Types and Common Causes of Dry Eye Syndrome

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Abstract Based on abnormalities in tear film structure and dynamics, dry eye syndrome is primarily classified into five types: aqueous-deficient, mucin-deficient, evaporative/lipid-deficient, tear dynamics disorder, and mixed type. The disease has diverse triggers, commonly including: lacrimal gland dysfunction; meibomian gland dysfunction accelerating tear evaporation; reduced blinking due to prolonged electronic device use; contact lens wear interfering with the tear film; medication side effects; environmental factors; hormonal fluctuations; certain ophthalmic surgeries, for example, LASIK. Treatment requires targeting specific pathogenic mechanisms, with the core focus on controlling inflammation, restoring tear film stability, and improving related gland function.

Key words Dry eye syndrome, types of dry eye syndrome, Causes of dry eye syndrome

1 Introduction

Dry Eye Disease (DED) is a common, multifactorial disorder characterized by tear film instability and ocular surface inflammation, along with neurosensory abnormalities, leading to tear film instability or imbalance in the ocular surface microenvironment. It is often accompanied by inflammatory responses, corneal damage, and neural abnormalities[1-2]. Characteristic clinical symptoms include ocular redness, dryness, fatigue, gritty sensation, burning, and soreness[1,3]. Comprising lipid, aqueous, and mucin layers, the tear film provides the basis for classifying DED into aqueous-deficient, lipid-abnormal, mucin-abnormal, tear dynamics disorder, and mixed types[1,4]. Studies indicate a global DED prevalence ranging from 5% to 50%, with 78% of patients being female. Among adults over 40 years old, prevalence may reach as high as 75%[5-7]. Advanced age, female gender, Asian ethnicity, and low-humidity environmental exposure are independent risk factors for DED[5,8], while autoimmune diseases such as Sjögren's syndrome (SS) and rheumatoid arthritis represent high-risk factors[2,5,9].

2 Types of dry eye syndrome

2.1 Aqueous deficient dry eye The core pathological mechanisms of aqueous deficient dry eye include lacrimal gland dysfunction, structural abnormalities of the tear layer, ocular surface inflammatory responses, and neural regulatory dysfunction[10-13]. Impaired lacrimal gland function leads to reduced tear secretion and thinning of the aqueous layer in the tear film, depriving the ocular surface of lubrication and nutritional support, thereby exacerbating symptoms such as dryness and foreign body sensation[10,14]. Structural abnormalities of the tear layer accelerate tear evaporation; particularly when lipid layer function is compromised, accelerated tear evaporation intensifies ocular surface dryness[11,15]. Ocular surface inflammation is a key characteristic of this dry eye subtype, where insufficient tear fluid triggers the release of inflammatory factors (such as interleukins and tumor necrosis factor), damaging the lacrimal glands and creating a vicious cycle between reduced tear production and inflammation[12,16]. Neural regulatory disorders cause abnormal function of corneal sensory receptors, diminishing the reflex regulatory capacity for tear secretion and further aggravating dry eye symptoms[13,17].

2.2 Mucin-deficient dry eye The pathological mechanisms of mucin-deficient dry eye primarily include deficiency of mucin, tear film instability, corneal and conjunctival damage, and ocular surface inflammatory responses. Secreted by conjunctival goblet cells, mucin functions to lubricate and facilitate the even distribution of tears[16-17], ensuring the formation of a stable tear film over the corneal and conjunctival surfaces. When mucin secretion is insufficient, the inner layer of the tear film fails to adhere properly to the ocular surface, leading to uneven tear distribution, increased tear film breakup and evaporation, and ultimately causing ocular surface dryness[18-20]. The main causes of mucin deficiency include goblet cell dysfunction, ocular surface inflammation, or environmental factors. Reduction in goblet cell count or impaired secretory function significantly decreases mucin levels, thereby compromising tear film stability.

Inflammatory response is a key mechanism in mucin-deficient dry eye[19-23]. Chronic inflammation on the ocular surface can damage conjunctival goblet cells and inhibit their mucin-secreting function. Simultaneously, inflammatory factors (such as interleukins and tumor necrosis factor-alpha, TNF-α) further damage ocular surface tissues, exacerbating tissue injury and forming a vicious cycle between inflammation and mucin deficiency. The deficiency of mucin leaves the cornea and conjunctiva inadequately protected, increasing mechanical friction and leading to damage of the corneal and conjunctival epithelium. This damage not only causes symptoms such as dry eyes, stinging, and foreign body sensation but also triggers further inflammatory responses, resulting in an additional reduction in goblet cell count. Moreover, due to tear film instability, tears evaporate more readily, depriving the ocular surface of essential lubrication and moisture, ultimately exacerbating dry eye symptoms.

In summary, the pathological mechanism of mucin-deficient dry eye centers on goblet cell dysfunction and chronic ocular surface inflammation, leading to tear film instability, corneal and conjunctival damage, thereby initiating and aggravating dry eye symptoms. Therapeutic efforts should focus on restoring mucin se-

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cretion and controlling inflammation to improve tear film stability and ocular surface health.

2.3 Evaporative dry eye (lipid-deficient type) The pathological mechanisms of evaporative dry eye (lipid-deficient type) primarily involve dysfunction of the tear film lipid layer, leading to excessive tear evaporation and consequent chronic inflammation of the ocular surface[1,23]. Under normal conditions, the tear film consists of three layers: the innermost mucin layer, the middle aqueous layer, and the outermost lipid layer. The lipid layer, primarily composed of lipids secreted by the meibomian glands, functions to reduce tear evaporation and maintain ocular surface moisture and smoothness[23-24]. When meibomian gland dysfunction or insufficient lipid secretion occurs, the lipid layer of the tear film becomes thinner or functionally impaired, resulting in a significantly increased tear evaporation rate and ultimately causing ocular surface dryness[23,25].

The disease process of lipid-deficient dry eye is typically accompanied by persistent ocular surface inflammation. Due to tear film breakup and rapid tear evaporation, lubrication on the corneal and conjunctival surfaces diminishes, exposing the ocular surface to the external environment and increasing vulnerability to mechanical stimuli and harmful external factors. This chronic ocular surface dryness and inflammation induce corneal epithelial damage, heighten tear film instability, and further exacerbate dry eye symptoms[25-27].

Moreover, patients with lipid-deficient dry eye commonly experience symptoms such as dryness, burning sensation, foreign body sensation, and visual fatigue. In severe cases, it may lead to reduced visual acuity and significantly impaired quality of life[23,27]. Meibomian gland dysfunction (MGD) is a critical etiological factor in this dry eye subtype. Conditions including meibomian gland obstruction, atrophy, or inflammation can cause abnormalities in the quantity or quality of the lipid layer[24-25]. Studies indicate that MGD correlates with aging, gender differences, and environmental factors, particularly prolonged electronic screen use and exposure to air pollutants, which may accelerate functional decline of the meibomian glands[25,28].

Regarding treatment, interventions for lipid-deficient dry eye primarily focus on improving meibomian gland function and restoring the normal state of the tear film lipid layer[23,29]. Common therapeutic approaches include: warm compresses and meibomian gland massage, artificial tear substitutes, anti-inflammatory medications. These measures aim to reduce tear evaporation and alleviate ocular surface inflammation. Concurrently, patients should avoid prolonged exposure to dry or heavily polluted environments and limit extended use of electronic devices to mitigate symptoms.

2.4 Abnormal tear dynamics The core pathological mechanism of tear dynamics-deficient dry eye involves abnormalities in tear secretion, distribution, and drainage processes, leading to tear film instability and chronic ocular surface inflammation[10,30]. Under physiological conditions, the tear film comprises the mucin layer, aqueous layer, and lipid layer, which act in concert to maintain ocular surface moisture, provide lubrication, and create a smooth optical surface for clear vision[30]. When tear dynamics are impaired, the production and drainage of tears as well as tear film stability are compromised, resulting in persistent ocular surface dryness, corneal damage, and sustained inflammatory responses[10-11,13].

The pathological mechanisms of tear dynamics-deficient dry eye can be categorized into two primary aspects: insufficient tear secretion and excessively rapid tear drainage. Insufficient tear secretion is typically associated with lacrimal gland dysfunction. Chronic inflammation, atrophy, or damage to the lacrimal gland reduces tear production, consequently diminishing the thickness of the aqueous layer in the tear film and destabilizing it[10,14]. This compromises the normal lubrication of the ocular surface. Causes of lacrimal gland dysfunction include aging, systemic diseases (Sjögren's syndrome, for instance), long-term medication use, and external environmental stimuli[10,31].

Besides, excessively rapid tear drainage, may relate to drainage dysfunction. Premature tear clearance or excessive evaporation is often caused by lipid layer dysfunction or abnormal blinking[11,13]. Weakened lipid layer function accelerates evaporation of the aqueous layer, resulting in rapid tear film breakup. This exposes the ocular surface to air, leading to dryness of the corneal and conjunctival surfaces. In addition, abnormal lacrimal duct function may cause excessive tear drainage, shortening tear retention time on the ocular surface[14] and preventing adequate lubrication and protection. These tear dynamics abnormalities are frequently accompanied by ocular surface inflammation. Tear film breakup, excessive evaporation, or rapid drainage impairs the ocular surface barrier, facilitating invasion of harmful external substances that irritate the cornea and conjunctiva, thereby triggering inflammation. This chronic inflammation further damages the lacrimal gland and tear film, creating a vicious cycle[13,26,30] that exacerbates dry eye symptoms.

Patients with tear dynamics-deficient dry eye typically present with dryness, foreign body sensation, burning sensation, and visual fatigue. In severe cases, visual impairment may occur. Therapeutically, interventions targeting insufficient secretion or abnormal drainage, such as artificial tears, secretagogues, or punctal occlusion—are required to restore tear film stability and reduce ocular surface damage and inflammation.

2.5 Mixed type dry eye Mixed type dry eye is a complex ocular surface disorder jointly triggered by insufficient tear secretion and excessive tear evaporation. Its pathological mechanisms involve multifaceted factors including multilayer tear film imbalance, lacrimal gland dysfunction, meibomian gland insufficiency, and ocular surface inflammation[1-2]. Under normal conditions, the tear film consists of the mucin layer, aqueous layer, and lipid layer, which collectively maintain ocular surface stability and lubrication[1]. When insufficient tear secretion coexists with accelerated tear evaporation, tear film stability becomes severely compromised, resulting in chronic ocular surface dryness and persis-

tent inflammatory responses[3,26-27].

Regarding insufficient tear secretion, lacrimal gland dysfunction represents the primary etiology. Chronic inflammation, atrophy, or immune-mediated disorders (for example, Sjögren's syndrome) affecting the lacrimal glands lead to reduced aqueous layer production and diminished tear film thickness. This compromises tear film integrity, predisposing it to rupture and impairing its ability to maintain normal ocular surface moisture[2,11]. Besides, exposure of the cornea and conjunctiva to the external environment increases vulnerability to mechanical stimuli and harmful agents, further exacerbating ocular surface damage and inflammation.

In addition, meibomian gland insufficiency causes inadequate secretion or qualitative deterioration of the lipid layer, impairing its capacity to effectively suppress tear evaporation[23-24,27-28]. Lipid layer deficiency significantly accelerates evaporation of the aqueous layer, shortens tear retention time on the ocular surface, and intensifies tear film instability[26-28]. Common contributors to meibomian gland dysfunction include chronic blepharitis, aging, air pollution, and prolonged digital screen exposure.

The pathogenesis of mixed dry eye also involves chronic ocular surface inflammation[10-11]. Tear film breakup and excessive evaporation compromise the barrier function of the corneal epithelium. Prolonged exposure to air heightens susceptibility to external irritants and pathogens, triggering persistent ocular surface inflammation. This inflammatory response further damages lacrimal and meibomian gland function, establishing a vicious cycle that promotes disease recurrence[2,10].

Patients typically present with dryness, foreign body sensation, burning sensation, and visual fatigue. Severe cases may develop corneal epithelial damage and even visual impairment. Therapeutic strategies for mixed dry eye require a multimodal approach addressing both insufficient secretion and excessive evaporation, while concurrently mitigating ocular surface inflammation and tissue damage.

3 Common causes of dry eye syndrome

The occurrence of dry eye syndrome is usually the result of a combination of factors. The following are some common causes of dry eye syndrome.

3.1 Insufficient tear secretion This is a main cause of dry eye and is often associated with decreased lacrimal gland function. Inflammation, injury, or degeneration of the lacrimal glands can reduce tear production. Aging, systemic diseases (such as Sjogren's syndrome, rheumatoid arthritis), and changes in hormone levels (such as hormonal fluctuations in postmenopausal women)[2,5] all affect lacrimal gland function, resulting in inadequate tear secretion.

3.2 Excessive tear evaporation Accelerated tear evaporation is often associated with meibomian gland dysfunction. Lipids secreted by the meibomian glands help form the lipid layer of the tear film and prevent tear evaporation. When the meibomian gland is blocked or impaired, the lipid layer of the tear film thins or disappears, resulting in increased evaporation of the watery layer and inducing dry eye. In addition, long-term exposure to dry, windy or air-conditioned environments can also accelerate tear evaporation[32-33].

3.3 Prolonged use of digital and electronic equipment Prolonged use of digital devices such as computers and smartphones reduces blink frequency. Insufficient blinking shortens tear film breakup time[34], accelerating tear evaporation and ultimately causing dry eyes. People whose modern work and lifestyle heavily rely on electronic devices are therefore more susceptible to dry eye syndrome.

3.4 Prolonged wearing of contact lenses Contact lenses mechanically affect the tear film, disrupting its stability and increasing tear evaporation rate[35]. Furthermore, prolonged wear of contact lenses may also cause corneal hypoxia and ocular surface inflammation, which can further exacerbate dry eye symptoms.

3.5 Drug effects Certain drugs, such as antihistamines, antidepressants, antihypertensive drugs, hormones, *etc.*, may inhibit tear secretion[36], resulting in insufficient tear secretion, thus causing or aggravating dry eye symptoms.

3.6 Environmental factors Living and working in dry, windy environments with severe air pollution or prolonged exposure to air conditioning can easily increase tear evaporation from the ocular surface, thereby contributing to dry eye syndrome[32-33]. In particular, airborne pollutants such as dust and smoke may directly irritate the ocular surface, triggering inflammatory responses.

3.7 Systemic disease Some systemic diseases, such as Sjogren's syndrome, rheumatoid arthritis and diabetes mellitus, may affect the function of lacrimal gland or meibomian gland through the disorder of immune system or metabolic abnormalities, resulting in decreased tear secretion or abnormal tear film function[2,5,37], thus causing dry eye.

3.8 Changes in hormone levels During pregnancy, in the postmenopausal period, or while using hormonal contraceptives, fluctuations in hormone levels may affect the secretory function of the lacrimal and meibomian glands[5-6], thereby increasing the risk of dry eye syndrome.

3.9 Certain eye surgery For example, laser corneal refractive surgery (such as LASIK) may temporarily or permanently impair corneal nerves[26], compromising tear secretion and contributing to dry eye syndrome. These factors often interact[3-26] and collectively promote the development of dry eye syndrome. Understanding these causes is essential for effective prevention and treatment strategies tailored to different types of dry eye.

4 Conclusions

Dry eye disease (DED), as a complex condition arising from multifactorial interplay, presents heightened demands for clinical diagnosis and personalized treatment due to the heterogeneity in its subtypes and pathogenic causes. Although significant progress has been made in understanding the pathogenesis of DED in recent years, with related classification systems gradually refined, practi-

cal clinical application still faces numerous challenges, including difficulties in identifying etiologies, unclear therapeutic targets, and limited management approaches. Currently, the continuous emergence of novel risk factors, such as environmental and societal behavioral changes (the ubiquity of electronic devices, for instance), population aging, and endocrine disorders, has led to an increasingly severe prevalence trend of DED and a continually expanding patient population. In the future, DED research urgently requires breakthroughs in molecular mechanisms, precise subtyping, biomarker screening, and personalized interventions. Through the application of interdisciplinary approaches and advanced technologies like big data analytics, it is anticipated that more fundamental pathogenic mechanisms of DED will be revealed, paving novel avenues for precise prevention and treatment, ultimately improving patients' long-term prognosis and quality of life.

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