

# Rosacea

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# Disclosures

- Galderma – investigator and speaker
- Ortho Dermatologics – advisory board, author
- Almirall – advisory board and author
- L’Oreal – advisory board and author
- National Dairy Council - advisor

# Outline

- Epidemiology
- Classification of Rosacea
- Review of Treatments
- Photosensitive or thermosensitive disease?
- Long term maintenance
- Rosacea in the skin of color patient
- Botulinum toxin for flushing?
- Look for the take home messages



# Epidemiology

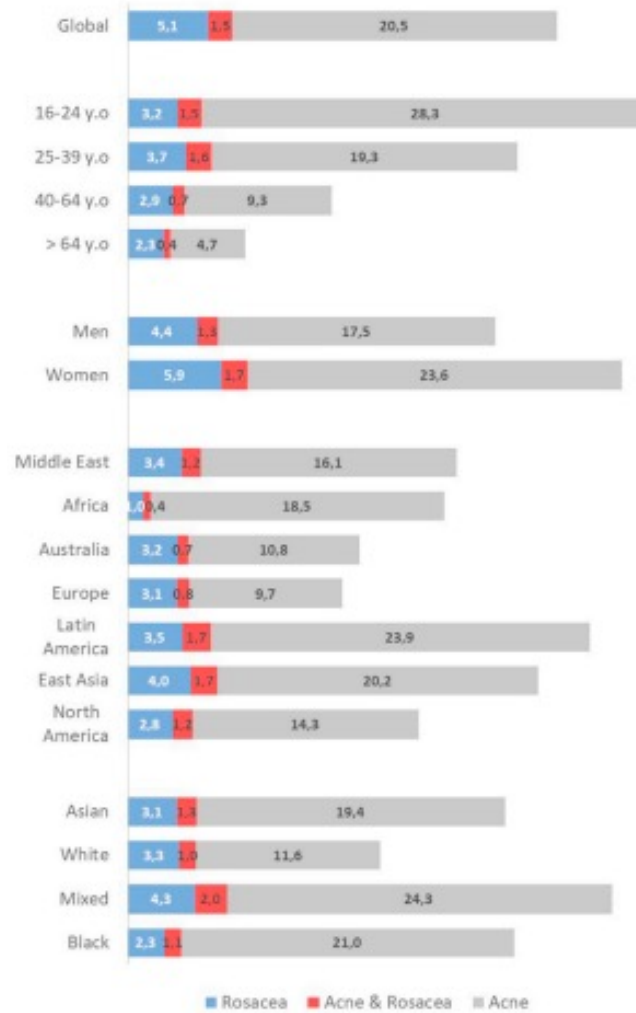
- This study showed an overall prevalence of rosacea of 5.1%.
- Prevalence by age group:
  - Years old 25 to 39 (3.7%)
  - Years old 40 to 64 (2.9%)
    - **Contrary** to other studies with highest estimates above 40 years old.
- Regarding rosacea:
  - highest prevalence was in East Asia
  - lowest in Africa

# Epidemiology

- Individuals with **mixed ethnicity** had the highest prevalence of acne and rosacea, followed by Asian for acne and White for rosacea.
- Significantly lower quality of life and higher stigmatization was noted when having **both disorders** vs having one of them.
- Rosacea had a significantly higher impact on quality of life

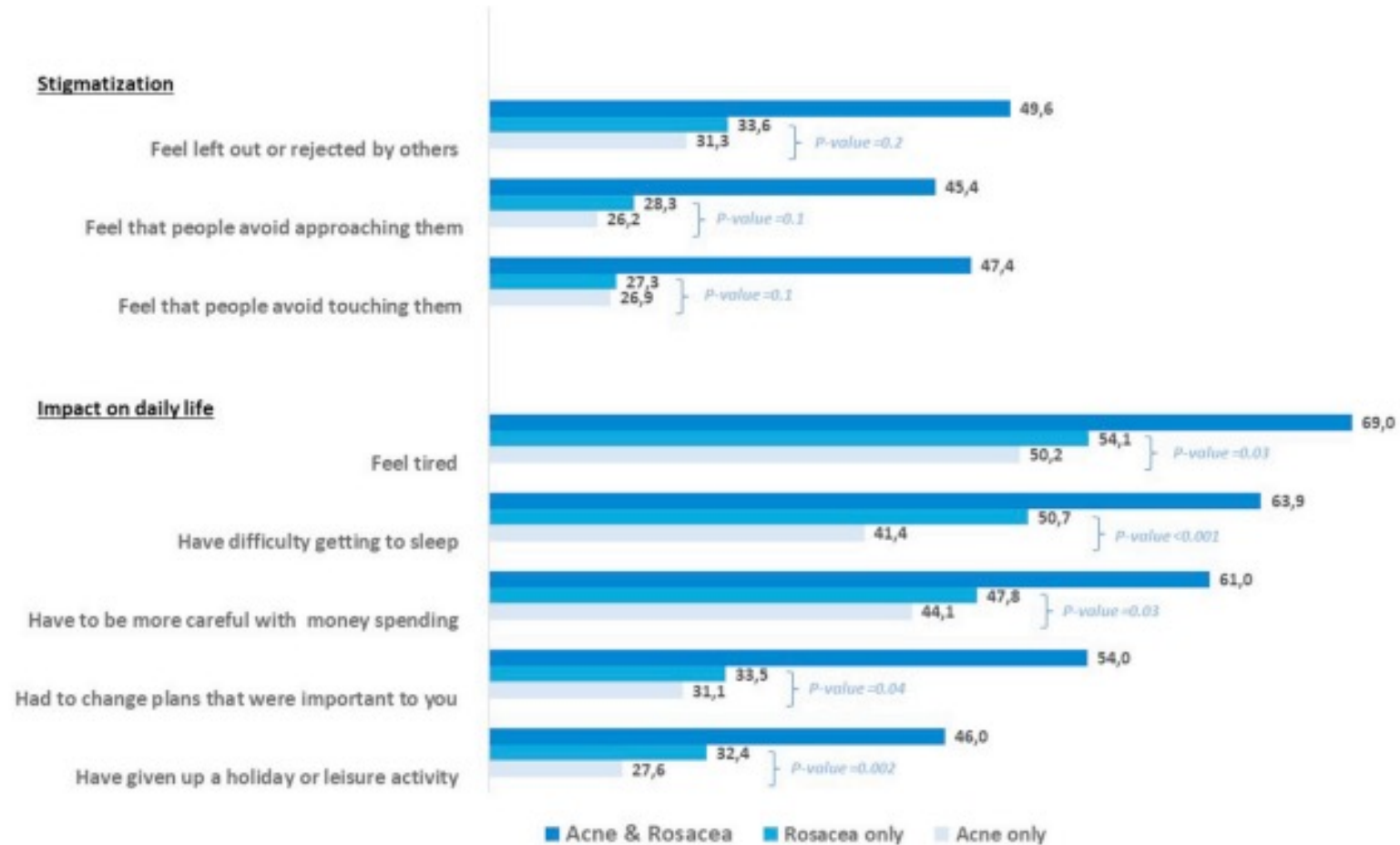


# Prevalence of Rosacea



Saurat JH, Halioua B, Baissac C, Cullell NP, Ben Hayoun Y, Aroman MS, Taieb C, Skayem C. Epidemiology of acne and rosacea: A worldwide global study. J Am Acad Dermatol. 2024 May;90(5):1016-1018. doi: 10.1016/j.jaad.2023.12.038. Epub 2024 Jan 4

# Quality of Life



Saurat JH, Halioua B, Baissac C, Cullell NP, Ben Hayoun Y, Aroman MS, Taieb C, Skayem C. Epidemiology of acne and rosacea: A worldwide global study. J Am Acad Dermatol. 2024 May;90(5):1016-1018. doi: 10.1016/j.jaad.2023.12.038. Epub 2024 Jan 4

# New Classification of Rosacea

Diagnostic <sup>*</sup>	Major <sup>†</sup>	Secondary
<ul style="list-style-type: none"> <li>• Fixed centrofacial erythema in a characteristic pattern that may periodically intensify</li> <li>• Phymatous changes</li> </ul>	<ul style="list-style-type: none"> <li>• Flushing</li> <li>• Papules and pustules</li> <li>• Telangiectasia</li> <li>• Ocular manifestations</li> <li>• Lid margin telangiectasia</li> <li>• Interpalpebral conjunctival injection</li> <li>• Spade-shaped infiltrates in the cornea</li> <li>• Scleritis and sclerokeratitis</li> </ul>	<ul style="list-style-type: none"> <li>• Burning sensation</li> <li>• Stinging sensation</li> <li>• Edema</li> <li>• Dryness</li> <li>• Ocular manifestations</li> <li>• “Honey crust” and collarette accumulation at the base of the lashes</li> <li>• Irregularity of the lid margin</li> <li>• Evaporative tear dysfunction (rapid tear breakup time)</li> </ul>

- **\* These features by themselves are diagnostic of rosacea.**
- **† Two or more major features may be considered diagnostic**

Richard L Gallo , Richard D Granstein , Sewon Kang , Mark Mannis , Martin Steinhoff , Jerry Tan , Diane Thiboutot.

Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee. J Am Acad Dermatol. 2018 Jan;78(1):148-155.



# New Classification of Rosacea

- **Diagnostic:**

- Fixed centropacial erythema in a characteristic pattern that may periodically intensify
- Phymatous changes

- Gallo RL, Granstein RD, Kang S, Mannis M, Steinhoff M, Tan J, Thiboutot D. Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee. *J Am Acad Dermatol.* 2018 Jan;78(1):148-155.

# New Classification of Rosacea

## Major Criteria (phenotypes)

- Flushing
- Papules and pustules
- Telangiectasia
- Ocular manifestations
  - Lid margin telangiectasia, interpalpebral conjunctival injection, spade-shaped infiltrates in the cornea, scleritis and sclerokeratitis
- 2 or more major features may be considered diagnostic
- Gallo RL, Granstein RD, Kang S, Mannis M, Steinhoff M, Tan J, Thiboutot D. Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee. *J Am Acad Dermatol*. 2018 Jan;78(1):148-155.

# New Classification of Rosacea

## Secondary Criteria (phenotypes)

- Burning sensation
- Stinging sensation
- Edema
- Dryness
- Ocular manifestations
  - “Honey crust” and collarette accumulation at the base of the lashes, irregularity of the lid margin, evaporative tear dysfunction (rapid tear breakup time)
- Gallo RL, Granstein RD, Kang S, Mannis M, Steinhoff M, Tan J, Thiboutot D. Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee. *J Am Acad Dermatol.* 2018 Jan;78(1):148-155.

# Rosacea – Papulopustular and early Phymatous



Rosacea



Rosacea

# Treatments

# Topical Treatments for Rosacea

Hala Daou, Michela Paradiso, Kerry Hennessy, and Lucia Seminario-Vidal. Rosacea and the Microbiome: A Systematic Review. *Dermatol Ther (Heidelb)*. 2021 Feb; 11(1): 1–12.

Drug	Mechanism of action	Side effects
Brimonidine tartrate (0.33% gel)	Vasoconstrictive $\alpha^2$ -adrenergic agonist	Erythema, flushing, skin burning, contact dermatitis
Azelaic acid (20% cream/lotion or 15% foam/gel) twice daily	May be related to reductions in mRNA for cathelicidin and kallikrein-5	Burning, itching, stinging
Metronidazole (0.75% cream/gel/lotion; 1% cream/gel) once or twice daily	May involve antimicrobial, anti-inflammatory, and/or antioxidant properties	Irritation, xeroderma, stinging
Oxymetazoline HCl (1% cream)	$\alpha^{1A}$ -adrenergic agonist	Contact dermatitis, worsening of inflammatory rosacea lesions, pain, pruritis, erythema
Ivermectin (1% cream) once daily	May be related to anti- <i>Demodex</i> and anti-inflammatory activity	NA
Sodium sulfacetamide (10%) and sulfur (5%) cream or lotion once or twice daily	Antiseptic, antiparasitic, antiseborrheic, and keratolytic	Local irritation, allergic reactions
Erythromycin (2% solution) twice daily	Antimicrobial and anti-inflammatory properties	Erythema, pruritus, burning, stinging
Clindamycin (1% lotion) daily	Antimicrobial and anti-inflammatory properties	Xeroderma, erythema, burning, pruritus
Benzoyl peroxide 5% plus clindamycin 1% daily	Free radical oxidation of anaerobic bacteria and antimicrobial activity	Xeroderma, itching, stinging
Permethrin (5% cream) daily–weekly	Unknown, may be related to anti- <i>Demodex</i> activity	Burning, numbness, tingling
Tretinoin (0.025% cream; 0.05% cream; 0.01% gel) daily	Alters epidermal keratinization	Irritation

# Treatment options - topical

- Metronidazole
- Azelaic Acid
- Sulfur and sodium sulfacetamide
- Ivermectin
- Topical Vasoconstrictors (brimonidine and oxymetazoline)
- Topical Antibiotics (minocycline, erythromycin, clindamycin)
- Topical Immunomodulators
- Topical Benzoyl Peroxide
- Permethrin
- Sensitive skin care

# Oral Therapy

- Doxycycline - 100mg BID
  - Submicrobial dosing 40mg a day or 20mg twice a day
- Minocycline - 100mg BID
- Tetracycline - 500mg BID
- Sarecycline – weight based dosing
- Trimethoprim/sulfamethoxazole - a tab BID
- Erythromycin - 500mg BID
- Azithromycin 250-500mg QD (pulse doses)
- Amoxicillin 500mg BID to TID



# Other Oral Therapies

- Isotretinoin
- Carvedilol, Propranolol, Nadolol
- Ampicillin
- Metronidazole
- Dapsone
- Clonidine
- Estrogen
- Prednisone
- Probiotics

# Review of Beta-blockers for Flushing

- Review looks at nine (9) studies
  - Review propranolol, nadolol and carvedilol
  - Small sample sizes
  - Effective treatment option for facial erythema and flushing that doesn't respond to traditional therapy
  - Watch for hypotension, lowered heart rate, nausea, dizziness
- 
- Jade G M Logger , Jill I Olydam , Rieke J B Driessen 3. Use of beta-blockers for rosacea-associated facial erythema and flushing: A systematic review and update on proposed mode of action. J Am Acad Dermatol. 2020 Oct;83(4):1088-1097.

# Carvedilol for flushing

- Twenty-four (24) rosacea patients with flushing
- Retrospective review
- All patients were prescribed carvedilol 6.25 mg either once or twice per day, and the daily dose was gradually titrated up to 12.5 mg.
- Clinical erythema severity was assessed by:
  - Clinician's Erythema Assessment (CEA)
  - Patient's Self-Assessment (PSA) scales.
- Mean change of  $-1.6$  in the CEA score (clinician)
- Mean change of  $-1.8$  in the PSA score (patient)
- Erythematotelangiectatic rosacea (ETR) patients did better than non-ETA patients (53.8% vs 16.7% [P = .035.]
- No serious adverse event was observed.

# Carvedilol

- Non-selective Beta-blocker
- Used for facial erythema and flushing
- Dosing 3.125 to 6.25 twice daily to start
- Doses usually to 12.5 daily to twice daily
- Max dose from referenced studies is 25mg



# Rosacea and Cardiometabolic Diseases

- Meta-analysis
- Thirteen studies (13) were included, representing 50,442 patients with rosacea.
- Patients with rosacea had higher prevalence of each of the following:
  - Dyslipidemia
  - Hypertension
  - Higher total cholesterol
  - Higher low-density lipoprotein,
  - Higher triglycerides
  - **Higher systolic blood pressure,**
  - **Higher diastolic blood pressure**
  - Higher fasting blood glucose.
- Rosacea was **not associated with ischemic heart disease, stroke, diabetes, and high-density lipoprotein.**
- Qi Chen, Xiao Shi, Yan Tang, Ben Wang, Hong-Fu Xie, Wei Shi, Ji Li. Association between rosacea and cardiometabolic disease: A systematic review and meta-analysis. *J Am Acad Dermatol.* 2020 Nov;83(5):1331-1340.

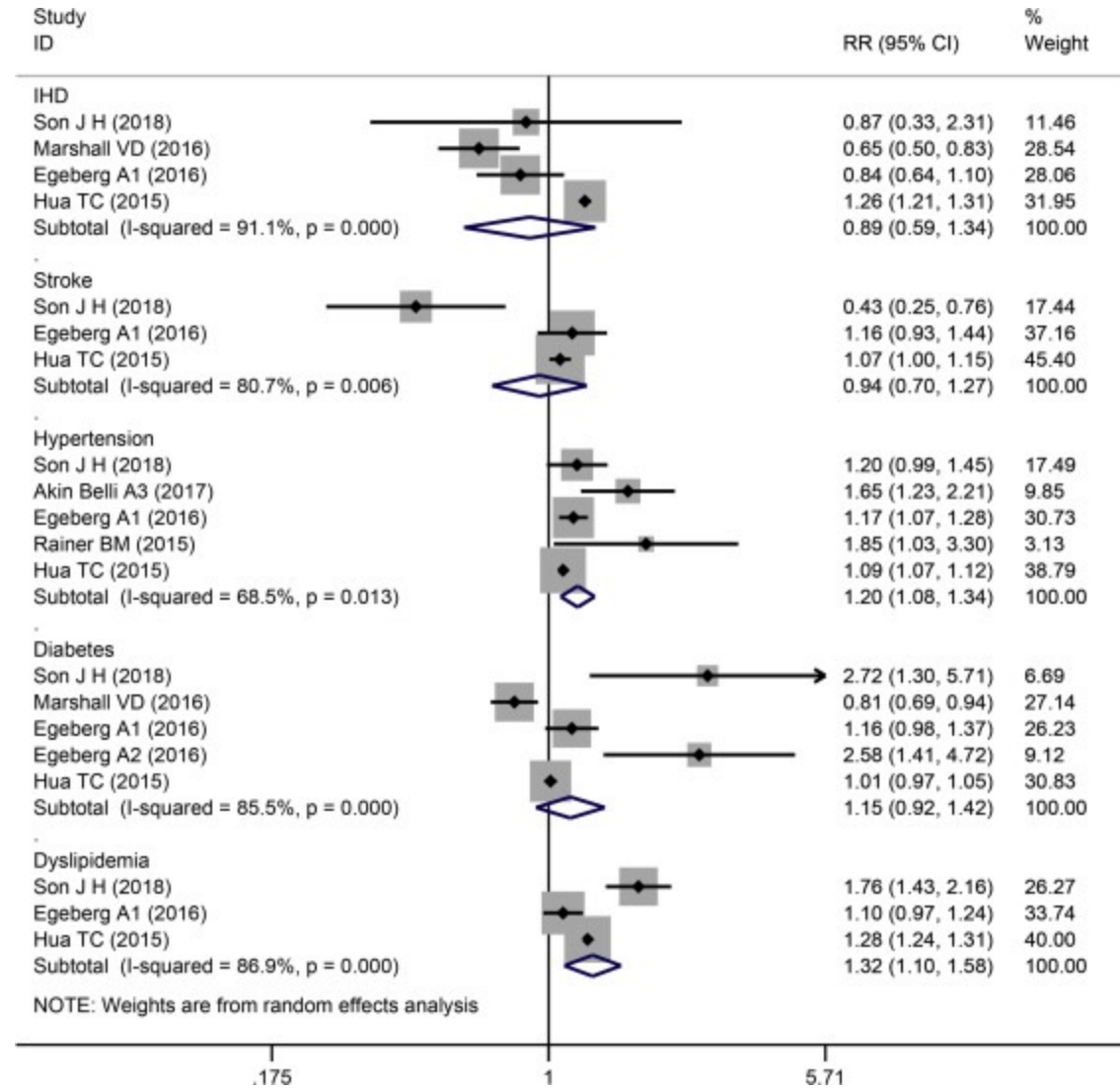
## Ischemic Heart Disease

## Stroke

## Hypertension

## Diabetes

## Dyslipidemia



- Qi Chen, Xiao Shi, Yan Tang, Ben Wang, Hong-Fu Xie, Wei Shi, Ji Li. Association between rosacea and cardiometabolic disease: A systematic review and meta-analysis. *J Am Acad Dermatol.* 2020 Nov;83(5):1331-1340.

# Take Home on: Rosacea and Disease Associations

- Rosacea and Stroke and Ischemic Heart Disease – **no association**
- Rosacea and Diabetes – can't make connection but Rosacea patients do have higher fasting blood sugar levels
- Rosacea associated with dyslipidemia
- Rosacea statistically **significant association with hypertension**



Photosensitive or Thermosensitive Disease?



# Is it the heat or the sun or both that aggravates rosacea?

- The evidence varies.
- Most recently a **small report suggested that not the sun but actually the heat** may be more involved.<sup>1</sup>
- This study was disputed, suggesting UV exposure in rosacea is still involved in this condition
- **Take home – use physical sun protection that protects against both UV irradiation and heat.**

- Chen L, Jin R, Zhang S, Zheng J. Heat stimuli test by infrared reveals rosacea as a heat sensitive skin disorder. *J Am Acad Dermatol.* 2024 Jan;90(1):196-198.
- Zhou C, Yin Z. Rosacea: a thermosensitive or photosensitive skin disease? *J Am Acad Dermatol.* 2024 Apr 5:S0190-9622(24)00570-X. doi: 10.1016/j.jaad.2024.01.092. Online ahead of print.



# Maintenance Therapy for Rosacea

- Expert consensus
- Daily skincare regimen and sunscreen are crucial.
- Active treatment phase should be recommended if signs or symptoms reappear or worsen.

- **Don't let the rosacea get worse.**



- (Recommendations were made if the specialists had 75% agreement.)


- Almeida LMC, Ianhez M, Dal'Forno T, Picosse FR, Ravelli F, Kamamoto C, Sarlos P, Gold LFS. Long-term maintenance treatment of rosacea: experts' opinion. Int J Dermatol. 2024 Jan;63(1):94-101.

# Initial Treatment Plan for Rosacea

- Topical treatments as discussed
  - **Regular use** is very important to repair the barrier
  - Oral antibiotics or if severe isotretinoin
- 
- Avoid triggers – keep diary of triggers
  - Education
  - Rule out serious reasons for flushing



# Skin of Color and Rosacea

- Rosacea is more common in skin of color (SOC) populations than previously reported.
- Clinical presentation of rosacea includes the clinical subtypes observed in other populations but **may be less conspicuous**
- **Index of suspicion may be lower** in SOC populations. 
- To avoid underdiagnosis, consider rosacea in the differential diagnosis of any patient presenting with:
  - history of skin sensitivity
  - central facial erythema, papules, and pustules

# Skin of Color and Rosacea

- The compromised barrier in rosacea contributes to skin sensitivity for all skin types.
- Studied Chinese rosacea patients showed that using a moisturizer and sunscreen **negatively correlated with rosacea**
- **Conclusions:** The use of skincare could improve rosacea symptomatology. These products are recommended before and during prescription therapy and as part of a maintenance regimen as adjuncts.

# Questions for Skin of Color Rosacea Patients

Archana M Sangha.  
Diagnosing and  
Treating Rosacea in  
Skin of Color Patients.  
J Clin Aesthet  
Dermatol. 2023  
Dec;16(12 Suppl  
2):S14-S15

**TABLE 1.** Pertinent questions to ask when assessing skin of color patients for rosacea<sup>5,6</sup>

Do you experience a warm sensation over the face?

Do you notice any redness on the face?

Do you feel any stinging or burning with skincare products? If yes, ask which products.

Ask about timing of symptoms. (Are they associated with known triggers? i.e. heat, stress, spicy foods?)

Have you been treated with acne medications recently? If so, have you noticed any improvement? (SOC patients with rosacea are often misdiagnosed as having acne).

Have you or are you currently applying any steroid creams to the face? (Screens for steroid-induced rosacea).

Regarding your eyes, do you experience: itching, burning, a gritty sensation or dryness? If so, how often?

# Treating Rosacea with Botulinum Toxin

- A total of 22 studies were included
- 9 of which were randomized controlled trials involving 720 subjects
- After treatment, **all studies showed varying degrees** of improvement in patient signs and symptoms along with reduced **Clinician's Erythema Assessment (CEA) scores**. The improvement was maintained for several month
- Adverse effects were mild and self-limiting.

- He G, Yang Q, Wu J, Huang Y, Zheng H, Cheng H. Treating rosacea with botulism toxin: Protocol for a systematic review and meta-analysis. J Cosmet Dermatol. 2024 Jan;23(1):44-61.

# Treating Rosacea with Botulinum Toxin

- Articles reviewed range of botulinum toxin used:
- 16 Units to 50 Units
- Done weekly for 3 weeks or every 3 months
- Botulinum Toxin types:
- Ona-
- Inco-
- Abo-
- Lan-

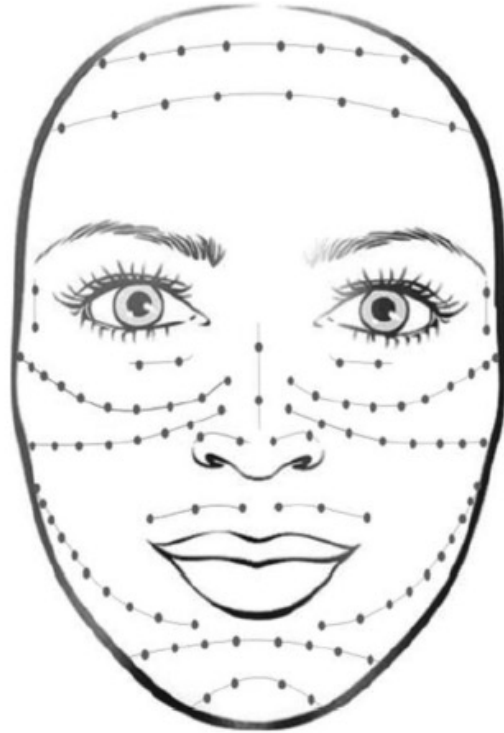


# Microdosing of Botulinum Toxin

- Standard botox for rhytides and then:
- Microdosing of botox .625U/.01ml over the face for erythema.
- Digital dermoscopy showed a marked reduction of erythema and telangiectasias.
- Erythema and telangiectasias improved both on objective and subjective measurements.
- Skin oleosity, static rhytids, papules and pustules and enlarged pores improved on subjective measurements.
- Patient satisfaction was high (93%) despite the high rate of adverse events (56%).

# Microdosing of Botulinum Toxin

Doris Hexsel, Indira Valente-Bezerra, et al. Subjective and Objective Measurements of the Facial Effects of Microdoses of Botulinum Toxin. *Dermatol Pract Concept.* 2023 Jul 1;13(3):e2023168.



**Figure 1.** Injection points for the microdoses of Botulinum Toxin. The 100 points of injection were distanced 1cm from each other, were applied as symmetrically as possible and were evenly distributed between the left and right sides and the 3 thirds of the face.

# Conclusions:

- New Epidemiology Study shows rosacea is worldwide and affects people's quality of life
- Many topicals and systemic treatments
- Rosacea is aggravated by heat and UVlight
- Heart disease associations and heart medications for rosacea patients
- Microdosing of botulinum toxin for the erythematous type of rosacea

Thank you!