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# Rosacea Phenotypes Explained: Selecting Targeted Therapies That Work

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# Disclosures

- **Henry Yu, PA:** Consultant/advisory board – AbbVie, Amgen, Arcutis, Boehringer Ingelheim, BMS, Organon, Galderma, Incyte, J&J, LEO Pharma, Novartis, Pfizer, Regeneron, Sun Pharma, UCB; speaker's bureau – AbbVie, Amgen, Arcutis, Boehringer Ingelheim, BMS, Organon, Galderma, Incyte, J&J, LEO Pharma, Pfizer, Sun Pharma, UCB; principal investigator – Target Derm, Castle Biosciences; sub-investigator – Amgen, Pfizer

- I will be discussing off-label use of medication

# Learning Objectives

- Classify rosacea using the 2017 NRS (National Rosacea Society) phenotype-based framework and identify co-existing phenotypes in a single patient
- Select evidence-based topical, oral, and device therapies matched to each rosacea phenotype
- Apply a phenotype-first treatment algorithm to optimize combination therapy and long-term management

# Rosacea: More than a Red Face

### ~5% Global Prevalence

Chronic inflammatory dermatosis of the central face

### Gender Paradox

Women diagnosed more often; men present with greater severity

### QoL Impact

Social anxiety, depression, occupational impairment

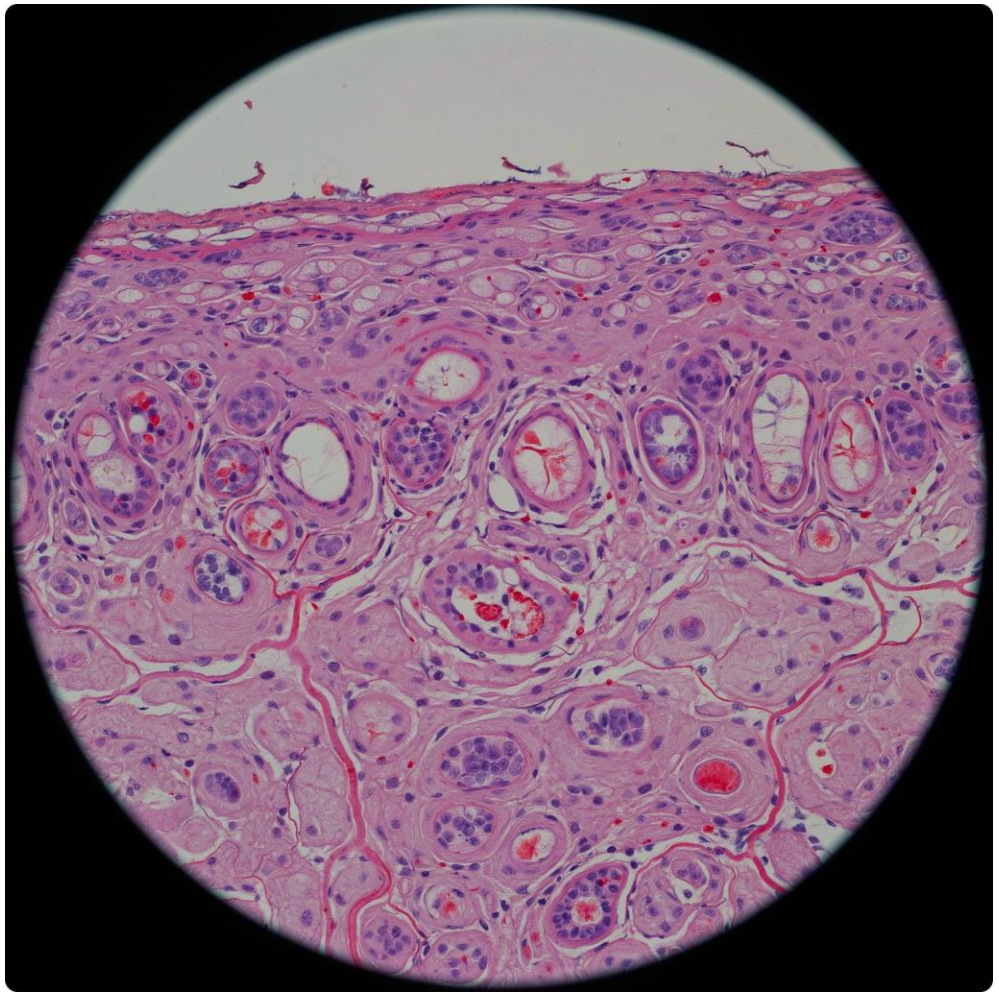
### No Cure

Phenotype-targeted long-term control is the goal



**Tan J, et al. *Br J Dermatol*. 2017;176(2):431-438.**

# Pathophysiology: The Inflammatory Triad



## Innate Immune Dysregulation

LL-37 cathelicidin overexpression via TLR2 (toll-like receptor 2) is thought to drive cutaneous inflammation.

## Neurovascular Hyperreactivity

TRPV1 (transient receptor potential vanilloid 1) activation is associated with flushing; dysregulated angiogenesis is linked to telangiectasias.

## Microbial Dysbiosis

*Demodex folliculorum* overgrowth and gut dysbiosis (SIBO, small intestinal bacterial overgrowth) may amplify inflammatory flares.

**REF**

# Common Triggers to Counsel Every Patient



- Environmental
  - UV exposure
  - Heat & cold wind



- Dietary
  - Alcohol (red wine)
  - Spicy foods, hot beverages



- Physiologic
  - Exercise & stress
  - Menopause



- Topical
  - Harsh cleansers, astringents
  - Topical steroids

Trigger avoidance + gentle skincare + daily SPF 50+ = the foundation of every plan

# The 2017 Shift: Subtypes → Phenotypes

## Old Model: 4 Subtypes

### Subtype 1: Erythematotelangiectatic

Flushing, redness, visible vessels

### Subtype 2: Papulopustular

Acne-like breakouts

### Subtype 3: Phymatous

Skin thickening, rhinophyma

### Subtype 4: Ocular

Eye involvement

*Rigid, siloed, imprecise — one patient, one box*

## New Model: 6 Phenotypes (NRS 2017)



Persistent Central Erythema



Flushing



Papules & Pustules



Telangiectasias



Phymatous Changes



Ocular Rosacea

*Flexible, overlapping, combinable — one patient, many phenotypes*

**Tan J, et al. *Br J Dermatol*. 2017;176(2):431-438.**

# Skin of Color: Don't Miss it



### Altered Erythema Presentation

In Fitzpatrick types V–VI, erythema appears **brown or violaceous** — or may be absent entirely

### Symptom-Based Clues

Burning, stinging, and flushing are key diagnostic indicators when erythema is subtle

### Dermoscopy Advantage

Aids visualization of telangiectasias in darker skin phototypes

**Lim HS, et al. *J Clin Aesthet Dermatol*. 2022;15(3):14-19.**

# Topical Therapies: Match the Phenotype

| Agent | Phenotype | Mechanism / Notes | Dosing |
|---|---|---|---|
| Brimonidine 0.33% gel | PCE (persistent central erythema); flushing (off-label) | α2-agonist; onset ~30 min, lasts 8–12 hrs | QD |
| Oxymetazoline 1% cream | PCE; flushing (off-label) | α1-agonist; longer duration than brimonidine | QD |
| Ivermectin 1% cream | PPR (papular pustular rosacea) | Anti-inflammatory + anti-Demodex; studies show improved relapse prevention vs metronidazole | QD |
| Metronidazole 0.75%/1% | PPR | Anti-inflammatory; PPR maintenance | BID/QD |
| Azelaic acid 15% | PPR + mild erythema | Anti-inflammatory, keratolytic | BID |

**Thiboutot D, et al. *J Am Acad Dermatol*. 2020;82(6):1501-1510. van Zuuren EJ, et al. *Cochrane Database Syst Rev*. 2019;(9):CD003262.**

# Oral Therapies: When to Step Up

### Doxycycline 40 mg MR

FDA-approved; sub-antimicrobial dose; **first-line oral** for moderate–severe PPR

### Doxycycline 100 mg (off-label)

Off-label induction 6–8 wks → step down to doxycycline 40 mg MR

### Isotretinoin 10–20 mg/day (off-label)

Off-label low-dose; refractory PPR + phymatous disease; requires **iPLEDGE enrollment**

### Carvedilol / propranolol (off-label)

Off-label; β-blockade for refractory flushing



**Off-label use of isotretinoin and beta-blockers for rosacea is based on published case series and expert consensus; not FDA-approved for these indications.**
**Thiboutot D, et al. *J Am Acad Dermatol*. 2020;82(6):1501-1510.**

# Newer FDA-Approved & Adjunct Options

| | |
|---|---|
| 1 | **Minocycline 1.5% foam**<br>FDA-approved 2020; once-daily PPR; minimal systemic absorption |
| 2 | **Encapsulated benzoyl peroxide 5%**<br>FDA-approved 2022; PPR; encapsulation reduces irritation vs. standard BPO |
| 3 | **Spironolactone 50–100 mg (off-label)**<br>Off-label use; hormonal flushing in women |



**Off-label use of spironolactone for rosacea is based on clinical experience and published case reports; not FDA-approved for this indication.**

**Fowler J Jr, et al. *J Am Acad Dermatol*. 2020;82(6):1395-1403. Stein Gold L, et al. *J Drugs Dermatol*. 2022;21(9):956-963.**

# Laser & Light: The Vascular Toolkit

### PDL (pulsed dye laser) 595 nm — well-established first-line option

Targets oxyhemoglobin; strong evidence for telangiectasias + persistent cutaneous erythema (PCE); typically 3–5 sessions

### IPL (intense pulsed light) 515–1200 nm

Meta-analysis data suggest >75% clearance rate; lower pain threshold compared to PDL

### KTP (potassium titanyl phosphate) 532 nm

Targets superficial vessels; studies suggest fewer adverse effects than IPL

### Nd:YAG (neodymium-doped yttrium aluminum garnet) 1064 nm

Targets deeper vessels; evidence supports use in patients with darker skin types

### Picosecond 755-nm — off-label use

Picosecond laser; similar wavelength to PDL targets; emerging off-label use for vascular lesions and erythema in rosacea; shorter pulse duration may reduce thermal damage per preliminary data

**Picosecond 755-nm for vascular lesions in rosacea: Off-label use based on emerging preliminary data and presenter clinical experience.**
**Wat H, et al. *Dermatol Surg*. 2014;40(4):359-377. Patel NU, et al. *Dermatol Clin*. 2018;36(2):167-178. Gold MH, et al. *J Drugs Dermatol*. 2023;22(1):45-51.**

# Ablative Lasers for Phymatous Disease

## CO2 laser

Sculpts rhinophyma; studies show favorable long-term outcomes; **1–2 weeks downtime**

## Er:YAG laser

Superficial ablation; less thermal damage; faster healing for milder phymatous changes

## Pre-treatment protocol

Low-dose isotretinoin (off-label) pre-treatment may reduce sebaceous activity before ablation

## ⚠️ Skin of color precaution

Higher risk of post-inflammatory hyperpigmentation (PIH) and dyspigmentation in Fitzpatrick types IV–VI. Use conservative settings, test spots, and consider Er:YAG over CO2 to minimize thermal damage. Pre- and post-treatment with hydroquinone or azelaic acid may reduce PIH risk

**Pre-treatment with low-dose isotretinoin prior to ablative laser for phymatous rosacea is off-label and based on presenter clinical experience and published expert opinion.**

**Aloi F, et al. *Dermatol Surg*. 2002;28(7):614-619. Orenstein A, et al. *Lasers Surg Med*. 2001;29(3):230-235. Patel NU, et al. *Dermatol Clin*. 2018;36(2):167-178.**

# Rosacea Cheat Sheet

| Phenotype | First-Line | Step-Up | Device |
|---|---|---|---|
| PCE / Flushing | brimonidine 0.33% or oxymetazoline 1%<br>*[FDA-approved PCE; flushing off-label]* | β-blockers: carvedilol/propranolol (off-label) | IPL or PDL |
| Telangiectasias | brimonidine 0.33% or oxymetazoline 1% | — | PDL → KTP or Nd:YAG |
| PPR Mild–Moderate | ivermectin 1% or azelaic acid 15% | + doxycycline 40 mg MR | IPL (adjunct) |
| PPR Severe | doxycycline 100 mg induction → step down (off-label) | isotretinoin 10–20 mg (off-label) | — |
| Phymatous | isotretinoin low-dose (off-label) | — | CO2 or Er:YAG |
| Ocular | Lid hygiene + omega-3 | cyclosporine 0.05% ophthalmic | Ophthalmology referral |

# Putting It All Together

## Combination Therapy: Real-World Approach

### Most Patients Have ≥2 Phenotypes

Monotherapy is often insufficient — assess every phenotype at every visit

### Classic Combo

Doxycycline 40 mg MR + ivermectin 1% cream → studies show faster clearance and improved maintenance

### Vascular + Inflammatory

IPL series + ivermectin 1% cream simultaneously for dual phenotype control

### Sequence Matters

Control active inflammation before laser to reduce post-procedure flares

## Your Phenotype-First Prescription

### Identify

Map every phenotype at the visit — not just the chief complaint

### Prioritize

Treat the phenotype causing the most distress first

### Combine

Pair topical/oral with device therapy when vascular or phymatous features are present

### Maintain

Rosacea is managed, not cured — follow up at 8–12 weeks

**Schaller M, et al. *Br J Dermatol*. 2017;176(2):465-471. Thiboutot D, et al. *J Am Acad Dermatol*. 2020;82(6):1501-1510.**

# *Mark your calendar*
## for what's coming up next!

### masterclasses in dermatology annual meeting

**February 18–21, 2027**
Signia by Hilton
Orlando Bonnet Creek

### masterclasses in dermatology NP/PA institute

**September 11–12, 2027**
New York Marriott Marquis

**October 23–24, 2027**
Thompson Dallas by Hyatt

### masterclasses in dermatology saturday morning live

**Two 2026 dates remaining:**
November 14, 2026
December 19, 2026