Acne
Mechanisms that contribute to acne

1. **Follicular Keratinization**
   - (↓ thyroid, ↓ vitamin A)
   - Excess skin cells clogging the pore.

2. **Sebaceous Activity**
   - (↓ estrogens in women, ↑ testo & DHEA, GH)
   => Excess sebum, mixes with the dead skin cells, causing a blackhead.

3. **Inflammation**
   - (↓ cortisol, ↓ zinc)
   = inflammatory response causes redness & swelling

4. **Propionibacterium Acnes (P. Acnes)**
   - (↓ thyroid, ↓ cortisol)
   lies deep within the pore and can break down the heavy oil in the sebaceous gland, which causes inflammation and results in blemishes and breakouts
White, closed comedones

Whiteheads (closed comedones) = the earliest lesions of acne.
Blackheads, or open comedones, are common in acne. Clogged hair follicles reflect light irregularly to produce this black hue.
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Pimple
Pïmples => cysts
Cystic disease
Acne: Grades

The grades of acne

- **Grade I**
  - Comedones (open, closed)
  - Few papules

- **Grade II**
  - Comedones
  - Papules
  - Few pustules

- **Grade III**
  - Comedones
  - Papules
  - Pustules
  - Few nodules

- **Grade IV**
  - Comedones
  - Papules
  - Pustules
  - Nodules
  - Cysts
Acne: Causes

1. Wrong food (chocolate, yoghurt, baked fats, …)
2. Sufficient or high DHEA, testosterone levels
3. Low estrogens (women), low thyroid
4. Low cortisol, zinc => purulent acne

2 essential causes (usually they need to be both present)
2 aggravating factors
Wrong food + hormone or nutrient imbalance = cause of acne
↑ milk intake => ↑ acne in girls

SUBJECTS: 6,094 girls, aged 9-15 years  BLOOD TESTS: Women + acne (vs normal controls)

• The result did not change appreciably when we excluded girls who reported use of contraceptives & when we restricted our analysis to those < 11 years of age at baseline.

=> positive association between intake of milk & acne

<table>
<thead>
<tr>
<th></th>
<th>Lowest milk intake (&lt;1 per week)</th>
<th>Highest milk intake (≥ 2 servings/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total milk</td>
<td>1</td>
<td>1.20 (1.09, 1.31; &lt;0.001)</td>
</tr>
<tr>
<td>Whole milk</td>
<td>1</td>
<td>1.19 (1.06, 1.32; &lt;0.001)</td>
</tr>
<tr>
<td>Low fat milk</td>
<td>1</td>
<td>1.17 (1.04, 1.31; 0.002)</td>
</tr>
<tr>
<td>Skim milk</td>
<td>1</td>
<td>1.19 (1.08, 1.31; &lt;0.001)</td>
</tr>
</tbody>
</table>

Milk & cheese intake => acne in girls

SUBJECTS: 47,355 women + severe teenage acne + questionnaires on retrospective food intake

Positive association between intake of milk & acne

⇒ Instant breakfast drink, sherbet, cottage cheese, & cream cheese were also positively associated with acne.

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<td>(&lt;1 per week)</td>
<td>(≥ 2 servings/day)</td>
</tr>
<tr>
<td>Total milk</td>
<td>1</td>
<td>1.22 (1.03, 1.44; .002)</td>
</tr>
<tr>
<td>Whole milk</td>
<td>1</td>
<td>1.12 (1.00, 1.25; .56)</td>
</tr>
<tr>
<td>Low fat milk</td>
<td>1</td>
<td>1.16 (1.01, 1.34; .25)</td>
</tr>
<tr>
<td>Skim milk</td>
<td>1</td>
<td>1.44 (1.21, 1.72; .003)</td>
</tr>
</tbody>
</table>

↓ carb diet => ↓ acne in male patients

SUBJECTS: 43 male patients + acne

BLOOD TESTS: ↓ glycemic-load diet (vs conventional, high glycemic-load diet): during 12 weeks
- Greater ↓ total acne lesion counts (-21.9 vs -13.8 P = .01).
- ↓ weight (P = .001),
- ↓ free androgen index (P = .04)
- IGFBP-1 (P = .001)

LIMITATIONS: possible role of weight loss in the overall treatment effect.

↑ Testosterone

⇒ ↑ risk of acne in men
Testosterone treatment => ↑ skin surface lipids, esp. Cholesterol & free fatty acids, ↑ Propionibacteria acnes

SUBJECTS: healthy young men

TREATMENT: self-administered 8 weeks of ↑ doses of testosterone & anabolic steroids during a 12-week strength training period.

• ↑ amount of dissolved skin surface lipids (SSL),
• ↑ Colony Forming Units/cm² of Propionibacteria acnes (p < 0.01).
• Changed % values of dissolved SSL constituents:
  ↑ cholesterol & relative values of free fatty acids

CCL: ↑ doses of testosterone & anabolic steroids => may ↑ dissolved skin surface lipids, the Propionibacteria acnes population, & the % of the cholesterol & free fatty acids of the skin surface lipids in healthy young men

Severe Acne caused by ↑↑↑↑ androgen treatment
Testosterone Excess + wrong food
Acne fulminans after testo for excessively tallness in boys


Acne fulminans after testo for treatment of Klinefelter syndrome

↑ Estrogens

=> ↑ risk of acne in men (but ↓ acne in women)
Men with acne => (↑ testosterone => estradiol conversion) => ↑ estradiol

SUBJECTS: 27 male acne patients & 38 healthy subjects

FINDINGS: Male patients with acne
• normal serum testosterone levels, but
• sign. Higher (40%) serum estradiol levels than in healthy males.

CCL: male acne patients should not be treated with estrogen,

↑ Testosterone

=> ↑ risk of acne

in women
Women with acne
=> higher serum testosterone

SUBJECTS: 18 female acne patients & 38 healthy subjects

FINDINGS: Female patients:
• normal serum estradiol, but
• sign. higher (47%) testosterone than in healthy females.
• 16 /18 female acne patients had various degrees of menstrual dysfunction, and some even had slight hirsutism.
Women with acne

=> ↑ Serum free testo, DHT & DHEA-

<table>
<thead>
<tr>
<th>Study</th>
<th>University</th>
<th>Androgens =&gt; acne</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aizawa H, Niimura M. Adrenal androgen abnormalities in women with late onset and persistent acne. Arch Dermatol Res. 1993;284(8):451-5.</td>
<td>Jikei University School of Medicine, Tokyo, Japan</td>
<td>↑ Serum free testo, DHT &amp; DHEA-S in acne patients (both 34 women with mild acne &amp; 29 women with moderate or severe acne) compared to the 34 healthy control subjects. No significant differences of other hormone levels (total testosterone, androstenedione &amp; SHBG). Dexamethasone suppression test =&gt; ↑ DHT &amp; T of adrenal origin in the acne patients.</td>
<td>In acne patients, hyper-androgenaemia is likely to develop as a result of adrenal androgen excess.</td>
</tr>
</tbody>
</table>
Topical anti-androgen cyproterone acetate => ↓ acne

**SUBJECTS:** 40 women + acne =>

- **oral** 0.035 mg of ethinyl estradiol & 2 mg of cyproterone acetate (n=12),
- **topical** 20 mg of cyproterone acetate lotion (n=12), or placebo lotion (n=16)

**TREATMENT:** After 3 months of **topical cyproterone acetate** (vs oral or placebo)

- ↓ **mean facial acne grade** from 1.57 to 0.67, sign. better (P<.05) than placebo (1.57 to 1.25), but similar to oral cyprot. (1.56 to 0.75) (P>.05).
- **4x ↓ lesion counts** from 35.9 to 9.1 in the topical cyproterone acetate group vs oral medication (45.4 to 15.5: 3x less) (P>.05) & placebo (38.2 to 23.1) (P<.05).
- **10x ↓ serum cyproterone acetate levels** than those after oral cyproterone acetate

**CCL:** **topically applied cyproterone acetate** for acne treatment was clearly demonstrated. Topically applied sexual steroids in combination with liposomes are as effective as oral antiandrogen medication in acne treatment, while reducing the risk of adverse effects

↓ Estrogens/
Androgen ratio

=> ↑ risk of acne
Ratio Estrogens/Androgens (DHEAs + testo) => acne in women

Acne patients (vs controls):

- Not sign. ↑ DHEA, testosterone
- NI E2 levels

Topical therapy

=> ↓ acne
Topical Estriol => ↓ acne in women

SUBJECTS: 12 women + acne

RESULTS: acne patients => local efficacy of the estriol-ointment.
• Clinical results ranged between good and excellent in 8 out of 12 patients.
• ↓ number of skin lesions decreased
• the skin itself looked "improved".

↑ DHEAs

=> ↑ risk of acne
Adolescent girls with acne => ↑ serum DHEAs
No correlation of serum androgens w/ acne severity

SUBJECTS: 15 women + adolescent acne & 13 healthy controls

TREATMENT:
• No sign. Diff. between the mean levels of total testosterone, free testosterone, dihydrotestosterone levels in patients & controls
• Sign. +47% ↑ mean serum DHEA-S in the patient population (1886 +/- 829 ng/ml) were significantly (p < 0.05) than normal controls (1287 +/- 620 ng/ml).
• no correlation between androgen levels & acne severity

CCL: unlikely that serum androgens play a principal role in women with adolescent acne.

DHEA therapy => Fewer side effects at lower doses

Figure: 6-12 weeks of 5, 10, 15, to 50 mg per day of DHEA to 100 women, aged 46-74 yrs, with adrenopause in order to raise serum DHEAs into the physiological range of younger adults, gave fewer side effects when the adequate (lower) dose was found.

Glucocorticoid therapy => ↓ acne
Glucocorticoid treatment =>
down acne in hyperandrogenic women

SUBJECTS: 158 women + acne, ages 16 to 40

TREATMENT: Prednisone at a maximum daily dose ranging from 7.5 to 15 mg for a period of at least 6 months
• Only 19% of patients + pretreatment testosterone < (below) upper limits (40 ng/dl) of normal range => with prednisolone => 92.4% + testosterone levels < 40ng/dl
• 39.9% => acne completely cleared; 50.6 % => sign. improved, & in only 9.5% => acne => not affected by the medication
• the % drop in testosterone = greatest in those who cleared their acne (p<0.05)
• Pretreatment testosterone levels were not sign. different in those who cleared, improved or did neither.

Acne: Treatment

1. Stop wrong food (chocolate, yoghurt, baked fats, …)
2. Take less DHEA, testosterone levels
3. Add estrogens, possibly locally (women), correct thyroid deficiency
4. Correct any cortisol or zinc deficiency
Acne: treatment in women

Cause:
imbalance between high androgens (derived from DHEA) & low female hormones (progesterone & estrogens) not sufficiently secreted by the ovaries & allowing compensatory higher levels of testosterone

Treatment:
- Stop eating sweets, milk products and cooked fats, and drinking soft drinks
- Reduce -50% testosterone & DHEA treatments
- in case of premenstrual acne: progesterone alone
- in case of continuous acne: estrogen & progesterone in association
Acne: treatment in men

Cause:
imbalance between high androgens (derived from DHEA) & low female hormones (progesterone & estrogens) not sufficiently secreted by the ovaries & allowing compensatory higher levels of testosterone

Treatment:
- Stop eating sweets, milk products and cooked fats, and drinking soft drinks
- Reduce -50 to -70% testosterone & DHEA treatments
- Correct any zinc, thyroid (and/or cortisol) deficiency
# Hormone & nutrients against Acne

<table>
<thead>
<tr>
<th>Causes or co-factors</th>
<th>Best Treatments</th>
<th>Dose (adult)</th>
<th>Duration</th>
<th>Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone or DHEA excess</td>
<td>Stop or reduce the dose</td>
<td>Women should avoid androgenic pills</td>
<td>Several months</td>
<td></td>
</tr>
<tr>
<td>Thyroid deficiency</td>
<td>Armour Thyroid</td>
<td>45-210 mg/day dep. on the degree of the deficiency</td>
<td>constant</td>
<td>85-100 % improvement after 3-6 months if diet is good enough</td>
</tr>
<tr>
<td></td>
<td>Synthetic T3 + T4</td>
<td>¾ to 2.5 tablets/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisol deficiency</td>
<td>Prednisolone (synthetic )</td>
<td>2.5 to 5 mg/day following the deficit</td>
<td>2 to permanent</td>
<td></td>
</tr>
<tr>
<td>Zinc deficiency</td>
<td>Zinc</td>
<td>30 to 50 mg/day</td>
<td>4-8 months</td>
<td></td>
</tr>
<tr>
<td>Wrong food choice</td>
<td>Avoid sweets, milk products &amp; baked fat</td>
<td>Minimally 3 months, then after 5 to 6 days a week without the wrong food</td>
<td>Permanent dietary improvement</td>
<td></td>
</tr>
</tbody>
</table>
Acne scars: treatment

Treatment:
- Local citapmin A
- Topical/local melatonin
- Hormone mesotherapy
- Derma-roller
Estriol or Vit. A derivative => Acne scars

SUBJECTS: 18 women + acne scars => topical estriol by iontophoresis

ESTRIOL TREATMENT: new noninvasive treatment method consisting of local iontophoresis

- 100 % of women improved (in contrast ‘only’ 93% of 28 other patients improved with a vitamin A derivative, tretinoin, applied by iontophoresis).
- No hormonal changes
- No side effects (while tretinoin treatment produced increased dryness & retinoid dermatitis in 1 on 7 patients)

Greasy hair, oily skin

Cause:
Excess (androgen) stimulation of sebum

Treatment:
- ↓ or avoid foods that stimulate insulin and sebum production as sweets (chocolate esp.) & milk products (esp. yoghurt)
- ↓ dose of DHEA and/or other androgens
- ↑ female hormones esp. estrogen & progesterone in association