الجمهورية الجزائرية الديمقراطية الشعبية
DEMOCRATIC AND POPULAR ALGERIAN REPUBLIC
وزارة التعليم العالي والبحث العلمي
MINISTRY OF HIGHER EDUCATION AND SCIENTIFIC RESEARCH
جامعة الشهيد حمه لخضر الوادي
ECHAHID HAMMA LAKHDAR UNIVERSITY OF EL-OUED
كلية العلوم الطبيعية والحياة
FACULTY OF NATURAL SCIENCES AND LIFE
قسم البيولوجيا الخلوية والجزيئية
DEPARTMENT OF CELLULAR AND MOLECULAR BIOLOGY

Master's Thesis

In order to obtain a diploma of an Academic Master

In biological sciences

Specialty: Applied Biochemistry

Theme

Evaluation of Risk Factors and Predictive Biomarkers in Ocular Inflammatory Diseases: A Receiver Operating Characteristic Curve-Based Study

Presented by:

Miss: ROUAG Amani

Miss: HATHROUBI Khadidja

President	**Dr. Kadri Mounira**	**M.C. A**	**El-Oued University**
Examiner	**Dr. Aouimeur Meriem**	**M.A. A**	**El-Oued University**
Supervisor	**Prof. DEROUICHE Samir**	**Professor**	**El-Oued University**
Co-Supervisor	**Dr. CHETTHOUNA Sara**	**M.C. A**	**M'sila University**

University year: 2026/2025

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ

سورة يوسف الآية 76

صَدَقَ اللَّهُ العَظِيمُ

إهداء

إلى نفسي...

إلى تلك الفتاة التي حملت أحلامها بين يديها وسارت بها وسط الطرق الوعرة، إلى التي تعثرت أحيانًا لكنها لم تسمح للسقوط أن يكون نهاية الحكاية، إلى التي قاومت التعب والقلق والخذلان وضغط الأيام، وآمنت أن وراء كل ليلة طويلة فجرًا يستحق الانتظار. أهدي هذا الإنجاز لنفسي، لأنني كنتُ شاهدة على كل معركة خضتها بصمت، وعلى كل دمعة أخفيتها خلف ابتسامة، وعلى كل مرة اخترت فيها الاستمرار رغم صعوبة الطريق.

أبي الغالي...

إلى أول رجل آمنت بقوته، وإلى السند الذي لم يخذلني يومًا، إلى من علمني أن النجاح يُصنع بالإرادة والعمل، إلى من كان دعمه صامتًا لكنه عظيم الأثر في قلبي، أهديك هذا العمل عربون حب ووفاء، وأسأل الله أن يطيل في عمرك ويجزيك عني خير الجزاء.

أمي الحبيبة ...

إلى الحضن الذي أعود إليه مهما أثقلتني الحياة، إلى القلب الذي أحبني قبل أن يراني أحد، إلى المرأة التي كانت تدعو لي في الخفاء بينما كنت أسعى في العلن، إلى التي سهرت من أجل راحتي، وفرحت لفرحي أكثر مما فرحت أنا به، وتألمت لألمي دون أن تشكو. يا أمي، مهما كتبت فلن أوفيك حقك، فكل نجاح أصل إليه يحمل بصمتك، وكل خطوة أخطوها نحو المستقبل تقف خلفها تضحياتك العظيمة. حفظك الله وأدامك نورًا يضيء حياتي وسندًا لا يميل.

أختي الوحيدة رانيا...

إلى قطعة من قلبي لا تشبه أحدًا، إلى من شاركتني تفاصيل العمر وأسراره، وضحكاته ودموعه، إلى أخت لم تكن يومًا مجرد أخت، بل كانت صديقة ورفيقة وسندًا في أوقات كثيرة. وجودك في حياتي نعمة أحمد الله عليها كل يوم، وأدعو أن تبقي دائمًا قريبة من قلبي كما كنتِ دائمًا.

إخوتي الأعزاء توفيق ومحمد إبراهيم...

إلى من يجمعني بهم رابط لا تصنعه الأيام ولا تضعفه المسافات، إلى إخوتي الذين كانوا جزءًا من كل ذكرى جميلة في حياتي، والذين كنت أجد في وجودهم قوة وطمأنينة. أهديكم هذا الإنجاز بمحبة كبيرة، وأتمنى أن يكون فخرنا ببعضنا دائمًا أكبر من كل نجاح نحققه.

صديقتي ورفيقة دربي في هذا العمل خديجة...

إلى صديقة العمر، ورفيقة السنوات الجميلة، إلى الأخت التي لم تلدها أمي، إلى من كانت شاهدة على أحلامي ومخاوفي، وعلى لحظات ضعفي وقوتي، إلى من شاركتني تفاصيل هذه الرحلة العلمية يومًا بيوم، وفرحتي قبل أن تكتمل، وتعبي قبل أن يُروى.

لم تكوني مجرد شريكة في إنجاز هذه المذكرة، بل كنتِ رفيقة دربٍ حقيقية، نتقاسم الأمل حين يشتد التعب، ونزرع التفاؤل حين تتراكم الصعوبات. شكراً لأنك كنتِ السند في لحظات الإرهاق، والرفقة الطيبة في أيام العمل الطويلة، والصديقة التي أزداد فخرًا بها كلما مرت السنوات.

سيبقى هذا العمل شاهدًا على رحلة جمعت بين الاجتهاد والصداقة، وستبقى ذكريات هذه المرحلة من أجمل ما أحمله في قلبي ما حييت.

أستاذتي الفاضلة الدكتورة ساره شتحونه...

إلى من أنارت لي الطريق بعلمها وتوجيهها، وكانت سنداً أكاديمياً حقيقياً خلال هذه الرحلة، إلى من لم تبخل عليّ بوقتها ولا بنصائحها، فكان لحضورها ودعمها أثرٌ كبير في إتمام هذا العمل.

شكراً لكِ لأنكِ كنتِ مثالاً للعطاء والإخلاص، ولأنكِ تركتِ في نفسي أثراً سيبقى أكبر من صفحات هذه المذكرة. أسأل الله أن يجزيكِ عني خير الجزاء، وأن يبارك في علمكِ وعملكِ.

إلى أستاذي الفاضل البروفيسور سمير درويش...

إلى القامة العلمية التي طالما كانت مصدر فخرٍ واعتزاز لطلبتها، وإلى القدوة التي تعلمنا منها أن العلم لا يكتمل إلا بالتواضع والأخلاق والإخلاص.

شكراً لكم على ما قدمتموه من علمٍ نافع وتوجيهٍ قيّم، وعلى دعمكم ومرافقتكم لنا في هذه الرحلة العلمية. لقد كنتم بالنسبة لنا أكثر من أستاذ ومؤطر؛ كنتم مثالاً يُحتذى به في الجدية والعطاء والتميز، وشخصيةً تركت أثرها في نفوس طلبتها قبل عقولهم.

أسأل الله أن يجزيكم خير الجزاء، وأن يبارك في علمكم وعملكم، وأن تبقوا منارةً يستضيء بها كل طالب علم يسعى للنجاح والتميز.

وأخيرًا...

إلى كل من ترك في حياتي أثرًا جميلًا، إلى كل من منحني كلمة تشجيع في وقت احتجتها، أو رفع يديه داعيًا لي بالتوفيق، أهديكم جميعًا ثمرة سنوات من الجهد والأمل، وأسأل الله أن يجعل هذا العمل بداية لأحلام أكبر، ونجاحات أجمل، ومستقبل يليق بكل ما بذلته من أجل الوصول إلى هذه اللحظة.

إهداء

بسم الله الرحمن الرحيم، والحمد لله الذي بنعمته تتم الصالحات، والذي وفقني ومنحني القوة والصبر حتى أصل إلى هذه اللحظة التي أقطف فيها ثمرة سنوات من الاجتهاد والتعب.

إلى نفسي...

إلى تلك التي لم ترَ الطريق سهلًا يومًا، لكنها لم تتوقف رغم التعب، ولم تنكسر رغم الضغط، ولم تتراجع رغم كل لحظات الشك، إلى من حملت حلمها بصمت، وواجهت العالم بقوة هادئة لا يعرفها إلا قلبها.

أهدي هذا الإنجاز بكل ما فيه من تعب وسهر وصبر، وبكل لحظة كنت فيها على وشك الاستسلام ثم اخترت أن أكمّل. أنا لست مجرد نتيجة، بل رحلة طويلة من الإصرار، من السقوط والقيام، من الألم الذي تحوّل إلى قوة.

اليوم أقف بفخر... ليس لأن الطريق انتهى، بل لأنني كنت أنا الطريق، وكنت أنا من صنع هذا الوصول.

أبي الغالي...

إلى الرجل الذي كان ولا يزال مصدر الأمان والقوة في حياتي، إلى من تعب وسعى وضحّى من أجل أن يراني في أعلى المراتب. مهما كتبت من كلمات فلن أوفيك حقك، فأنت السند الذي استندت إليه كلما تعبت، وأنت الفخر الذي أحمله في قلبي أينما ذهبت. أهديك هذا الإنجاز عربون محبة وامتنان، وأسأل الله أن يحفظك ويمدك بالصحة والعافية.

أمي الحبيبة...

إلى القلب الذي أحبني دون شروط، وإلى اليد التي امتدت بالدعاء في كل حين، وإلى الروح التي كانت تبث في نفسي الطمأنينة كلما ضاقت بي السبل. أمي، لولا دعواتك وصبرك وحنانك لما وصلت إلى ما أنا عليه اليوم. هذا النجاح هو جزء من عطائك، وأنتِ أول من يستحق أن أُهدي إليه ثمرة هذا الجهد.

أخواتي العزيزات نسرين وخولة...

إلى من شاركوني تفاصيل حياتي وفرحتي وأحلامي، إلى من وجدت معهما المحبة الصادقة والاهتمام والدعم في كل المراحل. شكرًا لكل كلمة تشجيع، ولكل لحظة وقفتما فيها إلى جانبي، ولكل دعاء صادق خرج من قلبيكما من أجلي. وجودكما كان نعمة عظيمة وسندًا جميلًا لا يقدر بثمن.

إخوتي الأعزاء سليم وبلال وكمال...

إلى من كانوا دائمًا مصدر قوة وفخر، وإلى من تقاسمت معهم أجمل الذكريات وأصدق المشاعر. أشكركم على دعمكم المتواصل ومحبتكم الصادقة، وعلى ثقتكم الدائمة بي. أسأل الله أن يديم بيننا المودة وأن يرزقكم من النجاح والسعادة أضعاف ما تتمنونه لي.

صديقة العمر أماني...

توأم الروح ورفيقة أجمل سنوات الدراسة، إلى من كانت تشاركني أحلامي وتفاصيلي الصغيرة قبل الكبيرة، وإلى من كانت حاضرة في لحظات التعب قبل الفرح. شكراً لأنك كنتِ دائمًا ذلك الوجه المطمئن والكلمة الصادقة والقلب الذي أجد فيه الدعم دون أن أطلبه. لقد كانت رحلتي الجامعية أجمل بوجودك، وستبقى ذكرياتنا معًا من أثمن ما أحمله من هذه المرحلة. أسأل الله أن يديم صداقتنا وأن يجمع بيننا دائمًا على الخير والمحبة.

الدكتورة ساره شتحونه...

أستاذتي الفاضلة التي لم تبخل عليّ يومًا بعلمها ونصحها وتوجيهاتها، والتي رافقت هذا العمل بعناية وصبر واهتمام.

أتقدم لكِ بخالص الشكر والامتنان على كل جهد بذلته من أجلي، وعلى كل كلمة تشجيع منحتني الثقة للاستمرار. سيبقى فضلكِ محفورًا في ذاكرتي، وسيبقى تقديري لكِ كبيرًا بقدر ما قدمتِه لي من دعم ومرافقة خلال إنجاز هذه المذكرة.

البروفيسور سمير درويش...

أكتب هذه الكلمات وكلّي امتنان لا تستطيع العبارات أن تفيه حقه، فقد كان لإشرافه على هذه المذكرة أثرٌ بالغ في كل مراحل إنجازها، إذ لم يكن مجرد مشرف، بل كان سندًا علميًا حقيقيًا، بتوجيهاته الدقيقة ونصائحه الصادقة التي كانت تنير لي الطريق كلما تعثّرت الخطوات.

أتقدم بجزيل الشكر على صبره واهتمامه وتشجيعه الذي منحني القوة للاستمرار رغم الصعوبات، وعلى ثقته التي كانت دافعًا لي لتقديم الأفضل في كل مرة، وسيبقى اسمه محفورًا في هذه المرحلة من مسيرتي العلمية بكل تقدير وامتنان، وأسأل الله أن يجزيه عني خير الجزاء وأن يبارك له في علمه وعمله.

إلى السيد بوبكر نصيرة

مسيّر مكتبة الباحث، بكل مشاعر الامتنان والوفاء، تقديرًا لما قدمه لنا من دعم ومساعدة طوال خمس سنوات من مسيرتنا الجامعية. كان حاضرًا بعلمه وتعاونه وطيب أخلاقه، فترك في نفوسنا أثرًا جميلًا سيبقى راسخًا في الذاكرة. فله منا أسمى عبارات الشكر والتقدير والاحترام.

ختاما

ها قد أسدلت الستائر على هذه المذكرة، لكنها ليست نهاية، بل بداية جديدة على طريق العلم والمعرفة. كل صفحة كتبتها، وكل فكرة بحثتها، كانت خطوة في رحلة طويلة من التعلم والتحدي، رحلة علمتني أن الاجتهاد والصبر يولدان النتائج

ما هذا الإنجاز إلا بداية لطريق أطول من الطموح والعطاء، وأسأل الله أن يوفقني ومن أحب إلى كل خير ونجاح.

Acknowledgements

First and foremost, we thank Allah, the Almighty, for granting us the strength, patience, and guidance to complete this work.

We would like to express our deepest gratitude to our supervisor, ***Prof. DEROUICHE Samir****, for his valuable advice, continuous support, and encouragement throughout this research. We also extend our sincere thanks to our co-supervisor,* ***Dr. CHETTHOUNA Sara****, for her guidance, scientific insights, and kind support during our work.*

We are honored to express our sincere gratitude to the members of the jury for their time, interest, and for accepting to evaluate our research work.

We would like to express our special thanks to the staff and administration of the Cuba Friendship Hospital for Ophthalmology El-Oued and Al Wifaq Clinic (Clinique El Wifaq) for their valuable cooperation, assistance, and continuous support, which greatly contributed to the successful completion of this study.

We also extend our appreciation to the University Interface Center (Incubator) for their support and for providing the necessary environment to conduct this research.

Our heartfelt thanks go to our families for their unconditional love, encouragement, and sacrifices throughout our academic journey. Finally, we would like to thank all our colleagues, friends, and everyone who contributed, directly or indirectly, to the successful completion of this academic project.

May Allah reward them all for their support and kindness.

Abstract

Ocular inflammatory diseases represent a multifactorial health problem whose occurrence and progression depend on the interaction of environmental, occupational, clinical, biological, and oxidative stress-related factors. Although the eye possesses natural defense mechanisms, including tears, eyelids, and local immune responses, it remains highly susceptible to external aggressors that may induce bacterial, viral, and allergic inflammation. The aim of this study was to investigate the main risk factors associated with these different forms of ocular inflammation and to evaluate the diagnostic value of selected biological and oxidative stress markers. Our socioeconomic risk factors study based on a questionnaire involving 121 participants, including 61 healthy individuals and 60 patients suffering from ocular inflammation. In addition, a biological study was conducted on 38 volunteers in order to analyze selected biological markers (Hematological, Biochemical and oxidative stress markers) related to inflammation. The results obtained in this study highlighted the diversity of factors involved in ocular inflammation. Bacterial ocular infections were strongly associated with several environmental and occupational exposures, particularly dust exposure (OR = 100.000), machine and factory smoke (OR = 44.348), foreign body entry into the eye (OR = 28.889), and industrial work (OR = 15.818), indicating that environmental and workplace conditions play a major role in the development and aggravation of bacterial ocular inflammation. Clinical factors also showed significant associations, with eye rubbing emerging as the strongest risk factor (OR = 140.000), followed by the use of antibiotic eye drops (OR = 95.145), severe ocular itching (OR = 52.308), and family history (OR = 12.727), suggesting that ocular irritation, repeated mechanical trauma, and individual susceptibility contribute substantially to bacterial infection. Viral ocular inflammation was found to be more closely associated with factors related to disease transmission and direct contact. Eye rubbing and contact with individuals presenting similar symptoms represented the strongest risk factors (OR = 240.000 for both), while severe itchy eye and skin allergy (OR = 90.000 for both) were also significantly associated with viral inflammation. These findings suggest that direct transmission, close interpersonal contact, and behavioral factors play a crucial role in the spread and persistence of viral ocular infections. Similarly, allergic ocular inflammation showed strong associations with environmental allergens and clinical predisposition factors. Dust exposure represented the most important environmental risk factor (OR = 120.000), followed by exposure to animals (OR = 40.000) and pollen (OR = 30.000), confirming the major contribution of airborne allergens to disease onset. In addition, eye rubbing (OR = 165.000), mild itchy eye (OR = 390.000), and antihistamine use (OR = 390.000) showed very strong associations, while seasonal variation and family history further contributed to disease occurrence, indicating that allergic ocular

disease results from a complex interaction between environmental exposure, behavioral factors, and genetic predisposition. The analysis of oxidative stress and biological markers revealed significant diagnostic and predictive performance in ocular inflammatory diseases. In bacterial infections, plasma and tears MDA and GSH showed excellent diagnostic accuracy with high sensitivity (100%) and AUC values of 1.000, while protein, platelet, neutrophil, and basophil count also demonstrated perfect predictive performance (AUC = 1.000), suggesting that both oxidative stress imbalance and hematological changes play a major role in bacterial ocular inflammation. In contrast, SOD and catalase showed low or non-significant diagnostic value, indicating limited predictive relevance. In viral ocular inflammation, tears MDA (AUC = 0.960) and plasma MDA (AUC = 0.880) demonstrated strong predictive performance, alongside monocyte count (AUC = 0.960) and platelet count (AUC = 1.000), indicating that oxidative stress and immune cell alterations are closely involved in viral infection progression. Conversely, SOD, catalase, and several routine biochemical parameters showed weak or non-significant diagnostic value, suggesting limited utility as predictive biomarkers. In allergic ocular inflammation, most oxidative stress markers including plasma and tears MDA, GSH, catalase, and several hematological parameters demonstrated excellent predictive performance with AUC values reaching 1.000 in most cases. Monocyte count also showed strong diagnostic value (AUC = 0.980), indicating a major role of immune response activation and oxidative imbalance in allergic ocular disease pathophysiology. In conclusion, ocular inflammatory diseases are influenced by a combination of environmental, occupational, clinical, and immunological factors. In addition, oxidative stress and hematological alterations appear to play a central role in disease mechanisms and demonstrate strong diagnostic and predictive value, particularly MDA, GSH, platelet, and neutrophil-related parameters. These findings highlight the importance of early diagnosis, accurate differentiation between inflammatory types, and the use of oxidative stress biomarkers as potential tools for screening, monitoring, and therapeutic follow-up of ocular inflammatory diseases.

Key Words:

Ocular inflammatory diseases, Risk factors, Predictive biomarkers, Oxidative stress, ROC curve

Résumé

Les maladies inflammatoires oculaires représentent un problème de santé multifactoriel dont l'apparition et la progression dépendent de l'interaction de facteurs environnementaux, professionnels, cliniques, biologiques et liés au stress oxydatif. Bien que l'œil possède des mécanismes naturels de défense, notamment les larmes, les paupières et les réponses immunitaires locales, il demeure très vulnérable aux agressions externes pouvant provoquer des inflammations bactériennes, virales et allergiques. Cette étude avait pour objectif d'identifier les principaux facteurs de risque associés à ces différentes formes d'inflammation oculaire et d'évaluer la valeur diagnostique de certains marqueurs biologiques et du stress oxydatif. Notre étude des facteurs de risque socio-économiques a été réalisée à l'aide d'un questionnaire impliquant 121 participants, dont 61 sujets sains et 60 patients atteints d'inflammation oculaire. En outre, une étude biologique a été menée sur 38 volontaires afin d'analyser plusieurs marqueurs biologiques sélectionnés (hématologiques, biochimiques et du stress oxydatif) liés à l'inflammation. Les résultats ont mis en évidence la diversité des facteurs impliqués dans l'inflammation oculaire. Les infections oculaires bactériennes étaient fortement associées à plusieurs expositions environnementales et professionnelles, notamment l'exposition à la poussière (OR = 100,000), à la fumée des machines et des usines (OR = 44,348), à l'introduction de corps étrangers dans l'œil (OR = 28,889) et au travail industriel (OR = 15,818). Ces résultats indiquent que les conditions environnementales et professionnelles jouent un rôle majeur dans le développement et l'aggravation de l'inflammation oculaire bactérienne. Les facteurs cliniques ont également montré des associations significatives, le frottement des yeux constituant le principal facteur de risque (OR = 140,000), suivi de l'utilisation de collyres antibiotiques (OR = 95,145), du prurit oculaire sévère (OR = 52,308) et des antécédents familiaux (OR = 12,727). L'inflammation oculaire virale était davantage associée aux facteurs liés à la transmission de la maladie et au contact direct. Le frottement des yeux et le contact avec des personnes présentant des symptômes similaires représentaient les facteurs de risque les plus importants (OR = 240,000 pour chacun), tandis que le prurit oculaire sévère et les allergies cutanées (OR = 90,000 pour chacun) étaient également fortement associés à cette forme d'inflammation. De même, l'inflammation oculaire allergique présentait de fortes associations avec les allergènes environnementaux et les facteurs de prédisposition clinique. L'exposition à la poussière représentait le principal facteur de risque environnemental (OR = 120,000), suivie de l'exposition aux animaux (OR = 40,000) et au pollen (OR = 30,000). En outre, le frottement des yeux (OR = 165,000), le prurit oculaire léger (OR = 390,000) et l'utilisation d'antihistaminiques (OR = 390,000) ont montré des associations très fortes. L'analyse des marqueurs du stress oxydatif et des paramètres biologiques a révélé une

performance diagnostique et prédictive significative dans les maladies inflammatoires oculaires. Dans les infections bactériennes, le MDA et le GSH plasmatiques et lacrymaux ont présenté une excellente précision diagnostique avec une sensibilité de 100 % et une AUC de 1,000. Les protéines totales, les plaquettes, les neutrophiles et les basophiles ont également montré une performance prédictive parfaite (AUC = 1,000). En revanche, la SOD et la catalase ont présenté une faible valeur diagnostique. Dans l'inflammation oculaire virale, le MDA lacrymal (AUC = 0,960), le MDA plasmatique (AUC = 0,880), les monocytes (AUC = 0,960) et les plaquettes (AUC = 1,000) ont montré une forte capacité prédictive. À l'inverse, la SOD, la catalase et plusieurs paramètres biochimiques de routine ont présenté une faible utilité diagnostique. Dans l'inflammation oculaire allergique, la majorité des marqueurs du stress oxydatif, notamment le MDA, le GSH et la catalase, ainsi que plusieurs paramètres hématologiques, ont présenté d'excellentes performances prédictives avec des valeurs d'AUC atteignant 1,000 dans la plupart des cas. Les monocytes ont également montré une forte valeur diagnostique (AUC = 0,980). En conclusion, les maladies inflammatoires oculaires sont influencées par une combinaison de facteurs environnementaux, professionnels, cliniques et immunologiques. De plus, le stress oxydatif et les altérations hématologiques semblent jouer un rôle central dans les mécanismes pathologiques et présentent une forte valeur diagnostique et prédictive, en particulier le MDA, le GSH, les plaquettes et les neutrophiles. Ces résultats soulignent l'importance du diagnostic précoce, de la différenciation précise entre les différents types d'inflammation et de l'utilisation des biomarqueurs du stress oxydatif comme outils potentiels de dépistage, de suivi et d'évaluation thérapeutique.

Mots-clés :

Maladies inflammatoires oculaires, Facteurs de risque, Biomarqueurs prédictifs, Stress oxydatif, Courbe ROC.

الملخص

تمثل الأمراض الالتهابية العينية مشكلة صحية متعددة العوامل، إذ يعتمد حدوثها وتطورها على التفاعل بين العوامل البيئية والمهنية والسريرية والبيولوجية والعوامل المرتبطة بالإجهاد التأكسدي. وعلى الرغم من امتلاك العين لآليات دفاع طبيعية تشمل الدموع والجفون والاستجابات المناعية الموضعية، فإنها تظل شديدة التأثر بالعوامل الخارجية التي قد تؤدي إلى حدوث التهابات بكتيرية أو فيروسية أو تحسسية. هدفت هذه الدراسة إلى تحديد أهم عوامل الخطر المرتبطة بهذه الأشكال المختلفة من الالتهابات العينية، وتقييم القيمة التشخيصية لبعض المؤشرات البيولوجية ومؤشرات الإجهاد التأكسدي المختارة. أُجريت دراسة عوامل الخطر الاجتماعية والاقتصادية باستخدام استبيان شمل 121 مشاركًا، منهم 61 فردًا سليمًا و60 مريضًا يعانون من التهابات عينية. بالإضافة إلى ذلك، أُجريت دراسة بيولوجية على 38 متطوعًا لتحليل مجموعة من المؤشرات البيولوجية المرتبطة بالالتهاب، بما في ذلك المؤشرات الدموية والكيميائية الحيوية ومؤشرات الإجهاد التأكسدي. أظهرت النتائج تنوع العوامل المتدخلة في حدوث الالتهابات العينية. فقد ارتبطت الالتهابات العينية البكتيرية بشكل قوي بعدة عوامل بيئية ومهنية، خاصة التعرض للغبار (OR = 100.000)، ودخان الآلات والمصانع(OR = 44.348) ، ودخول الأجسام الغريبة إلى العين (OR = 28.889)، والعمل الصناعي .(OR = 15.818) كما أظهرت العوامل السريرية ارتباطات مهمة، حيث كان فرك العينين أقوى عامل خطر(OR = 140.000) ، يليه استعمال القطرات العينية المضادة للمضادات الحيوية(OR = 95.145) ، والحكة العينية الشديدة(OR = 52.308) ، والتاريخ العائلي المرضي (OR = 12.727). أما الالتهابات العينية الفيروسية فقد ارتبطت بصورة أكبر بعوامل انتقال العدوى والاتصال المباشر. وكان فرك العينين والاتصال بأشخاص لديهم أعراض مشابهة من أقوى عوامل الخطر (OR = 240.000)لكل منهما، كما ارتبطت الحكة العينية الشديدة والحساسية الجلدية ارتباطًا قويًا بهذا النوع من الالتهاب. وبالمثل، أظهرت الالتهابات العينية التحسسية ارتباطًا وثيقًا بالمحسسات البيئية وعوامل الاستعداد السريري. وكان التعرض للغبار أهم عامل بيئي(OR = 120.000) ، يليه التعرض للحيوانات (OR = 40.000)وحبوب اللقاح .(OR = 30.000) كما أظهر فرك العينين(OR = 165.000) ، والحكة العينية الخفيفة(OR = 390.000) ، واستعمال مضادات الهيستامين (OR = 390.000) ارتباطات قوية جدًا. كشفت تحاليل مؤشرات الإجهاد التأكسدي والمؤشرات البيولوجية عن أداء تشخيصي وتنبؤي مهم في الأمراض الالتهابية العينية. ففي الالتهابات البكتيرية، أظهر كل من MDA و GSHفي البلازما والدموع دقة تشخيصية ممتازة مع حساسية بلغت 100% وقيم AUC بلغت 1.000. كما أظهرت البروتينات الكلية والصفائح الدموية والعدلات والخلايا القاعدية أداءً تنبؤيًا مثاليًا .(AUC = 1.000) في المقابل، أظهرت إنزيمات SOD و Catalaseقيمة تشخيصية ضعيفة أو غير معنوية. في الالتهابات الفيروسية، أظهر MDAفي الدموع (AUC = 0.960) و MDAالبلازمي (AUC = 0.880) أداءً تنبؤيًا قويًا، إلى جانب عدد الوحيدات (AUC = 0.960) والصفائح الدموية .(AUC = 1.000) بينما كانت القيمة التشخيصية

لـ SOD و Catalaseوعدة مؤشرات كيميائية حيوية روتينية محدودة. أما في الالتهابات التحسسية، فقد أظهرت معظم مؤشرات الإجهاد التأكسدي، بما فيها MDA و GSHوCatalase، بالإضافة إلى عدة مؤشرات دموية، أداءً تنبؤيًا ممتازًا مع قيم AUC بلغت 1.000 في أغلب الحالات. كما أظهر عدد الوحيدات قيمة تشخيصية مرتفعة.(AUC = 0.980)

في الختام، تتأثر الأمراض الالتهابية العينية بمزيج من العوامل البيئية والمهنية والسريرية والمناعية. كما يبدو أن الإجهاد التأكسدي والتغيرات الدموية يلعبان دورًا محوريًا في آليات المرض، ويظهران قيمة تشخيصية وتنبؤية عالية، خاصة بالنسبة لـ MDA و GSHوالصفائح الدموية والعدلات. وتبرز هذه النتائج أهمية التشخيص المبكر، والتمييز الدقيق بين أنواع الالتهابات المختلفة، واستخدام مؤشرات الإجهاد التأكسدي كأدوات محتملة للكشف المبكر والمتابعة والتقييم العلاجي للأمراض الالتهابية العينية.

الكلمات المفتاحية:

الأمراض الالتهابية العينية؛ عوامل الخطر؛ المؤشرات الحيوية التنبؤية؛ الإجهاد التأكسدي؛ منحنى ROC.

Abbreviation List

4-HNE:	4-Hydroxynonenal
AUC:	Area Under the Curve
BHT:	Butylated Hydroxytoluene
BK:	Bacterial Keratitis
CAT:	Catalase
CL:	Contact Lens
CRP:	C-Reactive Protein
DNA:	Deoxyribonucleic Acid
DTNB:	5,5'-Dithiobis-(2-nitrobenzoic acid)
GSH:	Reduced Glutathione
HAdV:	Human Adenovirus
HSV:	Herpes Simplex Virus
HSV-1:	Herpes Simplex Virus Type 1
MDA:	Malondialdehyde
NBT:	Nitro blue Tetrazolium
NO Synthase:	Nitric Oxide Synthase
OR:	Odds Ratio
OSDI:	Ocular Surface Disease Index
RBC:	Red Blood Cells
RNS:	Reactive Nitrogen Species
ROC:	Receiver Operating Characteristic
ROS:	Reactive Oxygen Species
SOD:	Superoxide Dismutase
TBA:	Thio barbituric Acid
TBUT:	Tear Break-Up Time
TCA:	Trichloroacetic Acid
TLR:	Toll-Like Receptor
UVR:	Ultraviolet Radiation

List of Figures

Figure 1: Schematic drawing of the human eye 4
Figure 2: The schematic of the cornea layers. 5
Figure 3: Basic scleral anatomy 5
Figure 4: Conjunctiva of the eye 6
Figure 5: The Structure of the Crystalline Lens 7
Figure 6: The neuroanatomy of the retina 8
Figure 7: Lacrimal system anatomy 8
Figure 8: Current conceptualization of tear film structure.. 10
Figure 9: The major cells and molecules promoting ocular surface immune homeostasis. 12
Figure 10: Clinical manifestations of bacterial keratitis showing different severities of corneal infiltration and ulceration. 13
Figure 11: Schematic representation of HSV-1 ocular infection, latency, and reactivation pathway involving the cornea and trigeminal ganglion 17
Figure 12: Eye with conjunctivitis 20
Figure 13: Diseases of the ocular surface caused by a hypersensitivity mechanism 21
Figure 14: Schematic illustration depicts the various endogenous and exogenous sources contributing to the generation of reactive oxygen species (ROS) within a cell. 25
Figure 15: Canonical schematic outlines the sources and biochemical pathways of reactive nitrogen species (RNS). 26
Figure 16: The body's oxidative stress defense mechanisms. 28
Figure 17: Role of oxidative stress in the pathogenesis of dry eye disease. 30
Figure 18: ROC curves of biological markers in patients with bacterial ocular inflammation. 52
Figure 19: ROC curves of biological markers in patients with viral ocular inflammation. 54
Figure 20: ROC curves of biological markers in patients with allergic ocular inflammation. 55

List of Table

Table 1: Diagnosis of Epithelial, Stromal, and Endothelial Forms of Herpes Simplex Keratitis 19
Table 2: Classification and treatment of herpes simplex keratitis..... 19
Table 3: Characteristics of the different types of allergic conjunctivitis..... 21
Table 4: Treatment in Allergic Conjunctivitis 23
Table 5: Some examples of reactive oxygen and nitrogen species 24
Table 6: Description of the study population according to the type of eye inflammation 42
Table 7: Comparison between bacterial inflammation cases and controls regarding socioeconomic and environmental factors (N=121) 43
Table 8: Comparison between viral inflammation cases and controls regarding socioeconomic and environmental factors (N=121) 44
Table 9: Comparison between allergic inflammation cases and controls regarding socioeconomic and environmental factors (N=121) 45
Table 10: Comparison between bacterial inflammation cases and controls regarding clinical factors (N=121) 46
Table 11: Comparison between viral inflammation cases and controls regarding clinical factors (N=121) 47
Table 12: Comparison between allergic inflammation cases and controls regarding clinical factors (N=121) 48
Table 13: Hematological parameters levels in control, bacterial, viral and allergic groups. 49
Table 14: Biochemical parameters in blood of control, bacterial, viral and allergic groups..... 49
Table 15: Oxidative stress marker in blood of control, bacterial, viral and allergic groups 50
Table 16: Oxidative stress marker in tears of control, bacterial, viral and allergic groups..... 51
Table 17: Sensitivity, specificity and AUC values of some oxidative stress markers in patients with bacterial ocular inflammation..... 51
Table 18: Sensitivity, specificity and AUC values of some biochemical and hematological parameters in in patients with bacterial ocular inflammation 52
Table 19: Sensitivity, specificity and AUC values of some oxidative stress markers in patients with viral ocular inflammation 53
Table 20: Sensitivity, specificity and AUC values of some biochemical and hematological parameters in patients with viral ocular inflammation..... 53
Table 21: Sensitivity, specificity and AUC values of some oxidative stress markers in patients with allergic ocular inflammation..... 54
Table 22: Sensitivity, specificity and AUC values of some biochemical and hematological parameters in patients with allergic ocular inflammation 55

Table of contents

إهداء .....

إهداء .....

Acknowledgements .....

Abstract ..... **I**

Résumé ..... **III**

الملخص ..... **V**

Abbreviation List ..... **VII**

List of Figures ..... **VIII**

List of Table ..... **IX**

Table of contents ..... **X**

Introduction .....

First Part: Bibliographic Part

I. Anatomy of The Human Eyes: 4

I.1. External and Protective Structures: 4

I.2. Middle Structures (Uveal Tract): 6

I.3. Optical Structures: 6

I.4. Inner Layer: 7

I.5. Ocular Adnexa: 8

II. Physiology of The Eye: 9

II.1. Tears Film: 9

II.2. Protective Ocular Barriers: 11

II.3. Ocular Immune Defense System: 11

III. Eye Inflammation Disease: 12

III.1 Bacterial Eye Inflammation Disease: 12

III.2. Viral Eye Inflammation Disease: 16

III.3. Allergic Eye Inflammation Disease: 20

IV. Oxidative Stress: 24

IV.1. Free Radicals: 24

IV.2. Antioxidants: 26

IV.3. Oxidative Stress in Eye Disease: 28

Second part: Experimental part

Material and Methods

I. Materiel 33
I.1. Study Period: 33
I.2. Risk Factors Study: 33
I.3. Biological Study: 33
II. Methods: 34
II.1. Collection of Data: 34
II.2. Method of Hematological Analysis: 34
II.3. Biochemical Parameters Assay: 34
II.4. Method of Estimating Oxidative Stress Parameters: 34
II.5. Statistical Analysis: 39

Result & Discussion

I. Result: 41
I.1. Clinical and Demographic Characteristics of The Study Population: 41
I.2. Study Of Socioeconomic and Environmental Factors: 42
I.3. Clinical Factors: 45
I.4. Study Of Biological Markers and Predictive Factor: 48
II. Discussion: 56
II.1. The Study Population: 56
II.2. Study of Socioeconomic and Environmental Factors: 60
II.3. Clinical Factors: 63
II.4. Study of Biological Markers and Predictive Factors: 68
II.4.3. Oxidative Stress Markers: 73
II.4.4. Oxidative Stress Marker in Tears: 74
II.4.5. Predictive Factors Study: 76

Conclusion 79
Bibliographical References 82
ANNEX 92

Introduction

Ocular inflammatory diseases represent a significant public health concern because they affect structures essential for visual function, including the cornea, conjunctiva, tear film, eyelids, and lacrimal glands. These structures are continuously exposed to microbial pathogens, allergens, and environmental stressors, making them particularly vulnerable to inflammatory disorders. Ocular inflammation may result from infectious causes, such as bacterial and viral infections, or non-infectious causes, including allergic reactions. Despite differences in their underlying pathophysiological mechanisms, these conditions frequently present with similar clinical manifestations such as redness, tearing, itching, pain, and visual discomfort, which often complicates accurate diagnosis and appropriate treatment (Ting, *et al*., 2021).

Among infectious ocular diseases, bacterial keratitis is considered one of the most severe forms of ocular inflammation because it can rapidly progress to corneal ulceration, stromal destruction, scarring, and permanent vision loss if not diagnosed and treated promptly. Several risk factors have been associated with bacterial keratitis, including contact lens wear, ocular trauma, ocular surface diseases, and immunosuppression, while *Staphylococcus* species and *Pseudomonas aeruginosa* remain among the most common causative pathogens (Ting, *et al*., 2021).

Viral ocular inflammation is predominantly represented by herpes simplex keratitis, a recurrent corneal infection caused by the herpes simplex virus (HSV). Following primary infection, the virus may remain latent within the trigeminal ganglion and reactivate under various triggering conditions, resulting in recurrent episodes of corneal inflammation that may ultimately compromise vision (Azher, *et al*., 2017).

Allergic conjunctivitis is one of the most prevalent non-infectious ocular inflammatory disorders and results from hypersensitivity reactions to environmental allergens such as pollen, dust mites, and animal dander. It is typically characterized by itching, conjunctival hyperemia, tearing, and eyelid swelling. Although generally not vision-threatening, recurrent or chronic allergic conjunctivitis can significantly impair patients' quality of life (Bielory, *et al*., 2020).

Recent evidence has highlighted the important role of oxidative stress in the development and progression of ocular inflammatory diseases. Oxidative stress arises from an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense system, leading to lipid peroxidation, protein oxidation, DNA damage, and activation of inflammatory pathways. Biomarkers such as malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) have been widely used to assess oxidative status and have been associated with several ocular disorders (Böhm, *et al*., 2023).

Although substantial progress has been made in understanding ocular inflammatory diseases, differentiating between bacterial, viral, and allergic forms remains a major clinical challenge because of their overlapping symptoms and shared risk factors. Furthermore, diagnosis often relies primarily on clinical examination, which may not always provide sufficient accuracy for early disease identification and classification. Consequently, there is a growing need to identify reliable biological markers that could facilitate differential diagnosis and potentially predict disease occurrence before severe complications develop.

Therefore, the central research question of the present study is whether risk factors, biochemical parameters, hematological indicators, and oxidative stress biomarkers can effectively distinguish bacterial, viral, and allergic ocular inflammatory diseases and serve as reliable predictive tools for early diagnosis in patients from the El Oued region.

Accordingly, this study aims to investigate the major risk factors associated with ocular inflammatory diseases in the El Oued region and to evaluate the diagnostic and predictive value of selected biochemical, hematological, and oxidative stress markers. In addition, Receiver Operating Characteristic (ROC) curve analysis will be employed to assess the sensitivity, specificity, and discriminative performance of these biomarkers, with the ultimate goal of identifying the most effective indicators for differential diagnosis and early detection of ocular inflammatory diseases.

First Part: Bibliographic Part

I. Anatomy of The Human Eyes:

The eye is a unique organ, in that it contains several highly different structures with specific physiological functions (Edman, 2019). The ocular surface is a very important part of the eye. It consists of the conjunctiva and the cornea, together with elements such as the lacrimal gland, lacrimal drainage apparatus and associated eyelid structures. This part of the eye has unique properties and is associated with special physiological mechanisms, for example tear production and (Martin Herranz, *et al*., 2013), this chapter is a short overview of the optical structure and function of the human eye. It mentions briefly some important aspects such as the cornea, the lens, and ocular axes (Atchison, *et al*., 2023). The main anatomical structures of the eye are presented below:

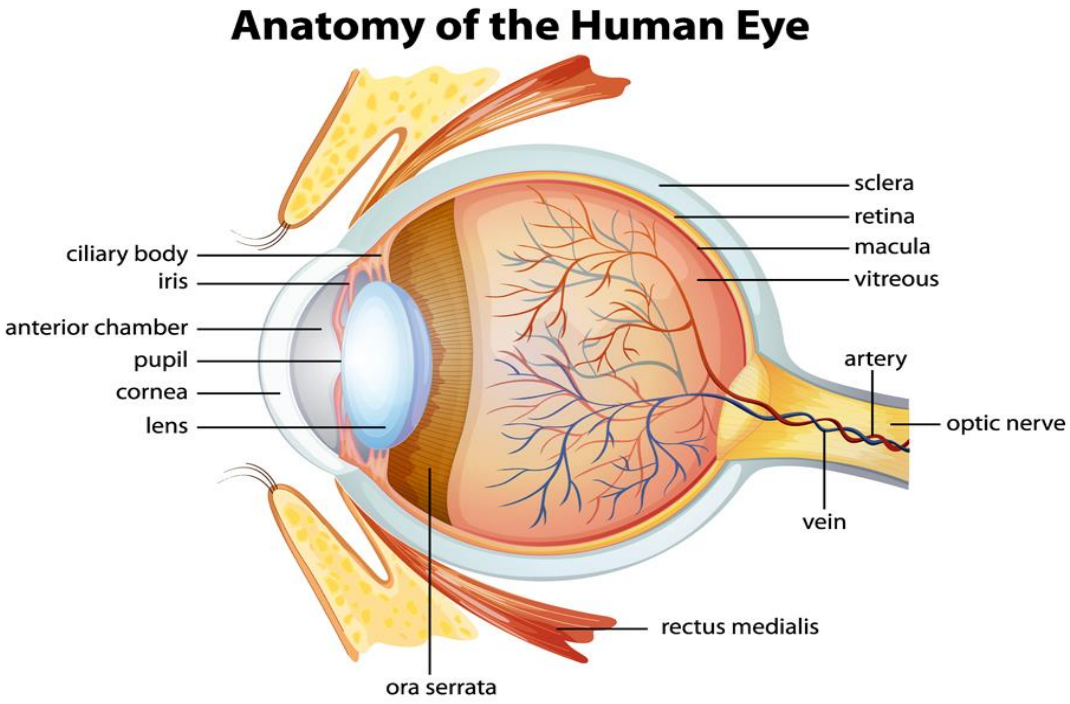


Figure 1: Schematic drawing of the human eye (Martin Herranz, *et al*., 2013).

I.1. External and Protective Structures:

I.1.1 Cornea:

The cornea is a transparent avascular tissue that acts as a structural barrier and protects the eye against infections. Along with the tear film (Sridhar, 2018) .The cornea is composed of both cellular elements keratocytes and endothelial cells and non-cellular components, including collagen and glycosaminoglycans. The epithelial cells originate from the epidermal ectoderm, whereas keratocytes and endothelial cells are derived from the neural crest. The cornea is

organized into five distinct layers: three cellular layers (epithelium, stroma, and endothelium) and two acellular interfaces (Bowman's membrane and Descemet's membrane) (Ozkan, 2021).

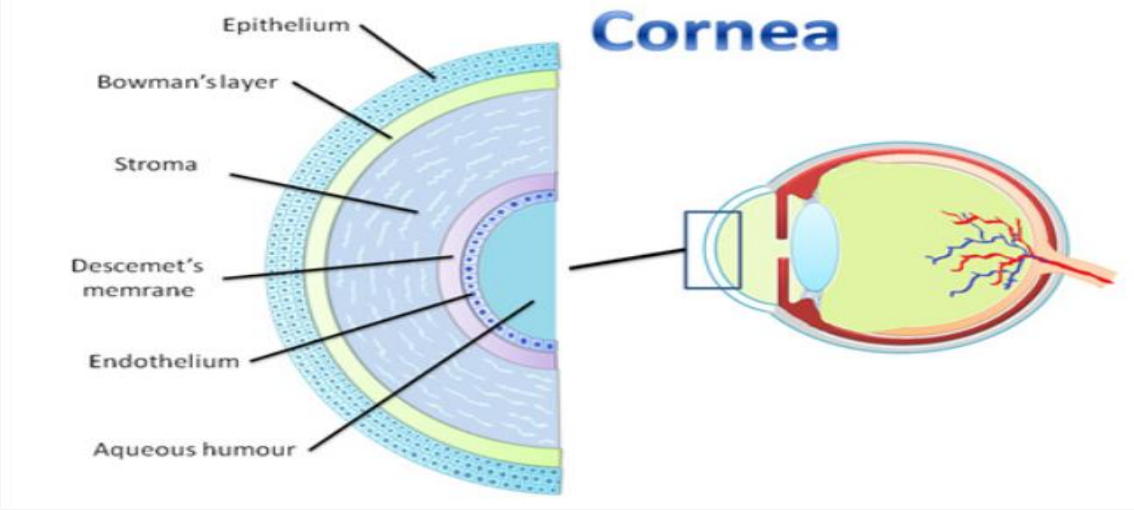


Figure 2: The schematic of the cornea layers (Balyen, 2022).

I.1.2 Sclera:

The sclera is the white, protective outer layer of the eye. It is a tough, fibrous tissue that forms the structural foundation of the eyeball (Aljaberi, 2024). The sclera is opaque and forms the posterior five-sixths of the eyeball. It is composed of dense fibrous tissue which is firm and maintains the shape of the eyeball. It is thickest behind, near the entrance of the optic nerve, and thinnest about 6 mm behind the sclerocorneal junction where the recti muscles are inserted (Garg, 2024) the sclera merges with the corneal perimeter at the limbus and extends backward to form an approximate sphere of vertical diameter ~24mm. The axial length of the emmetropic adult human eye is 24–25mm (Craig Boote, 2020).

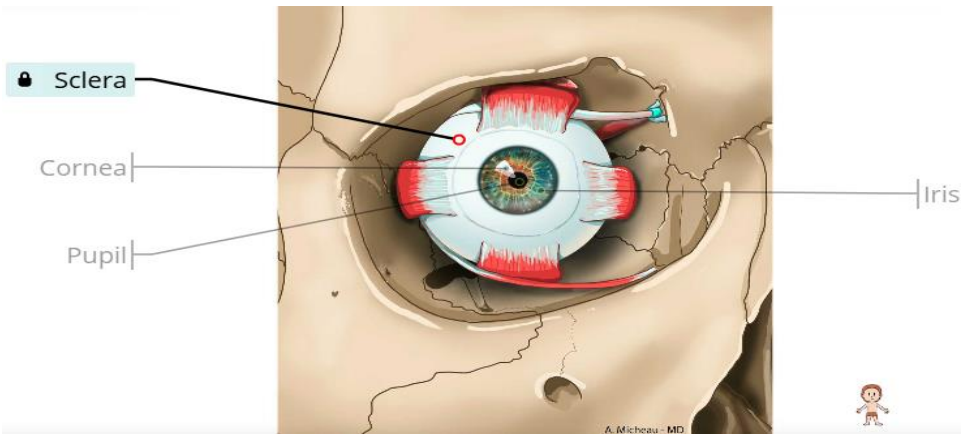


Figure 3: Basic scleral anatomy (IMAIOS, (n.d.)).

I.1.3 Conjunctiva:

The conjunctiva is a transparent mucous membrane that lines the inner surface of the eyelids (palpebral conjunctiva) and the anterior surface of the sclera (bulbar conjunctiva) (Awh, *et al*., 2022). The conjunctiva can be divided into three regions: the palpebral and tarsal conjunctiva, the bulbar or ocular conjunctiva, and the conjunctival fornixes. The palpebral conjunctiva is further divided into the marginal, tarsal, and orbital regions. The bulbar conjunctiva is divided into scleral and limbal parts. Finally, the conjunctival fornixes are divided into the superior, inferior, lateral, and medial regions. The conjunctiva has an average thickness of 33 microns (Wade, *et al*., 2023).

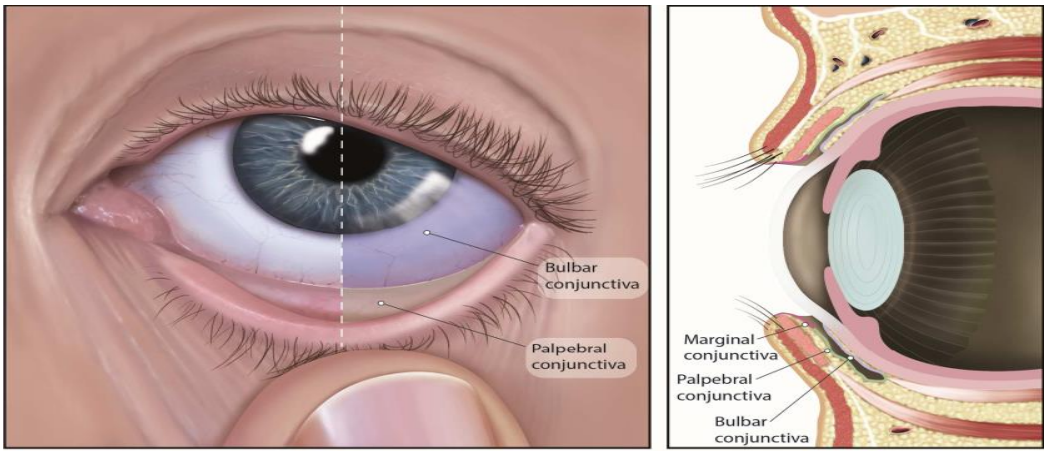


Figure 4: Conjunctiva of the eye (Downie, *et al*., 2021).

I.2. Middle Structures (Uveal Tract):

I.2.1 Iris:

The iris is the colored part of the eye that surrounds the pupil, which controls the amount of light that enters the eye. It is responsible for regulating the size of the pupil and the amount of light that enters the eye (Raj Kumar, 2024). The Iris is composed of, from front to the back, anterior surface, Stroma, sphincter and dilator muscle and posterior double layers of iris pigment epithelium. Anterior surface which is part of the stroma and stroma structure are extremely variable in different individuals, but the iris muscles and posterior double layered iris pigment epithelium is relatively constant (Moazed, 2020).

I.3. Optical Structures:

I.3.1. Lens:

The lens is a transparent biconvex structure which is placed between the anterior and posterior segments of the eye (Chaurasia, 2023). The lens consists of four parts the lens

capsule, the epithelial cells, the lens fibers and the zonules (Ruan, *et al*., 2020).The function of the lens or the eye lens, is to direct light onto the retina**.** The retina is the light-sensitive layer at the back of the eye. The ciliary muscles that surround the lens help to change the shape of the lens to ensure light hits the retina correctly, according to (Aliancy JF and Mamalis N). The retina takes light that the eye receives and turns this into electrical signals. These electrical signals are then taken to the brain via the optic nerve and turned into images (Oscar Wylee Team / Editorial content, 2025).

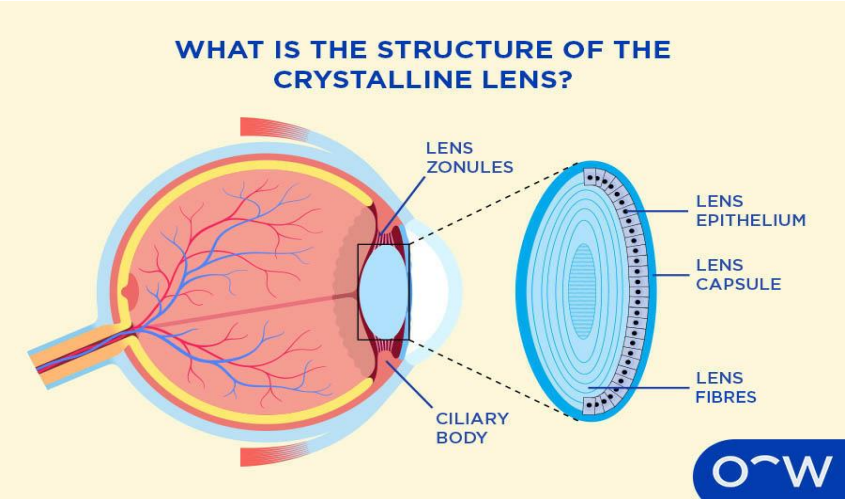


Figure 5: The Structure of the Crystalline Lens (Oscar Wylee Team / Editorial content, 2025).

I.4. Inner Layer:

I.4.1 Retina:

The retina is a layer of photoreceptors cells and glial cells within the eye that captures incoming photons and transmits them along neuronal pathways as both electrical and chemical signals for the brain to perceive a visual picture (Tadi, *et al*., 2023).The retina is arguably the most important, yet delicate, part of the eye that enables vision. It's a thin, light-sensitive layer of tissue that covers approximately 65 percent of the back of the eye. The retina consists of photoreceptors called rods and cones. Rods are responsible for detecting low levels of light in dim conditions, while cones are responsible for processing detailed, color vision (Banani, 2023).

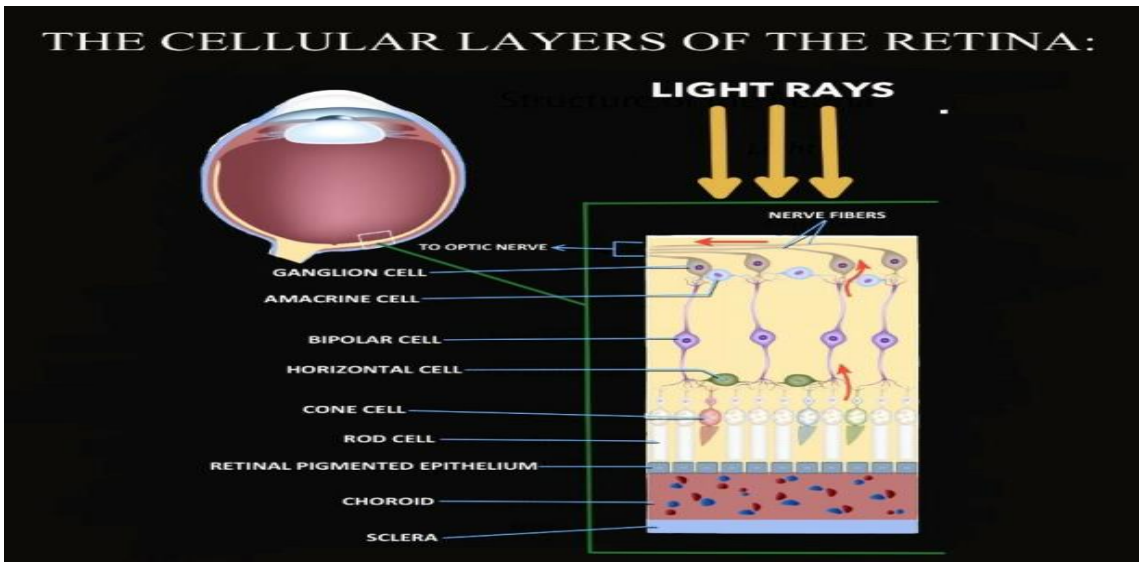


Figure 6: The neuroanatomy of the retina (Banani, 2023).

I.5. Ocular Adnexa:

❖ **Lacrimal Apparatus:**

The structures that make up the lacrimal apparatus include the lacrimal gland, accessory lacrimal glands (Krause and Wolfing glands), excretory ductules, lacrimal puncta, lacrimal canaliculi, lacrimal sac, and nasolacrimal duct. The lacrimal gland and accessory lacrimal glands form the secretion system, while the other structures make up the drainage system (Açar, *et al.*, 2025).

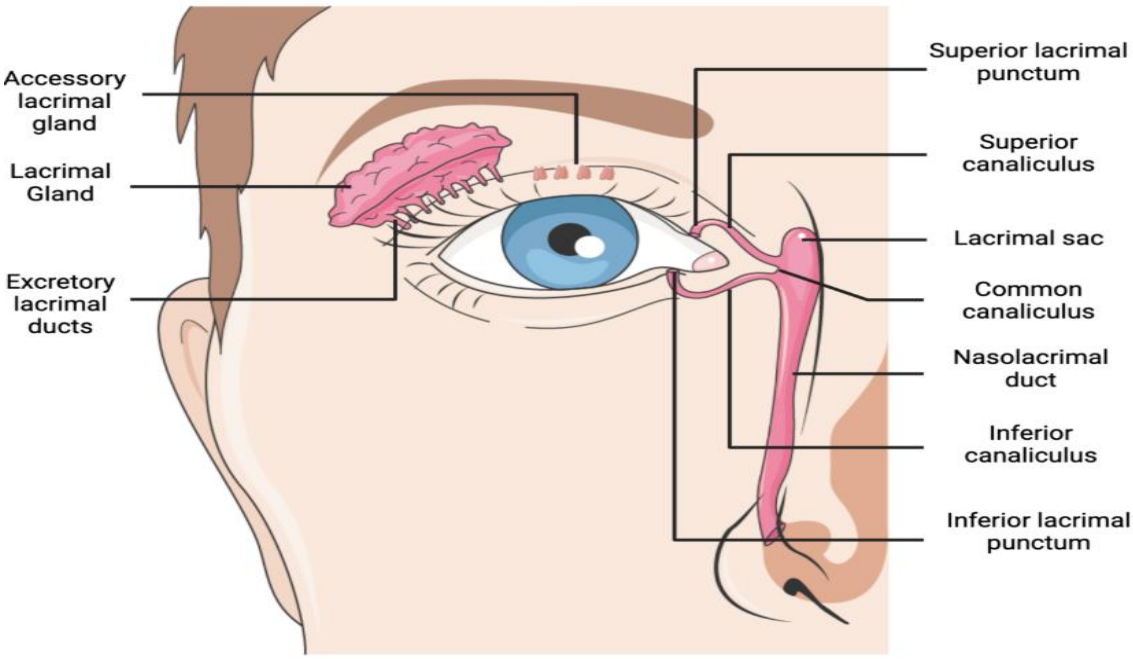


Figure 7: Lacrimal system anatomy. Created with BioRender.com and Servier Medical Art (Wu, *et al.*, 2024).

❖ **Lacrimal Gland:**

The lacrimal gland is a tubuloacinar exocrine gland responsible for tear secretion, located in the superolateral aspect of the orbit, within the fossa for the lacrimal gland of the frontal bone (Açar, *et al*., 2025). The tendon of levator palpebrae superioris bisects the lacrimal gland, giving rise to 2 lobes: a smaller palpebral component found continuous with the inner eyelid, and a larger orbital component. Its histological composition is mixed serous and mucinous acini, myoepithelial cells, and small interconnecting ductules (Machiele, *et al*., 2023).The lacrimal gland measures approximately 20 mm in length and 12 mm in width. The thickness of the orbital part is around 5 mm, whereas the palpebral part measures approximately 3 mm (Açar, *et al*., 2025).the primary function of secreting the aqueous portion of the tear film, thereby maintaining the ocular surface (Machiele, *et al*., 2023).

II. Physiology of The Eye:

II.1. Tears Film:

The tear film is a mixture of ocular surface secretions from the main lacrimal and accessory lacrimal glands, meibomian glands and the corneal and conjunctival epithelium (Martin Herranz, *et al*., 2013).

II.1.1. Components of Tears:

Tears consist of three layers: the mucin layer, aqueous layer, and lipid layer:

- Mucin Layer: This is the innermost and thinnest layer of the tear film, with a thickness of 0.02-0.05 µm. The mucin content, composed of mucopolysaccharides and glycoproteins, tends to adhere to foreign substances present on the cornea and conjunctiva, and it plays a physiological cleansing role in a normal eye.
- Aqueous Layer: This is the middle and thickest layer of the tear film, due to the large water content, this layer performs functions of lubrication and mechanical cleaning. It also helps maintain the neutral pH (7.4-7.5) of tears.
- Lipid Layer: Is the outermost layer of the tear film, which is in contact with the atmosphere. It is produced by the Meibomian, Zeiss, and Moll glands. This layer reduces the evaporation of tears and contributes to vertical stability, preventing the tear film from flowing toward the lower eyelid margin (Açar, *et al*., 2025).

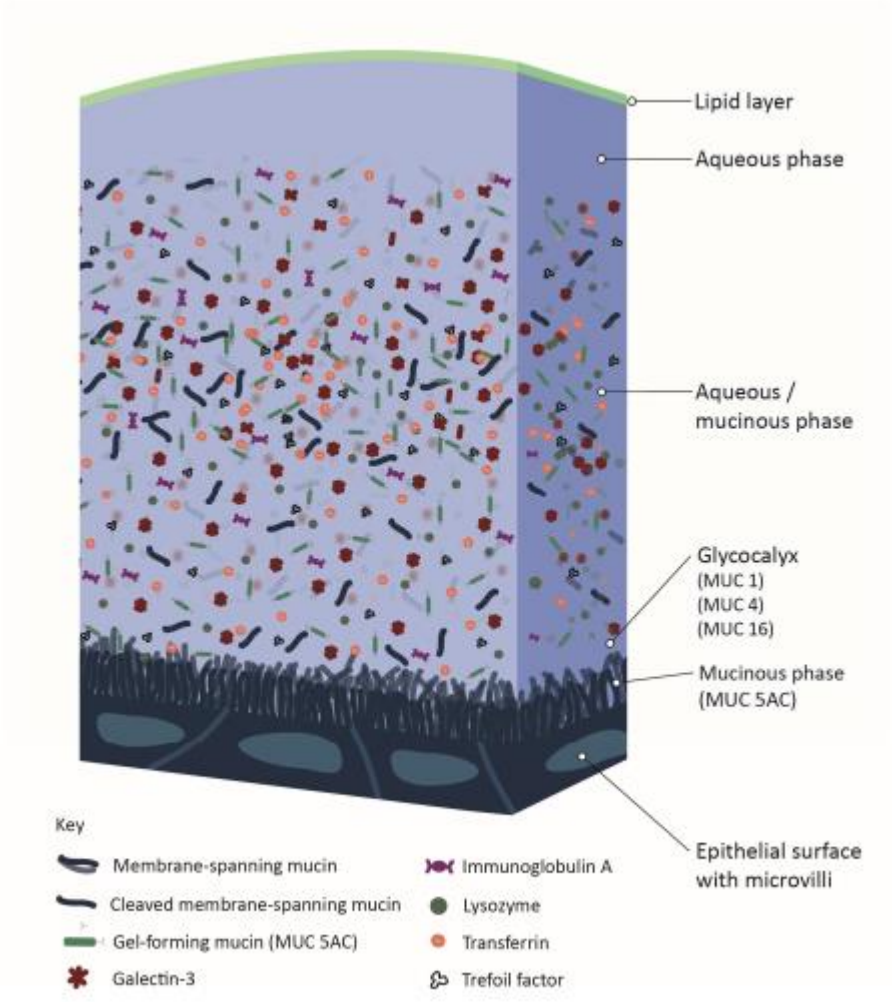


Figure 8: Current conceptualization of tear film structure. Copyright BCLA 2021 (Downie, *et al*., 2021).

II.1.2. Function of The Tear Film:

- ✓ Functions of the tear film include providing lubrication to the ocular surface and eyelid, antimicrobial defense, providing a smooth ocular surface for refraction, and supplying oxygen and nutrition to the avascular corneal epithelium.
- ✓ The tear film forms a protective barrier between the ocular surface and the external environment, and it contains antimicrobial properties. Key antimicrobial factors found in the tear film include lysozyme, lactoferrin, transferrin, ceruloplasmin, IgA, IgG, IgE, complement, glycoprotein, and anti-proteinase, which are found in the aqueous layer of the tear film (Chang, *et al*., 2023).

II.2. Protective Ocular Barriers:

II.2.1. Eyelids:

The eyelids (palpebrae) are critical anatomical and functional components of the ocular adnexa, playing an essential role in preserving the health and integrity of the ocular surface. Their specialized structure ensures mechanical protection, tear film distribution, and immune defense (Ozkan, *et al*., 2025) , the eyelid structure consists of four layers. The first or outermost layer includes the skin, eyelashes and associated glands. The second layer comprises the muscular layer, namely the orbicularis oculi, the circular sphincter-like muscles responsible for closing the eyelids. The third fibrous layer, important for mechanical stability of the eyelid, consists mainly of the tarsal plate. The innermost layer of the eyelid is the palpebral conjunctiva. The first two layers are sometimes termed anterior lamella of the eyelid, whereas the last two layers are termed posterior lamella of the eyelid (Martin Herranz, *et al*., 2013).

II.2.2. Eyelashes:

The eyelashes are hairs growing at the edge of the eyelids. They are positioned in the anterior portion of the lid margin, lined by skin epithelium. The eyelashes are surrounded by the glands of Zeis (modified sebaceous and the glands) of Moll (modified sweat glands). The eyelashes help to keep foreign particles from entering the ocular surface system, as well as increase the sensitivity of the eye to touch (Martin Herranz, *et al*., 2013).

II.3. Ocular Immune Defense System:

Despite constant exposure to various environmental stimuli, the ocular surface remains intact and uninflamed. This 'immune privilege of the ocular surface is not simply a result of the physical barrier function of the mucosal lining but, more importantly, is actively maintained through a variety of immunoregulatory mechanisms that prevent the disruption of immune homeostasis (Chen, *et al*., 2022).

Various cells and molecules participate in ocular immune responses:

II.3.1. Innate Immune System:

This includes physical barriers, antimicrobial peptides and cells like macrophages and neutrophils that provide the first line of defense against pathogens.

II.3.2. Adaptive Immune System:

Involves T cells and B cells, which can be activated in response to infections or in autoimmune diseases affecting the eye (Konov, 2024).

Similar to other immune privileged tissues in the body, such as the brain, the eye has limited regenerative capacity. For example, the corneal endothelium does not proliferate sufficiently to compensate for age-related cell loss (Amouzegar, *et al*., 2018).

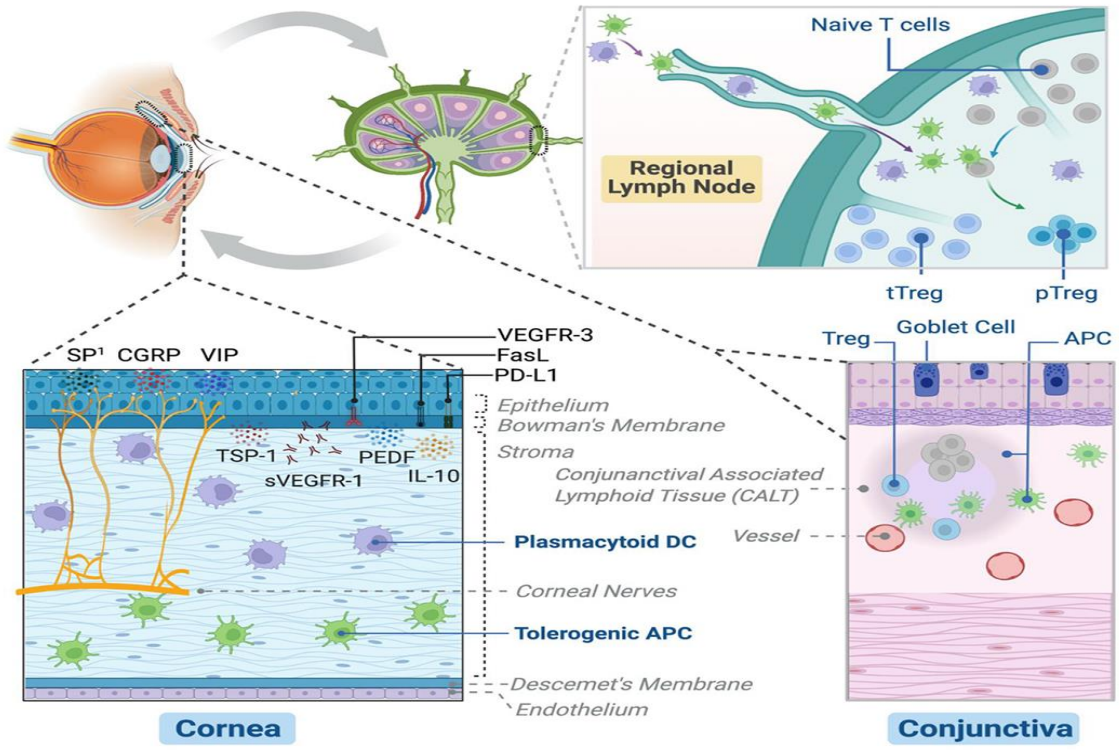


Figure 9: The major cells and molecules promoting ocular surface immune homeostasis (Chen, *et al*., 2022).

III. Eye Inflammation Disease :

III.1 Bacterial Eye Inflammation Disease:

Inflammatory eye disease encompasses a wide spectrum of conditions, ranging from the relatively benign to sight-threatening emergencies. The ocular inflammation can be infectious or non-infectious in an etiology. All parts of the eye may be variably affected, and eye inflammation can occur in isolation or as part of a systemic inflammatory disease (Miller, *et al*., 2022). Eye infections can be acute or chronic, and can range from mild to severe. Common types of eye infections include conjunctivitis, keratitis, blepharitis, and uveitis. Eye infections can be caused by a variety of things, such as viruses, bacteria, allergens (Khoo, 2023).

III.1.1. Bacterial Keratitis:

"Among the types of eye inflammation, keratitis was specifically addressed as an important example illustrating the mechanisms of infection and pathological effects on the surface of the eye."

Bacterial keratitis (BK) is the most common type among all types of infectious keratitis. BK accounts for approximately 65–90% of all microbial keratitis (Chlasta-Twardzik, *et al*., 2024), is an infection and inflammation of the cornea that cause pain, reduced vision, light sensitivity and tearing or discharge from the eye (Janumala, *et al*., 2012).BK is caused by varied bacterial species, and it can be an acute, chronic, or transient infectious process of the cornea. BK is one of the most common causes of visual impairment in working-age adults (Chlasta-Twardzik, *et al*., 2024). That can, in severe cases cause loss of vision. Bacterial keratitis progresses rapidly and corneal destruction may be complete in 24 - 48 hours (Janumala, *et al*., 2012).

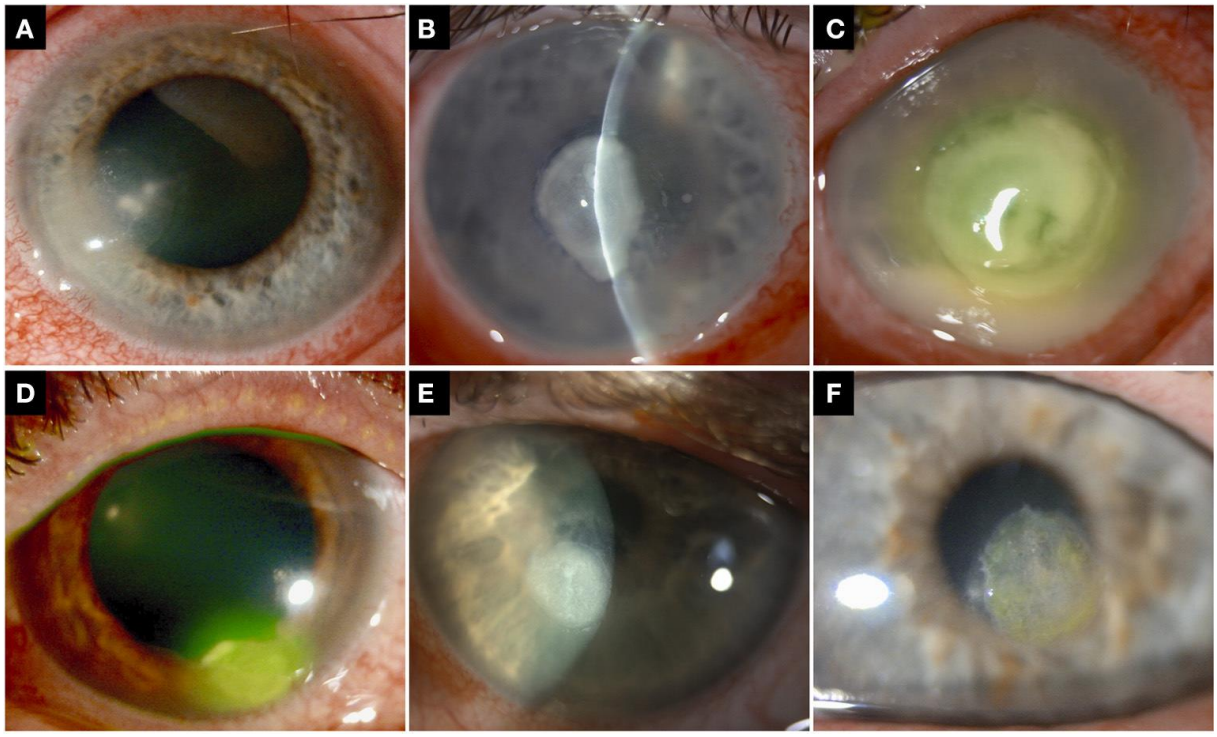


Figure 10: Clinical manifestations of bacterial keratitis showing different severities of corneal infiltration and ulceration (Ting, *et al*., 2021).

((A–C) Examples of bacterial keratitis with varying severity, including (A) small infiltrate (≤3 mm), (B) moderate infiltrate (3.1–6 mm), and (C) large infiltrate (>6 mm). (D–F) Examples of bacterial keratitis in different locations, including (D) peripheral, (E) paracentral, and (F) central location).

A. Common Causative Bacteria:

- The most common species causing bacterial keratitis include: *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and species of the Enterobacteriaceae family.
- The bacterial species that can penetrate the intact corneal epithelium are: *Neisseria gonorrhoeae*, *Corynebacterium diphtheriae*, *Hemophilus Aegyptus*, and *Listeria monocytogenes* (Gurnani, *et al*., 2023).

B. Clinical Features:

The development of a bacterial corneal inflammation may occur as a number of clinical features. We should keep in mind that in BK signs are more common than symptoms (Chlasta-Twardzik, *et al*., 2024). A bacterial corneal ulcer usually presents with chemosis and conjunctival injection, eyelid edema, decreased vision, pain, tearing, photophobia, and purulent discharge. It manifests a predominantly papillary conjunctival response, with limbal injection, a gray-white infiltrate corneal epithelial and stromal infiltrate which may appear necrotic, corneal edema, an anterior chamber reaction, and fibrin plates on the endothelium in severe cases with a fibrinoid aqueous or hypopyon (Ezisi, *et al*., 2018).

C. Risk feature:

- ✓ Contact lens usage (overnight wear, inadequate disinfection, use of contact lenses without a doctor's prescription and follow-up, or swimming, using a hot tub, or showering while wearing contact lenses).
- ✓ Topical antibiotics and glaucoma medications (chronic and multiple ophthalmic drug usage containing preservatives, especially benzalkonium chloride).
- ✓ Lacrimal disorders (dry eye, dacryocystitis) (Egrilmez, *et al*., 2020).

D. Pathophysiology:

The process of bacterial keratitis initiates once the epithelial is breached by any means. When a critical number of pathogens is exceeded, defense mechanisms fail and the stroma of the cornea is invaded by bacteria. This is facilitated by breaking the continuity of the epithelium. Only a small number of bacteria are able to break the continuous epithelium, these are gonorrhea, *Corynebacterium diphtheria*, *Corynebacterium a Egyptian*, *Listeria*, and *Shigella* (Chlasta-Twardzik, *et al*., 2024).

The development of bacterial keratitis progresses through four stages: Stage of progressive infiltration-Stage of active ulceration, stage of regression, stage of cicatrization (Gurnani, *et al*., 2023).

An important feature that determines pathogenicity is the ability of the bacterium to produce enzymes that facilitate penetration into tissues and their destruction. *Pseudomonas aeruginosa*, which produces protease, trypsin, elastase, and hemolysin, is particularly dangerous. These enzymes lead to rapidly progressing liquefied necrosis of the tissue. This bacterium should always be considered and differential as a cause of acute keratitis in CL users. Another mechanism of tissue damage by the bacteria is the production of toxins in the form of exotoxins and the release of endotoxins after cell death that damage host cells. The final course of bacterial keratitis is dependent on the virulence of the offending bacteria, host defensive mechanisms, and the treatment received (Chlasta-Twardzik, *et al*., 2024).

E. Diagnostic tests:

A diagnosis of BK is made from the patient's history as well as microbiology tests. Preferably, all corneal ulcers should be cultured for the identification of the causal organism and the antibiotic susceptibility before commencing antimicrobial therapy, the American Academy of Ophthalmology (AAO), BK preferred practice pattern, recommends smears and cultures in the following situations.

- ✓ Central and large corneal infiltrate and associated with significant stromal involvement or melting.
- ✓ Chronic or unresponsive infection to broad-spectrum antibiotic therapy.
- ✓ History of corneal surgeries.
- ✓ Atypical clinical features suggesting fungal, amoebic or mycobacterial keratitis
- ✓ Multiple infiltrates on the cornea (Cabrera-Aguas, *et al*., 2022).

F. Treatment:

❖ **Antibiotics treatment:**

The main group of antibiotics used in bacterial keratitis is fluoroquinolones. Fluoroquinolones are the group of antibiotics that provide excellent tissue penetration, quickly reaching high concentrations within tissues and have a broad spectrum of bactericidal activity (Chlasta-Twardzik, *et al*., 2024).

❖ **Other topical drugs therapy:**

Cycloplegics medications are commonly used as adjuvant drugs to relieve the pain, reduce ciliary spasm, and reduce cells and flare, as well as to prevent posterior synechiae formation that is often associated with iritis accompanying BK. They are indicated in cases with significant anterior chamber inflammation. Antiglaucoma drugs are useful to control and reducing intraocular pressure by help drain the hypopyon by opening the trabecular meshwork and drainage channels, as well as to help in controlling trabeculitis secondary to the inflammatory process. A total of 0.5% timolol is commonly used. Two groups of topical drugs should be avoided, namely prostaglandin analogs and miotics because they exacerbate inflammation of the eye (Chlasta-Twardzik, *et al*., 2024).

❖ **Surgical Treatment:**

Gunderson Flap: This treatment is beneficial when a donor cornea is not available to salvage a perforated corneal ulcer. The upper conjunctiva is dissected, and a thin flap of the conjunctiva is covered over the cornea and sutured. It acts as metabolic support for the cornea (Gurnani, *et al*., 2023).

III.2. Viral Eye Inflammation Disease:

III.2.1. Herpes Simplex Virus (HSV) Keratitis:

"Among the types of viral eye inflammation, keratitis was specifically addressed as an important example illustrating the mechanisms of infection and pathological effects on the surface of the eye."

Herpes simplex virus keratitis is one of the leading causes of blindness worldwide (Michalska-Małecka, *et al*., 2025). HSV is an enveloped, double-stranded DNA virus that belongs to the Alpha herpes virinae subfamily of the Herpesviridae family. The structure of HSV-1 includes the viral envelope with glycoproteins, viral tegument, capsid, and DNA genome. It has tropism for mucoepithelial cells and neurons. It causes lytic infection of epithelial cells and latent infection of most neurons. There is about 50% sequence homology between HSV-1 and HSV-2 (Labib, *et al*., 2022).

A. Classification of Herpesviridae Family:

There are three subfamilies of herpesviruses: alpha-, beta-, and gamma-herpesviruses. The human viruses included in the alpha-subfamily are herpes simplex virus type-1 (HSV-1), herpes simplex virus type-2 (HSV-2), and varicella-zoster virus (VZV). The alpha-subfamily

differs from its relatives in that it has the widest host range and a relatively short replicative cycle (Shukla, *et al*., 2019).

B. Risk Factors:

Risk factors associated with the severe disease include:

- ✓ Frequent recurrent episodes
- ✓ Atopic eye disease
- ✓ Pediatric age group
- ✓ Immunodeficiency or immunosuppression
- ✓ Malnourishment
- ✓ Alcoholism
- ✓ Fever
- ✓ Stress
- ✓ Malaria
- ✓ Inappropriate topical steroids may result in geographical ulceration (Patel, *et al*., 2024) .

C. Pathophysiology:

The virus enters the cell in different ways depending on the type of cell, e.g., merging with the membrane of the host cell, or through endocytosis. The capsid is then transported to the nucleus for viral genome replication using the host cell's DNA polymerase. The new virions produced are released from the cell to infect neighboring cells. HSV can replicate by infecting nearby cells or enter a latent state, reaching the trigeminal ganglion via the cornea. Reactivation from the state of latency is responsible for the persistence of the infection throughout the life of the host (Petrillo, *et al*., 2022).

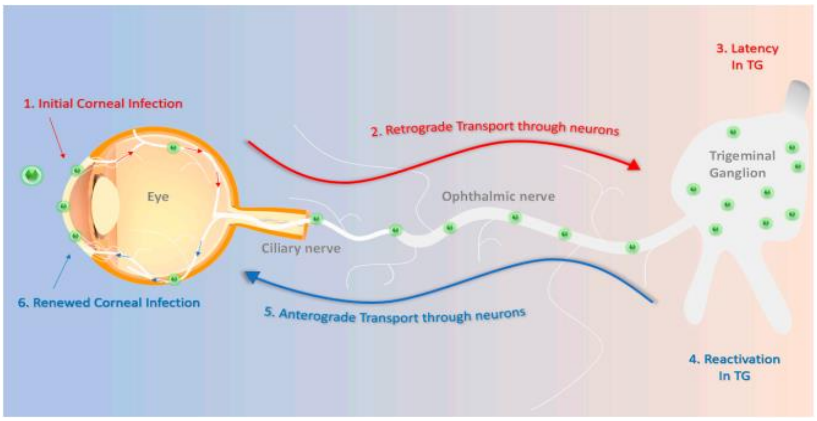


Figure 11: Schematic representation of HSV-1 ocular infection, latency, and reactivation pathway involving the cornea and trigeminal ganglion (Shukla, *et al*., 2019).

D. Modes of Transmission:

- ✓ Herpes simplex virus is typically spread by direct contact, most often from virus shed into saliva or genital secretions. Herpes simplex virus can be acquired following contact with an active Oro-labial lesion.
- ✓ Asymptomatic individuals regularly shed HSV in their saliva, and therefore, HSV can also be acquired by contact with virus-laden saliva of asymptomatic patients.
- ✓ While symptomatic patients shed more HSV viral DNA than asymptomatic patients, the asymptomatic patients are likely the more common source of transmission since there are many more of them (White, *et al*., 2014).

E. SYMPTOMS:

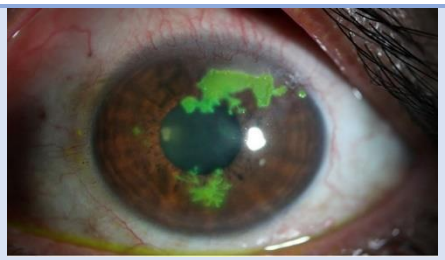
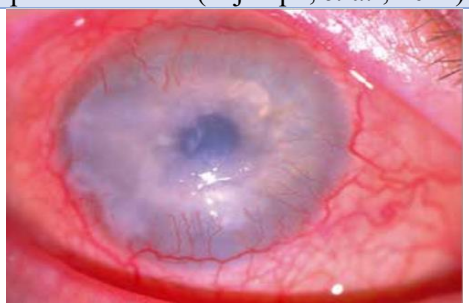
- ✓ Blurry vision
- ✓ Photophobia
- ✓ Eye redness
- ✓ Eye pain (Aijarapu, *et al*., 2021).
- ✓ Epiphora (tearing).
- ✓ History of previous episodes (Tidy, 2022).

F. Examination:

- ✓ Assess visual acuity.
- ✓ Examine lids and conjunctiva for evidence of inflammation. Involvement here is less common in secondary infection although conjunctival injection (red eye) is almost universal. There may be erosions around the lid margin with the presence of small vesicles or pustules.
- ✓ Observe cornea: any opacities or haziness? This may suggest stromal involvement.
- ✓ Test corneal sensation (twist the corner of a clean, dry tissue paper to a point and gently touch the corneal surface: this should elicit brisk blepharospasm and some sort of negative comment from the patient) - this can be reduced in epithelial disease.
- ✓ Stain the cornea and look for evidence of ulcers by staining with fluorescein (Tidy, 2022) .

G. Diagnosis:

Table 1: Diagnosis of Epithelial, Stromal, and Endothelial Forms of Herpes Simplex Keratitis

Form (HSV) keratitis	Diagnosis	Figure
Epithelial keratitis	This is based on typical clinical signs. Occasionally, it may be necessary to confirm the diagnosis with a sample taken from a corneal scraping which is sent for virological examination, cell culture or Polymérase Chain réaction (PCR) (Bagga, *et al*., 2020).	 Fig (1): Slit-lamp photograph showing epithelial keratit (Aijarapu, *et al*., 2021).
Stromal keratitis	The diagnosis of stromal keratitis is made clinically, and no investigations are required. For confirmation, the virus can be detected in a corneal scrape using cell culture, indirect immunofluorescence (IFA) or PCR. It is important to also exclude secondary bacterial infection. (Bagga, *et al*., 2020).	 Fig (2): Severe herpetic keratitis complicated by the formation of fibrovascular tissue (Serkies-Minuth, *et al*., 2025) .
Endotheliitis	The diagnosis is made clinically.	 Fig (3): Disciform endothelitis (Bagga, *et al*., 2020).

H. Treatment:

Table 2: Classification and treatment of herpes simplex keratitis (Michalska-Małecka, *et al*., 2025).

Form of herpetic keratitis	Alternative nomenclature	Treatment
Epithelial keratitis	Dendritic keratitis Geographic ulceration	Antiviral (topical/oral)
Stromal keratitis without ulceration	Non-necrotizing keratitis Endothelial keratitis Immune keratitis	Topical steroid therapy + oral antiviral medication at a prophylactic dose
Stromal keratitis with ulceration	Necrotizing keratitis	Topical steroid therapy + oral antiviral medication at a therapeutic dose
Endothelial keratitis	Disciform keratitis	

III.3. Allergic Eye Inflammation Disease:

III.3.1. Allergic Conjunctivitis:

"Among the types of Allergic eye inflammation, Conjunctivitis was specifically addressed as an important example illustrating the mechanisms of infection and pathological effects on the surface of the eye."

Allergic conjunctivitis (AC) is an inflammatory disease of the conjunctiva caused mainly by an IgE-mediated mechanism. It is the most common type of ocular allergy (Sánchez-Hernández, *et al*., 2015), is affecting up to 40% of the world's population (Bielory, *et al*., 2020).The pathogenesis of AC results from the interplay between genetic predisposition and complex environmental factors (Bao, 2025) (such as pollens, environmental antigens (e.g. dust), and animal dander) (Schellack, *et al*., 2021) , manifesting as a complex network of multiple cell types and molecular mediators on the ocular surface (Bao, 2025).

Figure 12: Eye with conjunctivitis (Patel, *et al*., 2024).

A. Types of Allergic Conjunctivitis:

The classification of allergic conjunctivitis has been revised recently by the Ocular Allergy group of the European Academy of Allergy and Clinical Immunology (EAACI), which distinguishes two types of ocular surface hypersensitivity disorders: ocular allergy or ocular nonallergic hypersensitivity (Villegas, *et al*., 2021).

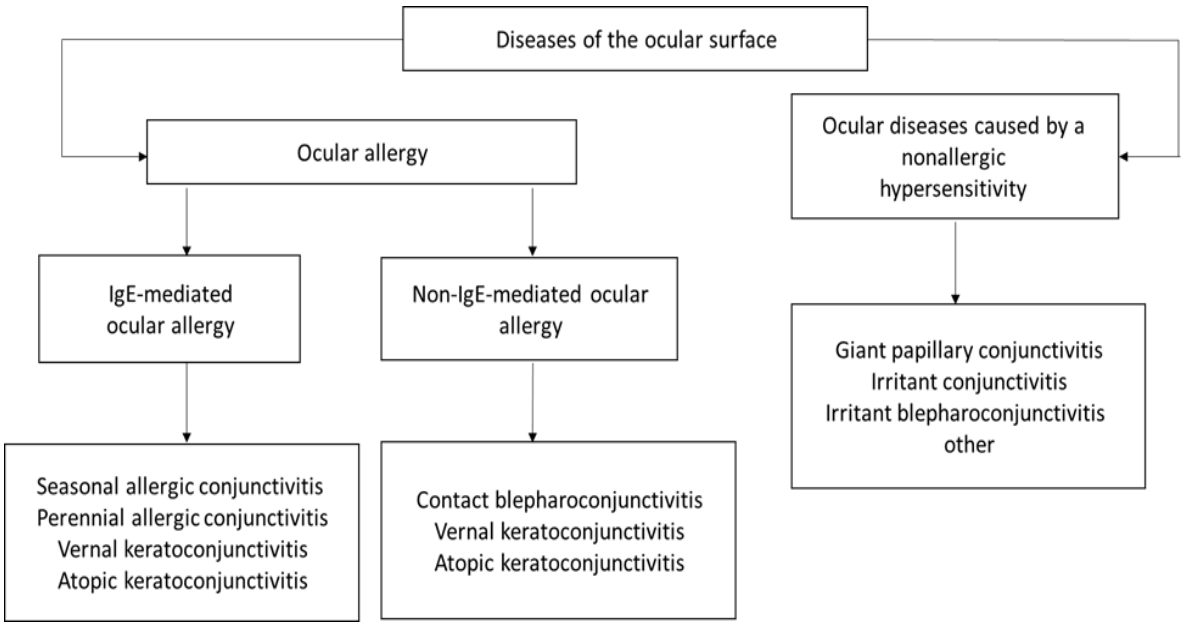


Figure 13: Diseases of the ocular surface caused by a hypersensitivity mechanism (Sánchez-Hernández, *et al*., 2015).

In the following sections, we will review the most common forms of allergic conjunctivitis, their clinical expression and management, and future prospects for their treatment (Table 3).

Table 3: Characteristics of the different types of allergic conjunctivitis (Villegas, 2021).

Characteristics of the different types of allergic conjunctivitis				
	Seasonal/Perennial allergic conjunctivitis (SAC/PAC)	Vernal Keratoconjunctivitis (VKC)	Atopic Keratoconjunctivitis (AKC)	Giant papillary reaction (GPC)
Disease Course	Seasonal or perennial with seasonal recurrence	Spring and summer months, may be perennial in warm climates	Chronic course with intermittent exacerbations	Avoiding precipitating cause resolves signs and symptoms
Mechanism	Allergen IgE-mediated mast cell degranulation	Hypersensitivity: Th2 lymphocytes, eosinophils, mast cells	Type IV: Th1 lymphocytes and eosinophils, mast cells	Mechanical irritation. Protein coating of irregular surfaces
Clinical characteristics	Hyperemia, watery discharge, chemosis, minimal papillary reaction, severe itching.	Cobblestoning of superior tarsal conjunctiva or limbal with Horner-Trantas dots, corneal implication, itching, mucous discharge	Lid eczema, superior and inferior tarsal papillae, photophobia, conjunctival cicatrization, severe itching	Giant papillae of the superior tarsal conjunctiva, itching, eye discomfort
Predisposing or risk factors/ Sex / Age	Environmental allergens PAC: dust mites, animal hair, etc. SAC: seasonal allergens such as pollens / Both sexes / All ages	Environmental allergens Hot and dry climates or months / Males / School age or puberty	Atopic dermatitis personal and/or family history / Males / Peak 30-50 years, resolves around 5th decade of life.	Irregular ocular surface, exposed sutures, scleral buckles, ocular prosthesis, contact lens use / Both sexes / All ages

B. Risk factors:

Risk factors associated with allergic conjunctivitis include a family history of allergies:

People with a family history of allergies have an increased risk of developing allergic conjunctivitis. Asthma and other allergic conditions: People with asthma, allergic rhinitis, or other allergic conditions are more likely to develop allergic conjunctivitis (Tiutiuca, *et al*., 2023).

C. Pathophysiology:

AC is the only ocular disease to involve solely a type I allergic reaction. In sensitized individuals, Th2 cells release pro-inflammatory cytokines (IL-3, IL-4, IL-5, IL-13) that stimulate immunoglobulin E (IgE) production by the B cells. The IgE become membrane-bound to mast cells and subsequent cross-linking by their respective allergen's triggers mast cell degranulation and release of preformed (histamine, tryptase) and newly formed mediators (leukotrienes, prostaglandins). The early phase of the allergic cascade begins within seconds to minutes after exposure and clinically lasts 20–30 minutes. During the early phase, mast cell release of mediators causes symptoms such as pruritus, tearing, redness, conjunctival injection, chemosis and a papillary reaction. The late phase begins a few hours later and is characterized by epithelial infiltration of inflammatory cells like neutrophils, lymphocytes, basophils and eosinophils, which lead to continued inflammation, persistent symptoms and increased likelihood of tissue damage. As the reaction progresses, hypersecretion of tears increases drainage through the lacrimal ducts carrying allergens directly into the nasal passage (Dupuis, 2020).

D. Clinical Features:

Allergic conjunctivitis is usually bilateral with common eye symptoms and signs that include the following:

- Itching, the hallmark of allergic eye disease
- Foreign body sensation
- Serous or mucous discharge
- Conjunctival hyperemia
- Tarsal papillary reaction

The symptoms can be differentiated into those that manifest primarily during the early or the late phase of the disease. Early signs are caused by coupling of histamine with its receptors and include: tearing, itching, redness, and edema (either conjunctival or palpebral), which are

expressed by the acronym TIREd, first suggested by Fauquert. Late signs occur hours later and are characterized by epithelial infiltration with a variety of cells: lymphocytes, neutrophils, basophils and eosinophils. This later phase leads to chronic inflammation, manifested by photophobia, ocular pain, visual impairment, and discharge, which are expressed by the acronym POVD (Villegas, *et al*., 2021).

E. Diagnosis of Allergic Conjunctivitis:

The diagnosis of ocular allergy is primarily clinical, but there are laboratory tests that can be useful in supporting the diagnosis. Allergists can perform skin testing for specific allergens by scratch tests or intradermal injections of allergen. In-vitro tests for IgE antibodies to specific allergens are widely used. Allergic tests would help in differentiating intrinsic and extrinsic forms and would, therefore, be helpful in the treatment (La Rosa, *et al*., 2013).

F. Treatment of Allergic Conjunctivitis:

The first objective when treating AC consists of avoidance or minimization of contact between the allergen and the conjunctiva by means of a series of nonpharmacologic measures. If the allergic inflammatory process is triggered in the conjunctiva, the characteristic signs and symptoms of AC that appear can be treated with pharmacologic measures, such as antihistamines, membrane stabilizing agents, multiple action drugs, vasoconstrictors, nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids. An aternative approach, specific immunotherapy, attempts to suppress or regulate the immune response triggered by the allergen in sensitized individuals and thus not only intervenes in the control of symptoms, but also modifies progression of the allergic disease (Table 4).

Table 4: Treatment in Allergic Conjunctivitis (Sánchez-Hernández, *et al*., 2015).

Nonpharmacologic	**Avoid allergens / Cold compresses / Artificial lubricants**	
Pharmacologic		
Ocular topical	Antihistamines Vasoconstrictors Mast cell stabilizers Dual action agents Corticosteroids	Antazoline, emedastine, levocabastine, pheniramine Naphazoline, oxymetazoline, phenylephrine, tetrahydrozoline Nedocromil, lodoxamide, sodium cromoglycate, spaglumic acid Diclofenac, flurbiprofen, ketorolac Azelastine, epinastine, ketotifen, olopatadine, Betamethasone, dexamethasone, fluorometholone, loteprednol, medrysone, prednisolone, rimexolone
Oral	Antihistamines	Bilastine, cetirizine, desloratadine, ebastine, fexofenadine, levocetirizine, loratadine, mizolastine, rupatadine
Nasal topical	Corticosteroids	Fluticasone, mometasone

IV. Oxidative Stress:

The definition of OS indicates "an imbalance between pro-oxidants and antioxidants with concomitant dysregulation of redox circuits and macromolecular damage". OS involves the chemistry of the reactions of so-called reactive oxygen species (ROS), reactive nitrogen species (RNS), reactive lipid species and free radicals (Albano, *et al*., 2022). OS has been associated with many pathological conditions in biological systems and plays a significant role in the pathogenesis of a range of diseases such as aging, cancer, cardiovascular diseases, and neurological disorders (Onur, 2024).

IV.1. Free Radicals:

Free radicals are molecular species that exist independently and contain an unpaired form of an electron in their atomic orbital. These radicals are highly unstable and reactive. They either donate or accept an electron, therefore acting as oxidants and reductants (Chaudhary, *et al*., 2023) These reactive oxygen species (ROS) and reactive nitrogen species (RNS) are produced both endogenously and exogenously (Chandimali, 2025), which include the free radicals and the non-free radicals (Table 5).

Table 5: Some examples of reactive oxygen and nitrogen species (Chouikh, *et al*., 2025)

Reactive oxygen species (ROS)			
Radicals	Symbol	Non-radicals	Symbol
Superoxide	$O_2^{\bullet-}$	Hydrogen peroxide	H_2O_2
Hydroxyl radical	$OH^{\bullet}$	Hypochlorous acid	HOCl
Peroxyl radical	$ROO^{\bullet}$	Hypobromous acid	HOBr
Alkoxyl radical	$RO^{\bullet}$	Ozone	O_3
Hydroperoxyl radical	$HO_2^{\bullet}$	Singlet oxygen	$^1\Delta g$
Lipid peroxyl radical	$LOO^{\bullet}$	Lipid peroxide	LOOH
Reactive nitrogen species (RNS)			
Radicals	Symbol	Non-radicals	Symbol
Nitric oxide	$NO^{\bullet}$	Nitrous acid	HNO_2
Nitrogen dioxide	$NO_2^{\bullet}$	Nitrosylcation	NO^+
		Nitroxyl anion	NO^-
		Dinitrogen tetroxide	N_2O_4
		Dinitrogen trioxide	N_2O_3
		Peroxynitrite	$ONOO^-$

IV.1.1. Sources of Free Radicals:

- **Intracellular Sources of ROS:**

There are several intracellular sources of ROS such as the mitochondria and NADPH oxidases (NOX), the major sources of intracellular ROS. Interestingly, both sources have

interactions between them, which contribute to the gradual progression of oxidative stress. Other sources of ROS include uncoupled NO synthase, cytochrome p450, xanthine oxidase (XO), the endoplasmic reticulum, peroxidases, and cyclooxygenases (Almeida, *et al*., 2022).

- **Exogenous Sources of ROS:**

There are several factors such as nutrients, alcohol, drugs (halothane, doxorubicin, and metronidazole), industrial solvents, heavy metals (Fe, Cu, Co, and Cr), transition metals (Cd, Hg, Pb, and As), air pollution, physical stressors (UV, X-rays, and among others) and lifestyle that act as exogenous sources of ROS (Almeida, *et al*., 2022).

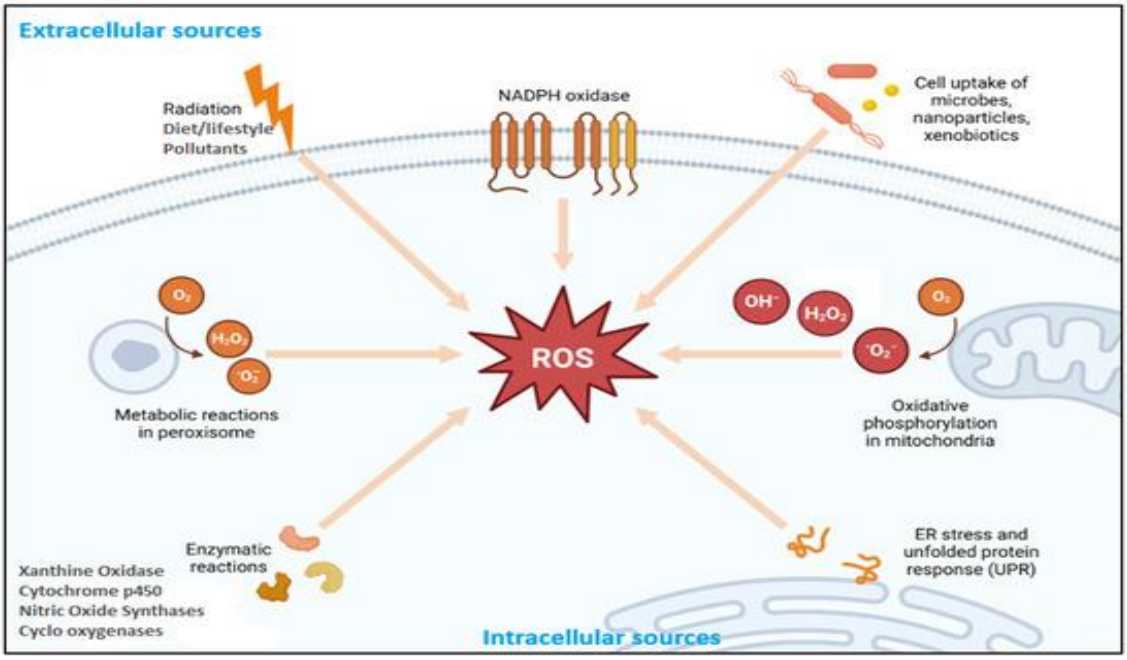


Figure 14: Schematic illustration depicts the various endogenous and exogenous sources contributing to the generation of reactive oxygen species (ROS) within a cell (Manful, *et al*., 2025).

- **Endogenous Sources of RNS:**

The endogenous production of RNS occurs primarily through tightly regulated enzymatic pathways that are crucial for physiological signaling but can contribute to pathological processes under the conditions of oxidative stress (Figure 15), the principal RNS, NO•, is synthesized by NOS enzymes, which catalyze the oxidation of L-arginine to produce NO• and citrulline (Manful, *et al*., 2025).

- **Exogenous Sources of RNS:**

The exogenous sources of RNS arise primarily from environmental exposures and dietary inputs, contributing significantly to systemic nitrosative stress (Figure15). The inhalation of

airborne pollutants, such as cigarette smoke, vehicle exhaust, and industrial emissions, introduces reactive nitrogen oxides (NO_x), including •NO2 and NO•, which readily penetrate lung tissues and initiate inflammatory cascades in the respiratory tract (Manful, *et al*., 2025).

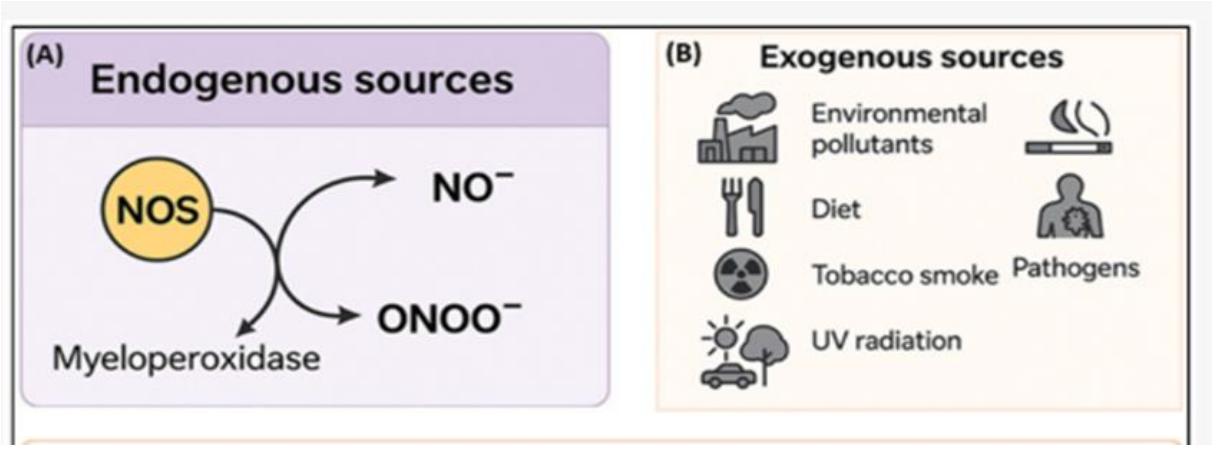


Figure 15: Canonical schematic outlines the sources and biochemical pathways of reactive nitrogen species (RNS) (Manful, *et al*., 2025).

IV.2. Antioxidants:

are defined as molecules that dispose of, scavenge, and inhibit the formation of Reactive oxygen species (ROS) or oppose their actions. In other words, antioxidants are chemicals that bind with free radicals and nullify their effect by causing damage to biological molecules. They bind with them by giving up their electrons. This results in the termination of oxidative chain reactions, and the free radicals are no longer able to attack the cell. Antioxidants attain a state of free radicals after donating their electrons. It can accommodate the change in electrons without becoming reactive, which is why they are not harmful (Chouikh, *et al*., 2025). The role of antioxidants is to lower or terminate these chain reactions by removing free radicals or inhibiting other oxidation reactions by being oxidized themselves. So, antioxidants are often reducing agents such as polyphenols or thiols (Adwas, *et al*., 2019).

IV.2.1. Endogenous Antioxidants:

The human body is equipped with a variety of antioxidants that serve to counterbalance the effect of oxidants. For all practical purposes, these can be divided into 2 categories: enzymatic and nonenzymatic (Birben, *et al*., 2012).

A. Enzymatic antioxidant:

Endogenous enzymatic antioxidants are the primary protection against oxidative and nitrosative stress (Manful, *et al*., 2025). The enzymatic antioxidants include superoxide

dismutase (SOD), catalase, glutathione reductase (GRx) and glutathione peroxidase (GPx) (Chouikh, *et al*., 2025). These enzymes facilitate the detoxification of ROS and RNS through highly regulated catalytic reactions, preserving redox balance and preventing macromolecular damage (Manful, *et al*., 2025).

B. Non-enzymatic antioxidants:

They are also known as synthetic antioxidants or dietary supplements. They are usually low-molecular-weight antioxidant (LMWA) compounds capable of preventing oxidative damage either by directly interacting with Reactive oxygen species (ROS) or indirectly by chelating metals (Chouikh, *et al*., 2025). Glutathione, uric acid, albumin, selenium, melatonin, bilirubin, coenzyme Q10, ceruloplasmin, α-lipoic acid and transferrin are examples of non-enzymatic antioxidants (Onur, 2024).

IV.2.2. Exogenous Antioxidants:

Exogenous antioxidants can be categorized into two distinct groups: exogenous antioxidants, both in the form of vitamins and as medicinal substances. Exogenous vitamin antioxidants, such as α-tocopherol (vitamin E), β-carotene (vitamin A), ascorbic acid (vitamin C), and folic acid (vitamin B9), are generated from vitamins and are consumed externally (Onur, 2024). derived from food and other dietary sources. Several herbs, spices, vitamins, foods, vegetables etc. exhibits antioxidant activities. Therefore, antioxidants-based drugs for the treatment of various pathological diseases have gained attraction in clinical as well as research areas (Noori, 2012).

The Factors protecting against the generation of free radicals and participating in their transformation into inactive derivatives. These include both exogenous and endogenous compounds, which form a complex antioxidant system with enzymatic and non-enzymatic properties (Korczowska-Łącka, *et al*., 2023).

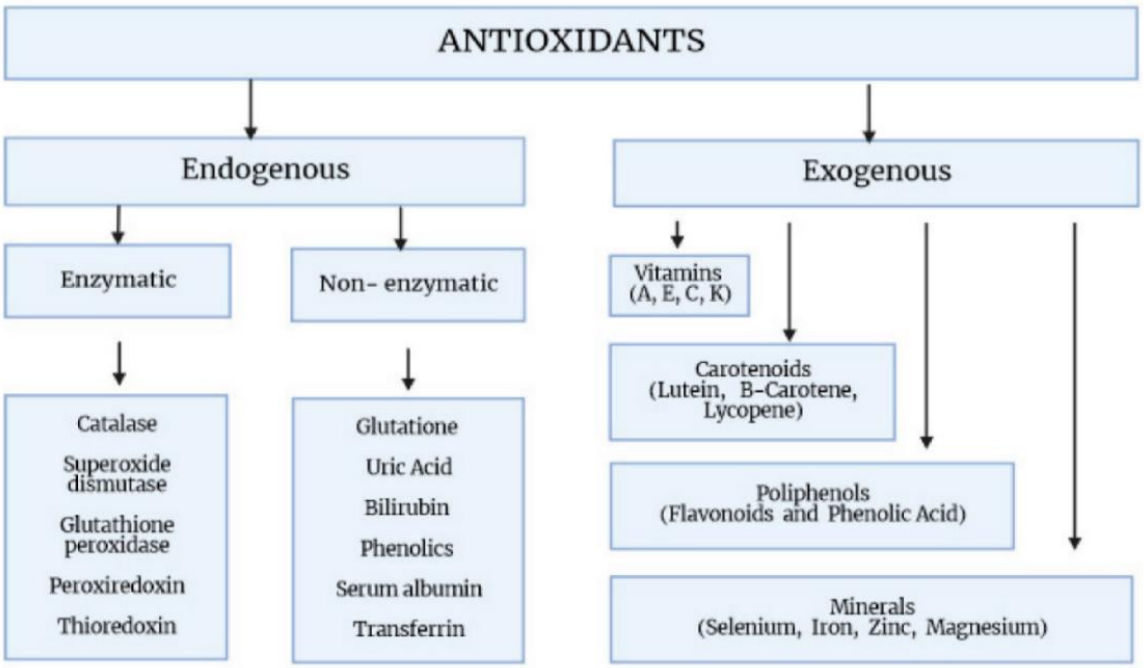


Figure 16: The body's oxidative stress defense mechanisms (Korczowska-Łącka, *et al*., 2023).

IV.3. Oxidative Stress in Eye Disease:

The eyes are unique as they are constantly exposed to sunlight, atmospheric oxygen, environmental chemicals and physical abrasion. In addition, these potentially deleterious ROS are generated internally by oxygen metabolism. Therefore, the eyes are at risk to be exposed to higher levels of free radicals and to increased levels of oxidative stress. The accumulation of ROS in the ocular surface leads to dry eye disease, and meibomian gland disease (Labib, *et al*., 2022).

"Dry eye disease was used as an example to show that oxidative stress contributes to the exacerbation of eye inflammation by disrupting the redox balance and enhancing the ocular inflammation response."

IV.3.1. Dry Eye Disease (Ded):

is a multifactorial condition defined by disturbances in the tear film due to reduced tear production or excessive evaporation. As one of the most prevalent ocular surfaces diseases the ocular inflammation response (Akbulut Yağcı, *et al*., 2025). The global prevalence of DED has been reported to be between 5 and 35% (Simpson, *et al*., 2022), DED involves oxidative damage alongside inflammation. It can arise from systemic inflammatory conditions, localized ocular issues, or the use of common medications. Additionally, environmental factors like pollutants, UV radiation, and ozone contribute to increased OS, inflammation, and tear film

osmolarity, further impacting the ocular surface. Hyperosmolarity is a key driver in DED pathology, perpetuating oxidative stress-induced damage to ocular epithelial cells. This stress leads to mitochondrial DNA (mtDNA) damage and lipid peroxidation in cell membranes (Akbulut Yağcı, *et al*., 2025), various oxidative stress markers, including lipid peroxide, myeloperoxidase, NO synthase, xanthine oxidase/ oxidoreductase, 4-HNE, and MDA were found to be elevated in tear fluid and conjunctival specimens from patients with DED. Moreover, impaired antioxidant functions have been detected in DED patients. For example, expression of CAT, GPX, and SOD was reduced in conjunctival epithelial cells from patients with DED compared to healthy controls (Böhm, *et al*., 2023). OS activates inflammatory cascades that release mediators serving as biomarkers in tears. For example, interleukin-6 in tears and conjunctiva stimulates the production of ROS, prostaglandins, and enzymes under conditions of low antioxidant presence (Akbulut Yağcı, *et al*., 2025).

Aging is another well-established risk factor for DED, associated with a decline in antioxidant defense mechanisms and an increase in oxidative stress. The rate of O2•− and H2O2 production increases, inducing a pro-oxidative shift and accumulation of oxidatively damaged molecules (Böhm, *et al*., 2023).

Environmental factors, such as air pollution, particulate matter, gaseous substances or UVR as well as aging lead to increased inflammation with consequent imbalance between ROS generation and the antioxidant defense. Additionally, hyperosmolarity and instability of the tear film further aggravates inflammation and oxidative stress contributing to the vicious circle of dry eye disease. DED: dry eye disease; UVR: ultraviolet radiation; IL-1: interleukin 1; IL-6: interleukin 6; TNF-α: tumor necrosis factor α; O2•−: superoxide; H2O2: hydroxyl peroxide; Nrf2: nuclear factor erythroid 2-related factor 2; SOD: superoxide dismutase; CAT: catalase (Böhm, *et al*., 2023).

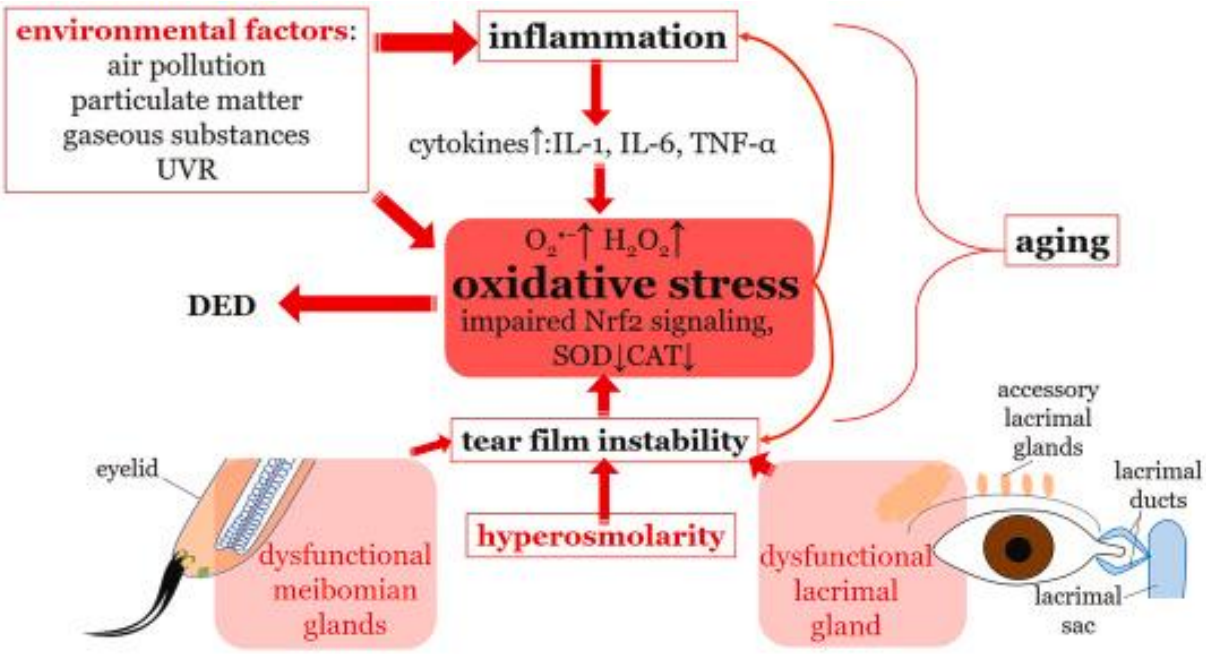


Figure 17: Role of oxidative stress in the pathogenesis of dry eye disease (Böhm, *et al*., 2023).

Second part:
Experimental part

Material and Methods

Conclusion

Ocular inflammatory diseases represent a multifactorial health problem whose occurrence and progression depend on the interaction of various biological, environmental, and immunological factors. Although the eye possesses effective natural defense mechanisms, including tears, eyelids, and local immune protection, it remains particularly vulnerable to external aggressors that may induce different forms of inflammation.

Bacterial infections were found to be mainly associated with certain environmental and occupational conditions, particularly frequent exposure to dust, industrial smoke, and poor hygiene practices. These findings suggest that environmental and occupational exposures, together with inadequate hygiene measures, constitute important risk factors for bacterial ocular inflammation.

Viral inflammations appeared to be more closely related to person-to-person transmission and direct contact with infected individuals. This indicates that preventive measures aimed at limiting contagion and improving hygiene practices are essential for reducing the spread of viral ocular infections.

Allergic manifestations were more frequently observed among subjects exposed to various allergens or those with a personal or family history of allergic diseases. These observations support the role of both environmental exposure and genetic predisposition in the development of ocular allergic disorders.

The analysis of selected biological parameters revealed variations suggesting the presence of a systemic inflammatory response associated with ocular disorders. This finding highlights that ocular inflammation may not be restricted to the eye alone but can also reflect broader systemic inflammatory processes.

Biological alterations were also suggestive of an imbalance in the body's oxidative status. This supports the hypothesis that oxidative stress may contribute to the pathophysiology and progression of certain ocular inflammatory diseases.

Overall, the results emphasize the importance of adopting a comprehensive approach to ocular inflammatory diseases that considers both local ocular factors and systemic biological mechanisms. They also underline the need for early and accurate diagnosis to distinguish between different forms of ocular inflammation and ensure appropriate therapeutic management. Furthermore, prevention remains a key strategy and should focus on improving personal and occupational hygiene, reducing exposure to irritants and allergens, avoiding eye rubbing, and promoting public awareness of ocular health and protective measures.

❖ **Perspectives:**

In light of the findings obtained, several research perspectives may be proposed:

- Conduct studies involving larger sample sizes to confirm and further expand the present findings.
- Investigate more deeply the role of oxidative stress in the development and progression of ocular inflammatory diseases.
- Explore new biological biomarkers that could improve the early diagnosis of these disorders.
- Evaluate the effectiveness of preventive strategies aimed at reducing exposure to environmental factors associated with ocular inflammation.
- Develop innovative therapeutic approaches incorporating antioxidant and anti-inflammatory agents.
- Strengthen awareness and educational programs regarding ocular hygiene and the risks associated with occupational and environmental exposures.

Bibliographical References

Abraham, M., Gola, J., & Cometto-Muñiz, J. (2016). An assessment of air quality reflecting the chemosensory irritation impact of mixtures of volatile organic compounds. *Environment International*, pp. 86,84-91.

Açar, G., & Çiçekcibaşı, A. (2025). *Overview of Head & Neck Clinical Anatomy*. Lyon: Livre de Lyon.

Adwas, A. A., Elsayed, A. S., & Azab, A. E. (2019, February 21). Oxidative stress and antioxidant mechanisms in human body. *Journal of Applied Biotechnology & Bioengineering.*, pp. 6(1):43-47.

Agrahari, G., Sah, S., Lee, M., Bang, C., Kim, Y., Kim, H.-Y., & Kim, T.-Y. (2022, January). Inhibitory effects of superoxide dismutase 3 on IgE production in B cells. *Biochemistry and Biophysics Reports*, p. 29:101226.

Aijarapu, L., Wilson, A., & Jennifer, J. (2021, February 23). Interstitial keratitis secondary to Herpes Simplex Virus (HSV). *EyeRounds.org*. The University of Iowa.

Aishwarya, A., Agarwal, A., Saxena, D., Jain, V., Singh, A., & Agarwal, R. (2024, October-December). Clinical Features and Epidemiological Insights of Acute Epidemic Conjunctivitis: A Multicentric Cross-Sectional Study in North Central India. *Romanian Journal of Ophthalmology*, pp. 68(4),372-378.

Akbulut Yağcı, B., & Erdal, H. (2025, March 27). The Role of Oxidative Stress in the Pathogenesis of Eye Diseases. *Advances in Health, Sports and Technology Sciences*, pp. 2(1):33–39.

Akkurt Arslan, M., Brignole-Baudouin, F., Chardonnet, S., Pionneau, C., Blond, F., Baudouin, C., & Kessal, K. (2023, September 14). Profiling tear film enzymes reveals major metabolic pathways involved in the homeostasis of the ocular surface. *Scientific Reports*, p. 13(1):15231.

Albano, G. D., P., G. R., & Montalbano, A. M. (2022, November 13). Overview of the Mechanism of Oxidative Stress: Impact in Inflammation of the Airway Diseases. *Antioxidants*, p. 11(11):2237.

Alghareeb, S., Alfhili, M., & Fatima, S. (2023, March 7). Molecular Mechanisms and Pathophysiological Significance of Eryptosis. *International Journal of Molecular Sciences*, p. 24(6):5079.

AlHarthi, A. S. (2025). Seasonal variation in conjunctivitis in Saudi Arabia and reduction of searches during the COVID-19 pandemic: Analysis of Google Trends data. *JMIR Formative Research*, pp. 9,73845.

Aljaberi, H. A. (2024). *Anatomy of the Eye: Choroid & Sclera.* Al-Mustaqbal University, College of Health and Medical Technologies, Department of Optics Techniques.

Almeida, A. J., Oliveira, J. C., Pontes, L. V., Souza Júnior, J. F., Gonçalves, T. A., Dantas, S. H., . . . Medeiros, I. A. (2022, October 19). ROS: Basic Concepts, Sources, Cellular Signaling, and its Implications in Aging Pathways. *Oxidative Medicine and Cellular Longevity*, p. 2022:1225578.

Amouzegar, A., Chauhan, S. K., & Dana, R. (2018, April). When clarity is crucial: regulating ocular surface immunity. *Trends in Immunology*, pp. 39(4):288-301.

Atchison, D. A., & Smith, ,. G. (2023). *Optics of the human eye.* CRC Press (Taylor & Francis Group, LLC).

Austermann, J., Roth, J., & Barczyk-Kahlert, K. (2022, June 20). The Good and the Bad: Monocytes' and Macrophages' Diverse Functions in Inflammation. *Cells*, p. 11(12):1979.

Awh, C., & Wilson, M. (2022, November 17). *Basic Histology of the Eye and Accessory Structures*. Récupéré sur https://2u.pw/RsYu0j

Ay, İ., Palanbek Yavaş, S., & Baysan, C. (2022, October). A cross-sectional study on marble

workers: Occupational eye health problems and risk factors. pp. 85(4),548-556.

Ayala, A., Muñoz, M., & Argüelles, S. (2014). Lipid peroxidation: Production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. *Oxidative Medicine and Cellular Longevity*, p. 360438.

Azari, A., & Arabi, A. (2020, April 25). Conjunctivitis: A Systematic Review. *Journal of Ophthalmic and Vision Research*, pp. 15 (3): 372–395.

Azari, A., & Barney, N. (2013, October). conjunctivitis: A systematic review of diagnosis and treatment. *The Journal of the American Medical*, pp. 310(16),1721-1730.

Azher, T. N., Yin, X.-T., Tajfirouz, D., Huang, A. J., & Stuart, P. M. (2017, January 19). Herpes simplex keratitis: challenges in diagnosis and clinical management. *Clinical Ophthalmology*, pp. 11:185–191.

Baab, S., Le, P., Gurnani, B., & Kinzer, E. (2024). Allergic Conjunctivitis. *StatPearls*. Treasure island,FL, United ststes: StatPearls Publishing.

Bafana, A., Dutt, S., Kumar, A., Kumar, S., & Ahuja, P. (2011). The basic and applied aspects of superoxide dismutase. *Journal of Molecular Catalysis B: Enzymatic*, pp. 68(2),129-138.

Bagga, B., Kate, A., Joseph, J., & Dave, V. P. (2020). Herpes simplex infection of the eye: An introduction. *Community Eye Health Journal*, pp. 33(108),68-70.

Balyen, L. (. (2022). *The Physiology of Cornea.* JOJ Ophthalmology.

Banani, A. (2023). *The Anatomy of the Human Eye Explained.* Amirali Banani Publishing.

Bao, J. W. (2025, August 29). Decoding allergic conjunctivitis: Latest perspectives on etiological drivers and immunopathological mechanisms. *Clinical Reviews in Allergy & Immunology*, p. 68(1):85.

Bergmann, M., Williams, J., & Gomes, P. (2014, August). Treatment of allergic conjunctivitis with bepotastine besilate ophthalmic solution 1.5%. *Clinical Ophthalmology*, pp. 13(8),505-1495.

Bielory, L., Delgado, L., Katelaris, C., Leonardi, A., Rosario, N., & Vichyanoud, P. (2020, January). Diagnosis and management of allergic conjunctivitis. *Annals of Allergy, Asthma & Immunology*, pp. 124(2),118-134.

Bilkhu, P., Wolffsohn, J., & Naroo, S. (2012, February). A review of non-pharmacological and pharmacological management of seasonal and perennial allergic conjunctivitis. *Contact Lens and Anterior Eye*, pp. 35(1),9-16.

Birben, E., Sahiner, U. M., Sackesen, C., Erzurum, S., & Kalayci, O. (2012, January 13). Oxidative Stress and Antioxidant Defense. *World Allergy Organization Journal.*, pp. 5(1):9–19.

Biswas, R., Anish, D., Shobha Rani, R. H., Nagendra Prasad, K., Paranjyothi, K., Anita, L., . . . Sangeetha, S. (2025, june 23). Comprehensive Analysis of Allergens Exposure and Symptoms Onset for Allergic Conjunctivitis A Retrospective Cohort Study. *Ophthalmology Research: An International Journal*, pp. 20(4),16-23.

Bitko, V., Garmon, N. E., Cao, T., Estrada, B., Oakes, J. E., Lausch, R. N., & Barik, S. (2004, July 15). Activation of cytokines and NF-kappa B in corneal epithelial cells infected by respiratory syncytial virus: potential relevance in ocular inflammation and respiratory infection. *BMC Microbiology*, p. 4:28. doi: 10.1186.

Böhm, E., Buonfiglio, F., Voigt, A., Bachmann, P., Safi, T., Pfeiffer, N., & Gericke, A. (2023, November 18). Oxidative stress in the eye and its role in the pathophysiology of ocular diseases. *Redox Biology*, p. 68:102967.

Cabrera-Aguas, M., Khoo, P., & Watson, S. L. (2022, jun 21). Infectious keratitis: A review. *Clinical & Experimental Ophthalmology*, pp. 50(5): 543–562.

Camodeca, A. J., & & Anderson, E. P. (2025, January 22). *Corneal Foreign Body*. Récupéré sur StatPearls: https://www.ncbi.nlm.nih.gov/books/NBK536977/

Chandimali, N. B.-J.-S.-K.-K. (2025, January 24). Free radicals and their impact on health and

antioxidant defenses: A review. *Cell Death Discovery*, p. 11:19.

Chang, A., & Purt, B. (2023). *Biochemistry, Tear Film.* Treasure Island (FL): StatPearls Publishing LLC.

Charlie-Silva, I., Klein, A., Gomes, J., Prado, E., Moraes, A., Eto, S., . . . Belo, M. (2019). Acute-phase proteins during inflammatory reaction by bacterial infection: Fish-model. *Scientific Reports*, pp. 9(1),4776.

Chaudhary, P., Janmeda, ,. P., Docea, ,. A., Yeskaliyeva, ,. B., Abdull Razis, ,. A., Modu, ,. B., . . . & Sharifi-Rad, ,. J. (2023, May 10). Oxidative stress, free radicals and antioxidants: Potential crosstalk in the pathophysiology of human diseases. *Frontiers in Chemistry*, p. 11:1158198.

Chaurasia, B. D. (2023). *Human Anatomy for Dental Students Fifth Edition.* CBS Publishers & Distributors Pvt Ltd.

Chen, R., Yang, J., Zhang, C., Li, B., Bergmann, S., Zeng, F., . . . Wang, B. (2019). Global associations of air pollution and conjunctivitis diseases: A systematic review and meta-analysis. *International Journal of Environmental Research and Public Health*, pp. 16(19), 3652.

Chen, Y., Wang, S., Alemi, H., Dohlman, T., & Dana. (2022, May). Immune regulation of the ocular surface. *Experimental Eye Research (Exp Eye Res)*, p. 218: 109007. doi:10.1016.

Chen, Y.-Y., Liu, A.-H., Nurmatov, U., van Schayck, O., & Kuo, I. (2023, March). Antibiotics versus placebo for acute bacterial conjunctivitis. *Cochrane Database of Systematic Reviews*, pp. Reviews, (3), Article CD001211.

Cheung, A., Choi, D., Ahmad, S., Amescua, G., Jhanji, V., Lin, V., . . . Varu, D. (2024). Conjunctivitis PPP 2023. *Ophthalmology*, pp. 131(4),134-204.

Chigbu, D., Karbach, N., Abu, S., & Hehar, N. (2024). Cytokines in Allergic Conjunctivitis: Unraveling Their Pathophysiological Roles. *Life*, pp. 14(3), 350.

Chlasta-Twardzik, E., & Nowińska, A. (2024). *Keratitis - Current Perspectives.* London: IntechOpen.

Chouikh, A., Chenguel, A., & Ben Ali, A. (2025, February 15). Understanding the Role of Free Radicals, Oxidative Stress, and Antioxidants: A Comprehensive Review. *Letters in Applied NanoBioscience*, p. 14(2):Article 66.

Cordiano, R., Di Gioacchino, M., Mangifesta, R., Panzera, C., Gangemi, S., & Minciullo, P. (2023, August 9). Malondialdehyde as a Potential Oxidative Stress Marker for Allergy-Oriented Diseases: An Update. *Molecules*, p. 28(16):5979.

Craig Boote, I. A. (2020). *Scleral structure and biomechanics.* : Progress in Retinal and Eye Research (Elsevier).

Dammak, A., Pastrana, C., Martin-Gil, A., Carpena-Torres, C., Peral Cerda, A., Simovart, M., . . . Carracedo, G. (2023, January 20). Oxidative Stress in the Anterior Ocular Diseases: Diagnostic and Treatment. *Biomedicines*, pp. 11(2),292.

Daruich, A., Sauvain, J.-J., Matet, A., Eperon, S., Schweizer, C., Berthet, A., . . . Behar-Cohen, F. (2020, October 15). Levels of the oxidative stress biomarker malondialdehyde in tears of patients with central serous chorioretinopathy relate to disease activity. *Molecular Vision*, pp. 26:722-730.

Delis, C., Chatzidimitriou, C., & Georgiou, S. (2024, April 15). Biomarkers of Oxidative Stress in Tear Fluid: A Review of Sampling, Analytical Methods, and Clinical Applications. *Journal of Ophthalmic and Vision Research*, pp. 19(2),180-195.

Di Zazzo, A., Zhu, A. Y., Nischal, K., & & Fung, S. S. (2024, February 15). Vernal keratoconjunctivitis in adults: a narrative review of prevalence, pathogenesis, and management. pp. 4,1328953.

Dias, S., Brouwer, M., & van de Beek, D. (2022, September). Sex and Gender Differences in Bacterial Infections. *Infection and Immunity*, pp. 90(10),e00283-22.

Doan, S., Papadopoulos, N. G., Lee, J. K., Leonardi, S., Manti, S., Lau, S., . . . & Lazarewicz, S. B. (2023, October). Vernal keratoconjunctivitis: Current immunological and clinical evidence and the potential role of omalizumab. pp. 16(6),100788.

Downie, L. E., Bandlitz, S., Bergmanson, J. P., Craig, J. P., Dutta, D., Maldonado-Codina, C., . . . Wolffsohn, J. S. (2021, April). Anatomy and Physiology of the Anterior Eye. *Contact Lens and Anterior Eye*, pp. 44(2):132-156.

Dupuis, P. P. (2020). A contemporary look at allergic conjunctivitis. *Allergy, Asthma & Clinical Immunology*, p. 16: Article 5.

Edman, P. (2019). *Biopharmaceutics of Ocular drug delivery.* Boca Raton, Florida.: CRC Press.

Egrilmez, S., & Yildirim Theveny, S. (2020, january). Treatment-Resistant Bacterial Keratitis: Challenges and Solutions. *Clinical Ophthalmology*, pp. 14, 287–297.

Elberling, J., Duus Johansen, J., Dirksen, A., & Mosbech, H. (2006). Exposure of eyes to perfume: a double-blind, placebo-controlled experiment. pp. 16,273-281.

Epps, S., Boldison, S., Stimpson, M., Khera, T., Lait, P., Copland, D., . . . Nicholson, L. (2018, July). Re-programming immunosurveillance in persistent non-infectious ocular inflammation. *Progress in Retinal and Eye Research*, pp. 65 (2018) 93–106.

Ezisi, C. N., Ogbonnaya, C. E., Okoye, O., Ezeanosike, E., Ginger-Eke, H., & Arinze, O. C. (2018, January-June). Microbial keratitis: A review of epidemiology, pathogenesis, diagnosis, and management. *Nigerian Journal of Ophthalmology*, pp. 26(1):13–23.

Foutch, B. K., Sandberg, K. A., Bennett, E. S., & Naeger, L. L. (2020, June 20). Effects of Oral Antihistamines on Tear Volume, Tear Stability, and Intraocular Pressure. *Vision(MDPI)*, p. 20;4(2):32.

Fujishima, H., Satake, Y., Okada, N., Kawashima, S., Matsumoto, K., & Saito, H. (2013). Effects of diesel exhaust particles on primary cultured healthy human conjunctival epithelium. *Annals of Allergy, Asthma & Immunology*, pp. 110(1), 39-43.

Garg, K. (2024). *B. D. Chaurasia's Human Anatomy for Dental Students.* CBS Publishers & Distributors.

Ghosh, S., & Klein, R. (2017, March 1). Sex drives dimorphic immune responses to viral infections. *The Journal of Immunology*, pp. 198(5):1782-1790.

Ghouali, W., Gendron, G., Baudouin, C., & Labbé, A. (2023, February). From ocular itching to eye rubbing: a review of the literature. *French Journal of Ophthalmology*, pp. 46(2),173-184.

Gomes, P., Ciolino, J., Arranz, P., & Hernánde. (2023, July). Efficacy of once-daily ophthalmic bilastine for the treatment of allergic conjunctivitis: A dose-finding study. *ournal of Investigational Allergology and Clinical Immunology*, pp. 33(4),271-280.

Gulhar, R., Ashraf, M., & Jialal, I. (2023). Physiology, Acute Phase Reactants. *StatPearls*. Treasure Island (FL).: StatPearls Publishing.

Guo, M., Diaz, G., Yu, Y., Patel, C., Farrar, J., Asbell, P., & Ying, G.-S. (2024, April). Association between systemic medication use and severity of dry eye signs and symptoms in the DRy eye assessment and management (DREAM) study. *The Ocular Surface*, pp. 32: 112–119.

Gurnani, B., & Kaur, K. (2023). *Bacterial Keratitis.* Treasure Island, Florida: StatPearls Publishing.

Hamzeh-Cognasse, H., Damien, P., Chabert, A., Pozzetto, B., Cognasse, F., & Garraud, O. (2015, February 26). Platelets and infections – complex interactions with bacteria. *Frontiers in Immunology*, p. 6:82.

Hashmi, M., Gurnani, B., & Benson, S. (2024, January 26). Conjunctivitis. *StatPearls*. StatPearls Publishing.

Hoffmann, A., Cheng, G., & Baltimore, D. (2025). NF-κB: master regulator of cellular responses in health and disease. *Immunity & Inflammation*, p. 1(1):2. doi: 10.1007.

Hom, J., Dulmovits, B., Mohandas, N., & Blanc, L. (2015, December). The erythroblastic island as an emerging paradigm in the anemia of inflammation. *Immunology Research*, pp. 63(0): 75–89.

Hottz, E., Bozza, F., & Bozza, P. (2018, April 30). Platelets in Immune Response to Virus and Immunopathology of Viral Infections. *Frontiers in Medicine*, p. 5:121.

Hou, A., Tin, M., & Tong, L. (2017, July). Toll-like receptor 2-mediated NF-kappa B pathway activation in ocular surface epithelial cells. *Eye and Vision*, p. 4:17. doi: 10.1186.

Howell, M., Wollenberg, A., Gallo, R., Flaig, M., Streib, J., Wong, C., . . . Leung, D. (2006). Cathelicidin deficiency predisposes to eczema herpeticum. *Journal of Allergy and Clinical Immunology*, pp. 117(4),41-836.

Huang, S.-C., Lei, Y.-P., Hsiao, M.-C., Hsieh, Y.-K., Tang, Q.-P., Chen, C., & Hsu, M.-Y. (2025, January 16). Multicomponent Dietary Supplementation: Impact on Tear Secretion and Ocular Surface Inflammation in Dry Eye Syndrome Patients. *Antioxidants*, p. 14(1):103.

Hwang, J., Jin, J., Jeon, S., Moon, S., Park, M., Yum, D.-Y., . . . Oh, G. (2020). SOD1 suppresses pro-inflammatory immune responses by protecting against oxidative stress in colitis. *Redox Biology*, pp. 37,101760.

Idzko, M., Pitchford, S., & Page, C. (2015, June). Role of platelets in allergic airway inflammation. *Journal of Allergy and Clinical Immunology*, pp. 135(6):1416-23.

IMAIOS. ((n.d.)). *Eye. e-Anatomy.* Récupéré sur https://2u.pw/RsYu0j

Janumala, H., Sehgal, P. K., & Mandal, A. B. (2012). Keratitis. London: IntechOpen.

Jhanji, V., Chan, T. C., Li, E. Y., Agarwal, K., & & Vajpayee, R. B. (2015, September–October). Adenoviral keratoconjunctivitis. *Survey of Ophthalmology*, pp. 60(5),435-443.

Jin, Y., Jones, L., & Gorbet, M. (2026, April 14). Phenotype of Tear Leukocytes in Seasonal Ocular Allergy and Their Potential Impacts on Ocular Surface Inflammation. *Ocular Immunology and Inflammation*, pp. 2026,34(4).

Kakaire, S., & Mulumba, T. (2024, April 8). Factors leading to the prevalence of viral conjunctivitis among patients receiving eye care services at Jinja Regional Referral Hospital. *SJ Ophthalmology Africa*, p. 1(1).

Katipoğlu, Z., & & Zengin, N. (2021, June 7). Dust exposure: a novel environmental risk factor for conjunctivochalasis. *Therapeutic Advances in Ophthalmology*, pp. 13,1-7.

Khoo, M. (2023). Overview of eye infections and their signs and treatment. *Journal of Laboratory Medicine*, pp. 4(1),1000110.

Kiernan, M., Keith, A., Stein, A., Jenkins, T., Sebastian, T., Meece, J., . . . Frost, H. (2024, August). Secondary household transmission of conjunctivitis in children. *Journal of American Association for Pediatric Ophthalmology and Strabismus*, p. 28(4): 103953.

Kim, M., & Tauber, J. (2025, October 26). Clinical considerations and recommended diagnostic algorithm for the differential diagnosis of conjunctivitis: a clinical practice review. *Annals of Eye Science*, pp. 2025,10-31.

Kishimoto, T., Kang, S., & Tanaka, T. (2015). IL-6: A New Era for the Treatment of Autoimmune Inflammatory Diseases. Tokyo, Japan: Springer.

Konov, A. (2024, May 28). Ocular Immunology: Immune Responses and Mechanisms Occurring Within the Eye. *Journal of Clinical and Cellular*, pp. 15(3),1000720.

Korczowska-Łącka, I., Słowikowski, B., Piekuł, T., Hurła, M., Banaszek, N., zymanowicz, O., . . . Dorszewska, J. (2023, September 29). Disorders of Endogenous and Exogenous Antioxidants in Neurological Diseases. *Antioxidants*, p. 12(10):1811.

La Rosa, M., Lionetti, E., Reibaldi, M., Russo, A., Longo, A., Leonardi, S., . . . Reibaldi, A. (2013). Allergic conjunctivitis: A comprehensive review of the literature. *Italian Journal of Pediatrics*, p. 39:Article 18.

Labib, B., & Chigbu, D. (2022, September 29). Clinical Management of Herpes Simplex Virus Keratitis. pp. 12(10),2368.

Lai, Y.-F., Lin, T.-Y., Chen, Y.-H., & Lu, D.-W. (2023, February 3). Erythropoietin in Glaucoma: From Mechanism to Therapy. *International Journal of Molecular Sciences*, pp. 2023, 24, 2985.

Lee, Y., Ju, H., Kwon, J., & Bae, J. (2020, June). Seasonality of allergic diseases: Real-world evidence from a nationwide population-based study. *Immunity, Inflammation and Disease*, pp. 8(3),360–362.

Li, J., Lu, X. X., Jiang, B., Du, Y., Yang, Y., Qian, H., . . . Wang, Q. (2018). Adenovirus-associated acute conjunctivitis in Beijing, China, 2011–2013. *BMC Infectious Diseases*, pp. 18,135.

Li, Z., Bian, X., Yin, J., Zhang, X., & & Mu, G. (2016, May 9). The Effect of Air Pollution on the Occurrence of Nonspecific Conjunctivitis. *Journal of Ophthalmology*, pp. 3628762, 3 pages.

Lorente, L., Martín, M., Abreu-González, P., Domínguez-Rodríguez, A., Labarta, L., Díaz, C., . . . Jiménez, A. (2013). Sustained high serum malondialdehyde levels are associated with severity and mortality in septic patients. *Critical Care*, pp. 17(6),R290.

Lushchak, V. I. (2012). Glutathione Homeostasis and Functions: Potential Targets for Medical Interventions. *Journal of Amino Acids*, pp. 2012,736837.

Machiele, R., Lopez, M. J., & Czyz, C. N. (2023, july 24). *Anatomy, Head and Neck: Eye Lacrimal Gland.* Treasure Island (FL), Florida, United states: StatPearls Publishing.

Mahoney, M. J., Bekibele, R., Notermann, S. L., Reuter, T. G., & Borman-Shoap, E. C. (2023, April 29). Pediatric Conjunctivitis: A Review of Clinical Manifestations, Diagnosis, and Management. *children*, pp. 10(5),808.

Manful, C. F., Fordjour, E., Subramaniam, D., Sey, A. A., Abbey, L., & Thomas, R. (2025, August 4). Antioxidants and Reactive Oxygen Species: Shaping Human Health and Disease Outcomes. *International Journal of Molecular Sciences*, p. 26(15) :7520.

Marchitti, S., Chen, Y., Thompson, D., & Vasiliou, V. (2011). Ultraviolet Radiation: Cellular Antioxidant Response and the Role of Ocular Aldehyde Dehydrogenase Enzymes. *Eye & Contact Lens*, pp. 37(4),13-106.

Martin Herranz, R., & Corrales, R. (2013). *Ocular Surface: Anatomy and Physiology, Disorders and Therapeutic Care.* CRC Press.

Michailopoulos, P., Almaliotis, D., Georgiadou, I., Papakosta, D., Gougoulias, K., Giouleka, P., . . . Karampatakis, V. (2017). Allergic Conjunctivitis in Patients with Respiratory Allergic Symptoms; a Retrospective Study in Greece. *Medical Hypothesis Discovery and Innovation in Ophthalmology.*, pp. 6(1),3–9.

Michalska-Małecka, E., Serkies-Minuth, P., & Glasn. (2025, December 5). Herpes Simplex Virus Keratitis – Diagnostic and Therapeutic Challenges. *Ophthalmology/Okulistyka*, pp. (3),44-48.

Miller, J., & Hanumunthadu, D. (2022, March). Inflammatory eye disease: An overview of clinical presentation and management. *Clinical Medicine*, pp. 22(2):100-103.

Miyake, K., Shibata, S., Yoshikawa, S., & Karasuyama, H. (2021, June 15). Basophils and their effector molecules in allergic disorders. *Allergy*, pp. 76(6):1693-1706.

Moazed, K. T. (2020). *The Iris: Understanding the Essentials.* Springer Nature Switzerland AG.

Moghadam, M. M., Yari, M. M., Jalilian, F. A., Amini, R., & & Bazzazi, N. (2019). Epidemiology and molecular diagnosis of acute conjunctivitis in patients attending Hamadan, west Iran ophthalmology clinics 2016–2017. *Clinical Optometry*, pp. 2019,11, 105–111.

Mohammed, A., Ali, M., & Zenebe, M. (2020, March). Bacterial etiology of ocular and periocular infections, antimicrobial susceptibility profile and associated factors among patients attending eye unit of Shashemene comprehensive specialized hospital, Shashemene, Ethiopia. *BMC Ophthalmology*, p. (2020) 20:124 .

Naquin, E. R., Garg, R., Chen, W. J., Karmakar, E., Prasad, A., Mandadi, S., . . . Gnana-Prakasam, J. P. (2025, September 16). Iron: More than Meets the Eye. *Nutrients*, pp. 2025, 17, 2964.

Navel, V., Sapin, V., Henrioux, F., Blanchon, L., Labbé, A., Chiambaretta, F., . . . Duthei, F. (2022, January 9). Oxidative and antioxidative stress markers in dry eye disease: A systematic review and meta-analysis. *Acta Ophthalmologica*, pp. 45 - 57.

Njinaka, I., Uhumwangho, O., Edema, O., Dawodu, O., & Omoti, A. (2011, july- september). A comparison study of conjunctiva disorders in technical and administrative sawmill workers in Nigeria. pp. 18(3),43-48.

Noori, S. (2012, November 3). An Overview of Oxidative Stress and Antioxidant Defensive System. *Open Access Scientific Reports*, p. 1:8.

Onur, S. (. (2024). *Oxidative Stress and Antioxidant Defense Systems.* Ankara, Turkey.: Serüven Yayınevi.

Orrico, F., Laurance, S., Lopez, A., Lefevre, S., Thomson, L., Möller, M., & Ostuni, M. (2023, August 18). Oxidative Stress in Healthy and Pathological Red Blood Cells. *Biomolecules*, p. 17(18):2964.

Oscar Wylee Team / Editorial content. (2025, October 3). Crystalline Lens: Anatomy, Function, and Associated Eye Problems. Canada: Oscar Wylee.

Ozkan. (2021). *Clinical anatomy: cornea and ocular surface.* Medical Hypothesis, Discovery & Innovation Ophthalmology Journal.

Ozkan, O., & Utine, C. (2025, Received:June; Accepted: August Received: 24 June ; Accepted: 29 August). Clinical anatomy: cornea and ocular surface. *Medical Hypothesis, Discovery & Innovation in Ophthalmology*, pp. 14(3):72-60.

Parrey, M., Alenazi, A., Alenezi, M., Albathali, H., & Aldaghmi, A. (2019, May). Allergic conjunctivitis: Prevalence, symptoms, precipitating and risk factors among Saudi population of Arar. *Indo American Journal of Pharmaceutical Sciences*, pp. 06 (05), 9164-9171.

Patel, A. K., Chandra, P., Sachan, N., & Singh, N. (2024, March 30). A review on pathophysiology and managements of allergic conjunctivitis. *Indian Journal of Clinical and Experimental Ophthalmology*, pp. 10(1):13-20.

Patel, B. A., Gurnani, B., & Bhupendra, C. (2024, March 10). *Herpes Simplex Keratitis.* StatPearls Publishing.

Patel, P., Jamal, Z., & Ramphul, K. (2023). Immunoglobulin. *StatPearls*. Treasure Island (FL), United States: StatPearls Publishing.

Pennington, M., Saha, A., Painter, D., Gavazzi, C., Ismail, A., Zhou, X., . . . Rajaiya, J. (2019, September). Disparate Entry of Adenoviruses Dictates Differential Innate Immune Responses on the Ocular Surface. *Microorganisms.*, pp. 7(9), 351.

Petrillo, F., Petrillo, A., Sasso, F. P., Schettino, A., Maione, A., & Galdiero, M. (2022, November 10). Viral Infection and Antiviral Treatments in Ocular Pathologie. *Microorganisms*, p. 10(11).

Pippin, M., & Le, J. (2023, Augus 17). Bacterial Conjunctivitis. *StatPearls*. StatPearls Publishing.

Qiu, Y., Song, Z., Zhu, L., Wang, Z., Shan, W., Liao, Y., . . . Ruan, Z. (2026). Ambient sulfur dioxide and daily outpatient visits for allergic conjunctivitis: a multi-city time-stratified case-crossover study in China. *BMC Public Health*, p. 26(390).

Raj Kumar, S. K. (2024, June 12). Anatomy and Physiology of the Uveal Tract. *Uveitis - Basics, Diagnosis, and Treatment*. IntechOpen.

Rosa, M., Lionetti, E., Reibaldi, M., Russo, A., Longo, A., Leonardi, S., . . . Reibaldi, A. (2013). Allergic conjunctivitis: a comprehensive review of the literature. *Italian Journal of Pediatrics*, p. 39(18).

Ruan, X., Liu, Z., Luo, L., & Liu, Y. (2020, August 24). Structure of the lens and its associations with the visual quality. *BMJ Open Ophthalmology*, pp. 5(1),e000459.

Sacchetti, M., Lambiase, A., Moretti, C., Mantelli, F., & & Bonini, S. (2015, January). Sex Hormones in Allergic Conjunctivitis: Altered Levels of Circulating Androgens and Estrogens in Children and Adolescents with Vernal Keratoconjunctivitis. pp. 2015,945317.

Sánchez-Hernández, M. C., Montero, J., Rondon, C., Benitez del Castillo, J. M., Velázquez, E., Herreras, J. M., . . . González. (2015). Consensus document on allergic conjunctivitis (DECA). *journal of Investigational Allergology and Clinical Immunolog*, pp. 25(2), 94–106.

Schellack, N., Shirindza, N., Mokoena, T., & Flepi. (2021). An overview of allergic conjunctivitis. *South African Pharmaceutical Journal*, pp. 88(1):21-32.

Sebastián-Morelló, M., Alambiaga-Caravaca, A., Calatayud-Pascual, M., Rodilla, V., Balaguer-Fernández, C., Miranda, M., & López-Castellano, A. (2020). Ex-vivo trans-corneal and trans-scleral diffusion studies with ocular formulations of glutathione as an antioxidant treatment for ocular diseases. *Pharmaceutics*, pp. 12(9),861.

Sedlak, L., Zych, M., Wojnar, W., & Wyględowska-Promieńska, D. (2019, July 11). Effect of Topical Prostaglandin F2α Analogs on Selected Oxidative Stress Parameters in the Tear Film. *Medicina*, p. 55(7):366.

Serkies-Minuth, E., Glasner, P., & Michalska-Małec. (2025). Herpes simplex virus keratitis – Diagnostic and therapeutic challenges. *Ophthalmology/Okulistyka*, pp. 28(3),48-44.

Shah, H., Eisenbarth, S., Tormey, C., & Siddon, A. (2021, May 19). Behind the scenes with basophils: an emerging therapeutic target. *Immunotherapy Advances*, pp. 2021,1(1).

Shannon, A. H., Adelman, S. A., Hisey, E. A., Potnis, S. S., Rozo, V., Yung, M. W., . . . Leonard, B. C. (2022, June 2). Antimicrobial Peptide Expression at the Ocular Surface and Their Therapeutic Use in the Treatment of Microbial Keratitis. *Frontiers in Microbiology*, pp. Volume 13 - article 857735.

Shi, C., & Pamer, E. (2014, March 9). Monocyte recruitment during infection and inflammation. *Nature Reviews Immunology*, pp. 11, 762–774 (2011).

Shorter, E., Whiteside, M., Harthan, J., Morettin, C., Perera, C., Johnson, S., . . . Gordon, M. (2022, September). Diagnostic accuracy of clinical signs, symptoms and point-of-care testing for early adenoviral conjunctivitis. *Clinical and Experimental Optometry*, pp. 102(7),702-707.

Shrivastava, A., & Rawat, K. (2022, October 26). Neutrophils as emerging protagonists and targets in chronic inflammatory diseases. *Inflammation Research*, pp. 71(12):1477-1488.

Shukla, R., Koganti, T., & Yadavalli, D. (2019, October 10). Current and Emerging Therapies for Ocular Herpes Simplex Virus Type-1 Infections. *Microorganisms*, pp. 7(10), 429.

Simpson, C., Asbell, P., & Roy, N. (2022, August 04). Review of the role of oxidative stress in ocular surface disease and use of MDA and 4-HNE in tears as potential markers. *Journal of Ophthalmic Research and Vision Care*, p. 4(1):Article JORVC2200108.

Solano, D., Fu, L., & Czyz, C. N. (2023, August). Viral Conjunctivitis. *StatPearls*. Treasure Island, Florida, United States (USA): StatPearls Publishing.

Sridhar, M. S. (2018). *Anatomy of cornea and ocular surface.* All India Ophthalmological Society.

Tadi, K., Nguyen, B. C., & Patel, P. (2023). *Anatomy, Head and Neck: Retina*. StatPearls Publishing.

Tariq, F. (2024). Allergic Conjunctivitis: Review of Current Types, Treatments, and Trends. *Life*, pp. 14(6), 650.

Tidy, C. (2022, December 15). Herpes simplex eye infections. *Patient.info*. Patient.info.

Ting, D. S., Cairns, J., Gopal, ,. B., Ho, C. S., Krstic, L., Elsahn, A., . . . Dua, H. S. (2021, august 11). Risk Factors, Clinical Outcomes, and Prognostic Factors of Bacterial Keratitis: The Nottingham Infectious Keratitis Study. *Frontiers in Medicine*, p. 715118.8.

Ting, D., Ho, C., Deshmukh, R., Said, D., & Dua, H. (2021, January 7). Infectious keratitis: an update on epidemiology, causative microorganisms, risk factors, and antimicrobial resistance. *Eye*, pp. 35(4):1084–1101.

Tiutiuca, C., Voicu, D. C., Indrei, L., Bratu, A. M., Caraiane, A., & Iulian, C. (2023). Description and presentation of the allergic conjunctivitis casuistic. *Romanian Journal of Oral Rehabilitation*, pp. 15(3): 1–6.

van de Sande, N., Ahmed, S., van Deurse, W., Jansen, W., Den Braber, A., Visser, P., . . . Ashok. (2026, April 2). Association of tear fluid glutathione synthetase and glutathione levels with amyloid positivity. *Scientific Reports*, p. 16(1):17143.

Villegas, B., & Benitez-del-Castillo , J. (2021). Current knowledge in allergic conjunctivitis. *Turkish Journal of Ophthalmology*, pp. 51(1):45–54.

Wade, C., Shumway, M., & Motlagh, M. (2023, August 28). Anatomy, Head and Neck, Eye Conjunctiva. StatPearls Publishing.

Waggoner, D., Wain, K. E., Dubuc, A. M., Conlin, L., Hickey, S. E., Lamb, A. N., . . . Miller, D. T. (2018, October). Yield of Additional Genetic Testing after Chromosomal Microarray for Diagnosis of Neurodevelopmental Disability and Congenital Anomalies: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genetics in Medicine*, pp. 20(10): 1105–1113.

Wakamatsu, T., Dogru, M., Ayako, I., Takano, Y., Matsumoto, Y., Ibrahim, O., . . . Fujishima, H. (2010, November 19). Evaluation of lipid oxidative stress status and inflammation in atopic ocular surface disease. *Molecular Vision*, pp. 16:2465-75.

White, M. L., & Chodosh, J. (2014, May). *Herpes Simplex Virus Keratitis: A Treatment Guideline.* Boston,MA,USA: American Academy of Ophthalmology (AAO).

Wu, J., Sigler, A., Pfaff, A., Cen, N., Ercal, N., & Shi, H. (2021, September 15). Development of a HPLC-MS/MS Method for Assessment of Thiol Redox Status in Human Tear Fluids. *Analytical Biochemistry*, p. 629: 114295.

Wu, K. Y., Dave, A., Daigle, P., & Tran, S. D. (2024, November 6). Advanced Biomaterials for Lacrimal Tissue Engineering: A Review. *Materials*, p. 17(22): 5425.

Wu, K., Borba, A., Deng, P., & Armstrong, A. (2019, June). Association between atopic dermatitis and conjunctivitis in adults: a population-based study in the United States. *Journal of Dermatological Treatment.*, pp. 32(4),455-459.

Yang, J., Zhang, L., Yu, C., Yang, X.-F., & Wang, H. (2014). Monocyte and macrophage differentiation: circulation inflammatory monocyte as biomarker for inflammatory diseases. *Biomarker Research*, pp. 2014, 2:1.

ANNEX

Diagnostic Questionnaire for Differentiating Eye Inflammation

Purpose: This questionnaire aims to collect clinical, environmental, seasonal, and hereditary data from patients in order to contribute to the differentiation of various types of eye inflammation.

Question	**Response**
1. Gender	□ Male □ Female
2. Age Group	□ Less than 15 years □ 15–30 years □ 31–50 years □ More than 50 years
3. Onset of Symptoms	□ Sudden □ Gradual
4. Duration of Symptoms	□ Less than 3 days □ 3–7 days □ More than one week
5. Is the Condition?	□ Persistent □ Recurrent
6. Number of Episodes per Year	□ Once □ 2–3 times □ More than 3 times
7. Severity of Symptoms	□ Mild □ Moderate □ Severe
8. Eye Involved	□ One eye □ Both eyes
9. Are There Any Eye Discharges?	□ Yes □ No
10. Type of Discharge	□ Watery □ Mucoid □ Purulent (yellow/green)
11. Do You Wake Up with Eyelids Stuck Together?	□ Yes □ No
12. Do You Experience Eye Itching?	□ Severe □ Mild □ None
13. Do You Have Excessive Tearing?	□ Yes □ No
14. Do You Have Eye Pain?	□ Yes □ No
15. Do You Have Headache?	□ Yes □ No
16. Do You Suffer From?	□ Common cold □ Sore throat □ Fever □ Other
17. Do You Experience Sneezing and Nasal Congestion?	□ Yes □ No
18. Does the Nature of Your Work Affect Your Eye Health?	□ Yes □ No
19. If Yes, What Is the Nature of Your Work?	□ Office work (screens) □ Industrial/workshops □ Agricultural □ Healthcare
20. Are You Frequently Exposed to Dust?	□ Yes □ No

21. Are You Exposed to:	□ Smoke □ Chemicals □ Strong odors □ Other
22. Do You Use Eye Protection Equipment?	□ Yes □ No
23. Does the Condition Worsen During:	□ Spring □ Summer □ Autumn □ Winter
24. Do Symptoms Improve in a Particular Season?	□ Yes □ No
25. If Yes, During Which Season?	□ Winter □ Summer □ Spring □ Autumn
26. Do Symptoms Increase When Exposed To:	□ Dust □ Pollen □ Animals □ Perfumes
27. Do You Suffer From:	□ Allergic rhinitis □ Asthma □ Skin allergy □ Other
28. Is There a Family History of Allergy or Eye Inflammation?	□ Yes □ No
29. Has a Foreign Body Entered Your Eye Before Symptoms Appeared?	□ Yes □ No
30. If Yes, Who Has a history?	□ One parent □ Siblings □ Other relatives
31. Type of Foreign Body	□ Dust □ Sand □ Insect □ Other
32. Did You Rub Your Eye Before Symptoms Appeared?	□ Yes □ No
33. Was Your Hand Contaminated When Touching Your Eye?	□ Yes □ No □ I do not know
34. Do You Use Shared Personal Items?	□ Yes □ No
35. Have You Been in Contact with Someone Having the Same Symptoms?	□ Yes □ No
36. Was the Infection Transmitted to a Family Member?	□ Yes □ No
37. Have You Used an Ophthalmic Antibiotic?	□ Yes □ No
38. If Yes, Did the Condition Improve?	□ Yes □ No
39. Have You Used Anti-Allergic Medication?	□ Yes □ No
40. If Yes, Did the Condition Improve?	□ Yes □ No

41. Other Remarks:

……

……...

……...