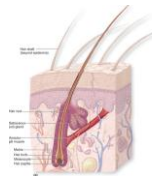


Management of acne

รศ. พญ. เพ็ญพรรณ วัฒนไกร
หน่วยโรคผิวหนัง
ภาควิชาอายุศาสตร์
รพ.รามธิบดี

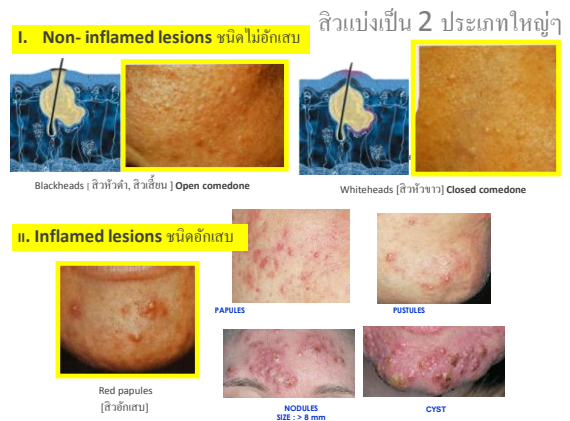
Acne

- A common disease of the pilosebaceous unit (หน่วยรูขุมขนและต่อมไขมัน)
- Significant psychologic and economic impact
- Clinically characterized by comedones, papules, pustules, cysts and scarring



Acne management

- Pathogenesis
- Evaluation and DDX
- Treatment



Acne severity

- **(mild acne)** mostly comedones / papules, pustules < 10
- **(moderate acne)** papules, pustules < 10 and/or nodules < 5
- **(severe acne)** papules, pustules, nodules, cysts จำนวนมาก, sinus tract

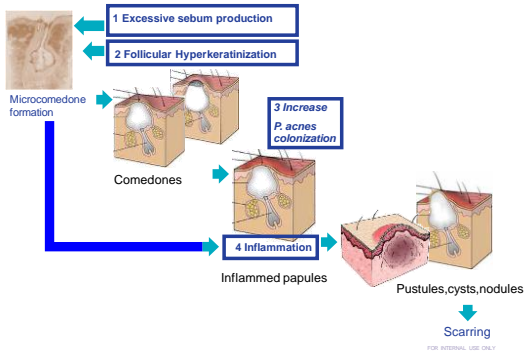
Treatment of Acne

- pathogenesis of acne



Pathogenesis of acne

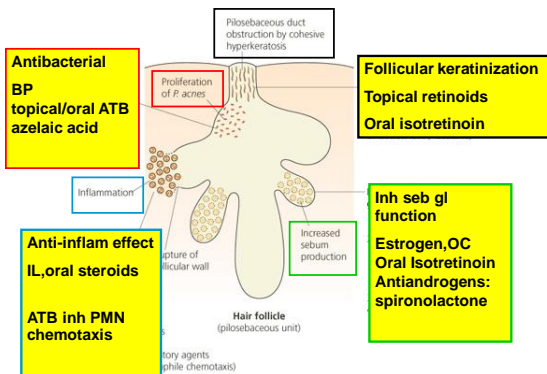
4 key factors causing acne



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



Global Alliance consensus on Acne Rx

- Retinoids:
 - Normalize follicular proliferation and differentiation
 - Target the 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

Global Alliance consensus on Acne Rx

- Antibiotics:
 - Minimize the use of antibiotics (<12 weeks)
 - Avoid antibiotics as monotherapy
- BPO:
 - Has a greater and faster effect in suppressing P. acnes > topical ATBs
 - No antibiotic resistance
- Topical ATBs/Antimicrobials
 - Benzoyl peroxide
 - Clindamycin
 - Erythromycin (Eryacne)
 - Azelaic acid (Skinoren® 20%)
 - Dapsone gel

Global Alliance consensus on 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

Best management of 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 **Hyperandrogen**
 - deepening of the voice **Endocrine abn.**
 - precocious puberty
 - increase in libido

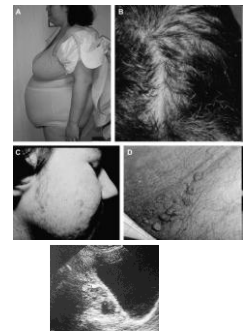
Hyperandrogenism

- PCOS
- CAH
- Adrenal neoplasia
- Ovarian neoplasms



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

- In young children may be manifested by body odor, axillary or pubic hair, and clitoromegaly.
- Adult women may present with recalcitrant or late-onset acne, infrequent menses, hirsutism, male or female pattern alopecia, infertility, acanthosis nigricans, and truncal obesity.



DDx in acne

Acne=disease of the sebaceous gland
Sebaceous gland normal flora

Differential diagnosis

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

• Acne/acneiform eruptions
due to topical or systemic
drugs

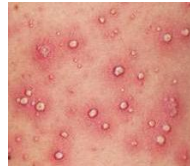
do not have comedos
monomorphous

• acne vulgaris



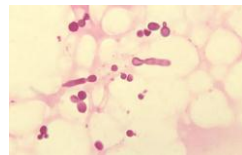
• variety of acne lesions
(comedones, pustules,
papules, and nodules)
• on the face, back, or chest

Folliculitis
Bacterial folliculitis



- Bacterial folliculitis commonly
due to *Staphylococcus aureus*
- **Gram-negative folliculitis**
- Due to *Pseudomonas aeruginosa*, *Klebsiella*, *Enterobacter*, *Proteus* spp.
- Usually in acne patients receiving long-term antibiotic

Drug-induced folliculitis
(acneiform eruption)



Pityrosporum folliculitis
gram stain: oval, round yeast with budding yeast

- corticosteroids
- Anabolic steroids (danazole and testosterone)
- androgenic hormones,
- iodides, bromides,
- lithium,
- isoniazid
- Anticonvulsant :phenytoin
- inhibitors of the epidermal growth factor receptor (EGFR)
- Less often, azathioprine, cyclosporine, vitamins B1-2-12, vitamin D₂, phenobarbital, PTU propylthiouracil,

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)

Epidermal Growth Factor Receptor (EGFR) Inhibitor–Associated Eruption

- gefitinib, cetuximab, erlotinib,
- ☒ EGFR inhibitors are used to Rx advance malignancies
- **Clinically** : eruptive, monomorphous follicular pustules and papules
- the face, scalp and upper trunk



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 the expression of genes involved in 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

- Benzoyl peroxide (BPO) 2.5-5%
- nonspecific bactericidal effective against *P. acnes*, and
- bacterial resistance to benzoyl peroxide has not been reported
- 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

Topical Therapy

- Topical antibiotics (e.g., erythromycin and clindamycin)
- effective acne treatments.
- use of these agents alone - associated with development of bacterial resistance.
- resistance is lessened if topical antibiotics are used in combination with BPO

Topical Therapy-Others

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

Topical Therapy

- Salicylic acid= lipid soluble beta-hydroxy acid, comedolytic
- conc. 0.5-2%
- Resorcinol= antimicrobial
- Sulfur= 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

การรักษาโดยใช้ยารับประทาน

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

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.
- First line ATB : tetracyclines, macrolides
- Other antibiotics, such as amoxicillin, clindamycin and trimethoprim/sulfamethoxazole are second line treatments.

Problems with Antibiotics use in general

- Vaginal candidiasis;
- Bacterial resistant strains;
- gram-negative folliculitis;
- pseudomembranous colitis (especially clindamycin and broad spectrum antibiotics).

Tetracycline

- P. acnes sensitive;
- inexpensive; 500-1000 mg/d
- dietary restriction, dairy products
- **tooth discoloration (under age 9); avoid during pregnancy;**
- photosensitivity
- **500-1000 mg/day 1 hour a.c. or 2 p.c.**
- **Use in children >= 12 years**

Doxycycline

- Lipophilic;
- P. acnes very sensitive; resistance rare; photosensitivity,
- More expensive; better GI absorption
- avoid during pregnancy and in children
- 100-200mg/d pc

Erythromycin

- increasing P acnes resistance;
- gastrointestinal upset
- hepatotoxicity more with estolate form;
- inexpensive;
- ok in pregnancy, children < 9 years of age;
- not first line ATB therapy in acne.
- 1000 mg/d pc

Trimethoprim-Sulfamethoxazole

- Lipophilic;
- P. acnes very sensitive;
- gram -ve folliculitis
- crystalluria (push fluids);
- FDE, hepatitis, bone marrow suppression;
- hypersensitivity reactions (erythema multiforme, SJS, toxic epidermal necrolysis).

Clindamycin

- P. acnes very sensitive;
- somewhat lipophilic;
- pseudomembranous colitis makes it third-line drug.
- Mainly used topical form, in combination+BPO

Amoxicillin

- 250 mg twice daily to 500 mg three times a day
- alternative Rx and may be useful in pregnancy

แนวทางเพื่อลด ATB resistance

- Topical ATB in mild acne use with BPO/RA
- Oral ATB in moderate to severe acne
- กำหนดระยะเวลาการใช้ ATB 3-6m และประเมินผลการรักษาใน 6-12 wk

Hormonal Rx

Antiandrogens: Spironolactone

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

- oral contraceptives,
- glucocorticoids,
- gonadotropin-releasing hormone (GnRH) agonists

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 excretion by 70%,
 3. anti-inflammatory,
 4. reduces *P acnes*.

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 such as oral antibiotics.
- acne variants: acne conglobata, acne fulminans (in combination with corticosteroids)
- acne with gram-negative folliculitis

Oral isotretinoin, Administration and dosage

- varies from 0.5 to 1 mg/kg. divided in two doses.
- no clinical response expected earlier than **1 to 2 months** from initiation of treatment ,
- **A flare of acne** several weeks after initiation of treatment in **6% of patients**.
- The usual duration of treatment varies with **a total cumulative treatment dose of 120 to 150 mg/kg**.

Low dose isotretinoin

- (eg, 0.1 to 0.40 mg/kg daily, or 10 mg daily to 10 mg thrice weekly)
- effective and very well tolerated.
- Less Remissions when patients do not complete a cumulative dosage

Oral isotretinoin

- **40–60%** of patients remain acne-free after a single course of isotretinoin.
- **Relapse**
1/3 of the relapsing pt need only topical Rx
2/3 oral treatments.

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 –
- ไม่ควรใช้ในเด็ก อายุ < 18

common side effects

- pruritus, mucocutaneous SE dryness of skin eyes, lips, mouth, and nose (treatment with emollients),
- Lipid abnormalities (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).
- psychiatric side effects, including depression, suicide ideation, and suicide **controversial**

??

การรักษาเสริม adjunctive therapy



COSMETICS / SKIN CARE

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



DIET in acne

- ? may be link between milk, high-glycemic index foods and acne.
- ? the role of chocolate, sweets, milk, high-glycemic index foods, and fatty foods in acne requires further study

กดสิว



- Topical Comedolytic 3-4 wks prior for easier extraction

การฉีดยาใต้หัวสิว

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

- AHA, glycolic acid peels
- BHA salicylic acid peels



Laser / Light



- สิ่งนี้อาจเกิดขึ้นหลังทำเลเซอร์
- pain -discomfort, erythema, edema, crusting ,
- hyper-hypopigmentation

Before

After



Take home message

- Acne vulgaris is a common disorder of the sebaceous glands
- characterized clinically by comedones, papules, pustules, cysts and scarring.
- Many other acneform eruptions exist

Evaluation of acne patients

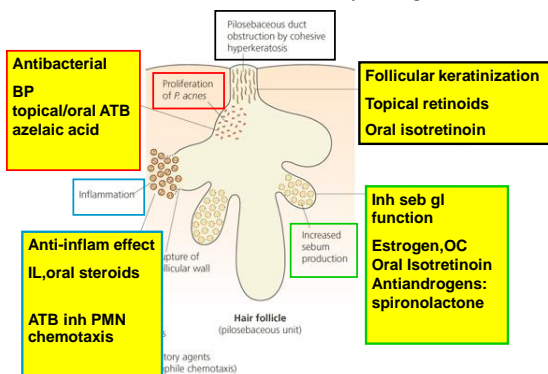


Acne treatment

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

- Aim to Target the 4 pathogenic factors of acne

Mode of action of Acne therapeutic agents



Acne Rx the clinical severity grade

- extent of affected areas
- types of lesions
 - noninflammatory comedones;
 - inflammatory papules, pustules, nodules
- presence or absence of scarring and/or dyspigmentation.



Acne Rx

- **Topical**
- retinoids and
- antimicrobials
 - benzoyl peroxide,
 - antibiotics,
 - azelaic acid
- **Systemic**
- antibiotics,
- oral isotretinoin,
- hormonal Rx in females

Combination therapies work better

TREATMENT ALGORITHM					
	Mild	Moderate	Moderate	Severe	Severe
	A.comedonica ¹	A.pap.pust. ¹	A.pap.pust. ¹	A.pap.pust.nod. ^{1,2}	A.conglobata
1st Choice	Topical Retinoid	Top. Retinoid plus topical anti-microbial agent	Oral Antibiotic plus topical retinoid +/- BPO	Oral Antibiotic plus topical retinoid plus BPO	Oral Isotretinoin ³ Not anymore first choice
Alternatives	All. Top. Retinoid or Azelaic Acid or Salicylic Acid	Alternative top. Retinoid plus Alternative Antimicrobial agent / Azelaic Acid	Alternative Oral Antibiotic plus Alternative top. Retinoid +/- BPO / Azelaic Acid	Oral Isotretinoin or Alternat. Oral Antibiotic plus Alt. Top. Retinoid BPO / Azelaic Acid	High Dose Oral Antibiotic + Topical Retinoid + BPO
Alternatives or Females⁴	See 1 st Choice	See 1 st Choice	Oral Antiandrogen ⁵ plus Top. Retinoid / Azelaic Acid +/- BPO	Oral Antiandrogen ⁵ plus Top. Retinoid / Azelaic Acid +/- BPO	High dose ⁵ Oral Antiandrogen plus Top. Retinoid / Azelaic Acid +/- BPO
Maintenance Therapy:	Top. Retinoid			Top. Retinoid +/- BPO	

1)* plus physical removal of comedones 2)* with small nodes (0.5 - 1cm) 3)* 2nd course in case of relapse 4)* for pregnancy refer for local regulations 5)* any type of antiandrogenic anticonceptive pill

Goilnick, Cunliffe et al (2003) JAAD



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 / Patient's compliance
- play an important role in the overall response and outcome.



แนวทางการดูแลรักษาโรค Acne Clinical Practice Guideline Acne

- รองศาสตราจารย์นายแพทย์มงคล นพคุณ
- ศาสตราจารย์แพทย์หญิงเพ็ญศรี พิมพ์บพิงค์
- รองศาสตราจารย์แพทย์หญิงวันเนศรี สันสุภักดิ์
- รองศาสตราจารย์แพทย์หญิงเพ็ญพรรณ วิวัฒน์ไกร
- แพทย์หญิงวิศน์ ฉัตรพันธ์
- แพทย์หญิงนลินี สุทธิไพศาล
- ร้อยโทหญิงแพทย์หญิงวิรัชานี คนเจริญ อยุธยา
- รองศาสตราจารย์นายแพทย์นิยม ต้นศิคุน
- นายแพทย์รัฐกรณ์ อีเมการณ
- นายแพทย์วิบูลย์ ใจจนวานิช
- แพทย์หญิงภาวณี อุภรณ์มิตร
- นายแพทย์เจษฎ์ วิฑิตสุวรรณกุล