

## REVIEW

## DRY EYE DISEASE AND RISKS OF URBAN AIR POLLUTION – LITERATURE REVIEW

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## Abstract

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**Key words:** dry eye, air pollution, eye allergy

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Air pollution has a major impact on health, and it particularly affects the mucous membranes of the respiratory tract and the eyes. The ocular effects of chronic, long-term exposure to high levels of air pollution are still unclear. The increase in air pollution levels can be associated with an increase in the instability of the tear film. The aim of this paper is to evaluate and discuss the available data about chronic eye diseases in regions with high air pollution. Furthermore, the review also offers a certain understanding of the link between chronic dry eye disease (DED) and air pollution. Materials and methods: Specific keywords (dry eye, air pollution, and urban) were used to search the medical databases of PubMed and Medline. This research technique led to obtaining 103 papers, dating from 1995 to 2021. Out of those, 15 were used as the basis of this paper. Results: The pathophysiological mechanisms of oxidative stress and ocular surface inflammation involve the selective binding of environmental agents to ocular surface membrane receptors, leading to the activation of proinflammatory signaling pathways with changes in the extracellular stromal matrix and consequent occurrence of inflammation of the ocular surface with epithelial defects. Conclusions: Dry eye disease, pollution, and eye allergy overlap, but their presentations can be different. Future advancements in monitoring technology and the development of modern, non-invasive diagnostic methods will help prove the link between air pollutants and DED. The points should be aimed at preventing the global risks of antigenic stimulation of „urban eye“.

## ПРЕГЛЕД НА ЛИТЕРАТУРА

## СУВО ОКО И УРБАНОТО ЗАГАДУВАЊЕ НА ВОЗДУХОТ КАКО РИЗИК ФАКТОР- ПРЕГЛЕД НА ЛИТЕРАТУРА

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## Извадок

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**Клучни зборови:** суво око, загадување на воздухот, алергија на око.

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**Печатарски права:** ©2022 Наташа Трпевска-Шекеринов, Андријана Петрушевска, Емилија Гошевска-Даштевска, Тони Шекеринов, Јана Нивичка-Каева. Оваа статија е со отворен пристап дистрибуирана под условите на некаленизирана лиценца, која овозможува неограничена употреба, дистрибуција и репродукција на било кој медиум, доколку се цитираат оригиналните(ите) автор(и) и изворот.

**Конкурентски интереси:** Авторот изјавува дека нема конкурентски интереси.

Загадувањето на воздухот има големо влијание врз здравјето, а особено влијае на мукозните мембрани на респираторниот тракт и очите. Окуларните ефекти од хроничната, долготрајна изложеност на високи нивоа на загадување на воздухот сè уште се нејасни. Зголемувањето на нивото на загаденост на воздухот може да биде поврзано со зголемување на нестабилноста на солзниот филм. Целта на овој труд е да се евалуираат и дискутираат достапните податоци за хроничните очни болести во регионите со високо загадување на воздухот. Понатаму, прегледот нуди и одредено толкување за врската помеѓу хроничната болест на суво око и загадувањето на воздухот. Материјали и методи: Специфични клучни зборови (суво око, загадување на воздухот и урбано) беа користени за пребарување на медицинските бази на податоци на PubMed and Medline. Пронајдовме 103 трудови, кои датираат од 1995 до 2021 година. Од нив, 15 беа користени како основа на овој труд. Резултати: Патофизиолошките механизми на оксидативниот стрес и воспалението на окуларната површина вклучуваат селективно врзување на агенсите од средината за рецепторите на окуларната површина што доведува до активирање на проинфламаторните сигнални патишта со промени во екстрацелуларната стромална матрица и последователна појава на воспаление на окуларната површина со дефекти на епителот. Заклучок: Суво око, загадувањето и алергијата на очите се преклопуваат, но нивните презентации може да бидат различни. Идните достигнувања во технологијата за следење и развојот на современи, неинвазивни дијагностички методи ќе помогнат да се докаже врската помеѓу загадувањето на воздухот и сувото око. Мерките треба да бидат насочени кон спречување на глобалните ризици од антигенска стимулација на „урбаното око“.

## Introduction

Dry eye disease is a chronic condition. Being very common, it affects millions of people worldwide and is one of the most common causes for patients to visit ophthalmologists<sup>1</sup>. It is a multifactorial disease, and incidence can be significantly increased by climatic conditions, the environmental pollution, traffic, extreme temperatures, and relative humidity. Studies prove that there is a correlation between low relative humidity and the increased prevalence of DED. Namely, air-conditioned offices and vehicles, extremely hot air, and air pollution with high levels of PM particles lead to tear film instability.

The National Eye Institute and Industry of workshop on Clinical Trials in Dry Eyes held in 1995 proposed a global definition for this entity, as disorder of the tear film due to tear deficiency or excessive tear evaporation, which cause damage to the interpalpebral ocular surface, associated with ocular discomfort. Both of these factors lead to the damage of the interpalpebral ocular surface, which is associated with ocular discomfort<sup>2</sup>.

According to epidemiological studies, more than 6 % of people over the age of 40 suffer from dry eye, with the prevalence increasing to 15 % when it comes to adults age 65 and older. Several environmental factors have been linked to DED, including high altitude, wind, air pollution, allergens, adjuvants, temperature, relative humidity (RH), and UV radiation<sup>3</sup>.

Air pollution has a major impact on health, and it particularly affects

the mucous membranes of the respiratory tract and the eyes.

It appears that the contamination related to traffic emissions is associated with DED and other allergic diseases; thus, lowering pollution levels caused by exhaust gas is necessary to mitigate this health problem.

The ocular effects of chronic, long-term exposure to high levels of air pollution are still unclear. The increase in air pollution levels can be associated with an increase in the instability of the tear film.

It is considered that the abnormalities of the ocular surfaces caused by high levels of air pollution are subtypes of the dry eye disease<sup>2</sup>. Furthermore, the rise in temperature, which results from the ongoing climate changes, causes high rates of tear evaporation in patients with DED. Global warming contributes to the prolongation of the allergy season and leads to the development of allergy-triggered DED. Since environmental conditions like these can't be bypassed, prevention strategies must be created with those suffering from the disease taken into account.

There aren't any large studies on the link between air pollution and DED while focusing on multiple air pollutants. On the other hand, there is an important knowledge gap when it comes to how environmental factors (especially air pollution along with weather conditions) affect the frequency of detrimental changes to the eye.

Main inductors contains air pollution, exposure to pollutants: particulate matter (PM10, PM2.5), in-

creased ozone and nitrogen oxides (O<sub>3</sub>, NO<sub>x</sub>), increased allergenic bio particles, chronic use of preserved eye drops, reduced enzymes – nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, pollen-associated lipid mediators (PALMs) and allergic proteins. In fact, reactive oxygen radicals (ROS) present on the PM particles can act anti-oxidative barrier of the tear film<sup>2,3</sup>.

The lacrimal gland reduces the production of mucin and increases tears evaporation, which reduces the protective barrier and facilitates the flow of antigens.

According to the World Health Organization, the air quality in the countries of the Western Balkans is terrible. The air in each country of this region contains large quantities of harmful PM 2.5 particles; in fact, the concentration of PM 2.5 and PM 10 particles is often 10 times the allowable level. The biggest polluters in this part of the world are coal power plants and old cars<sup>4</sup>.

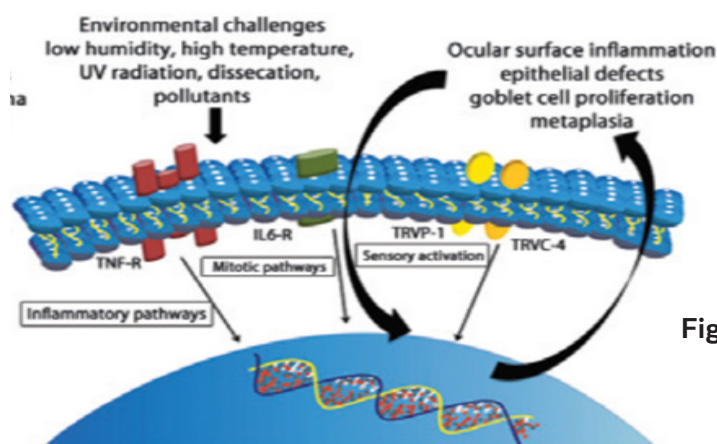
The aim of this paper is to evaluate and discuss the available data about chronic eye diseases in regions with high air pollution. Furthermore, the review also offers a certain understanding of the link between chronic dry eye disease and air pollution.

## Materials and methods

In this paper we were focused on recent DED-related studies to identify the urban eye allergy syndrome associated with DED and perennial conjunctivitis (PAC). We are presenting update about some hypothetical mechanisms of changes in the structure of allergen with acceleration of immune reaction of conjunctiva. The studies discussed in this paper suggest objective diagnostic methods for DED. Specific keywords (dry eye, air pollution, and urban) were used to search the medical databases of PubMed and Medline. This research technique led to obtaining 103 papers, dating from 1995 to 2021. Out of those, 15 were used as the basis of this paper.

## Results

The pathophysiological mechanisms of oxidative stress and ocular surface inflammation involve the selective binding of environmental agents to ocular surface membrane receptors leading to the activation of pro-inflammatory signaling pathways with changes in the extracellular stromal matrix and consequent occurrence of inflammation of the ocular surface with epithelial defects<sup>3</sup>.(Figure 1)



**Fig. 1.** Pathophysiological mechanisms of DED at the cellular level  
Source: Alves M. et al., Arq Bras Oftalmol. 2014

There is increasing evidence that the dry eye disease leads to inflammation of the ocular surface and is partially responsible for ocular surface epithelial diseases and irritation symptoms that develop. Inflammation may be caused by different factors, including desiccation, hyperosmolarity, alteration in the tear film composition, and micro trauma of the eyelids. Whatever the initial etiology of DED, once it develops, inflammation becomes the core mechanism of ocular surface disease.

Exposure to ozone exacerbates the adverse effects of allergic reactions by enhancing the production of the IgE. Current studies show that patients with chronic allergic or atopic tendencies may have less tolerance for additional environmental antigen stimulation<sup>5</sup>.

Antioxidative defenses in the ocular surface occur in the form of tear proteins such as lactoferrin and S100A proteins and enzymes like superoxide dismutase (SOD), peroxidase, catalase, and mitochondrial oxidative enzymes. An imbalance between the level of reactive oxygen species (ROS) and the action of protective enzymes will lead to oxidative damage and possibly inflammation<sup>5</sup>.

The manifestations of the pseudo-allergic form of irritating conjunctivitis include the following eye problems as immediate effects of exposure: watering, burning, redness, irritation, itching, stinging, chronic discomfort, dry eye symptoms, foreign body sensation, blurred vision, increased sensitivity to light, inflammation of the cornea, and worsening of allergic symptoms, which can be minimal, middle or chronic<sup>6</sup>. (Figure 2, 3)



**Fig. 2.** Figure 2, 3 Manifestations of the pseudo- allergic form of irritating conjunctivitis

The latest articles describes the tear film as an interactive hydrated mucin gel with the presence of lipids and proteins distributed throughout the gel. Eye moisture, which is of optical and physiological importance, is maintained by the secretion of lipids and aqueous solution and the mucous layer. Lipids pre-

vent evaporation and stabilize the tear film, and any disruption of the lipid secretion process will result in increased evaporation and destabilization of the tear film and consequently lead to DED.

Kjaeregaard et *al.* confirm that there is a link between high humidity and

the stability of the tear film, emphasizing that air in a room should be dry, cool, and with a humidity level of 40%<sup>7</sup>.

In their study, Hwang et al. point out that high ozone levels and low humidity are the main causes of DED in the Korean population<sup>8</sup>.

Another study showed that outpatient visits for conjunctivitis significantly increase during periods of higher levels of air pollution and the presence of PM particles in the air<sup>9</sup> (Fu et al.).

Furthermore, the authors of the study suggest a complexity of the clinical picture of DED, with symptoms of the condition including not only those related to the dry eye disease, but eye infections and irritation, dry cough, itching of the nose, fluctuation vision, etc. Analyses confirm that PM particles present on the surface of the eye are more damaging for eyes affected by the dry eye disease than they are for healthy eyes, suggesting that poor air quality might be a factor in the development of DED.

## Discussion

Recognizing that insufficient tear production and increased evaporation are two different components of DED that interact with the condition differently can lead to a significant progress in the management of this disease<sup>10</sup>.

Identifying the presence of volatile film instability in the various stages of DED and understanding that the thickness of the lipid layer can determine the stability of the tear film can also improve the treatment

plans of individuals with the condition.

Evaluations of the effects of exposure to pollution in patients with irritating and perennial conjunctivitis (PAC) contain evaluation of the conjunctiva (hyperemia, hyperplasia, chemosis); evaluation of the tear film lipid layer; ocular surface staining and corneal involving; corneal sensation; Schirmer test and Tear film break up time; cultures from the ocular surface or associated tissue and serum antibody biomarkers and/or other serological tests<sup>11,12</sup>.

The diversity of the existing clinical forms of DED and other conjunctival and corneal diseases that may have similar symptoms and clinical presentations leads to the conclusion that diagnosing DED is not easy and that it should be done by obtaining different information with various procedures.

New, non-invasive imaging methods include the following: optical coherence tomography (AS-OCT) for tear meniscus; corneal biopsy for evaluating the thickness and structure of the cornea; corneal topography for measuring the tear break-up time and tear meniscus height; meibomian gland imaging and osmolarity testing, which measure the adverse effects that exposure to high levels of air pollution has on the ocular surface; and using the Inflammation Dry Detector (RPS) to detect the production of the inflammatory MMP-9 cytokine marker.

Findings about the link between inflammation with reduced secretion of tears and subsequent damage to the ocular surface have led to a proposal for a unified concept of DED<sup>13</sup>.

Air pollutants may create temporary eye irritations, but eye redness typically clears up when pollution levels decrease. However, people living in areas where the air contains many pollutants are three to four times more likely to develop an eye condition called dry eye syndrome. Four years of monitoring the air after the conclusion of the New York State Department of Environmental Conservation's (NYSDEC's) Tonawanda Community Air Quality Study showed a reduction in the concentrations of benzene and other air pollutants within the Tonawanda community<sup>14</sup>.

The interactions between different microenvironment components during the development of DED need to be investigated as well. The ultimate goal of DED management is to revert the ocular surface and tear film to their normal homeostatic state. A wide range of therapeutics is available in treating DED, but evaluating whether certain treatment interventions can interfere with the functions of other components and cause unrelated complications or exacerbate DED is crucial<sup>15</sup>.

Ophthalmologists need to check the environmental histories of patients with dry eyes and allergic conjunctivitis. Environmental manipulations, such as increasing local humidity and decreasing the exposure to air pollution, and encouraging frequent blinking hydration, the use of sunglasses, and the finding of ways to increase indoor humidity and making the necessary lifestyle changes (AQI) are vital in preventing DED<sup>14</sup>.

## Conclusion

Dry eye disease, pollution, and eye allergy overlap, but their presentations can be different.

Future advancements in monitoring technology and the development of modern, non-invasive diagnostic methods will help prove the link between air pollutants and DED. The points should be aimed at preventing the global risks of antigenic stimulation of "urban eye".

The best way to alleviate the effects of air pollution on the eyes is to avoid the same, but this is not always possible. A reasonable prevention strategy would be to keep the eyes well lubricated with artificial tears that don't contain preservatives and to keep an eye on cleaning the caps and eyelashes after long-term exposure to high levels of pollution.

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