Received: 29 August 2023 | Revised: 5 January 2024 | Accepted: 26 January 2024

DOI: 10.1111/ceo.14364

REVIEW

Clinical & Experimental Ophthalmology WILEY

Gender differences in retinal diseases: A review

Anne Tillmann MD[1] | **Lala Ceklic MD**[2,3] | **Chantal Dysli MD, PhD**[2,3] | **Marion R. Munk MD, PhD**[1,2,3,4]

[1]Augenarzt-Praxisgemeinschaft Gutblick, Pfäffikon, Switzerland

[2]Department of Ophthalmology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

[3]Bern Photographic Reading Center, Inselspital, University Hospital Bern, Bern, Switzerland

[4]Department of Ophthalmology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA

Correspondence
Marion R. Munk, Augenarzt Praxisgemeinschaft Gutblick AG, Pfäffikon, Switzerland.
Email: marion_munk@hotmail.com

Abstract

Gender medicine is a medical specialty that addresses gender differences in health and disease. Traditionally, medical research and clinical practice have often been focused on male subjects and patients. As a result, gender differences in medicine have been overlooked. Gender medicine considers the biological, psychological, and social differences between the genders and how these differences affect the development, diagnosis, treatment, and prevention of disease. For ophthalmological diseases epidemiological differences are known. However, there are not yet any gender-based ophthalmic treatment approaches for women and men. This review provides an overview of gender differences in retinal diseases. It is intended to make ophthalmologists, especially retinologists, more sensitive to the topic of gender medicine. The goal is to enhance comprehension of these aspects by highlighting fundamental gender differences. Integrating gender medicine into ophthalmological practice helps promote personalized and gender-responsive health care and makes medical research more accurate and relevant to the entire population.

KEYWORDS

epidemiological differences, gender medicine, retinal diseases, sex difference, sex hormones

1 | INTRODUCTION

"Gender medicine" looks at differences between women and men in different physiological and pathological processes, taking into account both the biological ("sex") and the sociocultural ("gender") dimensions. Biological "sex" refers to a person's biological and physical characteristics, which are classified based on their reproductive functions such as reproductive organs, sex hormones, and gene expression of the X and Y chromosomes. The term "gender," on the other hand, refers to the social, cultural, psychological, and behavioral aspects associated with gender in a particular society or culture. Gender is a social construct and refers to the expectations, roles, norms, and behaviors attributed to a particular gender identity in a society. Men and women differ in terms of prevalence and incidence of diseases; but also in the diseases themselves, their courses and reactions to different therapies and drugs.

"Gender-specific medicine" emerged in the 1980s, particularly in the field of cardiology. In "The Yentl Syndrome" Healy reports that much of the cardiology research in the 1980s focused predominantly on the symptoms of ischemic heart disease (IHD) in male patients. In contrast, the adverse effects of IHD in women received less attention. In addition, women were underdiagnosed and undertreated.[1] The name "Yentl" was inspired by the main character in the short story "Yentl." In the narrative, Yentl adopts a male identity to pursue Talmudic studies at a male Jewish school in 19th-century Poland.[2] Since the publication of Healey's work, there have been increased efforts to support and advance gender medicine.

© 2024 Royal Australian and New Zealand College of Ophthalmologists.

Further studies reported worse outcomes of women with heart attacks as their symptoms are more unspecific and different from the classic symptoms like those of men. Gastrointestinal complaints or general fatigue were not always interpreted as cardiac-related. Therefore, misdiagnosis was more frequent, there were delays in diagnosis, therapy and increased mortality rates compared to men.[3,4] Norberg et al. addressed the significant difference between the proportion of females in the big randomized trials and the real-world heart failure population. In this discrepancy, they saw a significant factor that adds to the current knowledge gap in the treatment of women with heart failure.[5] In 2001, a recommendation on the development and implementation of strategies for gender-specific health care was published by the World Health Organization.[6] Despite this recommendation, gender medicine is still relatively unknown today.

In ophthalmology, gender medicine is not a common topic either. Epidemiological differences in some diseases are known. However, these differences have not yet resulted in a distinct methodology for the practical approach including diagnostics and treatment of patients.

Ophthalmologists should approach and treat patients with a "gender-sensitive" view. With this review we would like to highlight gender differences in different retinal diseases and sharpen the "gender-sensitive" view. A better understanding of gender health disparities will help make patient treatment and care more individualized and equitable. A summary of gender prevalence rates of the here discussed retinal pathologies can be found in Table 1.

2 | ANATOMICAL DIFFERENCES

In 2018, Polin et al. published that they were able to predict the patient's gender using their deep learning (DL) model based on color fundus photographs.[54] Further studies have followed, which confirmed that gender can be very accurately distinguished using DL models on color fundus imaging but also on single OCT scans.[55] Accordingly, there must be differences between males and females at the posterior pole that are not easily identifiable for the ophthalmologist at first glance. The physiologic cause and effect relationships of this gender prediction mystery are still not readily apparent. Further attention map analysis showed that characteristics within the optic disc area are suggestive of a male prediction, while specific features at the macula region were important for the algorithm to predict a female sex[54] (Figure 1). In case the fovea or the optic nerve head was not clearly visible on the photographs, prediction was rather random[55] (Figure 2).

Also, on OCT scans the algorithm focused on the foveal regions. Between the sexes, the relative sizes, levels of brightness etc. appear to be similar. This implies the presence of structural but localized differences in the retinas of men and women.[56]

Studies using spectral-domain optical coherence tomography have shown that the central retina is substantially thicker in men.[57,58] These differences in retinal thickness already appear to exist in young patients: in a study of children suffering from type I diabetes and healthy controls, the retina was thicker in both diabetics and controls in boys than in girls.[59] Further studies looked at the individual structures and showed that only the outer plexiform layer (OPL), inner nuclear layer (INL), outer nuclear layer (ONL) and photoreceptor outer segment length are greater in men.[60,61]

In contrast, the layer of the retinal nerve fiber is greater in women.[60,62]

In addition, the foveolar avascular zone (FAZ) differs: Goméz-Ulla et al. were able to show that female sex is associated with a significantly larger FAZ. This applies to both the superficial and deep macular FAZ. In women, the FAZ size seems to change with age.[63] It was observed that the FAZ was significantly smaller in younger age groups compared to older ones. In men, it appears that age does not have an influence on the size of the FAZ. Hormonal changes in women with increasing age may be the cause for these differences in changes in retinal structures.

Many differences between the genders can be attributed to hormonal factors, which is why a pure gender comparison is often complex. Sex hormone receptors have been identified in various tissues of the eye. Women experience distinct hormonal fluctuations at different life stages, including prepubertal, pubertal, menstrual, and postmenopausal phases. Additionally, variations in hormone concentrations are evident during different menstrual cycle phases and pregnancy, leading to more significant fluctuations in women's hormonal profiles throughout their lives compared to men. This dynamic nature makes direct comparisons with men challenging. To better understand gender differences, it is useful to consider the influence of these hormonal changes. An example of this might be to examine the prevalence rates of certain conditions, such as diabetic retinopathy (DR), in males and females at different lifetime stages. By comparing prevalence rates, one could identify potential sex-specific associations.

It is also discussed that altered regulation of blood flow may contribute to gender differences in the incidence of ocular disease.[64] However, knowledge on differences between men and women in ocular blood flow and how this is controlled is limited. Reported findings from

TABLE 1 Overview of gender differences in various retinal diseases.

Retinal disease	Gender differences
Vascular diseases	
DR	Controversial results. Multiple factors such as age, type of diabetes and ethnicity need to be taken into account.
RVO	<55 years: higher prevalence in women >55 years: higher prevalence in men[7,8]
Mac Tel	Type 1A: predominantly men[9] 1B: predominantly men[10] 2: probably slightly higher prevalence in women (68%)[11,12] 3: limited data
Degenerative diseases	
CSCR	M:F = 6:1[13]
AMD	Worldwide controversial results: ethnicity and access to health care need to be taken into account presumably higher prevalence in Caucasian women[14–17]
Pathologic myopia	Anterior myopia[a]: higher prevalence in (younger) men, posterior myopia[b]: higher prevalence in (older) women[18]
RD	Higher prevalence in men[19]
Macular holes	M:F = 1:1,2 (India) to 1:7 (China)[20–22]
Hereditary diseases	
RP	Slightly higher prevalence in men[23]
Stargardt Disease	Controversial results. potential effect of different risk alleles potentially higher prevalence in women[24] with mild ABCA4 alleles.
Uveitis infectious	
Syphilis	Higher prevalence in men (87%–90%)[25–27]
Tuberculosis	No gender differences[28,29]
CMV	Controversial results: potentially higher prevalence in women[30,31]
Toxoplasmosis	No gender differences[32–34]
Non-infectious	
JIA	Dependent on subtype, overall 50%–80% of JIA patients are female[35] Oligoarticular JIA (highest risk of uveitis): higher prevalence in young female patients[25]
SLE	Higher prevalence in women (88%–90.5%),[36–38] ocular involvement M:F = 1:17[39]
MS	Higher prevalence in women (78%),[40] MS-associated uveitis: higher prevalence in women (75%)[41]
Sarcoidosis	higher prevalence in women (55%–64%),[42,43] ocular sarcoidosis: M:F = 1:3[25,44]
VKH	Higher prevalence in women (70% in Brazil,[45] 78.7% in USA,[46] 84.4% in India[47])
BD	Higher prevalence in men (54%–85%)[48,49] ocular manifestations: higher prevalence in men (also more common: posterior segment complication and poorer visual outcomes)[25,50]
HLA-B27- associated anterior uveitis	Higher prevalence in men: F:M = 1: 2.5[51]
WDS	Higher prevalence in women: MEWDS (50%–91%), BSCR (58%), MCP (75%), PIC (85%), AZOOR (79%), potentially higher prevalence in men: APMPPE (54%)[52,53]

Abbreviations: AMD, age related macular degeneration; APMPPE, acute posterior multifocal placoid pigment epitheliopathy; AZOOR, acute zonal occult outer retinopathy; BD, Behçet disease; BSCR, birdshot chorioretinopathy; CMV, cytomegalovirus; CSCR, central serous chorioretinopathy; DR, diabetic retinopathy; HLA, human leukocyte antigen; JIA, juvenile idiopathic arthritis; Mac Tel, macular telangiectasia; MCP, multifocal choroiditis and panuveitis; MEWDS, multiple evanescent white dot syndrome; MS, multiple sclerosis; PIC, punctate inner choroidopathy; RD, retinal detachment; RP, retinitis pigmentosa; RVO, retinal vein occlusion; SLE, systemic lupus erythematosus; VKH, Vogt-Koyanagi-Harada; WDS, white dot syndromes.

[a]Defined as lattice degeneration, rhegmatogenous retinal detachment, retinal tear or retinoschisis.

[b]Defined as myopic maculopathy, macular hole, staphyloma, angioid streaks, retinal neovascularization, cystoid macular degeneration, exudative retinopathy, retinal pigmented epithelium detachment, vitreomacular adhesion or epiretinal membrane.

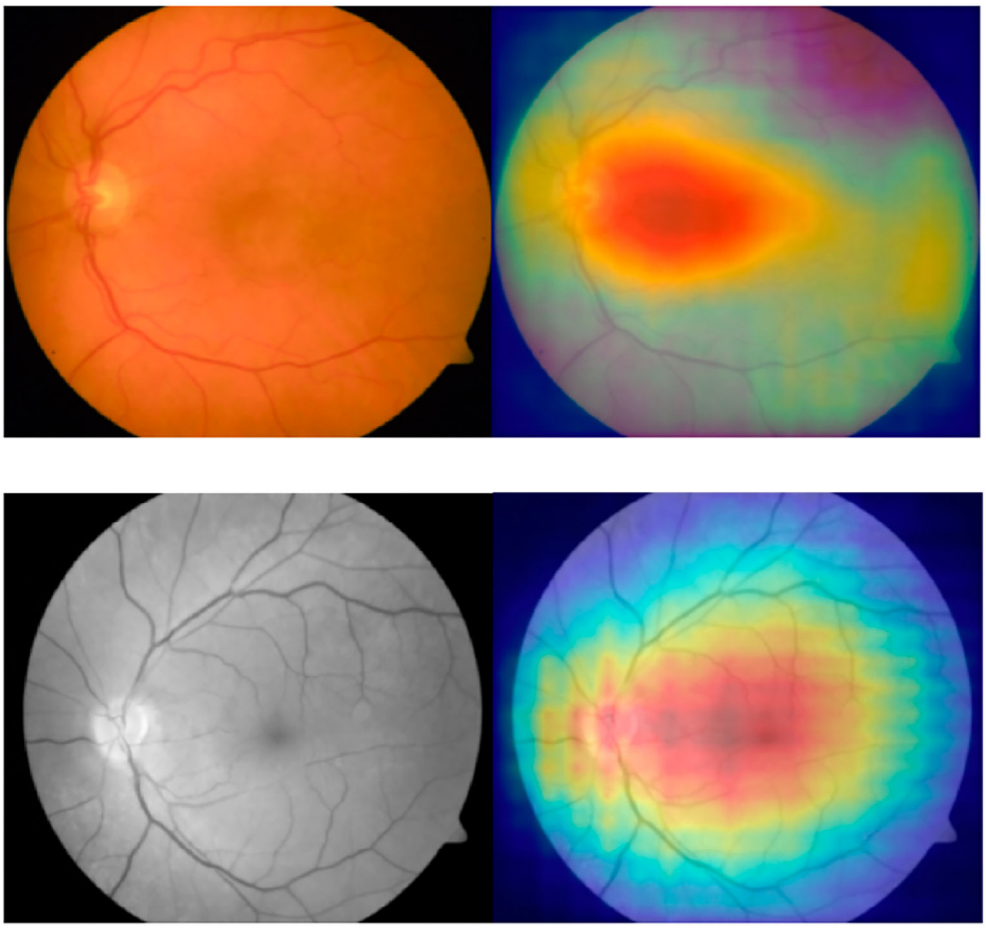

FIGURE 1 Attention maps of fundus images with correct prediction, top row: male patient, bottom row: female patient.[55]

a study conducted on normal and glaucomatous eyes of adult Chinese aged 40 years and older indicate significantly thinner arteries in glaucomatous eyes.[65] However, there were no significant differences identified in terms of gender. The analysis of data from the Beaver Dam Eye Study in contrast showed that men exhibited slightly smaller mean retinal arteriolar diameters (202.5 vs. 201.0 μm) and venular diameters (232.4 vs. 227.1 μm) compared to women.[66] Given that both studies included only patients aged 40 and older, it should be noted that gender differences may be present in younger subjects. Further studies could find a higher retrobulbar blood velocity in the ophthalmic artery and a lower blood velocity for the short posterior ciliary artery in male patients in contrast to female patients (not taking hormone supplements). The results showed statistical significance solely for patients <40 years.[67] In addition, in male patients age did not appear to influence the flow in the choroid. A notable increase in choroidal blood flow was observed in women <40 years compared with women >55 years. None of the women involved in the study were on oral contraceptives and none used hormone therapy.[68] It is highly probable, that these differences are attributed to sex hormones as well.

Beside that many potential differences at a more molecular level may be present. Some studies investigated a potential gender difference in macular pigment (MP) density for example. Hammond et al investigated potential sex differences in MP density in relation to plasma carotenoid concentration and dietary patterns. They found a 38% higher MP density in males despite similar plasma carotenoid concentrations and diet.[69] No gender difference however was found in a more recent study, where MP optical density was measured using the macular pigment optical density (MPOD) module of a multicolor spectralis in elderly Japanese.[70] These divergent findings may be based on the different measurement methods or they may be due to ethnical differences.

3 | VASCULAR RETINAL DISEASES

3.1 | Diabetic retinopathy (DR)

DR is a big contributor to avoidable vision impairment in diabetic patients between 20 and 64 years.[71] The literature reveals disparities between male and female diabetics in

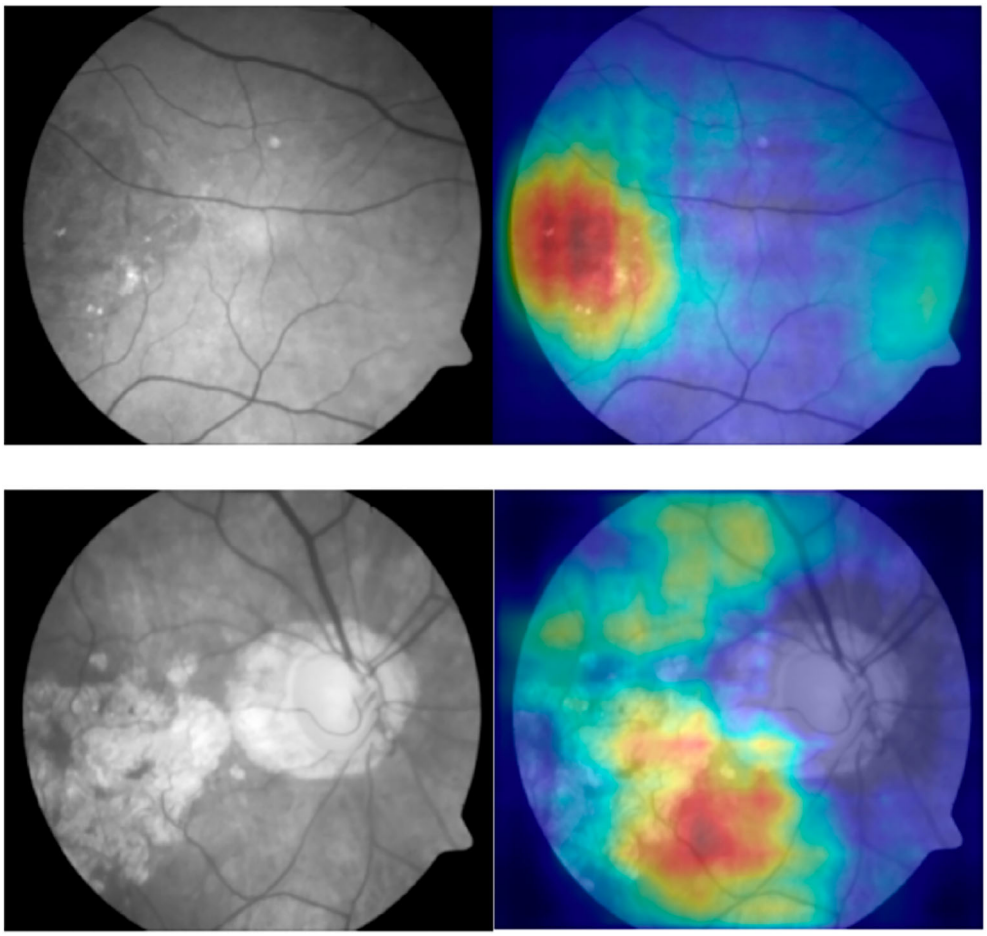

FIGURE 2 Attention maps of fundus images with incorrect prediction, top row: male patient, bottom row: female patient.[55]

terms of diabetes incidence and rates of complications. These differences are applicable to both type 1 (T1D) and type 2 (T2D) diabetes: For T1D, girls and boys seem to be equally affected in young populations.[72] High T1D incidence areas report a higher number of males affected, while low T1D incidence areas observe an excess in women.[73–75] Populations of European origin reported an increase of T1D cases in male adults following puberty.[75] For T2D, incidence and prevalence data were reported to be higher in female vs. male subjects in young populations.[76,77] In adulthood, the gender imbalance in T2D shifts towards a more equitable distribution between both genders.[78]

Controversial results exist in literature regarding gender differences and DR. While some studies report a higher prevalence of DR in men,[79–81] others observed a higher prevalence in women.[82–84] These controversial results might be related to ethnic differences, different age groups and mixed T1D and T2D subjects in the study populations. There is also a sex discrepancy in terms of microvascular complications in T1D. Women of a younger age face an elevated risk of encountering microvascular complications earlier in the disease course.[85] Potentially, differences in microvascular patterns could play a role here, as females presented with wider venular caliber and a decreased arteriolar length-to-diameter-ratio in this population.[86]

The progression of DR during pregnancy[87] implies a potential involvement of sex hormones in the retinal pathophysiology in diabetic patients.

Recently, Schiefelbein et al. showed that women with diabetic macular edema had worse baseline values (visual acuity and retinal thickness) at diagnosis and therapy initiation than their male counterparts. The difference between the genders was not resolved after the same number of intravitreal injections; thus, women were diagnosed and treated at a later and worse stage than men, and ended up with worse visual acuity and thicker retinas.[88]

A gender-based therapeutic approach seems useful and necessary to differentiate between high-risk and low-risk patients. Especially women with diabetic macular edema should be involved in diagnosis and therapy early on.

3.2 | Retinal vascular occlusions

For retinal vein occlusions (RVO) and retinal artery occlusions, a predominance in men was found in different studies.[89–91] In a big retrospective registry cohort

study with 1 251 476 cases, different occlusion subtypes were analyzed. They reported slightly more women in transient retinal artery occlusion, venous engorgement and branch retinal vein occlusion, and more men in partial retinal artery occlusion, branch retinal artery occlusion, central retinal artery occlusion and central retinal vein occlusion.[92] Venous thromboembolism seems to occur more frequently in females <55 years due to factors including pregnancy, postpartum conditions, and oral contraceptive use. In the elderly population, instances seem to be more prevalent in males, which may be due to cardiovascular risk factors.[7,8]

3.3 | Macular telangiectasia

Previous research suggests that there are gender differences in macular telangiectasia (Mac Tel) that may indicate certain characteristics and clinical aspects. Mac Tel is usually divided into 3 main groups. Subgroup type 1A within this subgroup ranks as the second most frequent, predominantly occurring in males ages 15–54 years.[9]

Type 1B is less common and mainly impacts men who are in the middle-aged category, typically between 40 and 54 years of age.[10] For Type 2 Mac Tel, there was no evident gender preference in a cohort of 92 cases reported by Gass and Blodi.[11]

However, according to the MacTel multicenter study ($n = 310$), the proportion of women was higher at 64%.[12] Mac Tel type 3 is extremely rare, and no clear gender predilection has been identified to date. Additional research is needed to gain a deeper understanding of these gender disparities in macular telangiectasia and to verify their existence. The exact reasons for these differences are not yet fully understood. A blend of genetic, hormonal, anatomic, and other factors might play a role in this context.

4 | DEGENERATIVE RETINAL AND MACULAR DISEASES

4.1 | Central serous chorioretinopathy (CSCR)

CSCR is a retinal condition for which gender differences are most widely known. Men in their 30s–50s face a greater risk of developing CSCR than women. In the Olmsted County, Minnesota population study, CSCR was sixfold more common in males than in females.[13] In 1996, Spaide et al.[93] found a male-to-female ratio (2.6–1.0) that significantly differed from the ones reported before[94] and discussed a relationship with stress (representing a suspected risk factor) in this regard. Due to the changing role of women in society with increased stress of work, family and household, woman may be put at greater risk for stress-related conditions such as CSCR.

The etiology of CSCR is currently unknown. However, it has been linked with various risk factors such as male gender, exogenous steroid use, stress, pregnancy and obstructive sleep apnea.[95] The incidence in pregnancy is estimated to increase to 0.008% per year, and in women developing pre-eclampsia these values are even much higher. Especially elevated levels of cortisol are thought to be linked to that fact.[96,97] In a thorough investigation of the steroid hormone system in 46 male patients with CSCR, elevated levels of four hormones were observed in comparison to the control group. Besides, the relationship between steroid hormones was modified, suggesting an imbalance in the steroid hormone system of individuals with CSCR.[98] Currently, the role of androsterone, etiocholanolone, androstenedione and estrone in the etiology of CSCR is still unknown. Each of these compounds plays a notable role within the sex hormone sector of the steroid hormone system. Androsterone, androstenedione and etiocholanolone are weak androgens and metabolites for testosterone. Estrone is a mild estrogen hormone known to have increased levels in postmenopausal women.

Looking at the age distribution of CSCR patients, studies showed one peak for males (50–54 years).[98] For females there seems to be two peaks in the range of 50–54 years and over 65 years.

The onset age of CSCR in females and the second peak in the age distribution might be related to significantly greater fluctuations in the concentrations of different hormones over the course of their lives compared to men. Thus, for example estrogen receptor α has been detected in the retina and its pigment epithelium of females with younger age. However, it has not been found in male retinas or postmenopausal women.[99]

Recently, Hanumunthadu et al.[100] retrospectively looked at 310 CSCR cases with a follow-up period of approximately 8 months. Female patients had less hyperreflective foci and reduced retinal pigment epithelium (RPE) alteration (with fewer subretinal deposits, pigment epithelial detachment (PED), RPE irregularities). Fluorescein angiography (FA) and indocyanine green angiography (ICGA) showed more RPE disruption with diffuse RPE leakage, RPE tracs and point leakage in male patients. At follow-up, female patients exhibited a decrease in subretinal deposits and significantly better outcomes compared to their male counterparts. It would be interesting to see how these structural variations would be affected by treatment.

4.2 | Age related macular degeneration (AMD)

Numerous factors have been named as contributors to the pathophysiology of AMD. Age, particularly advanced age, consistently emerges as the most prominent factor linked with the onset and progression of AMD in extensive research studies.[14,101–103] Data on gender differences, however, are conflicting and the consideration of sex as an additional potential risk factor has been a topic of debate for many years. Epidemiological studies have found a higher prevalence in females,[14–17] however similar studies in Asia and a Mexican-American population indicated that AMD is more prevalent in male patients.[104,105] Other studies found no gender differences.[106–109]

Sasaki et al. demonstrated distinct associations between early AMD and genetic factors based on gender in a Japanese population: Women with ARMS2 A69S polymorphisms are at higher risk for early AMD.[110] An association with AMD was also demonstrated for the synonymous single nucleotide polymorphism (SNP) rs17810398, located in death-associated protein-like 1 (DAPL1). This association was marked by a highly significant sex disparity, as it was notably restricted to females.[111]

Sex hormones also appear to be involved in the pathophysiology of AMD. In a review by Kwon et al.[112] they examined fundus photographs of patients with sex hormone deficiency lasting more than 12 months. The study found that sex hormone deficiency and its duration were linked to the development and progression of soft drusen in female patients, but not in male. A sub-analysis within the Blue Mountains Eye Study investigated whether there is an elevated risk of AMD associated with early menopause. The study revealed a significant reduction in early AMD with increasing years from menarche to menopause.[113] A sub-study of the Rotterdam study with over 3000 women indicated a heightened relative risk of AMD among women who experienced early menopause due to external factors (ovariectomy) compared to those with naturally occurring early menopause.[114] A decreased duration of endogenous production may increase the risk of AMD. Furthermore, exogenous estrogens supplements may favorably effect and mitigate the risk of developing AMD in postmenopausal women.[115–117] While data of Edwards et al. indicate that birth control pills might have significant protective effects in women with AMD,[115] another study from Korea found a negative effect of oral contraceptive pills.[118] Assessment and management of sex hormone deficiency in female AMD patients as a gender-based therapeutic approach should be further investigated.

4.3 | Pathologic myopia

The origin of high myopia involves multiple factors, with both environmental and genetic influences contributing to the elongation of the eye's axial length.[119] Earlier studies have indicated that being female is associated with an increased risk of developing myopia.[120,121] The exact mechanism behind this phenomenon remains unclear, and gender-specific elements like the age of growth spurt have been proposed as potential factors. Myopia prevalence also seems to differ with age: Enthoven showed that myopia was more common in girls in the young generation, but more common in men in the older generation (>44 years). Ludwig et al. conducted a detailed investigation of pathological findings in high myopia and categorized them into anterior (lattice degeneration, rhegmatogenous retinal detachment, retinal tear, and retinoschisis) and posterior (myopic maculopathy, macular hole, staphyloma, angioid streaks, retinal neovascularization, cystoid macular degeneration, exudative retinopathy, retinal pigmented epithelium detachment, vitreomacular adhesion, and epiretinal membrane) high myopia. This classification exhibits distinct risk profiles associated with gender and age and indicate different etiologies for these manifestations: anterior myopic patients are more likely to be younger males and posterior myopic patients to be older females. Younger patients are more likely to be diagnosed with anterior myopia while older patients are more likely to have posterior myopia.[18]

Estrogen receptor mRNA is expressed in the cornea, meibomian glands, retinal/choroidal and retinal pigment epithelial cells of rats, rabbits and humans.[122] Estrogen exerts a specific influence on corneal thickness and shows a positive correlation with the degree of myopia. Xie et al. measured the levels of different serum sex hormones (luteinizing hormone (LH), follicle-stimulating hormone (FSH), E2, and testosterone) in a large sample of young students (12–14 years old) with varying degrees of myopia and non-myopic controls.[123] Myopia severity was negatively correlated with the estrogen level. Understanding the underlying mechanism could offer insights for tailored drug therapies in individualized treatment approaches in the future.

4.4 | Retinal detachment

Large population-based studies showed that male eyes (mean axial length 23.93 mm) are longer than female eyes (mean axial length 23.51 mm).[124] An elevation in axial length is correlated with a higher risk of rhegmatogenous retinal detachment (RRD).[125] In a substantial observational study comprising 1202 cases of primary

RRD, a predominance of males (13.09 vs. 7.41 per 100 000 of population) was found.[19] This imbalance of gender was also observed in other population-based studies and is probably correlated to differences in axial length. Wang et al. reported gender disparities in the anatomy of the vitreoretinal base[126]: in their series of 58 pairs of donor eyes, they observed a significant age-related migration of the posterior border of the vitreous base in male donor eyes compared to female donor eyes. Mitry et al. propose that this increased posterior migration of the vitreous base might also make males more susceptible to retinal breaks. This susceptibility could arise from increased dynamic vitreoretinal traction and rise in vitreoretinal irregularities along the posterior border.[19]

Recently, a retrospective cohort study showed that not only the incidence of RRD, but also the incidence of laser retinopexy[127] or surgical intervention[128] for retinal tears, is higher in male patients: in the United States, insured women are less likely than insured men to undergo surgical intervention for RRD. As the authors suggest, this difference is probably attributed to a complex interplay of factors including access to healthcare, societal gender roles and potentially biological variation in the types of RRDs.

4.5 | Macular holes

Idiopathic macular holes (IMHs) seem to have a higher prevalence among women. Nevertheless, the male-to-female ratios exhibit significant variations across studies, spanning from 1:1,2 (India) to 1:7 (China).[20–22] In 1996, Kishi et al. conducted an assessment of the vitreous in 64 eyes of patients with IMHs before and during vitreous surgery. They found that tangential traction, seemingly originating solely from the premacular vitreous cortex that constitutes the posterior wall of the premacular liquefied pocket, is responsible for causing IMHs.[129] In addition to this local factor, underlying systemic factors are unclear in the pathophysiology of IMHs.

Female sex as well as hormonal fluctuations during menopause, a history of hysterectomy, and the use of hormone replacement therapy have been mentioned as possible risk factors.[130,131] Other studies, however, reported no association with estrogen exposure.[132] Estrogen has several effects on different tissues in the body and estrogen receptors have been found in bovine and rat retinas as well.[133] Estrogen also effects the production of collagenase in the cervix of guinea pigs[134] and can inhibit collagen gel contraction by glial cells.[135] The metabolic alteration of estrogen post-menopause might affect ocular collagen metabolism, potentially leading to the contraction of the posterior vitreous membrane and the development of IMHs. Inokuchi et al. examined vitreous estrogen levels in IMH patients and reported significant higher estradiol concentrations in the vitreous samples of IMH patients in contrast to their controls suggesting an association with the pathogenesis of IMH.[136]

5 | HEREDITARY RETINAL AND MACULAR DISEASES

Inherited retinal (IRD) and macular diseases can vary in their presentation and progression in men and women. Genetics plays a significant role in these diseases. Certain mutations can have different effects on men and women, leading to variable symptoms and presentations. First and foremost, of course X-linked IRDs, where males will present with the pathologic phenotype while females will be (mostly) asymptomatic carriers. Given the large number of IRDs, the high amount of different genetic aberrations and their rarity in daily clinic, we will focus only on the two most IRDs in this chapter.

5.1 | Retinitis pigmentosa (RP)

RP is the most prevalent inherited retinal disease worldwide, with an approximate prevalence of one in 5000 (in nonsyndromic retinitis pigmentosa). Males are somewhat more frequently affected than females, primarily due to the X-linked form that is more frequently expressed in males.[23] In an animal model of retinitis pigmentosa, gender-related disparities in onset and progression of the disease were found. The onset of rod degeneration occurred significantly earlier in female rd10 mice compared to male rd10 mice. As the disease advanced, cones degenerated more rapidly in the retinas of females. Female rd10 mice were more vulnerable to retinal degeneration, indicating that female sex may be a risk factor for RP.[137] This has not yet been proven in studies on human eyes.

5.2 | Stargardt disease

Stargardt disease is the most common inherited macular dystrophy.[138] Runhart et al. looked at 550 cases of genetically confirmed Stargardt disease and observed a greater prevalence among females in the group of patients carrying either of the two most common and less severe ABCA4 alleles, in comparison to patients who did not carry a presumed mild ABCA4 allele.[24] However, another separate analysis study of a bigger cohort could not confirm the association between gender and specific mild ABCA4 alleles.[139]

6 | UVEITIS

Studies show that sex hormones, beyond their role in sexual differentiation and reproduction, also seem to have an impact on the immune system. Therefore, females tend to exhibit greater resistance to certain infections, characterized by more robust cellular and humoral immune responses. Males are more susceptible to infections caused by various pathogens. However, females experience a higher incidence of autoimmune diseases. Sex steroids, specifically androgens in males and estrogens in females, modulate different aspects of host immunity and affect genes and behaviors that influence susceptibility and resistance to infection.[140,141] Estrogen seems to increase autoimmune response whereas androgens suppress it.

Uveitis, a diverse category of intraocular inflammatory diseases encompassing both infectious and non-infectious types, has exhibited gender-related differences in many of its manifestations.[25]

6.1 | Infectious uveitis

The biological basis for the susceptibility of men or women to infectious uveitis remains uncertain. For infectious uveitis it remains unclear whether there is a biological basis for a higher susceptibility in either males or females. As mentioned above, men appear to be more vulnerable to infections caused by several species.[141] Unlike noninfectious uveitis, infectious uveitis is more closely related to occupational exposures, sexual behaviors and other environmental factors that vary between males and females. These factors may obscure any true biological disparities in susceptibility to ocular manifestations of infection. For non-sexually transmitted types of infectious uveitis where data is accessible, there seems to be no big difference in the prevalence of ocular disease when comparing males and females suggesting that sexual hormones might not be significant factors. However, in the case of sexually transmitted diseases, behavioral factors might outweigh any biological effects associated with sex-specific gene expression.[26]

6.1.1 | Sexually transmitted diseases

The prevalence of both systemic and ocular syphilis is significantly higher in males ranging from 87% to 90%.[25–27] In men who have sex with men the prevalence is 15–20 times greater than in the broader male population.[142] Therefore, the male predominance is believed to be primarily attributed to unsafe sexual practices. In human immunodeficiency virus (HIV) + patients, syphilitic uveitis is predominantly seen in men.[143] A small case series from China ($n = 14$) reported no big gender imbalances in non-HIV infected, syphilitic uveitis patients. Nevertheless, regional factors may also contribute to these results.[144]

6.1.2 | Nonsexually transmitted diseases

One could assume that infectious uveitis triggered by pathogens not related to sexual transmission would generally be less likely to show significant differences between the sexes. However, it should be borne in mind that HIV is also a risk factor for non-sexually transmitted infectious diseases. Since the sex ratio varies here depending on the geographical region, women are at different levels of risk.

A study involving HIV patients, and patients with infections of herpes viruses excluding cytomegalovirus (CMV), (including zoster, simplex) Cryptococcus, atypical Mycobacterium and Toxoplasmosis displayed comparable prevalence rates in both males and females.[145] Also in non-HIV infected patients, literature does not indicate a significantly higher proportion of men among those with herpetic uveitis.[146,147] A large survey[28] and review[29] from Saudi Arabia also found no specific sex imbalances in tuberculosis (TB) associated uveitis in non-HIV infected patients.

However, when looking at complications in viral uveitis including acute retinal necrosis (ARN), the prevalence in men is increased with 56%–72% of ARN patients being male.[148,149] Besides, male gender is correlated with an increased likelihood of experiencing a more severe form of the disease and is associated with severe vision loss at 6 and 12 months.[150]

Literature on progressive outer retinal necrosis reported a higher prevalence in men (83%–86%) as well.[151,152]

CMV can be sexually transmitted but also by contact with infectious body fluids, e. g. trough breastfeeding, kissing, blood products and organ transplants. CMV used to be the leading cause of visual impairment in HIV+ patients before the advent of highly-active-antiretroviral-treatment (HAART). In the pre-HAART era, the occurrence of AIDS-related infections was primarily linked to the level of immune suppression more than sex.[153] However, following the introduction of HAART, literature showed that new cases of CMV-retinitis (CMVR) in 2002 were more prevalent in females than in males.[30] Gender specific disparities in healthcare access were seen as the primary contributing factor in this context. Individuals lacking insurance or remaining untreated at the beginning of the study were also linked to a higher incidence of CMVR, implying that economic disadvantage was

another influencing factor.[25,30] However, a re-analysis of this dataset in 2012 did not reveal any disparity in the incidence of CMVR between males and females.[154] CMV can also spread through contact within households, making women who care for infected young children particularly vulnerable. In contrast to syphilis and regardless of HIV status, studies show that healthy females are generally more prone to this virus compared to men (odds ratio 1.17 [1.14–1.21]).[31]

For ocular toxoplasmosis extensive clinical-based studies have demonstrated no significant gender specific difference in the disease rate.[32–34] In regions of Brazil where toxoplasma seropositivity is prevalent among individuals of all ages and genders living in the same households, the clustering implies that transmission via foodborne routes is a significant factor in this form of non-sexually transmitted infectious uveitis. In situations where all individuals are primarily exposed through their diet, an even gender distribution would be anticipated.[155] A recent observational study of 262 toxoplasmosis patients in Brazil aimed to assess how gender influences the clinical characteristics and results of ocular toxoplasmosis.[156] While the clinical features and outcomes were largely comparable between men and women, some noteworthy distinctions emerged. The study could show that male patients had a significantly higher likelihood of initially presenting with primary active disease, while female patients had a higher probability of presenting with recurrent active disease. Additionally, a higher occurrence of atypical ocular toxoplasmosis was observed in male patients, and some of these men were HIV+. Furthermore, they found that woman exhibited a notably higher incidence of Toxo lesions situated at the posterior pole of the eye. Female patients tended to have multiple lesions in a single eye more frequently, while male patients were more inclined to have one single lesion. The exact relationships and causes of these gender differences are not fully understood. Lyons et al. list potential explanations for this. The development of ocular toxoplasmosis is shaped by various factors, encompassing both parasite-related and host-related elements, with the host's immune system playing a pivotal role. This could potentially have implications on the development of ocular disease, with different types of infection (via oocysts, bradyzoites, or tachyzoites) and variations in parasite genotype and load playing a role. The different types of infection are affected by occupational and sociocultural behaviors and these behaviors may exhibit gender-related variations. Another important aspect to consider is gender-related attitudes to seeking health care. However, the largest clinical studies reported no major gender differences regarding presenting to uveitis services.[32–34] Fernandes et al. found more reactivations of ocular toxoplasmosis in females compared to males and proposed a potential connection with immunological alterations by the menstrual cycle.[157] Data concerning the influence of pregnancy and period of postpartum on reactivation are conflicting: while Braakenburg et al. found no alteration in recurrence rate during pregnancy,[158] Reich et al. documented a mitigation in the risk of recurrence during pregnancy.[159] Brydak-Godowska et al. even observed an elevated risk of recurrence during pregnancy and postpartum.[160]

6.2 | Non-infectious uveitis

Along with the finding that women suffer more frequently from systemic autoimmune diseases, autoimmune associated uveitis seems to be more frequent in women than in men.[161]

6.2.1 | Uveitis with systemic involvement

Among pediatric patients, uveitis is most frequently associated with juvenile idiopathic arthritis (JIA) when considering systemic diseases. It affects children below the age of 16. In different sub-types, 50%–80% of JIA patients are female.[35] Uveitis is more commonly linked to the most prevalent subtype of JIA, which is oligoarticular JIA, and this subtype is predominantly observed in young female patients.[25] Uveitis occurs in 10%–45% of JIA patients.[162–164] The highest risk of uveitis carries the oligoarticular subtype among girls who are ANA-positive and have an earlier age of onset.[35] While uveitis is more common in females, the ocular complication rate, when uveitis happens in male patients, is often higher and complications are more severe. In a group of individuals with JIA-associated uveitis, observed over a period of 8 years, 40% of male patients encountered at least one ocular complication, contrasting with 10% among women.[165] However, other data could not support this correlation between sex and disease severity.[166]

Systemic lupus erythematosus (SLE) is an autoimmune condition associated with the production of autoantibodies against nuclear material that affects the eye as well as skin, kidney, joints, lungs and central nervous system (CNS). Females experience a significantly higher rate of occurrence than males, particularly during the ages of 20–40 years. According to the literature, 88%–90.5% of SLE patients are women.[36–38] Men, however, seem to be more susceptible to SLE-related complications including CNS involvement and systemic thromboses. Being male has been suggested as a predictor for unfavorable systemic outcomes.[167,168] Literature reports ocular

involvement in almost every second patient (47.3%) with a ratio of 17 females to 1 male.[39] During puberty, and after menopause, the incidence is much lower. Hormone replacement therapy after menopause seems to increase the incidence and severity of SLE uveitis again, which could be an indication of sex hormone involvement.[169] Elevated concentrations of estrogen and progesterone might cause worsening of SLE by promoting an upregulation of a Th2 immune response, resulting in an increase of antibody synthesis.[170] Attempts to influence disease course through androgen therapy showed minimal to no effect in several trials.[171,172]

Multiple sclerosis (MS) is another non-infectious autoimmune disease, which is much more prevalent in women (78%).[40] In addition to epigenetic, environmental factors are suspected due to geographical variations in incidence and hormonal changes have been implicated in the disease.[173] Women seem to be affected significantly more often during the reproductive phase, and an earlier onset of menarche has been correlated with a heightened risk higher risk for MS. Therefore, female hormones may influence the inflammatory and neurodegenerative processes involved. While women have a higher risk for MS, the female gender also appears to be protective against severe, progressive courses with cognitive loss.[174] Multiple sclerosis-associated uveitis, typically bilateral intermediate uveitis, is observed in 1%–10% of MS patients and precedes MS diagnosis in ~25% of patients.[175,176] Another study involving 1916 uveitis patients found that MS was present in 3.1% of patients. Of the patients who had both MS and uveitis, about three-quarters were of the female sex.[41] This statistical gender distribution highlights gender differences in the underlying autoimmune disease.

Sarcoidosis appears to have a slightly higher prevalence in female patients (55%–64%).[42,43] Most patients are in the range of 10–40 years, but there is another age peak in patients >50 years, especially in women.[177] Ocular involvement is more common in females.[178] For ocular sarcoidosis patients, the ratio of women to men was reported to be 3:1.[25,44] The female sex has been linked to a less favorable visual prognosis.[179]

Vogt-Koyanagi-Harada (VKH) disease primarily impacts pigmented individuals including Asians, Native Americans, Middle Easterners and Hispanics.[180] It tends to have a more pronounced impact on women. Literature reports the following proportions of women in the different ethnic groups: 70% in Brazil,[45] 78.7% in USA,[46] 84.4% in India.[47] It was suggested that being male may predict a less favorable visual outcome although the precise cause is not understood. In an Indian study, it was observed that approximately 40% of male patients diagnosed with VKH had vision that was worse than 20/80, whereas only 3% of the female VKH cohort had vision below the 20/80 threshold.[181] The increased occurrence of VKH in women might be attributed more to genetic aspects than hormonal ones. The most robust association was observed with the HLA-DRB1*04:05 haplotype which again was associated with female sex only.[182]

Behçet disease (BD) is an infrequent systemic vasculitis, which predominantly occurs in patients with genetic heritage linked to the Silk Road. The HLA-B51 allele represents a highly correlated genetic risk factor. 54%–85% of patients are male[48,49] and BD tends to manifest with greater severity in men. However, gender preference in BD has been a subject of long-standing debate.[25] Clinical characteristics of BD differ between the genders: while women often experience more frequent and severe oral ulcers, genital ulcers and skin lesions, males tend to suffer more often from ocular and vascular involvement and neurologic disease.[25,183] Different studies showed that young males with BD are at higher risk of dying from the disease.[50]

In BD patients, around 50%–80% of cases show ocular manifestations, with men more commonly experiencing posterior segment issues and poorer visual outcomes.[25,50] Men generally exhibit a less favorable response to ocular BD treatment,[184] while women tend to have less severe and non-recurrent manifestations of ocular involvement.[185] Discussed here is a protective effect of estrogen in females through down-modulation of inflammatory genes in the vascular endothelium, as shown in animal studies.[186]

Human leukocyte antigen (HLA)-B27-associated anterior uveitis is the most frequent form of acute anterior uveitis and this condition predominantly affects men. Men have a 2.5 times higher likelihood of being affected compared to women.[51] Other HLA-B27-associated diseases include ankylosing spondylitis (AS), reactive arthritis syndrome, inflammatory bowel disease and psoriatic arthritis. All of these appear to exhibit a higher prevalence in men[187] and uveitis is known to affect up to 37% of individuals within this specific patient population.[188] Males seem to have a greater susceptibility to developing occlusive retinal vasculitis in association with this condition, and they also tend to experience an earlier onset (at younger age).[187,189–192] However, there doesn't appear to be a sex-based difference in the risk of hypopyon, vitritis, cystoid macular edema, secondary glaucoma or final visual acuity as reported in the literature.[187,193]

6.2.2 | Uveitis without systemic involvement

White dot syndromes (WDS) are a category of inflammatory disorders distinguished by the presence of yellow-white or grayish foci within the outer retina, the retinal

pigment epithelium, and the choroid. An increased proportion of women was described for the majority of the diseases[52,53]: for Multiple Evanescent White Dot Syndrome (50%–91% Female (F)), Birdshot Chorioretinopathy (58% F), Multifocal Choroiditis and Panuveitis (75% F), Punctate Inner Choroidopathy (85% F) and Acute Zonal Occult Outer Retinopathy (79% F) a female predilection has been shown. Only Acute Posterior Multifocal Placoid Pigment Epitheliopathy (54% M) appears to be more prevalent in males or have an equal gender distribution.[52] Why these gender differences exist and whether there are hormonal causes here as well is unclear so far. Furthermore, in all WDS, for disease severity or symptoms no gender differences were reported.[52]

7 | CONCLUSION

Investigating and understanding gender medicine in ophthalmology is still in its infancy. This review highlights gender differences in epidemiology, disease severity, treatment response, and prognosis of various retinal diseases. It demonstrates that the significance of gender in retinal diseases has been a subject of ongoing debate and remains relevant.

It is crucial to highlight that disparities between genders in retinal diseases are intricate and frequently shaped by various factors. Genetics, hormones, lifestyle, environmental factors, and social determinants may all have influence on the development and progression of these diseases. Additional research is necessary to deepen understanding of these relationships and some data that might seem contradictory at the present time.

Providing fair and equitable healthcare is rooted in ensuring that everyone, regardless of their gender, receives the necessary medical services. Overcoming gender gaps in access to health care requires targeted interventions that address the needs and challenges of women and men equally. These include promoting gender-responsive health systems, raising awareness of gender-specific health issues among medical staff, and empowering women with regard to their health.

New diagnostic possibilities will help to gain important insights and a better understanding of gender-related differences in certain diseases and their correlations.

There is some evidence that response to certain medications or treatments for retinal diseases may vary between men and women. So far, the knowledge has not yet been translated into different ophthalmic treatment approaches for women and men. Gender-specific treatment response in retinal diseases will require more detailed investigation in the future in order to promote gender-responsive health care that addresses the individual needs of men and women equally. This could make a significant contribution to individualized therapy for each patient.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Anne Tillmann https://orcid.org/0000-0002-4763-6167
Chantal Dysli https://orcid.org/0000-0002-3926-0825
Marion R. Munk https://orcid.org/0000-0002-6227-2242

REFERENCES

1. Healy B. The Yentl syndrome. *N Engl J Med*. 1991;25(325):274-276.
2. Singer IB. *Gimpel the Fool and other stories*. Noonday Press; 1957.
3. Maynard C, Litwin PE, Martin JS, Weaver WD. Gender differences in the treatment and outcome of acute myocardial infarction. Results from the Myocardial Infarction Triage and Intervention Registry. *Arch Intern Med*. 1992;152:972-976.
4. Chiamvimonvat V, Sternberg L. Coronary artery disease in women. *Can Fam Physician*. 1998;44:2709-2717.
5. Norberg H, Pranic V, Bergdahl E, Lindmark K. Differences in medical treatment and clinical characteristics between men and women with heart failure: a single-centre multivariable analysis. *Eur J Clin Pharmacol*. 2020;76:539-546.
6. WHO. A/RES/55/69, February. 2001.
7. Kappert K, Böhm M, Schmieder R, et al. Impact of sex on cardiovascular outcome in patients at high cardiovascular risk. *Circulation*. 2012;126:934-941.
8. Silverstein MD, Heit JA, Mohr DN, et al. Trends in the incidence of deep vein thrombosis and pulmonary embolism. *Arch Intern Med*. 1998;158:585-593.
9. Gass JD, Oyakawa RT. Idiopathic juxtafoveolar retinal telangiectasis. *Arch Ophthalmol*. 1982;100:769-780.
10. Friedman N, Kaiser P, Pineda R. *The Massachusetts Eye and Ear Infirmary Illustrated Manual of Ophthalmology*. 3rd ed. Saunders Elsevier; 2009:352-353.
11. Gass JD, Blodi BA. Idiopathic juxtafoveolar retinal telangiectasis. Update of classification and follow-up study. *Ophthalmology*. 1993;100:1536-1546.
12. Clemons TE, Gillies MC, Chew EY, et al. Baseline characteristics of participants in the natural history study of macular telangiectasia (MacTel) MacTel Project Report No. 2. *Ophthalmic Epidemiol*. 2010;17:66-73.
13. Kitzmann AS, Pulido JS, Diehl NN, Hodge DO, Burke JP. The incidence of central serous chorioretinopathy in Olmsted County, Minnesota, 1980-2002. *Ophthalmology*. 2008;115:169-173.
14. Age-Related Eye Disease Study Research Group. Risk factors associated with age-related macular degeneration. A case-control

study in the age-related eye disease study: age-related eye disease study report number 3. *Ophthalmology*. 2000;107:2224-2232.
15. Klein R, Klein BE, Jensen SC, Meuer SM. The five-year incidence and progression of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology*. 1997;104:7-21.
16. Mitchell P, Smith W, Attebo K, Wang JJ. Prevalence of age-related maculopathy in Australia. The blue mountains eye study. *Ophthalmology*. 1995;102:1450-1460.
17. Rudnicka AR, Jarrar Z, Wormald R, Cook DG, Fletcher A, Owen CG. Age and gender variations in age-related macular degeneration prevalence in populations of European ancestry: a meta-analysis. *Ophthalmology*. 2012;119:571-580.
18. Ludwig CA, Shields RA, Chen TA, et al. A novel classification of high myopia into anterior and posterior pathologic subtypes. *Graefes Arch Clin Exp Ophthalmol*. 2018;256:1847-1856. doi:10.1007/s00417-018-4071-0
19. Mitry D, Tuft S, McLeod D, et al. Laterality and gender imbalances in retinal detachment. *Graefes Arch Clin Exp Ophthalmol*. 2010;249:1109-1110.
20. McCannel CA, Ensminger JL, Diehl NN, et al. Population based incidence of macular holes. *Opthalmology*. 2009;116:1366.
21. Wang S, Xu L, Jonas JB. Prevalence of full-thickness macular holes in urban and rural adult Chinese: the Beijing Eye Study. *Am J Ophthalmol*. 2006;141:589-591.
22. Sen P, Bhargava A, Vijaya L, George R. Prevalence of idiopathic macular hole in adult rural and urban south Indian population. *Clin Exp Ophthalmol*. 2008;36:257-260.
23. StatPearls (Treasure Island (FL)). O'Neal TB, Luther EE. *Retinitis Pigmentosa*. 2023. Accessed July 2023 https://www.ncbi.nlm.nih.gov/books/NBK519518/
24. Runhart EH, Khan M, Cornelis SS, et al. Association of Sex With Frequent and Mild ABCA4 Alleles in Stargardt Disease. *JAMA Ophthalmol*. 2020;138:1035-1042.
25. Sen HN, Davis J, Ucar D, Fox A, Chan CC, Goldstein DA. Gender disparities in ocular inflammatory disorders. *Curr Eye Res*. 2015;40:146-161.
26. Davis JL. Sex and reproduction in the transmission of infectious uveitis. *J Ophthalmol*. 2014;2014:683246.
27. Mathew RG, Goh BT, Westcott MC. British Ocular Syphilis Study (BOSS): 2-year national surveillance study of intraocular inflammation secondary to ocular syphilis. *Invest Ophthalmol Vis Sci*. 2014;55:5394-5400.
28. Al-Mezaine HS, Kangave D, Abu El-Asrar AM. Patterns of uveitis in patients admitted to a university hospital in Riyadh, Saudi Arabia. *Ocular Immunol Inflamm*. 2010;18:424-431.
29. Abu El-Asrar AM, Abouammoh M, Al-Mezaine HS. Tuberculous uveitis. *Int Ophthalmol Clin*. 2010;50:19-39.
30. Jabs DA, Van Natta ML, Kempen JH, et al. Characteristics of patients with cytomegalovirus retinitis in the era of highly active antiretroviral therapy. *Am J Ophthalmol*. 2002;133:48-61.
31. Staras SA, Flanders WD, Dollard SC, Pass RF, McGowan JE Jr, Cannon MJ. Cytomegalovirus seroprevalence and childhood sources of infection: a population-based study among pre-adolescents in the United States. *J Clin Virol*. 2008;43:266-271.
32. Bosch- Driessen LEH, Berendschot TTJM, Ongkosuwito JV, et al. Ocular toxoplasmosis: clinical features and prognosis of 154 patients. *Ophthalmology*. 2002;109:869-878.
33. Aleixo ALQ, Curi AL, Benchimol EI, Amendoeira MR. Toxoplasmic Retinochoroiditis: Clinical characteristics and visual outcome in a prospective study. *PLoS Negl Trop Dis*. 2016;10:e0004685.
34. Arruda S, Vieira BR, Garcia DM, et al. Clinical manifestations and visual outcomes associated with ocular Toxoplasmosis in a Brazilian population. *Sci Rep*. 2021;11:3137.
35. Heiligenhaus A, Heinz C, Edelsten C, Kotaniemi K, Minden K. Review for disease of the year: epidemiology of juvenile idiopathic arthritis and its associated uveitis: the probable risk factors. *Ocul Immunol Inflamm*. 2013;21:180-191.
36. Gaudreau MC, Johnson BM, Gudi R, et al. Gender bias in lupus: does immune response initiated in the gut mucosa have a role? *Clin Exp Immunol*. 2015;180:393-407.
37. Cervera R, Doria A, Amoura Z, et al. Patterns of systemic lupus erythematosus expression in Europe. *Autoimmun Rev*. 2014;13:621-629.
38. Tedeschi SK, Bermas B, Costenbader KH. Sexual disparities in the incidence and course of SLE and RA. *Clin Immunol*. 2013;149:211-218.
39. Sitaula R, Shah DN, Singh D. The spectrum of ocular involvement in systemic lupus erythematosus in a tertiary eye care center in Nepal. *Ocul Immunol Inflamm*. 2011;19:422-425.
40. Harbo HF, Gold R, Tintore M. Sex and gender issues in multiple sclerosis. *Ther Adv Neurol Disord*. 2013;6:237-248.
41. Jakob E, Reuland MS, Mackensen F, et al. Uveitis subtypes in a german interdisciplinary uveitis center: analysis of 1916 patients. *J Rheumatol*. 2009;36:127-136.
42. Siltzbach LE, James DG, Neville E, et al. Course and prognosis of sarcoidosis around the world. *Am J Med*. 1974;57:v847-v852.
43. Lobo A, Barton K, Minassian D, et al. Visual loss in sarcoid-related uveitis. *Clin Exp Ophthalmol*. 2003;31:310-316.
44. Birnbaum AD, Oh FS, Chakrabarti A, Tessler HH, Goldstein DA. Clinical features and diagnostic evaluation of biopsy-proven ocular sarcoidosis. *Arch Ophthalmol*. 2011;129:409-413.
45. Belfort Junior R, Nishi M, Hayashi S, et al. Vogt-Koyanagi-Harada's disease in Brazil. *Jpn J Ophthalmol*. 1988;32:344-347.
46. Lertsumitkul S, Whitcup SM, Nussenblatt RB, et al. Subretinal fibrosis and choroidal neovascularization in Vogt-Koyanagi-Harada syndrome. *Graefes Arch Clin Exp Ophthalmol*. 1999;237:1039-1045.
47. Murthy SI, Moreker MR, Sangwan VS, et al. The spectrum of Vogt-Koyanagi-Harada disease in South India. *Int Ophthalmol*. 2007;27:131-136.
48. Citirik M, Berker N, Songur MS, et al. Ocular manifestations of late-onset behcet disease. *Ophthalmologica*. 2011;225:21-26.
49. Liberman P, Gauro F, Berger O, et al. Causes of uveitis in a tertiary center in Chile: a cross-sectional retrospective review. *Ocul Immunol Inflamm*. 2015;23:339-345.
50. Seyahi E, Yazici H. Prognosis in Behcet's Syndrome. In: Yazici Y, Yazici H, eds. *Behcet's syndrome*. Springer; 2010:285-295.
51. Wakefield D, Chang JH, Amjadi S, Maconochie Z, Abu El-Asrar A, McCluskey P. What is new HLA-B27 acute anterior uveitis? *Ocul Immunol Inflamm*. 2011;19:139-144.
52. Faia LJ. Gender differences in birdshot chorioretinopathy and the white dot syndromes: do they exist? *J Ophthalmol*. 2014;2014:146768.

53. Abu-Yaghi NE, Hartono SP, Hodge DO, Pulido JS, Bakri SJ. White dot syndromes: a 20-year study of incidence, clinical features, and outcomes. *Ocul Immunol Inflamm*. 2011;19:426-430.
54. Poplin R, Varadarajan AV, Blumer K, et al. Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. *Nat Biomed Eng*. 2018;2:158-164.
55. Munk MR, Kurmann T, Márquez-Neila P, Zinkernagel MS, Wolf S, Sznitman R. Assessment of patient specific information in the wild on fundus photography and optical coherence tomography. *Sci Rep*. 2021;11:8621.
56. Ilanchezian I, Kobak D, Faber H, Ziemssen F, Berens P, Ayhan MS. Interpretable gender classification from retinal fundus images using BagNets. medRxiv. 2021. doi:10.1101/2021.06.21.21259243
57. Song WK, Lee SC, Lee ES, Kim CY, Kim SS. Macular thickness variations with sex, age, and axial length in healthy subjects: a spectral domain-optical coherence tomography study. *Invest Ophthalmol Vis Sci*. 2010;51:3913-3918.
58. Mauschitz MM, Holz FG, Finger RP, Breteler MMB. Determinants of macular layers and optic disc characteristics on SD-OCT: The Rhineland study. *Transl Vis Sci Technol*. 2019;8:34.
59. Niestrata-Ortiz M, Fichna P, Stankiewicz W, Stopa M. Sex-related variations of retinal and choroidal thickness and foveal avascular zone in healthy and diabetic children assessed by optical coherence tomography imaging. *Ophthalmologica*. 2019;241:173-178.
60. Ooto S, Hangai M, Tomidokoro A, et al. Effects of age, sex, and axial length on the three-dimensional profile of normal macular layer structures. *Invest Ophthalmol Vis Sci*. 2011;52:8769-8779.
61. Maden G, Cakir A, Icar D, Erden B, Bolukbasi S, Elcioglu M. The distribution of the photoreceptor outer segment length in a healthy population. *J Ophthalmol*. 2017;2017:4641902.
62. Li D, Rauscher FG, Choi EY, et al. Sex-specific differences in circumpapillary retinal nerve fiber layer thickness. *Ophthalmology*. 2020;127:357-368.
63. Gómez-Ulla F, Cutrin P, Santos P, et al. Age and gender influence on foveal avascular zone in healthy eyes. *Exp Eye Res*. 2019;189:107856.
64. Schmidl D, Schmetterer L, Garhöfer G, Popa-Cherecheanu A. Gender differences in ocular blood flow. *Curr Eye Res*. 2015;40:201-212.
65. Wang S, Xu L, Wang Y, Wang Y, Jonas JB. Retinal vessel diameter in normal and glaucomatous eyes: the Beijing eye study. *Clin Exp Ophthalmol*. 2007;35:800-807.
66. Wong TY, Klein R, Klein BE, Meuer SM, Hubbard LD. Retinal vessel diameters and their associations with age and blood pressure. *Invest Ophthalmol Vis Sci*. 2003;44:4644-4650.
67. Ustymowicz A, Mariak Z, Weigele J, Lyson T, Kochanowicz J, Krejza J. Normal reference intervals and ranges of side-to-side and day-to-day variability of ocular blood flow Doppler parameters. *Ultrasound Med Biol*. 2005;31:895-903.
68. Kavroulaki D, Gugleta K, Kochkorov A, Katamay R, Flammer J, Orgul S. Influence of gender and menopausal status on peripheral and choroidal circulation. *Acta Ophthalmol*. 2010;88:850-853.
69. Hammond BR Jr, Curran-Celentano J, Judd S, et al. Sex differences in macular pigment optical density: relation to plasma carotenoid concentrations and dietary patterns. *Vision Res*. 1996;36(13):2001-2012. doi:10.1016/0042-6989(95)00290-1
70. Obana A, Gohto Y, Sasano H, et al. Spatial distribution of macular pigment estimated by autofluorescence imaging in elderly Japanese individuals. *Jpn J Ophthalmol*. 2020;64(2):160-170. doi:10.1007/s10384-020-00716-5
71. Zhang X, Saaddine JB, Chou CF, et al. Prevalence of diabetic retinopathy in the United States, 2005-2008. *JAMA*. 2010;304:649-656.
72. Soltesz G, Patterson CC, Dahlquist G, EURODIAB Study Group. Worldwide childhood type 1 diabetes incidence: what can we learn from epidemiology? *Pediatr Diabetes*. 2007;6:6-14.
73. Green A, Gale EA, Patterson CC. Incidence of childhood-onset insulin-dependent diabetes mellitus: the EURODIAB ACE Study. *Lancet*. 1992;339:905-909.
74. Karvonen M, Pitkäniemi M, Pitkäniemi J, Kohtamäki K, Tajima N, Tuomilehto J. Sex difference in the incidence of insulin-dependent diabetes mellitus: an analysis of the recent epidemiological data. World Health Organization DIAMOND Project Group. *Diabetes Metab Rev*. 1997;13:275-291.
75. Maahs DM, West NA, Lawrence JM, Mayer-Davis EJ. Epidemiology of type 1 diabetes. *Endocrinol Metab Clin North Am*. 2010;39:481-497.
76. SEARCH for Diabetes in Youth Study Group, Liese AD, D'Agostino RB, Hamman RF, et al. The burden of diabetes mellitus among US youth: prevalence estimates from the SEARCH for Diabetes in Youth Study. *Pediatrics*. 2006;118:1510-1518.
77. Fazeli Farsani S, van der Aa MP, van der Vorst MM, Knibbe CA, de Boer A. Global trends in the incidence and prevalence of type 2 diabetes in children and adolescents: a systematic review and evaluation of methodological approaches. *Diabetologia*. 2013;56:1471-1488.
78. Ozawa GY, Bearse MA, Adams AJ. Male-female differences in diabetic retinopathy? *Curr Eye Res*. 2015;40:234-246.
79. Al-Rubeaan K, Abu El-Asrar AM, Youssef AM, et al. Diabetic retinopathy and its risk factors in a society with a type 2 diabetes epidemic: a Saudi National Diabetes Registry-based study. *Acta Ophthalmol*. 2015;93:e140-e147.
80. Kashani AH, Zimmer-Galler IE, Shah SM, et al. Retinal thickness analysis by race, gender, and age using Stratus OCT. *Am J Ophthalmol*. 2010;149:496-502.e1.
81. Hammes HP, Welp R, Kempe HP, Wagner C, Siegel E, Holl RW. Risk factors for retinopathy and DME in type 2 diabetes-results from the German/Austrian DPV database. *PloS One*. 2015;10:e0132492.
82. Constable IJ, Knuiman MW, Welborn TA, et al. Assessing the risk of diabetic retinopathy. *Am J Ophthalmol*. 1984;97:53-61.
83. West KM, Ahuja MM, Bennett PH, et al. Interrelationships of microangiopathy, plasma glucose and other risk factors in 3583 diabetic patients: a multinational study. *Diabetologia*. 1982;22:412-420.
84. Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. *Phys Ther*. 2008;88:1254-1264.
85. Amin R, Widmer B, Prevost AT, et al. Risk of microalbuminuria and progression to macroalbuminuria in a cohort with childhood onset type 1 diabetes: prospective observational study. *BMJ*. 2008;336:697-701.

86. Benitez-Aguirre P, Craig ME, Cass HG, et al. Sex differences in retinal microvasculature through puberty in type 1 diabetes: are girls at greater risk of diabetic microvascular complications? *Invest Ophthalmol Vis Sci*. 2014;56:571-577.
87. Moloney JB, Drury MI. The effect of pregnancy on the natural course of diabetic retinopathy. *Am J Ophthalmol*. 1982;93:745-756.
88. Schiefelbein J, Müller M, Kern C, et al. Gender-related differences in patients treated with intravitreal anti-vascular endothelial growth factor medication for diabetic macular oedema. *Eur J Ophthalmol*. 2020;30:1410-1417.
89. Thapa R, Bajimaya S, Paudyal G, et al. Prevalence, pattern and risk factors of retinal vein occlusion in an elderly population in Nepal: the Bhaktapur retina study. *BMC Ophthalmol*. 2017;17(1):162.
90. Schwaber EJ, Fogelman N, Sobol EK, et al. Associations with retinal vascular occlusions in a diverse, urban population. *Ophthal Epidemiol*. 2018;25:220-226.
91. Ponto KA, Elbaz H, Peto T, et al. Prevalence and risk factors of retinal vein occlusion: the Gutenberg Health Study. *J Thromb Haemost*. 2015;13:1254-1263.
92. Li Y, Hall NE, Pershing S, et al. Age, gender, and laterality of retinal vascular occlusion: a retrospective study from the iris® registry. *Ophthalmol Retina*. 2022;6:161-171.
93. Spaide RF, Campeas L, Haas A, et al. Central serous chorioretinopathy in younger and older adults. *Ophthalmology*. 1996;103:2070-2079.
94. Gilbert CM, Owens SL, Smith PD, Fine SL. Long-term follow-up of central serous chorioretinopathy. *Br J Ophthalmol*. 1984;68:815-820.
95. Chatziralli I, Kabanarou SA, Parikakis E, Chatzirallis A, Xirou T, Mitropoulos P. Risk factors for central serous chorioretinopathy: multivariate approach in a case-control study. *Curr Eye Res*. 2017;42:1069-1073.
96. Said-Ahmed K, Moustafa G, Fawzy M. Incidence and natural course of symptomatic central serous chorioretinopathy in pregnant women in a maternity hospital in Kuwait. *Middle East Afr J Ophthalmol*. 2012;19:273-276.
97. Al-Mujaini A, Wali U, Ganesh A, Montana C. Natural course of central serous chorioretinopathy without subretinal exudates in normal pregnancy. *Can J Ophthalmol*. 2008;43:588-590.
98. Schellevis RL, Altay L, Kalisingh A, et al. Elevated steroid hormone levels in active chronic central serous chorioretinopathy. *Invest Ophthalmol Vis Sci*. 2019;60:3407-3413.
99. Ogueta SB, Schwartz SD, Yamashita CK, Farber DB. Estrogen receptor in the human eye: influence of gender and age on gene expression. *Invest Ophthalmol Vis Sci*. 1999;40:1906-1911.
100. Hanumunthadu D, Van Dijk EHC, Gangakhedkar S, et al. Gender variation in central serous chorioretinopathy. *Eye (Lond)*. 2018;32:1703-1709.
101. Lim LS, Mitchell P, Seddon JM, Holz FG, Wong TY. Age-related macular degeneration. *Lancet*. 2012;379(9827):1728-1738.
102. Yonekawa Y, Miller JW, Kim IK. Age-related macular degeneration: advances in management and diagnosis. *J Clin Med*. 2015;4:343-359.
103. Smith W, Assink J, Klein R, et al. Risk factors for age-related macular degeneration: pooled findings from three continents. *Ophthalmology*. 2001;108:697-704.
104. Fraser-Bell S, Donofrio J, Wu J, et al. Sociodemographic factors and age-related macular degeneration in Latinos: the Los Angeles Latino Eye Study. *Am J Ophthalmol*. 2005;139:30-38.
105. Kawasaki R, Yasuda M, Song SJ, et al. The prevalence of age-related macular degeneration in Asians: a systematic review and meta-analysis. *Ophthalmology*. 2010;117:921-927.
106. Vingerling JR, Dielemans I, Hofman A, et al. The prevalence of age-related maculopathy in the Rotterdam Study. *Ophthalmology*. 1995;102:205-210.
107. Winkler TW, Brandl C, Grassmann F, et al. Investigating the modulation of genetic effects on late AMD by age and sex: Lessons learned and two additional loci. *PloS One*. 2018;13:e0194321.
108. Friedman DS, O'Colmain BJ, Muñoz B, et al. Prevalence of age-related macular degeneration in the United States. *Arch Ophthalmol*. 2004;122:564-572.
109. Klein R, Klein BE, Linton KL. Prevalence of age-related maculopathy. The Beaver Dam Eye Study. *Ophthalmology*. 1992;99:933-943.
110. Sasaki M, Harada S, Kawasaki Y, et al. Gender-specific association of early age-related macular degeneration with systemic and genetic factors in a Japanese population. *Sci Rep*. 2018;8:785.
111. Grassmann F, Friedrich U, Fauser S, et al. A candidate gene association study identifies DAPL1 as a female-specific susceptibility locus for age-related macular degeneration (AMD). *Neuromolecular Med*. 2015;17:111-120.
112. Kwon HJ, Lee SM, Pak KY, Park SW, Lee JE, Byon IS. Gender differences in the relationship between sex hormone deficiency and soft drusen. *Curr Eye Res*. 2017;42:1527-1536.
113. Smith W, Mitchell P, Wang JJ. Gender, oestrogen, hormone replacement and age-related macular degeneration: results from the Blue Mountains Eye Study. *Aust N Z J Ophthalmol*. 1997;25:13-15.
114. Vingerling JR, Dielemans I, Witteman JC, Hofman A, Grobbee DE, de Jong PT. Macular degeneration and early menopause: a case-control study. *BMJ*. 1995;310:1570-1571.
115. Edwards DR, Gallins P, Polk M, et al. Inverse association of female hormone replacement therapy with age-related macular degeneration and interactions with ARMS2 polymorphisms. *Invest Ophthalmol Vis Sci*. 2010;51:1873-1879.
116. Snow KK, Cote J, Yang W, Davis NJ, Seddon JM. Association between reproductive and hormonal factors and age-related maculopathy in postmenopausal women. *Am J Ophthalmol*. 2002;134:842-848.
117. Patnaik JL, Lynch AM, Wagner BD, et al. Hormone therapy as a protective factor for age-related macular degeneration. *Ophthalmic Epidemiol*. 2020;27:148-154.
118. Cho BJ, Heo JW, Shin JP, Ahn J, Kim TW, Chung H. Association between reproductive factors and age-related macular degeneration in postmenopausal women: the Korea National Health and Nutrition Examination Survey 2010-2012. *PloS One*. 2014;9:e102816.
119. Chakraborty R, Read SA, Vincent SJ. Understanding myopia: pathogenesis and mechanisms. In: Ang M, Wong TY, eds. *Updates on Myopia: A Clinical Perspective*. Springer; 2020:65-94.
120. Vitale S, Sperduto RD, Ferris FL. 3 rd Increased prevalence of myopia in the United States between 1971–1972 and 1999–2004. *Arch Ophthalmol*. 2009;127:1632-1639.

121. Gong JF, Xie HL, Mao XJ, et al. Relevant factors of estrogen changes of myopia in adolescent females. *Chin Med J (Engl)*. 2015;128(5):659-663. doi:10.4103/0366-6999.151669
122. Wickham LA, Gao J, Toda I, Rocha EM, Ono M, Sullivan DA. Identification of androgen, estrogen and progesterone receptor mRNAs in the eye. *Acta Ophthalmol Scand*. 2000 Apr; 78(2):146-153. doi:10.1034/j.1600-0420.2000.078002146.x
123. Xie HL, Mao XJ, Yang HH, Xie ZK, Pan Y, Gao Y. Analysis on the relationship between adolescent myopia and serum sex hormone. *Natl Med J China*. 2014;94:1294-1297.
124. Lee KE, Klein BE, Klein R, Quandt Z, Wong TY. Association of age, stature, and education with ocular dimensions in an older white population. *Arch Ophthalmol*. 2009;127:88-93.
125. Mitry D, Charteris DG, Fleck BW, Campbell H, Singh J. The epidemiology of rhegmatogenous retinal detachment: geographical variation and clinical associations. *Br J Ophthalmol*. 2010;94:678-684.
126. Wang J, McLeod D, Henson DB, Bishop PN. Age-dependent changes in the basal retinovitreous adhesion. *Invest Ophthalmol Vis Sci*. 2003;44:1793-1800.
127. Mahroo OA, Mitry D, Williamson TH, et al. Exploring sex and Laterality imbalances in patients undergoing laser Retinopexy. *JAMA Ophthalmol*. 2015;133:1334-1336.
128. Callaway NF, Vail D, Al-Moujahed A, et al. Sex Differences in the Repair of Retinal Detachments in the United States. *Am J Ophthalmol*. 2020;219:284-294.
129. Kishi S, Hagimura N, Shimizu K. The role of the premacular liquefied pocket and premacular vitreous cortex in idiopathic macular hole development. *Am J Ophthalmol*. 1996;122: 622-628.
130. McDonnell PJ, Fine SL, Hillis AI. Clinical features of idiopathic macular cysts and holes. *Am J Ophthalmol*. 1982;93: 777-786.
131. James M, Feman SS. Macular holes. *Albrecht Von Graefes Arch Klin Exp Ophthalmol*. 1980;215:59-63.
132. The Eye Disease Case-Control Study Group. Risk factors for idiopathic macular holes. *Am J Ophthalmol*. 1994;118:754-761.
133. Kobayashi K, Kobayashi H, Ueda M, Honda Y. Estrogen receptor expression in bovine and rat retinas. *Invest Ophthalmol Vis Sci*. 1998;39:2105-2110.
134. Rajabi MR, Solomon S, Poole AR. Activation of protein kinase C stimulates collagenase production by cultured cells of the cervix of the pregnant guinea pig. *Am J Obstet Gynecol*. 1992; 167:194-200.
135. Qiu QH, Chen ZY, Yin LL, Zheng Z, Wu XW. Effects of estrogen on collagen gel contraction by human retinal glial cells. *Chin Med J (Engl)*. 2012;125:4098-4103.
136. Inokuchi N, Ikeda T, Nakamura K, et al. Vitreous estrogen levels in patients with an idiopathic macular hole. *Clin Ophthalmol*. 2015;9:549-552.
137. Li B, Grafe S, Munchow A, Lopez-Toledano M, Pan ZH, Shen W. Sex-related differences in the progressive retinal degeneration of the rd10 mouse. *Exp Eye Res*. 2019;187:107773.
138. Blacharski P. Fundus flavimaculatus. In: Newsome DA, ed. *Retinal Dystrophies and Degenerations*. Raven Press; 1988: 135-139.
139. Lee W, Zernant J, Nagasaki T, Allikmets R. Reevaluating the association of sex with ABCA4 alleles in patients with stargardt disease. *JAMA Ophthalmol.* 2021;139:654-657.
140. Bouman A, Heineman MJ, Faas MM. Sex hormones and the immune response in humans. *Hum Reprod Update*. 2005;11: 411-423.
141. Klein SL. The effects of hormones on sex differences in infection: from genes to behavior. *Neurosci Biobehav Rev*. 2000;24:627-638.
142. Cáceres CF, Konda KA, Klausner JD. Syphilis in men who have sex with men: advancing research and human rights. *Lancet Glob Health*. 2021;9:e1039-e1040.
143. Tucker JD, Li JZ, Robbins GK, et al. Ocular syphilis among HIV-infected patients: a systematic analysis of the literature. *Sex Transm Infect*. 2011;87:4-8.
144. Yang P, Zhang N, Li F, Chen Y, Kijlstra A. Ocular manifestations of syphilitic uveitis in Chinese patients. *Retina*. 2012;32: 1906-1914.
145. Gangaputra S, Drye L, Vaidya V, Thorne JE, Jabs DA, Lyon AT. Non-cytomegalovirus ocular opportunistic infections in patients with acquired immunodeficiency syndrome. *Am J Ophthalmol*. 2013;155:206-212.e5.
146. Borkar DS, Tham VM, Esterberg E, et al. Incidence of herpes zoster ophthalmicus: results from the pacific ocular inflammation study. *Ophthalmology*. 2013;120:451-456.
147. Tugal-Tutkun I, Ötük-Yasar B, Altinkurt E. Clinical features and prognosis of herpetic anterior uveitis: a retrospective study of 111 cases. *Int Ophthalmol*. 2010;30:559-565.
148. Nakahara H, Kaburaki T, Takamoto M, et al. Statistical analyses of endogenous uveitis patients (2007–2009) in central Tokyo area and comparison with previous studies (1963–2006). *Ocul Immunol Inflamm*. 2015;23:291-296.
149. Roy R, Pal BP, Mathur G, et al. Acute retinal necrosis: clinical features, management and outcomes: a 10 year consecutive case series. *Ocul Immunol Inflamm*. 2014;22:170-174.
150. Sims JL, Yeoh J, Stawell RJ. Acute retinal necrosis: a case series with clinical features and treatment outcomes. *Clin Exp Ophthalmol*. 2009;37:473-477.
151. Spaide RF, Martin DF, Teich SA, et al. Successful treatment of progressive outer retinal necrosis syndrome. *Retina*. 1996;16: 479-487.
152. Sittivarakul W, Aui-aree N. Clinical features, management and outcomes of progressive outer retinal necrosis (PORN) in southern Thailand. *J Med Assoc Thai*. 2009;92:360-366.
153. Farizo KM, Buehler JW, Chamberland ME, et al. Spectrum of disease in persons with human immunodeficiency virus infection in the United States. *JAMA*. 1992;267:1798-1805.
154. Sugar EA, Jabs DA, Ahuja A, Thorne JE, Danis RP, Meinert CL. Incidence of cytomegalovirus retinitis in the era of highly active antiretroviral therapy. *Am J Ophthalmol*. 2012; 153:1016-1024.
155. Portela RW, Bethony J, Costa MI, et al. A multihousehold study reveals a positive correlation between age, severity of ocular toxoplasmosis, and levels of glycoinositolphospholipid-specific immunoglobulin A. *J Infect Dis*. 2004;190:175-183.
156. Lyons MR, Arantes T, Vieira BR, Furtado JM, Smith JR. Impact of gender on clinical features and outcomes of ocular toxoplasmosis. *Br J Ophthalmol*. 2023;bjo-2023-323227.
157. Fernandes Felix JP, Cavalcanti Lira RP, Grupenmacher AT, et al. Long-term results of trimethoprim-sulfamethoxazole versus placebo to reduce the risk of recurrent Toxoplasma Gondii Retinochoroiditis. *Am J Ophthalmol*. 2020;213: 195-202.

158. Braakenburg AMD, Crespi CM, Holland GN, et al. Recurrence rates of ocular toxoplasmosis during pregnancy. *Am J Ophthalmol*. 2014;157:767-773.
159. Reich M, Ruppenstein M, Becker MD, et al. Risk of recurrence of preexisting ocular toxoplasmosis during pregnancy. *Ocul Immunol Inflamm*. 2015;23:240-245.
160. Brydak- Godowska J, Borkowski PK, Rabczenko D, et al. Do pregnancy, postpartum period and lactation predispose to recurrent toxoplasmic retinochoroiditis. *Med Sci Monit*. 2015; 21:582-584.
161. Fairweather D, Frisancho-Kiss S, Rose NR. Sex differences in autoimmune disease from a pathological perspective. *Am J Pathol*. 2008;173:600-609.
162. Ravelli A, Felici E, Magni-Manzoni S, et al. Patients with antinuclear antibody-positive juvenile idiopathic arthritis constitute a homogeneous subgroup irrespective of the course of joint disease. *Arthritis Rheum*. 2005;52:826-832.
163. Hahn YS, Kim JG. Pathogenesis and clinical manifestations of juvenile rheumatoid arthritis. *Korean J Pediatr*. 2010;53: 921-930.
164. Kalinina Ayuso V, Makhotkina N, van Tent-Hoeve M, et al. Pathogenesis of juvenile idiopathic arthritis associated uveitis: the known and unknown. *Surv Ophthalmol*. 2014;59:517-531.
165. Edelsten C, Lee V, Bentley CR, et al. An evaluation of baseline risk factors predicting severity in juvenile idiopathic arthritis associated uveitis and other chronic anterior uveitis in early childhood. *Br J Ophthalmol*. 2002;86:51-56.
166. Saurenmann RK, Levin AV, Feldman BM, Laxer RM, Schneider R, Silverman ED. Risk factors for development of uveitis differ between girls and boys with juvenile idiopathic arthritis. *Arthritis Rheum*. 2010;62:1824-1828.
167. Ding Y, He J, Guo JP, et al. Gender differences are associated with the clinical features of systemic lupus erythematosus. *Chin Med J (Engl)*. 2012;125:2477-2481.
168. Stefanidou S, Benos A, Galanopoulou V, et al. Clinical expression and morbidity of systemic lupus erythematosus during a post-diagnostic 5-year follow-up: a male:female comparison. *Lupus*. 2011;20:1090-1094.
169. Costenbader KH, Feskanich D, Stampfer MJ, et al. Reproductive and menopausal factors and risk of systemic lupus erythematosus in women. *Arthritis Rheum*. 2007;56:1251-1262.
170. Rider V, Li X, Peterson G, et al. Differential expression of estrogen receptors in women with systemic lupus erythematosus. *J Rheumatol*. 2006;33:1093-1101.
171. Crosbie D, Black C, McIntyre L, Royle PL, Thomas S. Dehydroepiandrosterone for systemic lupus erythematosus. *Cochrane Database Syst Rev*. 2007;2007:CD005114.
172. Alvarez-Nemegyei J, Cobarrubias-Cobos A, Escalante-Triay F, Sosa-Muñoz J, Miranda JM, Jara LJ. Bromocriptine in systemic lupus erythematosus: a double-blind, randomized, placebo-controlled study. *Lupus*. 1998;7:414-419.
173. Rosati G. The prevalence of multiple sclerosis in the world: an update. *Neurol Sci*. 2001;22:117-139.
174. Bergamaschi R. Prognostic factors in multiple sclerosis. *Int Rev Neurobiol*. 2007;79:423-447.
175. Zein G, Berta A, Foster CS. Multiple sclerosis-associated uveitis. *Ocul Immunol Inflamm*. 2004;12:137-142.
176. Chen L, Gordon LK. Ocular manifestations of multiple sclerosis. *Curr Opin Ophthalmol*. 2005;16:315-320.
177. Hillerdal G, Nöu E, Osterman K, Schmekel B. Sarcoidosis: epidemiology and prognosis. A 15-year European study. *Am Rev Respir Dis*. 1984;130:29-32.
178. Judson MA, Boan AD, Lackland DT. The clinical course of sarcoidosis: presentation, diagnosis, and treatment in a large white and black cohort in the United States. *Sarcoidosis Vasc Diffuse Lung Dis*. 2012;29:119-127.
179. Umur KA, Tayfun B, Oguzhan O. Different ophthalmologic manifestations of sarcoidosis. *Curr Opin Ophthalmol*. 2012;23: 477-484.
180. Bordaberry MF. Vogt-Koyanagi-Harada disease: diagnosis and treatments update. *Curr Opin Ophthalmol*. 2010;21:430-435.
181. Elias A, Gopalakrishnan M, Bhat S, et al. Vogt-Koyanagi-Harada disease clinical course, therapy, complications and prognosistic factors. *World J Retina Vitreous*. 2012;2:46-52.
182. Aláez C, Flores-A H, Concha del Río LE, et al. Major histocompatibility complex and strong human leukocyte antigen-DRB1 and gender association with Vogt-Koyanagi-Harada syndrome in Mexican Mestizos. *Hum Immunol*. 2011;72:1198-1203.
183. Wang LY, Zhao DB, Gu J, Dai SM. Clinical characteristics of Behçet's disease in China. *Rheumatol Int*. 2010;30:1191-1196.
184. Yazici H, Tuzun Y, Tanman AB, et al. Male patients with Behcet's syndrome have stronger pathergy reactions. *Clin Exp Rheumatol*. 1985;3:137-141.
185. Matsuo T, Itami M. Recurrent versus non-recurrent or no eye involvement in Behcet's disease. *Ocul Immunol Inflamm*. 2005;13:73-77.
186. Miayamoto N, Mandai M, Suzuma I, et al. Estrogen protects against cellular infiltration by reducing the expressions of E-selectin and IL-6 in endotoxin-induced uveitis. *J Immunol*. 1999;163:374-379.
187. Smith WM. Gender and spondyloarthropathy-associated uveitis. *J Ophthalmol*. 2013;2013:928264.
188. Suhler EB, Martin TM, Rosenbaum JT. HLA-B27-associated uveitis: overview and current perspectives. *Curr Opin Ophthalmol*. 2003;14:378-383.
189. Monnet D, Breban M, Hudry C, et al. Ophthalmic findings and frequency of extraocular manifestations in patients with HLA-B27 uveitis: a study of 175 cases. *Ophthalmology*. 2004; 111:802-809.
190. Uy HS, Christen WG, Foster CS. HLA-B27-associated uveitis and cystoid macular edema. *Ocul Immunol Inflamm*. 2001;9:177-183.
191. Braakenburg AM, de Valk HW, de Boer J, et al. Human leukocyte antigen-B27-associated uveitis: long-term follow-up and gender differences. *Am J Ophthalmol*. 2008;145:472-479.
192. Agnani S, Choi D, Martin TM, et al. Gender and laterality affect recurrences of acute anterior uveitis. *Br J Ophthalmol*. 2010;94:1643-1647.
193. Yeung IY, Popp NA, Chan CC. The role of gender in uveitis and ocular inflammation. *Int Ophthalmol Clin*. 2015;55:111-131.

How to cite this article: Tillmann A, Ceklic L, Dysli C, Munk MR. Gender differences in retinal diseases: A review. *Clin Exp Ophthalmol*. 2024; 1-17. doi:10.1111/ceo.14364