

BEATING ROSACEA: Vascular, Ocular & Acne Forms

By Geoffrey Nase, PhD

Partial Excerpt from:

**CHAPTER 10
ROSACEA TREATMENT BY THERAPY TYPE**

Note: The complete e-book can be found at <http://www.drnase.com>

CHAPTER 10
ROSACEA TREATMENT BY THERAPY TYPE

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WARNING

This chapter contains in-depth treatment information for rosacea sufferers. Most of the treatment regimens are detailed in peer-reviewed medical articles; however, some regimens are based on cutting-edge approaches that have not yet made their way into medical journals or textbooks. This chapter is only meant for educational purposes ~ physicians and their patients need to be better informed about the current treatment options available for rosacea.

Treatment of rosacea should only be performed by a qualified medical physician because there are many variables that a physician must consider before choosing a proper treatment regimen for his or her patient:

- Some rosacea sufferers have underlying medical disorders in addition to their rosacea.
- Some rosacea sufferers are taking prescriptions, nutritional supplements, or herbs that may interact with rosacea medications.
- A small percentage of rosacea sufferers may experience unpredictable reactions or serious side effects to treatment therapy. This can occur with any type of therapy or medication.

I encourage each rosacea sufferer to consult with his or her physician about common and serious side effects of prescribed treatments, as it is impossible to list all of them in this chapter.

Rosacea sufferers and their physicians will have to decide together what the potential side effects are for certain treatments, and whether they are worth the risk. If there are any doubts, please seek additional medical advice. It is a sign of wisdom, not cowardice, to seek a second or third professional opinion.

I. ORAL THERAPY (PRESCRIPTION)

1. ORAL ANTIBIOTICS

Effect on rosacea symptoms:

- Extremely effective at reducing facial papules and pustules.
- Moderately effective at reducing facial inflammation.
- Minimally effective at reducing constant facial redness and burning sensations.
- Not effective at reducing facial flushing, telangiectasia, or heart of the disorder.

ORAL ANTIBIOTICS: TETRACYCLINE, DOXYCYCLINE & MINOCYCLINE

Oral antibiotics have been used for more than 30 years to treat rosacea symptoms. Today, these drugs are the mainstay of therapy due to their relative safety and effectiveness. Medical specialists now know that antibiotics work primarily through their anti-inflammatory actions; they are not used for 'antibacterial' actions because rosacea is not caused by facial bacteria. ^(1,3)

Tetracycline

Due to their effectiveness and low cost, oral tetracycline antibiotics are usually the first choice for rosacea treatment. Oral tetracycline antibiotics (tetracycline-HCL or oxytetracycline) are usually quite effective at decreasing rosacea papules and pustules, and moderately effective at reducing facial inflammation. ^(4,5) In some patients, reduction in facial inflammation may help to alleviate chronic facial redness and burning sensations.

Tetracycline dosage: The usual starting dose is 250 milligrams four times daily, or 500 milligrams, twice daily. These antibiotics should not be taken with meals due to decreased absorption of the medication. Patients are instructed to take this medication one hour before, or two hours after meals.^(4,6) If the patient responds adequately within one to three months, the dose may be tapered to the lowest level that maintains control.⁽⁷⁾

Tetracycline side effects: The most common side effects include gastrointestinal disturbances (upset stomach, diarrhea and constipation), and photosensitization (facial skin becomes more sensitive to sunlight).

Doxycycline

Doxycycline is a tetracycline-derivative that has several potential advantages over standard tetracyclines. First, it is absorbed by the gastrointestinal tract much more efficiently than standard tetracyclines, and therefore may be taken in smaller dosages. Second, it has a much longer half-life than standard tetracyclines, making it effective for longer periods of time. Third, it is much gentler on the stomach and may be taken with meals if needed.⁽⁸⁾ Doxycycline is very effective at reducing rosacea papules and pustules, and moderately effective on facial inflammation.^(5,9,10) In some patients, reduction in facial inflammation may help to decrease chronic facial redness and burning sensations.

Doxycycline dosage: The normal dose for rosacea treatment is 50 to 100 milligrams, one to two times daily.⁽⁴⁾

Doxycycline side effects: Doxycycline is a strong photosensitizer (it is much easier to get sunburn while on this medication). Due to this side effect, experts do not prescribe this drug to patients who spend a great deal of time outdoors, or whom cannot wear sunscreen on a daily basis.⁽⁸⁾

Minocycline

Minocycline is very similar to doxycycline; it is a tetracycline-derivative that is well absorbed by the gastrointestinal tract and is long acting. Minocycline

has an additional advantage - it usually does not cause photosensitization. Minocycline⁽¹¹⁾ is very effective in the treatment of rosacea papules and pustules, and moderately effective at reducing facial inflammation.^(4,7,12) In some patients, reduction in facial inflammation may help to alleviate chronic facial redness and burning sensations. Personal reports from hundreds of rosacea sufferers, and dozens of physicians indicate that minocycline is one of the most popular antibiotics used for rosacea treatment.

Minocycline dosage: The usual starting dose for rosacea treatment is 50 to 100 milligrams, one to two times daily.^(4,6)

Minocycline side effects: Some patients experience bouts of dizziness the first couple weeks of treatment. In order to minimize dizzy spells, experts recommend starting patients on low doses for the first two weeks (50 milligrams twice a day), and then gradually increasing the dose to 100 milligrams, twice a day.⁽⁸⁾

ORAL ANTIBIOTICS:

CLARITHROMYCIN & AZITHROMYCIN

Medical experts now realize that the most effective oral antibiotics are those with the greatest anti-inflammatory actions. In this respect, the newer macrolide antibiotics may offer significant advantages over tetracycline antibiotics. Numerous studies demonstrate that macrolide antibiotics possess anti-inflammatory actions that are much greater than tetracycline antibiotics.^(1,9,13,14) Two of the most popular macrolide antibiotics are clarithromycin and azithromycin.

Clarithromycin

Clarithromycin is a recently synthesized macrolide antibiotic that possesses strong anti-inflammatory actions.⁽⁹⁾ Clarithromycin is also highly bioavailable, extremely long acting, can be taken with or without food, and has very few side effects. Medical experts indicate that all of these attributes make clarithromycin a great choice for rosacea treatment.^(1,9,15)

In a recent study, "*Clarithromycin Versus Doxycycline in the Treatment of Rosacea*", medical experts compared the effects of doxycycline to clarithromycin in 40 rosacea patients.⁽⁹⁾ After 4 weeks of treatment, facial papules and redness were significantly better in the clarithromycin-treated group. The clarithromycin-treated group also experienced fewer side effects associated with treatment. The physicians conducting the study concluded that clarithromycin was an extremely effective rosacea medication that was virtually free of side effects.^(11,9)

In a more recent article, "*Clarithromycin: A New Perspective in Rosacea Treatment*", Dr. Torressani documented that oral clarithromycin was effective in the treatment of inflammatory skin disorders such as acne vulgaris, perioral dermatitis, and steroid-induced rosacea.⁽¹⁾ He stated, "*The effectiveness of clarithromycin in treating steroid-induced rosacea is truly impressive.*"

In his medical practice, Dr. Torressani has found that clarithromycin is superior to standard antibiotics in the treatment of rosacea.⁽¹⁾ In fact, he has documented a case in which a rosacea patient, who was previously unresponsive to standard antibiotics, cleared dramatically with clarithromycin.

Clarithromycin dosage: The standard rosacea treatment protocol is 250 milligrams, twice daily for the first month, followed by 250 milligrams once daily for the remainder of treatment.⁽⁹⁾ Experts point out that due to its strong anti-inflammatory actions, long-lasting effectiveness, and quick onset of action, clarithromycin may also be used intermittently each month (pulse-dosing) to maintain rosacea clearance.⁽¹⁾

My personal experience with clarithromycin:

Throughout the years, I have tried many oral antibiotics including tetracycline-HCL, doxycycline, minocycline, and clarithromycin. In my particular case, clarithromycin was the fastest- and best-acting antibiotic. Clarithromycin was moderately effective on my facial papules, pustules, and inflammation (while the standard antibiotics had no visible effect on my symptoms). I did not experience any side effects while on clarithromycin, even at high dosages.

Azithromycin

Azithromycin is a macrolide antibiotic that also possesses strong anti-inflammatory actions. Two recent studies have shown azithromycin to be a powerful tool in the fight against rosacea.

At a recent *American Academy of Dermatology Meeting (1998)*, Dr. Thomas Fitzpatrick of Harvard Medical School detailed an effective rosacea treatment regimen that consisted of pulse dosing with azithromycin.⁽¹⁴⁾ Pulse-dosing therapy is possible with azithromycin due to its fast onset of action, powerful anti-inflammatory actions, and long half- life (it remains in the body for extended periods of time, maintaining therapeutic serum levels for 6 days following discontinuation of the drug). In this study, Dr. Fitzpatrick treated his patients for only 10 days out of the month; azithromycin was given on the first of the month for 5 straight days, and on the fifteenth of the month for 5 straight days. All rosacea patients reported significant reductions in symptoms while on this treatment regimen.

In agreement with the above study, Dr. Fernandez-Obregon, of the Hudson Dermatology Skincare Center, demonstrated that azithromycin is one of the more effective antibiotics for rosacea treatment.⁽¹³⁾ In this clinical study, he treated 10 rosacea patients with azithromycin (each of whom did not respond to previous treatment with standard antibiotics). His treatment protocol consisted of a single dose of azithromycin (250 milligrams), three times a week. Within three to four weeks, all patients reported moderate to excellent improvement in their rosacea symptoms. So, not only did these patients respond to low doses of azithromycin, but they did so very quickly.

Azithromycin dosage: Although there are no guidelines yet for rosacea treatment, the mild to moderate sufferers may only need pulse-dose therapy (250 milligrams three times a week).^(13, 14) In the more severe cases, daily treatment may be needed for one to three months in order to control the symptoms. After adequate control, pulse dosing may be employed to maintain clearance.

Important: Limitations of Oral Antibiotics

While oral antibiotics are the mainstay of rosacea treatment and are relatively safe, it must be stressed that these medications only decrease some of the superficial symptoms. They do not treat the underlying disease. ⁽¹⁶⁾ While patients are often grateful for reduced symptoms, they are usually not satisfied with the effect of antibiotics on the vascular symptoms. *These medications do not result in a "story book ending" for most sufferers with moderate to severe rosacea.* In fact, there are numerous medical reports suggesting that moderate to severe rosacea sufferers may only experience minor improvements on oral antibiotics, or may not respond at all:

- In a study of 20 rosacea sufferers with moderate to severe rosacea, oral antibiotic treatment had no significant effect on their rosacea symptoms. ⁽¹⁷⁾
- In a review of 27 rosacea patients, oral antibiotics were only moderately effective at reducing some of the papules and pustules, and were not effective at treating facial flushing, redness, inflammation, and telangiectasia. ⁽¹⁸⁾
- In four different medical reviews, rosacea experts stress that oral antibiotics are not effective in treating the underlying vascular disorder such as facial flushing, chronic redness, and telangiectasia. ^(16,19-21)
- In agreement with the above, Dr. Groussans states, *"Tetracycline and metronidazole are very useful for therapy, but they only influence the cutaneous and ocular complications and do not act upon the basic vascular trouble."* ⁽²²⁾
- In clinical case reports, medical specialists document that some rosacea sufferers do not respond at all to oral antibiotics. ⁽²³⁾
- Medical experts indicate that the main problem with standard antibiotic therapy is that they, *"Treat the symptoms rather than the root cause or causes of this chronic disorder, and must be used on a long-term basis."* ⁽²⁴⁾

2. ORAL ISOTRETINOIN

Effect on rosacea symptoms:

- Extremely effective at reducing facial papules, pustules, inflammation, and rhinophyma.
- Moderately effective at reducing constant facial redness, burning, and swelling.
- Not effective at reducing flushing, telangiectasia, or heart of the disorder.

Isotretinoin (Accutane™, Roche Laboratories) is a vitamin A analog that has been used with great success in the treatment of severe acne and inflammatory skin disorders. Oral isotretinoin has potent anti-inflammatory properties, suppresses overactive immune cells in the skin, and physically shrinks sebaceous glands. ⁽²⁵⁾ For these reasons, isotretinoin is now being recommended for the treatment of moderate to severe rosacea sufferers with facial papules, pustules, redness, inflammation, burning, swelling, and rhinophyma. In many cases, isotretinoin's beneficial actions are long lasting. Some synopses of important articles are included below:

General Findings on Isotretinoin: Effect on Skin Inflammation

- Numerous clinical studies demonstrate that oral isotretinoin has potent anti-inflammatory actions in the skin. ⁽²⁶⁻²⁹⁾ In one excellent medical review, Drs. Orfanos and Bauer present clinical evidence demonstrating that oral isotretinoin is very effective in treating patients with inflammatory skin disorders. ⁽²⁹⁾ In this review they highlight two important findings. First, they document that oral isotretinoin can actually lower skin temperature in patients with inflammatory skin disorders (within 3 days of oral isotretinoin treatment, skin temperatures decreased by up to 1° Celsius). Second, they document that oral isotretinoin can greatly reduce the size of dilated skin blood vessels within 3 weeks of treatment. Both of these actions can help bring relief to patients and break the inflammatory cycle.

Note: Partial excerpt only. The complete e-book can be found at <http://www.drnose.com>

Rosacea Treatment by Therapy Type

- Additional studies by medical experts demonstrate that oral isotretinoin is one of most effective anti-inflammatory agents for skin disorders.^{(30) (31)} In one study on 16 patients with inflammatory skin disorders, Drs. Plewig and Wagner demonstrated that oral isotretinoin cleared most signs of skin inflammation including skin redness, swelling, papules, and pustules.
- There is medical evidence demonstrating that isotretinoin can successfully treat skin inflammation associated with lupus erythematosus.^(32,33) In a clinical case study, medical investigators documented that isotretinoin greatly reduced facial inflammation and redness associated with lupus. These physicians included an impressive series of colored photographs showing the lupus patient before isotretinoin treatment (with a severe fire-red face), and after treatment (with a completely normal, white face).⁽³²⁾ In a second study on a lupus patient who suffered with severe facial inflammation for 15 years, four weeks of low-dose isotretinoin resulted in remarkable clearance of skin inflammation.⁽³³⁾

General Findings on Isotretinoin: Effect on Rosacea

- Dr. Shalita and colleagues report that most rosacea sufferers respond very well to oral isotretinoin.⁽³⁴⁾ In their experience, oral isotretinoin results in dramatic clearance of moderate to severe rosacea. They have also found that this treatment greatly reduces the bulbous red nose of rhinophyma. They state, *"A 4- to 5-month course characteristically results in a striking involution of the disease process followed by remissions, even though therapy is discontinued"*.
- Dr. Orfanos reports that oral isotretinoin is extremely effective in treating severe rosacea sufferers with inflammatory papules, pustules, nodular lesions, redness, swelling, and rhinophyma.⁽²⁵⁾ He has found that most patients notice dramatic improvement within 4 to 8 weeks of treatment.
- Drs. Nikolowski and Plewig report excellent success with isotretinoin in 13 rosacea sufferers with severe inflammatory papules, pustules, swelling, and rhinophyma. Within 2 weeks of treatment, 50% of the inflammatory lesions were healed; after 8 weeks, over 95% of the lesions were completely gone. In this study, most patients also reported significant reductions in facial swelling. All patients (including rhinophyma patients) were in full remission at the 12-month follow up interview.
- In a clinical study on 6 rosacea sufferers, isotretinoin treatment resulted in excellent clearance of inflammatory papules and pustules.⁽³⁶⁾ In this study, all patients were symptom free at a follow-up interview, 14.8 months later.
- Numerous other clinical studies demonstrate that oral isotretinoin is a safe and effective form of treatment for rosacea sufferers.⁽³⁷⁻⁴⁵⁾

Low-Dose Isotretinoin: Effect on Rosacea

- In a superb clinical study, medical experts demonstrated that low-dose isotretinoin had potent anti-inflammatory actions on rosacea patients.⁽⁴⁶⁾ These specialists stated that isotretinoin, *"Controlled rosacea in every single patient faster and better than any other previously administered drug. The erythema and edema became much less prominent, and rhinophyma shrank an appreciable amount. Histologically, the severe inflammation in the upper dermis and the accompanying edema disappeared. The first patients on this protocol were in full remission for over 15 months at the time of writing."* In these patients, the average number of papules and pustules per face was 16 prior to treatment, and 0 during treatment. The mean scores for facial redness and swelling were 2.8 before treatment and 0.6 after treatment. The physicians conclude, *"These results indicate that inflammation was almost completely blocked by isotretinoin therapy"*.
- In a study performed on 47 rosacea patients treated with low-dose isotretinoin for 5 months, very good to excellent clearance was achieved in all patients. At follow-up examinations over a year later, 40 of 47 patients were found to be symptom free.⁽⁴⁷⁾

Note: Partial excerpt only. The complete e-book can be found at <http://www.drnose.com>

A clinical trial on 92 rosacea patients was undertaken to evaluate the effectiveness of a 5-month course of low-dose isotretinoin on rosacea symptoms. ⁽⁴⁸⁾ Isotretinoin was found to be extremely effective in clearing papules and pustules in most patients. Facial swelling and redness also improved considerably in most sufferers. In this study, sebaceous gland abnormalities (hyperplasia) disappeared, and rhinophyma shrank remarkably.

In a clinical study on 18 patients with severe rosacea, excellent results were achieved with low-dose isotretinoin. ⁽⁴⁹⁾

In a small clinical study, low-dose isotretinoin resulted in excellent clearance in 8 patients with rosacea. ⁽⁵⁰⁾

In an interesting study performed on 12 patients with vascular rosacea, low-dose isotretinoin was shown to decrease facial blood flow. ⁽⁵¹⁾ In this study, physicians measured cutaneous blood flow (via laser doppler) on the facial cheeks of all patients before and after isotretinoin treatment. They measured blood flow during normal room temperatures and high room temperatures (93.2 degrees Fahrenheit); *they found that after 10 weeks of isotretinoin treatment, blood flow through the rosacea cheeks decreased by an average of 40%.*

Very-Low-Dose Isotretinoin: Effect on Rosacea

In a clinical study on 22 rosacea patients, very-low-dose isotretinoin (10 milligrams per day) significantly decreased facial redness, papules and pustules. ⁽²⁾ Furthermore, burning sensations that had been reported by 18 patients at the beginning of the study were significantly decreased in all patients by the sixth week of treatment. In patients with rhinophyma, isotretinoin caused regression of at least 50% during treatment. No significant side effects were noted at this dosage.

In a second study on 8 rosacea subjects, very-low-dose isotretinoin (10 milligrams per day) resulted in significant clearance of facial papules, pustules

and facial redness. ⁽⁵³⁾ In this study, the medical experts speculate that a dose as low as 5 milligrams per day may be extremely beneficial to rosacea patients (with very little chance for side effects).

- In a third study on 6 rosacea patients, very-low-dose isotretinoin resulted in significant reductions in facial papules, pustules and rhinophyma. ⁽⁵⁴⁾ In this study, the remissions were long lasting and no significant side effects were observed.
- In a clinical study performed on 20 rosacea sufferers, very-low-dose isotretinoin treatment for 3 to 6 months resulted in good to excellent clearance of papules, pustules and facial redness. ⁽¹⁷⁾ After one year, 17 out of 20 patients remained in full remission demonstrating that isotretinoin has long-lasting favorable effects on rosacea.
- Drs. Jansen and Plewig recommend very-low dose isotretinoin (2.5 or 5.0 milligrams daily) for the treatment of rosacea. ⁽⁵⁵⁾ They state, *"This dose is surprisingly helpful in many forms of the disease "*. Patients on very-low-dose isotretinoin may respond slower than those on high starting doses, and may need to take isotretinoin for longer periods of time, but the side effects are greatly reduced, and the anti-inflammatory actions are substantial.
- Dr. Richard Odom, chair and professor of dermatology at the University of California, San Francisco, uses very-low-dose isotretinoin to treat facial papules, pustules, and redness of moderate to severe rosacea. ⁽⁵⁵⁾ For certain patients, he suggests using, *"10 milligrams of oral isotretinoin 2 to 3 times a week, or 20 milligrams 2 times per week."* Dr. Odom gives oral isotretinoin for up to a year, at which point he likes to decrease the dosage and eventually discontinue the drug. Noteworthy is the fact that side effects at this dosage are minimal to non-existent.
- In the 1999 medical textbook, *"Primary Dermatologic Care"*, medical specialists recommend the use of long-term, very-low-dose isotretinoin for the treatment of rosacea. They state, *"Very-low-dose therapy of 10 milligrams every other day may suppress the disease when used over a long period of time (years) and may*

also be helpful in the treatment of rhinophyma."⁽¹⁷⁾

- Consistent with the above reports, several medical experts are now recommending very-low-dose isotretinoin for the treatment of facial redness, inflammation, swelling, inflammatory lesions, and rhinophyma associated with rosacea.^(46,57,58)

Isotretinoin dosage: It is important for rosacea sufferers and their physicians to understand that there is a significant difference between very-high-dose isotretinoin treatment (used for nodulocystic acne), high-dose isotretinoin treatment (used for moderate acne), and very-low-dose isotretinoin (now recommended for rosacea). At the high dosages, isotretinoin may actually worsen facial redness and flushing; while at very low dosages, isotretinoin is a potent anti-inflammatory that usually decreases facial redness and inflammation.

Below is a general guideline for isotretinoin treatment (dosages are based on body weight). The dosages are given for the average male weight (150 pounds = 68 kilograms), and average female weight (100 pounds = 45 kilograms). *Rosacea sufferers should focus on the low- and very-low-dosages:*

Very-High Dose Isotretinoin
(2.0 milligrams/kilogram/day)

Average male = 136 milligrams per day
Average female = 90 milligrams per day

High-Dose Isotretinoin
(1.0 milligrams/kilogram/day)

Average male = 68 milligrams per day
Average female = 45 milligrams per day

******Low-Dose Isotretinoin******
(0.5 milligrams/kilogram/day)

Average male = 34 milligrams per day
Average female = 22.5

******Very-Low-Dose Isotretinoin******
(0.2 milligrams/kilogram/day)

Average male = 14 milligrams per day
Average female = 9 milligrams per day

******Very-Low-Dose Isotretinoin******
(0.1 milligrams/kilogram/day)

Average male = 6.8 milligrams per day
Average female = 4.5 milligrams per day

As the reader can appreciate, very-high doses of 136 milligrams per day for an average male (which causes facial redness), is quite different from very-low doses of 6.8 milligrams per day (which usually decreases facial redness).

Note on isotretinoin dosage: In some areas of Europe, oral isotretinoin is available in 2.5 and 5.0 milligrams capsules. In the United States and Canada, the smallest pre-made dose is 10 milligrams; however, all compounding pharmacies are able to make 2.5 or 5.0-milligram capsules.

My personal experience with isotretinoin: I was treated with very-low-dose isotretinoin for 1 year for my facial redness, papules, swelling, burning sensations, and rhinophyma. Oral isotretinoin was extremely effective on my facial papules, swelling and rhinophyma, and moderately effective on my facial redness and burning sensations. This was a true Godsend for me because I could not treat my face with any topical medication due to extreme skin sensitivity. Oral isotretinoin broke the vicious inflammatory cycle, and has resulted in long-lasting improvement in many aspects of my rosacea. Consistent with my experience, medical experts are now finding that 1 or 2 courses of very-low-dose isotretinoin may decrease the entire disease process.

Isotretinoin side effects: Oral isotretinoin is a serious medication that comes with a long list of potential side effects, some minor and others major. Some common side effects include dry lips and skin,

Note: Partial excerpt only. The complete e-book can be found at <http://www.drnase.com>

a transient elevation in cholesterol and triglyceride levels, mild headaches, and dry eyes.^{159-)} One serious side effect, and the one that causes most physicians to not use this medication, is that it can cause severe deformities to the unborn fetus. Thus, its use is contraindicated in women who are trying to get pregnant, or who are not using birth control (at least two forms) while sexually active. All patients considering this medication should sit down with their physicians and thoroughly discuss the most common side effects and the 'worst case scenarios' before starting treatment.

In a recent medical review in *Dermatology* titled, "*How Safe is Oral Isotretinoin* ", noted dermatologist Dr. Meigel thoroughly reviews isotretinoin including dosing, duration of treatment, and new insights into optimal treatment.⁽⁵⁹⁾ In this article Dr. Meigel emphasizes several important points. First, he stresses that the most common side effects are dryness of lips, nasal mucosa and eyes. In his experience, "*Pretreatment counseling and concomitant use of moisturizing agents usually manage these side effects effectively; in unusual cases of particularly poor tolerability, dose adjustments suffice*". All of these side effects are reversible upon discontinuation of the drug. Second, systemic side effects, which are much less frequent, can include joint and muscle stiffness, skeletal changes, and transient elevations in cholesterol and lipids. Third, Dr. Meigel indicates that isotretinoin is generally safe when used in moderation; in fact, he states, "*Patients with serious concomitant disease, such as insulin-dependent diabetes, epilepsy, spina bifida, transplant patients, renal failure patients, multiple sclerosis motor neuron disease, and others can safely be treated with isotretinoin at a standard cumulative dose of 120 milligrams/kilograms per treatment course.*"⁽⁵⁹⁾

A special warning must also be given to those rosacea sufferers taking isotretinoin who are planning on laser surgery for removal of blood vessels or rhinophyma. Facial surgery should **not** be performed while on this medication because there is an increased chance of poor wound healing and scarring.⁽⁵⁾ Patients are usually instructed to wait at least 6 months after stopping isotretinoin before undergoing any form of facial surgery.

3. ORAL ANTIHYPERTENSIVE MEDICATIONS

Effect on rosacea symptoms:

- **Moderately** effective at reducing some forms of flushing associated with nerve and hormonal activity.
- **Minimally** effective at reducing facial inflammation.
- Not effective at reducing papules, pustules, chronic redness, burning sensations, swelling, telangiectasia, or heart of the disorder.

Oral antihypertensive medications are now being used to reduce facial flushing that is mediated by sympathetic nerves and hormonal surges — i.e., those evoked by the 'fight-or-flight response', anxiety, stress, certain emotions, and spontaneous discharges.^(5,8,12,61) By decreasing major bouts of facial flushing, oral antihypertensive medications may also reduce facial inflammation in some patients.

ORAL ANTIHYPERTENSIVE MEDICATIONS: BETA-BLOCKERS (NADOLOL & PROPRANOLOL)

Nadolol

Oral beta-blockers work by blocking receptors in the heart and skin blood vessels that respond to neural and hormonal stimuli. These actions are helpful in reducing some forms of vascular flushing triggered by fight or flight situations, stress, anxiety, and certain emotional upsets. In the superb article, "*Recognizing and Managing Rosacea*"; Dr. Wilkin indicates that nadolol, a non-selective beta-blocker, may be somewhat helpful in reducing the flushing and blushing reaction to emotions and anxiety.⁽⁶⁾ Furthermore, in the study, "*Effect of Nadolol on Flushing Reactions in Rosacea*", Dr. Wilkin documented that nadolol may be helpful in reducing the intensity and duration of spontaneous flushing in some rosacea sufferers.⁽⁶²⁾

Note: Partial excerpt only. The complete e-book can be found at <http://www.drnose.com>

Rosacea Treatment by Therapy Type

Nadolol dosage: Dr. Wilkin recommends that rosacea sufferers take 40 milligrams of nadolol every morning.⁽⁸⁾ In a small percentage of patients, he sometimes increases the dosage to 80 milligrams. He states, *"The goal is to follow the heart rate: lowering the heart rate by 8 to 10 beats per minute is sufficient to alleviate - but not completely block - the anxiety-induced tachycardia and flushing."*⁽⁸⁾

Nadolol side effects: In general, nadolol is a very safe medication. Some subjects report mild sedation and light-headedness. The body usually adjusts to these side effects within the first few weeks of treatment.

Propranolol

Propranolol is a type of beta-blocker that may also be useful in the treatment of rosacea flushing.⁽⁸⁾ Propranolol may reduce the intensity of neural or hormonal flushing associated with fight-or-flight situations, stress, anxiety, certain emotional upsets, and spontaneous discharges.

Propranolol dosage: While nadolol is Dr. Wilkin's first choice of beta-blocker, he states that, *"If long-acting propranolol is chosen for its low cost, it should be administered according to the migraine regimen outlined in the Physician's Desk Reference."*⁽⁸⁾

Propranolol side effects: In general, propranolol is a very safe medication. Some subjects report mild sedation and light-headedness. The body usually adjusts to these side effects within the first few weeks of treatment.

Important: Limitations of Oral Beta Blockers

Beta-blockers are moderately effective at reducing some forms of facial flushing; however, general physicians should be aware that these medications are not the final solution for most rosacea sufferers. Physicians should understand that while these are an important part of the rosacea arsenal, most sufferers will need additional treatment in order to achieve more complete rosacea clearance.

Consistent with this, Dr. Wilkin demonstrated in a study of 15 rosacea sufferers that beta-blockers have

benefits and limitations.⁽⁶²⁾ He suggests that while beta-blockers may reduce flushing to anxiety, certain emotional strains, and spontaneous discharges, they do not alter other forms of flushing such as those induced by hot water, alcohol, or niacin. Other medical specialists concur with the above report, indicating that beta-blockers are only moderately effective for treating some forms of rosacea flushing.^(16,23,61,63)

ORAL ANTIHYPERTENSIVE MEDICATIONS: CLONIDINE, RILMENIDINE AND MOXONODINE

Clonidine

Clonidine is an effective antihypertensive medication. Clonidine is also one of the most popular rosacea medications due to its effect on neural and hormonal flushing. In the study, *"Clonidine and Facial Flushing in Rosacea"*, Dr. Cunliffe and colleagues studied the effect of oral clonidine (0.05 milligrams 2 times daily) on 17 rosacea patients who experienced frequent bouts of flushing.⁽⁶⁴⁾ These physicians found that low-dose clonidine significantly decreased the frequency and severity of flushing attacks in some sufferers. They concluded that clonidine may be beneficial to rosacea patients whose primary complaint is frequent flushing. In support of this, Dr. Wilkin indicates that in his clinical experience, oral clonidine can effectively reduce certain forms of neural and hormonal rosacea flushing.⁽⁶⁵⁾ Dr. Wilkin cites several reasons why clonidine may be effective in alleviating certain forms of rosacea flushing:

1. Clonidine may act directly on the facial blood vessels to cause mild constriction.
2. Clonidine may act centrally within the brain to decrease sympathetic nerve-mediated flushing.
3. Clonidine may act centrally to decrease internal body temperature.

Note: Partial excerpt only. The complete e-book can be found at <http://www.drnose.com>

It is also well documented that clonidine can reduce facial flushing associated with menopausal hot flashes. ⁽⁸⁾

Clonidine dosage: The recommended dosage for rosacea treatment is 0.05 milligrams 2 times daily. ^(8, 65) Some rosacea sufferers may experience greater benefits at higher dosages such as 0.05 milligrams 3 times daily, or 0.1 milligrams 2 times daily. ⁽⁶⁶⁾ High-dose treatment should only be performed under the tight supervision of a medical physician, and should only be increased gradually to this level.

Clonidine side effects: At the onset of treatment clonidine may cause sedation, mouth dryness, and fatigue. ⁽⁶⁷⁾ The body usually adjusts to these side effects within the first month of treatment. Patients are also cautioned not to abruptly stop this medication due to blood pressure-related side effects. Patients are always instructed to gradually taper off of this medication.

Rilmenidine

Rilmenidine is an antihypertensive medication that acts centrally within the brain to decrease sympathetic nerve activity. ⁽⁶⁸⁾ This oral medication has great potential for rosacea flushing due to its effectiveness in decreasing sympathetic nerve activity and its relative lack of side effects. This medication is more selective and potent than clonidine. Some medical references on rilmenidine's actions are included below:

- Numerous clinical and experimental studies demonstrate that rilmenidine is very effective at reducing sympathetic nerve activity. ⁽⁶⁹⁻⁷¹⁾
- A series of recent medical articles in the *Journal of Hypertension* demonstrates that rilmenidine dramatically reduces sympathetic nerve activity. ⁽⁷²⁾ These studies indicate that rilmenidine

helps to normalize human disease resulting from overactive sympathetic nerves. ^(71,73)

- In a 1999 multicenter study conducted in France, 18,235 hypertensive patients were treated with low-dose rilmenidine for 12 months and then re-evaluated. ⁽⁷⁴⁾ Low-dose rilmenidine (1 to 2 milligrams daily) was found to lower sympathetic nerve activity in 83% of the patients. Patients reported that side effects of treatment were generally mild and transient.
- A recent experimental study demonstrated that oral rilmenidine lowers resting sympathetic nerve activity, and decreases overactive sympathetic nerve activity in response to certain stress responses. ⁽⁷⁵⁾

Rilmenidine and rosacea: In a recent clinical study, "*Rilmenidine in Rosacea: A Double-Blind Study Versus Placebo*", physicians evaluated the effect of rilmenidine on rosacea symptoms (1 milligram per day for 3 months). ⁽⁷⁶⁾ Rilmenidine's main action was in reducing the number of rosacea flushes per day. Physicians stressed that these were only preliminary results and that other studies should be performed in order to evaluate rilmenidine's actions on the neuro-vascular component of rosacea. It is important to note that higher daily doses may be needed to achieve more complete sympathetic nerve blockade.

Rilmenidine dosage: There are currently no general guidelines for rilmenidine dosing in rosacea treatment. In the above study, rilmenidine was given at 1 milligram per day. ⁽⁷⁶⁾

Rilmenidine side effects: This medication has fewer side effects than clonidine because it is very selective for certain receptors within the brain. It does not usually cause sedation, mouth dryness, and fatigue like clonidine. ⁽⁶⁷⁾

Moxonodine

Moxonodine is an antihypertensive medication that also acts centrally within the brain to decrease sympathetic nerve activity.⁽⁶⁸⁾ Numerous clinical studies demonstrate that moxonodine is very effective at reducing sympathetic nerve activity.⁽⁶⁹⁻⁷¹⁾ In a recent medical review comparing moxonodine to rilmenidine, moxonodine was found to be more potent and selective than rilmenidine.⁽⁶⁸⁾

Oral moxonodine has great potential for rosacea sufferers; however, clinical studies have not yet been performed on rosacea sufferers.

My personal experience with moxonodine: I found moxonodine (Physiotens filmtabs™, Solvay Pharma, 0.4 milligrams) to be one of the most effective oral medications on my sympathetic nerve- induced flushing (fight-or-flight flush, thermoregulatory flush, anxiety/stress flush, and spontaneous flush). It was not a cure, but it significantly decreased the number and intensity of nerve-induced flushes. I personally found it to be much more effective than clonidine, with fewer side effects.

Moxonodine dosage: There are currently no general guidelines for moxonodine dosing in rosacea treatment. Rosacea sufferers may be instructed to follow the general guidelines used for the treatment of hypertension.

Moxonodine side effects: This medication has fewer side effects than clonidine because it is very selective for certain receptors within the brain. It does not usually cause sedation, mouth dryness, and tiredness like clonidine.⁽⁶⁷⁾ In a 1998 medical article in *Drug Safety*, the safety and tolerability of moxonodine was reviewed over an 8-year period (1989 to 1997), including 74 clinical trials and an estimated 370,000 patient-years of exposure.⁽⁷⁷⁾ The safety profile was found to be excellent, and the adverse side effects were generally minor and transient.

4. ORAL NON-STEROIDAL ANTI-INFLAMMATORY MEDICATIONS

Effect on rosacea symptoms:

- Moderately effective at reducing facial inflammation, swelling and burning sensations.
- Minimally effective at reducing some forms of facial flushing and redness.
- Not effective on facial papules, pustules, general flushing, telangiectasia or heart of the disorder.

ORAL NON-STEROIDAL ANTI-INFLAMMATORY MEDICATIONS: NAPROXEN AND COX-2 INHIBITORS

Naproxen

Naproxen is a non-steroidal anti-inflammatory medication that inhibits the production of inflammatory prostaglandins. While the active flushing in rosacea is not usually due to prostaglandins, those sufferers who have longstanding facial inflammation may benefit from these anti-inflammatory medications (i.e., to help knock down the inflammatory environment and flushing intensity).

In the medical article, "*Tips from the Experts: Dermatologic Therapy*", Dr. John Epstein of San Francisco, California, indicates that he uses oral non-steroidal anti-inflammatory drugs such as naproxen to help alleviate some of the burning and flushing associated with rosacea.⁽⁷⁸⁾ He treats his patients with 250 milligrams of naproxen twice daily until symptoms respond, and then tapers the dosage down to 250 milligrams every other day. Drs. Hooper and Goldman also indicate that non-steroidal anti-inflammatory agents may help decrease facial inflammation associated with rosacea.⁽⁷⁾

Naproxen dosage: There are currently no general guidelines for naproxen dosing in the treatment of rosacea. Patients may notice improvement of rosacea symptoms with 250 milligrams once or twice daily.

Naproxen side effects: The most common side effects are gastrointestinal-related such as abdominal pain, diarrhea, and constipation. Some may also experience gastrointestinal bleeding and ulcer formation.

Cox-2 Inhibitors

A new class of anti-inflammatory medications called Cox-2 inhibitors is now available. Cox-2 inhibitors (nicknamed 'super aspirins') are potent inhibitors of an enzyme called Cox-2 that produces inflammatory prostaglandins.^(79,80) The main difference between Cox-2 inhibitors and traditional non-steroidal anti-inflammatory drugs (i.e., naproxen and aspirin) is that traditional non-steroidal medications usually cause more gastrointestinal side effects. To explain, researchers have identified two forms of Cox enzymes; Cox-1, which releases 'good' prostaglandins that protect the stomach and Cox-2, which releases 'bad' prostaglandins that cause inflammation. Traditional non-steroidal anti-inflammatory drugs such as naproxen inhibit both Cox-1 and Cox-2 enzymes. Since Cox-1 prostaglandins protect the stomach, diminishing them with naproxen treatment may lead to gastrointestinal side effects, stomach discomfort, bleeding, and peptic ulcers. The new Cox-2 inhibitors do not affect the protective prostaglandins of the stomach, but are very effective at blocking inflammatory prostaglandins that are produced in areas of chronic inflammation.^(79,80)

Like naproxen, Cox-2 inhibitors may be helpful in reducing chronic facial inflammation and decreasing the intensity of certain forms of flushing. Cox-2 inhibitors may also reduce facial burning sensations in moderate to severe rosacea sufferers.

Cox-2 inhibitor dosage: There are currently no general guidelines for Cox-2 inhibitor dosing in the treatment of rosacea. Celebrex™ (Searle & Pfizer Pharmaceuticals) is a popular Cox-2 inhibitor that is

generally taken in doses of 100 milligrams, two times daily.

Cox-2 inhibitor side effects: These medications have very few side effects and are generally much gentler on the gastrointestinal tract than naproxen.

5. ORAL ANTIHISTAMINES

Effect on rosacea symptoms:

- Moderately effective at reducing facial swelling, and itching or burning sensations.
- Minimally effective at reducing facial inflammation and some forms of flushing.
- Not effective at reducing facial redness, general flushing, papules, pustules, telangiectasia, or heart of the disorder.

ORAL ANTIHISTAMINES: ZYRTEC™

In a recent medical article, "*Drug Therapy of Rosacea: A Problem-Directed Approach*", Dr. Singer indicates that antihistamines may be helpful in decreasing rosacea symptoms.⁽⁵⁾ Antihistamines may be beneficial to rosacea sufferers for several reasons. First, allergy or food-related histamine release may cause or intensify facial flushing.⁽⁸¹⁻⁸⁴⁾ Second, histamine release is known to contribute to swelling and uncomfortable skin sensations such as itching and burning.⁽⁸⁵⁾ Third, histamine has been shown to play a role in long-standing inflammation and skin redness.⁽⁸⁶⁾ Therefore, blockade of histamine may potentially decrease some forms of rosacea flushing, and reduce facial swelling, general inflammation, and uncomfortable itching or burning sensations.

Newer, second-generation antihistamines such as cetirizine hydrochloride (Zyrtec™, Pfizer Labs) may play an important role in reducing some rosacea symptoms. Zyrtec™ is an effective histamine blocker that has several major advantages over the older, first-generation antihistamines:^(82,84,87)

Rosacea Treatment by Therapy Type

- Zyrtec™ is much longer acting (24-hour acting).
- Zyrtec™ does not affect the central nervous system (i.e., it does not cause drowsiness).
- Zyrtec™ does not have significant anti-cholinergic actions (i.e., it does not cause dry mouth).

Zyrtec™

Zyrtec™ may alleviate symptoms in moderate to severe rosacea sufferers by reducing flushing to allergies and histamine-containing foods, and decreasing facial swelling and inflammation. Consistent with this, studies have demonstrated that Zyrtec is able to reduce the severity of inflammatory skin disorders such as psoriasis and atopic dermatitis.^{(87), (88)}

Zyrtec™ dosage: There are currently no general guidelines for Zyrtec™ dosing in the treatment of rosacea. Zyrtec is usually taken once daily at dosages of 5 or 10 milligrams.

Zyrtec™ side effects: Although this second-generation antihistamine has fewer side effects than older antihistamines, it can still cause mild drowsiness and dry mouth in some subjects. In patients with moderate to severe ocular rosacea, antihistamine therapy may also exacerbate dry eye symptoms. This side effect is usually controlled by frequent use of moisturizing eye drops.