

Rosacea and its management: an overview

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ABSTRACT

Background Rosacea is a chronic inflammatory disorder that affects 10% of the population. The prevalence of rosacea is highest among fair-skinned individuals, particularly those of Celtic and northern European descent. Since a cure for rosacea does not yet exist, management and treatment regimens are designed to suppress the inflammatory lesions, erythema, and to a lesser extent, the telangiectasia involved with rosacea.

Objectives This review outlines the treatment options that are available to patients with rosacea.

Methods Published literature involving the treatment or management of rosacea was examined and summarized.

Results Patients who find that they blush and flush frequently, or have a family history of rosacea are advised to avoid the physiological and environmental stimuli that can cause increased facial redness. Topical agents such as metronidazole, azelaic acid cream or sulfur preparations are effective in managing rosacea. Patients who have progressed to erythematotelangiectatic and papulopustular rosacea may benefit from the use of an oral antibiotic, such as tetracycline, and in severe or recalcitrant cases, isotretinoin to bring the rosacea flare-up under control. Treatment with a topical agent, such as metronidazole, may help maintain remission. Patients with ocular involvement may benefit from a long-term course of an antibiotic and the use of metronidazole gel. A surgical alternative, laser therapy, is recommended for the treatment of telangiectasias and rhinophyma. Patients with distraught feelings due to their rosacea may consider cosmetic camouflage to cover the signs of rosacea.

Conclusions With the wide variety of oral and topical agents available for the effective management of rosacea, patients no longer need to feel self-conscious because of their disorder.

Key words: azelaic acid, isotretinoin, management, metronidazole, rosacea, tetracycline

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Rosacea is a chronic disorder, involving the mid facial region, and occasionally the neck and scalp and eyes.¹ It may progress from inflammatory lesions and/or erythema, to telangiectasia and rhinophyma, and sometimes also cause ocular involvement. The prevalence of rosacea is highest among fair-skinned individuals, especially those of Celtic and northern and eastern European heritage.² The onset of rosacea is usually between the ages of 20 and 50 years, with females more often affected than males; however, males more frequently progress to the end-stages of severe rosacea. Rosacea has been described as having four subtypes, erythematotelangiectatic rosacea, papulopustular rosacea, phymatous rosacea, and ocular rosacea, with one variant, granulomatous rosacea.³

Presently there is no cure for rosacea; management and treatment may provide only a method of suppressing its signs and symptoms. The choice of treatment is dependent primarily on the severity of the disorder and ranges from avoiding the factors that can trigger a flare-up, to the use of surgery for correcting the hypertrophied soft tissue of the nose (rhinophyma). This paper will discuss the treatment options rosacea patients have for managing their disorder.

Pre-rosacea (episodic erythema)

Avoidance policy

The earliest manifestation of rosacea includes frequent flushing and blushing, or episodic erythema. Patients, who experience

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Table 1 Rosacea trigger factors and management techniques

Rosacea triggering factors	Management factors
Foods: Meat: liver Dairy products: yogurt, sour cream, cheeses (not including cottage cheese) Vegetables: eggplant, tomatoes, spinach, lima and navy beans, peas Fruits: avocados, bananas, red plums, raisins, figs, and citrus fruits Condiments/flavoring: chocolate and vanilla, soy sauce and vinegars Other: hot and spicy foods, yeast extraction	Identify and avoid any foods that aggravate the condition
Beverages: Alcohol and hot beverages	Avoid alcoholic beverages, especially red wine, beer, bourbon, gin, vodka or champagne Avoid hot drinks, e.g. Tea, coffee, hot cider or hot chocolate
Emotional: Stress and anxiety	Practice stress management techniques, e.g. Yoga or breathing exercises
Weather: Sun, strong winds, cold, humidity	Use ski masks, scarves to protect from cold and windy conditions Use sunscreens (min. SPF 15)
Temperature: Any hot environment: saunas, hot baths, simple overheating	Avoid any hot or humid environment
Skin Care Products: Cosmetics and hairsprays especially those containing alcohol, witch hazel or fragrances Hydro-alcoholic or acetone substances Any substance that causes redness or stinging	Resist using skin products that are listed as irritating
Medications: Vasodilators, and topical steroids	If avoidance is not possible, they should not be taken for long periods of time
Medical Conditions: Menopause, caffeine withdrawal syndrome, chronic cough, frequent flushing	Not avoidable; however, avoiding other factors minimizes these conditions
Physical Exertion: Exercise, heavy lifting	Avoid long strenuous exercising and heavy lifting Use cool-down techniques: chewing on ice, or covering face with cool cloth after the workout

frequent blushing, have a family history of rosacea, or both may be entering prerosacea; these patients are advised to consider changing their lifestyle to control their blushing. The best approach to preventing the blushing and flushing associated with the stages of rosacea is the avoidance policy,⁴ where nonspecific physiological and environmental stimuli are avoided, and thus increased facial redness is lessened. One study reported 78% of rosacea patients felt that avoiding the factors that aggravate their rosacea was effective or at least somewhat effective in controlling their condition.⁵ The most common triggers of blushing include alcohol ingestion, spicy food, sun exposure, or stress. However, the causes may vary from patient to patient, and therefore it is important for a patient to avoid these causative agents as much as possible during their daily routine. Physicians of rosacea patients must be aware that rosacea is a recognized and controllable disorder; they should educate and monitor their patients for possible triggers and try to establish an individual risk factor profile.⁶ Table 1 outlines

some common factors that may trigger and aggravate rosacea flare-ups.

Drug therapy

Drug treatment trials for decreasing the flushing associated with rosacea have primarily been unsuccessful. Two drugs, clonidine and nadolol have been tried against rosacea flushing; neither was effective. One study demonstrated that twice-daily treatment with clonidine hydrochloride, 0.05 mg, taken for 2 weeks was unable to suppress the flushing reactions provoked with hot water (60 °C), red wine and chocolate in 23 of 24 patients with erythematotelangiectatic rosacea.⁷ Similarly, treatment with 40 mg of nadolol once or twice daily had no apparent effect on flushing induced by hot water (60 °C), ethanol, and niacin in 15 patients with erythematous telangiectatic rosacea.⁸ However, one double-blind study showed that 10-minute pretreatment with naloxone 0.8 mg in 2 mL saline

injected subcutaneously completely inhibited alcohol induced facial flushing in all five subjects.⁹ The mean forehead skin temperature increased by 1.1 ± 0.6 °C during flushing after saline administration, but by only 0.4 ± 0.2 °C after naloxone administration. Currently, there are no effective long-term drug therapies to control the flushing associated with rosacea.

Erythematotelangiectatic and papulopustular rosacea

Rosacea is a progressive disorder, and although not all patients necessarily pass through all stages, early diagnosis and management will prevent or lessen the chances that the rosacea will worsen. A variety of oral and topical treatments, with the ability of suppressing the disorder, are available for patients suffering with rosacea.

Systemic therapy

Several oral agents have been used in the treatment of rosacea. Table 2 summarizes the clinical trials evaluating the efficacy of these systemic drugs.

Oral antibiotics

Oral antibiotics have long been accepted as safe and effective treatments for rosacea, and are thought to exert their therapeutic effects primarily via anti-inflammatory rather than antibacterial methods. Antibiotic therapy is most effective against inflammatory papules and pustules, with minimal effects on erythema and telangiectasia.²⁶

Tetracycline has historically been the antibiotic of choice for treating rosacea, as it has been shown to be successful in reducing the number of papules and pustules. High doses are initially recommended until the disorder is brought under control, and then lower doses are used to maintain control. Total daily doses of up to 1000 mg, taken two to four times a day are recommended for up to 4 weeks, and then reduced by half for an additional 5 months.

Tetracycline has proven to be successful in treating patients diagnosed with rosacea. In one randomized, double-blind study, 78% of patients treated with tetracycline 250 mg twice daily for 1 month experienced the disappearance of pustules, the flattening of papules and the diminution of erythema.¹¹ In another randomized, double-blind clinical trial, compared with ampicillin, tetracycline 250 mg taken three times daily for the first week and then twice daily for the subsequent 5 weeks, did not significantly differ in the reduction of papules and pustules; however, post-treatment evaluation revealed that both treatments were effective in decreasing the mean number of papules and pustules in comparison with the pretreatment means ($P < 0.05$).¹²

The effects of doxycycline, 100 mg twice daily for 4 weeks, then once daily for another 4 weeks were compared with clarithromycin, 250 mg twice daily for 4 weeks, then once daily for another 4 weeks in patients with mild and moderate rosacea.¹³ The overall results of the treatment provide evidence of a higher clarithromycin efficacy profile in comparison with doxycycline. Significant differences were seen in erythema in favour of the clarithromycin group at weeks 4 and 6 ($P < 0.05$); however, after 8 weeks of treatment, no significant differences were seen in erythema. A significant difference between the mean values of the numbers and dimensions of telangiectasia in the two groups of patients was observed after 4 weeks of treatment. After 6 and 8 weeks of treatment, there were no significant differences between the two groups. A significantly faster decrease ($P < 0.0005$) of the mean number of papules and pustules was observed in the clarithromycin-treated patients, when compared with the doxycycline-treated patients after 4 and 6 weeks of therapy; however, after 8 weeks there was no significant difference in these two parameters between the two groups.

Treatment with antibiotics must be long-term, lasting a minimum of 6 months. Treatment failure with antibiotics is most commonly the result of patient noncompliance, particularly resulting from side-effects including nausea, and also because some antibiotics, such as tetracycline must be taken on an empty stomach; food and milk restrict its absorption.

Oral metronidazole

Oral metronidazole is a treatment alternative for rosacea patients who do not respond well to tetracycline. Two double-blind, randomized controlled trials assessed the efficacy of oral metronidazole.^{14,15} Metronidazole 200 mg, taken twice daily for 12 weeks proved to be as effective as oxytetracycline 250 mg taken twice daily in improving the papulo-pustules related to rosacea.¹⁴ In addition, 6 weeks of therapy with metronidazole 200 mg taken twice daily in combination with 1% hydrocortisone, applied twice daily produced 'definite improvement' in the overall clinical severity of the rosacea condition in 10 of 14 patients.¹⁵

Isotretinoin

Another effective therapy in the treatment of rosacea is isotretinoin. However, this treatment is suggested for patients with severe or recalcitrant rosacea. Patients may benefit from a trial with systemic tetracycline, metronidazole or topical metronidazole before the use of isotretinoin. Daily doses of isotretinoin usually range from 0.5 mg/kg to 1.0 mg/kg. The advantage of isotretinoin is that it has an immediate effect on papules and pustules. Four studies have shown isotretinoin to significantly decrease the mean number of papules and pustules compared to baseline^{17–20} within as little as 1 month of therapy.¹⁸ Isotretinoin also produces considerable improvement in erythema,^{17,20} however, the effects may be slow and

Table 2 Systemic therapies used in the treatment of rosacea

Study design	Regimen	Efficacy parameters			Physician assessment	Patient assessment	Other	Reference
		Inflammatory lesions	Erythema	Telangiectasia				
DB, R 1% clindamycin phosphate lotion vs. oral tetracycline <i>N</i> = 43; 12 weeks	1% clindamycin lotion b.i.d. + placebo or 250 mg tetracycline q.i.d. + placebo lotion for 9 weeks	Clindamycin: facial lesions decreased from baseline ($P < 0.05$) tetracycline: facial lesions decreased from baseline ($P < 0.05$)	No significant difference	No significant difference	Improvement in clindamycin: 94.7% of patients tetracycline: 94.4% of patients	Improvement seen in 81.8% of patients treated with clindamycin and 90.5% of tetracycline	N/A	Wilkin 1993 ¹⁰
DB, R Tetracycline vs. placebo <i>N</i> = 78; 4 weeks	Tetracycline 250 mg b.i.d. or placebo tablets b.i.d. for 4 weeks	N/A	N/A	N/A	N/A	N/A	Improvement in disappearance of pustules, flattening of papules, and diminution of erythema: Tetracycline: 78% Placebo: 45%	Sneddon 1966 ¹¹
DB, R Tetracycline vs. ampicillin <i>N</i> = 56; 6 weeks	t.i.d. for the first week then b.i.d. for 5 weeks	Tetracycline: decreased from 21.05 to 4.6 ampicillin: decreased from 21.06 to 9.53	No significant difference	N/A	N/A	Ampicillin marginally better than tetracycline	N/A	Marks 1971 ¹²
Clarithromycin vs. doxycycline <i>N</i> = 40; 8 weeks	Clarithromycin 250 mg b.i.d. for 4 weeks then q.i.d. for 4 weeks or doxycycline 100 mg b.i.d. for 4 weeks then q.i.d. for 4 weeks	No significant difference between treatments after 8 weeks	No significant difference between treatments after 8 weeks	No significant difference between treatments after 8 weeks		No significant difference between treatments after 8 weeks	N/A	Torresani 1997 ¹³
DB, R Metronidazole vs. oxytetracycline <i>N</i> = 38; 12 weeks	Metronidazole 200 mg b.i.d. or oxytetracycline 250 mg b.i.d. 12 weeks	N/A	N/A	N/A	Mean independent opinion of patient and 2 doctors No significant difference between groups; both improved from baseline ($P < 0.05$)		N/A	Saihan 1980 ¹⁴
DB, R Metronidazole vs. placebo <i>N</i> = 27; 6 weeks	Metronidazole 200 mg b.i.d. + 1% hydrocortisone cream daily or placebo + 1% hydrocortisone for 6 weeks	N/A	N/A	N/A	10 patients in metronidazole and 2 patients in placebo group showed good results ($P < 0.02$)	N/A	N/A	Pye 1976 ¹⁵

Table 2 Continued

Study design	Regimen	Efficacy parameters			Physician assessment	Patient assessment	Other	Reference
		Inflammatory lesions	Erythema	Telangiectasia				
DB, R Isotretinoin vs. tretinoin cream vs. combo $N = 20$; 32 weeks	Group 1: isotretinoin 10 mg/d + placebo cream for 16 weeks then placebo cream for 16 weeks or Group 2: 0.025% tretinoin cream + placebo tablets for 16 weeks then tretinoin cream for 16 weeks or Group 3: combo (isotretinoin and tretinoin) + placebo tablets for 16 weeks then tretinoin cream for 16 weeks	All groups showed significant difference from baseline ($P < 0.01$)	Group 1: 41% reduction Group 2: 27% reduction Group 3: 40% reduction	N/A	N/A	N/A	N/A	Ertle 1994 ¹⁶
Open label isotretinoin $N = 92$; 20 weeks	Isotretinoin 0.5 mg/kg/bw	Mean papules decreased from 42 to 5 mean pustules decreased from 11 to 0.6	Improved considerably	Improved considerably	Number of patients with good or very good response: 64	Number of patients fully or partially satisfied: 64	Edema improved considerably	Hoting 1986 ¹⁷
Open label isotretinoin $N = 20$; 6 months	Isotretinoin 0.5 mg/kg or 1.0 mg/kg for 3 months	N/A	N/A	N/A	N/A	N/A	Total clinical score (includes papules, pustules, erythema and oiliness): decreased from 7.5 to 1.25 ($P < 0.001$)	Turjanmaa 1987 ¹⁸
Open label isotretinoin $N = 7$; 20 weeks	Isotretinoin 1.0 mg/kg/bw for 12 weeks	Facial lesions decreased from 39.7 to 4 at 6 weeks ($P < 0.001$) and rose to 10.6 at week 20	Measured by reflectometer. Decreased from 10.8 units to 10.1 units at 12 weeks then to 9.1 at week 20	N/A	N/A	N/A	N/A	Marsden 1984 ¹⁹
Open label isotretinoin $N = 18$; 16 weeks	Isotretinoin 1.0 mg/kg/bw for 16 weeks	Significantly decreased from 8.86 to 2.55 ($P < 0.001$)	Significantly decreased ($P < 0.001$)	Significantly decreased ($P < 0.001$)				Erdogan 1998 ²⁰
DB, R Lemecycline vs. sulphur $N = 37$; 4 weeks	Lymecycline 150 mg 2 capsules b.i.d. for 1 week then 1 capsule b.i.d. for 3 weeks + placebo cream or 10% sulphur cream q.i.d. + placebo capsules for 4 weeks	Sulphur: number decreased from 213 to 17; Lymecycline: number decreased from 143 to 131	No significant difference	No significant difference	No significant difference	No significant difference	N/A	Blom 1984 ²¹

Table 2 Continued

Study design	Regimen	Efficacy parameters			Physician assessment	Patient assessment	Other	Reference
		Inflammatory lesions	Erythema	Telangiectasia				
DB, R Oxytetracycline vs. metronidazole <i>N</i> = 27; 9 weeks	Oxytetracycline 250 mg bid + placebo cream vs. Metronidazole 0.75% gel b.i.d. + placebo tablets for 9 weeks	Facial lesions decreased 100% in 75% of the Metronidazole-treated patients and in 66% of oxytetracycline-treated patients; No significant difference	Metronidazole: decreased from 2.5 to 1.1 Oxytetracycline: decreased from 2.4 to 1.1; No significant difference	N/A	Definite improvement in 75% of metronidazole treated patients and 80% of oxytetracycline treated patients	Definite improvement in 67% of metronidazole treated patients and 80% of oxytetracycline treated patients	N/A	Monk 1991 ²²
DB, R Tetracycline vs. metronidazole <i>N</i> = 75; 8 weeks	Tetracycline 250 mg b.i.d. + placebo cream or Metronidazole 1% cream q.i.d. for 8 weeks	Significantly more patients treated with tetracycline obtained 100% reduction of papules and pustules; No significant difference between treatments	Significant reduction from baseline. No significant difference between treatments	N/A	N/A	N/A	N/A	Weien 1986 ²³
DB, R Oxytetracycline vs. metronidazole <i>N</i> = 48; 2 months	Oxytetracycline 250 mg b.i.d. + placebo cream or metronidazole 1% cream q.i.d. + placebo tablets for 2 months	Reduction from baseline; No significant difference between groups	Reduction from baseline; No significant difference between groups	Number and extent of telangiectasia remained unchanged; No significant difference	Improved patients: metronidazole: 96% oxytetracycline: 96%; No significant difference	Improved patients: metronidazole: 88% oxytetracycline: 91%; No significant difference	Photographic evaluation Improved patients: metronidazole: 84% oxytetracycline: 91%; No significant difference	Nielson 1983 ²⁴
DB, R Tetracycline vs. metronidazole <i>N</i> = 101; 2 months	Tetracycline 250 mg t.i.d. + placebo cream or Metronidazole 1% cream q.i.d. for 2 months	Significantly fewer number of papules and pustules from baseline ($P < 0.05$) papule decrease: metronidazole: 68% tetracycline: 77% pustule decrease: metronidazole: 68% tetracycline: 77%	No differences in degree of erythema compared to baseline	No differences noted in degree of telangiectasia compared to baseline	N/A	Both groups showed much improvement	N/A	Schachter 1991 ²⁵

q.i.d., once daily; b.i.d., twice daily; t.i.d., thrice daily; DB, double-blind; R, random; N, number of patient.

incomplete.¹⁸ In addition, patients may remain in remission for at least 1 year after discontinuing treatment.¹⁸

One study performed ophthalmologic examinations in patients taking isotretinoin.¹⁷ Blepharitis and conjunctivitis, which are quite common symptoms in patients with rosacea, were present in 23 of 88 and 33 of 88 subjects, respectively, which decreased, respectively, to 17 of 54 and 25 of 54 subjects at week 20.

Although isotretinoin has been demonstrated to be effective in treating the papules and pustules associated with rosacea, considerable drug intolerance is seen. The most common side-effects that occur with isotretinoin are mucosal, such as dryness of the lips and nose. Other side-effects that may be seen are cheilitis, dermatitis, musculoskeletal pain, tinnitus, headache, and an increase in triglyceride levels. The number and extent of these side-effects may be the limiting factors to this form of therapy for rosacea treatment.

Topical treatments

Metronidazole 1% cream, Metronidazole 0.75% gel, lotion and cream

Topical metronidazole, available either as a gel or a cream, is the most popular topical agent for treating rosacea. Metronidazole 0.75% gel^{22,27–29} and metronidazole 1% cream,^{14,23,25,30–37} metronidazole 0.75% cream^{35,38} and metronidazole lotion³⁹ have been shown to be effective in treating rosacea when applied once or twice daily for 8–12 weeks. The results of these studies have demonstrated that both preparations significantly decrease the number of inflammatory lesions and reduce the erythema associated with rosacea. In addition, neither the cream nor the gel seemed to have an effect on the telangiectasia. However, Tan 2001,³⁶ reported that metronidazole 1% cream with sunscreen SPF 15 significantly decreased facial telangiectasia ($P = 0.043$).

Studies that have compared 1% metronidazole cream with tetracycline have found that although the end result shows no significant difference between topical metronidazole and tetracycline, tetracycline does have a faster onset than metronidazole.^{23–25} In addition, other studies have shown that following tetracycline withdrawal, the relapse rate is high. These findings suggest that the use of a topical agent following systemic therapy might be beneficial in preventing relapse after the oral agent is discontinued.

Other topical therapies

As a result of the positive effects of topical metronidazole, several other studies have evaluated the outcome of other topical agents in treating rosacea. Topical alternatives to metronidazole include: 1% clindamycin phosphate lotion,¹⁰ topical tretinoin,¹⁶ and 5% permethrin cream.^{40,41} The effectiveness of these topical agents has been compared to proven,

successful systemic and topical therapies. When 1% topical clindamycin phosphate lotion was compared with tetracycline,¹⁰ clindamycin phosphate reduced the mean number of pustules, papules, and nodules while tetracycline significantly reduced only papule and nodule counts from baseline. Comparison of topical tretinoin with isotretinoin¹⁶ revealed that both treatments were effective in decreasing the number of papules, pustules and erythema after 16 weeks of treatment, with no significant difference between the two treatment groups in papules and pustules. The results of 5% permethrin cream compared to 0.75% metronidazole gel showed that both treatments produced gradual improvement in erythema and papules.^{40,41}

The efficacy of two other topical preparations, sodium sulfacetamide 10%/sulphur 5% lotion^{42,43} and 10% sulphur cream²¹ were also evaluated in the treatment of rosacea. Both preparations proved to be effective in decreasing the number of papules and pustules in patients. The sodium sulfacetamide 10%/sulphur 5% lotion demonstrated significant reduction in erythema.^{42,43}

Another topical agent, 0.05% retinaldehyde cream was found to have beneficial effects on the vascular component of rosacea.⁴⁴ In an open-labelled study, 23 females with rosacea applied retinaldehyde 0.05% once daily for 6 months. Clinical response was obtained in approximately 75% of patients with erythema after 5 months of treatment ($P < 0.05$).

The antimicrobial, comedolytic and anti-inflammatory activity of azelaic acid 20% cream has been shown to be beneficial in the treatment of rosacea. Two studies that evaluated the efficacy and safety of azelaic acid 20% cream recorded that this agent produced significantly greater mean reductions in the number of papules, pustules and erythema than vehicle.^{45,46} Following twice-daily application of azelaic acid 20% cream, the mean number of papules and pustules decreased from 14.2 to 2.5 after 9 weeks of treatment,⁴⁵ and from 30.8 to 8.3 after 3 months of treatment.⁴⁶ Furthermore, Carmichael⁴⁵ found the erythema index decreased from 539.6 ± 13.4 to 500.6 ± 14.7 after 9 weeks of treatment. Bjerke⁴⁶ found the erythema severity score reduced by 47.9%. In addition, another study found twice-daily applications of azelaic acid 20% cream to be equivalent to twice-daily applications of metronidazole 0.75% cream in the treatment of inflammatory lesions, with no significant difference in efficacy between the two groups.³⁸

In addition to the azelaic acid cream treatments, recently, there has been investigation into a lower concentration (15%) azelaic acid gel (AzA gel) as a new treatment for papulopustular rosacea through two vehicle-controlled, randomized studies.⁴⁷ The study found that the AzA gel group yielded a statistically significantly higher reduction in mean inflammatory lesion count than its vehicle in both study 1 ($P = 0.0001$) and study 2 ($P = 0.0208$), with a reduction in 58% and 51%, respectively. This study also found that a significantly higher proportion of patients treated with AzA gel experienced improvement in

erythema when compared with the vehicle. In study 1, improvement of erythema severity was seen in 44% of patients in the AzA group, compared to only 29% of the vehicle group ($P = 0.0017$). Study 2, showed improvement in 46% of patients, while only 28% of the vehicle group improved ($P = 0.0005$). Furthermore, the study found that there were no serious treatment-related adverse events, and the final conclusion of the investigators was that AzA gel, used twice daily, is an efficacious, safe, and well-tolerated topical treatment for moderate, papulopustular rosacea.⁴⁷

All these topical preparations have demonstrated efficacy in the treatment of papules, pustules and to a certain extent the erythema associated with rosacea.

Demodex folliculorum

Demodex folliculorum mites, frequently found in facial follicles, were previously thought to be the cause of rosacea.⁴⁸ These mites may not play a significant role in the aetiology of rosacea. However, a high density of the *D. folliculorum* mites may aggravate the flare-up of rosacea. Patients with an increased colonization of mites may benefit from the use of antiparasite drugs like lindane, crotamiton, permethrin or benzoyl benzoate, as elimination of these mites may lead to improvement.⁴⁹ There are reports of patients diagnosed with rosacea, resistant to conventional rosacea therapies, who demonstrated success when treated with an antiparasitic drug.

Maintaining remission

It has been proposed that topical metronidazole be concurrently used with an oral agent, such as tetracycline, with continued use of the topical agent after cessation of tetracycline.⁴⁹ This combined method of treatment has shown to maintain remission of rosacea for longer periods of time.⁵⁰ In one study, oral tetracycline and topical metronidazole gel 0.75% were used in combination for up to 12 weeks.⁴⁹ At that time, those patients with significant clinical improvement (> 70% reduction in lesions) were randomized to apply either topical metronidazole 0.75% gel or placebo gel twice daily for an additional 6 months to determine relapse rates. The authors found that the continued use of topical metronidazole after discontinuation of tetracycline significantly prolonged the disease-free interval and minimized recurrence compared with subjects treated with the vehicle ($P < 0.05$). Forty-two percent (18/43) of the patients applying vehicle experienced relapse, compared to 23% (9/39) subjects applying metronidazole gel ($P < 0.05$).

Telangiectasia

By the time a patient starts showing telangiectasia on their face, it has progressed to the vascular stage in rosacea. The avoidance

policy and drug treatments are often ineffective in treating telangiectasia and a surgical alternative should be considered. Furthermore, drug therapy may actually lessen the redness of erythema and emphasize the existing telangiectasia on the face. When the ectatic vessels are slender and few in number, removal may be achieved by electrocautery. The availability of lasers has had a significant effect on the management of telangiectasias. Several laser therapies such as argon laser surgery,^{51–53} pulse dye laser (590–595 nm),⁵⁴ potassium-titanyl phosphate (KTP) laser surgery (532 nm),⁵⁴ flash lamp pumped dye (FLPD) laser surgery (585 nm), and intense pulsed light treatments⁵⁵ have been successful in treating telangiectasias. However, intense pulsed light treatments have very little study performed on them with respect to rosacea-associated erythema and telangiectasia. In fact the pilot study by Mark *et al.*⁵⁵ which found a 30% decrease in blood flow ($P < 0.05\%$), a 29% decrease in area of telangiectasia ($P < 0.05$), and a 21% decrease in erythema intensity ($P < 0.05$), is one of only two studies documenting the use of intense pulsed light treatment for rosacea.⁵⁵ When comparing the efficacy of long-pulse (590–595 nm) with that of KTP (532 nm) in the treatment of telangiectasia, one study found both to be effective treatments, with long-pulse dye demonstrating a slightly better outcome.⁵⁴ A complication seen after treatment with pulsed-dye laser was hyperpigmentation.⁵⁴ This iatrogenic condition is usually treatable with hydroquinone, glycolic acid, or retinoic acid, in combination or alone, for a duration of 6–12 weeks.⁵⁶

It is important to counsel patients about the effects of laser treatment, as ablation of telangiectasia will only ameliorate the flushing response for a variable period of time, and further treatments may be required.⁵⁶ Patients deciding between laser treatments should be aware of the course, outcome, healing process and possible complications of each treatment.

Rhinophyma

Occurring more frequently in males than in females, rhinophyma is the hyperplasia of sebaceous glands, connective tissue and blood vessels of the nose. Flushing and increased blood flow in the superficial dermis leads to an increase in the extracellular fluid that may be involved in rhinophyma.⁵⁶ The presence of rhinophyma represents the final stage of rosacea, and may be treated with both medical and surgical treatment modalities.⁵⁷ A suitable treatment is dependent on an appreciation of the progression of the disease from a minimal thickening of advanced rosacea to a massive tumorous condition.⁵⁸

Medical treatment

Patients with early rhinophyma consisting of minimal skin thickening without nasal deformity are not treated surgically and may benefit from medical therapy.⁵⁹ The patient should be instructed to practice good hygiene, including keeping the

nose clean, avoiding stress, and preventing infection. Steroids may prevent the complication of scar formation and antibiotics may prevent secondary infections;⁵⁷ however, the prolonged and indiscriminate use of topical corticosteroids may be associated with other adverse effects. In addition, treatment with isotretinoin may suppress the activity of sebaceous glands and substantially reduce sebum production.⁶⁰ Substantial regression of established disease, with or without medical treatment does not occur, and as a result of the limited success of medical therapy, surgery has become the accepted treatment for this stage.

Surgical treatment

Surgical treatment of rhinophyma is aimed at the restoration of a more normal contour of the nose while minimizing scar formation. Surgical methods are divided into two main groups.⁶¹ The first is complete excision, with primary closure for small lesions, or skin grafting for large lesions. The second group includes incomplete excision followed by re-epithelialization from the remaining glandular epithelium. Better cosmetic results have been consistently reported with incomplete excision, and this is now considered the treatment of choice. Methods of incomplete excision include cryosurgery, dermabrasion, electrosurgery, sharp blade excision, shaving with a razor, and laser surgery.

Cryosurgery involves destroying the sebaceous glands with low temperatures. A liquid nitrogen spray treats the rhinophyma with two freeze-thaw cycles, where each freeze time is 30 s and thaw time is 4 minutes.⁶² The main function of dermabrasion is contouring of the nasal profile, and is primarily utilized as an adjuvant to other methods of rhinophyma surgical procedures.⁶² Electrocautery is a procedure that utilizes a bipolar electrosurgical unit with a loop attachment that removes tissue in thin layers.⁶³ Tissue is destroyed with the heat produced when current passing through the tissue encounters electrical resistance. With this method, intraoperative crusting, exudation, and heat damage to the underlying cartilage frequently occurs. Scalpel excision involves the use of either a surgical scalpel or a razor blade. Although these are both excellent instruments to use in treating rhinophyma, the main problem encountered is haemostasis. This issue is addressed by the Shaw scalpel, which is heated to a temperature of 130–180 °C to coagulate most small and medium-sized vessels during the procedure.^{64,65} Although this method seems to be the ideal technique, the Shaw scalpel is not widely accepted because of the potential full-thickness tissue destruction.⁵⁷

Laser therapy is used as a method of vaporizing the excessive tissues present in rhinophyma, while maintaining minimal blood loss and good visualization. Two types of laser, carbon dioxide^{66–74} and argon^{75,76} have shown success in treating rhinophyma. The carbon dioxide laser vaporizes skin in several layers using a continuous beam with a spot size of 0.2–0.5 mm.⁶⁸

The laser beam is then defocused to vaporize the remaining excess tissue, and by securing haemostasis, sculpting is complete. Although the carbon dioxide laser gives good cosmetic results, provides a bloodless operating field, allows re-epithelialization from sebaceous pores, and maintains the normal porous architecture of the nose, the major disadvantage with this technique has been the extensive operating time required to laser resect the excessive tissue, obtain haemostasis, and then sculpt.

The argon laser has also been found to be effective in treating vascular disorders, such as telangiectasia and rhinophyma. The argon laser selectively coagulates small blood vessels, which leads to an effective treatment of telangiectasia. It also coagulates dermal connective tissue up to a depth of about 0.5 mm. This subsequently yields additional direct shrinkage of connective tissue.⁷⁵ However, the use of the argon laser is limited to reducing the generalized redness of the nose and improving the clinical appearance of the patients.⁷⁶ Potential adverse events of argon laser therapy include: atrophy, scarring, hyperpigmentation, and the possibility of no change or insufficient lightening to improve the clinical appearance.

Another type of laser, the long-pulsed dye laser, for example the Nd:YAG and Er:YAG, is a laser procedure that offers accuracy of tissue excision by reducing the depth of tissue vaporization and subsequent cell injury.^{77,78} Although Nd:YAG requires two visits to the operating room, first to sculpt the rhinophyma, and then 3 months later for a finer excision of the rhinophyma along the ala and the junction of rhinophyma and the normal skin, cosmetic results are excellent and tissue healing is comparable to that seen with the carbon dioxide laser.⁷⁹ Temporary postoperative oedema and proteinaceous exudates may, however, develop with the Nd:YAG laser treatment. The Er:YAG laser emits a wavelength that is the peak of light absorption in water, resulting in more efficient evaporation and minimal thermal injury to adjacent tissue. Surgical results with Er:YAG laser have been found to be good to excellent, with no postoperative complications.⁷⁸

Ocular rosacea

Ocular rosacea is a common associate of rosacea, however, is frequently misdiagnosed because ophthalmologists do not carefully examine the face of the patient and dermatologists do not routinely enquire for ocular symptoms. The most common symptoms of ocular rosacea are nonspecific and include a foreign body, gritty, or dry sensation, burning, tearing, or redness.⁷⁹ One study found the most common cutaneous signs were telangiectasia, irregularity of lid margins, and meibomian gland dysfunction.⁷⁹ Traditional therapy of ocular rosacea consists of lid hygiene and warm compresses combined with oral tetracycline or doxycycline.⁸⁰ Treatments for ocular rosacea have varied widely and have been generally unsuccessful.

Antibiotics

Tetracycline remains the treatment of choice for managing ocular rosacea. One study showed that 36 of 37 patients with ocular rosacea treated with cycles of tetracycline 250 mg four times a day for 3 weeks, followed by 1 week of no therapy improved markedly beginning 4 days to 3 weeks after initiation of therapy.⁸¹ Fifteen of these patients remained asymptomatic at the follow-up period, 5–28 months after discontinuing treatment.

In a double-blind, randomized study, 35 patients with ocular rosacea were treated for 6 weeks with 250 mg oxytetracycline twice daily, or placebo.⁸² Eleven of 17 patients receiving oxytetracycline therapy showed remissions in their signs and symptoms compared to five of 18 taking placebo. The authors concluded that the nonspecific signs of ocular rosacea (lid swelling, redness, blepharitis, chalazia and conjunctival hyperemia) respond well to treatment with oxytetracycline.

Two open-labelled studies demonstrated that doxycycline might be effective in treating ocular rosacea.^{83,84} In both studies, patients with ocular rosacea were treated with doxycycline 100 mg once daily. In the first study, 14 of 16 patients showed symptomatic improvement during the first 3 weeks of treatment. Eight of these patients remained on various doses of doxycycline throughout the study period of 3 months. In four of the patients, the dose was tapered and three of them discontinued treatment without the recurrence of symptoms. However, in two of the 14 patients that showed improvement, one developed a peripheral corneal infiltrate and the other had a phototoxic skin reaction. This study demonstrated similar results to those experienced by Jenkins *et al.*⁸¹ utilizing tetracycline 250 mg four times a day in the treatment of ocular rosacea.

In the second study, doxycycline 100 mg per day was prescribed for 12 weeks. The most frequent ocular symptoms were dryness, itching, blurred vision, and photosensitivity, all of which improved significantly by the end of the treatment period ($P < 0.05$).⁸⁴ Significant improvements were seen for scale, erythema and telangiectasia, ciliary base injection, bulbar injection, papillary hypertrophy, and punctate epithelial erosions ($P < 0.05$). In addition, the mean tear break-up time for patients with rosacea improved from 5.7 s at baseline to 10.8 s after 12 weeks of treatment with doxycycline ($P = 0.007$). Both studies illustrate the efficacy of doxycycline in the treatment of ocular rosacea.

Topical metronidazole gel

As a result of the success of metronidazole gel in the treatment of dermatological rosacea, its use was investigated in the treatment of ocular rosacea.⁸⁰ One eye of each of the 13 enrolled patients was assigned randomly to receive lid hygiene and warm compresses twice daily while the other eye received the lid hygiene and compresses twice daily followed by an application

Table 3 Cosmetic camouflage techniques

Cosmetic Products	Guidelines for Cosmetic Product Selection
Moisturizers	Choose a water-based moisturizer.
Pre-foundation	Try a colour-correcting pre-foundation base in shades of yellow or green to counter redness. Pre-foundation may be available in liquids, creams, or as concealer sticks.
Foundation	Match foundation with skin tone, choosing an oil-free product with moderate to heavy coverage. Avoid make up with pink or orange hues.
Products to avoid	Never use products that cause irritation or redness. Avoid ingredients such as alcohol, menthol, peppermint, eucalyptus oil, clove oil, witch hazel or products with heavy fragrances.

of topical metronidazole 0.75% gel to the eyelid margin twice daily. Eight of the 10 eyes treated with metronidazole gel and five of the 10 eyes treated with the control improved. Significant improvement was seen in both groups for the eyelid score ($P = 0.003$ for treatment group and $P = 0.025$ for control group). No significant improvement in the ocular surface score was seen for either group, however, when the eyelid and ocular surface scores were taken in combination, there was a significant improvement in the treated eyes ($P = 0.022$). Patients may require long-term therapy for ocular rosacea, and therefore may prefer a nonsystemic agent, such as metronidazole topical gel.

Cosmetic camouflage

The papules, pustules, and the redness of erythema seen on the faces of rosacea patients can cause some individuals great distress.⁸⁵ Cosmetic camouflage is a helpful method of disguising the stigmata involved with rosacea, and hence providing psychological benefit to rosacea patients. The camouflage technique involves the use of a number of non-irritating, covering creams, with excellent finish and high durability. These are blended onto the skin to achieve a perfect match with the surrounding area, and then set, with an untinted, unperfumed finishing powder. The results can be extremely natural.⁸⁶ Although an irregular, or pitted skin surface can make it difficult to achieve a satisfactory finish, once the correct blend of preparations has been achieved, the patient rapidly acquires skill in applying the camouflage. An effective application of camouflage to the face can sometimes bring increased self-confidence and other psychological advantages. Table 3 outlines some effective cosmetic camouflage techniques.

Conclusions

With the various available methods of controlling rosacea, patients no longer need to suffer from its signs and symptoms. Management of rosacea commences with identifying and

avoiding the nonspecific physiological and environmental factors that trigger a flare-up. Together with the avoidance policy, rosacea patients may benefit from a 6-month course of an oral agent, such as an antibiotic, and the concomitant use of a topical agent, such as metronidazole cream, gel, or lotion, azelaic acid, 1% clindamycin phosphate lotion, tretinoin, 5% permethrin cream, or a sulphur preparation. In severe, recalcitrant vascular or inflammatory rosacea, isotretinoin may be preferred. Patients with telangiectasia may benefit from therapy with an argon laser, pulse dye laser (590–595 nm), potassium-titanyl phosphate (KTP) laser (532 nm), or flash lamp pumped dye (FLPD) laser surgery (585 nm). In those patients whose rosacea that has progressed to rhinophyma, therapy begins with practicing good hygiene followed by laser surgery. In addition to drug therapy, signs of rosacea may be masked with oil-free, fragrance-free cosmetics in shades of yellow or green that counter the rosy redness of rosacea. Patients with ocular involvement may benefit from a long-term course of an antibiotic and continual use with metronidazole gel.

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