Acne management

- Pathogenesis
- Evaluation and DDx
- Treatment

Acne

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

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

1. Excessive sebum production
2. Follicular Hyperkeratinization
3. Increase 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

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 Antibacterial ATBs/Antimicrobials**
  - Benzoyl peroxide
  - Clindamycin
  - Erythromycin (Eryacne)
  - Azelaic acid (Skinoren 20%)

- **Topical retinoids**
  - Tretinoin (Retin-A, Retacnyl, StievaA)
  - Isotretinoin (Isotrex, Adapalene (Differin®)

- **Systemic retinoids**
  - Isotretinoin: Roaccutane, Acnotin, Sotret

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

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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.

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

Syndrome associated

Hyperandrogen Endocrine abn.

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

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)
- corticosteroids
- Anabolic steroids (danazole and testosterone)
- androgenic hormones,
- iodides, bromides,
- lithium,
- isoniazid
- Anticonvulsants: phenytoin
- inhibitors of the epidermal growth factor receptor (EGFR)
- Less often, azathioprine, cyclosporine, vitamins B1-2-12, vitamin D3, phenobarbital, PTU propylthiouracil,
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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

**ACNE (โรคสิว)

การรักษาโดยใช้ยา

ยาทะเลสาบ
ยาเฉพาะที่

การรักษาโดยวิธีทางกายภาพ

การกดสิว
การฉีดยาสตีรอยด์ใต้หัวสิว
Chemical Peeling

การรักษาโดยใช้ยาเฉพาะที่

• 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 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 =ลดการสร้างFFA, keratolytic
- OTC
  - Acne cream SA 0.5%+R2%+sulfur4%
  - Postacne cream: SA 0.8%+sulfur3%+calamine
  - Acne lotion: SA 0.8%+R8%+ZnO,talc
Topical Therapy

- **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 amoxycillin, 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

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.

Adverse effects

• Early epiphyseal closure –

Less common SE

• hepatitis
• photosensitivity (advise sun protection).

• psychiatric side effects, including depression, suicide ideation, and suicide controversial

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

การรักษาเสริม adjunctive therapy

“สิ”

Water-based, silicone-based (cyclomethicone, dimethicone), loose powder
DIET in acne

• May be a 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.

กลิ่น

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

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

- Hyperandrogenism
- Unusual clinical presentation
- Sudden acne
- Distribution
- Comedones
- Monomorphous
- Endocrine abn.
- Drug
- Folliculitis
  - Infection
  - Non-infection
- PCOS/Rare syndrome

Acne treatment

- Aim to target the 4 pathogenic factors of acne

Acne Rx

- **Topical**
  - Retinoids and
  - Antimicrobials
    - Benzoyl peroxide,
    - Antibiotics,
    - Azealaic acid
- **Systemic**
  - Antibiotics,
  - Oral isotretinoin,
  - Hormonal Rx in females

Combination therapies work better
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.