



Acne Vulgaris: Newest Guidelines

Heather Roebuck, DNP, FNP-BC, FAANP

drheatherroebuck@gmail.com

DISCLOSURES: **ANY BAGGAGE?**



- **Current Contract: iPLEDGE FDA ~~ACNE~~ Scientific Safety Board**
- **National Speaker: Aesthetic Medical Educators Training**
- **All relevant financial relationships have been mitigated**

Objectives

1

Identify at least **2** first line pharmacological treatment options for acne vulgaris

2

Identify at least **2** pharmacological treatment options for rosacea

3

Evaluate appropriate pharmacologic vehicles to prescribe based on patients

- **Age**
- **Gender**
- **Race**
- **Location**
- **Severity** of dermatologic disease

PATHOGENESIS: ACNE

Androgen

→ Sebocyte and Keratinocyte



Increased sebum &
Abnormal follicular keratinization



Follicular Plug

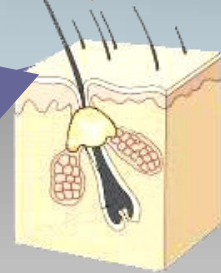


Non-inflammatory (comedones) -----→ Inflammatory lesions (papules, pustules, nodules)
c. acnes (previously *p. acnes*)

ACNE LESION: LIFE CYCLE



MICROCOMEDONES



- Topical Retinoids
- Benzoyl Peroxide
- Azelaic Acid

COMEDONES NONINFLAMMATORY

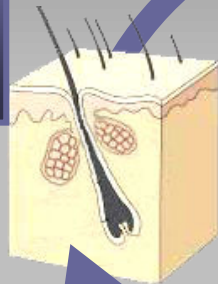


- Benzoyl Peroxide
- Antibiotics
- Dapsone
- Retinoids
- Azelaic Acid
- Sulfacetamide/Sulfur

INFLAMMATORY LESIONS

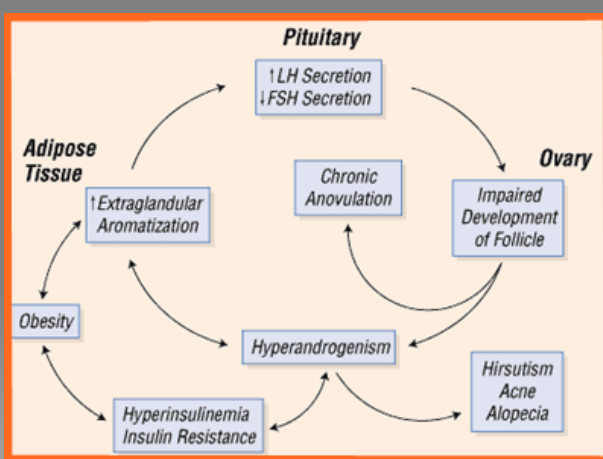


REPAIR



- Medical Devices
- Retinoids

- Intralesional Corticosteroids
- Isotretinoin



LABORATORY TESTING

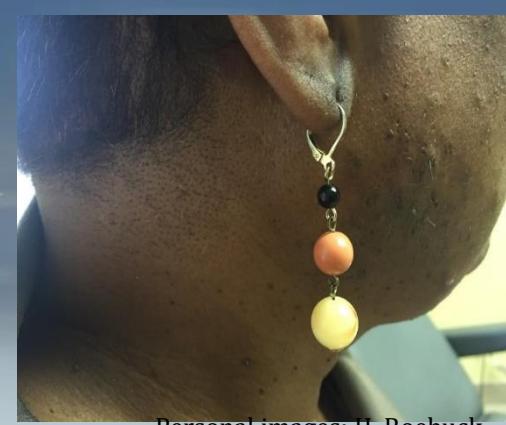
None Routinely Recommended Unless:

- Abnormal Menses
- Acanthosis Nigricans
- Hair Loss/Thinning
- Hirsutism
- Refractory to Conventional Therapy

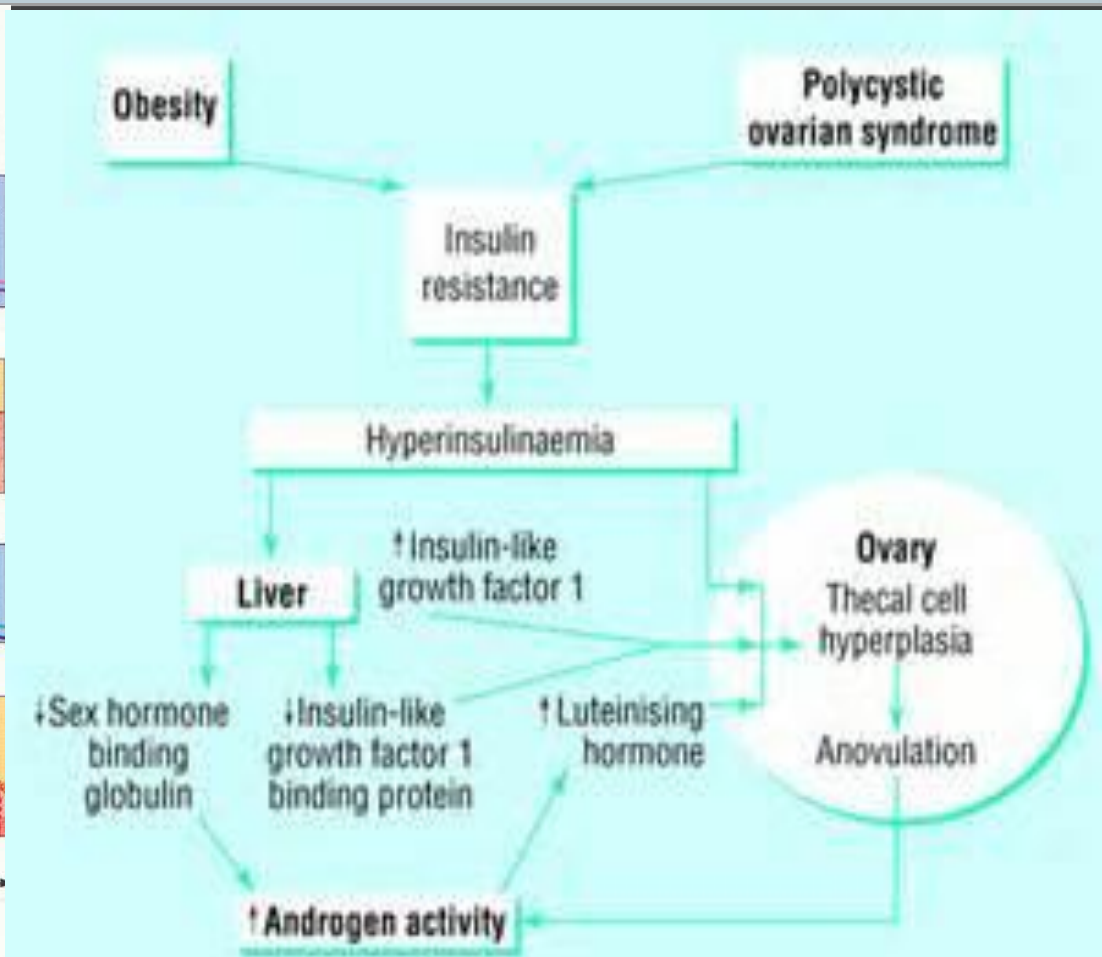
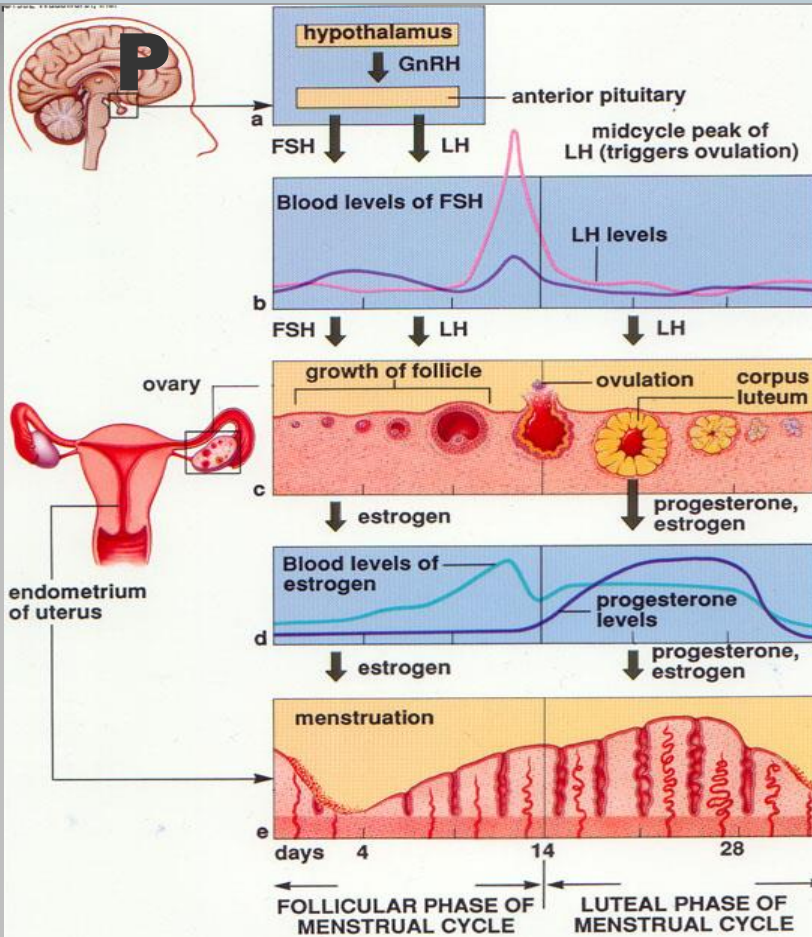


PHARMACOLOGY

- **OCP**
- **Metformin**
- **Spironolactone**



Personal images: H. Roebuck



EVALUATION FOR PCOS



Lab or Imaging Study	Expected Result or Explanation
Free testosterone	Elevated in PCOS
Total testosterone	Elevated in PCOS
Sex hormone binding globulin	Suppressed in PCOS
LH, FSH	Generally LH is higher than FSH; older criteria noted that LH is $2x > FSH$; however this is not always seen
Prolactin	To exclude hyperprolactinemia
TSH, free T4	To exclude hypothyroidism
DHEAS, 17 alpha-hydroxyprogesterone (17-OHP)	To screen for CAH, androgen-secreting tumors (in which case the DHEAS level is significantly elevated, generally over 600 – 700 mcg/dL)
Morning cortisol level and/or 24-hour urinary free cortisol	To exclude Cushing syndrome
Beta-HCG	To exclude pregnancy
Consider insulin-like growth factor 1 (IGF-1)	To exclude acromegaly IGF-1, like insulin, can increase androgen production and lower levels of sex hormone binding globulin
Lipid profile	To screen for hyperlipidemia
Hemoglobin A1c	To evaluate for glucose intolerance
Comprehensive metabolic profile	To evaluate renal and hepatic function prior to potential initiation of medication CMP also provides fasting blood glucose level
Oral glucose tolerance test	Should be performed in all girls with PCOS, regardless of BMI – not necessarily as part of screening labs, but once diagnosed
Pelvic ultrasound	To exclude masses and anatomical disorders causing menstrual dysfunction

Acne Treatment Guidelines

Definition

ACNE VULGARIS is a common, chronic, multifactorial, polymorphic, inflammatory, non-infectious disease involving the pilosebaceous unit (PSU).



Pathogenesis

Four factors play major roles:

- (1) abnormal desquamation of follicular keratinocytes; follicular epidermal hyperproliferation
- (2) excess sebum production
- (3) proliferation of anaerobic *Propionibacterium acnes* (*P. acnes*)
- (4) immune and inflammatory responses

Androgenic stimulation, genetic and external factors target both the sebocytes and keratinocytes. This leads to sebaceous hyperplasia/hyperseborrhea and follicular hyperkeratosis, respectively. Changes in the follicular homeostasis lead to accumulation of these materials and distention of sebaceous follicle lumina (microcomedo). Comedogenesis ensues and there is proliferation of *P. acnes*. Production of proinflammatory chemotactic and cytokine factors leads to inflammation of acne and the activation of host immune responses.

Classification of Acne Severity	
MILD	predominance of comedones ≤ 20 with few inflammatory papules ≤ 15
MODERATE	predominance of inflammatory papules and pustules ≥ 15 with comedones and few nodules ≤ 3
SEVERE	primarily nodules and cysts ≥ 3 with presence of comedones, papules and pustules

General Management Strategies in Acne

- Perform careful patient history
- Teach patients about gentle skin cleansing
- Show appropriate application technique for topical therapies
- Help patients to have realistic expectations of therapy
- Show empathy for patients' distress due to acne

Microbiologic Testing

- Routine microbiologic testing is unnecessary in the evaluation and management of patients with acne.
- Those who exhibit acne-like lesions suggestive of gram-negative folliculitis may benefit from microbiologic testing: bacterial cultures, including antibacterial sensitivities.

Endocrinologic Testing

- Routine endocrinologic evaluation (e.g., for androgen excess) is not indicated for the majority of patients with acne.

- Laboratory evaluation is indicated for patients who have acne and additional signs of androgen excess.
 - In prepubertal children, a hand film for bone age is a practical screen prior to specific hormonal testing.
 - Increased awareness of clinical signs of androgen excess will help identify those patients who may benefit from further evaluation and treatment by an endocrinologist or gynecologic endocrinologist.
 - The following laboratory tests may be helpful: free testosterone, dehydroepiandrosterone sulfate (DHEAS), luteinizing hormone (LH), and follicle stimulating hormone (FSH)

Acne Treatment General Guidelines	
MILD	
Comedonal First Choice Alternatives	Topical Retinoid Alternative Topical Retinoid or Azelaic Acid or Salicylic Acid
Papules/Pustules First Choice	Topical Retinoid + Topical Antimicrobial \pm Benzoyl Peroxide (BPO)
Alternatives	Alternative Topical Retinoid or Azelaic Acid + alternative Topical antimicrobial
MODERATE	
Papulopustules / Nodules First Choice	Topical Retinoid+ Oral Antibiotic \pm BPO
Alternatives	Alternative Oral Antibiotic + Alternative Topical Retinoid \pm BPO
Alternative for Females	Oral Antiandrogen + Topical Retinoid/Azelaic Acid \pm Topical Antimicrobial
SEVERE	
Nodulo-cystic First Choice Alternatives	Oral Isotretinoin High dose Oral Antibiotic + Topical Retinoid + BPO
Alternative for Females	High Dose Oral Antiandrogen + Topical Retinoid/ \pm Alternative Topical Antimicrobial

ADJUNCTIVE THERAPY

Comedo extraction, Intralesional steroid injection

MAINTENANCE THERAPY for all types of acne

Topical Retinoids \pm BPO

Topical Therapy

- Topical therapy is the standard of care in acne treatment.
- Topical retinoids are important in acne treatment. They reduce obstruction within the follicle and are useful in the management of both comedonal and inflammatory acne.
- Benzoyl peroxide is a bactericidal agent and combinations with erythromycin or clindamycin reduce bacterial resistance and enhance efficacy.
- Topical antibiotics (e.g., erythromycin and clindamycin) are effective acne treatments. However, the use of these agents alone can be associated with the development of bacterial resistance.
- Salicylic acid is a comedolytic/keratolytic that is moderately effective in the treatment of acne.
- Azelaic acid possesses comedolytic and antibacterial

PHARMACOLOGY: VEHICLE MATTERS

- Cream
- Foam
- Gel
- Lacquer
- Lotion
- Ointment
- Paste
- Powder
- Solution
- Spray
- Tincture

INTERACTIONS:

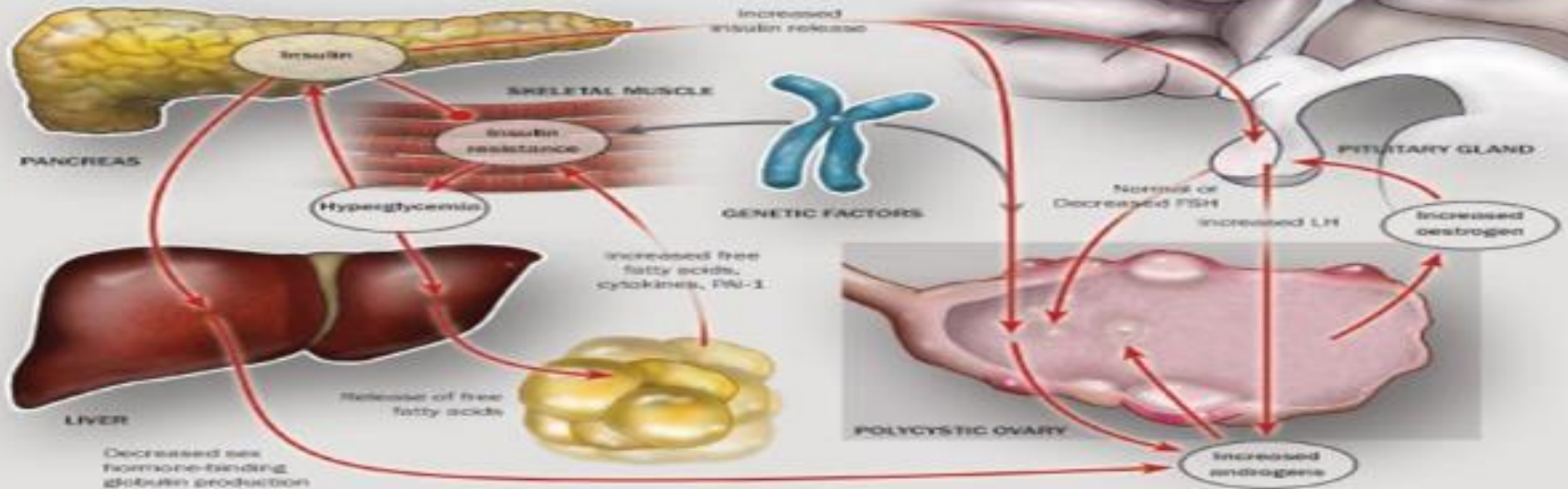




Rachel a 42 year old with severe **ACNE** and **ACANTHOSIS NIGRICANS** is suspected of having **PCOS**. Her quantitative HCG is 2 and her 75-G oral glucose tolerance test (OGTT) results show her 2 hour post-load glucose value is 152 mg/dL which indicates she has:

- A. Gestational diabetes
- B. Type 1 diabetes mellitus
- C. Type 2 diabetes mellitus
- D. Impaired glucose tolerance

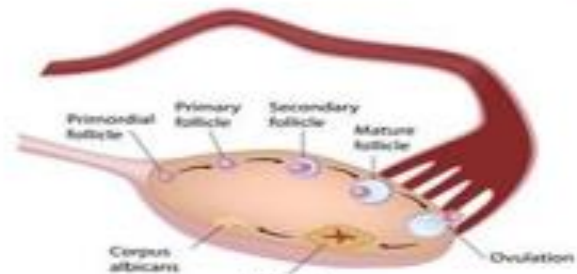




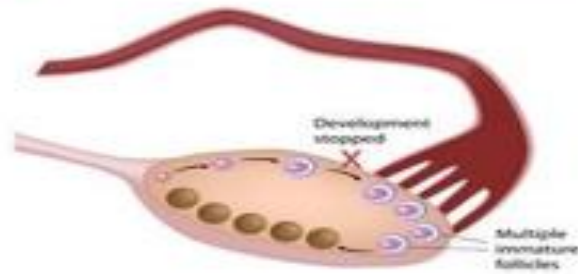
Arslanian S, Neider J, et al. New England Journal of Medicine 2008; 358: 27-34



Insulin resistance in women with polycystic ovary syndrome



Normal Ovary



Polycystic Ovary





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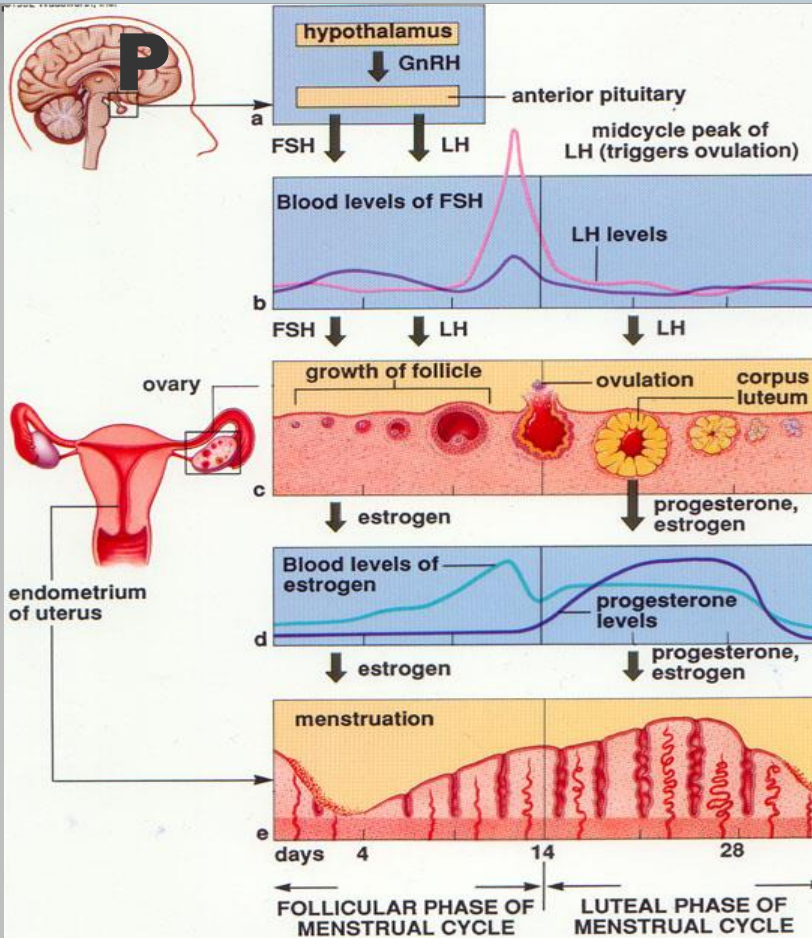
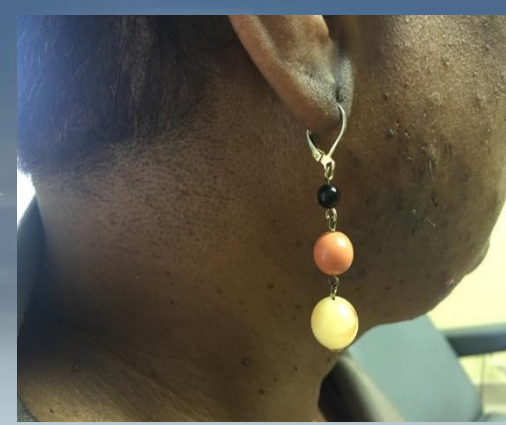


Diagnostic Criteria for PCOS

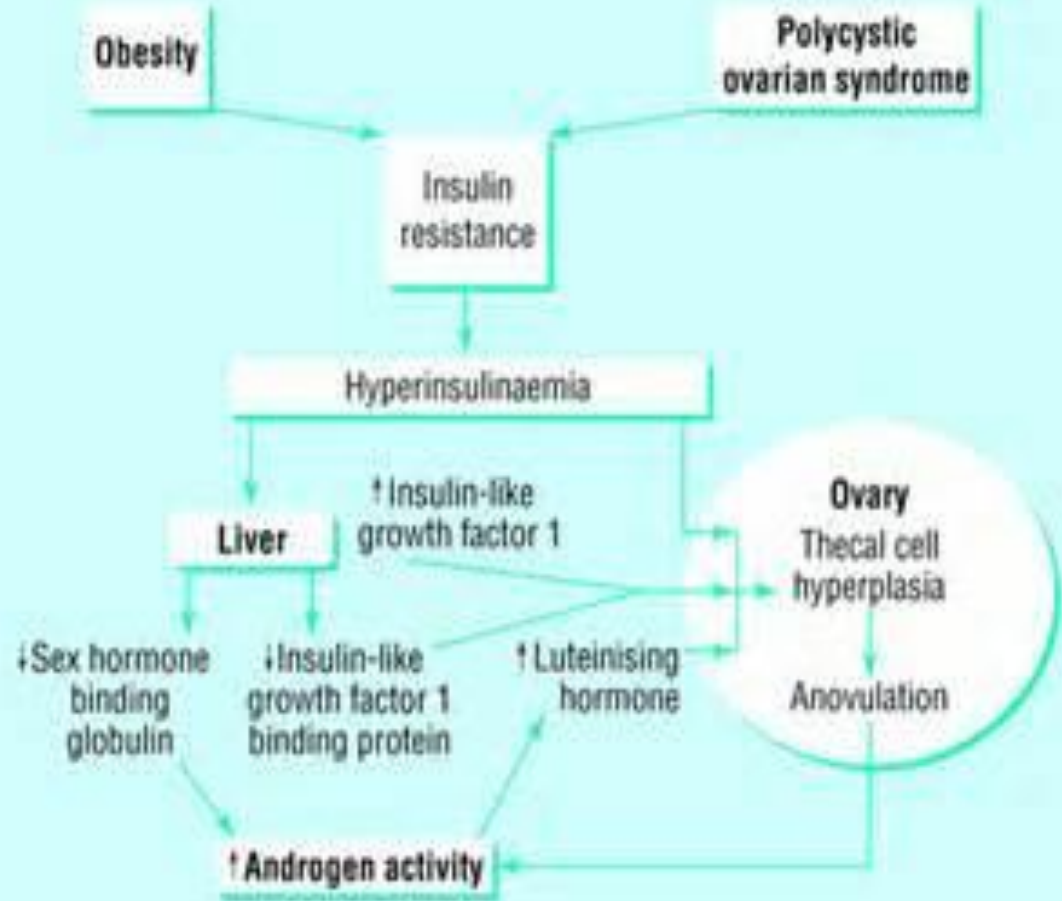
National Institutes of Health Criteria (1990)	Rotterdam Consensus Criteria (2003)	Androgen Excess and PCOS Society (2006)
<p>Must include all of the following:</p> <ul style="list-style-type: none">• Hyperandrogenism and/or hyperandrogenemia• Anovulation or oligo-ovulation• Exclusion of possible related disorders	<p>Must include two of the following:</p> <ul style="list-style-type: none">• Anovulation or oligo-ovulation• Clinical or biochemical signs of hyperandrogenism• Polycystic ovaries	<p>Requires all of the following:</p> <ul style="list-style-type: none">• Hyperandrogenism• Ovarian dysfunction• Exclusion of possible related disorders
<p>The presence of polycystic ovaries is not necessary for diagnosis</p>	<p>All possible related disorders must be ruled out for a diagnosis of PCOS to be made</p>	<p>Emphasizes that the diagnosis of PCOS should not be made without evidence of hyperandrogenism</p>
<p>First developed and most commonly used criteria today</p>	<p>Formulated to expand on NIH diagnostic definition of PCOS</p>	<p>Formulated to provide an evidence-based definition</p>

PHARMACOLOGY

- **OCP**
- **Metformin**
- **Spironolactone**



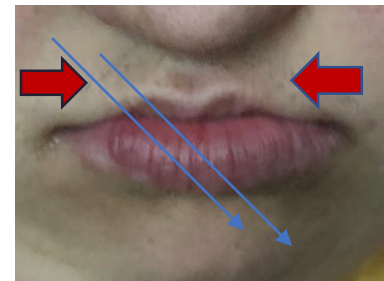
Personal image: H. Roebuck



Changing hormone levels during the menstrual cycle.

PEDIATRIC CASE STUDY

- 16 year old patient
- Acanthosis Nigricans Axillae
- Hair Thinning
- Hirsutism
- Hypothyroidism
- Menstrual Cycles: **6-8** per year
- Papulopustular and Nodular Truncal Acne
- Pacemaker and Open Heart Surgery History
- **PHARMACOLOGY RECOMMENDATIONS:**



CASE STUDY

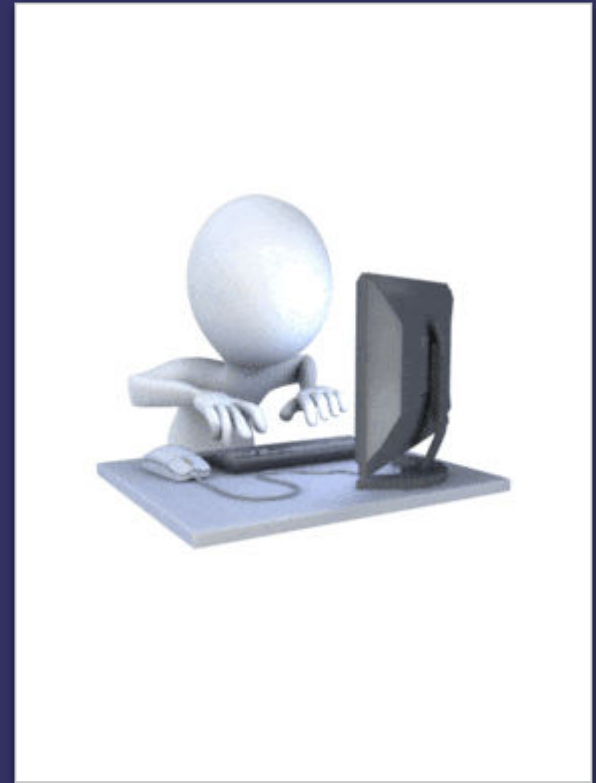
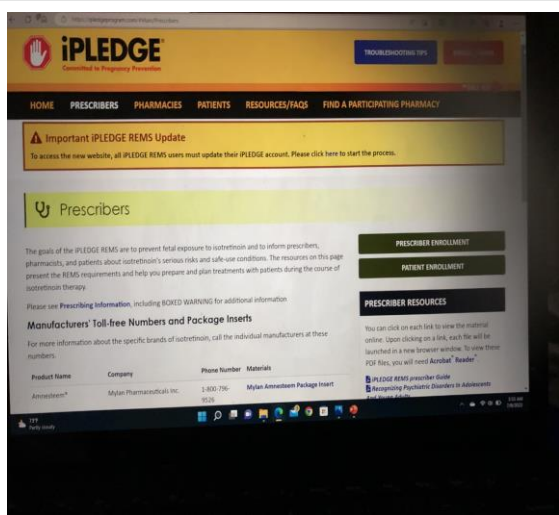
- 32 year old female
- Completed 3 courses of *isotretinoin*
- Dapsone 5% cream BID (Acne)
- Enalapril 5 mg QD (HTN)
- Ibuprofen 800 mg (Dysmenorrhea)
- Pseudoephedrine OTC (Allergy/Sinus)
- Remains on OCP: contains drospirenone/ethinyl estrodiol and levfomefolate calcium (Acne & PCOS)
- Spironolactone 100mg QD (Hirsutism & PCOS)
- Trimethoprim 100 mg BID (UTI)



WHICH OF HER MEDICATIONS CAN CAUSE HYPERKALEMIA?

- A. Dapsone, Pseudoephedrine, & Spironolactone
- B. Ibuprofen, Pseudoephedrine, & Tretinoin
- C. Enalapril, Spironolactone, & Trimethoprim
- D. Pseudoephedrine, Spironolactone, & Tretinoin





PHARMACOLOGY: FDA SAFETY PROGRAM

WHICH OF HER MEDICATIONS CAN CAUSE HYPERKALEMIA?

- A. Dapsone, Pseudoephedrine, & Spironolactone
- B. Ibuprofen, Pseudoephedrine, & Tretinoin
- C. **Enalapril, Spironolactone, & Trimethoprim**
- D. Pseudoephedrine, Spironolactone, & Tretinoin



ROSACEA

- Affects **16 million**
- Chronic Vascular Disease
- More common in Women **3:1**
- Men: More Phymata
- Ocular: Can lead to vision loss
- Pediatric Patients also found to experience genital flushing



DIAGNOSTIC CRITERIA



SOLE REQUISITE CRITERION:

Persistent **erythema** of the central face for a minimum of **3** months

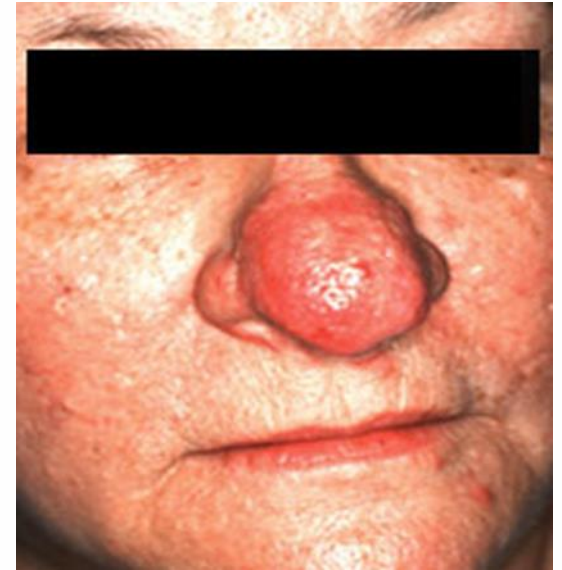
Supportive Findings:

- Flushing
- Papules
- Pustules
- Telangiectasia
- *Not Required*

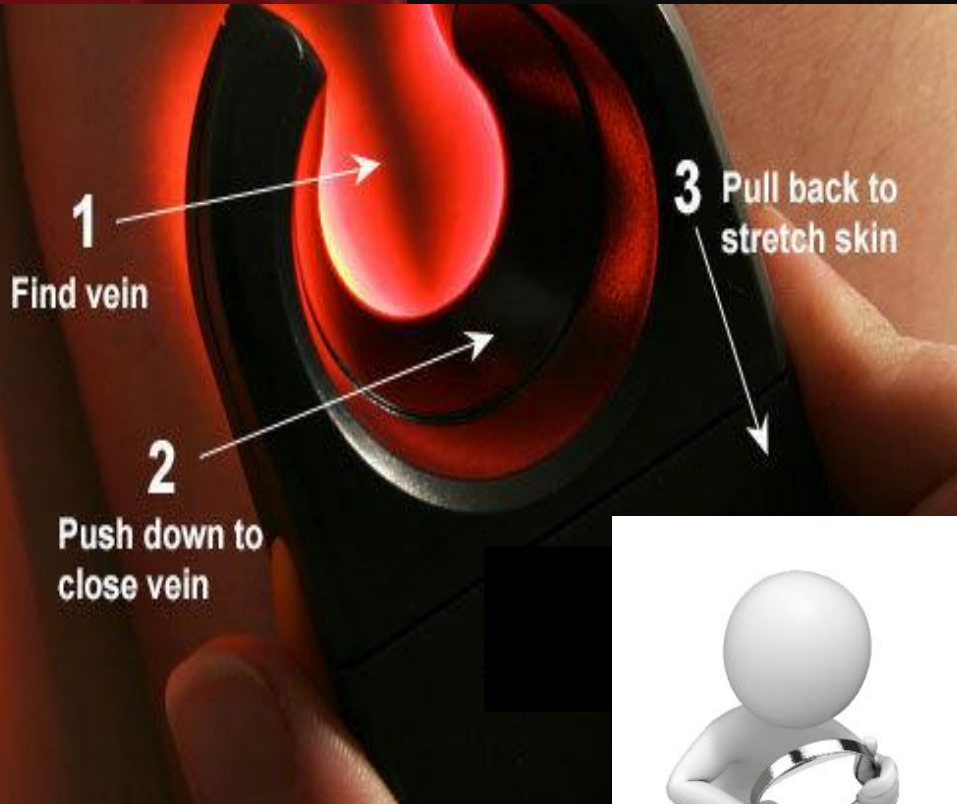
Secondary Features:

- Burning or stinging
- Edema
- Plaques
- Dry appearance
- Ocular manifestations
- Phymatous changes

ROSACEA: VARIANTS



TELANGIECTASIA ASSESSMENT



PAPULOPUSTULAR ROSACEA



- Inflammatory lesions:
- Papules and or Pustules
- Sparing of periocular skin
- Flushing though mild
- Edema sometimes noted

PHARMACOLOGY CASE STUDY:

- Comorbid Conditions
- Systemic Medication
- Tolerates Topicals

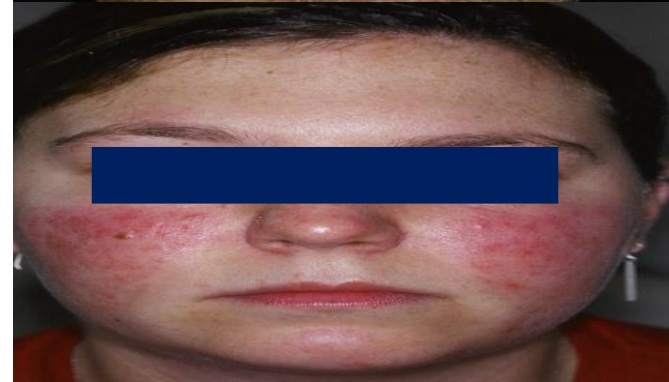
A



B



C



PHYMATOUS ROSACEA CASE STUDY

- **ACTINIC KERATOSES**
- **SEBACEOUS HYPERPLASIA**
- **SEBORRHEIC DERMATITIS**

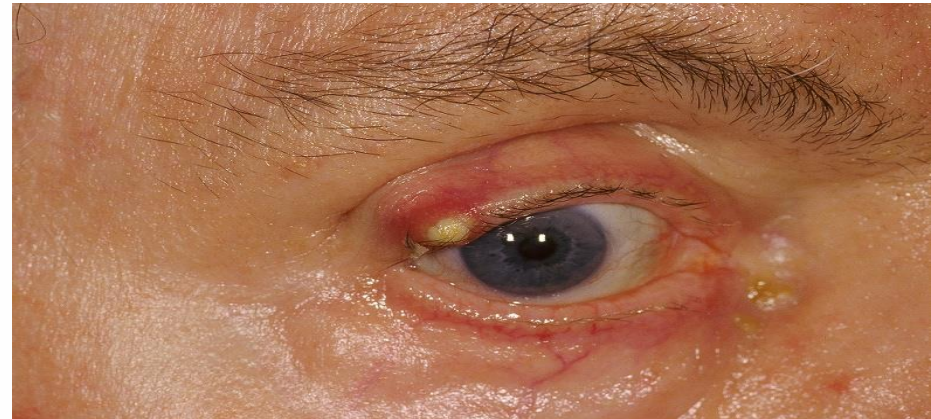
PHARMACOLOGY

- **Azelaic Acid**
- **Isotretinoin**
- **Retinoid**



OCULAR ROSACEA

- Can precede cutaneous signs
- Severity not proportional to the severity of facial rosacea
- **FREQUENT SYMPTOMS:**
- Burning, Stinging, Itching
- Blurred Vision
- Light-sensitivity
- Foreign Body sensation
- **50%** of all rosacea patients
- Blepharitis and Conjunctivitis
- **PHARMACOLOGY**
- Lid Hygiene
- Eye Drops
- Antibiotics



TRIGGER FACTORS

HEAT

Inside (eg, exercise, hot baths, overdressing)

Outside (eg, radiant heat)

Hot food/beverages

EXERTION

Exercise, chronic cough, lifting

EMOTIONS

Anger, stress, embarrassment

WEATHER

Hot, cold, strong winds, spring season

FOOD

Cayenne pepper 36%

Hot coffee 35%

Chocolate 33%

Tomatoes 31%

Hot tea 30%

Citrus fruits 27%

Black pepper 18%

Cheese 14%

Cured meats 14%

ALCOHOL

Red wine 48%

Liquor 37%

Beer 26%

TOPICAL PRODUCTS

Astringents

Irritants

Some cosmetics

DISEASE

Carcinoid syndrome

Mastocytosis, tumors

Migraine headaches

Hot flashes

DRUGS

Vasodilators, nicotinic acid, calcium channel

blockers, cholinergic

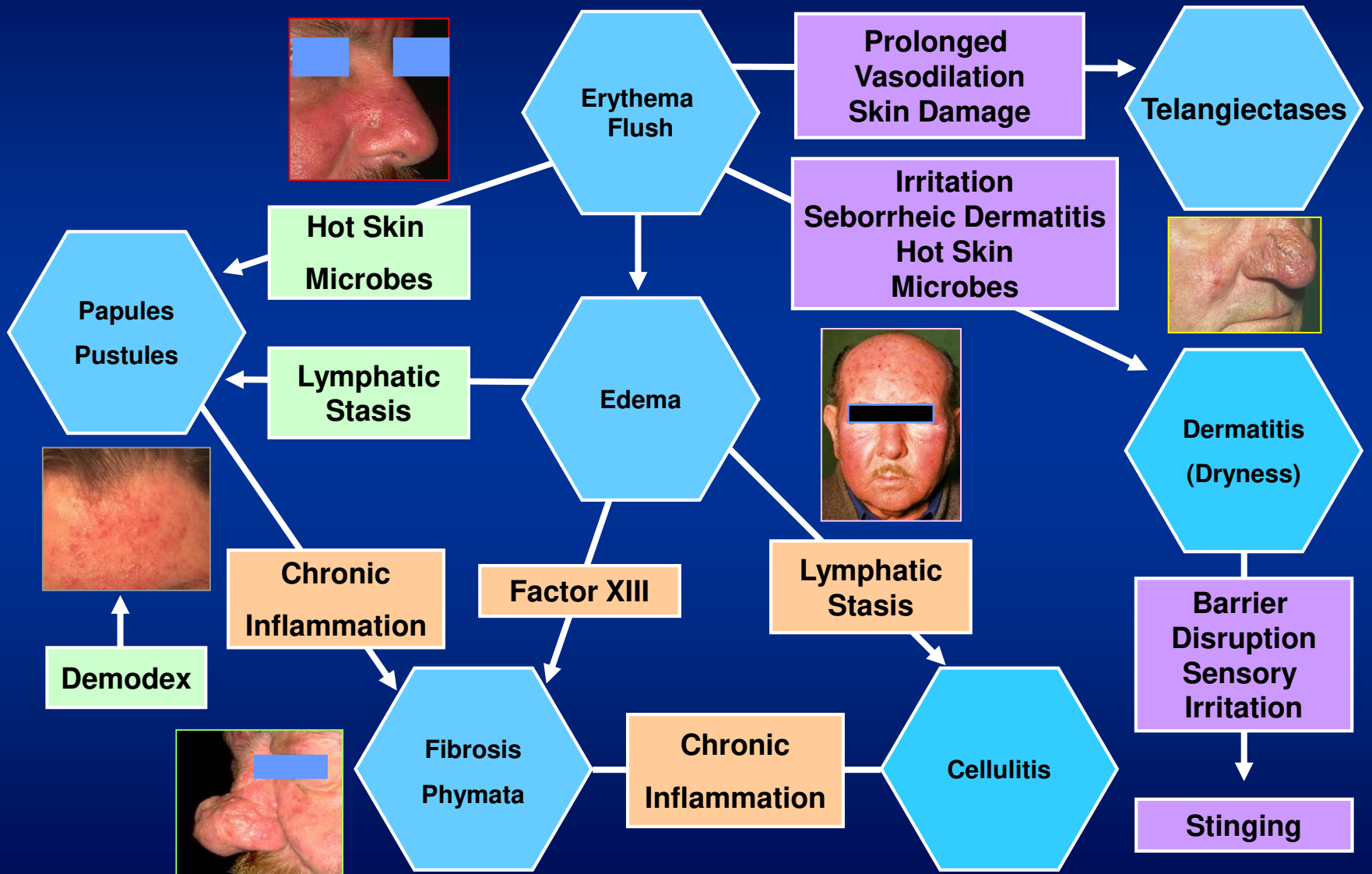
agents, cyclosporin A,

opiates, tamoxifen,

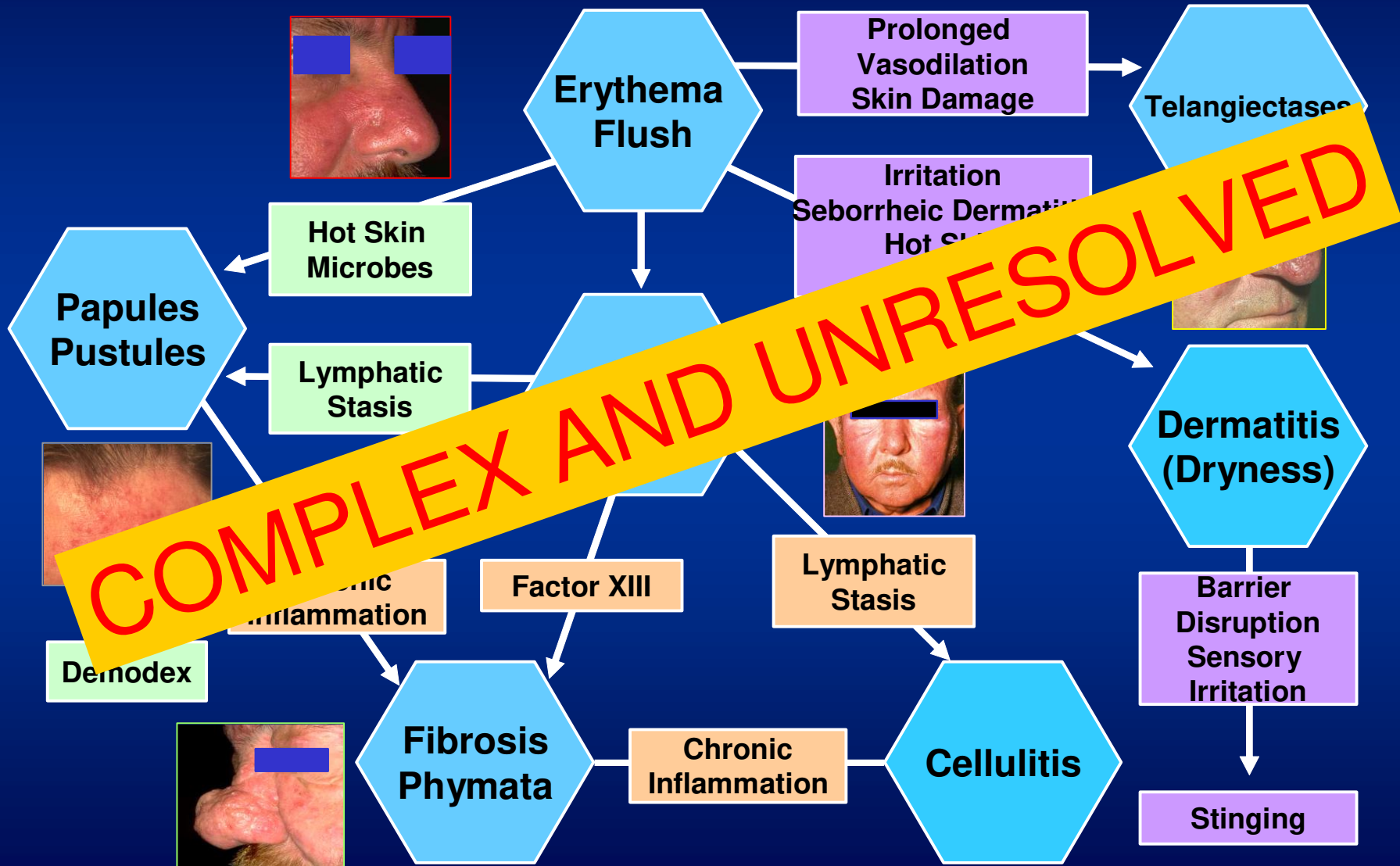
erectile dysfunction

Medications

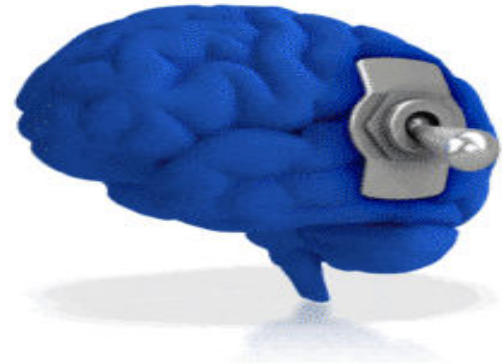
ROSACEA PATHOGENESIS



Rosacea Pathogenesis



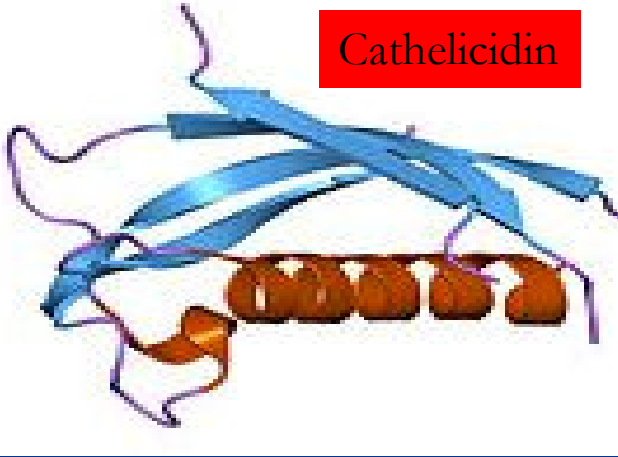
NEUROVASCULAR DYSREGULATION



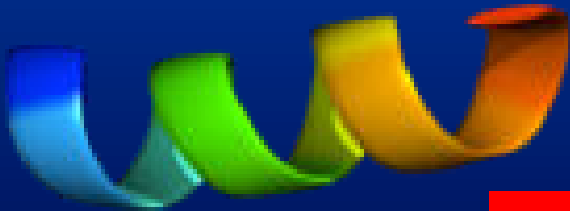
- **Flushing:** Increased facial blood flow
- **Neurosensory:** Stinging and burning
- **Neurogenic Inflammation:** Heat/warmth and spices
capsaicin
- **Norepinephrine Release:** presynaptic sensory nerve channels causes vasodilation
- **Emotional Stress:** activates sympathetic nervous system: releases chemicals that induce flushing, papules and pustules

CATHELICIDINS: ANTIMICROBIAL PEPTIDES (AMPS)

Cathelicidin



KLK-5 (SCTE)



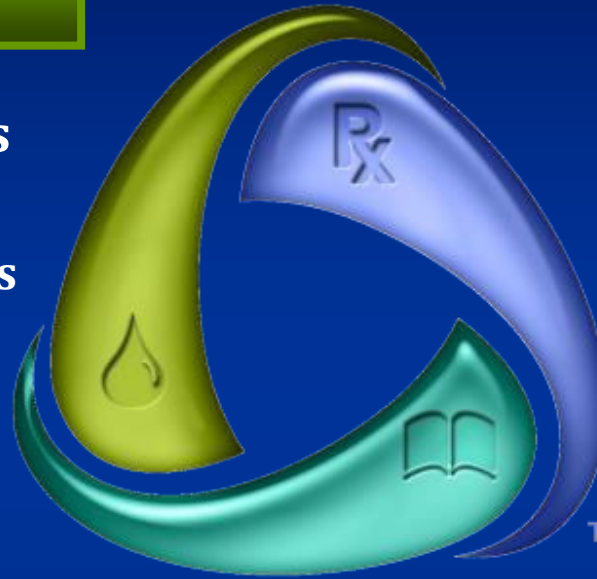
LL-37

- Patients with rosacea have elevated levels of **cathelicidin** and **KLK-5**
- **Cathelicidin** is cleaved into the antimicrobial peptide **LL-37** by both **kallikrein 5** serine proteases
- Excessive production of **LL-37** is suspected to be a contributing cause in **ALL variants** of *Rosacea*

ROSACEA: A Triad Approach to Patient Care

Skin Care

- Cleansers & Moisturizers
- Skin barrier repair
- Appropriate cosmeceuticals
- **SUN PROTECTION**



Prescriptions

- Flare control maintenance
- **PHARMACOLOGY:**
- Erythema
- Papules & Pustules
- Comorbid Conditions

Patient Education

- Inform patients about the chronic, long-term nature of rosacea
- Manage patient expectations about therapy
- Teach patients to identify and manage **trigger factors**
- Stress importance of adherence after initial improvement

Pharmacology: *Rosacea Therapies*

2013-Present

- Topical Brimonidine .33%
- Topical Ivermectin 1%
- Oxymetazoline HCL 1%
- Probiotics
- New Research: Genetics

1953

- Oral Tetracycline

1956

- Topical Sulfacetamide-Sulfur

1967

- Oral Doxycycline

Mid-1970s

- Topical Antibiotics
- Erythromycin
- Clindamycin

1972

- Oral Minocycline

2002

- Topical Azelaic Acid 15%
- Generic Metronidazole .75%

2005

- Topical Metronidazole 1.0%

2006

- Subantimicrobial Docycycline 40mg

1988

- Topical Metronidazole

Late 1990s - 2004

- Sulfacetamide-Sulfur Formulations

Pharmacology: Vehicle Matters

- Cream
- Foam
- Gel
- Lacquer
- Lotion
- Paste
- Powder
- Ointment
- Spray
- Tincture or Solution

Interaction



ROSACEA: A PHARMACOLOGIC PERSPECTIVE

- Dietary and lifestyle changes
- Free provider and patient information available:
- **WWW.ROSACEA.ORG**
- Topical Metronidazole: Cream, Gel, Lotion
- Azelaic Acid: Cream, Foam, Gel (Finacea®)
- Ivermectin 1% Cream (Soolantra®)
- Brimonidine 0.33% Gel (Mirvaso®)
- Oxymetazoline HCL 1% (Rhofade®)
- Topical retinoids: Cream, Foam, Gel
- Isotretinoin in severe cases: Oral (**iPLEDGE Program**)
- Ocular: Doxycycline (Oracea®) and Gentle Shampoo/Wipes



PHARMACOLOGY: TOPICAL AZALEIC ACID

- FDA approved 2003: **PAPULOPUSTULAR ROSACEA**
- Decreases cathelicidin expression after 4 weeks
- Decrease KLK-5 mRNA expression after 12 weeks
- Has comedolytic properties: **ACNE & MELASMA**
- Foam vehicle more tolerable than the cream or gel

PHARMACOLOGY: ORAL DOXYCYCLINE



- Subantimicrobial Dose:
- **ANTI-INFLAMMATORY**
- Doxycycline: 40mg Capsules Decreases LL-37 levels
- Doxycycline: 20 mg By Mouth BID
- Indirectly Inhibits Serine Protease Activity (SPA) by Inhibiting Matrix Metalloproteinases (**MMPS**)
- Improves **PAPULOPUSTULAR**
- Improves **OCULAR ROSACEA**
- **EDUCATE TO WEAR SUN PROTECTION**

DEMODEX FOLLICULORUM AND *BACILLUS OLERONIUS*



- *DEMODEX FOLLICULORUM* most common ectoparasites
- Increased mite prevalence found in people with **PAPULOPUSTULAR ROSACEA**
- New evidence suggests:
 - *DEMODEX* form a symbiotic relationship with *BACILLUS OLERONIUS*, an anaerobic bacterium able to eliminate lipid degradation products, which *DEMODEX* cannot


PHARMACOLOGY:

- *BACILLUS OLERONIUS*, not *DEMODEX*, is responsible for an increase in an **INFLAMMATORY REACTION**
- *BACILLUS OLERONIUS* TREATMENT:
 - Doxycycline, Erythromycin, Minocycline
 - Topical Ivermectin: Soolantra®

MMPS: ROSACEA, GLIOMAS, & PARKINSON'S

- **MMPs** may contribute to the link between **ROSACEA** and the risk for glioma and **PARKINSON'S DISEASE**
- MMP upregulation is seen in all three disease states and is associated with **NEUROINFLAMMATION**
- Incidence in **ROSACEA** patients **4** times Higher
- The incidence of **PARKINSON'S DISEASE** was 7.62 per 10,000 person-years among rosacea patients vs. 3.54 in the general population

THE NEUROPROTECTIVE EFFECT:

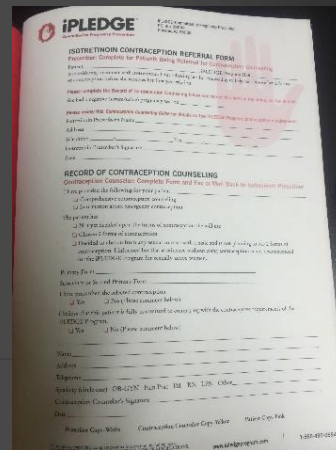
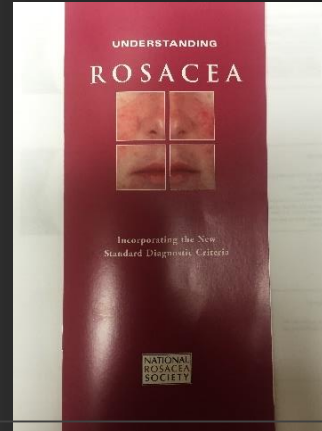
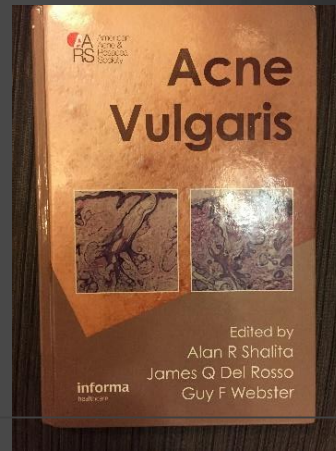
- TCN: Reduces risk of Parkinson's disease in patients with **ROSACEA**
- The Danish Study
- 2%  in Parkinsons if Tetracycline
- **INHIBITS MMP EXPRESSION:** may explain potential neuroprotective effect



SEX MAKES ROSACEA FLARE



UTILIZE RESOURCES



Patient & Provider = **Ticket** to Success!

➤ **Collaboration: iPledge Funding**

NEW ROSACEA TOOL KIT: 1-888-NO-Blush

Diagnostic Tool Sheet

Managing ROSACEA

ROSACEA Diary

NATIONAL ROSACEA SOCIETY

Rosacea Clinical Scorecard

Patient Name _____ Date: _____

Primary Features

Flushing (transient erythema)	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Nontransient erythema	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Papules and pustules	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Telangiectasia	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe

Secondary Features

Burning or stinging	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Plaques	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Dry appearance	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Edema	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
If present:	<input type="checkbox"/> Acute	<input type="checkbox"/> Chronic		
If chronic:	<input type="checkbox"/> Pitting	<input type="checkbox"/> Nonpitting		
Ocular manifestations	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Peripheral location	<input type="checkbox"/> Absent	<input type="checkbox"/> Present		
If present:	List location(s) _____			
Phymatous changes	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Granulomatous changes	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe

Global Assessment

Physician ratings by subtype

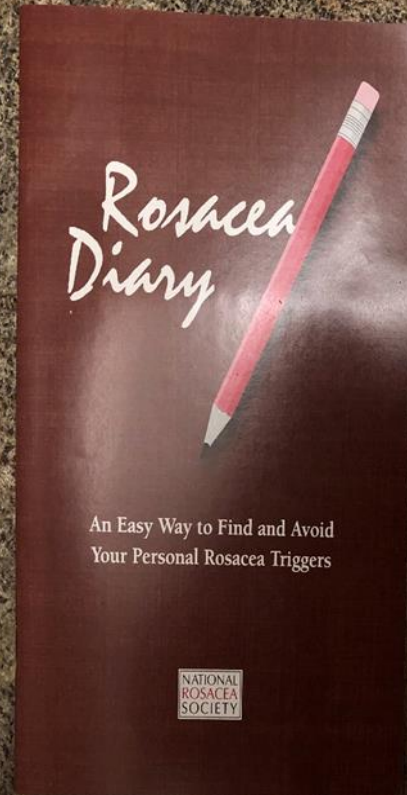
Subtype 1: Erythematotelangiectatic	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Subtype 2: Papulopustular	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Subtype 3: Phymatous	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe
Subtype 4: Ocular	<input type="checkbox"/> Absent	<input type="checkbox"/> Mild	<input type="checkbox"/> Moderate	<input type="checkbox"/> Severe

Patient's global assessment Clear Mild Moderate Severe

Initial symptoms occurred: _____
Treatment prescribed: _____
Comments: _____
Physician: _____

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This form made possible by a grant from the makers of Finacea®

Based on "Standard grading system for rosacea. Report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea." J Am Acad Dermatol 2004;50:957-12. PMA 10220.



Resources for Patients and Clinicians



- **Consumer Lab**: Identifies quality health and nutritional products through independent testing
- **American Botanical Council**: Reliable herbal medicine information

RESOURCES FOR THE HEALTHCARE COMMUNITY

FDA Listings of Generics and Biologics, Including Biosimilars



APPROVED DRUG PRODUCTS
With Therapeutic Equivalence Evaluations



The "Orange Book"



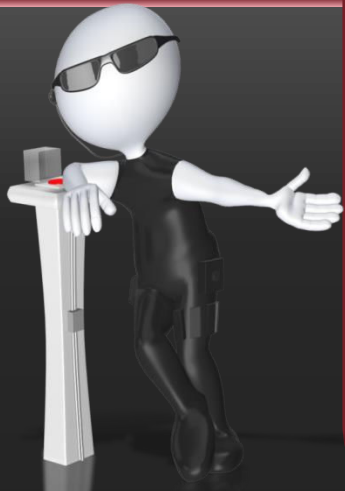
Purple Book

Lists of Licensed Biological Products

With Reference Product Exclusivity and
Biosimilarity or Interchangeability Evaluations

- A listing of approved **small-molecule drugs** and their **generic** equivalents

- Lists of **licensed biological products**, including **biosimilars** and interchangeability evaluations



What is Your Professional Imprint?

RESOURCES

- WWW.ROSACEA.ORG
- WWW.ACNEANDROSACEA.ORG
- [ADVERSE REACTIONS](#)
- 1800-FDA-1088
- www.accessdata.fda.gov
- World Health Organization:
Medication without Harm
www.who.int/patientsafety/medication-safety/en/
- www.fda.gov/health-professionals
- www.ncbi.nlm.nih.gov/home/learn/





*Enjoy
the
Journey!*

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