Rosacea: A Review of a Common Disorder
C Knox

Citation

Abstract
Rosacea is a common but often overlooked condition of unknown etiology. It mainly affects the central convexities of the face; the cheeks, chin, nose, and central forehead. While it is not a physically threatening syndrome, it can cause significant anxiety, depression, and social withdrawal. Rosacea is not curable, but treatments are available for symptoms of telangiectasias, papules, pustules, and ocular and phymatous changes. Treatments include topical and/or oral agents, laser and, more recently, intense pulsed light therapies. Health care providers need to be understanding and compassionate when treating those afflicted with this potentially disabling disorder.

INTRODUCTION
Millions of Americans have rosacea, experiencing symptoms that range from mild flushing of the facial skin, to papules and pustules resembling acne, to irritated eyes to disfiguring thickening of the skin. The cause of rosacea has not been determined and it cannot be cured. Health care providers need to help patients identify triggers of their exacerbations and educate them about the variety of treatments that exist. Effective therapy can help patients control their flares and prevent potentially permanent changes. Effective and compassionate care can improve a patient's quality of life.

EMOTIONAL IMPACT
When symptoms of rosacea flare, they can cause emotional distress and decreased social and professional interactions. Patients are often asked if they have a sunburn or they are subject to the social stigma and misconception that a red face and enlarged nose signals a problem of alcohol abuse. Others may think patients with rosacea have poor hygiene. Seventy-five percent of rosacea patients report decreased self-esteem and decreased quality of life due to their disorder. Seventy percent describe embarrassment about their appearance and 60% suffer from frustration with their symptoms. Impaired professional interactions are reported by 60% while 57% attribute adverse effects on their social life to the disorder. These percentages are higher than for patients with respiratory or orthopedic conditions, denoting the impact that rosacea has on self-esteem. Rosacea patients experience higher rates of depression, feelings of inadequacy and social isolation, marital problems, phobias and eating disorders than those without the syndrome.

EPIDEMIOLOGY
It is estimated that 13 million adults in the United States, including former president Bill Clinton, have rosacea, resulting in a prevalence in 5-10% of the population. The actual numbers of sufferers may be even higher as it is often overlooked by providers or not mentioned by those affected. It is most commonly diagnosed in fair skinned people of Northern European descent. In Sweden the prevalence is 10%. For this reason it has been coined “The curse of the Celts.” It is much less common in people with darker pigmented skin, though it has been diagnosed in all racial and ethnic groups, including African American and Asian patients.

Rosacea occurs most frequently among 20-60 year olds, and it is uncommon in children. Women are affected two to three times more often than men, and women usually develop the disorder at an earlier age, often in their late teens or early twenties. This may be because fewer men, especially young men, seek treatment as they may view the cosmetic symptoms as being less significant than women. Fourteen to thirty percent of women aged 35-55 have the disorder. Women may also have onset of symptoms during menopause when the initial trigger is the vasomotor instability that also causes hot flashes. Men, however, usually have more severe cases of rosacea, with skin thickening and phymatous changes.

The prevalence of rosacea is on the rise. This may be due to the aging of the “baby boomers” or a better recognition by providers.
IMPORTANCE OF DIAGNOSIS

Rosacea is an incurable and progressive disorder with an inflammatory component. Its course is marked by chronic remissions and relapses. Rosacea can have severe effects on a patient’s psychological, social and occupational well-being, so the importance of making the correct diagnosis and instituting effective treatment cannot be over-estimated. Patients may experience decreased self-esteem, embarrassment, anxiety over their symptoms. They may feel less sexually desirable, experience impediment in career advancement or be viewed as alcohol abusers by those around them. These issues can take an enormous toll on the patient.

PATHOPHYSIOLOGY/ETIOLOGY

The etiology and pathogenesis of rosacea is poorly understood. No histologic or serologic markers have been identified. There are several proposed etiologies, though none are yet proven. Researchers believe that rosacea may be due to both genetic and environmental factors, since those with a family history of rosacea and also a history of photodamage to the skin are more frequently inclined to developing rosacea. The proposed causes range from vascular components to facial mites to bacteria to steroid use to environmental factors and beyond.

Several vascular etiologies have been proposed. One theory is that adjacent vessel walls break down and vessels fuse, resulting in a dilation of the blood vessels. Another vascular theory states that the development of telangiectasias may be due to decreased integrity of upper dermal connective tissue, allowing for passive dilation of vessels.

Some studies have shown an association between rosacea and migraines. Migraines are 2-3 times more common in rosacea sufferers, suggesting a vascular instability as root cause. Also since many perimenopausal women develop rosacea, a theory of vasomotor instability secondary to hormonal imbalance or a flaw in autonomic innervation of cutaneous vasculature has been implicated. What has been determined is that there is widening of the dermal vessels, inflammation and fibromatous proliferation in the dermis.

Another theory proposes a bacterial cause for rosacea, possibly Helicobacter pylori. Several small studies in 1999 and 2000 suggested a possible link between H. pylori infection in the gastric mucosa and rosacea. They concluded that eradication of H. pylori led to improvement of rosacea symptoms, stating that rosacea was an extragastric symptom of this infection, but this has met with conflicting results in subsequent blinded studies. Mites in the facial hair follicles, specifically Demodex folliculorum have been named as a causative factor, provoking an allergic reaction in the skin, but this has not been confirmed. This mite can be found in follicles of normal skin, too, but may cause inflammation and result in rosacea if increased numbers of mites occur. The mite prefers to colonize enlarged sebaceous follicles that are found in rosacea patients. Uncontrolled trials using permethrin (Lindane) cream did not show clinically significant improvement, though.

Steroid use, especially prolonged or excessive use, has been suggested to precipitate or increase rosacea symptoms. Other theories have implicated vitamin deficiencies, hypertension, and gastrointestinal causes, however none of these theories alone can explain all cases of rosacea.

TRIGGERS

Patients with rosacea can cite many triggers for a flare of their symptoms, but the triggers are not the same for all patients. Common triggers are listed in Tables 1, 2, 3 and 4 and may include environmental factors such as sunlight (61%), sudden emotional change (60%) heat (53%), alcohol (45%), spicy foods (43%), exercise (39%), wind (38%), hot baths (37%), hot beverages (36%), cold weather (36%), topical skin products (24%), medications or other medical conditions. Health care providers should help patients identify their triggers and discuss ways to avoid them when possible.

Figure 1

Table 1: Common Triggers of Rosacea Flares

<table>
<thead>
<tr>
<th>Triggers</th>
<th>Wind</th>
<th>Humidity</th>
<th>Skin care products, including:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional stress</td>
<td>Headaches</td>
<td>Sunscreens</td>
<td></td>
</tr>
<tr>
<td>(laughter, embarrassment, anger, anxiety)</td>
<td>Asthmatics</td>
<td>Methylsalicylate</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>Soaps</td>
<td>Make up</td>
<td></td>
</tr>
<tr>
<td>Spicy food</td>
<td>Exfoliants</td>
<td>Make up</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>Perfumes</td>
<td>Make up</td>
<td></td>
</tr>
<tr>
<td>Hot baths, saunas, showers</td>
<td>Sunscreens</td>
<td>Make up</td>
<td></td>
</tr>
<tr>
<td>Hot drinks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold weather</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menses, menopausal hot flash</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>especially those containing alcohol</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sources: 1, 3, 5, 7, 9
CLINICAL PRESENTATION

The National Rosacea Society (NRS) has developed a standard classification system that is based on morphology to assist providers with diagnosis and classification of rosacea patients. This standardized terminology facilitates clear communication among providers. It has also helped create uniformity and enabled researchers to analyze results and compare data from different studies more effectively. The NRS describes four subtypes of the disorder including: erythematotelangiectatic, papulopustular, phymatous and ocular. Each subtype is graded on a scale of mild, moderate or severe.

Subtype 1, erythematotelangiectatic, is the most common type of rosacea. It consists of persistent, symmetrical, central facial redness with occasional flushing. The erythema may last hours to days or never remit. No pruritus is associated, but patients may experience stinging pain during a flush. Products such as cosmetics, cleansers, perfumes and sunscreens that were once well-tolerated may now cause sensitivity. Flushing is common and frequent, and triggers may be identified.

In subtype 2, papulopustular rosacea, the persistent central facial erythema continues, but now patients also experience transient papules and/or pustules of the central face. The papules are small, dome-shaped and red, and pustules may form, often in crops, usually involving the convex portions of the face. The lesions may also involve the perioral, perinasal or periocular areas and resemble acne. The distinguishing feature between rosacea and acne is that in rosacea no comedones develop. Acne and rosacea may co-exist, however, confusing the diagnosis. Telangiectasias may be seen or may be obscured.

Subtype 3 is phymatous rosacea. Patients with this type have the above symptoms, plus thickened skin and an irregular skin surface with nodule formation. Phymatous changes most commonly involve the nose, known as rhinophyma, but phymatous changes can also involve the chin, jaw, forehead, cheeks and ears. The follicles in these areas are prominent and patulous as the sebaceous glands exhibit hyperplasia. The connective tissue exudes protein which is deposited faster than the lymphatic drainage can remove it. The extracellular fluid accumulates leading to fibrosis of the tissue causing a hard, nonpitting, thickened skin. The thickening can be mild or severe and resemble the peau d'orange changes of lymphoma. Though this subtype is less common, it can become severe and disfiguring. Rhinophyma...
Rosacea: A Review of a Common Disorder

has been labeled as “whiskey nose” or a “gin blossom” because of misconceptions of its association with alcohol use. Males with this subtype outnumber females by a ratio of 20:1.

The final subtype of rosacea, subtype 4, is ocular. It is actually a fairly common type, occurring in approximately 50% of rosacea patients, but often goes unrecognized especially if it is mild or if there are no accompanying skin symptoms. Ocular symptoms can precede skin symptoms, but not commonly. It may also occur simultaneously with, or develop after the skin changes of rosacea. Providers need to consider a diagnosis of ocular rosacea when patients report symptoms of watery or bloodshot eyes, a sensation of foreign body, gritty, burning, stinging, dry, itchy, irritated or light sensitive eyes. An associated decreased tear production may exacerbate these symptoms. Patients may state they can no longer wear their contact lenses or may report blurred vision or the development of telangiectasias of the conjunctiva or lid margin. Patients may also exhibit blepharitis, conjunctivitis, chalazion, styte formation or chronic staphylococcal infections as presenting symptoms. Eye symptoms are usually of mild to moderate severity, but severe cases can occur and be potentially blinding. Corneal neovascularization and keratitis, though rare, can lead to corneal scarring and perforation, permanently affecting visual acuity. Ocular rosacea is usually best managed by an ophthalmologist because of these potential complications.

COURSE OF THE DISORDER

Rosacea is not uniformly progressive in severity, but it is commonly characterized by a chronic course with relapses and remissions that require long term treatment. Each flare up causes additional skin damage and exacerbates further eruptions. Medical treatment and lifestyle changes can effectively arrest progression of the disorder in many cases, and even control or eradicate symptoms altogether in some patients. Some patients may think that rosacea symptoms are a normal part of the aging process, while others may feel that nothing can be done to improve their symptoms and do not consult a healthcare provider. Healthcare providers can initiate the discussion of treatment for rosacea and alleviate much distress in patients by letting them know that this is a common disorder that is often effectively controlled with proper treatment.

TESTING

There is no current laboratory test to make the diagnosis of rosacea. Histologic changes of inflammation are not specific to this diagnosis. Rosacea is diagnosed clinically. Serologic testing and skin biopsy may be done, however, to rule other disorders that can cause similar signs and symptoms.

DIFFERENTIAL DIAGNOSIS

Rosacea can be mistaken for several other cutaneous disorders including acne vulgaris, steroid-induced acne, sunburn, or actinic changes. The flushing and telangiectasias of rosacea can be confused with some other rare disorders as well, including carcinoid syndrome, pheochromocytoma, and mastocytosis. Ocular rosacea is usually best managed by an ophthalmologist because of these potential complications.

The flushing and telangiectasias of rosacea can be confused with some other rare disorders as well, including carcinoid syndrome, pheochromocytoma, and mastocytosis. Ocular rosacea is usually best managed by an ophthalmologist because of these potential complications.

To differentiate the patient with rosacea from other rare disorders, additional historical questions can often provide the clue. Carcinoid syndrome patients may have flushing and telangiectasias, but these patients will also describe cardiac, pulmonary and gastrointestinal symptoms. Pheochromocytoma patients will describe heart and blood pressure symptoms, increased sweating, and headaches. Mastocytosis patients report additional findings of cardiac symptoms, bronchospasm and gastrointestinal symptoms. Patients with lupus often have the characteristic butterfly rash, sparing the other convexities of the face. A serum ANA can also aid in the diagnosis of lupus.
TREATMENT OPTIONS

Treatment is based on subtype. The efficacy and optimal duration of many of the therapies currently in use for rosacea are not evidenced based, and off-label prescription drug use is common. The four subtypes of rosacea, signs and symptoms of each and their corresponding treatments are summarized in Table 5.

The treatment of subtype 1, erythematotelangiectatic rosacea, is difficult. Effective methods for eradicating the erythema and flushing episodes are lacking. These patients have sensitive, easily irritated skin so behavior modification is key at this stage. Patients need to be taught how to recognize and avoid their own personal triggers. A diary may be helpful for patients to identify their own triggers. By doing so and by following medical regimens, patients have an increased chance of success of treatment and may avoid possible permanent disfiguration. While triggers inflame the condition, they do not cause it. Therapy is long term and side effects are possible. Patients need to be aware of these considerations to optimize success in managing their condition.

For erythema and flushing, topical and oral antibiotics are not effective. Several treatments for flushing have been tried, including low dose Beta-blockers, clonidine and spironolactone, but supportive evidence of their effectiveness is lacking. Topical steroids may appear to be initially helpful, but in the long run they aggravate the condition. Steroids also delay resolution of flare ups. Green-tinted cosmetics may help conceal the redness in the skin.

Telangiectasias have historically been treated with CO\textsubscript{2} lasers. CO\textsubscript{2} lasers have a small spot size and a tendency to cause purpura, though. This results in long treatment and recovery times making them less than ideal for panfacial, serial treatments that are needed in many rosacea patients. In the 1990’s Intense Pulsed Light (IPL) therapy was developed. This newer regimen is so far proving to provide better and longer lasting results in the treatment of telangiectasias. IPL causes selective photo-thermalysis that ablates vessels as it causes selective coagulation necrosis of target tissue with minimal heat damage to surrounding structures. IPL can penetrate more deeply and treat larger vessels than CO\textsubscript{2} lasers because the pulse duration can be varied. The wavelength is not fixed so vessels at different depths can be individually treated. A larger spot size also makes it easier to treat the whole face. There is less purpura formation with IPL so recovery times are shorter. IPL has afforded more versatile treatments, allowing the provider to tailor the treatment to the individual patient’s condition severity and skin type.

A study done in 2002 of 32 patients receiving IPL treatments showed that 83% of those treated had decreased redness, 75% had decreased flushing and improved skin texture and 64% had fewer popular/pustular breakouts following treatment. Side effects of IPL include some purpura, peeling and postinflammatory hyperpigmentation. These are all reversible with time. No scarring was seen. Treatments occurred at three week intervals and patients required an average of 3-6 treatments. IPL is still being studied, to determine optimal treatment parameters including ideal number of treatments, expected period of remission, and a maintenance schedule. Patients should be reminded that IPL is not curative and repeat treatments may be needed. Once a population of vessels is removed, antibiotic agents need to be used to help keep new vessel formation to a minimum.

In subtype II, papulopustular rosacea, several avenues of treatment are available to patients in addition to the measures above. Patients need to be taught to use gentle, water-soluble cleansers, and water-based moisturizers and make-up. Make-up should be non-comedogenic and should not contain alcohol, acid or oil. Patients should use sunscreen with an SPF of 15 or higher year round. Some patients find sunscreen to be a trigger, however, so careful selection is required.

For patients with a milder form of subtype 2, topical agents may be sufficient. Those with moderate or severe forms of subtype 2 will probably need systemic therapy. Topical agents can cause a burning sensation in some patients, necessitating oral therapy even in mild forms. Patients should be instructed to treat the whole face, not “spot treat” lesions. Topical agents can help control the inflammatory lesions, but do not resolve the telangiectasias. Many of these agents are limited in their long term use because of side effects.

For many years, topical treatment of rosacea has typically begun with 0.75% or 1% metronidazole (Flagyl) in cream, gel or lotion. It is gently massaged into the skin after gentle cleansing. Metronidazole has been shown to reduce papules and pustules by 60% and decrease erythema by 26-30%. It may cause a burning sensation or drying of the skin. In the pregnant patient, topical clindamycin has been used. More
recently, other topical agents such as azelaic acid, sulfacetamide, permethrin, and isotretinoin have been tried, with varying degrees of success.4-10

There is evidence of the efficacy of azelaic acid in the treatment of papulopustular rosacea. Azelaic acid (AzA) is a naturally occurring, saturated, straight-chain, 9-carbon atom dicarboxylic acid that has historically been used for many years in the treatment of acne. It has an anti-inflammatory effect that acts by inhibiting neutrophil counts and their effects. AzA is generally safe and can be used in pregnant women (Category B). No fatal or serious events have been reported in association with its use. It does not cause phototoxicity or photoallergenicity.11 In 2002, a study compared the efficacy, safety and tolerability of 15% azelaic acid gel (Finacea) to 0.75% metronidazole (Flagyl) for the topical treatment of mild to moderate papulopustular rosacea. Two-hundred and fifty patients participated in the study, with each group using either AzA or metronidazole twice daily for 15 weeks.4 In 2003, over 650 patients participated in another blinded study, again comparing these two agents.11 Results showed that neither AzA nor metronidazole caused any improvement in telangiectasias, but both were helpful in controlling inflammatory lesion counts and erythema, especially AzA. AzA continued to have effect through the 15th week of the study, while metronidazole plateaued at week 8.12 Further investigation into the long term effects of AzA gel is warranted.13 It had a low incidence (>10%) of stinging or itching in treatment groups.11 More severe cases of rosacea can also be treated with a higher strength 20% azelaic acid solution.4

A combination of 10% sodium sulfacetamide and 5% sulfur has been shown to be better than Flagyl, providing more options in the treatment of this condition.1

In 2003, researchers studied permethrin and its effectiveness on rosacea since the demodex mite was cited as a possible etiology. Sixty-three patients were involved in this small study. Patients used either permethrin 5% bid or metronidazole 0.75% or placebo. They concluded that permethrin was as effective as metronidazole and superior to placebo.10

For recalcitrant cases of subtype 2, isotretinoin (Accutane) may be used in either topical or oral form. It is effective in severe cases, and can be helpful for rosacea patients with oily skin. Its use is reserved for severe cases due to its possible severe side effects including dry eyes, dry skin, increased erythema and teratogenic effects.14-19

Oral antibiotic therapy commonly includes oral tetracycline 250-1000 mg daily, as it frequently provides rapid relief of papules and pustules.3 Minocycline 50-200 mg daily or doxycycline 100-200 mg daily are two other commonly used drugs, however there is less evidence for their effectiveness.1 If patients cannot tolerate tetracycline, erythromycin may be used.4 Metronidazole 200 mg orally bid has been shown to be equally as effective as tetracycline 250 bid.1

Some researchers have concerns about the development of resistant organisms on the skin.1 Others state that the efficacy of antibiotics is due to their anti-inflammatory effect more than their antibiotic effect. Metronidazole, for example, which is both antibacterial and antiprotozoal, modulates neutrophilic activity and blocks the cascade of inflammatory processes that cause and sustain rosacea.7

If oral antibiotics are employed, they should be continued for six weeks to relieve the exacerbation, then topical agents should be used for maintenance until the next flare occurs.3 One quarter of patients relapse within weeks after stopping oral treatment if no topical agent is used for maintenance, so continued use of topical agents is employed for an average of six months. Some patients can then reduce therapy to topical treatment every other day or twice weekly, while others will need another course of oral medications. This regimen usually helps to control the papules and pustules, but erythema may persist.1

Other oral medications have been tried, including clarithromycin, trimethoprim sulfamethoxazole, and isotretinoin. These have been less effective, or cause more side effects, however.9

Subtype 3, phymatous rosacea, has not been as extensively studied as it is less commonly encountered. Accutane has been used in some cases as it shrinks the sebaceous glands and so may be helpful in early rhinophyma.10 Hypertrophy of the tissue usually requires surgical intervention though, and previous isotretinoin use may increase the possibility of complications after laser therapy.2 Moderate to severe cases of phymatous rosacea can be afforded some relief with surgical excision, electrosurgery, dermabrasion, cryosurgery and CO2 laser therapy.15,11

For subtype 4, ocular rosacea, effective treatment measures can be undertaken to help control the symptoms. Patients are
advise to perform good lid hygiene, using warm soaks and baby shampoo for mild cases and for maintenance therapy. If patients experience dry, itchy, gritty eyes, they can use artificial tears for lubrication. If these conservative measures are not effective, topical fucidic acid or metronidazole gel to the lid margins or systemic antibiotics such as tetracycline or doxycycline may be indicated. These medications help avoid blepharitis and other inflammatory conditions. Oral antibiotics may be necessary for moderate to severe cases and are continued for 6-12 weeks. Severe cases of ocular rosacea should be managed by an ophthalmologist due to potential development of blinding keratitis.

CONCLUSION

Rosacea is a common dermatologic disorder. It is frequently overlooked or misdiagnosed, particularly when mild in nature. There are four subtypes, including erythematotelangiectatic, papulopustular, phymatous and ocular, as standardized by the National Rosacea Society. Identification of triggers and behavior modification are important in the management of symptoms. In more advanced cases, many different topical and systemic medications may be instituted. Intense pulsed light is a newer form of treatment for the persistent erythema and telangiectasias that cannot be effectively reduced with other treatments. If phymatous changes develop, surgical intervention is usually required. Ocular rosacea may be managed by the primary care provider if it is mild or moderate, but severe cases should be referred to an ophthalmologist. Though not life-threatening, rosacea is not curable and can cause severe anguish in patients because of the cosmetic disfiguration and common misconceptions surrounding it. Health care providers can improve a patient’s social and emotional well-being by being supportive and offering effective methods of treatment.

FOR MORE INFORMATION, CONTACT

National Rosacea Society 800 South Northwest Highway Suite 200 Barrington, IL 60010 888-NO BLUSH Web: http://www.rosacea.org E-mail: rosacea@aol.com

References

Author Information
Carolyn Knox, MS, PA-C
Assistant Professor/Clinical Coordinator, Physician Assistant Department, Gannon University