

# Update in acne management

รศ. พญ. เพ็ญพรรณ วัฒนไกร  
หน่วยโรคผิวหนัง  
ภาควิชาอายุศาสตร์  
รพ.รามธิบดี

J American Acad of Dermatology 2016; 74:945-73.  
**Guidelines of care for the management of acne vulgaris**

Work Group: Andrea L. Zaenglein, MD (Co-Chair),<sup>1</sup> Arun L. Pathy, MD (Co-Chair),<sup>2</sup> Bethanee J. Schlosser, MD, PhD,<sup>3</sup> Ali Alikhan, MD,<sup>4</sup> Hilary E. Balwin, MD,<sup>5</sup> Diane S. Berson, MD,<sup>5a</sup> Whitney P. Bowe, MD,<sup>6</sup> Emmy M. Graber, MD,<sup>6a</sup> Julie C. Harper, MD,<sup>7</sup> Sewon Kang, MD,<sup>8</sup> Jonette E. Keri, MD, PhD,<sup>1a</sup> James J. Leyden, MD,<sup>9</sup> Rachel V. Reynolds, MD,<sup>10</sup> Nanette B. Silverberg, MD,<sup>11</sup> Linda F. Stein Gold, MD,<sup>12</sup> Megha M. Tollefson, MD,<sup>13</sup> Jonathan S. Weiss, MD,<sup>14</sup> Nancy C. Dolan, MD,<sup>15</sup> Andrew A. Sagan, MD,<sup>16</sup> Mackenzie Stern,<sup>17</sup> Kevin M. Boyer, MPH,<sup>18</sup> and Reva Bhushan, MA, PhD<sup>19</sup>  
*Hershey and Philadelphia, Pennsylvania; Centennial, Colorado; Chicago and Schaumburg, Illinois; Cincinnati, Ohio; New York, New York; Boston, Massachusetts; Birmingham, Alabama; Baltimore, Maryland; Miami, Florida; Detroit, Michigan; Rochester, Minnesota; and Atlanta, Georgia*

J Dermatol 2015;42(10):945-53



REVIEW ARTICLE

**South-East Asia study alliance guidelines on the management of acne vulgaris in South-East Asian patients**

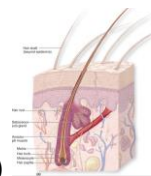
## Acne grading/classification scale

- No universal grading/classification
  - the numbers and types of acne lesion
  - disease severity
  - anatomic sites, and scarring
- to facilitate therapeutic decisions and assess response to treatment.

## Acne management

- Pathogenesis
- Evaluation and DDX
- Treatment

## Acne



- A common disease of the pilosebaceous unit (หน่วยรูขุมและต่อมไขมัน)
- Clinically characterized by comedones, papules, pustules, cysts and scarring
- Face chest back
- Puberty teenagers young adults
- Significant psychologic and economic impact

## Acne severity

- (**mild acne**) mostly comedones / few-several papules/pustules (<10)
- (**moderate acne**) Several to many papules/pustules (<10) Few to many nodules (<5)
- (**severe acne**) numerous papules/ pustules, many nodules / cysts , sinus tract

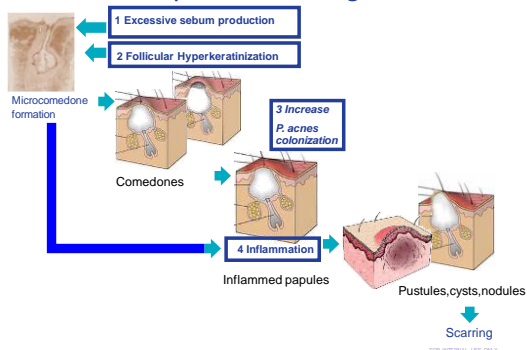
## Prognosis and Complications

- **Prognosis** overall prognosis is good.
- การดำเนินโรคของสิว มักจะเรื้อรัง และกลับเป็นซ้ำ (Recurrence or relapse)
- มักหายไปในช่วงอายุ 20-30 ปี แต่บางคนอาจเรื้อรัง จนเข้าสู่วัยผู้ใหญ่
- ร้อยละ 85 ของผู้เป็นสิว เป็นสิวนชนิดไม่รุนแรง ร้อยละ 15 ของผู้เป็นสิว เป็นสิวนอักเสบรุนแรง

## Prognosis and Complications

- **Complications**
- psychosocial impairment
- permanent scarring.

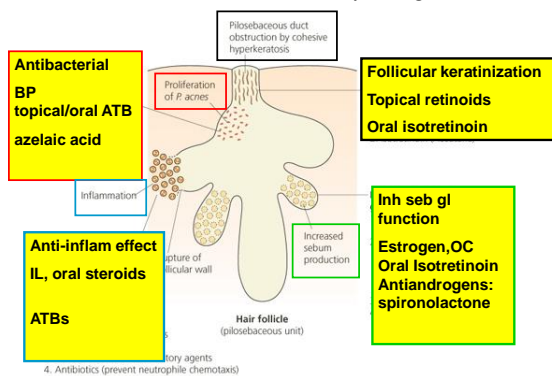
### Pathogenesis of acne 4 key factors causing acne



### Acne Rx: Target the pathogenesis

1. removing obstructions of the follicles (comedolytics)
2. reducing the rate of sebum secretion, (anti-androgens)
3. reducing the follicular P. acnes (antimicrobials)
4. anti-inflammatory agents

### Mode of action of Acne therapeutic agents



4. Antibiotics (prevent neutrophil chemotaxis)

# DDx in acne


### Evaluation of acne patients

- Severe/sudden acne **Drug/other precipitant**
  - Therapy-resistant acne
  - Unusual clinical
  - Rapid relapse post isotretinoin
  - Signs of hyperandrogenism **Syndrome associated**
    - severe acne
    - sudden onset
    - hirsutism
    - irregular menstrual periods
    - deepening of the voice
    - precocious puberty
    - increase in libido
- Hyperandrogen Endocrine abn.**

### DIFFERENTIAL DIAGNOSIS OF HYPERANDROGENISM IN FEMALES

- Polycystic ovary syndrome (80% of all hyperandrogenism in women)
- Androgen-secreting neoplasm (adrenal or ovary)
- Nonclassical congenital adrenal hyperplasia
- HAIR-AN (Hyperandrogenism, insulin resistance, acanthosis nigricans)
- Hyperandrogenism and hirsutism
- Exogenous steroid administration

Harper JC. JDD 2008;7(6):527-530.



### POLYCYSTIC OVARY SYNDROME

- Anovulation
- ovarian cysts
- irregular menses, obesity, androgenic alopecia, hirsutism, acne
- **increased risk of DM endometrial carcinoma**
  - Serum total testosterone 150 to 200 ng/dL
  - increased LH/FSH ratio (> 2.0)



### Endocrinologic Testing

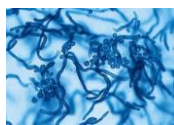
- Routine endocrinologic evaluation (e.g., for androgen excess) is not indicated for the majority of patients with acne.
- Laboratory evaluation is indicated for patients who have acne and additional signs of androgen excess.

### symptoms of hyperandrogenism

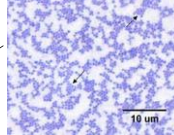
- young children : body odor, axillary or pubic hair, and clitoromegaly.
- Adult women : recalcitrant or late-onset acne, infrequent menses, hirsutism, male or female pattern alopecia, infertility, acanthosis nigricans, and truncal obesity.



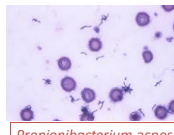
Acne=disease of the sebaceous gland  
Sebaceous gland normal flora




*Malassezia spp*



*Staph. epidermidis*



*Propionibacterium acnes*



mite *Demodex*

## Differential diagnosis

Folliculitis – staphylococcal,  
Gram-negative,  
eosinophilic, *Pityrosporum*,  
*Demodex*

- Acne/acneiform eruptions due to topical or systemic drugs



do not have comedos  
monomorphous

- acne vulgaris



- variety of acne lesions (comedones, pustules, papules, and nodules)

- on the face, back, or chest

## Drug-induced folliculitis (acneiform eruption)

- corticosteroids
- Anabolic steroids (danazole and testosterone)
- androgenic hormones,
- iodides, bromides,
- lithium,
- isoniazid
- Anticonvulsant :phenytoin
- inhibitors of the epidermal growth factor receptor (EGFR)

## การรักษาสิว ACNE

### การรักษาโดยใช้ยา

ยารับประทาน  
ยาทาเฉพาะที่

### การรักษาโดยวิธีทางกายภาพ

การกดสิว  
การฉีดยาสตีรอยด์ใต้หัวสิว  
Chemical Peeling

## ACNE (โรคสิว)

### การรักษาโดยใช้ยา

#### ยาทาเฉพาะที่

ใช้กับสิวไม่รุนแรง - ปานกลาง  
ใช้ร่วมกับยารับประทานเพื่อรักษาสิवरุนแรง

#### ยารับประทาน

ใช้กับสิवरุนแรงปานกลาง - รุนแรงมาก

## การรักษาโดยใช้ยาทาเฉพาะที่

- all topical treatments are preventative,
- use for 6–8 weeks is required to judge their efficacy.
- The entire acne affected area is treated, not just the lesions, and
- Long term usage is the rule.

## Topical Therapy

- Topical retinoids 0.01-0.1%
- จับและกระตุ้น nuclear retinoic acid receptors (RARs)
- Affects cell proliferation, differentiation, melanogenesis and inflammation
- comedolytic and anti-inflammatory
- Maintenance Rx

## Topical Therapy

- Topical retinoids 0.01-0.1%
- SE irritation / sun sensitivity
- Low concentration
- Cream VS alcohol-based gel
- hs / every- other- day or short contact 30 min daily
- + moisturizer
- Pregnancy category C

- Benzoyl peroxide (BPO) 2.5-5%
- antimicrobial properties against *P. acnes*, *Staph aureus*
- bacterial resistance to BPO has not been reported
- Mild comedolytic effects
- Ideal for combination Rx

## Topical Therapy

- Benzoyl peroxide 2.5-5%
- SE dryness, irritation
- Short contact to decrease irritation
- Topical application at least 1 hour to be effective
- Pregnancy category C

## Topical Therapy

- Topical antibiotics (e.g., erythromycin and clindamycin)
- Antibacterial + antiinflammatory mechanisms
- use of these agents alone - associated with development of bacterial resistance.

## Topical Therapy

- Topical antibiotics (e.g., erythromycin and clindamycin)
- Less resistance if topical antibiotics are used in combination with BPO
- Combination Topical antibiotic+BPO increases the bactericidal effects
- Pregnancy category B

## Topical Therapy-Others

- Salicylic acid
- Azelaic acid
- sulfur, resorcinol, sodium sulfacetamide, aluminum chloride, and zinc

## Topical Therapy

- **Salicylic acid**= BHA
- lipid soluble beta-hydroxy acid,
- comedolytic
- conc. 0.05-5%
- **Pregnancy category C**

## Hydroxy Acids

Hydroxy acid	Solubility	source	penetration	action
Alpha HA	Water soluble		dermis	Exfoliative,
Glycolic Lactic		Sugar cane Sour milk		
Beta HA salicylic	Lipid soluble	Willow bark, winter green, sweet birch	Epidermis+ pilosebaceous unit	Exfoliative, comedolytic anti-inflam

## Topical Therapy

- **Resorcinol**= antimicrobial
- **Sulfur**= antifungal and bacteriostatic properties ลดการสร้าง FFA, keratolytic
- **OTC**
- Acne cream SA0.5%+R2%+sulfur4%
- Postacne cream: SA0.8%+sulfur3%+calamine
- Acne lotion: SA0.8%+R8%+ZnO,talc

## Topical Therapy

- **Azelaic acid**: dicarboxylic acid
- 20% cream
- Antimicrobial , comedolytic, competitive inh of tyrosinase
- Rx mild – mod acne with PIH
- **Pregnancy category B**

## Topical Therapy

- Topical dapsone** 5% gel
- Mechanism antiinflammatoty
  - Apply bid
  - for inflammatory acne, particularly in adult females with acne > males, adolescents
  - Glucose-6-phosphate dehydrogenase testing not required
  - **Pregnancy category C**

## Oral antibiotics

- INDICATIONS
- moderate and severe acne and treatment resistant forms of inflammatory acne.
- chest, back, truncal acne
- patients in whom absolute control is essential; scarring, post inflammatory hyperpigmentation.

## Problems with Antibiotics use in general

- Evidence supports the efficacy of tetracycline, doxycycline, minocycline, erythromycin, azithromycin, trimethoprim/ sulfamethoxazole (TMP/SMX), amoxicillin, and cephalixin.
- **First line ATB : tetracyclines, macrolides**
- Vaginal candidiasis;
- Bacterial resistant strains;
- gram-negative folliculitis;
- pseudomembranous colitis (especially clindamycin and broad spectrum antibiotics).

### Tetracycline class

- first-line systemic ATB in moderate to severe acne, except when contraindicated
  - tooth discoloration (avoid children  $\leq 8$  years of age)
  - Pregnancy category D: avoid during pregnancy;
  - Drug allergy
- MECH : Antibacterial P. acnes  
Antiinflammatory effects

### Tetracycline

- inexpensive
- dietary restriction: dairy products, Antacids
- photosensitivity
- 500-1000 mg/day 1 hour a.c. or 2 p.c.

### Doxycycline

- More expensive; better GI absorption
- 100-200mg/d pc

### MACROLIDES: Erythromycin

- increasing P acnes resistance;  
Antiinflammatory effects
- gastrointestinal upset
- hepatotoxicity more with estolate form;
- inexpensive;
- **Pregnancy category B: ok in pregnancy, children < 9 years of age;**
- 500-1000 mg/d pc

### Azithromycin

- Sensitivity spectrum similar to other macrolides;
- expensive
- less frequent dosing **250-500 mg x 3 times/week** (1 hour a.c. or 2 p.c.)
- low gastrointestinal intolerance;
- **Pregnancy category B**

## Trimethoprim-Sulfamethoxazole

- Lipophilic;
- *P. acnes* very sensitive;
- Rx of gram -ve folliculitis
- crystalluria (push fluids);
- **FDE, hepatitis, bone marrow suppression;**
- **hypersensitivity reactions (erythema multiforme, SJS, toxic epidermal necrolysis).**
- **Pregnancy category C**
- **Amoxicillin** 250 mg twice daily to 500 mg three times a day
- **Cephalexin** 500 mg twice daily
- Alternative Rx in acne
- **Pregnancy category B**, may be used in pregnancy
- **safe pediatric use**

### คำแนะนำ เพื่อลดการเกิดเชื้อดื้อยา

- 1. หลีกเลี่ยงการใช้ยาด้านจุลชีพชนิดทาหรือรับประทาน ตัวเดียว (**Monotherapy**) ในการรักษาสิว
- 2. เพื่อป้องกันการดื้อยา ควรใช้ยาด้านจุลชีพชนิดทาและรับประทาน **+Benzoyl peroxide / Retinoid**
- 3. ยาด้านจุลชีพชนิดทาและรับประทานไม่ควรให้นานเกิน **12 สัปดาห์ (3-6 เดือน)** และไม่ควรให้น้อยกว่า 3 สัปดาห์ ซึ่งเป็นระยะเวลาที่จะเริ่มเห็นผลจากยาด้านจุลชีพ
- Topical ATB      in mild acne use with BPO/RA
- Oral ATB        in moderate to severe acne

## Oral isotretinoin

- Isotretinoin is a systemic retinoid that is highly effective in the treatment of severe, recalcitrant acne vulgaris
- Oral Isotretinoin effects
  1. normalization of epidermal differentiation,
  2. depresses sebum production, excretion
  3. anti-inflammatory,
  4. reduces *P. acnes*.

## Hormonal Rx

Agents that decrease endogenous production of androgens by ovary or adrenal gland

- **Estrogen-containing combined oral contraceptives**
- glucocorticoids,
- gonadotropin-releasing hormone (GnRH) agonists

Antiandrogens: Spironolactone

## Indications oral isotretinoin

- severe acne not responding to antibiotics and topical therapy.
- less severe forms of acne that produce scarring or excessive psychologic distress
- acne that has demonstrated resistance to other conventional systemic treatments
- acne variants: acne conglobata, acne fulminans (in combination with corticosteroids)
- acne with gram-negative folliculitis



## Oral isotretinoin, Administration and dosage

- varies from 0.1- 0.5 to 1 mg/kg. with meals
- Severe acne : ≥12 years of age:  
0.5-1 mg/kg/day orally in 2 divided doses with food
- Rx resistant, Moderate acne: ≥12 years of age:  
0.3-0.5 mg/kg/day
- no clinical response expected earlier than 1 to 2 months from initiation of treatment ,
- flare of acne several weeks after initiation of treatment - Coadministration with steroids
- The usual duration of treatment varies with a total cumulative treatment dose of 120 to 150 mg/kg.

## Low dose isotretinoin

- Low dose (eg, 0.1 to 0.40 mg/kg daily, or 10 mg daily to 10 mg thrice weekly)
- effective and very well tolerated.
- Low, intermittent dosing (1wk/m) less effective

## Oral isotretinoin

- 40–60% of patients remain acne-free after a single course of isotretinoin.
- Relapse
  - 1/3 of relapsing pt need only topical Rx
  - 1/3 topical Rx +oral ATB
  - 1/3 2<sup>nd</sup> course oral isotretinoin
- Relapse more likely in younger or female patients

## Adverse effects

- Birth defects (pregnancy: category X)
- Retinoid embryopathy is characterized by craniofacial, cardiovascular, central nervous system, and thymus abnormalities
- Two forms of contraception must be used, from 1 month before therapy until 1 month after

## Adverse effects

- Early epiphyseal closure – 2 reported cases on short term isotretinoin for acne
- Safety in children < 12 not established

## common side effects

- pruritus, mucocutaneous SE dryness of skin eyes, lips, mouth, and nose (treatment with emollients),
- Lipid abnormalities- chol TG (dietary management),
- myalgia, and arthralgia (reduction of intense physical activity or use of analgesics)
- **SE dose-related, reversible, and respond to symptomatic therapy.**

## Less common SE

- hepatitis
- photosensitivity (advise sun protection).
- Changes in mood, depression, suicidal ideation reported sporadically
- To date, no studies to suggest an evidence-based link between isotretinoin and depression, anxiety, mood changes, or suicide

## Lab monitoring

- **Baseline monitoring** Liver function test, pregnancy test, lipid panel
- **Ongoing monitoring**
- Pregnancy test every 30 days for females
- Repeat liver function tests and lipid panel at least once during treatment

## COSMETICS / SKIN CARE

- Gentle nonirritant skin cleansing
- use moisturizers , non-comedogenic, non-acnegenic products
- Avoid : oil-based , waterproof , pressed powder
- Water-based, silicone-based (cyclomethicone, dimethicone), loose powder
- Sunprotection



## DIET in acne

- ? the role of milk, high-glycemic load diets , chocolate, sweets, milk, fatty foods and obesity (BMI) in acne
- Dairy products (skim milk > low fat/whole milk, ice-cream) associated with acne
- Not cheese, yoghurt
- Low glycemic load diet: improves acne, decrease seb gl size, decrease inflammation

## กดสิว



- Topical Comedolytic 3-4 wks prior for easier extraction

## การฉีดยาใต้ผิวหนัง

### Intralesional corticosteroid injections

- effective in the treatment of individual acne inflamed papules, nodules.
- Triamcinolone 1-10 mg/ml, 0.05-0.25 ml/lesion
- SE atrophy, hypopigmentation



## Chemical Peeling

- noninflammatory (comedonal) acne
- AHA, glycolic acid peels superficial scarring
- BHA salicylic acid peels inflammatory acne



## Laser / Light



- Lasers (เช่น Pulsed dye laser, KTP laser, Infrared lasers ),
- Narrowband lights เช่น blue light, red light
- แสงความเข้มสูง (Intense pulse light) Photopneumatic therapy
- Photodynamic therapy (PDT)
- Radiofrequency



Figure 1. (A) Multiple inflammatory papules and pustules on the right cheek (penetration). (B) Two weeks after the third session of treatment with topical AHA and 9%. 100% clearance in acne lesions was observed (penetration).

## Take home message

- Acne vulgaris is a common chronic inflammatory disorder of the sebaceous glands
- characterized clinically by comedones, inflammatory lesions (papules, pustules, or nodules ,cysts) and scarring.
- Many other acneform eruptions exist

## Evaluation of acne patients

- Hyperandrogenism
- Unusual clinical presentation
- sudden acne
- Distribution
- Comedones
- Monomorphous
- **Endocrine abn.**
- **Drug**
- **Folliculitis**
  - Infection
  - non-infection
- **Rare syndrome**

## Acne treatment

- Aim to Target the 4 pathogenic factors of acne

Acne pathogenesis	Follicular Hyperproliferation	Increased Sebum production	P acnes proliferation	Inflammation
<b>Targets / Mechanism of action</b>	Correct follicular keratinization	Inhibit sebaceous gland	Antimicrobial effect follicular P acnes	Anti-inflammatory effect
<b>Topical treatment</b>				
Retinoids: Tretinoin, Adapalene, Isotretinoin	++			+
Antimicrobials: Benzoyl peroxide Clindamycin, Erythromycin Azelaic acid Salicylic acid	+		+++ ++	+ +
<b>Systemic treatment</b>				
Antibiotics: Tetracyclines, Macrolides			+++	++
Oral contraceptives Oral isotretinoin	+++	++ +++	++	++

### Acne Rx

- **Retinoids:**
  - Normalize follicular proliferation and differentiation
  - Comedolytic+Targets formation of comedone
  - Anti-inflammatory action
  - Treatment and maintenance
- **Topical retinoids**
  - Tretinoin (Retin-A, Retacnyl, StievaA)
  - Isotretinoin (Isotrex)
  - Adapalene (Differin®)
- **Systemic retinoids**
  - Isotretinoin : Roaccutane, Acnotin, Sotret

FOR INTERNAL USE ONLY

### Acne Rx

- **Antibiotics/ Antimicrobials**
- **Topical / systemic**
  - **Topical ATBs/Antimicrobials**
    - Benzoyl peroxide
      - Has a greater and faster effect in suppressing *P. acnes* > topical ATBs
      - No antibiotic resistance
    - Clindamycin
    - Erythromycin (Eryacne)
    - Avoid antibiotics as monotherapy**
  - Azelaic acid (Skinoren® 20%)
  - Dapsone gel

FOR INTERNAL USE ONLY

### Acne Rx

- **Combination therapy:**
  - **Antimicrobials + retinoids**
  - Mild to moderate acne
  - **Faster and better results in reduction of lesions**
- Adapalene–benzoyl peroxide (Epiduo Gel®, Galderma)
- Benzoyl peroxide–clindamycin (Duac®, Stiefel)
- Isotretinoin-erythromycin (Isotrexin gel, Stiefel)
- Benzoyl peroxide–erythromycin
- Tretinoin-clindamycin

FOR INTERNAL USE ONLY

### Acne Rx

#### Assess clinical severity grade

- to facilitate therapeutic decisions and assess treatment response.
- types of lesions/ severity
  - noninflammatory comedones;
  - inflammatory papules, pustules, nodules
- scarring and/or dyspigmentation.
- extent of affected areas

#### สรุปแนวทางการรักษาสิวตามความรุนแรงของสิว

	การรักษาแนะนำ (Recommend)	การรักษาอื่น (Alternative)
สิวง่ายน้อย (Mild Acne)	Topical Treatment: <ul style="list-style-type: none"> <li>• Comedones: Retinoids</li> <li>• Inflamed lesions: Benzoyl peroxide +/- Topical antibiotics*</li> </ul>	Topical Treatment: <ul style="list-style-type: none"> <li>Azelaic acid</li> <li>Salicylic acid</li> <li>Sulfur</li> <li>Dapsone<sup>Δ</sup></li> </ul>
สิวง่ายปานกลาง (Moderate acne)	เหมือน Mild Acne + Oral Antibiotics*	เหมือน Mild Acne ในเพศหญิง Combined Oral Contraceptive
สิวง่ายรุนแรง (Moderate acne) นาน 6-8 สัปดาห์	Oral isotretinoin	ในเพศหญิง Combined Oral Contraceptive
การรักษาเพื่อควบคุมอาการ (Maintenance Treatment)	Topical retinoids +/- Benzoyl peroxide	Azelaic acid

\* ไม่ควรใช้ยาล้างจุดสิว (Antibiotics) ชนิดทาหรือรับประทาน สิวเดียว (Monotherapy) ในการรักษาสิว Δ ยังไม่มีจำหน่ายในประเทศไทย

## Acne treatment

- Begin with topical treatment whenever appropriate,
- systemic therapy whenever necessary,
- limit use of antibiotics—oral or topical—whenever possible

## Take home message

- With early and adequate treatment, the risk of permanent scarring can be reduced
- All acne treatments work relatively slow improvement is generally after 2-3 months of Rx

## Take home message

- Doctor's Knowledge
- Patient's education + compliance
- play an important role in the overall response and outcome.



### แนวทางการดูแลรักษาโรค Acne Clinical Practice Guideline Acne

- รองศาสตราจารย์นายแพทย์มงคล นพคุณ
- ศาสตราจารย์แพทย์หญิงเพ็ญศรี ทิมพัฒน์พงศ์
- รองศาสตราจารย์แพทย์หญิงวันเนศรี สันสุภักดิ์
- รองศาสตราจารย์แพทย์หญิงเพ็ญพรรณ วิวัฒน์ไกร
- แพทย์หญิงวิศน์ ฉัตรพันธ์
- แพทย์หญิงนลินี สุทธิไพศาล
- ร้อยโทหญิงแพทย์หญิงวิรัชยาณี คนจร ฅ อออุธยา
- รองศาสตราจารย์นายแพทย์นิยม ตันติคุณ
- นายแพทย์รัฐกรณ์ นีระการณ
- นายแพทย์วิบูลย์ ใจจนวานิช
- แพทย์หญิงภาวณี อุภรณ์มิตร
- นายแพทย์เจษฎ์ วิฑิตสุวรรณกุล