Acne management

• Pathogenesis
• Evaluation and DDx
• Treatment

Acne

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

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 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.
- **Complications**
  - Psychosocial impairment
  - Permanent scarring.

### Prognosis and Complications

- **Prognosis**
  - การด าเนินโรคของสิว มักจะเรื้อรัง และกลับเป็นซ้ ้า (Recurrence or relapse)
  - มักหายไปในช่วงอายุ 20-30 ปีแต่บางคนอาจยังคงเข้าสู่วัยผู้ใหญ่
  - ร้อยละ 85 ของผู้เป็นสิว เป็นสิวชนิดไม่รุนแรง ร้อยละ 15 ของผู้เป็นสิว เป็นสิวอักเสบรุนแรง

### Pathogenesis of acne

**4 key factors causing acne**

1. Excessive sebum production
2. Follicular Hyperkeratinization
3. Increased P. acnes colonization
4. Inflammation

### 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

- **Antibacterial**
  - BP, topical/oral ATB, azelaic acid
- **Follicular keratinization**
  - Topical retinoids, Oral isotretinoin
- **Anti-inflammatory**
  - IL, oral steroids, ATBs
- **Antibiotics**
  - Prevent excess P. acnes colonization
Evaluation of acne patients

- Severe/sudden acne
- Therapy-resistant acne
- Unusual clinical
- Rapid relapse post isotretinoin
- Signs of hyperandrogenism
  - severe acne
  - sudden onset
  - hirsutism
  - irregular menstrual periods
  - deepening of the voice
  - precocious puberty
  - increase in libido

Drug/other precipitant

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


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
Propionibacterium acnes
Staph. epidermidis
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)

ACNE (โรคสิว)

การรักษาโดยใช้ยา

ยาทาระยะยาว
ยาทาระยะสั้น

การรักษาโดยวิธีทางกายภาพ

การกดสิว
การเร็มยาด้วยคลื่น diğerเรซิ่ง
Chemical Peeling

การรักษาโดยใช้ยาทาระยะชั้น

• 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

Topical Therapy

- Benzoyl peroxide (BPO)2.5-5%
- antimicrobial properties against \textit{P acnes}, \textit{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- Others

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

Topical Therapy- Others

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

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

Hydroxy Acids

<table>
<thead>
<tr>
<th>Hydroxy acid</th>
<th>Solubility</th>
<th>source</th>
<th>penetration</th>
<th>action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha HA Glycolic</td>
<td>Water soluble</td>
<td>Sugar cane Sour milk</td>
<td>dermis</td>
<td>Exfoliative,</td>
</tr>
<tr>
<td>Lactic</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Beta HA salicylic</td>
<td>Lipid soluble</td>
<td>Willow bark, winter green, sweet birch</td>
<td>Epidermis+pilosebaceous unit</td>
<td>Exfoliative, comedolytic anti-inflamm</td>
</tr>
</tbody>
</table>

Topical Therapy

• Resorcinol = antimicrobial
• Sulfur = antifungal and bacteriostatic properties, FFA, keratolytic
• OTC
• Acne cream: SA0.5%+R2%+sulfer4%
• Postacne cream: SA0.8%+sulfer3%+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 antiinflammation
• 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.
• Evidence supports the efficacy of tetracycline, doxycycline, minocycline, erythromycin, azithromycin, trimethoprim/ sulfamethoxazole (TMP/SMX), amoxicillin, and cephalexin.

• First line ATB: tetracyclines, macrolides

Problems with Antibiotics use in general

• 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<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

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

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.

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 2nd 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

- 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

**كدية**

- Topical Comedolytic 3-4 wks prior for easier extraction
**Chemical Peeling**

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

**Laser / Light**

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

**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
- Endocrine abn.
- Drug
- Folliculitis
  - Infection
  - non-infection
- Distribution
- Rare syndrome
- Comedones
- Monomorphous

**Acne treatment**

- Aim to Target the 4 pathogenic factors of acne
Acne pathogenesis

<table>
<thead>
<tr>
<th>Targets / Mechanism of action</th>
<th>Follicular Hyperproliferation</th>
<th>Increased Sebum production</th>
<th>P. acnes proliferation</th>
<th>Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct follicular keratinization</td>
<td>Inhibit sebaceous gland</td>
<td>Antimicrobial effect follicular</td>
<td>Anti-inflammatory effect</td>
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Acne Rx

**Topical Retinoids:**
- Normalize follicular proliferation and differentiation
- Comedolytic-Targets formation of comedone
- Anti-inflammatory action
- Treatment and maintenance

**Systemic Retinoids:**
- Isotretinoin (Isotrex)
- Adapalene (Differin®)

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

**Antibiotics/Antimicrobials**
- Tetracyclines
- Macrolides
- Oral contraceptives
- Oral isotretinoin

**Systemic treatment**
- Antibiotics:
  - Tetracyclines
  - Macrolides
  - Oral contraceptives

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

**Combination therapy:**
- **Antimicrobials + retinoids**
  - Mild to moderate acne
  - Faster and better results in reduction of lesions

Acne Rx

- Adapalene–benzoyl peroxide (Epiduo Gel®, Galderma)
- Benzoyl peroxide–clindamycin (Duac®, Stiefel)
- Isotretinoin-erythromycin (Isotrexin gel, Stiefel)
- Benzoyl peroxide–erythromycin
- Tretinoin-clindamycin

*Not available in Thailand*
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.