central area of the lens. It is an acceleration of the normal aging process characterized by changes in the structural proteins of the lens. Observation with a slit lamp shows a yellowish hue; when the condition progresses, the nucleus of the lens appears brown. Nuclear cataract often causes a myopic shift due increased refractive index. (Bowling & Kanski 2015, 270).

- *Cortical cataract* involves the cortex of the lens. It can develop in the anterior, posterior, or equatorial cortex. It first starts as clefts and vacuoles in the outer segment of the lens and later develops into sharper wedge shaped or radial opacities. These opacities develop due

to changes in the water content of the cortex. These opacities typically cause glare. (Bowling and Kanski, 2015, 270).

- *Subcapsular cataract* can locate either anteriorly or posteriorly. Anterior subcapsular cataract is located under the anterior lens capsule and is caused by the metaplasia of the lens epithelium cells. Posterior subcapsular cataract is formed in front of the posterior lens capsule and is caused by migrated epithelial cells. It has an opaque appearance, and due to its central location, it usually affects vision profoundly. It typically causes glare, especially when exposed to bright lights. (Bowling & Kanski 2015, 270).

Age-related macular degeneration (AMD) is the most typical reason for vision loss in people over the age of 65 in developed countries. Approximately 200 million people globally are affected by the disease. (Stahl, 2020). In Finland, over a hundred thousand are diagnosed with AMD (Holopainen et al., 2018, 192). AMD is a progressive disorder that impacts the macula often leading to progressive loss of vision. Typical clinical findings in AMD are drusen and changes in the retinal pigment epithelium. (Bowling and Kanski, 2015, 598). AMD is classified by the type into dry and wet forms. The dry form of AMD is far more common and makes up 90 percent of the cases. The wet form is quite rare, but it is more severe and progresses fast into visual impairment. AMD can also be classified by the severity of clinical findings into early, intermediate, and late forms (Table 2). (Bowling and Kanski, 2015, 598, 600). This information can be valuable in clinical work when assessing whether the retinal abnormalities are only age-related or possibly indicating a disease.

Table 2, Classification of AMD

Category	Definition by the presence of lesions within two-disc diameters of the fovea
No apparent aging changes	No drusen No pigmentary AMD abnormalities
Normal aging changes	Only drupelets No pigmentary AMD abnormalities
Early AMD	Medium drusen (>63um but <125um) No pigmentary AMD abnormalities
Intermediate AMD	Large drusen (>125um) Any pigmentary AMD abnormalities
Late AMD	Neovascular AMD and/or any geographic atrophy

(Bowling & Kanski 2015, 600).

Main risk factors for AMD include age, positive family history and genetics, white race (late AMD), smoking, nutritional factors, hypertension, and Alzheimer's disease (Bowling and Kanski, 2015, 600–601; Heesterbeek et al., 2020). AMD is often asymptomatic in the early and intermediate stages of the disease. When the disease progresses, patients might experience blurred vision, difficulties seeing in dim light, distorted vision (metamorphopsia), and decreased contrast sensitivity. In the wet form where neovascularisation is present the symptoms are more profound and might progress rapidly. These symptoms include severe distortion of the vision and/or central scotoma. (Heesterbeek et al., 2020). According to Stahl (2020) the patient history can give valuable information that can reveal the presence of AMD. Patients often report blurred vision in one or both eyes especially in dim light. They might report seeing faces disfigured and might experience that the image is seen in different size between two eyes. It is important to ask these patients about metamorphopsia which indicates the presence of macular disease. (Stahl, 2020.) The Amsler grid is a good tool to evaluate distortion and the presence of macular scotoma (Thomas & al. 2021).

2.6 General Health Status and History

Many systemic diseases have ocular manifestations, and it is therefore important for the optometrist to ask about patients' systemic history. When it comes to health status, for example diabetes and

blood pressure, treatment balance is something the examiner should ask further about since it can affect the state of vision and eye health as well. The systemic history might also help to find out about possible medications. Many patients are unaware of the connection of systemic health to the eyes and don't necessarily know about the possible ocular side effects of medications.

2.6.1 Ears, Nose, Throat (ENT) and Mouth

Ears, nose, throat (ENT) and mouth are all connected. The throat (pharynx) is located behind the nose and mouth and connected to both. The middle ear is connected to the nasal cavities and back of the throat through eustachian tubes, which drain mucus from the ears. Around the skull, there are air filled cavities called sinuses that are connected to the nose by small tubes. Eyes are located adjacent to these sinuses and connected to the nose through nasolacrimal ducts. (Berger 2017). Infections caused by bacteria and viruses can quite easily spread through these passageways and affect all structures. Ears and eyes are connected by the vestibulo-ocular reflex (VOR), which is the reflex responsible for gaze stabilization. When the head is moving the eye muscles must move the eyes in the opposite direction to keep the gaze steady. If there is a disturbance in this reflex it can cause oscillopsia and atypical nystagmus. (Somisetty & Das 2021).

It is important to inquire the patient about history of ENT and mouth related problems since there might be a link to the eyes as well. Next, we discuss some selected conditions of the ENT and mouth that can affect the eyes or migrate to the eyes form the neighbouring structures.

In **preseptal cellulitis** there is an infection in the eyelid and surrounding tissues anterior to the orbital septum. The causative agent is typically Staphylococcus aureus or Streptococcus pyogenes. The infection can spread from sinusitis, skin trauma, conjunctivitis, upper respiratory tract, or ear infection. Signs and symptoms include a swollen, red eyelid, and fever. Visual acuity typically stays good, and there is no chemosis or proptosis present. (Salmon 2020, 124).

The most typical cause of vertigo is an inner ear disorder known as **Benign Paroxysmal Positional Vertigo (BPPV)**. It typically affects people in their 5th to 7th decade and is more common in females. Typical signs and symptoms include recurring sudden vertigo that is triggered by head movement. BPPV can be diagnosed by a test called Dix-Hallpike maneuer that shows positional nystagmus of the eyes. (Kim et al. 2021).

Inflammation of the vestibular region of the vestibulocochlear nerve causes **Vestibular neuritis** that results in vertigo, nausea, oscillopsia, and difficulties with the gait. The cause of the inflammation is thought to be viral. Diagnosis can be made if spontaneous horizontal-torsional nystagmus is present, there is an abnormal head impulse test on the affected site, and other neurological symptoms are missing. (Kim 2020).

Sjogren's syndrome is an inflammatory disorder of the immune system that causes the destruction of the lacrimal and salivary glands. It is more common in females; the peak age is usually during perimenopause. It can be classified as a primary or secondary disease. The latter is associated with other autoimmune diseases like systemic lupus erythematosus and rheumatoid arthritis. Sjogren's syndrome mainly presents with sicca symptoms such as dry mouth and dry eyes. Patients with keratoconjunctivitis sicca experience foreign body sensation, soreness and burning of the eyes and photophobia. (Stefanski & al. 2017; Vivino 2017).

2.6.2 Diabetes

Diabetes is a group of diseases with high blood glucose levels. Normal blood glucose concentration after fasting should be under 6mmol/ and in a glucose tolerance test at the two-hour point under 7.8 mmol/l. If blood glucose levels are between 6.1-6,9 mmol/l, it is regarded as impaired fasting glucose, and if the glucose tolerance test at the two-hour point shows glucose levels between 7.8-11 mmol/l, it is regarded as impaired glucose tolerance. For the diagnosis of diabetes, the fasting blood glucose levels must be 7mmol/l or higher in two separate tests and if in glucose tolerance test blood glucose levels are 11mmol/or more. (Diabetes: Käypä hoito -suositus, 2018).

The most common types of diabetes include diabetes type I, diabetes type II and gestational diabetes (What is diabetes 2021). According to International Diabetes Federation (2021) over 500 million people worldwide are living with diabetes. In Finland, there are 450 000 people diagnosed with diabetes and most of these patients (400 000) suffer from type II diabetes (Tilastotietoa - Diabetesliitto, 2021).

Diabetes type I typically occurs in childhood or young adulthood. It is caused by an autoimmune reaction against the body`s insulin producing pancreatic islet cells. Consequently, very little or no insulin is produced causing blood glucose levels to rise. The exact risk factors are unknown but

positive family history and exposure to viral infections might increase the risk. (Type 1 diabetes 2020).

Diabetes type II accounts for around 90 percent of diabetes cases. It is more commonly diagnosed in older adults, but the incidence has increased in children and young adults. In diabetes type II, the cells don't respond to insulin properly making the glucose levels rise and making the pancreas release even more insulin. Sometimes as a result the pancreas gets exhausted and is unable to produce enough insulin. (Type 2 diabetes 2020). Risk factors for type II diabetes include poor diet, obesity, inactive lifestyle, increasing age, high blood pressure, short sleep duration and quality, stress and depression, smoking, low socioeconomic status. (Type 2 diabetes 2020; Kolb & Martin 2017).

In **Gestational diabetes** blood glucose levels are high during pregnancy. It usually disappears afterward, but the affected women and their children are at increased risk for developing type II diabetes later. (Gestational diabetes 2020).There might also be some neonatal complications including a higher risk for cesarean delivery and injury during birth. This is believed to be the result of the bigger size of the fetus (Szmuilowicz et al., 2019). Risk factors for gestational diabetes include overweight, advanced maternal age and positive family history of diabetes (Plows et al., 2018).

Ocular complications of diabetes are numerous, including unstable refraction, diabetic retinopathy, diabetic macular edema, glaucoma, cataract, ocular surface disease and dry eye syndrome (Sayin, Kara & Pekel 2015; Bowling & Kanski 2015, 520). These complications are discussed in more detail next.

Unstable blood glucose levels might cause *unstable refraction*. Excess blood glucose can cause physiological changes in the crystalline lens. These changes are considered to be the reason for the refractive changes in patients with diabetes. Asking the patient about glycaemic control is important. A new prescription for corrective lenses should not be given before the blood glucose levels have been stabilized. (Stern & Haddadin 2021)

Diabetic retinopathy (DR) affects around 40 percent of people with diabetes. Risk factors for developing diabetic retinopathy include the duration and control of the disease, pregnancy, neuropathy, hypertension, hyperlipidemia, obesity, smoking, and anemia. (Bowling and Kanski,

2015, p. 521). Novel risk factors identified include inflammation, vitamin D insufficiency, oxidative stress, hormonal influence (leptin and adiponectin) and genetic factors (Broe 2010). DR is a disease that affects all small retinal vessels making them more susceptible to damage.

DR can be classified into background diabetic retinopathy, diabetic maculopathy (diabetic macular edema), proliferative diabetic retinopathy, and advanced diabetic eye disease. (Bowling and Kanski, 2015, 521). The classification of diabetic retinopathy by The Early Treatment Diabetic Retinopathy Study (ETDRS) is shown in the table below (Table 3).

Table 3

Category	Signs
Non-Proliferative Diabetic Retinopathy	
Very mild DR	Microaneurysms only
Mild NPDR	Any or all: microaneurysms, retinal haemorrhages, exudates, cotton wool spots, no IRMA or significant beading
Moderate NPDR	Severe retinal haemorrhage in 1-3 quadrants or mild IRMA, significant venous beading can be present in no more than 1 quadrant, cotton wool spots commonly present
Severe NPDR	The 4:2:1 rule; one or more of: Severe haemorrhage in all 4 quadrants Significant venous beading in 2 or more quadrants IRMA in one quadrant in 1 or more quadrants
Very severe NPDR	Two or more of the criteria for severe NPDR
Proliferative Diabetic Retinopathy (PDR)	
Mild-moderate PDR	New vessel on the disc or new vessels elsewhere but extent insufficient to meet the high-risk criteria
High-risk PDR	New vessel at the disc greater than 1/3 disc area Any NVD with vitreous haemorrhage NVE greater than 1/2 disc area with vitreous haemorrhage
Advanced Diabetic eye Disease	Preretinal and/or intragel haemorrhages Tractional retinal detachment Rubeosis irides

(Bowling & Kanski 2015, 522).

DR can be asymptomatic in the early course of the disease. Symptoms that might be experienced include blurry vision, fluctuation of vision, decreased colour vision, floaters, poor night vision, and

central scotoma. Early detection is important to prevent more serious complications. (Diabetic Retinopathy: Causes, Symptoms, Treatment - American Academy of Ophthalmology 2021).

Diabetic macular edema (DMO) is the primary cause of vision loss in diabetic eyes. It happens when the leaky blood vessel of the retina leaks fluid into the macula causing the macula to thicken. Focal thickening is caused by the focal leakage of microaneurysms and enlarged capillary sections. Diffuse edema is caused by the leakage of vessels throughout the posterior pole. DMO can take place in any stage of the disease and should therefore be assessed separately. (Bowling and Kanski, 2015, 524; Sayin et al., 2015).

Clinically significant macular edema (CSME) is described by the ETDRS by retinal thickening within 500um from the centre of the macula, hard exudates that are situated within 500um from the macula with adjoining macular thickening, retinal thickening that is 1500um or larger in any part which is within one disc diameter from the fovea. (Bowling and Kanski, 2015, 526).

Neovascular glaucoma is a rare eye disease and is mostly caused by diabetes. The association between diabetes and other types of glaucoma is controversial. Several studies report diabetes as a risk factor for both open-angle and angle closure glaucoma. (Sayin et al., 2015).

There is a 2-5 times higher risk for diabetic patients to develop cataract. The cause of *diabetic cataract* is believed to be hyperglycemia, which causes the glucose converting enzyme of the lens to build up into the lens causing cataract. (Sayin et al., 2015).

Diabetes is known to affect *ocular surface* health by many mechanisms such as abnormal corneal sensitivity, reduced tear production and impaired corneal wound healing. (Sayin et al., 2015). Diabetic eyes are at higher risk of developing dry eye disease, recurrent corneal erosions, persistent epithelial defects, and punctate epithelial erosions (Co Shih et al., 2017).

2.6.3 Endocrine Diseases

In **hyperthyroidism**, there is an increase in thyroid hormone production and excretion. Typical symptoms include tachycardia in rest, exaggeration of reflexes, warm peripheries, tremors, weight loss, fatigue, and lid lag. Hypothyroidism is primarily caused by Grave`s disease, which often

comes with ocular manifestations. Around 25 percent of patients with Grave`s disease show signs of Grave`s ophthalmopathy. (De Leo, Lee & Braverman 2016).

Grave`s ophthalmopathy also known as thyroid eye disease, can cause severe ocular complications. Symptoms include dry or gritty eyes, photophobia, lacrimation, pressure behind the eyes and double vision. Clinically the disease can manifest as lid lag, swelling and redness of periorbital tissues and conjunctiva and proptosis. More severe complications are relatively rare and affect around 3-5 percent of patients with Grave`s ophthalmopathy. These complications include corneal ulcers and compressive optic neuropathy. (Bahn, 2010).

Hypothyroidism is a relatively common condition characterized by a decrease in the level of thyroid hormones circulating in the body (Chaker et al., 2017). It is more prevalent in females and white population. Typical symptoms include fatigue, gaining weight, apathy, trouble tolerating cold, constipation, and dry skin. Clinical signs vary greatly and therefore the diagnosis is often delayed. (Chaker & al. 2017). Hypothyroidism is not usually associated with ocular problems. Some patients might experience swelling around the eyelids (Mustajoki 2021). The medication Levothyroxine used for treating hypothyroidism can rarely cause pseudotumor cerebri (idiopathic intracranial hypertension) in paediatric patients in the case of overdosing (Strickler & Pilon 2007).

2.6.4 Systemic Infections with Ocular Manifestations

Trachoma is an ocular disease caused by an infection with the bacterium Chlamydia trachomatis (C. trachomatis). C. trachomatis also causes Chlamydia, a sexually transmitted disease. The serotypes of C. trachomatis associated with trachoma are serotypes A-D. Trachoma is the main cause of infectious vision loss worldwide and is associated with poverty, crowded living spaces, and poor sanitation.(Ahmad & Patel 2021b). Optometrists in Finland may meet patients with trachoma since there is immigration from the countries where trachoma is still a problem. Ocular manifestations of trachoma can be divided into findings associated with active and chronic stages of the disease. The active inflammation is more common among children and manifests as follicular mixed conjunctivitis, mucopurulent discharge, superior epithelial keratitis, and pannus formation. The chronic stage is common in middle age and manifests as stellate conjunctival scarring, trichiasis, distichiasis, entropion, dry eyes, and corneal opacification. (Salmon 2020, 175).

Toxoplasmosis is a disease resulting from an infection by the parasite Toxoplasma gondii. Sources of infection include contaminated water or soil, eating contaminated undercooked meat, exposure to cat feces, or through vertical transmission. Immunocompetent patients usually have mild initial symptoms and don't require treatment. (Smith & al. 2021). Ocular toxoplasmosis can be caused by the reactivation of congenital toxoplasmosis or by acquired infection. Ocular toxoplasmosis infection is the most common cause of posterior uveitis. Symptoms include blurred vision and floaters; visual acuity might be reduced if the infection affects the macula. (Soheilian et al. 2011). The hallmark finding of ocular toxoplasmosis is retinochoroiditis. Typically, it looks like a white-yellowish lesion in the retina (Reynolds et al. 2012).

Tuberculosis is a disease resulting from an infection with Mycobacterium tuberculosis. WHO (World Health Organization) estimated that in 2020 around ten million people were infected by tuberculosis (Tuberculosis -WHO, 2021). In Finland, an infection caused by tuberculosis is rare. In 2020 only 174 people got infected (Tuberkuloosin esiintyvyys Suomessa 2021). Tuberculosis mainly involves the lungs but can also occur in other organs. Ocular tuberculosis usually manifests as posterior uveitis, although it can infect any ocular tissue. (Haq et al. 2021).

Lyme`s disease is an infection caused by Borrelia burgdorferi. Transmission occurs through a tick bite (Kanski, 2003, 698). In Finland, 6000 people get infected by borrelia yearly. In the acute phase, the symptoms are usually fatigue, headache, fever, and a characteristic clinical finding is skin rash (erythema migrans). If left untreated, symptoms might spread to joints, skin, eyes, heart, and the nervous system. (Lumio 2021). Ocular manifestations include conjunctivitis, keratitis, anterior or intermediate uveitis, optic neuritis, neuroretinitis, and ocular motor nerve palsies (Kanski 2003, 698).

Herpes viruses are DNA viruses that cause lifelong infections. Eight herpes viruses are known to infect humans (Connolly, Jardetzky & Longnecker 2021). In this chapter, the ones with ocular manifestations are introduced.

Herpes simplex virus is a common virus in humans. It is a DNA virus and can be further classified into HSV-1 and HSV-2 viruses. HSV-1 causes infection above the waist (facial area) and HSV-2 below the waist (genital herpes). HSV-2 rarely infects the eye. Primary infection of HSV usually takes place in childhood by droplet transmission. The initial infection might be asymptomatic, or it can cause mild fever, malaise, and upper respiratory tract infection. Following the primary infection,

the virus travels along the fifth cranial nerve (trigeminal nerve) to its ganglia and stays in a latent state. The virus might later reactivate, start to replicate, and travel down the sensory axon to its target tissue, where it causes recurrent disease. (Kanski 2003, 107–108). Ocular manifestations caused by herpes simplex virus are presented in chapter 2.5.7.

The initial infection by *Varicella zoster virus (VZV)* causes chickenpox. After the primary infection, the virus can stay inactive for many years. The virus usually stays latent in healthy individuals, but in immunocompromised patients, it might reactivate. When the virus reactivates, it causes shingles (herpes zoster). If the activated virus is in the ophthalmic division of the trigeminal nerve, it causes herpes zoster ophthalmicus (HZO). (Meduri, Grenga & Kaufman 2022). The risk of getting shingles is higher in older age, and affected patients are predominantly over sixty. Also, immunocompromised patients are at higher risk of developing a more severe disease. A rash at the tip or side of the nose, called Hutchinson´s sign relates strongly to ocular involvement. (Bowling & Kanski 2015, 189). Herpes zoster ophthalmicus is characterized by a unilateral skin rash that respects the midline. The rash is associated with fever, malaise, and headache. In the acute stage, around 50 percent of the patients develop epithelial keratitis (dendritic lesions are smaller in size and more faint compared to those caused by HSV). Other ocular manifestations include conjunctivitis, episcleritis, scleritis, anterior, stromal, or disciform keratitis, and anterior or posterior uveitis. In the chronic stage of the disease, patients might develop neurotrophic keratopathy due to compromised corneal innervation that results in decreased corneal sensation. (Salmon 2020, 226–229).

Cytomegalovirus (CMV) belongs to the herpes viruses. Like other herpes viruses, it causes lifelong infections. In healthy individuals, CMV is usually asymptomatic, but the virus can cause severe complications in immunocompromised patients. (Gugliesi et al. 2021). For patients with acquired immunodeficiency syndrome (AIDS), Cytomegalovirus is the commonest cause of visual impairment (Rice & Steffen 2020). The most typical complication of Cytomegalovirus for immunocompromised patients is CMV retinitis, that if left untreated, can lead to vision loss (Tang & al. 2020).

Adenovirus is a widespread virus that causes respiratory tract, gastrointestinal, genitourinary, and ocular infections. The most typical ocular manifestation of adenovirus is bilateral conjunctivitis which presents with a sudden onset of watery red eyes and is typically seen with a sore throat. There are four phenotypes for adenoviral conjunctivitis. Next a brief introduction to the phenotypes

of adenoviral conjunctivitis. Chronic keratoconjunctivitis caused by adenovirus will not be discussed in the next chapter since it is so rare. (Hoffman 2020).

Epidemic keratoconjunctivitis (EKC) is the most serious form of adenoviral infection since it is the only form where the cornea is involved. Initially, EKC presents with swollen pre-auricular lymph nodes, follicular conjunctivitis, pseudo membrane/true membrane formation, small conjunctival hemorrhages, and punctate epithelial keratitis. Later, subepithelial infiltrates are formed. EKC presents unilaterally in two-thirds of the cases. Patients typically report symptoms like foreign body sensation, photophobia, redness, and excess tearing. Fever and sore throat are not typically present. (Chigbu & Labib 2018; Jonas, Ung, Rajaiya & Chodosh 2020).

Pharyngoconjunctival fever is associated with systemic symptoms like fever, sore throat, swollen pre-auricular lymph nodes, and acute follicular conjunctivitis. It is most found in children and presents bilaterally. Acute follicular conjunctivitis develops a few days after the systematic symptoms appear, causing irritation, burning, and tearing. Follicles are predominately located in the lower tarsal conjunctiva. (Hoffman 2020).

Acute non-specific follicular conjunctivitis is a mild form of conjunctivitis. It is self-limiting and resolves typically in 7-10 days. Symptoms and signs include redness, tearing, soreness and follicles in the tarsal conjunctiva. (Hoffman 2020).

2.6.5 Cardiovascular Diseases

Overview

Cardiovascular diseases are a variety of different disorders that affect the heart and blood vessels. It is the primary cause of death in the world. (Cardiovascular diseases 2021). Risk factors for developing cardiovascular disease include hypertension, hyperlipidemia, smoking, excess alcohol use, diabetes, inactivity, overweight, family history, ethnicity (African, Caribbean, South Asian), and age. There are four main types of CVD. They are coronary artery disease, cerebrovascular disease (strokes and transient ischemic attack), peripheral arterial disease, and aortic disease. (Cardiovascular disease - NHS 2018).

Several cardiovascular diseases and eye diseases share the same pathophysiology, risk factors and treatment options (Stuart, 2015b). Since retinal vasculature share comparable characteristics with cerebral and coronary circulation, abnormalities in retinal vasculature such as narrowing of arterioles, arteriovenous nicking, tortuosity of the veins, widening of arterial light reflex and embolies can be indicators of systemic cardiovascular diseases. (Wong et al. 2001).

Risk factors for cardiovascular diseases and their relevance to eyes:

Atherosclerosis is an inflammatory disorder due to the accumulation of plaque in the artery's innermost layer, reducing the blood flow (Santos et al. 2021). Atherosclerosis in carotid vessels increases the risk for age-related macular degeneration and diabetic retinopathy (Stuart 2015).

In *Arteriosclerosis* the medium and large artery walls thicken and lose their elasticity. This can cause restricted blood flow to organs and tissues (Santos et al. 2021).

In *arteriolosclerosis*, the walls of arterioles or small arteries thicken due to systematic elevation of arterial pressure (Santos & al. 2021). In the eyes, arteriolosclerosis typically manifests as arteriovenous nicking (Bowling and Kanski, 2015, 557).

A blood clot forming in a vessel is called *a thrombus*. It blocks the blood flow, causing thrombosis (Villines, 2021). Retinal vein occlusions are typically caused by thrombosis (Blair & Czyz 2022).

An embolus can be anything that moves through blood vessels till it reaches a vessel small enough to prevent it from passing through, thus causing an embolism (Villines 2021). Retinal emboli originate from the carotid artery and can be formed from cholesterol (Hollenhorst plaques), calcium, or platelet-fibrin (Kanski, 2003, 463). In the eye, carotid artery emboli can cause monocular transient vision loss (amaurosis fugax), which is often a transient ischemic attack (TIA) symptom. This can be a precursor for a stroke and should be considered an emergency. (Jeffery, Chen & Lueck 2021).

Hyperlipidemia is a condition where the lipid concentration of the blood increases. These lipids can be cholesterol or triglycerides (Nelson 2013). Hyperlipidemia can increase the risk of stroke and heart attack. High cholesterol can manifest in the eyes in several ways. Typical findings in middle aged or elderly patients associated with hyperlipidemia are xanthelasma and arcus senilis.

Xanthelasma manifests as yellow plaque-like findings on or around the eyelids, whereas arcus senile is a whitish arc in the superior and inferior peripheral cornea. (Salmon, 2020, 41, 261).

Dyslipidemia refers to an imbalance of lipids or lipoproteins in the blood (Dyslipidemia eli rasva-aineenvaihdunnan häiriö - Terveyskylä 2021). Dyslipidemia increases the risk of developing coronary artery disease and is also associated with an increased risk of a stroke (Parnianfard, Sadat-Ebrahimi & Hoseini 2020). In the eyes, dyslipidemia can manifest as an embolus from a carotid artery plaque (Hollenhorst plaque) that can cause amaurosis fugax (Suhr 2014).

Hypertension (high blood pressure) is represented by systolic and diastolic blood pressure. The unit used is millimeters of mercury (mmHg). (High blood pressure (hypertension) - NHS 2019). According to current guidelines, hypertension is diagnosed when the systolic blood pressure is ≥140 mm Hg and the diastolic blood pressure is ≥90 mm Hg (Unger & al. 2020).

Hypertension can affect the eyes in various ways. Patients with hypertension might develop hypertensive retinopathy or choroidopathy and optic neuropathy. It also increases the risk of branch retinal vein occlusion (BRVO), central retinal vein occlusion (CRVO), branch retinal artery occlusion (BRAO), central retinal artery occlusion (CRAO), and non-arthritic anterior ischemic optic neuropathy (NAION). (Tsukikawa & Stacey 2020). Patients might be asymptomatic or might experience headaches, blurred vision, and occasional vision changes (Suhr, 2014).

Retinal vascular diseases

Retinal vascular diseases refer to a group of disorders that impact the vasculature of the eye. There is an interaction between the functions and risk factors of cardiovascular diseases and the development and incidence of vascular eye disorders. (Flammer & al. 2013a).

In *hypertensive retinopathy*, elevated blood pressure causes arteriolosclerotic changes in the retina. Clinical signs include general arteriole narrowing, arteriovenous nicking, copper or silver wiring, retinal hemorrhages, hard exudates, cotton wool spots, and in the severe form, optic disc swelling. (Bowling & Kanski 2015, 557). The Keith-Wakener-Barker classification of hypertensive retinopathy classifies hypertensive patients into four groups. (Table 4). Stages 3 and 4 are associated with an increased risk of cardiovascular issues but are quite rarely seen. (Flammer & al. 2013a).

Table 4 The Keith-Wakener-Barker classification

Stage	Description
Stage 1	Mild arterial narrowing
Stage 2	Moderate arterial narrowing, arteriovenous nicking, and changes in the light reflex
Stage 3	Arterial narrowing and constriction, flame shaped haemorrhages, cotton wool spots, hard exudates, retinal edema
Stage 4	All the above + optic disc swelling

(Flammer & al. 2013b).

The main risk factor for retinal vein occlusion (RVO) in older patients is hypertension. Hyperlipidemia is a common risk factor for younger patients but should also be considered an important risk factor for older patients. (Schmidt-Erfurth & al. 2019). Other risk factors include age older than 65 years, diabetes mellitus, glaucoma, contraceptive pills, and smoking (Bowling & Kanski 2015, 538). There are two types of RVO:

Branch retinal vein occlusion (BRVO) is caused when there is an obstruction of one of the smaller retinal branch veins. Typically, this happens when arteriolosclerotic stiffening of a branch retinal arteriole combined with arteriovenous nicking leads to thrombus formation. (Bowling and Kanski, 2015, 538). Clinical signs of BRVO include dilation and tortuosity of the impacted venous section with flame shaped and dot/plot hemorrhages. Symptoms vary depending on where the occlusion is located. Peripheral occlusion might be asymptomatic. With macular involvement, the visual disturbance is more noticeable; metamorphopsia and sudden painless onset of blurred vision are observed. (Salmon, 2020, 515).

Central retinal vein occlusion (CRVO) is caused when the central retinal vein gets occluded completely or partly posterior to the lamina cribrosa. It is caused by the same mechanism as branch occlusion, so it is typically caused by thrombosis. (Blair & Czyz 2022). If the central vein is not completely occluded, it is called impending or partial retinal vein occlusion and is commonly seen in younger individuals. Symptoms might be absent, or there might be a slight blurring of the vision that is worse upon awakening. Fundoscopy shows mild tortuosity and veins dilation accompanied by dot and blot hemorrhages. (Salmon 2020, 518).

There are two forms of CRVO: non-ischemic and ischemic. In the more common non-ischemic type, patients suffer from sudden unilateral blurred vision. Fundoscopy reveals tortuosity and dilation on all branches of the central vein. Flame shaped and dot/blot hemorrhages are present and there might be mild edema in the macula and optic disc. The ischemic form is more severe. The clinical signs and symptoms are more extensive, and the visual acuity is usually very poor as well as the prognosis for the vision. (Salmon, 2020, 519).

Atherosclerosis related thrombosis is the primary cause of *retinal artery occlusion (RAO)* (Salmon, 2020, 525). Other causes include carotid embolism, giant cell arthritis, cardiac embolism, thrombophilic disorders, arrhythmia, and migraine. Retinal artery occlusion can be classified into branch retinal artery occlusion (BRAO), central retinal artery occlusion (CRAO), and cilioretinal artery occlusion. (Kanski, 2003, 462).

Branch retinal artery occlusion (BRAO) refers to an obstruction of one of the branches of retinal artery. It is mostly caused by an embolism. It usually presents with a sudden unilateral altitudinal or sectoral vision loss. In fundoscopy an embolus might be present and there is clouding of the subsequent area. (Kanski 2003, 463).

Central retinal artery occlusion (CRAO) is an analog of an ischemic stroke, and it is considered a precursor for further cerebrovascular or cardiovascular events. Most of the cases are caused by carotid artery stenosis (narrowing) that is due to atherosclerosis. Another common cause of CRAO is cardiac embolus. (Mac Grory & al. 2021). Clinical findings include a cherry-red spot at the foveola surrounded by a pale cloudy macula, APD is present, or the pupil might not respond to light. Visual acuity is poor, except if the papillomacular bundle is spared by the cilioretinal artery. (Kanski, 2003, 464).

Anterior ischemic neuropathy (AION) can be divided into two subtypes: non-arteritic anterior ischemic optic neuropathy (NAION) and arteritic anterior ischemic optic neuropathy (AAION). AION causes vision loss due to reduced blood flow to the optic nerve. (Patel & Margo 2017).

In *NAION,* there is reduced blood flow to the optic nerve without inflammation (arthritis), causing optic nerve ischemia. Patients experience painless progressive loss of vision in one eye. Swelling of the optic disc is a typical clinical sign; it can be sectoral or diffuse. Retinal hemorrhages might be absent or present. Reported risk factors include male gender, hypertension, hyperlipidemia,

diabetes mellitus, coronary heart disease, history of cardiovascular medications, and obstructive sleep apnea. (Liu et al.2021).

In *AAION* there is reduced blood flow to the optic nerve due to an inflammation of the arteries that supply the optic nerve. AAION is nearly always associated with Giant Cell Arthritis (GCA, see chapter 2.6.6). Clinical signs show optic disc edema with haemorrhages and sometimes exudates. Visual symptoms are the same as in NAION but because of the association with GCA the systematic symptoms are numerous. (Chacko, Chacko & Salter 2015).

Ocular ischemic syndrome results from atherosclerotic narrowing or occlusion of the carotid artery, leading to ocular hypoperfusion. Risk factors include age over 65, male gender, hypertension, diabetes, and cardiovascular and cerebrovascular diseases. The ocular symptoms vary from mild to severe. Typically, patients experience a gradual loss of vision in one eye, but sometimes the loss might be sudden. About 40 percent of the patients experience ocular or periocular pain. Visual field defects might be present or absent. Clinical signs include episcleral redness, anterior chamber flare, and a few cells, neovascularization of the iris, mid-dilated and minimally reactive pupil, venous and arterial changes, retinal hemorrhages, and sometimes disc edema and cotton wool spots. (Terelak-Borys, Skonieczna & Grabska-Liberek 2012; Bowling & Kanski 2015, 556).

2.6.6 Immunologic and Inflammatory Diseases

Rheumatoid arthritis is an autoimmune disease that usually affects small and medium joints. Ocular manifestations can be the first sign of this disease. It most typically involves the anterior part of the eye but can affect any part. Ocular manifestations include keratoconjunctivitis sicca, episcleritis and scleritis, peripheral ulcerative keratitis, anterior uveitis, and retinal vasculitis. (Bhamra & al. 2019).

Spondyloarthropathies (SpA) are a group of inflammatory disorders with strong association to the HLA-B27 surface antigen. Spondyloarthropathies include ankylosing spondylitis, reactive arthritis, psoriatic arthritis, inflammatory bowel disease associated spondylarthritis and undifferentiated spondylarthritis. Spondyloarthropathies typically affect the spine, joints, and limbs but they can also involve the skin, eyes, and intestines. (Gill and Rosenbaum, 2021; Spondylarthritis, 2021). Ocular inflammatory disorders like uveitis are common manifestations of

these diseases, HLA-B27 associated anterior uveitis being the most prevalent type (Traian-Costin et al., 2018; Zagora and McCluskey, 2014).

Spondyloarthropathies (SpA) is an umbrella term for a group of inflammatory disorders with a strong association with the HLA-B27 surface antigen. Spondyloarthropathies include ankylosing spondylitis, reactive arthritis, psoriatic arthritis, inflammatory bowel disease associated spondylarthritis, and undifferentiated spondylarthritis. Spondyloarthropathies typically affect the spine, joints, and limbs, but they can also involve the skin, eyes, and intestines. (Gill and Rosenbaum, 2021; Spondylarthritis, 2021). Ocular inflammatory disorders like uveitis are common manifestations of these diseases, HLA-B27 associated anterior uveitis being the most prevalent type (Traian-Costin et al., 2018; Zagora and McCluskey, 2014).

Myasthenia gravis is an autoimmune disease in which an antibody-mediated blockage or destruction of the neurotransmitter receptors leads to faulty communication between motor neurons and muscle fibers. Typically, in the disease, the acetylcholine receptors are affected. The hallmark finding of Myasthenia gravis is muscle weakness that occurs after the muscle group has been used and lessens after rest. This can affect the ocular, bulbar, limbal, and respiratory muscles. Most patients present with ocular symptoms. Since the extraocular muscles are affected, patients might experience double vision and ptosis. (Dresser, Wlodarski, Rezania & Soliven 2021).

Giant Cell Arthritis (GCA) is an autoimmune disease. It causes inflammation of the arteries, typically in the head and neck. GCA predominantly affects the elderly, and it is rarely seen in patients under fifty. It is more commonly seen in whites of European origin and affects women more often than men. Some people may have a genetic predilection for this condition. Typical symptoms include headache in the temples, scalp tenderness, jaw claudication, fever, and malaise. Sudden vision loss can be an indicative finding for GCA. The other eye is usually affected as well within days or weeks. 15-20% of the patients with GCA suffer from permanent vision loss, so it is crucial to recognize the symptoms early. (Chacko & al. 2015).

Sarcoidosis is a granulomatous inflammatory disease of unknown origin. It can affect any organ, but the lungs and lymph nodes are most often affected (Gerke 2020). Sarcoidosis is most prevalent in African American and Scandinavian people (Sève et al., 2021). Ocular sarcoidosis most commonly presents as uveitis; however, all structures of the eye can be affected. Other ocular

manifestations include conjunctival granulomas, keratoconjunctivitis sicca, and rarely optic neuritis. (Sève et al. 2021; Kanski 2003, 710).

2.6.7 Genitourinary Diseases

Kidneys and eyes share similar developmental and structural pathways. Therefore, kidney disease and ocular disease can be closely connected. **Chronic kidney disease (CKD)** is a disease where the kidneys gradually stop functioning. CKD and common eye diseases like AMD, diabetic retinopathy, glaucoma, and cataract share common risk factors. These risk factors include age, hypertension, hyperlipidemia, obesity, and smoking. Patients suffering from CKD have a higher risk of being affected by major eye diseases. (Wong et al. 2014).

CKD might progress into **end stage renal disease (ESRD)**, which in turn increases the risk of developing band keratopathy. Band keratopathy is a degenerative disease where calcium deposits accumulate on the cornea, creating a band like greyish or whitish opacity. (Weng & al. 2016).

Congenital abnormalities also affect the eyes and kidneys (oculorenal syndromes). These syndromes include WAGR, Alport and Fabry`s, and Senior-Loken syndrome. The ocular abnormalities of these disorders include aniridia, coloboma, and microphthalmia. (Wong & al. 2014). These congenital abnormalities are rare and won't be further discussed in the scope of this work.

Benign prostate hyperplasia (BPH) is a common disorder where the prostate becomes enlarged. BPH typically affects men over fifty years old. Other risk factors are obesity, type II diabetes, positive family history, and physical inactivity. Typical symptoms include the need to urinate more frequently, difficulty emptying the bladder, and difficulty starting the urination. (NIDDK 2014). The disease doesn't affect the eyes, but the medications used to treat the condition (alpha-blockers) have ocular side effects that will be discussed in chapter 2.8.2.

2.6.8 Gastrointestinal Diseases

Inflammatory bowel disease (IBD) mainly means Crohn's disease or Ulcerative colitis. IBD is a chronic inflammatory disease that affects the gastrointestinal tract, although it can also involve

other organs and systems. The eye is often affected, and typical manifestations are episcleritis and uveitis. (Lopes et al. 2017).

2.6.9 Hereditary Connective Tissue Disorders

Hereditary disorders of connective tissue (HDCT) are a group of disorders affecting various connective tissues of the body. These disorders often affect multiple organ systems, including the skin, joints, heart, blood vessels, bones, eyes, and lungs. (Meester & al. 2017).

Marfan Syndrome (MFS) is a hereditary disorder affecting the body's connective tissue. The causative agent is a mutation in the FBN1 gene, which is known to encode the fibrillin-1 protein, an essential part of the extracellular matrix. MFS typically has skeletal, cardiovascular, and ocular manifestations. MFS patients typically have chest and foot deformities, overly flexible joints, long arms span, long and curved fingers, scoliosis, and overbite. The ectopia lentis (luxation of the lens) is the most typical ocular manifestation. Other ocular manifestations include a long axial length of the eye which raises the risk of retinal detachment. Patients with MFS tend to develop cataract and glaucoma more commonly due to ectopia lentis. (Meester et al., 2017).

Ehlers-Danlos Syndrome (EDS) is a hereditary disorder. It affects connective tissues such as skin, joints, ligaments, blood vessels, and internal organs. Typical manifestations are hypermobility of the joints, unusually elastic skin, and frail tissues. EDS was previously classified into six subtypes, but currently, there are 13 recognized subtypes of the disease. (Meester & al. 2017). Only a few of the subtypes have ocular manifestations. Brittle cornea syndrome mainly causes eye problems, including thin cornea, keratoconus, keratoglobus, and blue sclera. Kyphoscoliotic EDS and dermatosparaxis EDS can sometimes have ocular manifestations such as blue sclera and refractive errors. (Malfait et al. 2017).

2.6.10 Diseases of the Respiratory System

Although there are generally no reported ocular manifestations of respiratory diseases, the medications used for these conditions have been associated with ocular side effects. It is therefore important to inquire the patient about any respiratory diseases.

Asthma is a pulmonary condition that causes inflammation and narrowing of the airways, resulting in breathing difficulties. It affects over 250 million people worldwide (Asthma-WHO, 2021). There are generally no reported ocular manifestations of asthma. Still, in a study by Huang et al. (2018), people with asthma were more susceptible to having dry eye disease than those without asthma. However, in this study the increased prevalence of dry eye disease among the asthma group could also be due to the prescribed medications. (Huang et al.2018). Systemic medications used for the treatment of asthma have been associated with adverse ocular effects like cataracts, glaucoma, and dry eye disease. (Bielory 2006).

Obstructive sleep apnea is sleep related breathing disorder. It manifests as partial or complete obstruction of the airways during sleep. It poses a risk for cardiovascular and cerebrovascular comorbidities and mortality. (Bouzerda 2018). Ocular complications of the disease include floppy eyelid syndrome, non-arthritic anterior ischemic optic neuropathy (NAAION), central serous retinopathy, retinal vein occlusion (RVO) and glaucoma. (Santos & Hofmann 2017).

2.6.11 Dermatological and Mucous Membrane Diseases

Skin and eye are closely related organs and therefore ocular manifestations are common in dermatological diseases (Akrash et al. 2021). Next, we will go through some common dermatological diseases with ocular manifestations.

Atopic dermatitis is a chronic skin disorder. It makes the skin red, scaly, and itchy. It might be associated with asthma and allergic rhinitis and is often hereditary. It is most often seen in young children but might develop at any age. (Kanski 2003, 686). Ocular manifestations are numerous, including blepharitis, atopic keratoconjunctivitis, tear film imbalance, keratoconus, uveitis, cataract, and rarely retinal detachment (Pietruszyńska et al. 2020).

Acne rosacea is a chronic skin condition typically affecting the facial skin. It is usually seen in middle aged patients and seems more common among females and fair-skinned individuals. It typically manifests as blushing or flushing, pimples or small pus-filled bumps, and small superficial blood vessel dilation. (Airola, 2022). Approximately half of the patients also have ocular manifestations such as dry eyes, blepharitis, conjunctivitis, conjunctival telangiectasis, and meibomian gland dysfunction (Airola 2022; Thiboutot & al. 2020).

Mucous membrane pemphigoid (MMP) is an uncommon autoimmune disease that causes blistering lesions on mucous membranes. The mouth and conjunctiva are most often affected. (Xu, Werth, Parisi & Sollecito 2013). Ocular MMP is a subtype of MMP that can cause serious ocular complications including severe dry eye syndrome, corneal erosions, corneal scarring, and entropion (Branisteanu & al. 2020).

2.6.12 Haematologic Disorders

Hematologic disorders refer to disorders of the blood and blood forming organs. Ocular manifestations can many times be the first sign of underlying hematologic disease. (Reynolds & Rodman 2009). Next, some of the most common hematologic disorders that can have ocular manifestations are discussed.

Anemia refers to a condition where the level of hemoglobin is decreased due to a reduced number of red blood cells or a decreased amount of hemoglobin in red blood cells. Anemia can be caused by iron deficiency, vitamin B12 or folic acid deficiency, increased breakdown of red blood cells, increased bleeding, certain autoimmune diseases, or diseases of the bone marrow. Anemia is diagnosed when the level of hemoglobin is less than 134g/l in men and less than 117g/l in women. (Salonen 2020). Hemoglobin levels naturally fluctuate by sex, age, genetic factors, environmental factors, pregnancy, and race (Chaparro & Suchdev 2019). In the eyes, anemia manifests as conjunctival pallor, cotton wool spots, flame shaped hemorrhages, dot and blot hemorrhages, Roth spots hemorrhages, tortuosity of veins, macular edema, and optic nerve changes (Kumar, Singh & Garg 2020).

Sickle cell disease (SCD) is a hereditary blood disease. Its prevalence is highest among sub-Saharan Africans. SCD leads to a typical “sickle” shape of red blood cells that causes disturbance in the blood flow to small vessels leading to inflammation and ischemia. SCD can affect almost every organ, including the eye. (Ware et al. 2017). All eye structures can be affected by SCD, but the most common ophthalmic manifestation is sickle cell retinopathy. It is classified into two forms: non-proliferative and proliferative, the latter being the major cause of vision loss among SCD patients. (Abdalla Elsayed & al. 2019). Clinical findings in the non-proliferative form include oval shaped hemorrhages (salmon patch hemorrhage), sunburst black lesions, iridescent spots, dark

red spots on the disc, vessel tortuosity, angioid streaks, abnormal retinal light reflex, and retinoschisis. In the proliferative form, neovascularization is present as in other vascular re**ti**nopathies. (Pahl, Green, Bhatia & Chen 2017).

2.6.13 Neurological Disorders

Neurological disorders are a group of disorders that affect the central and peripheral nervous systems. The visual system consists of the eye and retina, optic nerve, optic tract, and visual cortex. Since a relatively large portion of the brain is dedicated to vision, neurodegenerative disorders have numerous ocular manifestations. (Waxman 2013, 201; Guidoboni et al. 2020).

A stroke is a neurological disorder. It happens when there is a disturbance of blood flow to the brain. It is the second leading cause of death worldwide and affects approximately 14 million people. The major non-modifiable risk factor for stroke is age, but the incidence of strokes is rising among younger individuals. Other non-modifiable risk factors include genetics, black or Hispanic race, and female gender. The modifiable risk factors include systemic conditions such as hypertension, hyperlipidemia, diabetes, and atrial fibrillation. Alcohol and drug abuse, smoking, inactivity, and poor diet also increase the risk of a stroke. (Kuriakose & Xiao 2020).

Strokes can be categorized as *hemorrhagic and ischemic strokes*, from which the latter accounts for roughly 85% of the cases. In an ischemic stroke, the blood flow to the brain is reduced or blocked by thrombosis or embolism. If the blood flow is temporarily obstructed, the condition is considered a transient ischemic attack (TIA, a mini stroke). The less common form of stroke is a hemorrhagic stroke which happens when blood vessels in the brain leak or rupture. (Kuriakose & Xiao 2020).

Visual symptoms after a stroke are common. A stroke can affect a specific part of the visual pathway or an area of the brain processing visual information, therefore affecting vision. Typical visual symptoms after a stroke include transient monocular vision loss or permanent vision loss with reduced visual acuity or visual field defects (due to retinal ischemia), bitemporal hemianopia (due to chiasmal ischemia), homonymous hemianopia (due to post chiasmal ischemia), incongruous loss of visual field (due to optic tract and lateral geniculate body ischemia), incongruous homonymous hemianopia or quadrantanopia (due to ischemia of optic radiation), congruous homonymous hemianopia (due to occipital lobe ischemia). (Guidoboni et al., 2020).

Multiple Sclerosis (MS) is a disease attacking the central nervous system (CNS). It is the most common disease affecting the physical and functional ability of young adults. In Multiple Sclerosis, the body´s immune system attacks the myelin sheath around nerve cell axons in the CNS. This results in miscommunication with the rest of the body, causing various symptoms. These symptoms include muscle weakness, numbness and tingling, vision problems, dizziness, and cognitive problems. The cause of the disease is unknown. Still, various factors can increase the risk of MS: age (20-40), female gender, positive family history, infections (Epstein-Barr virus), vitamin D insufficiency, North European ethnicity, smoking, and obesity. (Atula 2019).

Visual symptoms are common findings in MS. In approximately 20 percent of the patients, optic neuritis (ON) is the first sign of the disease. ON manifests as a unilateral loss of vision, altered colour vision, abnormal pupillary light reflex, and pain with ocular movements. Other ocular manifestations of MS disease include oculomotor dysfunction, cranial nerve palsies (usually VI and III), nystagmus, and saccadic dysfunction. (Hoff et al. 2019).

With the increasing use of Optical Coherence Tomography (OCT) the knowledge of the pathophysiology of MS has increased. Retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thickness can be measured with OCT. The thickness reduction of these layers is an indicator of neuroaxonal loss, which is typical for neurodegenerative diseases. (Guerrieri, Comi & Leocani 2021). Axonal loss has been demonstrated to occur in the early stages of the disease even before optic neuritis (Britze & Frederiksen 2018).

Parkinsonism, also known as atypical Parkinson`s or Parkinson`s plus, is a term used to describe symptoms and signs that are characteristically like those seen in Parkinson`s disease. These include tremors, stiffness, slowness of movement and problems with balance. Parkinson`s disease is the most familiar form of parkinsonism. Other less common types of parkinsonism include dementia with Lewy bodies, progressive supranuclear palsy, multiple system atrophy, and corticobasal degeneration. (Levin et al. 2016). Parkinson´s disease and Parkinson´s plus comes with different ocular signs and symptoms. Therefore, in the next chapter these are shortly introduced, and their ocular signs and symptoms are presented.

Parkinson´s Disease (PD) is a neuro-degenerative disease that progresses over time. The risk of getting PD increases with age; affected individuals are typically over fifty. PD is somewhat more

common among men than women. Interestingly, smoking is known to decrease the risk of developing PD. The disease is caused by the degeneration of dopamine producing neurons in a specific area of the brain (substantia nigra). One characteristic pathological feature is the aggregation of alpha synuclein proteins within these cells, causing damage and eventual cell death. As a result, typical motor symptoms are seen with PD, such as stiffness, tremor, and bradykinesia. The symptoms generally start on one side of the body and gradually worsen over time. (Atula 2018). There are a variety of ocular symptoms with PD. These symptoms include reduced blinking rate resulting in dry eyes, decrease in visual acuity, color vision and contrast sensitivity, impaired oculomotor control, abnormal pupil reactivity and larger pupil size, reduced depth reception, insufficient convergence and optokinetic nystagmus, and visual hallucinations. (Armstrong 2015). Structural imaging of the retina with OCT has shown thinning of the retinal nerve fiber layer and inner retinal layers in many PD patients. (Guo et al. 2018).

Progressive supranuclear palsy is an untypical degenerative disorder of the nervous system in which tau protein accumulates in certain areas of the brain, damaging nerve cells. This causes walking, balance, vision, speech, and swallowing problems and alters behavior and thinking. Early in the disease, it is often misdiagnosed as Parkinson´s due to similar motor symptoms. Most patients will develop ocular manifestations, including slow eye movements, restricted up and down eye movement (vertical gaze palsy), impaired control of eyelids, and a tendency to move the head when looking in different directions. (Progressive Supranuclear Palsy Fact Sheet 2021).

Multiple System Atrophy (MSA) is an untypical degenerative disorder of the nervous system with multiple signs and symptoms. It typically manifests as parkinsonism, cerebellar ataxia, and autonomic dysfunction. (Armstrong 2014). In MSA, there is an accumulation of alpha-synuclein protein in nerve cells as in Parkinson`s, but in this case also in oligodendrocytes - glial cells that do not have axons or dendrites but perform in other roles in the central nervous system (Valera & Masliah 2018). Since many of the areas in the brain that are affected by MSA involve visual functions, many ocular signs and symptoms are reported with MSA. The most common are blepharospasm, square-wave jerks, abnormal fixation, decreased smooth pursuit eye movements, and abnormal pupil reflexes. (Armstrong 2014).

Dementia with Lewy Bodies (DLB) is a usual cause of neurodegenerative dementia. Also, in DLB there is an abnormal accumulation of alpha-synuclein protein in the brain, but in this disease in the area which is involved in thinking, memory, and motor control. (Outeiro & al. 2019). DLB shares

many of the same clinical features as Alzheimer´s Disease, as it is often misdiagnosed. Up to 80 percent of DLB patients experience vivid visual hallucinations, which can often help with the diagnosis. (Barrett & Armstrong 2017).

Alzheimer's Disease (AD) is the most typical cause of dementia. Age increases the risk of developing AD, which seems to be slightly more prevalent among females. Other risk factors include a positive family history of the disease, head injuries, severe depression, cardiovascular disease, obesity, excess alcohol use and smoking. AD is caused by an abnormal accumulation of amyloid β (Aβ) and tau protein in the brain resulting in the degeneration of nerve cells and neuronal connections. This leads to memory problems and a decline in cognition. (Juva 2021).

The retina's neurons are in many ways comparable to the ones in the brain, therefore, neurodegenerative diseases like AD can have various ocular manifestations. In the eye, AD can manifest as abnormal pupil reactivity and increased pupil size, retinal nerve fiber layer thinning, ganglion cell layer degeneration (superior and inferior peripheral retina), choroidal thinning, increased cup-disc ratio and optic nerve pallor, Aβ deposits in the retina, lens, and aqueous humor. Visual manifestations include reduced visual acuity, contrast sensitivity and color vision, visual field defects (inferior hemifield), reduced depth reception, and problems with the oculomotor functions. (Javaid, Brenton, Guo & Cordeiro 2016).

Epilepsy belongs to the most prevalent neurological diseases globally. It affects both sexes and people of all ages, races, and social classes (Beghi 2020). It is a chronic disease of the brain and is characterized by episodes of seizures. These seizures are caused by abnormal electrical activity in the brain. The underlying cause is unidentified in about half of the cases, but in many cases, an underlying disease or mechanism is causing the seizures. These causes can be genetic, structural, infectious, metabolic, or immune related causes. (Epilepsy-WHO, 2022). Epilepsy seizures can be classified into focal, generalized, or unknown onset. The signs and symptoms depend on the type of seizure. (Thijs, Surges, O'Brien & Sander 2019). Epilepsy can cause several visual and ocular symptoms during the seizure; however, this doesn't usually affect vision permanently. Ocular manifestations of epilepsy include staring, rapid blinking, eye deviation, visual field loss, and visual hallucinations. (Vision and Eye Changes with Epilepsy | National Epilepsy Month 2019). If the occipital lobe is involved, visual disturbances are often present. A hallmark finding of occipital epilepsy is vivid visual hallucinations. These often manifest as colorful circles or balls that may

flash, change the size, and move around, lasting seconds. Sometimes these visual disturbances might be misdiagnosed as a migraine. (Taylor, Scheffer & Berkovic 2003).

As people commonly understand **headaches** as a condition related to eyesight, an optometrist´s office may be the first location where treatment is sought. Therefore, the optometrist must be aware of the most common headache disorders.

Headache disorders are described as recurrent headaches and are among the most common neurological disorders, the prevalence being around 50 percent in the adult population. Headache disorders affect people of all races, ages and gender but are more common among females. Headache disorders can be categorized into primary and secondary disorders. The secondary disorders (for example idiopathic intracranial hypertension, giant cell arthritis and intracranial tumors) are unusual, but they might be life threatening, so their recognition is crucial. Primary and secondary headaches can share similar neurological symptoms such as anisocoria and careful history taking can help to differentiate between these two categories. Primary headaches comprise most headache disorders and are divided into three major categories: migraine headache, tension type headache and cluster headache. Migraine and tension type headaches have the highest prevalence. Cluster headaches are unusual but are often misdiagnosed. (Ahmed 2012, Payne, Blair & Barret 2022).

- *Migraine* is a chronic neurological disorder. It typically manifests as headache attacks with transient neurological symptoms. The most common migraine associated symptoms are sensitivity to light, sound and smells, cutaneous allodynia, nausea, vomiting, dizziness, and vertigo. Migraine headache is reported as unilateral in around 60 percent of the cases. It is often described as a pulsating pain that worsens with physical activity, so patients prefer to lie in a dark room. The pain lasts a few hours or even a couple of days. About 30 percent of the patients experience a migraine aura (known as classic migraine) before or during the attack; the aura can also occur without the headache. (Dodick 2018). The visual aura typically starts as a paracentral scotoma or zigzag pattern and flashing lights that expand to the peripheral visual field. The auras usually last between 5 and 60 minutes. A migraine aura can mimic an epilepsy aura and a transient ischemic attack (TIA), so differentiation is essential. (Eren et al. 2021).

- *Tension type headache (TTH)* is the most common headache disorder. It doesn't have associated symptoms, and it typically manifests as an aching head and a feeling of a tight band around the head. TTH usually comes in episodes and is far less disabling than migraine. TTH is not reported to have visual symptoms. (Ahmed, 2012).

- *Cluster headache* is characterized as a short, intense, and strictly unilateral headache. Associated symptoms are tearing, conjunctival injection, ptosis, and runny nose. Cluster headaches are more common among young men who smoke. (Ahmed 2012).

2.6.14 Cancer

The most common cancers worldwide are breast cancer in women and lung cancer in men (Worldwide cancer data | World Cancer Research Fund International 2022). These are also the most typical cancers to metastasize to the eye. Metastasis to the eye usually occurs in the later stages of cancer. However, with lung cancer, metastasis can happen early on, and the optometrist can be the first to detect the tumor. Ocular metastasis is not often seen, although they are the most common intraocular tumor of the eyes. Although cancer can metastasize in several structures of the eye, the most typical site is the uveal tract, especially the choroid. A typical fundus finding is a creamy yellow concentration associated with subretinal fluid and changes in the retinal pigment epithelium. The most common symptom is blurry vision followed by flashes and floaters. Sometimes patients might be asymptomatic. (Pahlevan 2017; Cohen 2013).

2.6.15 Mental Disorders

Mental disorders include depression, anxiety, bipolar disorder, ADHD (Attention-Deficit Hyperactivity Disorder), and many more (Cherry 2022). Although mental disorders are not reported to have ocular manifestations, the medications used for treating these conditions often affect the eyes and vision (Bhawan 2016). These medications will be further discussed in chapter 2.8.2.

2.6.16 Pregnancy and Breast Feeding

Pregnancy can have physiological and pathological effects on the eyes. All ocular structures can be affected during pregnancy. Physiological changes during pregnancy can include lens curvature and corneal thickness changes, causing refractive changes and accommodative problems. These problems have been reported during pregnancy and the postnatal breastfeeding phase, so renewing eyeglasses or a contact lens prescription is not recommended until after stopping breastfeeding. Pregnancy can also cause changes in the tear film resulting in dry eyes. Changes in the cornea and tear film increase the intolerance of contact lenses. Intraocular pressure and corneal sensitivity are reported to decrease during pregnancy. (Yenerel & Küçümen 2015; Anton & al. 2021).

Pathological changes can be classified as the following: ocular changes that emerge first time during pregnancy (dry eyes, keratoconus), pre-existing ocular diseases that are modified by pregnancy (glaucoma, diabetic retinopathy), pregnancy related systemic diseases with ocular manifestations (pre-eclampsia/eclampsia) and diseases that occur more often during pregnancy (idiopathic intracranial hypertension and Grave`s disease). (Anton & al. 2021).

2.7 Family Ocular and Medical History

Asking about family history is an important part of the medical history to determine if there is a genetic predisposition to disease (Nichol, Sundjaja & Nelson 2021). Many diseases are hereditary, or genes may increase the risk of developing certain conditions. Diseases like Alzheimer´s, heart disease and diabetes have a multifactorial inheritance pattern meaning that they are not caused by a single mutation of the genet, but instead by a mixture of environmental and genetic factors. (Levin, et al. 2017). The same applies to certain eye diseases. While genes are more profound in diseases like retinitis pigmentosa and corneal dystrophies, the effect is less significant in AMD and glaucoma. (Iwata 2018).

AMD is a multifactorial disease with a robust genetic component. More than 50 susceptibility loci (location of a gene on a chromosome) are associated with the disease. (Mitchell et al. 2018). Patients with a sibling or parent with AMD have a 12 to 27 percent higher risk of developing the disease themselves (DeAngelis & al. 2017).

Glaucoma is a problematic disease since it can be asymptomatic for years. Up to 50 percent of affected people are unaware of having it. There might even be a ten-fold increased risk for glaucoma if a first degree relative like a sibling has the disease. Identifying the higher risk patients is a key factor in preventing the progression of the disease. (Okeke 2016).

Corneal dystrophies are a group of disorders that usually run-in families. These disorders affect the cornea's transparency. These dystrophies can affect any layer of the cornea. Some of the most common corneal dystrophies encountered in optometrist's practice are epithelial basement membrane dystrophy (EBMD) and Fuchs endothelial corneal dystrophy. EBMD is common in people over fifty, so most cases are believed to result from age-dependent degeneration. (Levin & al. 2017, 39,44).

Retinitis pigmentosa (RP) is understood as a group of hereditary disorders affecting the retina, causing a gradual loss of vision. RP typically starts with a loss of night vision, progressing into peripheral loss of vision, and later the loss of central vision. (Levin & al. 2017).

There are two primary types of **refractive errors: myopia and hyperopia**. They are thought to be caused by a complex interplay between genetics and environmental factors. The knowledge of the genetic background of refractive error and myopia has increased significantly in recent years, and around 200 genetic loci have been recognized for refractive error and myopia. Since myopia can cause sight threatening pathologies, studies usually concentrate on the inheritance patterns of myopia. The heritability of myopia varies largely between different studies, but according to the IMI-Myopia Genetics Report (2019), it is estimated to be around 60-80 percent. (Tedja & al. 2019).

Systemic diseases and conditions affecting the eyes like diabetes, hypertension, and numerous autoimmune disorders, all have a strong genetic component. Still, they are multifactorial by origin, influenced by a complex interplay between genetics and environmental factors. (Yamamoto & Okada 2019; Dedmon 2020; Liguori, Mascolo & Vernì 2021; Arnett & Claas 2018).

2.8 Medications and Drug Allergies

Medications and drug allergies are a vital part of the patient history. Systemic medications can affect all structures and functions of the eyes. These adverse effects might be mild or more severe, causing transient disturbances or even permanent vision loss. Allergies are a crucial part of the patient history to avoid complications. (Dellabella & Andres 2015; Nichol & al. 2021). For optometrists, it is important to be aware of the most used systemic medications and their possible ocular and visual adverse effects and to be familiar with the contraindications of the medications used in the optometrist´s own practice.

2.8.1 Medications Used by the Finnish Optometrists

Finnish optometrists can use certain medications as a part of a clinical examination. More detailed discussion about the medications can be found in the thesis made by optometry students at Metropolia University of Applied Sciences in 2019, Diagnostisten lääkeaineiden hyödyntäminen työelämässä and the thesis made by optometry students in Oulu University of Applied Sciences in 2015, Diagnostiset lääkeaineet optikon käytössä. (Mäkelä & Sillanpää 2015; Lindroos & Malinina 2019). A short list of these medications and possible contraindications is written below.

Oftan Tropicamide belongs to the class of drugs known as anticholinergics and is used to dilate the pupil. It should not be used for patients allergic to tropicamide, with narrow anterior chamber angles, or angle-closure glaucoma since tropicamide might increase the intraocular pressure of these eyes. Oftan Tropicamide contains benzalkonium chloride, so an allergy to this preservative should also be asked about before use. It should be noted that tropicamide might increase the effect of alcohol, psychotropic medication, allergy medication, and arrhythmia medication. (Lääkeinfo.fi - lääkevalmisteiden pakkausselosteet - OFTAN TROPICAMID silmätipat, 2020).

Oftan Syklo is also an anticholinergic drug used for dilating the pupil. Oftan Syklo should not be used for patients allergic to its active ingredient cyclopentolate, who have narrow anterior chamber angles or angle-closure glaucoma since it might increase the intraocular pressure of these eyes. Oftan Syklo contains benzalkonium chloride, so an allergy to this preservative should also be asked about before use. Oftan Syklo might increase the effect of certain medications such as tricyclic antidepressants, antihistamines that make you sleepy, and certain medications used for

parkinsonism. (Lääkeinfo.fi – lääkevalmisteiden pakkausselosteet – OFTAN SYKLO silmätipat, 2020).

Oftan Metaoksedrin eye drops contain phenylephrine hydrochloride as the active ingredient. It is a sympathomimetic drug used for dilating the pupil. Oftan Metaoksedrin should not be used for patients allergic to phenylephrine hydrochloride who have narrow anterior chamber angles or angle-closure glaucoma since it might increase the intraocular pressure of these eyes. Oftan Metaoksedrin contains benzalkonium chloride, so an allergy to this preservative should also be asked about before use. Extra caution should be taken with elderly patients with high blood pressure, atherosclerosis, diabetes treated with insulin, hyperthyroidism, or heart failure. (Lääkeinfo.fi - lääkevalmisteiden pakkausselosteet - OFTAN METAOKSEDRIN silmätipat, 2020).

Oftan obucaine is a topical anesthetic that is used for short ophthalmic procedures. It contains oxybuprocaine, so an allergy to this ingredient should be asked about before using. The use of this medication might decrease the effect of sulphonamides. (Lääkeinfo.fi – lääkevalmisteiden pakkausselosteet – OFTAN OBUCAIN silmätipat, 2020).

Oftan flurekain is a topical anesthetic that contains yellow stain that helps to detect corneal damage. It is used for ophthalmic procedures like intraocular pressure measurement and detecting corneal damage. It contains oxybuprocaine and fluorescent sodium, so an allergy to these ingredients should be asked about before using. The use of this medication can cause temporary irritation of the eyes. Other ocular side effects are rare. (Lääkeinfo.fi – lääkevalmisteiden pakkausselosteet – OFTAN FLUREKAIN simätipat, 2019).

2.8.2 Selected Systemic Medications with Ocular Side Effects

In this chapter, selected systemic medications with ocular side effects are briefly introduced. There are several ways to classify medications. In this thesis, the ATC classification method will be used. This method classifies medications by their anatomical, therapeutic, and chemical properties. Medications are classified according to which organ or organ system they affect and their pharmacological, therapeutic, and chemical properties. Medications are classified into five different groups. The first level specifies the anatomical group of the drug. The second level specifies the therapeutic group. The third level specifies the therapeutic/pharmacological group. The fourth level

specifies the chemical/therapeutic/pharmacological group. Finally, the fifth level specifies the chemical substance. ATC code is structured based on these different levels; one drug might have several different codes. (ATC-luokitus - Fimea s.a.). In this thesis, only the first level (anatomical or pharmacological group) will be used to simplify the content (Table 5).

Table 5

A: Alimentary tract and metabolism
B: Blood and blood forming organs
C: Cardiovascular system
D: Dermatologicals
G: Genito-urinary system and sex hormones
H: Systemic hormonal preparations, excluding sex hormones and insulins
J: Anti-infectives for systemic use
L: Antineoplastics and immunomodulating agents
M: Musculoskeletal system
N: Nervous system
P: Antiparasitic products, insecticides, and repellents
R: Respiratory system
S: Sensory organs
V: Various

(ATC-luokitus - Fimea s.a.).

Next chapters discuss the most relevant anatomical or pharmacological groups related to eyes and vision.

C: Cardiovascular system

Amiodarone is an antiarrhythmic drug. It has been associated with ocular toxicities, the most common being corneal keratopathy (vortex keratopathy). Rarely, in less than 2 % of the cases, amiodarone has been associated with the development of optic neuropathy. Dry eyes and eyelid irritation are also reported side effects of this drug. Due to the high prevalence of ocular toxicity, the patients should be warned about the risks. (Dellabella & Andres 2015; Salmon 2020, 882, 889, 890).

Statins such as atorvastatin, simvastatin, and rosuvastatin are drugs used for treating high cholesterol. They are usually well tolerated and safe. A reported and relatively common ocular side effect is blurry vision. Statins may have protective effects on ocular health, but the results are inconsistent. (Ho, Gentry & Zimbalist 2020; Lääkeinfo.fi - lääkevalmisteiden pakkausselosteet - ATORVASTATIN ORION, 2018).

D: Dermatologicals

Isotretinoin is a derivate from vitamin A and is widely used for treating skin conditions like acne. The most recognized ocular side effect associated with Isotretinoin is dry eyes. Other possible side effects include blepharitis, conjunctivitis, decreased tolerance to contact lenses, and decreased adaptation in the dark. (Prakash et al. 2019; Ahmad & Mehta 2021).

G: Genito-urinary system and sex hormones

Combined oral contraceptives can cause various ocular side effects. The most recognized ocular side effects include dry eyes, corneal edema, intolerance to contact lenses, and lens opacities. More severe and rarely reported ocular manifestations include vascular (CRAO, CRVO, macular or papillary edema) or neuro-ophthalmic (sixth cranial nerve palsy, hemianopsia, retrobulbar neuritis) complications. For menopausal women, contraceptives might have positive effects, such as alleviating dry eye symptoms. (Nitoda & Moschos 2017).

Tamsulosin is an alpha-1 blocker medication used for treating benign prostatic hyperplasia in men and bladder problems in women. This medication is known to cause floppy iris syndrome, which increases the risk for complications during cataract surgery. (Dellabella & Andres 2015).

Sildenafil and tadalafil inhibit the action of phosphodiesterase type 5. These medications are widely used in erectile dysfunction and are associated with various ocular side effects. Typical ocular side effects are blurry vision and changes in color perception. (Dellabella & Andres 2015).

H: Systemic hormonal preparations, excluding sex hormones and insulins

Corticosteroids treat asthma, hay fever, arthritis, inflammatory bowel disease, lupus, and multiple sclerosis (Steroids - NHS 2020). The use of steroids, both systemic and topical, can lead to cataract formation. Typically, steroid induced cataract manifests as posterior subcapsular cataract. (Salmon 2020, 883). Using steroids can also increase the intraocular pressure leading to steroid induced glaucoma. (Phulke et al. 2017; Ahmad & Mehta 2021). Central serous chorioretinopathy is a condition where fluids accumulate under the retina, causing decreased visual acuity and distorted vision. This condition has been associated with systemic steroid use (Ahmad & Mehta 2021).

J: Anti-infectives for systemic use

Tetracycline is an antibiotic used to treat skin conditions and/or bacterial infections. Tetracycline can cause dry eyes, blurry vision, and in rare cases papilledema. (Ahmad & Mehta 2021).

L: Antineoplastics and immunomodulating agents

Methotrexate is an immunosuppressant which is used in the treatment of certain types of cancer and inflammatory conditions like rheumatoid arthritis and severe psoriasis. (Methotrexate – an immunosuppressant used to treat inflammatory conditions - NHS 2020). Methotrexate can cause optic neuropathy, but it is extremely rare. (Salmon 2020, 890).

Tamoxifen is an anti-estrogen that is used to lower the recurrence of breast cancer. Ocular manifestations are uncommon, but retinal toxicity might develop in patients using high doses. Tamoxifen induced retinopathy presents as crystalline deposits in the inner layers of the retina. Grey lacerations in the outer retina and retinal pigment epithelium (RPE) are also seen. (Salmon 2020, 887).

M: Musculoskeletal system

Bisphosphonates are typically used in the treatment of osteoporosis. They prevent bone resorption and activate a group of immune cells. This activation of T-cells is thought to be connected to the development of uveitis or scleritis in the patients using this medication. Inflammation typically occurs two days after administration. (Salmon 2020, 884).

N: Nervous system

Tricyclic antidepressants have been on the market since the late 1950s and are still commonly used for treating depression (Matti O 2017). These medications have anticholinergic properties, suppressing the action of the parasympathetic nervous system by blocking the action of acetylcholine (a type of neurotransmitter). This causes the ciliary muscle to relax, causing dilated pupils and decreased accommodation. They can also cause dry eyes by repressing parasympathetic activity. Patients with narrow anterior chamber angles have an increased risk of acute angle-closure glaucoma. (Ahmad & Mehta 2021).

SSRIs (selective serotonin reuptake inhibitors) are first-line medications for depression. They increase the levels of serotonin in the brain. SSRIs have fewer anticholinergic effects compared with older generation antidepressants. (Matti O 2017). The most common ocular side effect is dry eyes; however, they can cause increased pupil sizes (although less visual disturbances compared to Tricyclic antidepressants), and increased IOP (Constable et al. 2022).

Topiramate is an antiepileptic agent that can be used for treating epileptic seizures or as a prophylactic medication for migraine. It can cause acute angle-closure glaucoma due to swelling of the ciliary body. (Dellabella and Andres, 2015; Salmon, 2020, 882).

Vigabatrin is an antiepileptic drug with a high risk of causing progressive and permanent narrowing of the visual fields. Baseline assessment with visual fields and OCT is recommended before using vigabatrin, followed by reassessment every three months. (Dellabella & Andres 2015; Salmon 2020, 890).

Digoxin is a cardiac glycoside for heart conditions like atrial fibrillation and flutter. Visual problems are common, including yellowing of the vision, blurry vision, and a flickering spot of light in the visual field. (Ahmad & Mehta 2021).

P: Antiparasitic products, insecticides, and repellents

Antimalarial agents such as *hydroxychloroquine* and less often used *chloroquine* can cause ophthalmic toxicity. Hydroxychloroquine can be used for malaria, rheumatoid arthritis, systemic lupus erythematosus, and chronic inflammatory disorders of the skin. The risk of developing retinal toxicity is estimated to be around 7,5 percent when these medications are used for over five years. Hydroxychloroquine can also cause keratopathy. Chloroquine can also cause retinal toxicity but is less often used since hydroxychloroquine is much safer. (Salmon 2020, 885).

R: Respiratory system

Antihistamines are widely used for treating allergic conditions such as hay fever or insect bites. They work by preventing the action of histamine in the body. There are two main subtypes of antihistamines: H-1 receptor antagonists, which are used for allergic conditions, and H-2 receptor antagonists, which are used for gastrointestinal conditions. H-1 receptor antagonists are categorized into two groups: first-generation antihistamines and second-generation antihistamines. The first-generation antihistamines can pass through the brain-blood barrier and therefore cause drowsiness and interact with other medications. Second-generation antihistamines are safer since they can't pass through the blood-brain barrier. H-1 receptor antihistamines have anticholinergic effects, especially first-generation antihistamines. (Khelemsky et al. 2022). These medications suppress the action of acetylcholine (a type of neurotransmitter). This then suppresses the action of the parasympathetic nervous system causing the ciliary muscle to relax, resulting in dilated pupils and decreased accommodation. They can also cause dry eyes by repressing parasympathetic activity. (Ahmad & Mehta 2021).

Others

Herbal medicines and vitamins can also have ocular side effects. Patients tend to leave this out when asked about their medication. Therefore, asking the patient about using herbal medicines, vitamins, and food supplements is important. Next, a few selected examples are presented shortly.

Niacin (vitamin B3) which is used for its cholesterol lowering abilities can cause dry eyes, blurred vision, and cystoid macular edema. *Chamomile*, if used topically around the eyes, can cause severe conjunctivitis. *Ginkgo biloba*, which is used in treating dementia and Alzheimer's, can result in retinal hemorrhage and hyphemia. (Dellabella & Andres 2015).

2.8.3 Selected Systemic Medications that are Associated with Dry Eyes

Dry eyes can be caused by topical and systemic drugs. Systemic medications can reduce the production of tears, alter the reflex secretion of tears, and cause inflammation of the secretory glands of the eyes. Dry eyes can also be caused by mechanical irritation from drug crystals in tears. The Tear Film and Ocular Surface Society held a workshop on dry eyes (Dry Eye Workshop, DEWS) and prepared an iatrogenic report including a list of medications "known or suspected to cause, contribute, or aggravate dry eyes." (Gomes & al. 2017). The following list contains selected systemic medications with a known or possible association with dry eyes (Table 6).

Table 6

Category	Subcategory	Systemic drug (examples)
Analgesic	Antirheumatic	Aspirin, Ibuprofen
	Opioid	Morphine, Opium, Fentanyl
Anticholinergic	Antiarrhythmic/Broncho dilating	Disopyramide, Ipratropium
	Antihistamine	Cetirizine, Loratadine
	Antidepressant	Mirtazapine, Amitriptyline, Clomipramine
	Anti-Parkinson`s	Levodopa, Pramipexole

	Antipsychotics	Chlorpromazine, Clozapine, Aripiprazole
	Antispasmodic	Fesoterodine, Homatropine, Tolterodine
	Decongestant	Phenylephrine, Oxymetazoline, Xylometazoline
Antihypertensive	Adrenergic blocking	Metoprolol, Atenolol, Propranolol
	NaCl- Co-transporter (diuretics)	Bendroflumethiazide, Chlorothiazide, Hydrochlorothiazide
Antimalarial		Hydroxychloroquine
Antineoplastic		Methotrexate, Interferon
Anxiolytic/hypnotic		Diazepam, Eszopiclone, Lorazepam
Herbals and Vitamins		Isotretinoin, Niacin
Hormonal	Antiandrogen/Estrogen replacement	Tamsulosin, Estrogen/Progesteron

(Gomes & al. 2017).

2.9 Social History

Social history can help connect with the patient, offer important clues about the early signs of disease, and guide the examination. By getting to know the patients better, optometrists can provide better patient care. (Anderson & Schiedermayer 2010). The social history can contain information about the patient's alcohol, tobacco and drug use and other attributes such as

occupation, hobbies, and sexual activity (Nichol & al. 2021). Occupation is included in section “Patient information including demographics” and won’t be discussed below.

2.9.1 Hobbies

Information about hobbies and occupation is an important part of the patient history. This information can be utilized when choosing appropriate optical correction for the patient's needs. Patients playing sports involving sticks, pucks, and balls or those doing repair projects at home should be advised about protective eyewear. Patients in need of a wider visual field and those that are affected by fogging or rain could benefit from contact lenses. Different options regarding lens properties such as coatings, tints and polarization can be determined based on the information obtained from the patient history. (Elliot 2020).

2.9.2 Tobacco Smoking

According to Boyd (2022), tobacco smoking is considered a risk factor for eye diseases, including age-related macular degeneration, cataract, and Grave`s ophthalmopathy. People who smoke have a 2 to 4-fold higher risk of AMD than non-smokers. Smoking is also reported to increase the instability of the tear film, resulting in dry eyes. Corneal wound healing is prolonged in smokers, increasing the risk of keratitis and poor healing of an epithelial defect or an ulcer. (Boyd 2022; Garcia-Layana et al. 2017; Dhingra et al. 2019).

2.9.3 Use of Alcohol

Alcohol intake in short term use leads to ocular and visual changes, including dilated pupils, slow pupillary reaction, double vision, problems seeing in low light conditions, decreased contrast sensitivity, and red eyes. Chronic intake can lead to tear film instability resulting in dry eyes and cause chronic changes in the conjunctiva, increasing the risk of keratitis. With the chronic use of alcohol, the risk of AMD and external ophthalmoplegia increases. (Dhingra & al. 2019).

2.9.4 Use of Illegal Drugs

Many prohibited drugs cause physiological changes in the body, including the eyes. The adverse effects vary from mild symptoms to more severe complications. Next, some of the most common illicit drugs and their ocular side effects will be discussed. (Dhingra & al. 2019).

Cannabinoids can be smoked or ingested orally. When smoked, the typical ocular manifestation is red eyes. When ingested orally, the ocular manifestations include dilated pupils, conjunctival hyperemia, and reduced accommodation. Cannabis is also known to reduce intraocular pressure, but it should be smoked 6-8 times a day to have that effect. (Dhingra & al. 2019).

Opioids like heroin, morphine, oxycodone, and fentanyl cause pupillary constriction. Intravenous administration of heroin or morphine can cause problems with saccadic movements and eye fixation. It can also cause retinal micro embolism and endophthalmitis. In around thirty percent of cases, acute onset esotropia is associated with heroin withdrawal symptoms. Other withdrawal symptoms of opioids include mydriasis and anisocoria. (Dhingra & al. 2019).

Commonly used stimulants include **cocaine and amphetamine**. Cocaine causes pupils to dilate, and in higher doses, it can cause cycloplegia. Chronic use can cause exophthalmos and upper lid retraction. Amphetamine causes dilated pupils and can cause crystalline retinopathy if administrated intranasally. (Dhingra & al. 2019).

Hallucinogens such as LSD cause hallucinations, overstimulation of the central nervous system, and pupil dilation (Dhingra & al. 2019).

2.9.5 Sexually Transmitted Diseases

Sexually transmitted diseases (STDs) are caused by bacteria, viruses, or protozoa and are usually transmitted by unprotected sex or by the transplacental route. STDs can affect many organs, including the eye. The most common STDs all have ocular manifestations, and on many occasions, the eye is the primary location. (Gupta 2017).

Syphilis is caused by Treponema pallidum bacteria. Ocular involvement can be seen both in congenital and acquired forms and in any stage of the disease. Ocular infection can involve all eye structures, but panuveitis and posterior uveitis are the most common findings. Other common findings include interstitial keratitis, recurrent anterior uveitis, optic neuropathy, and retinal vasculitis. Syphilis is known to mimic other ocular diseases, and individuals with the ocular symptoms might be otherwise asymptomatic. (Koundanya & Tripathy 2022).

Chlamydia is caused by Chlamydia trachomatis (C. trachomatis) bacteria. It is the commonest sexually transmitted infection globally. Different types of C. trachomatis cause different kinds of infections. The ocular infections caused by C. trachomatis are trachoma (see chapter 2.6.4) and inclusion conjunctivitis. Inclusion conjunctivitis is caused by serotypes D-K and is typically sexually acquired. It is more common in developed countries, unlike trachoma. (Campbell et al. 2021; Leung & Abelson 2008). Ocular signs and symptoms of inclusion conjunctivitis include unilateral or bilateral redness, watery mucopurulent discharge, follicles in the inferior fornix and sometimes upper tarsal conjunctiva, superficial punctate epithelial keratitis, and tender preauricular lymph node (Salmon 2020, 173).

Gonorrhea is a sexually transmitted infection caused by Neisseria gonorrhea bacteria. Gonococcal conjunctivitis (GC) is an ocular infection caused by Neisseria gonorrhea. It is generally seen as a disease in newborn babies, but the incidence of adult gonococcal conjunctivitis has increased in recent years. The hallmark finding of GC is severe mucopurulent conjunctivitis. Other signs and symptoms include lid edema and tenderness, preauricular lymphadenopathy, and sometimes uveitis and severe keratitis. (McAnena et al. 2015).

3 THE PURPOSE, OBJECTIVES, AND TASKS OF THE RESEARCH AND DEVELOPMENT WORK AND THE DIFFERENT STAGES

3.1 Purpose of the Project

The purpose of this project was to produce evidence-based patient history guidelines for the Finnish Ethical Board of Optometry.

3.2 Statement of the Research Question

The demand for eye care has increased with the aging population, which has influenced the field of optometry in Finland. Optometrists are becoming more involved in assessing the health of the eyes and detecting early signs and symptoms of possible eye diseases. There is a need to increase the awareness and knowledge of the diseases, conditions and other factors that affect the eye and vision. Based on this need the research strived to answer the following question:

- What are the key elements (components) that Finnish optometrists should include in the patient history, and how these elements should be implemented in a form of a questionnaire?

3.3 Summary Description of the Experimental Design

This innovation project was performed as a literature review analysis-based research project for The Finnish Ethical Board of Optometry between fall 2021 and fall 2022.

The patient history guideline was implemented as a form (questionnaire) that serves optometrists in their everyday work. The form contains all key elements of a thorough patient history.

This project included the preparation of clinical guidelines for Finnish optometrists: Patient history. This project consisted of two main phases: in the first phase, a comprehensive descriptive literature review about the content of the patient history was written, and in the second phase, a patient history questionnaire was designed.

An IRB approval or a statistical approach were not required for literature review analysis-based research project.

3.4 Study Aims

The first aim was to search and select literature on the content of patient history.

The second aim was to analyze the selected literature for determining the key elements (main components) of the patient history, and further describe them in more detail.

The third aim was to define the content and structure of the patient history guideline.

3.5 Methodology

3.5.1 Literature Search and Selection

The primary search process was performed in the fall of 2021 by searching for already available guidelines on patient history. The search was conducted by using online databases and the key search terms were “optometry guidelines”, “clinical guidelines in optometry”, and “optometristi ohjeistus". Four guidelines were chosen for further analysis. From geographical point of view, it was natural to select guidelines from Finland and the guideline developed by the European Council of Optometry. The guideline developed by American Council of Optometry was chosen because the US represents the highest competence in the field of optometry. For the same competence point of view regarding Europe, the guideline developed by the College of Optometrist from the UK was selected.

The secondary search process was performed between the fall 2021 and spring 2022. The aim of this literature search was to gather evidence-based information on the parameters of a thorough patient history. The search was performed using PubMed, articles in medical journals, information prepared by official health organizations, and books relevant in this field. The aim was to select only studies no more than ten years old. However, if the information about a subject matter was still relevant, studies or textbooks older than ten years were accepted as a source. Only materials in English or Finnish were included. The PubMed database was searched using a wide range of

search terms, for example “patient history” AND “optometry”, “systemic diseases AND (vision OR eye)”, “eye diseases”, “hereditary diseases AND (eye OR vision)”, “medications effect on (vision OR eyes) AND ocular side-effects”, “pregnancy AND breastfeeding AND ocular side-effects OR vision OR eye)”, “Tobacco AND (eyes OR vision). Because the area of the research was so extensive, all the search terms used for the literature search were too broad to be itemized here. For the same reason the type of this literature review was chosen to be a narrative review, and no strict inclusion or exclusion criteria were formally used in the literature search.

3.5.2 Critical Analysis of the Selected Literature for Determining and Describing the Key Elements of the Patient History

In the guidelines chosen for further analysis, there were elements of the patient history that repeatedly occurred in each of the guidelines. This repetition justified their inclusion as key elements. More detailed information of the key elements (the sub-elements) was then obtained using the material from the secondary search.

The Finnish guidelines were used as a basis when determining the elements for the updated guidelines. The already existing elements were preserved; however, some elements were added and refined after analysing the other guidelines and materials as described above.

3.5.3 Defining the Content and Structure of the Patient History Guideline

The content for the final questionnaire was obtained after critical analysis of the evidence-based literature as described in the previous chapter. The format of the guideline was selected to be a questionnaire to ensure its usability. Examples of already existing questionnaires were used to support the design. To further support its usability, the questionnaire included several screening-type questions (yes or no question layout) and provided additional space for further details in case of a positive finding.

4 IMPLEMENTATION OF THE RESEARCH AND DEVELOPMENT WORK

4.1 Specific Aim 1, Search and Selection of Literature on the Content of Patient History

4.1.1 Methods

In the first phase of the literature search pre-existing recommendations concerning patient history were searched to better understand the subject. Geographical and competence point of views were used to select guidelines that would be further analysed. In the second phase, an extensive literature search was conducted and carefully assessed.

4.1.2 Results

The search and selection process identified the following guidelines for further analysis:

1. The Finnish Ethical Board of Optometry (OEN) guidelines for Finnish optometrists on the good eye and vision examination methodology (Hyvä optometristin tutkimuskäytäntö-ohjeistus 2019).
2. American Optometric Association (AOA) evidence-based clinical practice guidelines on the adult eye and vision examination (American Optometric Association 2015)
3. The European Council of Optometry and Optics (ECOO) guidelines for optometric and optical services in Europe (ECOO Guidelines for Optometric and Optical Services in Europe EXECUTIVE SUMMARY 2013)
4. The College of Optometrists (The professional body of optometry in the United Kingdom) – The routine eye examination (´sight test´) (The routine eye examination ('sight test') - College of Optometrists s.a.)

4.2 Specific Aim 2, Analysis of the Literature to Determine and Describe the Key Elements of the Patient History

4.2.1 Methods

After critical analysis of the evidence-based literature and four chosen guidelines, the key elements of the patient history were determined and described.

4.2.2 Results

As the first result of this part, the following were the key elements of the patient history:

- Patient information, including demographics
- Chief complaint, symptoms interview, and history of present illness
- Ocular status and ocular history
- General health status and history
- Family ocular and medical history
- Medications and drug allergies
- Social history

As the second result of this part, the key elements were further divided into sub-elements:

- Patient information, including demographics, is further divided into the following elements: age, gender, occupation, and ethnicity.
- Chief complaint is the reason for the visit given by the patient; symptoms interview covers a list of typical eye and vision-related symptoms (headaches, blurred vision, distorted vision, double vision, eye pain, floaters, flashes of light, itching, redness, irritation, foreign body sensation and tearing), the history of present illness is further investigated with a list of clarifying questions: onset, location, duration, characteristics, aggravating factors, relief, timing and severity of present illness
- Ocular status and ocular history are further divided into the following elements: optical correction and visual efficiency, previous visit, lazy eye/amblyopia, strabismus, eye surgery, ocular trauma, acute and/or recurrent eye diseases, and chronic eye diseases

- General health status and history is further divided into ears, nose, throat and mouth; diabetes; endocrine diseases; systemic infections with ocular manifestations; cardiovascular diseases; hereditary connective tissue disorders; diseases of the respiratory system; dermatological and mucous membrane diseases; hematologic disorders; neurological disorders; cancer; mental disorders; and pregnancy and breast feeding
- Family ocular and medical history is asked generally with no specific subcategories
- Medications and drug allergies are asked generally with no specific subcategories (non-prescription medications are included)
- Social history is further divided into hobbies, tobacco smoking, use of alcohol, and sexually transmitted diseases

The third result of this part was the narrative literature review further describing the elements of the patient history.

4.3 Specific Aim 3, Defining the Content and Structure of the Patient History Guideline

4.3.1 Methods

The final part of this project consisted of planning and creating a patient history guideline. The format of the guideline was selected to be a questionnaire.

4.3.2 Results

The Patient History Questionnaire that was designed during this innovation project is presented in the appendix.

5 DISCUSSION

Based on the literature search performed during this innovation project, it became clear that numerous major and minor factors can influence vision and eyes. Taking the patient history needs to investigate the most relevant factors without being unpractical.

According to the observations made during this project, it was found that some of the key elements of the patient history should be investigated in more detail compared with the current recommendations in Finland. Especially the following key elements should be emphasized more when taking the patient history:

- the symptoms interview, and the history of present illness
- the general health status and history
- the social history

Other elements of the patient history are equally important but are already included in the current guidelines. The results of this project confirm that the current guidelines need an update because they do not meet the requirements of a thorough patient history.

Long instructions on collecting patient history do not serve well in everyday work. Therefore, the guidelines were implemented as a structured questionnaire (see appendix). This should help the optometrist in collecting the required information.

The designing and structuring of the questionnaire raised some further thoughts. The author of this project found it challenging to correctly ask about the patient's ethnicity. Special consideration was used so that the question's wording would not seem offensive to any parties.

After this project, it seems evident that more education for the optometrist is needed to utilize the questionnaire. More knowledge about various diseases and conditions, and their related symptoms, helps optometrists refer suspected cases to an ophthalmologist. The literature review created in this project serves as a basis for educational material. However, a proper education process needs to be planned separately.

The project also had limitations. The literature review was labour intensive, considering that the scope of the information was so extensive. With each new topic, the author first had to become familiar with the subject to find the most relevant and topical information. This made the evaluation of the information sources challenging. Every section of the literature review required its own references; selecting them was very time consuming. As a result, it was not always possible to systematically assess the quality of the references. Therefore, the type of the literature review was chosen to be narrative. It can be characterized as an overview without strict rules. The materials used are extensive, and methodological rules do not limit the selection of materials. (Salminen 2011).

Taking new instructions first in limited pilot use is standard practice. One suggestion for further development could be to define a pilot project for testing the questionnaire in practice. Since the literature search and literature review were so time consuming there was not enough time to include that in this thesis.

The updated guidelines (questionnaire) require that more information is collected than what is currently the practice. Another suggestion for further development is that optometrists should be interviewed to determine how well their education and current knowledge support the task of using this questionnaire. This will help to plan what kind of additional education or guidance on how to use the information obtained from the questionnaire is potentially needed.

This Master`s thesis complies with ethical norms as described, for example, by Arene (Ammattikorkeakoulujen rehtorineuvosto Arene ry, 2020). This work did not involve any people as objects of the study, or clinical pharmaceutical studies or similar areas where ethical considerations are especially important.

6 CONCLUSIONS

Finland's population is aging. This has caused an increase in the number of age-related eye diseases. The healthcare system must handle this increasing workload. Optometrists will be required to expand their scope of work to fill the shortage of eyecare professionals. This requires changes in standard practices. To implement these changes, guidelines are needed to help standardize and unify the new practices in optometry in Finland.

Patient history is the foundation of the eye examination. Without going through the patient history systematically with the patient, some elements of the examination might be missed or done unnecessarily. A proper guideline on how to take patient history will benefit both the optometrist and the patient.

The Ethical Board of Optometry (OEN) in Finland has approached the Oulu University of Applied Sciences as they have seen a need to create more detailed guidelines for Finnish optometrists on how to take patient history. This innovation project also confirmed the need for updated guidelines.

As a result of this work, new guidelines were created. This project did not include the pilot use of these guidelines. That should be included in the next steps.

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APPENDIX: THE PATIENT HISTORY QUESTIONNAIRE

Patient History Questionnaire

Patient information

Name: _____

Date of Birth: ___/___/____

Address: _____

_____

Phone number: _____

Email: _____

Which ethnicity describes you the best

White/Caucasian	☐
Black/African American	☐
Hispanic/Latino	☐
Asian	☐
Other	☐

_____

Occupation: _____

Approximately how many hours do you spend on a computer daily? _____

Chief complaint:

_____
_____
_____

Previous visit to:

Optometrist_____

Ophthalmologist_____

Do you experience any of the following symptoms?

	Yes	No
Headaches	☐	☐
Blurred vision	☐	☐
Double vision	☐	☐
Distorted vision	☐	☐
Eye pain	☐	☐
Flashes and/or floaters	☐	☐
Itching, soreness, burning	☐	☐
Redness	☐	☐
Tearing	☐	☐

Please list any additional vision concerns:

_____

Optometrist will further ask

O = Onset
L = Location
D = Duration
C = Charachter
A = Aggrevating factors
R = Relief
T = Timing
S = Severity

	Yes	No	
Do you wear glasses?	☐	☐	**Type, and when renewed:** **_____**
Do you wear contact lenses?	☐	☐	**Type, and describe if any problems with the lenses:** **_____**

Ocular history

Any history of the following?

	Yes	No	Describe
Strabismus/crossed eyes	☐	☐	_____
Amblyopia/lazy eye	☐	☐	_____
Eye surgery	☐	☐	_____
Eye trauma	☐	☐	_____
Eye infection/inflammation	☐	☐	_____
Allergic eye disease	☐	☐	_____
Dry eyes	☐	☐	_____
Glaucoma	☐	☐	_____
Cataract	☐	☐	_____
Age-related macular degeneration	☐	☐	_____

List if any additional ocular conditions: _____

General health history and status (please fill in as best as you can, optometrist will review with you)

Do you have or have had a history of any of the following?

	Yes	No	Describe
Ear, nose, throat, mouth related problems	☐	☐	_____
Diabetes	☐	☐	_____
Endocrine diseases	☐	☐	_____
Systemic infections	☐	☐	_____
Cardiovascular diseases	☐	☐	_____
Immunologic and/or inflammatory diseases	☐	☐	_____
Genitourinary diseases	☐	☐	_____
Gastrointestinal diseases	☐	☐	_____
Diseases of the respiratory system	☐	☐	_____
Dermatological and mucous membrane diseases	☐	☐	_____
Hematologic disorders	☐	☐	_____
Neurological disorders	☐	☐	_____
Cancer	☐	☐	_____
Mental disorders	☐	☐	_____

List if any additional health problems: _____

	Yes	No
Are you currently pregnant or do you breastfeed?	☐	☐

Family ocular and health history (E.g. diabetes, hypertension, glaucoma, age-related macular degeneration):

_____
_____
_____

Medications (also non-prescription):

_____
_____

Allergies to medications:

_____
_____

Social history

Hobbies:

_____
_____

	Yes	No
Do you drive a car?	☐	☐

	Yes	No	If yes, type/amount/how long?
Do you smoke?	☐	☐	_____
Do you use alcohol?	☐	☐	_____
Do you use drugs?	☐	☐	_____

History of any sexually transmitted diseases?

_____
_____