



# MSS

## Pharmacology

LEC no. 2 v2



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# **Skin Pharmacology**

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# *Topical Therapy (Anti Comedonal Agents)*

 **Topical Retinoids 0.025% - 0.5%**

 **Azelaic acid**

 **Salicylic acid**

# Topical Retinoids (Adapalene, Differin)

## ✚ Topical Retinoids 0.025% - 0.5%

- **apply at night** Because it's photosensitive
- **always apply test dose**
- **start at low concentrations**
- **avoid in pregnancy**

## ✚ Side Effects:

- **pustular flare** (small pus-filled lesions)
- **Photosensitivity**
- **skin irritation and erythema** (redness)
- **dryness and peeling**



Also avoid the exposure of sunlight for a long period of time that's why we should use sunscreen

Works as skin exfoliant, so there would be more access to the antibacterial effect, washing...etc

Initially when we begin to use topical retinoids there will be flare up of the acne so once we begin use it, we will grow more acne. But this effect will decrease over time.

NOTE: the trend name of the drugs are NOT INCLUDED

The enzyme that converts testosterone to dehydrotestosterone.

Generating ROS, affecting those microbes

## *Azelaic Acid 20%*

+ **competitive inhibitor of mitochondrial oxidoreductases and of 5 alpha-reductase, inhibiting the conversion of testosterone to 5-dihydrotestosterone**. It also possesses **bacteriostatic activity** to both aerobic and anaerobic bacteria including **Propionibacterium acnes**

+ **applied twice daily** ( read only, no need to know the doses the doc said ;)

### + **Side Effects**

- **erythema and irritation**
- **decrease in pigmentation**(on other side,

it is such an advantage for people who have dark areas in the acne spot)

**5-dehydrotestosterone enzyme** the form of testosterone that's responsible for the secondary sex characteristics. In puberty age, males experience physical and hormonal changes include the facial and body hair deepening of the voice.

Now of course, we want to decrease the hormonal effect of dehydrotestosterone **only** at the site of a pimple. Our goal isn't to affect the puberty of patient.

# *Salicylic Acid 0.5 - 2%*

Making the pores more exposed to the effect of cleansing products

**Keratolytic (dissolves the keratin layer on the skin).** It belongs to the same class of drugs as

**aspirin (salicylates)** - (the structure of aspirin is acetylsalicylic acid and it is anti-inflammatory)

**Can reduce swelling and redness and unplugging blocked skin pores to allow pimples to shrink**

**applied twice daily**

**skin dryness and irritation**

**Other use of salicylic acid** is hyper keratinization such as onychogryphosis the nail grows into the surrounding skin causing inflammation and the treatment is done by patches that contain salicylic acid.

## *Topical Therapy (Anti Inflammatory Agents)*

✚ **Benzoyl Peroxide 2.5 - 10%**  
exhibits bactericidal effects against **Cutibacterium**

✚ **apply once to twice daily**

✚ **always apply test dose**

✚ **avoid use at night** (it's opposite of retinoids, we can apply it at night but for a short period of time. Wash after 30 minutes)

✚ **dryness of skin** (also it may cause irritation)

such as

**Hydrogen peroxide**  
**"hair color strippers"**

the patient should wear white because it stains on the clothes. Also because it's a peroxide, it'll generate ROS, to get rid of microorganisms.

# *Topical Therapy (Anti Inflammatory Agents)*

✚ **Clindamycin.**

✚ **Erythromycin.**

- **apply twice daily**
- **skin dryness**

Usually used in a combination. They are protein synthesis inhibitor drugs, and they can be used topically to treat mild to moderate acne and they have antibacterial effect as well

## *Combination therapy*

most of the time these drugs used in combination with other substances ex of these combinations:

✚ **%5 Benzoyl Peroxide and 3% Erythromycin**

✚ **%5 Benzoyl Peroxide and 1% Clindamycin Topical**

✚ **antibiotics and Azelaic acid or Tretinoin(**retinoid**)**



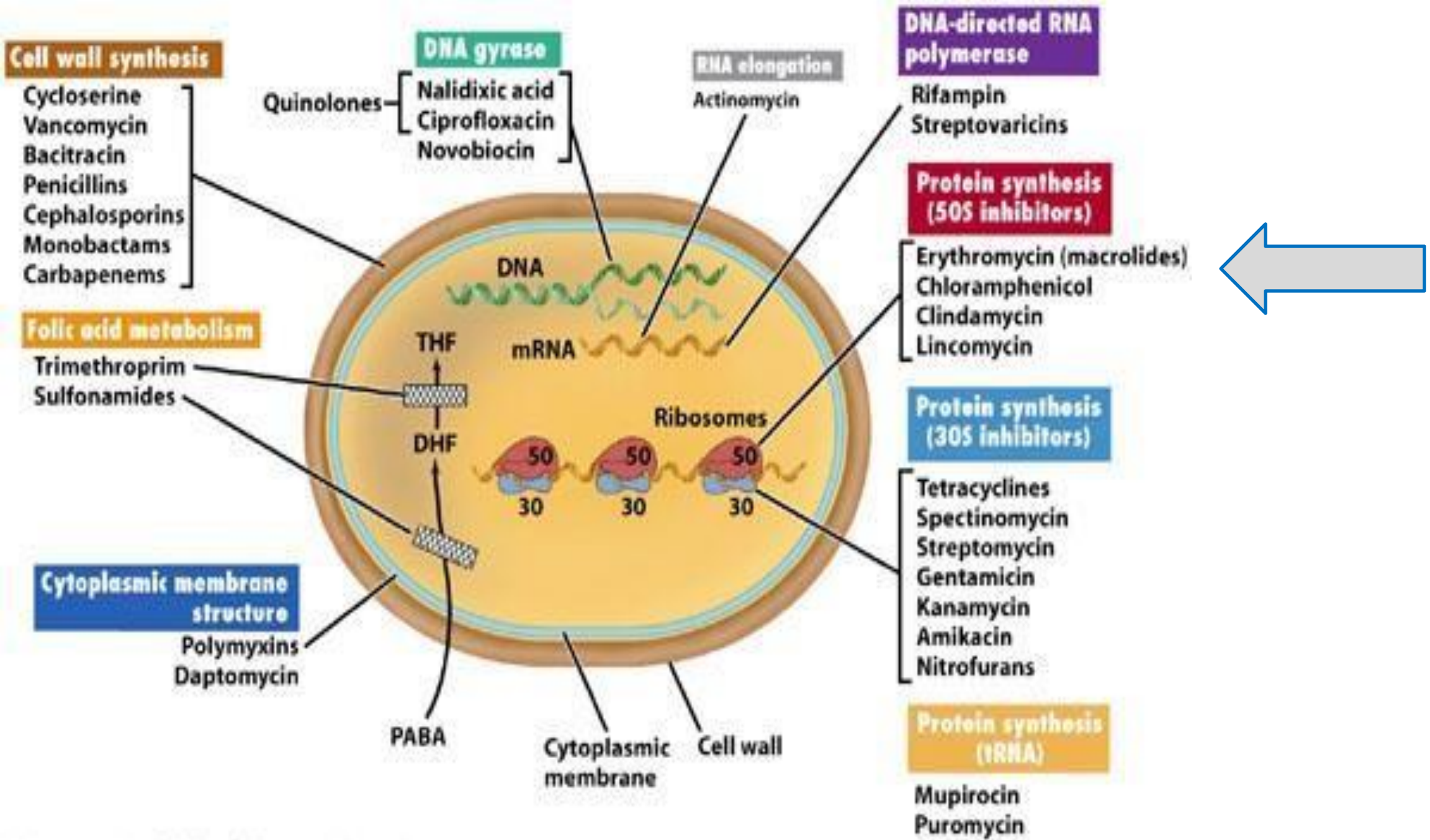


Figure 20-14 Brock Biology of Microorganisms 11/e  
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# Clindamycin

The topical side effects associated with these agents:

- **%10 absorbed, so, possibility of *Pseudomembranous colitis***
- The hydroalcoholic vehicle" drug delivery system from the origin form into my body" and foam formulation (Evoclin) .....may cause drying and irritation of the skin, with complaints of burning and stinging.
- The water-based gel and lotion formulations..... well tolerated and less likely to cause irritation. *Allergic contact dermatitis is uncommon .*
- Clindamycin is also available in fixed-combination topical gels with benzoyl peroxide (Acanya, BenzaClin, Duac), and with tretinoin (Ziana.)

NOTE: the trend name of the drugs are NOT INCLUDED  
We only what's to know the combination.

Special side effect of clindamycin:  
pseudomembranous colitis.  
(Caused by clostridium Defficile, and treated by Vancomycin or metronidazol).  
If a patient is suffering from diarrhea, it could be due to topical administration of clindamycin.

بين الأقواس الأسماء التجارية  
مش مطلوبة

# Erythromycin

Special side effect which is very common is **GI irritation**

(To remind you it is a protein synthesis inhibitor working on 50S subunit of the ribosome).

- In topical preparations, erythromycin base rather than a salt is used to facilitate penetration
- One of the possible complications of topical therapy is the development of antibiotic-resistant strains of organisms, including staphylococci
- Adverse local reactions to erythromycin solution may include a burning sensation at the time of application and drying and irritation of the skin
- Clindamycin is also available in fixed-combination topical gels with benzoyl peroxide (Acanya, BenzaClin, Duac), and with tretinoin (Ziana.)

# Metronidazole (Flagyl)

We use it for **parasites** for example amoeba, treating amoebiasis.

Other parasites it can treat, a small parasite called: Demodex brevis.

It's an antibacterial agent. Reduction reaction, then generation of ROS, which kills other microorganisms like parasites

Rosacea when patient has a dilation in blood vessels in the skin that lead to redness and erythema, and it may cause a small pus-filled bumps. in this case, a kind of acne can be coupled with rosacea.

- Effective in the treatment of **rosacea acne**
- Rosacea: common skin condition that causes blushing or flushing and visible blood vessels in your face(may lead to show up acne). It may also produce small, pus-filled bumps. These signs and symptoms may flare up for weeks to months and then go away for a while



# Metronidazole

Antibacterial agent to kill anaerobic bacteria and parasites

- The mechanism of action is unknown

- ✚ but it may relate to the inhibitory effects of metronidazole on **Demodex brevis**; This drug may act as an anti-inflammatory agent by direct effect on neutrophil cellular function

- ✚ Adverse local effects include dryness, burning, and stinging .

- ✚ Caution should be exercised when applying metronidazole near the eyes to avoid

**excessive tearing.**



Avoid the application of Metronidazole around the eye area

**Demodex folliculorum** is a small microorganism(parasite) that have been involved with rosacea ,that can make inflammatory response

Systemic therapy means when we give a pill, tablet or capsule (orally administered)

**Systemic therapy** (when the patient is resistant to topical therapy we will switch to systemic therapy)

**Indications:** (when to use systemic therapy)

- **Moderate inflammatory acne, non-responsive to topical therapy**
- **nodulocystic acne** (acne filled with pus and disburse all over the body)

## *Systemic therapy*

- ✚ **Oral Antibiotics**
- ✚ **Isotretinoin**
- ✚ **Hormonal Therapy**

We don't prescribe these drugs firstly because they have multiple side effects



Doses are **NOT FOR MEMORIZING**

## *Oral Antibiotics (used for 3-6 months)*

- ✚ **Tetracycline 500mg X BD** (main side effect is staining of **teeth**, we don't prefer use it for under age patients <18 because it's affect on the develop of teeth)
- ✚ **Doxycycline 100mg X BD**
- ✚ **Minocycline 100mg X OD**
- ✚ **Eythromycin 500mg X BD**
  
- ✚ **combined with topical therapy**

**OD:** once daily  
**BD:** twice daily

## *Isotretinoin (Accutane) indicated in (when to use this medicine)*

- ✚ **Severe nodulocystic acne**
- ✚ **Non-responsive acne**
- ✚ **Severe psychological distress**

We don't prefer to use it for young patients

May cause **depression** in a small subset of patients. So, we need an updated follow up of the patient's mental health.

### **!!! Important note:**

In general, you shouldn't give the patient an oral antibacterial with a topical antibacterial.



# Isotretinoin (RoAccutane) side effects

✚ **Teratogenic (major side effect)**, We don't give it during pregnancy, and even after stopping the medication the female patient must wait for a month or more (because it has a long half life) if she decides to get pregnant. In some countries, the woman who intends to get pregnant must pledge **تتعهد** to use at least two contraceptive methods alongside this medication.

✚ **mucosal dryness** (use eyedrops, lip balms, moisturizer and drink a lot of water)

✚ **photosensitivity** (use sunscreen)

✚ **arthralgias** (pain in joints and muscles)

✚ **alteration of liver enzymes**

**hypertriglyceridemia and hypercholesterolemia**

✚ **Tumerogenic in animals** This drug can cause a certain type of cancer in animals ,but nothing has been established yet in human. Some studies say that this drug causes some psychological problems such as depression

**Teratogenic:** abnormal development in fetus during pregnancy

Before we start treatment and every month while taking this drug the patient must perform many tests like: liver enzymes tests, and we look to lipid profile(triglyceride, cholesterol),if the patient has changing in these levels, we either lower the dose or stop drug for that patient for a period of time to make sure that everything goes back to normal.

# Isotretinoin (RoAccutane)

It's mechanism at the molecular or cellular level:



**Retinoic Acid( Tretinoin):** is the acid form of Vitamin

**A. Stabilizes lysosomes, increases RNA polymerase activity** (increase the transcription and translation so more proteins, and more regeneration/turnover of cells), **increases PGE<sub>2</sub>, cAMP, and cGMP levels**(cAMP and cGMP are 2nd messengers that bind to guanylate cyclase, work on ion channels leading to relaxation of muscles causing **vasodilation** which means increase in perfusion of blood toward the skin, more nutrients, enhancing the nature of skin), **and increases the incorporation of thymidine into DNA**(increase DNA replication).

All of these effects will increase the turn over or regeneration of the cells.



**Decreases cohesion between epidermal cells and increases epidermal cell turnover.** This will result in **expulsion of open comedones** (black heads) **and the transformation of closed comedones into open ones.** When the patient first starts using it, they will experience the formation of more pimples, then it'll start decreasing.



**Also, promotes dermal collagen synthesis** (so we can use at first stages of scarring), **new blood vessel formation, and thickening of the epidermis, which helps diminish fine lines and wrinkles.** Result: tight, baby-like skin!!

# Drugs for Psoriasis

**First-line treatment: Glucocorticoids;** suppressing the immune system. But it won't heal the origin of the problem; as Psoriasis may be genetically-tailored.

**Stronger drugs include:**

- **Acitretin:** (vitamin A derivative)
  - **Related to isotretinoin.**( first line treatment)
  - **Given orally.**
  - **Hepatotoxic and teratogenic .**
  - **Patient should not become pregnant for 3 years after stopping treatment. Also, should not donate blood, whether male or female.** Because what if they donate it to a pregnant lady? That'll affect her baby!!

**Psoriasis الصدفية** is an immune skin condition that causes inflamed thick layers, scaly patches on the skin. A keratinized layer can also form, called: plaque. Plaque psoriasis is the most common type of psoriasis (90%).

# Drugs for Psoriasis

- **Tazarotene:** (Tazarotene is a retinoic acid derivative, and it can be used to treat acne as well).

- Topical.
- **Anti-inflammatory and antiproliferative actions.**
- **Teratogenic. Also, can cause burning, stinging, peeling, erythema, and localized edema of skin.**

- **Calcipotriene:**

Activator of cell proliferation and it's lipid soluble, can cross the cell membrane and bind to intracellular receptor (transcription factor) and either activate or inhibit the transcription factors in nucleus. Modulating the immune system response & proliferation of cells.

Receptor: a transcription factor. Transcription factors are signaling molecules present the cell, they can be receptors for certain drugs/hormones

- **Synthetic vitamin D<sub>3</sub> derivative.**

(decrease the immune activity but can cause regeneration of healthy layers of the skin)

# New Drugs for Psoriasis

-approved in the last 5 years

-they suppress the immune system, increasing the chance of rare infections

## 1- Apremilast(Otezla)

Orally given + another inflammatory condition

- psoriasis and psoriatic arthritis .
- It may also be useful for other immune system-related inflammatory diseases .
- The drug acts as a selective **inhibitor** of the enzyme **phosphodiesterase 4 (PDE4)** (that degrades the cAMP and cGMP) and inhibits spontaneous production of TNF-alpha from human rheumatoid synovial cells.

**So Apremilast will:**

1. **Suppress the immune system**
2. **Promote growth of healthy, normal cells.**

# Apremilast

## Side Effects

- diarrhea
  - nausea.
  - stomach pain.
  - vomiting.
  - headache.
  - sore throat, cough, and fever.
  - sneezing, runny nose, and nasal congestion.
- e-to-severe psoriasis demonstrating superior efficacy to apremilast

it can cause upper respiratory symptoms that are similar to respiratory infection.

# New Drugs for Psoriasis

## 2- Deucravacitinib (Sotyktu)

- A new oral treatment option for adults with plaque psoriasis.
- moderate-to-severe plaque psoriasis
- It is a once-daily oral medication with its clinical trials in moderate-to-severe psoriasis demonstrating superior efficacy to apremilast
- MOA: Allosteric inhibitor of **TYK2** (tyrosine kinase A2)
- Side effects: runny nose, congestion, or sore throat, sore on mouth, lips, gums, tongue or roof of mouth, acne.

Because these drugs are new, we don't have an accurate profile of the severity of their side effects. So we have to be very conservative with them

## 3- Roflumilast (Zorvye) cream

Selective, long-acting inhibitor of the enzyme phosphodiesterase-4 (PDE-4). It has anti-inflammatory effects.

- Used for **chronic plaque psoriasis**
- Topical
- an effective topical therapy for use on all psoriasis-affected areas including body, face, and intertriginous areas





## New Drugs for Psoriasis

# 4- Tapinarof (Vtama)

**Tapinarof (Vtama)** is a topical (on the skin) medication used to treat plaque psoriasis in adults.

- MOA: immune modulation, skin-barrier normalization, and antioxidant activity(immune suppressor), because the psoriasis is an immune response.
- It's **convenient**(respond better )to use because it's only applied once daily

## Some of past paper questions

**1. Which of the following is correct regarding the use of isotretinoin in the treatment of acne?**

- A. Isotretinoin is given intravenously in the treatment of acne.
- B. Isotretinoin acts primarily on the membrane receptors.
- C. If given in high dosages, isotretinoin can indirectly increase the concentration of *Propionibacterium acnes* bacteria.
- D. Isotretinoin activates prostaglandin E<sub>2</sub> and collagenase, which causes the adverse effect of inflammation.
- E. Isotretinoin is contraindicated in pregnancy due to its high risk of birth defects.

**Correct answer = E.** Retinoic acids play an important role in mammalian embryogenesis. Excessive amounts of retinoid have been shown to cause teratogenicity, and the exact molecular mechanism is not known.

## Some of past paper questions

**2. All of the following are true combinations except :**

- A. Clindamycin with benzoyl peroxide
- B. Bacitracin with polymyxin or neomycin
- C. Erythromycin with benzoyl peroxide
- D. Amphotericin with Salicylic acid
- E. Salicylic acid with benzoyl peroxide

**Answer: D**

اللهم برِّدًا وسلامًا على غزة وأهلها ياربِّ .. احفظ غزة وأهلها  
اللهم إني أستودعك غزة وأهلها وسماؤها ورجالها ونسائها  
وأطفالها وشيوخها وشبابها وكل شبر في فلسطين.

ألا إنَّ نصرَ اللهِ قريبٌ 



**THANK YOU**  
**wish u a full mark**

V2

**Dihydrotestosterone instead of Dehydrotestosterone slide no.5**