Rosacea

A thorny problem with a rosy outlook

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Rosacea is a common and often underdiagnosed chronic inflammatory centrofacial dermatosis, with a diverse clinical presentation. Symptoms can have profound impacts on the social and psychological wellbeing of affected patients. Optimising management requires an accurate diagnosis and tailored treatment to the presenting features of the individual patient.

Rosacea is an often underdiagnosed chronic inflammatory centrofacial dermatosis.[1] It is diverse in its clinical presentation and is characterised by exacerbations and remissions.[2] Symptoms and signs encompass flushing, erythema, papules and pustules. Ocular involvement can occur in up to 50% of patients with rosacea and symptoms can be nonspecific.[3] Phymas or enlargement and thickening of the facial skin, particularly the nose in men, is a diagnostic feature of rosacea (Figure 1).[4] Initially, symptoms and signs may be transient, but persistent erythema with telangiectasia can develop over time due to repeated vasodilation.[5]

Rosacea is estimated to affect up to 5.5% of the global population.[6] It can occur in all skin types; however, it predominantly affects people with fair skin, especially those of Celtic heritage.[7] Men and women are both affected, although women have a slightly higher prevalence and men develop phymatous changes more frequently.[8,9] Typically, symptoms will peak from 30 to 50 years of age.[10]

Rosacea symptoms are often distressing and can have profound impacts on the social and psychological wellbeing of affected patients. People with rosacea have

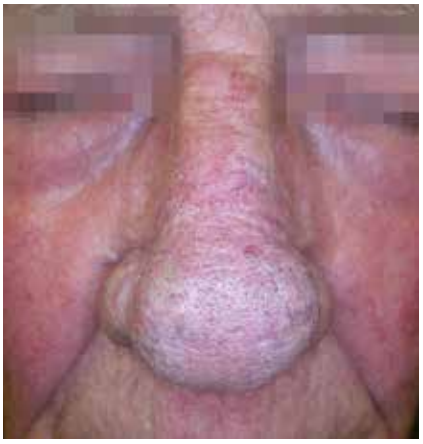

Figure 1. Rosacea complicated by phymatous changes.
Photo courtesy of A/Prof Alvin Chong.

KEY POINTS

- Rosacea is a common and often underdiagnosed inflammatory centrofacial dermatosis.
- Rosacea has a diverse clinical spectrum and includes symptoms of flushing, erythema, papules, pustules and, for some, skin thickening or ocular symptoms.
- Rosacea can have a profound impact on the social and psychological wellbeing of those affected.
- Early recognition and treatment can improve quality of life.
- Treatment options are diverse and should be tailored to the individual.

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1. DIFFERENTIAL DIAGNOSES OF ROSACEA[2,11,14]

- Seborrhoeic dermatitis
- Allergic/irritant contact dermatitis
- Photodamaged skin
- Periorificial dermatitis
- Acne
- Keratosis pilaris rubra
- Eczema
- Lupus erythematosus
- Steroid rosacea*
- 'Maskne' (acne mechanica)

* May occur after application of topical corticosteroids to the face.

2. DIAGNOSTIC CRITERIA FOR ROSACEA[2,9]

Primary diagnostic features
The following two features are independently diagnostic for rosacea:

- fixed centrofacial erythema: erythema in a characteristic centrofacial pattern that may periodically intensify (flushing)
- phymatous changes: patulous follicles, skin thickening or fibrosis, glandular hyperplasia and bulbous appearance of the nose (rhinophyma is the most common form)

Major features
In the absence of primary diagnostic features, the presence of two or more of the following major features can establish the diagnosis of rosacea:

- inflammatory papules and pustules
- flushing: frequent and typically prolonged
- telangiectasia: predominantly centrofacial in skin phototypes I to IV, rarely seen in darker phototypes
- ocular manifestations

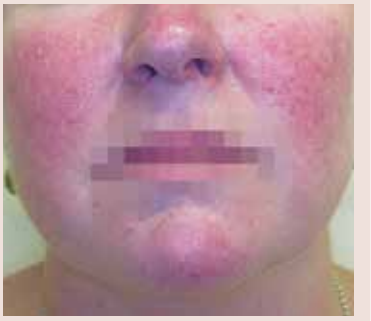
Minor features
The following minor features may also present with diagnostic or major features:

- burning and stinging sensation of the skin
- oedema: facial oedema
- dry appearance: central facial skin may be rough and scaly

3. A WOMAN WITH ERYTHEMATOTELANGIECTATIC ROSACEA

A 52-year-old woman presented with a several year history of periodic flushing and erythema to her cheeks, nose and chin. More recently, she had noticed the erythema was constantly present. On examination she was diagnosed with erythematotelangiectatic rosacea. Patient education focused on avoiding triggers and skin irritants in addition to the importance of photoprotection. She was effectively managed with vascular laser.

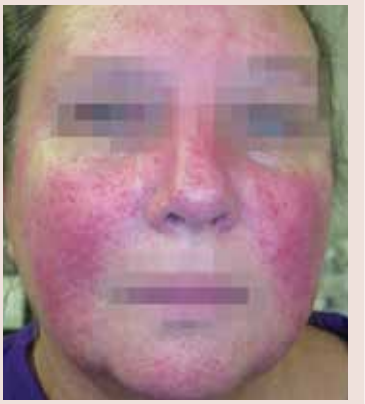
Photo courtesy of A/Prof Alvin Chong.



4. A WOMAN WITH ERYTHEMATOTELANGIECTATIC AND PAPULOPUSTULAR ROSACEA

A 55-year-old woman presented with a 10-year history of tender papules and pustules, periodic flushing and erythema to her cheeks, forehead, nose and chin. On examination, she had features of both erythematotelangiectatic rosacea and papulopustular rosacea. She was managed with 100 mg oral doxycycline daily for six months, along with daily application of topical ivermectin. Although she had a partial response to this regimen, she requires long-term oral isotretinoin to optimise control.

Photo courtesy of A/Prof Alvin Chong.



increased levels of embarrassment, social anxiety and depression and a decreased quality of life.[1] Appropriate treatment of symptoms and signs of rosacea results in an improved quality of life for affected patients.[1]

Pathophysiology

The pathophysiology of rosacea is yet to be fully elucidated but is known to be influenced by genetics and neurovascular dysregulation, in association with an abnormal cascading innate and adaptive immune response.[7,9]

Flushing and erythema develop from increased vascular reactivity, which contributes to increased blood vessel density near the skin surface.[11] Endogenous and exogenous triggers activate primary proinflammatory cytokines resulting in inflammation, which induces the characteristic histopathological features of rosacea. These triggers include sun exposure, heat and noxious cold, spicy food, smoking, exercise and alcohol.[12] Microbes such as the *Demodex* mite are thought to be an additional trigger for this inflammatory cascade.[13] In women during menopause, hot flashes may also trigger rosacea flares. Exposure to increased sunlight in the summertime may be a trigger for some people, whereas for others winter months will trigger symptoms through temperature fluctuations, cold temperature, icy winds and dry heat through heating systems.

Investigations

Rosacea is a clinical diagnosis and, as such, there are no histological or serological

markers. Histology, patch testing and serology should be considered for cases if there is diagnostic uncertainty, such as the need to exclude allergic contact dermatitis or lupus erythematosus.

Diagnosis

Erythematous facial dermatoses can pose significant diagnostic challenges. Differential diagnoses that need to be considered are outlined in Box 1.[2,11,14] It is important to remember that rosacea can coexist with other conditions (e.g. rosacea and photodamage or rosacea and perioral dermatitis) so it is possible to have more than one condition contributing to the presenting features.

Rosacea was previously classified into four subtypes (erythematotelangiectatic, papulopustular, phymatous, ocular) with one variant (granulomatous). In recent years, our understanding of rosacea has evolved. A new classification system has been developed based on diagnostic criteria, including major and minor features (Box 2).[9] The primary diagnostic features, which are independently diagnostic for rosacea, focus on persistent centrofacial erythema with periods of increased intensity and phymatous changes. In the absence of diagnostic features, a diagnosis of rosacea can be made if there are at least two major features, encompassing flushing (transient erythema), inflammatory papules and pustules, centrofacial telangiectasia and ocular manifestations. Minor features might also present with diagnostic or major features and encompass burning, stinging, oedema or dry sensation of the skin.[2]

Ocular symptoms are common and may include burning, itching, watering, grittiness, photosensitivity, lid margin or conjunctival erythema with or without recurrent stye and chalazion formation.

Comorbidities

Rosacea can often occur with other dermatological conditions, including extrinsic photoaging, telangiectasias, seborrhoeic dermatitis, acne, irritant contact dermatitis and keratosis pilaris. More recently, it has often been associated with 'maskne', or acne mechanica, from mask wearing in the context of the pandemic.[14] Maskne can be differentiated from rosacea as it will usually onset within six weeks of starting regular facial mask wear and will typically be distributed over the lower half of the face (underneath where the mask is worn). Maskne, unlike rosacea, will also typically present with comedones.[15]

There is also emerging evidence linking rosacea with other organ systems and

5. AN ELDERLY MAN WITH PAPULOPUSTULAR ROSACEA

A 75-year-old man presented with a 30-year history of tender facial papules, pustules and nodules with some background erythema. Examination showed severe papulopustular rosacea, particularly to the cheeks. He requires extensive periods of 100 mg daily oral doxycycline to maintain control.

Photo courtesy of A/Prof Alvin Chong.

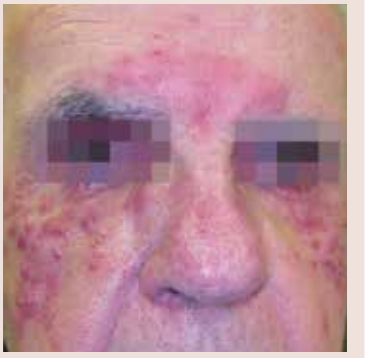


TABLE. COMMONLY USED TOPICAL THERAPIES AVAILABLE IN AUSTRALIA FOR ROSACEA

Topical medication	Application	Notes
Metronidazole	Twice daily for up to 3 to 4 months	• Targets inflammatory papulopustules • Available as 0.75% cream and gel formulations • Has a long history of safety and moderate efficacy • Mild stinging and burning can occur on application. Burning and stinging may be worsened with either gel or cream formulations, which may improve with change of formulation • Pregnancy category B2
Azelaic acid	Once daily	• Targets inflammatory papulopustules • Available as 15% gel and foam or 20% cream formulations • Similar efficacy to metronidazole • Pregnancy category B
Ivermectin	Once daily for up to 12 weeks	• Targets inflammatory papulopustules • Available as 1% cream • Reported to be more efficacious than 0.75% metronidazole cream[20] • Pregnancy category B3
Brimonidine tartrate	Once daily	• Used to manage moderate to severe facial erythema • Available as 0.33% gel • Has a rapid onset (in as little as 30 minutes) of noticeable reduction in erythema after the first application, lasting up to 12 hours • May be associated with a rebound erythema • Pregnancy category B3

comorbidities. Comorbidities include gastrointestinal, cardiovascular, respiratory and neurological disorders. Associations have also been found with several autoimmune diseases such as coeliac disease, rheumatoid arthritis, multiple sclerosis and diabetes mellitus.[16]

Treatment

Treatments should be tailored to the presenting features of the individual and the degree of distress caused by the condition (see the case studies in Boxes 3, 4 and 5). Optimising treatment begins with appropriate patient education. Education should highlight that rosacea is a treatable but not curable condition. Although the exact aetiology is unknown, it is caused by a combination of an overactive immune system, alongside heredity and environmental factors. Education should also emphasise the important role of reducing irritation through photoprotection and gentle skin cleansing as well as the avoidance of exacerbating factors and triggers.[5]

Skin care is important to maintain the epidermal barrier but ideally the cleansing and moisturising routine will be simple and contain a soap-free cleanser.[17] Scrubs and abrasive cleansers should be avoided, along with alpha and beta hydroxy acids such as salicylic or glycolic acid. Cosmetic products should be free from fragrance, colours and essential oils.[18] Patients should also be advised to avoid touching the face when possible throughout the day.[19]

Finding evidence-based and reliable patient information can be challenging, especially with the rise of social media. Although there is no Australian rosacea society, patients may find the US National Rosacea Society (rosacea.org) helpful for further information.

Topical agents

Topical agents are first-line therapy for the treatment of mild to moderate rosacea. They are typically used for their anti-inflammatory effects (such as metronidazole, ivermectin or azelaic acid) or their vasoconstrictive effects (such as brimonidine). Commonly used topical agents are outlined in the Table.[20] Typically, patients are reviewed after six weeks on topical treatment to assess for response.

Systemic agents

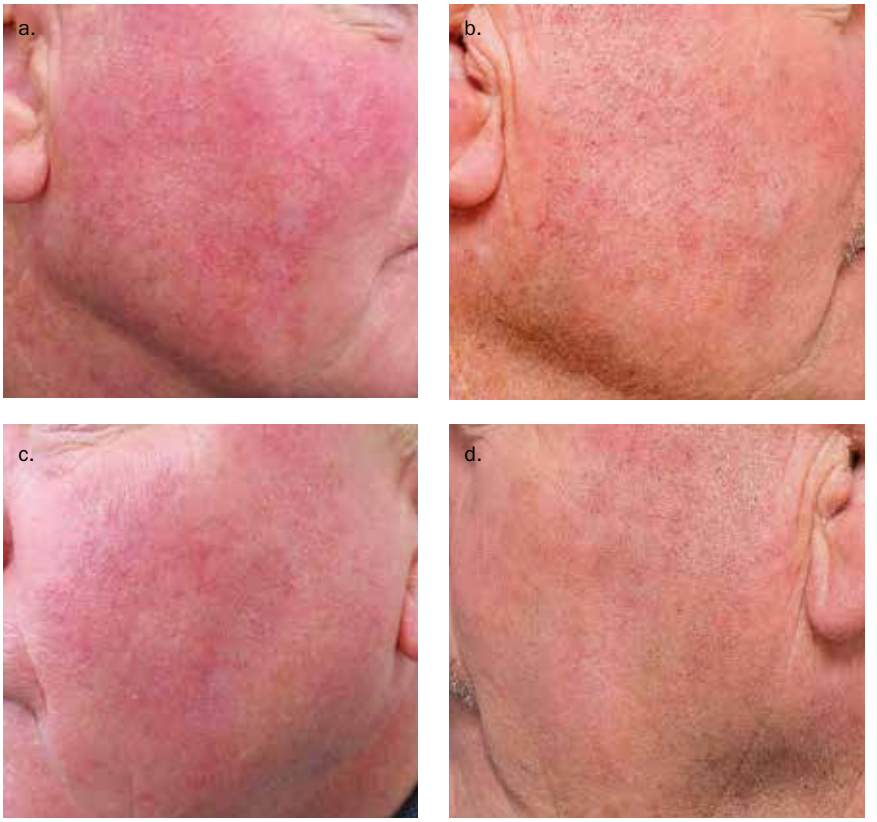
Oral antibiotics play a key role in the management of moderate to severe rosacea. Tetracyclines, such as doxycycline and minocycline, have been the long-term mainstay of papulopustular rosacea, but also have efficacy in ocular rosacea. The primary mode of action is anti-inflammatory. Typically, a patient is started on 50 to 100 mg doxycycline or 50 to 100 mg minocycline daily for six to eight weeks and then reviewed, with a view to ongoing treatment. If a patient fails to respond to doxycycline then referral to a dermatologist should be considered. Patients should not take doxycycline for longer than six months at

a time. Additionally, if they respond but papules and pustules rebound on cessation, requiring repeat courses, then referral to a dermatologist is also required. Adverse reactions of doxycycline may include photosensitivity, candida vaginitis and oesophagitis.[11] Treatment with minocycline should be limited to six months or less, due to the risks of iatrogenic hepatitis, drug-induced systemic lupus erythematosus and skin pigmentation changes. Erythromycin, although not always as effective, may also be trialled and has the benefit of being safe for use in pregnancy and breastfeeding.[21]

Off-label, low-dose oral isotretinoin, as prescribed by dermatologists, has good evidence of efficacy in people with rosacea, and has particular efficacy in the treatment of papulopustular rosacea variants.[22,23] Isotretinoin is thought to act through its downregulation of local cutaneous immunity, but its effect on lipid metabolism may also play a role.[5]

Laser and light devices

Laser and light devices are particularly valuable in the treatment of rosacea-associated erythema and telangiectasia. They can also remodel and rebuild dermal collagen, assisting in improving overall skin quality. Numerous different laser and light therapies are available, including pulsed dye laser (Figure 2), potassium titanyl phosphate laser, long-pulsed-neodymium-yttrium-aluminium garnet laser, intense pulsed light and nonablative and ablative lasers. The choice of laser or light devices should be tailored to the specific presentation of the patient.



Figures 2a to d. Erythematotelangiectatic rosacea responding to pulsed dye laser over four treatments. a (top left). The right side of face before laser treatment and b (top right) after four laser treatments. c (bottom left). The left side of face before laser treatment and d (bottom right) after four laser treatments.

Photos courtesy of Dr Belinda Welsh.

Management of specific features

Specific presentations of rosacea may require tailored management. Phymatous changes can be managed through oral isotretinoin, fully ablative carbon dioxide laser resurfacing or surgical excision.[24]

First-line therapies for ocular rosacea are eye hygiene measures and artificial tears. Often, patients will also benefit from use of systemic antibiotics such as tetracyclines. Early referral for ophthalmological care should be considered for moderate to severe cases.[24]

Treatment options for problematic flushing include beta-adrenergic blockers, such as propranolol or carvedilol. Monitoring for side effects such as bronchospasm, bradycardia and hypotension is important. Alpha-adrenergic receptor agonists, such as clonidine, may also be used but may be associated with systemic side effects.[5] Recently described emerging treatments include off-label use of botulinum toxin.[25]

Conclusion

Rosacea is an extremely common chronic centrofacial dermatosis with diagnostic features of erythema and flushing and tissue fibrosis (phymas). Its impact on the psychological wellbeing of patients should not be underestimated. Although our understanding of the pathophysiology of rosacea remains incomplete, current management strategies are very successful in controlling the signs and symptoms. Optimising management requires accurate diagnosis and tailored treatment to the unique circumstances of each patient and their presenting features. MT

References

A list of references is included in the online version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS: Dr Willems and Associate Professor Chong: None. Dr Welsh has received honoraria for a presentation on rosacea for the Candela Academy and from Galderma for media work for Rosacea Awareness Month.

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