RESEARCH PAPER

DRY EYE DISEASE: PATHOPHYSIOLOGY AND CURRENT MANAGEMENT STRATEGIES

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ABSTRACT

Dry Eye Disease (DED) is a multifactorial disorder of the ocular surface characterized by loss of tear film homeostasis, resulting in ocular discomfort, visual disturbance, and inflammation. It is increasingly recognized as a major public health concern due to rising digital screen exposure, aging populations, environmental pollution, and systemic diseases. Tear film dysfunction, hyperosmolarity, ocular surface inflammation, and neurosensory abnormalities form the core pathophysiological mechanisms underlying DED. The disease is broadly classified into aqueous-deficient and evaporative forms, with meibomian gland dysfunction representing the most common cause of evaporative dry eye. Current management strategies focus on restoring tear film stability, reducing inflammation, improving meibomian gland function, and relieving symptoms. Treatment modalities include artificial tears, anti-inflammatory agents, punctal occlusion, secretagogues, thermal pulsation therapy, intense pulsed light, and biologic tear substitutes. Lifestyle modifications such as screen-time regulation, nutritional optimization, hydration, environmental control, and eyelid hygiene play an essential supportive role. Recent advances include lipid-based tear substitutes, regenerative therapies, nanotechnology-based drug delivery systems, and neurosensory-targeted therapies. This review discusses the pathophysiology of DED, emphasizes tear film dysfunction, explores current medical and supportive management approaches, and highlights recent advances and future directions in DED care.

Keywords: Dry Eye Disease, Tear Film Dysfunction, Meibomian Gland Dysfunction, Ocular Surface Inflammation, Artificial Tears, Lifestyle Modification, Evaporative Dry Eye, Tear Hyperosmolarity.

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Introduction

Dry Eye Disease (DED) is one of the most prevalent ocular disorders encountered in ophthalmic practice. The Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop II defines DED as a multifactorial disease of the ocular surface characterized by a loss of tear film homeostasis accompanied by ocular symptoms, in which tear film instability, hyperosmolarity, inflammation, and neurosensory abnormalities play important etiological roles.[1] DED significantly affects visual function, daily activities, work productivity, and overall quality of life. Common symptoms include ocular dryness, burning sensation, foreign body sensation, redness, photophobia, fluctuating vision, and ocular fatigue. Increasing use of digital devices, prolonged exposure to air-conditioned environments, contact lens wear, and environmental pollution have contributed to the rising global prevalence of DED. Elderly individuals, postmenopausal women, and patients with autoimmune disorders such as Sjögren syndrome are particularly susceptible to developing the disease.[2]

DED is broadly classified into aqueous-deficient dry eye and evaporative dry eye, although overlap between these subtypes is frequently observed. Recent evidence has emphasized the role of chronic ocular surface inflammation, meibomian gland dysfunction, tear hyperosmolarity, and neurosensory dysregulation in the progression of the disease. Understanding the complex underlying pathophysiology is essential for accurate diagnosis and individualized treatment strategies.[3]

Dry eye disease is increasingly recognized as a major public health concern worldwide. Epidemiological studies have reported that the prevalence of DED ranges from approximately 5% to more than 30% in the general population, depending on the diagnostic criteria employed, age group studied, and environmental as well as cultural factors. The prevalence varies between 8.7% and 11.0% among Caucasian populations and between 16.7% and 33.4% in East Asian populations. Furthermore, DED occurs more commonly in women, and the risk is known to increase with advancing age. However, the incidence among younger individuals aged 18–50 years has also increased considerably due to

extensive use of smartphones, computers, and contact lenses.[4]

The TFOS DEWS II Task Force proposed an updated definition of DED, describing it as a disease of multifactorial etiology involving the ocular surface and characterized by disruption of tear film homeostasis. This process is associated with tear film instability, hyperosmolarity, ocular surface inflammation, and damage to the ocular surface barrier. In addition, abnormalities in neurosensory mechanisms contribute to the nature and severity of clinical manifestations, as further elaborated in the TFOS DEWS II and TFOS DEWS III reports.[5]The aim of this manuscript is to discuss the pathophysiology and risk factors of DED and to summarize current diagnostic and therapeutic approaches, including emerging innovations such as smart contact lenses, nanoformulations, emulsions, dendrimers, and nanomicellar drug delivery systems.

Methodology

This narrative review was conducted through a comprehensive literature search using electronic databases including PubMed, Scopus, Google Scholar, and Web of Science. Relevant articles published between 1995 and 2026 were reviewed, with particular emphasis on recent studies from the last five years focusing on dry eye disease pathophysiology, tear film dysfunction, ocular surface inflammation, meibomian gland dysfunction, medical management, lifestyle interventions, and recent therapeutic advances. Priority was given to systematic reviews, randomized controlled trials, TFOS DEWS II reports, and evidence-based review articles. The keywords and search phrases used included “DRY EYE DISEASE,” “DRY EYE SYNDROME,” “DRY EYE,” “OCULAR SURFACE,” “OCULAR SURFACE DISEASE,” “OCULAR SURFACE INFLAMMATION,” “TEAR FILM,” “TEAR FILM HOMEOSTASIS,” “TEAR FILM DYSFUNCTION,” “MEIBOMIAN GLAND DYSFUNCTION,” “MEDICAL MANAGEMENT,” AND “LIFESTYLE MODIFICATIONS.” Articles not published in English and studies with limited relevance to the review objectives were excluded.

Literature Review

Tear Film Anatomy and Physiology

The tear film is a highly specialized and dynamic trilaminar structure that plays a crucial role in maintaining the health and function of the ocular surface. It is composed of three interactive layers—the outer lipid layer, the middle aqueous layer, and the inner mucin layer—which together provide lubrication, optical smoothness, protection against microbial invasion, and nourishment to the corneal epithelium.[6]The superficial lipid layer is secreted primarily by the meibomian glands located within the tarsal plates of the eyelids. This layer consists mainly of nonpolar and polar lipids that reduce tear evaporation, stabilize the air–tear interface, and prevent contamination of the tear film by skin lipids. Dysfunction of the meibomian glands leads to increased evaporation and instability of the tear film, thereby contributing significantly to evaporative dry eye disease.[7]

The aqueous layer, which constitutes the largest portion of the tear film, is produced mainly by the main and accessory lacrimal glands. It contains water, electrolytes, proteins, enzymes, growth factors, immunoglobulins, and antimicrobial peptides such as lysozyme and lactoferrin. This layer is responsible for maintaining hydration of the ocular surface, supplying oxygen and nutrients to the avascular cornea, removing debris, and providing antimicrobial defensemechanisms.[8]The innermost mucin layer is secreted predominantly by conjunctival goblet cells and membrane-associated mucins of the corneal epithelium. It facilitates uniform spreading and adhesion of the aqueous layer over the hydrophobic corneal epithelial surface, thereby ensuring tear film stability and maintaining optical clarity.[9]

Disruption of any component of the tear film can result in tear film instability, increased evaporation, hyperosmolarity, inflammation, and epithelial damage to the ocular surface. Tear hyperosmolarity triggers inflammatory cascades and cellular stress responses that further impair tear production and ocular surface integrity. This creates a self-perpetuating “vicious cycle” that is considered the central pathophysiological mechanism underlying dry eye disease.[10]

Symptoms of Dry Eye Disease

Dry eye disease (DED) is a chronic multifactorial disorder of the ocular surface in which subjective symptoms play a central role in diagnosis, disease monitoring, and assessment of therapeutic outcomes. A characteristic feature of DED is its marked clinical heterogeneity and the frequent discrepancy between patient-reported symptoms and objective clinical findings, which presents a considerable challenge in both clinical practice and research. The symptoms of DED arise primarily from tear film instability, tear hyperosmolarity, ocular surface inflammation, and neurosensory abnormalities, and they may fluctuate over time depending on environmental exposure, visual activities, and behavioralfactors.[11]

Sensory Symptoms and Ocular Surface Discomfort

The most frequently reported symptoms of DED include ocular dryness, burning sensation, stinging, irritation, grittiness, and foreign body sensation. These manifestations are closely associated with tear film instability and reduced tear film break-up time (TBUT), particularly in patients with the short TBUT-type DED phenotype, in which severe subjective symptoms occur despite minimal ocular

surface damage. This phenotype has been observed more commonly in Asian populations but is increasingly recognized globally as an important clinical subtype of DED.[12]

Visual Disturbances and Visual Function Impairment

Visual symptoms are a major component of DED and include fluctuating vision, intermittent blurred vision, glare, photophobia, and difficulty maintaining visual focus during prolonged visual tasks. These disturbances result from irregularities in the precorneal tear film, leading to optical surface instability and impaired visual quality. Even in patients with normal visual acuity, tear film disruption may reduce contrast sensitivity and functional visual performance, thereby affecting activities such as reading, driving, computer work, and other tasks requiring sustained visual concentration.[13]

Paradoxical Tearing and Masking Symptoms

Some patients with DED present with excessive tearing or reflex epiphora as a compensatory response to ocular surface irritation. This paradoxical tearing may obscure the underlying tear film dysfunction and delay diagnosis. Such manifestations are commonly observed in younger individuals and contact lens wearers, in whom symptoms of ocular surface discomfort may coexist with apparently preserved tear secretion on routine quantitative tear testing.[14]

Symptoms Associated with Digital Screen Exposure

Prolonged digital screen exposure has emerged as a major contributor to the increasing prevalence of DED symptoms worldwide. Extended screen use is associated with reduced blink frequency and incomplete blinking, which promote excessive tear evaporation and tear film instability. Consequently, patients frequently experience ocular fatigue, dryness, eyelid heaviness, burning sensation, blurred vision, and visual discomfort following prolonged use of smartphones, computers, and other digital devices. These symptoms are particularly prevalent among children, adolescents, and young adults, reflecting the growing burden of DED in younger populations.[15]

Pain-Related Symptoms and Neurosensory Abnormalities

In certain patients, pain-related symptoms dominate the clinical presentation of DED. These include photophobia, burning ocular pain, hyperalgesia, allodynia, and persistent ocular discomfort that may occur independently of classical clinical signs. Such symptoms are associated with abnormalities in corneal nerve structure and sensory processing pathways, contributing to the pronounced discordance between subjective symptoms and objective findings observed in many patients with DED.[16]

Impact of DED Symptoms on Mental Health and Quality of Life

A substantial body of evidence demonstrates that DED significantly impairs quality of life and is associated with psychological distress. Patients with moderate-to-severe symptoms frequently report difficulties in daily functioning, reduced work productivity, sleep disturbances, anxiety, depressive symptoms, and social impairment. Meta-analyses have shown that individuals with DED are more likely to experience psychiatric comorbidities, and this relationship appears to be bidirectional, emphasizing the importance of holistic and patient-centered management strategies.[17]

Demographic and Clinical Factors Influencing Symptom Severity

The severity and pattern of DED symptoms vary according to demographic and clinical factors such as age, sex, hormonal status, refractive error, contact lens use, and systemic medication intake. Women generally report more severe symptoms than men, possibly due to hormonal influences and sex-related differences in pain perception. Increased symptom burden has also been documented among individuals with myopia, prolonged contact lens wear, autoimmune diseases, and chronic systemic medication use, highlighting the multifactorial and heterogeneous nature of DED.[18]

The discrepancy between subjective symptoms and objective clinical signs remains one of the most clinically significant aspects of DED. Patients may report severe ocular discomfort despite minimal findings on slit-lamp examination, whereas others may demonstrate substantial ocular surface damage with relatively mild symptoms. Large multicenter studies, including the DREAM study, have confirmed that the correlation between symptom severity measured by the Ocular Surface Disease Index (OSDI) and clinical tests such as TBUT, Schirmer test, and ocular surface staining is frequently weak. Furthermore, longitudinal changes in symptoms do not always parallel changes in clinical signs over time.[19] The short TBUT-type DED phenotype therefore requires special consideration during diagnosis, therapeutic planning, and evaluation of treatment response.[20]

Causes, Symptoms & Ocular Surface Dysfunction

Pathophysiology of Dry Eye Disease

Tear Hyperosmolarity and Inflammation in Dry Eye Disease

Tear hyperosmolarity and tear film instability are regarded as the principal pathogenic mechanisms underlying dry eye disease (DED).[21] Both major forms of DED—aqueous-deficient dry eye (ADDE) and evaporative dry eye (EDE)—ultimately lead to increased tear osmolarity and ocular surface dysfunction. In EDE, meibomian gland dysfunction results in an inadequate lipid layer, causing excessive tear evaporation despite normal lacrimal gland secretion. In contrast, ADDE occurs due to reduced aqueous tear production from lacrimal gland impairment, as observed in conditions such as Sjögren syndrome, resulting in hyperosmolar tears even with normal evaporation rates. These two forms frequently coexist and contribute to the mixed subtype of DED. Persistent tear hyperosmolarity initiates a vicious inflammatory cycle characterized by ocular surface stress, epithelial damage, goblet cell loss, and chronic inflammation.[22]

A variety of proinflammatory cytokines and mediators, including interleukin (IL)-1, IL-6, IL-8, tumor necrosis factor-alpha (TNF-α), transforming growth factor-beta (TGF-β), and chemokines, are elevated in patients with DED. These inflammatory mediators alter neural signaling, reduce lacrimal gland stimulation, and impair tear secretion. Neuroinflammatory substances such as substance P, calcitonin gene-related peptide (CGRP), and nerve growth factor (NGF) further contribute to ocular surface inflammation and epithelial injury. Elevated NGF levels correlate with conjunctival hyperemia and corneal fluorescein staining, reflecting ongoing epithelial damage and attempted tissue repair.[23] Inflammatory pathways involving nuclear factor kappa B (NF-κB) and intercellular adhesion molecules promote recruitment of lymphocytes to the ocular surface, perpetuating chronic inflammation and tissue destruction. Increased levels of matrix metalloproteinases (MMPs) additionally contribute to epithelial barrier disruption and apoptosis of conjunctival and lacrimal gland cells.

Mucin deficiency also plays a critical role in DED pathogenesis. Membrane-associated and secreted mucins, particularly MUC5AC produced by conjunctival goblet cells, are essential for tear film stability, hydration, and proper wetting of the corneal surface. Reduced mucin expression leads to tear film instability, epithelial desiccation, and ocular surface keratinization, even when aqueous tear production is relatively preserved.[24] Similarly, decreased tear proteins such as lactoferrin, lysozyme, lipocalin, and phospholipase A2 impair antimicrobial defense and destabilize the tear film. Lipocalin deficiency contributes to increased tear surface tension and formation of characteristic mucous strands in DED patients.

Sex hormone imbalance, particularly androgen deficiency, has also been implicated in the development of DED. Androgens exert trophic and anti-inflammatory effects on both lacrimal and meibomian glands by regulating lipid secretion and suppressing lymphocytic infiltration. Hormonal decline during menopause may impair tear secretion and meibomian gland function, contributing to the higher prevalence of DED among postmenopausal women. Clinical studies have demonstrated that androgen replacement therapy can improve tear breakup time, Schirmer test values, corneal staining, and symptom scores in androgen-deficient patients.[25] Furthermore, androgen deficiency alters the composition and viscosity of meibomian gland secretions, exacerbating evaporative tear loss and gland obstruction. Sjögren syndrome-associated DED represents a severe autoimmune subtype characterized by lymphocytic infiltration of lacrimal glands, production of autoantibodies, reduced reflex tearing, and progressive glandular destruction, ultimately resulting in chronic ocular surface inflammation and severe tear deficiency.

Etiology

The International Dry Eye WorkShop II (DEWS II) classifies dry eye disease (DED) into two major subtypes: aqueous-deficient dry eye (ADDE) and evaporative dry eye (EDE).[26] ADDE results primarily from inadequate aqueous tear production due to lacrimal gland dysfunction, whereas EDE is caused by excessive tear evaporation associated mainly with abnormalities of the tear film lipid layer. In clinical practice, both forms frequently coexist and contribute to a mixed pattern of disease.

Aqueous-deficient dry eye may occur in association with Sjögren syndrome (SS) or independently as non-Sjögren dry eye. Non-Sjögren ADDE may arise from age-related lacrimal gland degeneration, congenital alacrima, lacrimal gland infiltration by inflammatory or neoplastic disorders, infectious diseases, systemic vitamin A deficiency, endocrine disturbances, post-radiation fibrosis, ocular graft-versus-host disease, or adverse drug effects.[27] Several systemic medications, including antihistamines, beta blockers, anticholinergics, antidepressants, oral contraceptives, isotretinoin, and topical preservatives such as benzalkonium chloride, can impair aqueous tear secretion and destabilize the ocular surface. Reflex hyposecretion may also occur secondary to neurotrophic keratitis, refractive or corneal surgery, herpes simplex or herpes zoster infections, chronic contact lens wear, diabetes mellitus, aging, and cranial nerve dysfunction. Sjögren syndrome-associated DED is characterized by autoimmune-mediated destruction

of the lacrimal glands and may occur either as primary SS or secondary SS associated with connective tissue disorders such as rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, dermatomyositis, and autoimmune thyroid disease.[28]

Evaporative dry eye primarily results from meibomian gland dysfunction (MGD), which leads to deficiency or abnormality of the tear film lipid layer and increased tear evaporation. MGD may be hypersecretory, hyposecretory, or obstructive in nature and can occur secondary to local ocular disorders, systemic dermatologic diseases such as acne rosacea and seborrheic dermatitis, congenital syndromes, or medication-induced toxicity.[29] Reduced blink rate during prolonged visual tasks such as computer use, Parkinson disease, eyelid malposition, lagophthalmos, floppy eyelid syndrome, and ocular surface exposure disorders further contribute to evaporative tear loss. Drugs such as isotretinoin may also alter meibomian gland secretion and worsen tear film instability.

Extrinsic factors additionally play an important role in DED pathogenesis. Vitamin A deficiency impairs goblet cell differentiation and lacrimal gland function, resulting in ocular surface dryness and keratinization. Other external contributors include chronic contact lens wear, topical medications and preservatives causing epithelial toxicity, and ocular surface inflammatory disorders such as chronic blepharitis, allergic keratoconjunctivitis, ocular cicatricial pemphigoid, and Stevens–Johnson syndrome.[30] These diverse etiological factors collectively disrupt tear film homeostasis, induce ocular surface inflammation, and perpetuate the chronic cycle of dry eye disease.

Epidemiology

Dry eye disease (DED) is one of the most prevalent ocular surface disorders worldwide and represents a major public health concern. The prevalence of DED varies widely, ranging from approximately 5% to 50% depending on the diagnostic criteria used, geographic region, age group, and environmental influences.[26] The disease is particularly common among individuals older than 50 years, with epidemiological studies estimating that millions of adults are affected globally. Women are more frequently affected than men, especially postmenopausal women, likely because of hormonal influences on lacrimal and meibomian gland function.[27] Sjögren syndrome-associated dry eye also predominantly affects women and contributes significantly to severe aqueous-deficient dry eye cases.

In recent years, the prevalence of DED has increased considerably among younger adults due to lifestyle and environmental factors. Excessive use of digital devices such as smartphones, tablets, and computers, prolonged screen exposure, reduced blink rate, soft contact lens wear, and increased exposure to air-conditioned environments have all contributed to the growing incidence of dry eye symptoms in individuals aged 18–34 years.[28] Modern occupational demands and increased screen dependency have therefore made DED an increasingly important concern even in younger populations.

DED is among the most common reasons for seeking ophthalmic consultation and imposes a substantial socioeconomic burden on healthcare systems worldwide.[29] Patients with chronic dry eye often experience impaired visual performance, reduced work productivity, emotional stress, and diminished quality of life. The economic burden includes direct treatment expenses as well as indirect costs associated with reduced efficiency, absenteeism, and frequent medical visits. Meibomian gland dysfunction, a major cause of evaporative dry eye, is expected to increase further with the aging global population, thereby increasing the burden on ophthalmic practice and healthcare resources.[30] Additionally, studies suggest that DED may be more prevalent among Asian and Hispanic populations compared with White populations, although racial and ethnic epidemiological data remain limited.

Current Medical Management Strategies

Artificial tears and lubricating eye drops remain the first-line treatment for dry eye disease (DED) and are widely used to improve ocular surface lubrication, dilute inflammatory mediators, reduce friction during blinking, and restore tear film stability.[31] Preservative-free formulations are preferred in moderate-to-severe disease because chronic exposure to preservatives such as benzalkonium chloride may exacerbate ocular surface toxicity and inflammation. Lipid-containing artificial tears are particularly beneficial in evaporative dry eye associated with meibomian gland dysfunction (MGD), as they help replenish the deficient lipid layer and reduce tear evaporation.

Inflammation-targeted therapy has become a cornerstone in the modern management of DED because chronic ocular surface inflammation plays a central role in disease progression. Short-term topical corticosteroids rapidly suppress inflammatory cytokines, improve corneal staining, and relieve symptoms; however, prolonged use is limited by potential adverse effects such as cataract formation, elevated intraocular pressure, glaucoma, and secondary infection.[32] Topical cyclosporine A has emerged as an effective long-term immunomodulatory therapy that inhibits T-cell activation and inflammatory cytokine production, thereby improving tear secretion, goblet cell density, and ocular surface integrity in chronic DED. Lifitegrast, another anti-inflammatory agent, acts by blocking lymphocyte function-associated antigen-1 (LFA-1) interactions, thereby reducing T-

cell-mediated inflammation and improving both symptoms and signs of ocular surface disease.[33]

Secretagogues such as diquafosol and rebamipide stimulate aqueous and mucin secretion, enhance tear film quality, and promote epithelial healing by improving goblet cell function and mucin production. Punctal occlusion using punctal plugs is especially useful in aqueous-deficient dry eye, as it decreases tear drainage and prolongs tear retention on the ocular surface.[34] In severe or refractory cases, biologic tear substitutes such as autologous serum eye drops are increasingly used because they contain growth factors, vitamins, fibronectin, and anti-inflammatory mediators that support epithelial regeneration and ocular surface healing.

Management of meibomian gland dysfunction has also evolved significantly with the introduction of newer therapeutic modalities. Thermal pulsation systems, meibomian gland expression, microblepharoexfoliation, and intense pulsed light (IPL) therapy help improve meibomian gland secretion, reduce gland obstruction, and restore lipid layer stability, thereby reducing evaporative tear loss.[35] These multimodal treatment approaches emphasize individualized therapy based on the underlying pathophysiological mechanisms and severity of dry eye disease.

Diagnosis of Dry Eye Disease

The diagnosis of dry eye disease (DED) remains a significant clinical challenge because of its multifactorial etiology, heterogeneous presentation, fluctuating course, and the frequent discrepancy between subjective symptoms and objective clinical findings. Modern diagnostic strategies rely on a comprehensive and multidimensional approach integrating symptom assessment, clinical examination, tear film analysis, ocular surface imaging, and advanced digital technologies.[36] Earlier diagnostic approaches focused primarily on tear quantity measurement and detection of ocular surface damage; however, current understanding recognizes tear film homeostasis disruption, inflammation, and neurosensory abnormalities as central components of DED pathogenesis. Consequently, contemporary diagnostic algorithms emphasize the combined evaluation of patient-reported symptoms and objective tear film parameters.[37]

Symptom assessment serves as the initial step in DED diagnosis. Standardized questionnaires such as the Ocular Surface Disease Index (OSDI) and Dry Eye Questionnaire (DEQ-5) are commonly used to quantify symptom severity and evaluate the impact of DED on visual function and quality of life. Nevertheless, symptoms alone are insufficient because their severity often correlates poorly with objective ocular surface findings.[38] Classical diagnostic tests therefore remain essential for confirming the diagnosis and identifying disease subtype. The Schirmer test evaluates aqueous tear production by measuring wetting of filter paper strips placed in the lower conjunctival fornix. Values below normal thresholds indicate varying degrees of aqueous deficiency, although the test is limited by poor reproducibility and reflex tearing induced by irritation. Tear break-up time (TBUT), assessed following fluorescein instillation, evaluates tear film stability; values below 10 seconds indicate tear film instability and increased risk of DED. Ocular surface staining using fluorescein, lissamine green, or rose bengal identifies corneal and conjunctival epithelial damage and assists in grading disease severity.[39]

Additional diagnostic tools include the lid-parallel conjunctival folds (LIPCOF) scale, which evaluates conjunctival folds associated with ocular surface dryness, and tear osmolarity measurement, an objective biomarker of tear film hyperosmolarity. Elevated tear osmolarity values above 308 mOsm/L correlate strongly with DED severity and instability of the tear film.[40] Significant advances in DED diagnosis have also emerged through non-invasive tear film assessment techniques such as non-invasive tear break-up time (NIBUT), lipid layer interferometry, tear meniscus height analysis, and dynamic topographic tear film evaluation. These methods reduce patient discomfort while providing reproducible and quantitative assessments of tear film function.

Modern ocular surface imaging techniques play an increasingly important role in the diagnosis and management of DED. Meibography enables detailed visualization of meibomian gland morphology, allowing the assessment of gland dropout, atrophy, and structural abnormalities associated with evaporative dry eye. Advanced corneal imaging modalities, including optical coherence tomography (OCT) and corneal topography, permit precise evaluation of tear film distribution, epithelial integrity, and surface irregularities.[41] These imaging technologies provide objective information that assists in differentiating DED subtypes, monitoring treatment response, and identifying subtle pathological changes that may not be apparent during routine clinical examination.

In patients with systemic autoimmune disorders such as Sjögren syndrome, comprehensive ophthalmic evaluation is particularly important because ocular dryness may represent one of the earliest and most severe manifestations of systemic disease. Early recognition enables prompt interdisciplinary management and prevention of severe ocular complications including corneal ulceration and infection.[42]

Recent advances in artificial intelligence (AI) and machine learning (ML) have introduced a transformative approach to DED diagnosis and management. AI algorithms can analyze ocular surface images, meibography findings, tear film

parameters, and clinical datasets with high accuracy and reproducibility. Deep learning models and convolutional neural networks (CNNs) allow automated assessment of tear meniscus height, lipid layer quality, corneal staining, and meibomian gland morphology, significantly reducing interobserver variability and improving diagnostic precision.[43] AI-assisted meibography can detect subtle glandular abnormalities such as gland dropout and atrophy that may be overlooked during manual evaluation. Furthermore, ML algorithms can integrate multimodal clinical data—including Schirmer test results, TBUT, inflammatory biomarkers, and symptom scores—to classify disease severity, predict progression, and identify likely treatment responders.[44] Studies have demonstrated that AI-assisted diagnostic systems improve diagnostic accuracy, shorten image analysis time, and facilitate personalized treatment planning. AI also enables remote monitoring through mobile applications and digital imaging systems, allowing early detection of disease worsening and timely therapeutic intervention.[45] Although challenges remain regarding data standardization, population diversity, ethics, and privacy concerns, AI represents one of the most promising future directions in DED diagnostics, offering enhanced precision, reproducibility, individualized management, and improved patient outcomes.

Lifestyle and Supportive Care

Lifestyle modification and supportive care are essential components in the comprehensive management of dry eye disease (DED), particularly because environmental and behavioral factors significantly influence tear film stability and ocular surface health.[46] Increasing dependence on digital devices has emerged as a major contributor to DED, especially among younger populations. Prolonged screen exposure reduces blink frequency and increases incomplete blinking, leading to excessive tear evaporation and ocular surface desiccation. Patients are therefore advised to follow preventive strategies such as the "20-20-20 rule," which recommends looking at an object 20 feet away for 20 seconds every 20 minutes during screen use. Proper screen positioning below eye level and conscious blinking exercises also help reduce evaporative tear loss and visual fatigue.

Environmental modifications are equally important in minimizing tear film instability. Exposure to smoke, dust, air pollutants, wind, air conditioning, and low-humidity environments can aggravate ocular surface dryness and inflammation. The use of humidifiers, moisture chamber spectacles, and protective eyewear may help preserve tear film integrity and reduce ocular surface exposure.[47] Avoiding prolonged exposure to adverse environmental conditions can significantly improve patient comfort and symptom control.

Nutritional support has gained increasing attention in DED management. Omega-3 fatty acids possess anti-inflammatory properties and may improve meibomian gland function, tear film stability, and lipid layer quality. Dietary supplementation with omega-3 fatty acids has been associated with symptomatic relief and reduced ocular surface inflammation in several clinical studies.[48] Adequate hydration and balanced nutrition rich in vitamins, antioxidants, and essential fatty acids are also important for maintaining healthy tear production and ocular surface function.

Eyelid hygiene represents a fundamental supportive measure, particularly in patients with blepharitis and meibomian gland dysfunction. Regular eyelid cleansing, warm compresses, and gentle lid massage help improve meibomian gland secretion, reduce bacterial biofilm accumulation, and restore lipid layer function.[49] Consistent eyelid hygiene practices can significantly reduce evaporative tear loss and improve ocular comfort.

Behavioral and sleep-related factors also influence the severity of DED. Poor sleep quality, chronic stress, smoking, and prolonged contact lens wear have all been associated with worsening dry eye symptoms and ocular surface inflammation. Adequate sleep, stress reduction strategies, smoking cessation, and limiting contact lens use when symptoms are severe can substantially improve tear film stability and overall ocular surface health.[50] These lifestyle-based interventions complement pharmacological therapies and form an important part of long-term DED management.

Recent Advances in Management

Recent advances in the management of dry eye disease (DED) have increasingly focused on targeted therapy, personalized medicine, and the development of innovative technologies aimed at addressing the underlying pathophysiological mechanisms of the disease. Contemporary therapeutic strategies now extend beyond symptomatic lubrication and emphasize restoration of tear film homeostasis, suppression of inflammation, regeneration of ocular surface tissues, and optimization of meibomian gland function.[51] Lipid-based artificial tears and semifluorinated alkane formulations have emerged as important developments in the treatment of evaporative dry eye, particularly in patients with meibomian gland dysfunction. These formulations stabilize the tear film lipid layer, reduce evaporation, and improve ocular surface lubrication more effectively than conventional aqueous lubricants.

Novel anti-inflammatory therapies targeting specific inflammatory mediators and cytokine pathways are also under active investigation. Advanced immunomodulatory agents designed to inhibit T-cell activation, inflammatory cytokines, and oxidative stress pathways aim to provide more

selective and sustained control of ocular surface inflammation while minimizing adverse effects associated with long-term corticosteroid use.[52] Nanotechnology-based drug delivery systems have further improved therapeutic efficacy by enhancing ocular bioavailability, prolonging drug retention time, and enabling sustained-release medication delivery. Nanomicelles, nanoparticles, liposomes, and dendrimer-based carriers are being explored for more efficient delivery of anti-inflammatory drugs and tear substitutes to the ocular surface.

Regenerative medicine has emerged as another promising area in severe and refractory DED. Biologic tear substitutes such as autologous serum, platelet-rich plasma (PRP), and umbilical cord serum contain growth factors, cytokines, vitamins, and neurotrophic factors that promote epithelial healing and ocular surface regeneration.[53] Stem-cell-based therapies are also being investigated for their potential to restore damaged lacrimal gland tissue, regenerate conjunctival goblet cells, and improve corneal epithelial integrity. In addition, neuropathic pain-targeted therapies are gaining attention because neurosensory abnormalities contribute significantly to symptom severity in many DED patients.

Artificial intelligence (AI)-assisted diagnostics and tear biomarker analysis represent transformative advances in personalized DED management. AI systems can analyze tear film parameters, ocular imaging, and patient data to improve diagnostic precision, classify disease severity, and predict therapeutic response.[54] Tear biomarker profiling may allow identification of specific inflammatory phenotypes and facilitate individualized treatment selection. Emerging evidence also suggests that modulation of the ocular surface microbiome may play a future therapeutic role in controlling chronic inflammation and maintaining ocular surface health.

Advanced office-based procedures such as thermal pulsation therapy, intense pulsed light (IPL) treatment, meibomian gland probing, and microblepharoexfoliation are increasingly incorporated into routine clinical practice for the management of meibomian gland dysfunction and evaporative dry eye.[55] These modern approaches reflect the shift toward mechanism-based and patient-specific therapy aimed at improving long-term outcomes and quality of life in individuals with DED.

Future Directions

Future directions in dry eye disease (DED) research are increasingly focused on precision medicine approaches that target the specific pathogenic mechanisms involved in individual patients. As DED is a highly heterogeneous disorder with inflammatory, evaporative, aqueous-deficient, and neurosensory components, future therapeutic strategies are expected to move beyond generalized symptomatic treatment toward mechanism-based personalized care. The identification of reliable molecular and inflammatory biomarkers in tears and ocular surface tissues may allow improved disease classification, early diagnosis, prediction of disease progression, and individualized therapeutic selection. Biomarker-guided therapy could help clinicians determine which patients are most likely to benefit from immunomodulators, lipid-based therapies, regenerative treatments, or neurosensory-targeted interventions.

Emerging fields such as gene therapy and regenerative medicine are expected to significantly transform DED management in the future. Stem-cell therapy, lacrimal gland regeneration, tissue engineering, and biologic tear substitutes may offer long-term restoration of ocular surface function rather than temporary symptom relief. Neuroprotective and neuromodulatory therapies are also under investigation because neurosensory dysfunction plays a major role in symptom generation and chronic ocular discomfort.

Technological innovations, including artificial intelligence (AI)-based diagnostic systems, wearable tear monitoring devices, and digital ocular surface analysis platforms, may enable continuous disease monitoring, early detection of disease worsening, and real-time treatment optimization. Future DED therapies will likely integrate anti-inflammatory, regenerative, and neurosensory-targeted approaches to effectively interrupt the chronic vicious cycle of tear film instability, inflammation, and ocular surface damage.

Discussion

Dry eye disease (DED) is now recognized as a complex, multifactorial disorder involving tear film instability, ocular surface inflammation, meibomian gland dysfunction, epithelial injury, and neurosensory abnormalities. Contemporary understanding of DED has evolved considerably from the earlier concept of a simple tear deficiency disorder to that of a chronic inflammatory disease affecting the entire ocular surface functional unit.[56] Tear hyperosmolarity is considered a central pathogenic mechanism that initiates and perpetuates the vicious cycle of inflammation, epithelial apoptosis, goblet cell loss, and tear film instability. Persistent ocular surface inflammation further impairs lacrimal gland secretion and meibomian gland function, thereby worsening disease severity and contributing to chronic symptom progression. Increasing evidence also highlights the role of neurosensory dysfunction and ocular surface nerve alterations in symptom generation, which may explain the poor correlation often observed between clinical signs and patient-reported symptoms.

Over the past decade, management strategies for DED have undergone substantial transformation.

Conventional tear replacement therapy alone is frequently inadequate, particularly in moderate-to-severe disease, because it does not sufficiently address the underlying inflammatory and evaporative mechanisms. Modern therapeutic approaches therefore emphasize anti-inflammatory treatment, restoration of meibomian gland function, stabilization of the tear film lipid layer, and protection of the ocular surface epithelium.[57] Immunomodulatory agents such as cyclosporine and lifitegrast, biologic tear substitutes, and advanced meibomian gland therapies have improved the management of chronic and refractory cases. The growing understanding of DED heterogeneity has also reinforced the importance of individualized treatment strategies based on disease subtype, severity, associated systemic disorders, and patient-specific risk factors.[58]

Lifestyle and environmental factors have become increasingly important contributors to the rising global prevalence of DED. Extensive digital screen exposure, reduced blink rate, air-conditioned environments, pollution, sleep disturbances, and chronic stress significantly affect tear film stability and ocular surface health. Behavioral modifications, environmental optimization, eyelid hygiene, and nutritional interventions therefore play a critical supportive role alongside pharmacological therapy.[59] Such multimodal management strategies not only improve symptoms but also enhance long-term treatment adherence and patient quality of life.

Recent innovations in DED therapy, including lipid-based tear substitutes, nanotechnology-driven drug delivery systems, regenerative medicine, platelet-rich plasma therapy, and intense pulsed light treatment, have expanded available therapeutic options and provided promising results in selected patient populations. Advances in artificial intelligence-assisted diagnostics and tear biomarker analysis may further improve early diagnosis, disease classification, and personalized treatment planning in the future.[60] Nevertheless, important challenges remain regarding the long-term efficacy, accessibility, affordability, and standardization of newer interventions. Further large-scale clinical studies and translational research are required to optimize treatment algorithms, establish evidence-based protocols, and improve functional outcomes in patients with chronic dry eye disease.

Conclusion

Dry eye disease (DED) is a highly prevalent and multifactorial ocular surface disorder that significantly affects visual function, daily activities, and overall quality of life. Contemporary understanding of DED recognizes it as a chronic inflammatory disease involving tear film instability, hyperosmolarity, meibomian gland dysfunction, ocular surface damage, and neurosensory abnormalities. The complex interaction between these factors creates a self-perpetuating vicious cycle that contributes to disease progression and symptom chronicity.Advances in diagnostic techniques, including non-invasive tear film assessment, ocular surface imaging, biomarker analysis, and artificial intelligence-assisted systems, have improved the accuracy of diagnosis and facilitated individualized treatment planning. Modern management strategies extend beyond simple tear supplementation and now emphasize targeted anti-inflammatory therapy, restoration of meibomian gland function, biologic tear substitutes, and lifestyle modification. Supportive measures such as digital screen management, eyelid hygiene, nutritional optimization, and environmental control remain essential for long-term disease control.Emerging therapies involving regenerative medicine, nanotechnology-based drug delivery, neurosensory modulation, and personalized medicine hold considerable promise for future DED management. Continued research and innovation are essential to improve therapeutic outcomes, enhance patient satisfaction, and reduce the growing global burden of dry eye disease.

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