

Preferred practice patterns and review on rosacea.

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Rosacea is a relatively common facial dermatosis that affects up to 5.5% of the population, most notably those with fair skin.[1] It is associated with ocular disease in up to 58% of cases. It is frequently under-recognized by ophthalmologists, as ocular signs precede cutaneous disease in 15% of cases. While the ocular manifestations are usually mild, 41% of cases are associated with corneal involvement.[2 , 3] While not life threatening, rosacea is associated with significant psychosocial morbidity. Individuals with rosacea report increased depression and anxiety that may negatively impact routine daily activities.[4] Ocular rosacea has a significant impact on ocular morbidity and on patients' quality of life, and therefore, recognition of the condition is a key part of management. This becomes more important in pediatric ocular rosacea patients, where a delayed diagnosis is common. Demodex infestation has been associated with various facial dermatoses, though the cause–effect relationship has been difficult to establish.[5 , 6] In this review, we explore the preferred practices and the association of Demodex with rosacea.

The diagnosis of rosacea is clinical and based on specific features according to the ROSacea CONsensus expert panel (ROSCO) and the National Rosacea Society (NRS).[7 , 8] The original standard classification of rosacea identified the most common patterns or groupings of signs and symptoms and designated them as follows:

subtype 1—erythematotelangiectatic; subtype 2—papulopustular; subtype 3—phymatous; and subtype 4—ocular.

Although commonly used in practice, this classification made the management complicated as it was generalized for a given subtype, when in the real world, there was a significant overlap between subtypes, and many patients had more than one subtype. The revised standard diagnostic features were adopted on the basis of their positive predictive value as supported by rosacea experts. In addition, new scientific evidence has shown that rosacea's diverse features may be part of a continuum of inflammation that may not be clinically visible but is detectable histologically and biochemically.

On the clinical exclusion of other conditions with similar presenting features, the diagnosis of rosacea is established with either: (1) phymatous changes, or (2) centrofacial persistent erythema [Table 1].[9] In their absence, diagnosis can be established by the presence of any two of the following major features: flushing/transient erythema, papules and pustules, telangiectases [Table 1], or ocular rosacea [Table 2]. Minor features, such as burning, stinging, dry sensation of the skin, or edema are not diagnostic of rosacea.

Description of cutaneous rosacea. From the recommendations of the global ROSCO panel[7]

Description of ocular rosacea. From recommendations of the global ROSCO panel[7]

The global ROSCO 2019 panel (19 dermatologists and 2 ophthalmologists) reached the conclusion that optimal diagnosis of ocular rosacea (n = 21/21) and description of its features (n = 20/21) remain unmet needs, and that systematic, evidence-based guidelines for ocular rosacea are still required (n = 16/16).

Based on a meta-analysis of 32 studies, the global prevalence of rosacea has been estimated to be 5.46% of the adult population (range 0.09–24.1%).[1] The prevalence of ocular rosacea is reported to be much lower, ranging from 0.4 to 1.0%. While rosacea is considered to be more prevalent among Celts and northern European populations with photosensitive skin types (Fitzpatrick skin phototypes I and II), it also affects other racial groups and those with darker skin tones (Fitzpatrick skin phototypes III–VI). In a US national survey of known rosacea cases, 3.9% were individuals of Hispanic backgrounds and 2% of cases were in Asians and African-Americans.[10] Few studies from Saudi Arabia, China, South Korea, Japan, and Tunisia have shown that rosacea is comparatively less common in these populations and that sun exposure is the main triggering factor.[11 – 15] There is only one Indian study and that too describes steroid-induced rosacea.[16] Phymatous subtypes are rare in the population of dark tone. Epidemiological differences based on skin types may be due to the relative masking of facial flushing and erythema by the presence of skin pigmentation, the protective effects of melanin against ultraviolet (UV) radiation (as UV radiation can exacerbate rosacea), or genetic factors. It is therefore important to consider the diagnosis of rosacea and ocular rosacea in patients of all races. It also becomes important to consider secondary features like burning and stinging while making a diagnosis of rosacea in people with skin of color.[17]

Rosacea is observed in all age groups, although it is most commonly diagnosed after the age of 30 years, with a peak between 40 and 59 years.[18] Females are commonly diagnosed earlier and more frequently than men, although this may represent differences in the pattern of health-seeking behaviors. Phymatous skin changes occur more commonly in men. In contrast to rosacea, ocular disease occurs equally in both genders.[19]

Rosacea and ocular rosacea also occur in children. The reported incidence of rosacea in individuals aged less than 20 years in the UK was 0.89 per 1000 person-years.[18] Gupta et al . from India reported blepharoconjunctivitis as the most common diagnosis in a pediatric clinic, accounting for 12% of 5012 referrals, with a mean age of 6.7 years among affected children.[20]

The pathophysiology of rosacea is likely multifactorial, involving a combination of immune-mediated and neovascular-mediated responses, environmental triggers, and genetic factors.

Dysregulation of the innate immune system has a role in the pathogenesis of rosacea. Levels of cathelicidin (an antimicrobial peptide) and kallikrein 5 (a serine protease) are increased in rosacea. Kallikrein 5 cleaves cathelicidin into LL-37, its active peptide form. LL-37, in turn, has a role in upregulating the immune-mediated response to promote inflammation and angiogenesis. In patients with rosacea, LL-37 and kallikrein 5 are abundantly identified in the skin. Gene array studies have also identified a significant elevation of cathelicidin mRNA expression in all subtypes of rosacea. Elevated levels of pro-inflammatory markers in ocular rosacea patients have also been observed. Interleukin-1a and -b, gelatinase B (matrix metalloproteinase [MMP-9]), and collagenase-2 (MMP-8) have been identified in the tears of ocular rosacea patients. Significant overexpression of intercellular adhesion molecule-1 (ICAM-1) and human leukocyte antigen-DR (HLA-DR) isotype were also observed in conjunctival epithelial cells of rosacea patients, while interleukin-1b, interleukin-16, stem cell factor, monocyte chemotactic protein-1, and monokine induced by g-interferon have all been found in skin biopsy specimens.

The facial flushing, erythema, and telangiectasia seen in rosacea may be due to an altered neurovascular response. Triggers, such as spicy foods, UV radiation, and heat may promote the release of inflammatory mediators which lead to vasodilatation, erythema, and flushing, via a mechanism involving the transient receptor potential vallinoid (TRPV) family of cation channels. Increased expression of TRPV has been identified on neuronal cells (TRPV1), smooth muscles of blood vessels, macrophages, mast cells (TRPV2), keratinocytes (TRPV2-4), and immune cells (TRPV2-4) in skin biopsy specimens from patients with different subtypes of rosacea compared with healthy skin.

An increased expression of vascular endothelial growth factor (VEGF) and VEGF receptors (VEGF-R1, VEGF-R2) has also been demonstrated in the skin of rosacea patients. Interestingly, cathelicidin also modulates levels of VEGF within epidermal keratinocytes. It is therefore likely that both vascular and immune-mediated processes contribute to the pathophysiology of rosacea.

External triggers are believed to have a role in the activation of the vascular and immune-mediated responses in rosacea. These triggers include UV exposure, certain foods, and drinks (including spicy foods, dairy products, alcohol, and hot beverages), emotional stress, strenuous exercise, medications (including amiodarone, topical steroids, and nasal steroids), and high doses of vitamins B6 and B12. UV radiation may trigger rosacea via several mechanisms: by activating vitamin D in keratinocytes, which in turn, induces cathelicidin expression in keratinocytes; by causing overexpression of MMP-1 in the skin, which increases levels of kallikrein 5; and by inducing VEGF production from keratinocytes, leading to the increased vascularity seen in rosacea. UV radiation and other triggers may also lead to an increase in the levels of Toll-like receptor 2 (TLR2) in epidermal keratinocytes, as part of the innate immune response. In turn, TLR2 leads to an increase in the production and activity of kallikrein 5, leading to increased expression of LL-37.^{15 3.4 |}

Microorganisms are postulated to play a role in rosacea. In particular, Demodex (Demodex folliculorum and Demodex brevis), a microscopic mite found on hair follicles and sebaceous glands, is found in higher density in rosacea compared to unaffected skin. In a meta-analysis of 1513 patients, Demodex mites were more commonly observed in rosacea patients compared to controls (OR 9.039; 95% confidence interval, 4.827–16.925). The Demodex count from eyelash samples is also significantly higher in patients with facial rosacea and was seen more commonly in pediatric and adult patients with chalazia compared to controls (69.2% vs 20.3%). The presence of Demodex mites may lead to proinflammatory changes or may act as a vector for other microorganisms, which

activate TLR2 and the ensuing pro-inflammatory changes. Additional microbes that may be implicated include *Helicobacter pylori* and *Staphylococcus epidermidis*, which is a normal skin commensal; however, the effects of these additional microorganisms in the pathogenesis of rosacea remain controversial. Interestingly, a reduced concentration of group IIA phospholipase A2, an antimicrobial protein that is secreted into tears by the lacrimal glands has been observed in the tears of patients with ocular rosacea.

Rosacea, acne vulgaris (AV), and seborrheic dermatitis are the three most common inflammatory facial dermatoses; they affect the pilosebaceous unit and have a predilection for the sebaceous gland-rich facial areas. Demodex mites are also found in the pilosebaceous unit, causing inflammation and leading to immune reactions.

If the mites proliferate abnormally, or when they penetrate into the dermis, they can cause demodicosis. While demodicosis is clearly defined by its cause, rosacea is still currently defined by its symptoms. As the Demodex may be considered a symbiont on the skin surface, it is expected to be found in the diagnostic sample taken from its natural niche. Forton et al . applied three systems traditionally used to attribute causality to a disease (modified Koch criteria, Hill criteria for causality, and Rothman model) and made a compelling argument in favor of cause–effect relationship.[21] According to this hypothesis, Demodex exploits the host's protective immunotolerance mechanisms for its own advantage, its proliferation being also favored by other factors (ETR, large sebaceous glands, immunotolerance, severe immunodeficiency). This proliferation gives rise to an immunogenic reaction that can be diverted, via the immunosuppressive properties of VEGF, from its original defensive aim towards T-cell exhaustion ultimately favoring mite proliferation.

Other studies too have found a high incidence of Demodex positive blepharitis in papulopustular rosacea.[22 , 23] Güder et al . also found a high incidence of facial dermatoses in patients with blepharitis.[24] It was also found that most patients with demodicosis and papulopustular rosacea do respond to acaricidal treatment.[25 , 26]

The association between rosacea and ocular rosacea can vary between individuals. Only facial changes may appear as the primary feature in 53% of cases; simultaneous skin and ocular changes may occur in 27% of cases; and ocular changes may occur as the primary feature in up to 20% of cases.[27]

Rosacea is characterized by vasomotor changes within blood vessels, primarily in the facial and periocular areas. It results in transient or persistent erythema, telangiectasia, papules, pustules, and phymatous changes. Periodic exacerbation and remission of burning and stinging characterize the disease. It can also affect extra-facial locations, such as the neck, chest, scalp, ears, and back.

Ocular rosacea may occur in up to 58% of patients with rosacea. However, the severity of ocular involvement may not directly correlate with the extent of cutaneous changes. In the absence of clear guidelines, a diagnosis of ocular rosacea should therefore be considered in patients with diagnostic features, regardless of the presence of skin disease. The grading of ocular rosacea by the ROSCO panel is shown in Table 3 .

Grading of ocular rosacea. From the recommendations of the ROSCO panel[7]

Ocular manifestations are more often bilateral at the time of diagnosis; however, unilateral or sequential changes can occur. Symptoms include ocular irritation, itching, redness, photophobia and/or epiphora, and reduced vision in the presence of corneal involvement. The signs are described in more detail in this section. It should be noted that neither symptoms nor signs are specific to the disease.

The lid margin is typically erythematous with telangiectasia. Meibomian gland dysfunction (MGD) and posterior blepharitis are the most common findings. Meibomian gland secretions are produced

in an excessive quantity and can be of turbid consistency, leading to the plugging of the meibomian gland and chalazion formation.

It also results in an abnormal tear film, with a soapy, inferior tear meniscus, leading to evaporative dry eyes. Anterior blepharitis with cylindrical dandruff (CD) around the eyelashes is classically seen with *Demodex* mites at the root of eyelashes.

Chronic red eye is often the presenting feature of *Demodex* blepharoconjunctivitis. It is a non-specific, chronic conjunctivitis predominantly affecting the interpalpebral region. An arcade of dilated vessels in the superficial limbal plexus, typically in the inferior quadrant may be observed. Inferior conjunctival cicatrization can occur in chronic disease. Phlyctenulosis may occur.

Corneal involvement occurs in around one-third of cases with ocular rosacea. Inferior superficial corneal neovascularization is the most common finding in chronic blepharokeratoconjunctivitis, but can progress circumferentially and can involve the central cornea [Fig. 1].[28] Corneal pathology can range in severity from mild, inferior punctate epithelial erosions, to marginal keratitis, scarring, peripheral thinning, ulceration, and corneal perforation in the most severe cases.[28 , 29] Additional corneal changes include recurrent corneal epithelial erosions, Salzmann nodules, and phlyctenules. Episcleritis and scleritis have also been reported.[19]

(a) Right eye of a patient with history of chronic red eye with exacerbations and remission for ten years. Facial lesions were suggestive of papulopustular rosacea. (b) 6 weeks after treatment with a tapering dose of topical steroid drops, twice daily tea tree oil lid scrubs at home, and a course of oral ivermectin (12 mg) one week apart

In contrast to adult cases where ocular manifestations may precede cutaneous disease in 15% of cases, the ocular disease may precede skin disease in as many as 55% of affected children.[30] Dermatological features, where present, may also be more subtle compared to adults. Thus, ophthalmologists may be the first to diagnose the condition in young patients. However, the absence of skin changes frequently results in a delayed diagnosis. In a case series of 27 children from London, UK, the mean time from onset of symptoms to presentation at a specialty anterior segment clinic was 1.9 years. Ocular rosacea in the pediatric population also remains poorly recognized, in part, due to ambiguous diagnostic criteria and variable terms (including childhood blepharokeratoconjunctivitis, phlyctenular keratitis, and staphylococcal blepharokeratitis) which are all used to describe a wide spectrum of manifestations of the same disease.

Children with BKC had severer corneal disorders compared with adult BKC patients, which may be caused by a long-delayed diagnosis.[31]

On the first presentation, most pediatric patients have bilateral disease, although it may be asymmetric. Signs include recurrent chalazia, lid margin telangiectasia, MGD, anterior and posterior blepharitis, conjunctival hyperemia, inferior punctate epithelial erosions, corneal infiltrates, and phlyctenulosis. The presence of these signs and a positive family history of rosacea can provide clues to the diagnosis of ocular rosacea in this age group. However, due to delays in the diagnosis, corneal complications such as ulceration, pannus formation, vascularization, and scarring are more common on first presentation in pediatric patients compared to adults. It is frequently confused with herpetic eye disease or allergic eye disease.

While rosacea is typically considered a dermatological disorder, there is increasing evidence that it is associated with other systemic conditions. A meta-analysis found a higher prevalence of dyslipidemia, hypercholesterolemia, raised low-density lipoprotein, triglycerides and fasting blood glucose, and systolic hypertension among patients with rosacea. However, no statistically significant association was found with ischemic heart disease, stroke, diabetes, and high-density lipoprotein.[32] It has also been associated with gastrointestinal disorders (coeliac disease, ulcerative colitis, Crohn's disease, *H. pylori* infection) neurological disorders (depression, migraine,

dementia, Parkinson's disease), and rheumatoid arthritis.[33]

Rosacea and ocular rosacea currently remain a clinical diagnosis. Demodicosis can be confirmed by microscopic detection of Demodex mites in epilated eyelashes or in skin scrapings, which can be seen under the microscope under 20X magnification after dissolving the debris with sodium fluorescein.[34] Forton et al . described two consecutive standardized skin surface biopsies as an improved sampling method to evaluate Demodex density for the diagnosis of rosacea and demodicosis.[35] The optimal cutoff values for the two biopsies were combined and the resultant criterion (presence of a first biopsy density >5 Demodex/cm² or a second biopsy density >10 Demodex/cm²) enabled confirmation of a diagnosis of rosacea or demodicosis with a sensitivity of 98.7% and specificity of 95.5%.

Dermoscopy can also be performed by dermatologists where filaments surrounded by erythema or scales may be observed.

In vivo imaging of meibomian glands using meibography assists with the morphology of the glands in MGD.[36]

As rosacea is associated with systemic disorders including dyslipidemia, hypertension, and H. pylori infection, systemic investigations should be considered in conjunction with a general practitioner.

Depending on the severity of the disease, treatment usually involves one or a combination of, conservative measures, topical agents, systemic agents, and interventions. However, there is a lack of randomized, controlled trials assessing these treatments. Studies report small sample sizes, and many are not specific to ocular rosacea. An updated systematic review of rosacea treatment based on the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework is outlined in Table 4 .[37]

Treatment recommendations and certainty of evidence in ocular rosacea as per GRADE framework[37]

GRADE=Grading of Recommendations, Assessment, Development and Evaluations

Patient education is of paramount importance, as affected individuals need to understand the chronicity of the condition, with periods of exacerbations and remissions. Patients should also be aware of the systemic associations with rosacea so that monitoring can be undertaken where appropriate. Exposure to potential triggers should be minimized, such as recommending the use of sun protection to minimize UV exposure and minimizing hot showers, spicy foods, alcohol, and caffeine. Conservative measures to treat MGD are encouraged, including digital massage or the use of warm compresses and lid hygiene, twice daily, to treat posterior and anterior blepharitis. If conservative measures are insufficient in treating eyelid disease, concurrent topical and systemic agents may be required.

Demodex infection should be treated with tea tree oil therapy (weekly lid scrubs with 50% tea tree oil and daily lid scrubs with tea tree shampoo for a minimum of 6 weeks), warm compresses, intense pulsed light (IPL), topical ivermectin (1% once daily for 12 weeks) or systemic ivermectin (200 mg/mL as a single dose, which can be repeated after 7 days).

The aim of topical treatments for ocular rosacea is to treat dry eyes, MGD, and ocular surface inflammation. Preservative-free artificial tear supplements are recommended as it treats not only dry eyes but help to reduce ocular surface inflammation. In addition, topical steroids are frequently required during episodes of acute inflammation; however, long-term use is generally not recommended due to the increased risk of microbial keratitis and other steroid-associated complications. Cyclosporin is a potent inhibitor of T-cell function by selectively inhibiting calcineurin,

impairing the transcription of IL-2 and related cytokines in T-cells. It can be considered an adjunct treatment for ocular surface inflammation in rosacea. In a randomized, controlled trial, twice daily instillation of topical ciclosporin 0.05% was more efficacious than artificial tear supplements after 3 months of treatment in improving Schirmer score, mean tear break-up score, corneal staining, and ocular surface disease index (OSDI) score. Topical ciclosporin has also been reported to improve ocular symptoms and tear production to a greater extent than oral doxycycline, in part by increasing mucin production from goblet cells. Stinging and irritation are common side effects; however, it is generally well tolerated, with minimal long-term side effects reported.

There is less information on the use of other anti-inflammatory agents for ocular rosacea.

There is also one prospective, randomized, double-masked interventional case series on the use of topical tacrolimus ointment 0.03% twice daily for refractory posterior blepharitis. After 28 days, there was an improvement in symptoms, meibomian gland secretion, conjunctival hyperemia, lower lid telangiectasia, and corneal staining.

Topical azithromycin is approved to treat bacterial conjunctivitis. However, it may also be useful in treating MGD, although this indication is "off-label." In a randomized trial comparing azithromycin 1% with warm compresses, azithromycin was shown to improve eyelid signs, meibomian gland plugging, and symptoms. It can be used twice daily for 2 days and then once daily for a total of 30 days, although dosing regimens vary. It has also been used in pediatric cases.

Oral tetracyclines, such as doxycycline (a synthetic derivative of tetracycline), are beneficial in the treatment of rosacea through several potential mechanisms.[38] Tetracyclines inhibit the expression of MMPs and the activation of cathelicidin, which have a role in the pathophysiology of rosacea as described previously. Furthermore, tetracyclines reduce bacterial flora on the eyelids and reduce the production of lipase enzymes by staphylococci, which can improve the quality of meibomian gland secretions.[39] Tetracyclines also inhibit collagenase enzymes and may protect the cornea from thinning and perforation in more advanced cases.[40] Oral tetracycline and oral doxycycline have a similar mechanism and efficacy; however, tetracycline has a shorter half-life and is taken at a four times daily dose.[40] Doxycycline is, therefore, generally more commonly used and better tolerated. There are various dosing regimens that can be used. It is typically prescribed as a dose of 100 mg once daily, or 50 mg twice daily for 6 to 12 weeks, or tapered to a lower dose after 2 to 4 weeks. It can also be prescribed at 100 mg twice daily or 50 mg daily.[41 , 42] It should be noted that the optimal dose and duration of treatment have not been established and little evidence exists for the 50 mg daily dosing regimen to treat ocular rosacea.[43] Patients who have recurrent symptoms on discontinuation of the treatment may require longer-term use. However, long-term use of doxycycline may be associated with a higher side effect profile, including gastrointestinal symptoms, photosensitivity, and lower tolerance to the medication. In 2006, a lower dose doxycycline capsule was approved by the US Food and Drug Administration (FDA) specifically for rosacea in adults. It consists of 30 mg immediate-release and 10 mg delayed-release doxycycline and is taken once daily. Treatment with doxycycline 40 mg for a mean of 8 months resulted in an improvement in ocular rosacea symptoms and conjunctiva injection after a mean follow-up of 9 months.[44] A lower dose of 40 mg doxycycline is associated with fewer gastrointestinal side effects than conventional 100 mg or 50 mg doxycycline. It also has the advantage that 40 mg is a submicrobial dose, whereas 50 mg doxycycline once daily has a plasma concentration that exceeds the minimum inhibitory concentration for 2 to 3 hours.[45] Therefore, where available, the lower dose of 40 mg (30 mg immediate-release and 10 mg delayed-release) doxycycline should be used rather than 50 mg immediate-release doxycycline.

A combination of doxycycline and ciclosporin 0.05% has been shown to be more efficacious than doxycycline alone.[46] Another tetracycline, minocycline 100 mg taken once daily is commonly prescribed by dermatologists for rosacea, due to the lower incidence of gastrointestinal side effects and photosensitivity than doxycycline. It has been found to be non-inferior to doxycycline 40 mg once daily. However, the evidence for minocycline in the treatment of ocular rosacea is lacking, and risks include drug-induced lupus and other hypersensitivity syndromes.

The use of oral tetracyclines is not recommended in children under the age of 7 years, or in pregnancy and lactation. This is due to the potential complication of impaired bone growth and permanent discoloration of teeth, and its teratogenic potential. In such cases, oral erythromycin may be used as an alternative, 100 to 500 mg daily (as erythromycin base) for adults and 30 to 50 mg/kg (ethyl succinate formulation) in divided doses for children.[47] Alternatively, azithromycin can be prescribed 500 mg orally, 3 days a week for 3 or 4 weeks for adults and 5 mg/kg/day for children.[48 , 49] Erythromycin and azithromycin are macrolide antibiotics, considered to have polymodal immunomodulatory effects which can be used for the management of posterior blepharitis. They are generally well tolerated, although gastrointestinal side effects may be reported.

In a randomized, controlled trial of omega-3 fatty acids taken for 6 months for ocular rosacea, meibomian gland function, Schirmer score, tear break up time, and symptoms all improved at the end of the treatment.[50]

Conversely, the DREAM Study, a multi-center, randomized, double-masked clinical trial did not find any benefit from omega-3 fatty acid supplementation compared with olive oil control for the management of dry eyes, although this larger study was not specific for MGD and posterior blepharitis.[51]

Over recent years, thermal pulsation, IPL, and intraductal meibomian gland probing have gained popularity in the management of MGD.

Although the use of thermal pulsation has not been directly studied in ocular rosacea, the MGD associated with rosacea may be responsive to this treatment. In a prospective, randomized, cross-over, observer-masked trial, a single treatment with thermal pulsation was at least as effective as a 3-month, twice daily, eyelid hygiene regimen in improving OSDI, but not in tear break-up time, tear osmolarity, corneal and conjunctival staining, Schirmer test values, and tear meniscus height.[52] In other prospective studies, a single treatment of thermal pulsation led to a sustained improvement in OSDI and meibomian gland secretion scores after 1 year.[53]

IPL treatment consists of the use of polychromatic light with a wavelength spectrum of 500 to 1200 nm leading to selective photothermolysis. Its potential mechanisms of action may be in coagulation of telangiectatic vessels, reducing inflammation, causing liquefaction of meibum and reopening of meibomian gland ducts, and stabilizing the tear film. An American Academy of Ophthalmology Ophthalmic Technology Assessment concluded that IPL improves symptoms and signs of MGD despite methodological flaws in the studies examined. However, repeated treatments may be required.[54] For optimal results, IPL treatment should be combined with eyelid hygiene and warm compresses. While IPL may be an alternate option for ocular rosacea patients with MGD, its use is limited by its availability and cost. Further studies are required to directly compare its use to the more standard topical and oral treatments in ocular rosacea.

Intraductal meibomian gland probing is a simple, office-based procedure that can be performed at the slit lamp. Probes ranging from 1 to 4 mm in length can be used to relieve obstructed Meibomian gland orifices. In one case series, all 25 patients who were treated experienced symptomatic relief after 4 weeks, and 80% had continued improvement at 11.5 months after a single treatment.[55]

Corneal involvement such as persistent epithelial defects may benefit from additional treatments including amniotic membrane grafts and corneal perforations that may necessitate cyanoacrylate glue application and/or corneal transplantation.

Cutaneous rosacea should be co-managed with a dermatologist and a general practitioner or physician [Fig. 2]. Like the management of ocular rosacea, patients with skin disease should be encouraged to avoid any environmental triggers in addition to skincare. Topical treatments,

including topical sulfacetamide, metronidazole (0.75% and 1% formulations), and azelaic acid (15% gel or 20% cream), are used in the treatment of mild to moderate papulopustular rosacea, topical alpha-adrenergic receptor agonist, brimonidine (3.3 mg/g), can be used to treat facial erythema and topical ivermectin can be used to treat both papulopustular rosacea and demodicosis.[41] However, topical steroid treatment should be avoided as it can trigger steroid-induced rosacea.[56] If topical treatments are not sufficient in controlling the disease, systemic treatment with oral tetracyclines should be initiated. Tetracyclines minocycline and doxycycline are commonly used; oral isotretinoin (0.3–1.0 mg/kg/day) can be used in recalcitrant papulopustular rosacea, working via downgrading TLR2 expression, although the treatment is also associated with ocular side effects, most notably conjunctivitis.[57] The use of laser (e.g. pulsed dye laser and 532 nm potassium titanyl phosphate) and IPL treatments are reported in cases of persistent erythema or cutaneous telangiectasias.[9]

Rosacea is an underdiagnosed and underestimated condition, especially in populations of the skin of color. It should be considered as a diagnosis in all age groups with chronic eyelid inflammation associated with conjunctival and corneal changes. It can be a diagnostic challenge, particularly in pediatric cases where there may be minimal, or no, associated skin changes. Early treatment will provide symptomatic relief and reduce the risk of corneal complications. Treatment should involve minimizing environmental triggers, as well as a combination of conservative, topical, systemic, and potentially, interventional therapies.

New guidelines and consensus should be developed with multiple allied specialties for developing better management plans, especially for the dark skin tone population.