

# Acne and Rosacea: Lifestyle and pharmacologic intervention

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**Disclosures** 

- Speaker's Bureau for Abbvie, Beiersdorf, Eli Lilly, Janssen, Sanofi Genzyme, Sanofi-Aventis/Regeneron®, and Sun Pharma
- Strategic Advisor and Medical Board Member: Arcutis Biotherapeutics, Incyte Labs, Leo Pharma, and Novartis.
- No experimental or investigational use of drugs or devices will be presented.

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**Objectives** 

• At the end of this presentation, the participant will be able to:

Identify the pathophysiology of acne and rosacea.

Describe the most effective lifestyle and pharmacologic approaches for treatment.

Recognize new indications and cautions for established products.

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# Tips



- References
- Listed throughout and at the end of the presentation
- To facilitate your learning
- Specific tables/images can be viewed full page at the end of your handout.

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# **Acne Vulgaris**

- Acne vulgaris is considered a key driver of teen depression and suicidal ideation.
- However, many insurance companies will not cover acne treatments when the policy-holder becomes aged 18 or 21 years old.



#### **Introduction to Acne**

- Acne vulgaris accounts for 12% of all dermatology visits.
- Most common skin disorder in America, with 17 million people suffering at any given time
- #1 most common dermatology diagnosis
- Considered by many one of the most difficult conditions to treat.
- Drug resistance, compliance, access to medications, drug reactions, and home remedy additions/social media confusion

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# Acne Vulgaris (continued)

 At that point, it is considered "cosmetic" and thus not necessary for treatment.



# **Acne Fast Facts**

- Women affected slightly more than men, especially when older (age 40+ years).
- Not common in some non-Westernized peoples
- Cleopatra used sulfur soap.
- From Greek "ionthos" for "facial eruption," or Latin "acnae"
- Bacteria first observed in acne in the mid-1880s.



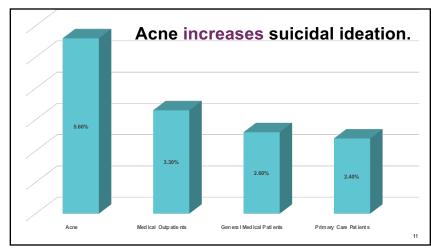
# Psychological Effects of Acne

- Acne can have profound social and psychological effects not related to its clinical severity.
- Affects around 85% of people between ages 12 and 25 years.
- Appearance linked to peer status
- Distress may result in depression and suicidal ideation.



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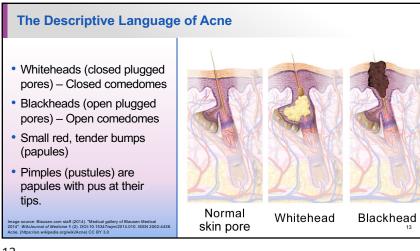
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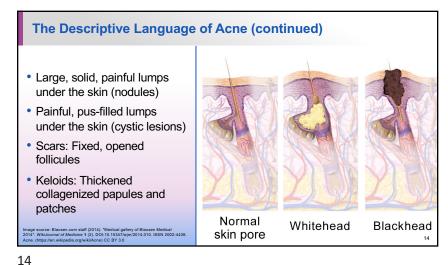


# **Psychological Impact of Acne (continued)**

- Teens say parents misguided in perceptions of severity
- Only 30% of teens seek medical help, 70% too discouraged.
- Of the teens who sought medical help, 91% reported improvement.
- Huge over-the-counter market
- Studies show severity of acne can affect job seekers.

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# **Another Case Study:**

What are the patient's concerns?

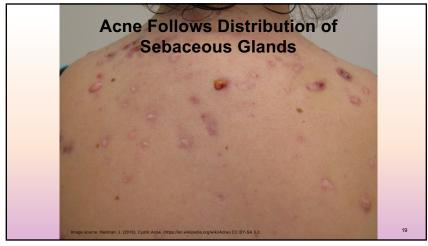
# **Risk Factors**

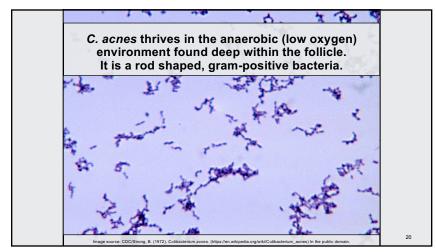
- Age: People of all ages can get acne, but it's most common in adolescents.
- Hormonal changes: Puberty, menopause, testosterone/ estrogen treatment, or pregnancy
- Family history: If both parents had acne, you're also likely to develop acne.

- Pressure on skin: Oily places breed acne.
- Hairstyles, caps, headphones, cellphones, helmets, tight collars and backpacks
- Diet: Sugar and dairy are highly inflammatory and promote hormonal androgenetic excess.

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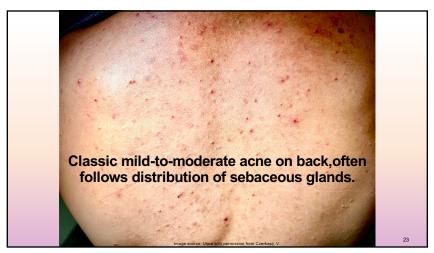


# **Acne: Multi-Factorial Inflammatory Disorder**

- Excess oil (sebum) production
- Hair follicles clogged by oil and dead skin cells
- · Bacteria (acne)
- Inflammatory cascade

- Diet research continues to support dairy avoidance.
- Think reverse engineering: If the previous four are the problem, going forward, how do we treat acne?

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# Acne Treatment

Inflammatory scarring is a challenge.

- "Domolene" popular mid-20<sup>th</sup> century topical treatment for acne
- It was simple hydrocortisone, which assisted in mild inflammation but did not address the acne proliferation or sebum production.
- Eventually caused atrophy

Image sources: Wellcome Collection gallery (2018-03-30): https://wellcomecollection.org/works/bs6b2h52 (2014)Jar of 
"Domolene" ointment (https://commons.wikimedia.org/wiki/File:Jar\_of\_%27Domolene%27\_ointment\_\_London\_\_England\_\_15



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# Social Media Recommendations for Acne Treatment: Recommend to Avoid Social Media!

- Do-it-yourself (DIY)
   "skinfluencers" share expertise with no real credentials except for millions of followers.
- Their main shtick: You can use "natural" products in your pantry or fridge to treat your skin issues, especially acne.
- The Great Toothpaste Hoax

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- Band-Aids on Every Pimple Prank
- Salt-water Spritzing Swindle
- The Lemon Juice Scar Treatment Fraud
- Drinking Chlorophyll Water Con
- The Skin Icing Dupe
- The Popular Potato Slice Ruse

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# **The Major Treatment Categories for Acne**

- Topical: Drying agents and topical antibiotic
- Oral antibiotics
- Hormonal/oral contraceptive
- Anti-inflammatory products
- Isotretinoin
- Combination therapy including diet
- Light and thermal devices

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# Realistic Treatment Goals with Acne

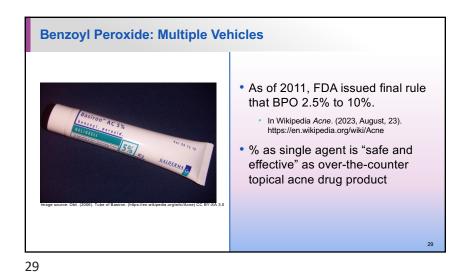
- Improve and control the condition for flares.
- Prevent the development of new lesions and scarring.
- Treat postinflammatory hyperpigmentation, if present.
- Avoid adverse effects from the medication regimen.
- DO NOT DO MONOTHERAPY TREATMENTS.

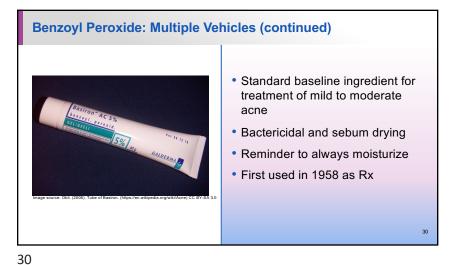
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# **Topical Therapy for Acne**

- Benzoyl peroxide (BPO) is bactericidal.
- Has never been shown to induce resistance
- More effective than topical clinda- and erythromycin in multiple studies
- Multiple concentrations and combinations in various vehicles, both prescription and OTC
- Can be applied topically to affected areas once a day
- Remind patients that it bleaches clothing!

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Salicylic Acid

From Latin "salix" or "willow tree"; basic compound of aspirin

Breaks down oily sebum in clogged pores, effective at 2%

10% to 40% will dissolve warts.

Begin with limited use to assess skin irritation possibilities.

Considered bacteriostatic

Image source: Obt al Einglath-language Wikipedia. (2008). Salicylic acid. (https://en.wikipedia.org/wikijSalicylic\_acid) CC BY SA.3.0

Clindamycin 1% Gel, Foam,
Solution, Cream, Lotion

Often applied to forehead, cheeks, chin,
and nose

Works best when combined with BPO use
Generic, bacteriostatic effect

Image source: Briamaflo520, (2019). Clindamycin phosphate topical solution
(https://commons.wikimedia.org/wikiFite.Clindamycin\* jeg) CC BY-SA 4.0

# **Azelaic Acid Foam or Cream**



- Azelaic acid both bacteriostatic and bactericidal, no inducement of antibiotic resistance
- Dicarboxylic acid, commonly found in wheat, rye, and barley
- Superior anti-inflammatory properties
- Not studied in pregnancy

Image source: Original book source: Prof. Dr. Otto Wilhelm Thomé Flora von Deutschland, Österreich und der Schweiz 1885, Gera, Germany. (https://en.wikipedia.org/wiki/Barley) In the public domain.

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## First-generation Retinoid Tretinoin: Multiple Vehicles

- Tretinoin Vitamin A derivative for both inflammatory and non-inflammatory acne.
- Often used in conjunction with other topicals to enhance follicular penetration
- Avoid with pregnant, breast-feeding women
- Photosensitivity is high

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 Effective, multiple vehicles and concentrations combined with oral antibiotics

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# First-generation Retinoid Tretinoin: Multiple Vehicles (continued)

- Excellent for photoaging problems and PIHP
- Developed in late 1950s with use on prison inmates in Pennsylvania
- First prescribed in 1962
- In the "Top 200" of all-time prescriptions

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# Second-generation Retinoid: Tazarotene

- Tazarotene 0.1% and 0.05% in cream, gel and foam bases
- Familiar in psoriasis and photodamage treatment
- Common adverse effects include worsening acne, sun sensitivity, dry skin, itching, redness, drying and cracking of skin.
- Adverse effects generally decrease after first 2–4 weeks of use.

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# Third-generation Retinoid: Adapalene 0.1% OTC and 0.3% Rx

- Synthetic retinoid that limits photosensitivity adverse effect: The tolerable retinoid
- Very helpful in bumpy, sharp keratotic papules

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- Enhances topical clindamycin gel/lotion use
- More stable chemical structure allows it to be combined with benzoyl peroxide in same formulation.

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#### Fourth-generation Retinoid: Rx 0.005% Trifarotene Cream

- Oral and topical dapsone used for acne since early 1950s.
- A sulfur compound antibiotic with bacteriostatic action, used chiefly in the treatment of leprosy in the past.
- Effective for inflammatory acne
- Minimal absorption, can be used twice a day
- Cannot be combined with BPO, as the skin can turn bright orange
- Controversy in dermatology if first- or second-line therapy
- Common adverse effects include nausea and loss of appetite.

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# Dapsone 5% and 7.5% Cream and Gel

- Indicated for the topical treatment of acne in people ages 9 years and older
- Contraindicated in pregnancy
- Little photosensitivity though still recommend evening application
- Superior results on truncal and facial acne
- Overall, considered quite gentle

# Androgenetic or Hormonal Therapy for Acne: An Option for Females

- Spironolactone: Potassiumsparing diuretic and aldosterone blocker
- Not FDA-approved for acne
- Longtime "well-established practice"
- Use for acne considered off-label in dermatology.
- 25 mg and 50 mg; 1 by mouth once or twice a day to begin and can be increased to 100 mg 1 PO qday.
- Also effective in female pattern hair loss, facial hirsutism and of course, at higher doses, blood pressure

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# Androgenetic or Hormonal Therapy for Acne: An Option for Females (continued)

Common adverse effects include...

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- More energy, tiredness, nipple tenderness, more frequent urination and dry mouth
- Blocks the conversion of testosterone to dihydrotestosterone
- Responsible for most hair growth alterations and acne

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# **Additional Information**

There are 4 FDA-approved combined oral contraceptives for treatment of acne. These take time *and* dermatology is leery.

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# Additional Information (continued)

- Newest topical cream: FDA-approved antiandrogen clascoterone 1%, for ages 12 years and older
- Blocks dihydrotestosterone (DHT) without secondary hormonal issues
- Good secondary product, being used also in rosacea
- Does not have drying as its primary action, but sebum reduction and not an antibiotic.
- Some feel it is more effective in males over females.

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# **The Relapsing Female Patient**

- Remember that pediatric endocrinology is your friend and an excellent referral option for the patient with suspected polycystic ovarian syndrome (PCOS).
- 17-hydroxylase deficiency should be considered.
- Congenital adrenal hyperplasia?
- Is there increased hirsutism?

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# **Controversial: The Use of Oral Prednisone for Treating Acne**

- Rapid-acting corticosteroid, very helpful as anti-inflammatory
- Key questions: Amount and time
- 5–10 mg; 1 PO qday for a month concomitantly with antibiotic or isotretinoin reasonable for severe acne
- Beware of rebound effect
- Overall, not a frontline recommendation

## **Oral Antibiotic Therapy in Acne**

- Doxycycline and minocycline extended release effective 1 mg/kg/day
- Markedly lower adverse effects
- Use in moderate to severe acne
- Enteric-coated doxycycline results in less GI adverse effects than immediate release formulations.
- Minimum one-month therapy; maximum three months
- Classic adverse effects are nausea, vomiting, diarrhea, dizziness and photosensitivity.
- Tetracycline not used much; new Rx sarecycline oral antibiotic is fourth generation of the -cyclines.

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#### How does acne become resistant to antibiotics?

- New resistant strains
- Failure to consider nare colonization
- Inadequate drug potency
- Inadequate treatment duration
- Inadequate patient education and compliance

**The Acne Vaccine** 

- Recent promising results in mice and humans
- Avoids topical regimens and improves compliance
- Limits use of antibiotics and subsequent resistance
- What are the results in the human body long-term?
- Should we neutralize a stable community of normal skin bacteria that is known to protect the skin from colonization by more harmful micro-organisms?
- Research continues as should questions.



#### The Isotretinoin Challenge: Will we practice on the evidence?

2/4/08 (San Antonio) – In the largest study of its kind, more than 9.6 million patient visits "failed to demonstrate an association between isotretinoin use and increased depression or suicide."

- Solid answer to antibiotic resistance
- American Academy of Dermatology 66<sup>th</sup> Annual Meeting
- Developed over 40 years ago, one of the safest and most predictable medications of the 20<sup>th</sup> century

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The Seminal New England Journal of Medicine Study 2005

- Nearly all patients achieve initial clearing of acne.
- 60% observe complete remission following one course of isotretinoin.
- 30% developed less severe acne.
- 10% relapse to warrant further treatment or an additional course of isotretinoin, without additional newer adverse effects.

The Seminal New England Journal of Medicine Study 2005 (continued)

- Isotretinoin-related depression, in one study, was found as "an idiosyncratic side effect." Often anxiety of potential adverse effects can bring on acne and depression, creating more anxiety.
  - Affects approximately 1% of patients on isotretinoin

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#### Isotretinoin is a vitamin A derivative.

- Brand names include Amnesteem<sup>®</sup>, Roaccutane<sup>®</sup>, Sotret<sup>®</sup>, Claravis<sup>™</sup>, Absorica<sup>®</sup> and Zenatane<sup>™</sup>, among others.
- The iPledge program protects patient and provider.
- Blood work to begin and once later in the 4–5-month course of treatment
- Adverse effects are generally predictable and consistent
- Dry eyes, nose, lips and skin

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# The iPledge Program, Summarized

- Blood work prior to prescribing for liver and lipid abnormality
- For females, two negative pregnancy tests and monthly thereafter
- Two forms of birth control
- iPledge online accessed monthly

- Prescribe for 30 days, no refills.
- Product dispensed and obtained within 7 days of qualification.
- Patient and parent educated with verbal discussion and written contract of warnings and hazards.

#### **Isotretinoin** is a vitamin A derivative. (continued)

- Severe adverse effects
- When drinking alcohol, photosensitivity, and birth defects
- · Females must have monthly pregnancy test.
- Can only dispense 30 pills at one time
- Mood improvement often observed.
- Be wary of bipolar, noncompliant, IBS, Crohns, hepatitis and the flippant.
- Always take with full meal.

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# The Skinny on Acne and Diet

- Foods that increase insulin levels magnify male hormone effect
- Dairy products boost insulin and are high in hormones made by pregnant cows that produce milk.
- Avoid dairy and sugar to lessen oil stimulus production.



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# Are there recommendations for reliable OTC skin maintenance products? Absolutely!

- Consider non-soap cleansers and sulfur-based soaps.
- Combination products with salicylic acid + niacinamide
- Niacinamide 10% with 1% zinc
- Vitamin C + vitamin E serums
- Combined are more effective.

- Retinoids + ceramides
- Glycolic washes and foams
- Hyaluronic B5 serums
- All combinations should not be used in combination or succession with BPO.

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# **Rosacea: An Introduction**



- Rosacea is an inflammatory condition as opposed to acne, which is primarily a bacterial disease.
- Older dermatology wrongly titled this condition "acne rosacea," though the treatment paradigms are quite different.
- They are both discouraging and require attention to care and detail.

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# **Rosacea: An Introduction (continued)**

- April is Rosacea Awareness month: Why do you think?
- Affects 16 million Americans
- The goals are control, not cure.
- 76% of rosacea patients experience lowered self-esteem and self-confidence.
- Pt must primarily become educated in daily skin care and trigger control.



# Famous People with Rosacea Left image source: Defensis (2019). Price Marry, Duke of Sustex. (https://en.wk.pedia.org/wki/Bil. Clinton). CC BY-SA 2.0. 60

# Famous People with Rosacea

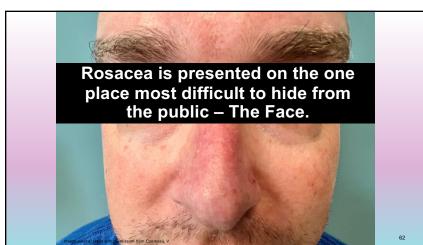




(Induction adapted on generating Co. Strong, Lemmeyer)

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# Rosacea Background

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- Rosacea is an inflammatory disease that affects primarily women 8>1 over men.
- Scots/Irish, Dutch/German and Scandinavian peoples ages 40 and older are the target population.
- Worst two triggers: Uncontrolled sunshine and increased stress.

- Other common triggers are...
- Coffee, chocolate, caffeine, hot foods, spicy foods, acidic foods (i.e., tomatoes, citrus, pineapple and strawberries) and wines
- Hispanic, Asian, and Black populations are not immune and often misdiagnosed, especially for acne.

**Rosacea Types and Variants** 

- Erythematotelangiectatic rosacea (ETR) has facial redness, flushing and visible blood vessels because of the ongoing inflammation.
- Papulopustular appears as acne in middle-aged women.
- Phymatous rosacea affects many men and thickens the nose.
- Ocular rosacea centers periorbitally and feels like grains of sand.

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# The Rosacea Challenge

Multiple challenges exist to address...

- Ongoing discussion of cause
- Provider inexperience to diagnose accurately
- Treatment combinations

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• Encouraging lifestyle change



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#### **Ocular Rosacea**

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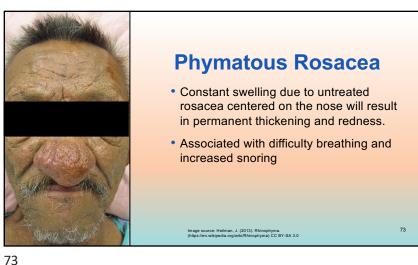
- Differentials include contact, perioral or seborrheic dermatitis, or true conjunctivitis.
- Itchy, scratchy, gritty eyes with swollen eyelids and tearing.
- 40 mg doxycycline helpful, as is ketoconazole 2% shampoo wash.

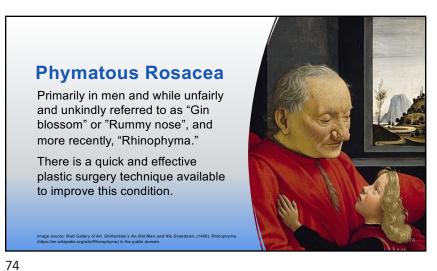
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# **Ocular Rosacea (continued)**

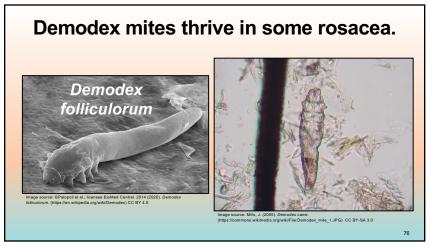
- Can occur prior to skin disease
- Abnormal Schirmer's test in 40% rosacea patients
- Topical corticosteroid eye drops effective for pruritus relief.











# **Classic Topical Therapies for Rosacea**

- Metronidazole 0.75% and 1% cream and gel
- Applied once or even twice daily
- Prescription brimonidine 0.33% is a topical alpha-adrenergic agonist gel for the treatment of persistent erythema (redness) in rosacea.
- Applied once daily or as needed
- Duration of peak effectiveness is three to six hours.

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#### **Classic Topical Therapies for Rosacea (continued)**

- Oxymetazoline 1% cream also reduces flushing by constricting blood vessels.
- Results occur within 12 hours after use.
- The effect on the blood vessels is temporary, so the medication needs to be applied regularly to maintain improvements.

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## **A Popular Rosacea Addendum Product**

- Sulfacetamide sodium/sulfur is a topical Rx medication used to treat rosacea.
- Effective for acne and seborrheic dermatitis

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- It is available in a variety of preparations including creams, gels and cleansers.
- Also available in several dosages – Most common is 10% sulfacetamide sodium/ 5% sulfur
- It is applied once or twice daily.
- Multiple OTC bar soap forms available over the counter.

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# **Key Therapies for Rosacea**

- Prescription azelaic acid foam and gel 15% and 20%
- Twice daily and avoid the eyes
- Decreases redness, swelling and blistering
- Hypopigmentation in darker skin is possible but rare.
- Look for any product with niacinamide as a co-ingredient.

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# **Ivermectin 1% Cream for Rosacea: Why?**

- Prescription ivermectin 1% cream can be used daily for rosacea control.
- · Marketed originally for its helpful anti-inflammatory effects.
- The reason for an antiparasitic was not lost on some providers.
- Generally, a very well-tolerated and helpful topical with blister and redness reduction when regularly used.
- Main complaints include drying and irritation.

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# Why do we use "-cyclines" for rosacea flares if rosacea is NOT bacterial?

- The anti-inflammatory effect of low-dose doxycycline and minocycline are very helpful for reducing flares.
- Recommend 100 mg 1 PO qday for up ten days for flares.
- Even better, consider sub-microbial 40 mg doxycycline
   1 PO qday for one-month.
- Since 2006, once daily 40 mg extended-release doxycycline has been the only oral treatment approved by the FDA.

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#### Rx 5% Benzoyl Peroxide Cream for Rosacea

- Although BPO may have previously been thought of as too irritating for rosacea skin, the BPO in this Rx product is formulated differently.
- Visible results as early as 2 weeks with blistering reduced by nearly 70% in 12 weeks.
- Nearly 50% of trial participants had clear or almost clear skin in 12 weeks.
- After 52 weeks of use in clinical trials, most people had mild adverse effects and were able to tolerate the medication daily.

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## On the Horizon for Rosacea Treatments

- Topical minocycline foam 4% was here during COVID and then disappeared as the company is restructuring. It may be back.
- The mainstay of daily therapy remains gentle cleansers and careful treatment of the facial skin.
- Stress and anxiety control is necessary for a foundation of maintaining clear skin.
- Sunscreen application of 30 SPF daily is part of the lifestyle.

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# End of Presentation Thank you for your time and attention.

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#### Rosacea Resources

- National Rosacea Society has free smart phone app for patients. See www.rosacea.org or popular app sites
- Rosacea Resource Center for providers at The American Academy of Dermatology Association, https://www.aad.org/public/diseases/rosacea

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