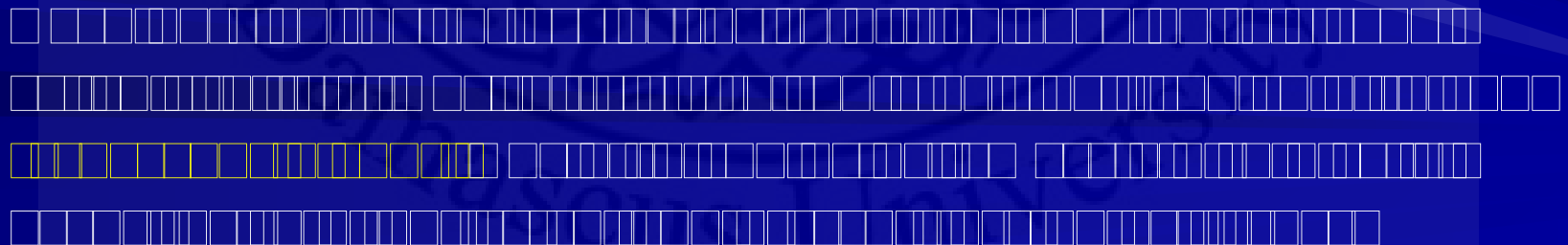


■ Acne

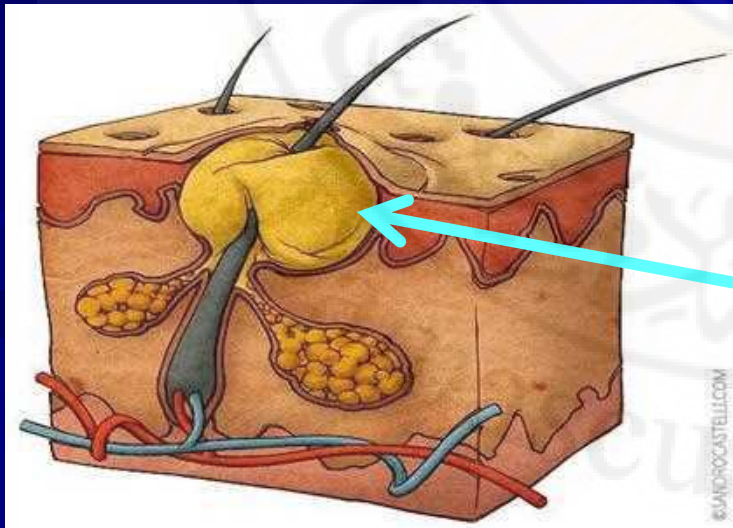
■ DEFINITION

- Acne vulgaris is a common, usually self-limiting, multifactorial disease involving inflammation of the sebaceous follicles of the face and upper trunk.
- Acne is a skin condition that causes spots. Acne usually affects the skin of the **face, back, neck, chest and arms** and the severity of the condition can vary.



■ PATHOPHYSIOLOGY

- increased sebum production, sloughing of keratinocytes, bacterial growth, and inflammation.
- If the follicular wall is damaged or ruptured, follicle contents may extrude into the dermis and present as a (pustule = حطاطة).



حطاطة

■ This increasing in sebum may be caused by:

■ **Increased androgen activity** at puberty triggers growth of sebaceous glands and enhanced sebum production. Sebum consists of **glycerides**, wax esters, squalene, and cholesterol. **Glyceride is converted to free fatty acids and glycerol by lipases, which are products of Propionibacterium acnes.** Free fatty acids may irritate the follicular wall and cause increased cell turnover and inflammation.

- **P. acnes** is a resident **anaerobic organism** that proliferates in the environment created by the mixture of excessive sebum and keratinocytes. **It is antigenic** and can **increase antibody formation** leading to an **inflammatory response**.

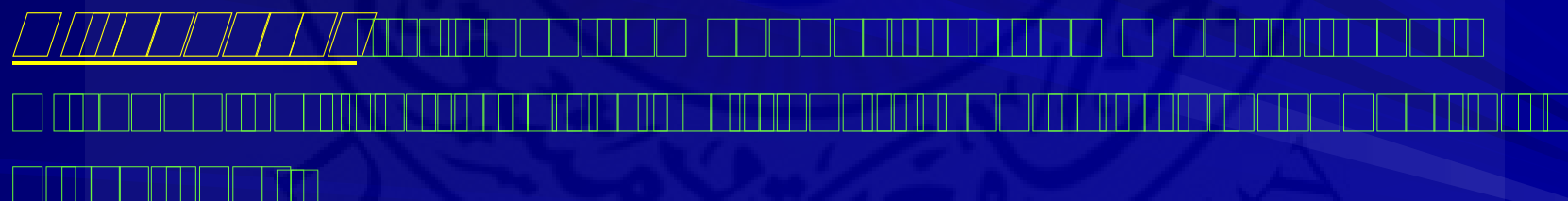
■ CLINICAL PRESENTATION

- Acne lesions **typically** occur on the **face**, **back**, **upper chest**, and **shoulders**. Lesions are classified primarily as either inflammatory or non inflammatory.
- The presentation can range from a **mild comedonal** (بثرة – حبة سوداء) form to **severe inflammatory necrotic acne** (نخري).
- Lesions may take **months to heal completely**, and *fibrosis* تَلَيُّف *associated with healing* قد تؤدي إلى ندبات permanent scarring

- **CLINICAL PRESENTATION, SYMPTOMS**
- *greasy skin*
- *blackheads (open comedones)* بثرة سوداء
- *whiteheads (closed comedones)* بثرة بيضاء
- *red or yellow spots (pustules)* (حطاطة)
- *deep inflamed lesions (nodules and cysts)* عقدي (كيسي)
- *Scars* ندبة =
-



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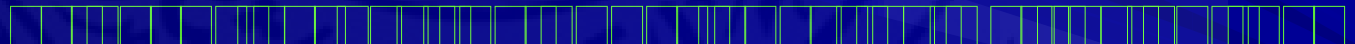


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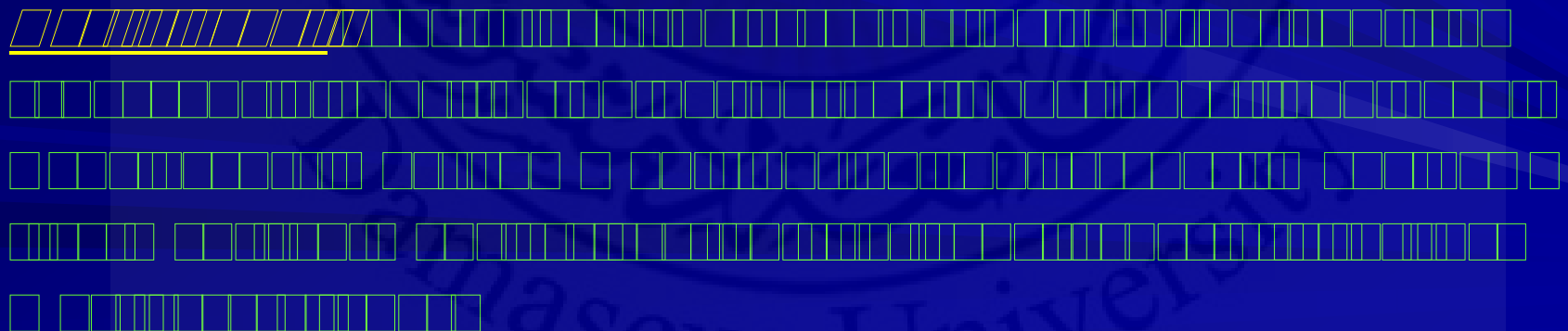




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Acne vulgaris is a common skin condition that affects the hair follicles and sebaceous glands.

It is characterized by the presence of comedones (blackheads and whiteheads), papules, pustules, and sometimes cysts.

The condition is caused by a combination of factors, including hormonal changes, increased sebum production, and bacterial infection.

Acne vulgaris can occur on any part of the body, but it is most commonly found on the face, back, and chest.

It is a chronic condition that can persist for years, but it is usually treatable.

■ ***Diagnosis of acne***

- Acne is easily recognized by the appearance of the spots and by their distribution on the body.
- Diagnosis is established by **observation** of acne lesions (e.g, **comedones** بثرة , **pustules** حطاطة , **papules**, **nodules** دَرَنَة , **cysts**) on the face, back, or chest.
- The presence of **5 to 10 comedones** is usually considered to be diagnostic.

■ DESIRED OUTCOME

- The goals of treatment are to :
- prevent the formation of new acne lesions,
- heal existing lesions, and
- prevent or minimize scarring (تندبات).

■ TREATMENT

■ NONPHARMACOLOGIC THERAPY

- **Surface skin cleansing with soap** and water has a relatively *small effect* on acne because it has minimal impact within follicles.
- **Skin scrubbing or excessive face washing** *does not necessarily*. Open or cleanse pores may lead to skin irritation.
- **Use of gentle, nondrying cleansing agents is important to avoid skin irritation** and dryness during some acne therapies.

■ TOPICAL PHARMACOLOGIC THERAPY

■ Benzoyl Peroxide

- Benzoyl peroxide may be used to **treat superficial inflammatory acne**. It is a non-antibiotic antibacterial that is bacteriostatic against *P. acnes*. It is decomposed on the skin by cysteine, liberating free oxygen radicals that oxidize bacterial proteins.

- Soaps, lotions, creams, washes, and gels are available in concentrations of 2.5% to 10%. The 10% concentration is not significantly more effective but may be more irritating. Gel formulations are usually most potent, whereas **lotions, creams, and soaps** have **weaker potency**. Alcohol-based gel preparations generally cause more dryness and irritation.
- *To limit irritation and increase tolerability,*
begin with a low-potency formulation (2.5%)
and increase either the strength (5% to 10%)
or application frequency (every other day,
each day, then twice daily).

- **Apply the formulation chosen to :**
- **cool, clean, dry skin no more often than twice daily to minimize irritation.**
- **Advise patients to apply the medication to dry skin at least 30 minutes after washing.**
- **Side effects include:**
- **dryness, irritation, and allergic contact dermatitis. It may bleach or discolor some fabrics (e.g., clothing, bed linen, towels).**

■ Tretinoin

- Tretinoin (a retinoid; topical vitamin A acid) is a **comedolytic** agent that **increases cell turnover in the follicular wall** and **decreases cohesiveness** of cells, leading to extrusion of comedones and inhibition of new comedo formation.
- It also decreases the number of cell layers in the stratum corneum **الطبقة القرنية** from about 14 to about 5. **البشرية**

■ Tretinoin

- Tretinoin is available as solution : 0.05% (most irritating), gels : 0.01% and 0.025%, and creams : 0.025%, 0.05%, and 0.1% (least irritating).
- Treatment initiation with:
 - 0.025% cream for mild acne in people with sensitive and non oily skin,
 - 0.01% gel for moderate acne on easily irritated skin in people with oily complexions, and 0.025% gel for moderate acne in those with non sensitive and oily skin.

- Patients should be **advised** to apply the medication **to dry skin** approximately
- *30 minutes after washing to minimize erythema and irritation.* Slowly increasing the application frequency from every other day to daily and then twice daily may also increase tolerability.
- **A flare of acne may appear suddenly after initiation of treatment**, followed by clinical clearing in 8 to 12 weeks. Once control is established, continue therapy at the lowest effective concentration and the longest effective interval that minimizes acne exacerbations.

- **Side effects** include : skin irritation, erythema = احمرار, peeling = تقشر, allergic contact dermatitis (*rare*), and increased sensitivity to sun exposure, wind, cold, and other irritants.
- **Concomitant use** of an **antibacterial** agent with **tretinoin** can decrease keratinization, inhibit *P. acnes*, and decrease inflammation.
- A combination of **benzoyl peroxide each morning** and **tretinoin at bedtime** may enhance efficacy and be less irritating than either agent used alone.

■ Adapalene

- Adapalene (Differin) is a **third-generation retinoid** with comedolytic, keratolytic, and anti-inflammatory activity. **It is available as 0.1% gel, cream, alcoholic solution, and pledgets.**
- **Adapalene** is indicated for mild to moderate acne vulgaris. The **0.1% gel** can be used as an **alternative** to **tretinoin 0.025% gel** to achieve better tolerability in some patients.
- Coadministration with a **topical or oral antibiotic** is reasonable for moderate forms of acne.

■ Tazarotene

- Tazarotene (Tazorac) is a synthetic **acetylenic retinoid** that is **converted to its active form, tazarotenic acid**, after topical application.
- It is used in the **treatment** of **mild to moderate acne vulgaris** and has **comedolytic, keratolytic, and anti-inflammatory action**.
- The product is available as a 0.05% and 0.1% **gel or cream**.
- Dose-related **adverse effects** include **erythema** حُمَامَى, **pruritus** حكة, **stinging**, and **burning**.

- **Erythromycin**
- Erythromycin with or without zinc is effective against inflammatory acne. Zinc combination products may enhance penetration of erythromycin into the pilosebaceous شَعْرِيٌّ زُهْمِيّ unit.
- Commonly used erythromycin formulations include 2% gel, lotion, solution, and disposable pads that are usually applied twice daily.
- Development of P. acnes resistance to erythromycin may be reduced by combination therapy with benzoyl peroxide.

■ **Clindamycin**

- Clindamycin inhibits *P. acnes* and provides comedolytic and anti-inflammatory activity.
- It is available as 1% or 2% concentrations in gel, lotion, solution, and disposable pad formulations and is usually applied twice daily.
- **Combination with benzoyl peroxide increases efficacy.**

■ SYSTEMIC THERAPY

■ Isotretinoin

■ Isotretinoin (Accutane) **decreases** sebum production, changes sebum composition, inhibits P. acnes growth within follicles, inhibits inflammation, and alters patterns of keratinization within follicles.

■ It is indicated for :

- **severe nodular (عقدي) or inflammatory acne** in patients unresponsive to conventional therapies,
- **scarring acne (ندبي)**,
- **for those with chronic relapsing acne**, **and**
- **acne associated with severe psychological distress.**

- A 6 - 12-month course is sufficient for most patients. Alternatively, an initial dose of
- 1 mg/kg/day for 3 months followed by
- 0.5 mg/kg/day (or 0.2 mg/kg/day if possible) for 3 to 9 more months may optimize the therapeutic outcome.

- **Adverse effects are** : drying of the mouth, nose, and eyes *is most common*. Cheilitis (التهاب شفاه) and skin desquamation (تقشر جلد).
- **Systemic adverse effects include:**
- ***transient increases in serum cholesterol*** and ***triglycerides***,
- ***increased*** : creatine kinase, hyperglycemia, photosensitivity, excess granulation tissue, bone abnormalities, muscle stiffness, headache.

- Patients should be counseled about and screened for depression during therapy, although a causal relationship to isotretinoin therapy is controversial.
- Because of teratogenicity, contraception is required in female patients beginning **1 month before therapy, continuing throughout treatment, and for up to 3 months after discontinuation of therapy.**

■ Oral Antibacterial Agents

- **Erythromycin- 250 – 1000**, has efficacy similar to tetracycline, but it induces higher rates of bacterial resistance. **Resistance may be reduced by combination therapy with topical benzoyl peroxide**. Erythromycin can be used for patients who require systemic antibiotics but cannot tolerate tetracyclines, or those who acquire bacterial resistance to tetracyclines.
- **Azithromycin – 500**, is a safe and effective alternative for moderate to severe inflammatory acne. **Its long half-life permits intermittent dosing 3 times a week.**

- **Tetracyclines – 250 – 500**, inhibit *P. acnes*, reduce the amount of keratin in sebaceous follicles, and inhibit chemotaxis, phagocytosis complement activation, and cell-mediated immunity.
- **Tetracyclines must not be combined with systemic retinoids because of the increase risk of intracranial hypertension.**
- Women taking oral contraceptives and given tetracycline should be informed of the potential for contraceptive failure.

- **Doxycycline** is commonly used for moderate to severe acne vulgaris. It is *more effective and produces less resistance than tetracycline.*
- The initial dose is 100 or 200 mg daily, followed by 50 mg daily as a maintenance dose after improvement is seen.

- **Trimethoprim-sulfamethoxazole** may be used for patients who do not tolerate tetracyclines and erythromycin or in cases of resistance to these antibiotics. The adult dose is usually 800 mg sulfamethoxazole and 160 mg trimethoprim twice daily.

■ **Drug-induced skin disorders**

■ **DEFINITION**

- Drug-induced skin disorders have been associated with most commonly used medications and may present as :
 - **maculopapular eruptions,**
 - **fixed-drug eruptions,**
 - **and photosensitivity reactions.**

■ **PATHOPHYSIOLOGY**

- Drug-induced cutaneous reactions tend to be immunologic in origin and relate to hypersensitivity, but some reactions are nonallergic. The pathogenesis of fixed-drug reactions is not well understood.

- Drug-induced photosensitivity reactions are divided **into**:
- **phototoxicity (a nonimmunologic reaction)** and
- **photoallergic reactions (an immunologic reaction)**. The latter form is far less common. Medications associated with photosensitivity reactions include fluoroquinolones, nonsteroidal anti-inflammatory drugs, phenothiazines, antihistamines, estrogens, progestins, sulfonamides, sulfonylureas, thiazide diuretics, and tricyclic antidepressants.

■ **CLINICAL PRESENTATION**

- Drug-induced cutaneous reactions are unpredictable, ranging from mild, self-limiting episodes to more severe, life-threatening conditions (Table 1-1). Maculopapular eruptions are most common and often involve the trunk or pressure areas in a symmetrical fashion. Early eruptions appear within a few hours to 3 days after drug ingestion, whereas late eruptions occur up to 9 days after exposure .

- A fixed-drug reaction usually **presents as** an erythematous or hyperpigmented round or oval lesion usually between a few millimeters to 20 cm in diameter. **The oral mucosa and genitalia are the most common sites involved**, but lesions can appear anywhere on the body. If the patient takes the **drug again**, the reaction tends to recur **within 30 minutes to 8 hours, often in the same location**. Although this is highly indicative of a fixed-drug reaction, rechallenge should be avoided when possible.

- **Sun-induced drug eruptions** appear **similar to a sunburn** and **present with: erythema, papules, edema, and sometimes vesicles**. They appear in areas exposed to sunlight (e.g., **the ears, nose, cheeks, forearms, and hands**).

■ **CUTANEOUS DRUG REACTIONS**

- Most maculopapular reactions **disappear within a few days after discontinuing the agent**, so symptomatic control of the affected area is the primary intervention. **Topical corticosteroids and oral antihistamines can relieve pruritus. In severe cases, a short course of systemic corticosteroids may be warranted.**

- Treatment of fixed drug reactions involves **removal of the offending agent. Other therapeutic measures include corticosteroids, antihistamines to relieve itching, and perhaps cool water compresses on the affected area.**



- Photosensitivity reactions typically **resolve with drug discontinuation**. *Some patients* benefit from **topical corticosteroids** and oral antihistamines, but these are often ineffective. **In some cases, systemic corticosteroids (e.g., oral prednisone 1 mg/kg/day tapered over 3 weeks) is more effective.**

Types of Drug-Induced Skin Eruptions

Clinical Presentation	Pattern and Distribution of Skin Lesions	Mucous Membrane Involvement	<i>Implicated Drugs</i>	<i>Treatment</i>
Erythema multiform	Target lesions, limbs	Absent	Anticonvulsants (including lamotrigine) sulfonamide antibiotics, allopurinol, NSAIDs, dapsone	Supportive
Stevens-Johnson syndrome	Atypical targets, widespread	Present	As above	Intravenous immunoglobulins, cyclosporine

Types of Drug-Induced Skin Eruptions

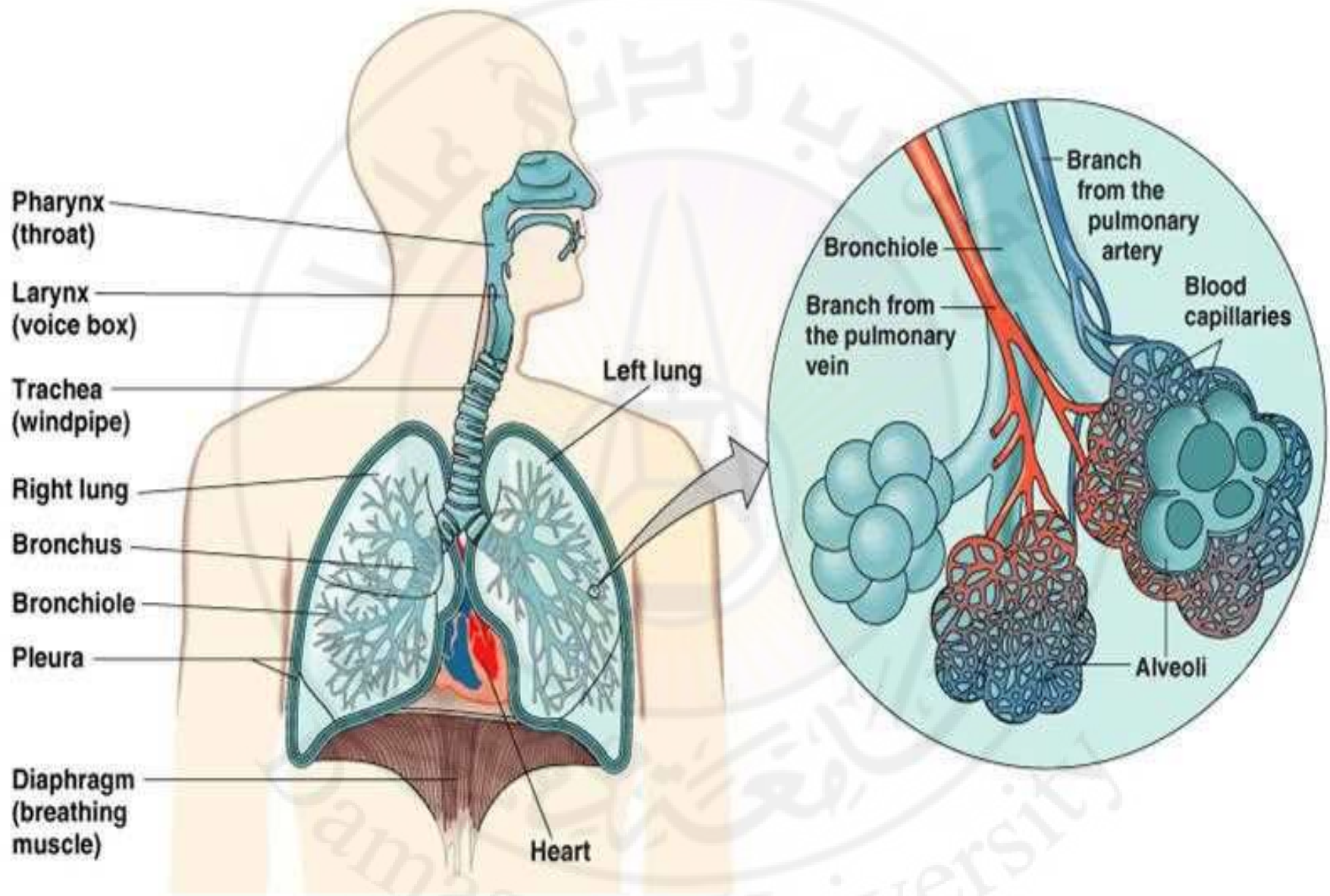
Clinical Presentation	Pattern and Distribution of Skin Lesions	Mucous Membrane Involvement	<i>Implicated Drugs</i>	<i>Treatment</i>
Toxic epidermal necrolysis	Epidermal necrosis with skin detachment	Present	As above	Supportive
Pseudoporphyria	Skin fragility, blister formation in photodistribution	Absent	Tetracycline furosemide, naproxen	Supportive

Types of Drug-Induced Skin Eruptions

Clinical Presentation	Pattern and Distribution of Skin Lesions	Mucous Membrane Involvement	<i>Implicated Drugs</i>	<i>Treatment</i>
Bullous pemphigoid	Tense bulla, widespread	Present or absent	Furosemide penicillamine , penicillins, sulfasalazine , captopril	Supportive Supportive care includes administration of systemic glucocorticoids until all symptoms of active disease disappear. NSAIDs, nonsteroidal anti-inflammatory drugs

Respiratory system disease





Respiratory tract anatomy

- The **pulmonary and circulatory systems** are designed to provide the body with a continuous supply of oxygen and quick removal of carbon dioxide. The pulmonary system controls the exchange of gases between the atmosphere and blood, while the circulatory system transports these gases between the lungs and the cells. A **dysfunction in either system** disrupts homeostasis, can cause **anoxia** (an inadequate level of oxygen) and even cell death.

- The organs used in the exchange of gases between the atmosphere and the blood are:

nose, pharynx البلعوم , **larynx** الحنجرة ,
trachea الرغامى , **bronchi** القصبات , and
lungs الرئة .

- **The Upper Airways including :**

- **nose,**

- **mouth,**

- **nasopharynx,** البلعوم الأنفي

- **oropharynx,** البلعوم الفموي

- **laryngopharynx,** البلعوم الحنجري and the
larynx الحنجرة .

Lower respiratory tract :

Trachea الرغامى, **and bronchi** القصبات
lungs الرئة

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- **Respiratory Tract Infections, Lower**
- **Lower respiratory tract infections include :**
- infectious processes of the lungs ,
- bronchitis التهاب قصبات ,
- Bronchiolitis التهاب قصيبات ,
- Pneumonia ذات رئة ,
- and lung abscess خراجات رئوية .

■ **BRONCHITIS**

■ **ACUTE BRONCHITIS**

- Bronchitis **refers to an inflammatory condition** of the large elements of the tracheo bronchial tree that is usually associated with a **generalized respiratory infection**. **The inflammatory process does not extend to include the alveoli.**
- **Acute bronchitis** most commonly **occurs during the winter months**. *Cold, damp climates and/or the presence of high concentrations of irritating substances such as air pollution or cigarette smoke may precipitate attacks.*

- **Pathophysiology**
- **Respiratory viruses :**
- **Rhinovirus and Coronavirus,**
and lower respiratory tract pathogens,
including : influenza virus, adenovirus,
respiratory syncytial virus (RSV).
- **Other bacterial causes include :**
- **Chlamydia pneumoniae, Mycoplasma pneumoniae**
and Bordetella pertussis.

Infection of the trachea and bronchi causes **edematous mucous membranes** and an **increase in bronchial secretions**.

In addition, the increase in bronchial secretions, which can become thick and tenacious, *further impairs mucociliary activity*. Recurrent acute respiratory infections may be associated with increased airway hyper-reactivity and possibly the pathogenesis of chronic obstructive lung disease.

■ Clinical Presentation

- The patient typically has **nonspecific complaints** such as: malaise and headache, coryza, and sore throat.
- Cough is the hallmark of acute bronchitis. It occurs early and will persist despite the resolution of nasal or nasopharyngeal complaints. Frequently, the cough is initially nonproductive but progresses, yielding mucopurulent sputum.

- **Treatment**
- **Symptomatic and supportive in nature.**
- **Bedrest** and mild analgesic-antipyretic therapy are often helpful in relieving the associated lethargy, malaise, and fever. **Aspirin or acetaminophen** (650 mg in adults or 10-15 mg/kg per dose in children with a maximum daily adult dose of 4 g and 60 mg/kg for children) or **ibuprofen** (200 to 800 mg in adults or 10 mg/kg per dose in children with a maximum daily dose of 3.2 g for adults and 40 mg/kg for children) is administered every 4 to 6 hours.
- Patients should be encouraged to drink fluids to prevent dehydration and possibly decrease the viscosity of respiratory secretions.

- In children, **aspirin should be avoided** and acetaminophen used as the preferred agent because of the possible association between aspirin use and the development of *Reye's syndrome*.
- **Persistent, mild cough**, which may be bothersome, **may be treated with dextromethorphan**; more severe coughs may require intermittent codeine or other similar agents.
- **Routine use of antibiotics** in the treatment of acute bronchitis is **discouraged**; however, in patients who exhibit persistent **fever** or **respiratory symptomatology** for **more than 2 to 3 days**, the possibility of a concurrent bacterial infection should be suspected.

- When possible, antibiotic therapy is directed toward anticipated respiratory pathogen(s).
- **M. pneumoniae**, if suspected or if confirmed by culture or serology, **may be treated with**
- **Erythromycin :Oral:**
- **Base: 250-500 mg every 6-12 hours**
- **Ethylsuccinate: 400-800 mg every 6-12 hours or its analogs such as :**
- **Clarithromycin: Oral: 250-500 mg every 12 hours**
- **PEDIATRIC: 15 mg/kg/day divided every 12 hours for 7 days, or**
- **Azithromycin : Oral: 2 g as a single dose.**
- **PEDIATRIC: 10 mg/kg/day for 2 days.**

- Also, a **fluoroquinolone** with activity against these pathogens :
- **Gatifloxacin : Oral:** 400 mg **once** a day for (**7-10 days**), or
- **Levofloxacin : Oral :** 500 mg **once** a day for at least (7-10 days) may be used in adults.
- During known epidemics **involving the influenza A virus,** **amantadine** or **rimantadine** may be effective in minimizing associated symptomatology **if administered early** in the course of the disease.

■ **CHRONIC BRONCHITIS**

- Chronic bronchitis is a nonspecific disease that primarily affects adults.

■ **Pathophysiology**

- factors, including cigarette smoking; exposure to occupational dusts, fumes, and environmental pollution; and bacterial (and possibly viral) infection.
- In chronic bronchitis, the bronchial wall is thickened and the **number of mucus-secreting goblet cells** in the surface epithelium of both larger and smaller bronchi is **markedly increased**.
- Continued progression of this pathology can result in residual scarring of small bronchi, augmenting airway obstruction and the **weakening of bronchial walls**.

- **By definition :**
- **any patient who reports coughing up sputum on most days for at least three consecutive months each year for two consecutive years suffers from chronic bronchitis.**

■ Clinical Presentation

- The **hallmark** of chronic bronchitis is **cough** that may range from a **mild cough to severe incessant coughing** productive of purulent sputum. Expectoration of the largest quantity of sputum usually occurs upon **arising in the morning**, although many patients expectorate sputum throughout the day. The expectorated **sputum** is usually **tenacious** and can vary in **color from white to yellow-green**.

- The physical examination of patients with mild to moderate chronic bronchitis is usually unremarkable (Table 1-1).

TAB 1-1. Clinical Presentation of Chronic Bronchitis

Signs and Symptoms

Cyanosis (advanced disease)
Obesity

Physical Examination

Chest auscultation usually reveals inspiratory and expiratory rales, rhonchi, and mild **wheezing** with an **expiratory** phase that is **frequently prolonged**.

■ **Treatment**

■ **General Principles**

- A complete occupational/environmental history for the determination of exposure to noxious, irritating gases, as well as cigarette smoking, must be assessed.
- Attempts must be made to reduce exposure to bronchial irritants.

- **Humidification of inspired air** may promote the hydration (liquefaction) of tenacious secretions, allowing for more effective sputum production. **The use of mucolytic aerosols** (e.g., N-acetylcysteine; deoxyribonuclease [DNase]) **is of questionable therapeutic value.**

■ Pharmacotherapy

- Oral or aerosolized bronchodilators may be of benefit to some patients during acute pulmonary exacerbations. **For patients who consistently demonstrate limitations in airflow, a therapeutic change of bronchodilators should be considered.**
- The use of antimicrobials has been controversial, although antibiotics are an important component of treatment. Agents should be selected that are effective against likely pathogens, have the lowest risk of drug interactions, and can be administered in a manner that promotes compliance (Table 1-2).

- Selection of antibiotics should consider that up to **30% to 40% of *H. influenzae*** and **95% of *M. pneumoniae*** are **β -lactamase producers**, and up to **30% of *S. pneumoniae*** are at least moderately penicillin resistant, (TABLE 1-2).

TAB 1-2. Oral Antibiotics Commonly Used for the Treatment of Acute Respiratory Exacerbations in Chronic Bronchitis

Antibiotic	Usual Adult Dose (g)	Dose Schedule (doses/day)
Ampicillin	0.25-0.5	4
Amoxicillin	0.5	3
Cefprozil	0.5	2
Cefuroxime	0.5	2

TAB 1-2. Oral Antibiotics Commonly Used for the Treatment of Acute Respiratory Exacerbations in Chronic Bronchitis

Ciprofloxacin	0.5-0.75	2
Gatifloxacin	0.4	1
Levofloxacin	0.5-0.75	1
Doxycycline	0.1	2
Minocycline	0.1	2
Tetracycline HCl	0.5	4
Amoxicillin-clavulanate	0.5	3

TAB 1-2. Oral Antibiotics Commonly Used for the Treatment of Acute Respiratory Exacerbations in Chronic Bronchitis

Supplemental Drugs

Azithromycin	0.25-0.5	1
Erythromycin	0.5	4
Clarithromycin	0.25-0.5	2
Cefixime	0.4	1
Cephalexin	0.5	4
Cefaclor	0.25-0.5	3

- **Ampicillin** is often considered the drug of choice for the treatment of acute exacerbations of chronic bronchitis. *Unfortunately*, the need for multiple repeat daily doses (4 times daily) and the incidence of penicillin-resistant β -lactamase-producing strains of bacteria **have limited the usefulness of this safe and cost-effective antibiotic.**
- The value of **macrolides** when Mycoplasma is involved is unquestioned. **Azithromycin** **should be considered as the macrolide of choice for Mycoplasma.**

- The **fluoroquinolones** are effective, particularly when **gram-negative** pathogens are involved, or for more severely ill patients. Many *S. pneumoniae* are resistant to older fluoroquinolones such as ciprofloxacin, necessitating the use of newer agents such as **gatifloxacin**.
- **In patients** whose history suggests recurrent exacerbations of **their disease** that might be **attributable to certain specific events** (i.e., seasonal, winter months), a trial of prophylactic antibiotics might be beneficial. If no clinical improvement is noted over an appropriate period (e.g., 2 to 3 months per year for 2 to 3 years), prophylactic therapy could be discontinued.

■ **BRONCHIOLITIS**

- Bronchiolitis is an **acute viral infection** of the **lower respiratory tract of infants** that shows a **definite seasonal pattern** (peaks during the winter months and persists through early spring). **The disease most commonly affects infants between the ages of 2 and 10 months.**
- **Respiratory syncytial virus** is the most common cause of bronchiolitis. **Parainfluenza viruses** are the second most common cause. Bacteria serve as secondary pathogens in only a small minority of cases.

TAB 1-3. Clinical Presentation of Bronchiolitis

Signs and Symptoms

Prodrome with irritability, restlessness, and mild fever
Cough and coryza.

Vomiting, diarrhea, noisy breathing, and an increase in respiratory rate as symptoms progress.

Labored breathing with retractions of the chest wall, nasal flaring, and grunting.

■ **Treatment**

- **Bronchiolitis is a self-limiting** illness and usually requires no therapy (other than reassurance and antipyretics) unless the infant is hypoxic or dehydrated.
- In severely affected children, the mainstays of therapy for bronchiolitis **are oxygen therapy and intravenous fluids.**
- Aerosolized β 2-adrenergic therapy appears to offer little benefit for the majority of patients but may be useful in the child with a predisposition toward bronchospasm.

- Because bacteria do not represent primary pathogens in the etiology of bronchiolitis, **antibiotics should not be routinely administered.**
- Ribavirin may be considered for bronchiolitis caused by respiratory syncytial virus in a subset of patients (those with underlying pulmonary or cardiac disease or with severe acute infection).

■ Glaucoma

■ DEFINITION

- Glaucomas are ocular disorders characterized by changes in the optic nerve head (optic disk) and by loss of visual sensitivity and field.

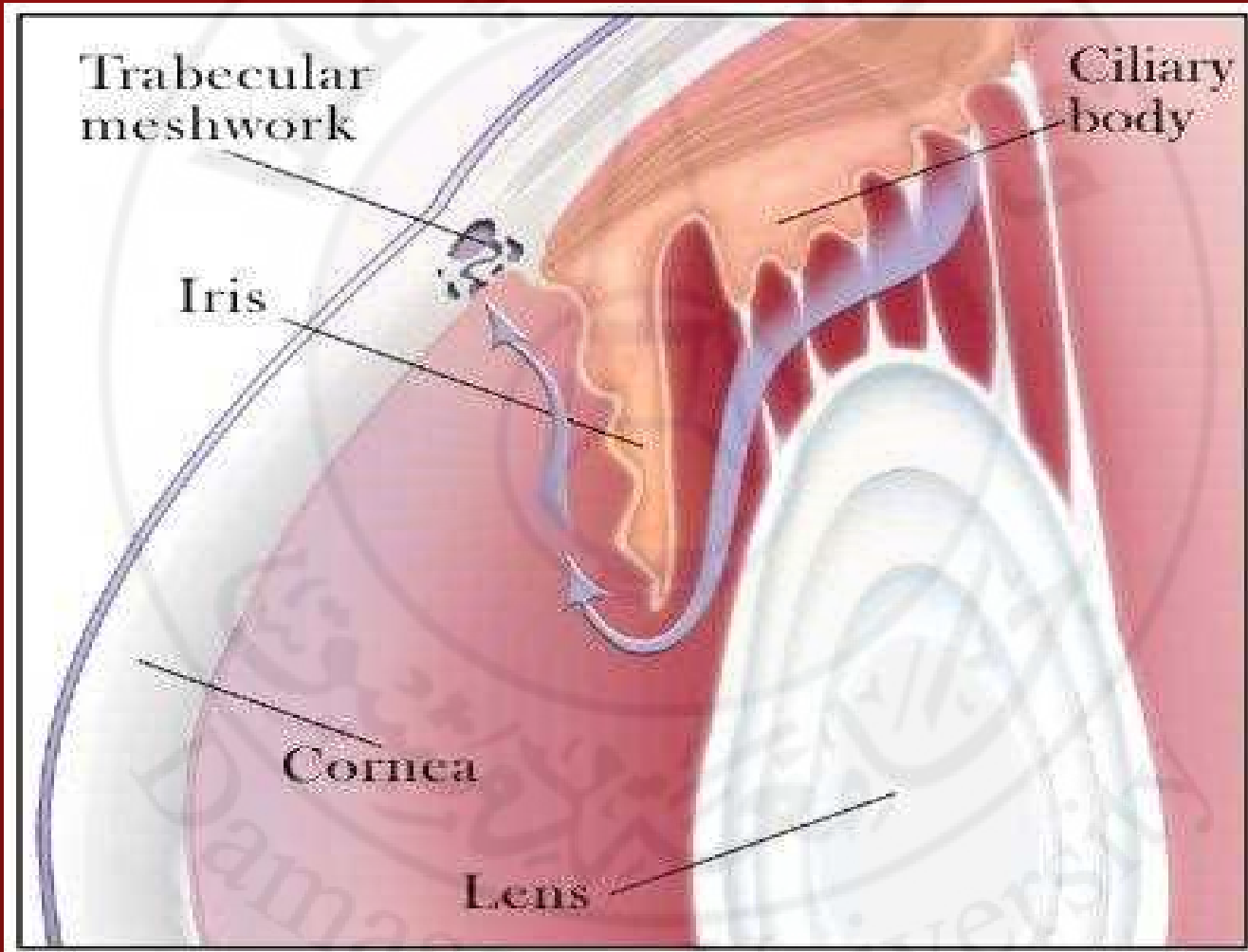
■ Glaucoma

■ DEFINITION

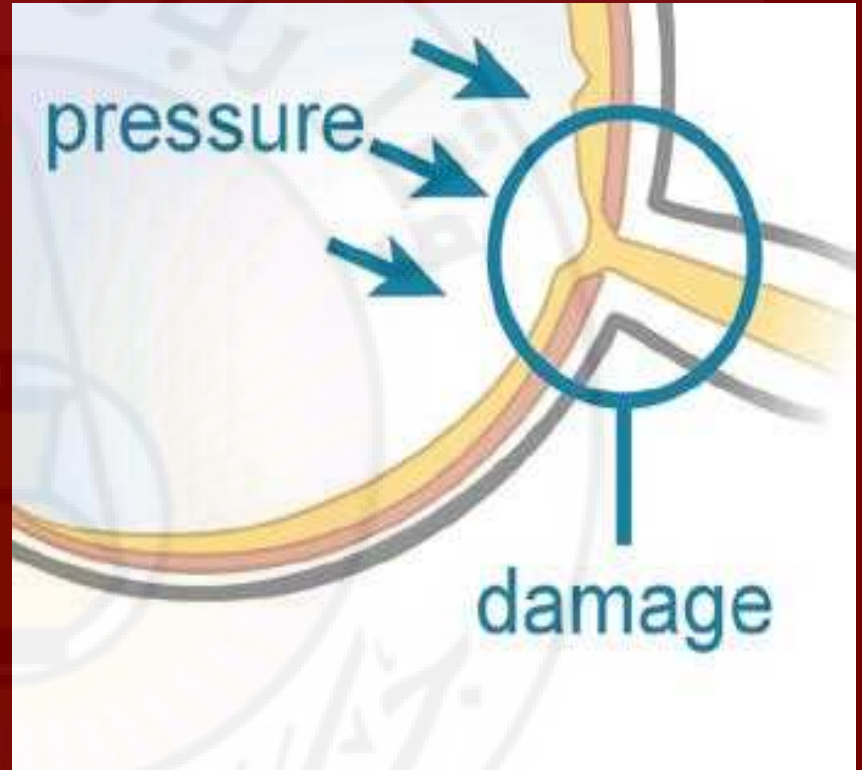
- Glaucoma is an eye disease that can cause vision loss or blindness. With glaucoma, **fluid builds up** in the eye, which puts **pressure on the back of the eye**. This pressure injures the optic nerve and causes vision loss. **Increased intraocular pressure** (ارتفاع الضغط في مقلة العين IOP)
- **Side vision is often affected first, followed by front vision.**

Ciliary body = الجسم الهدبي

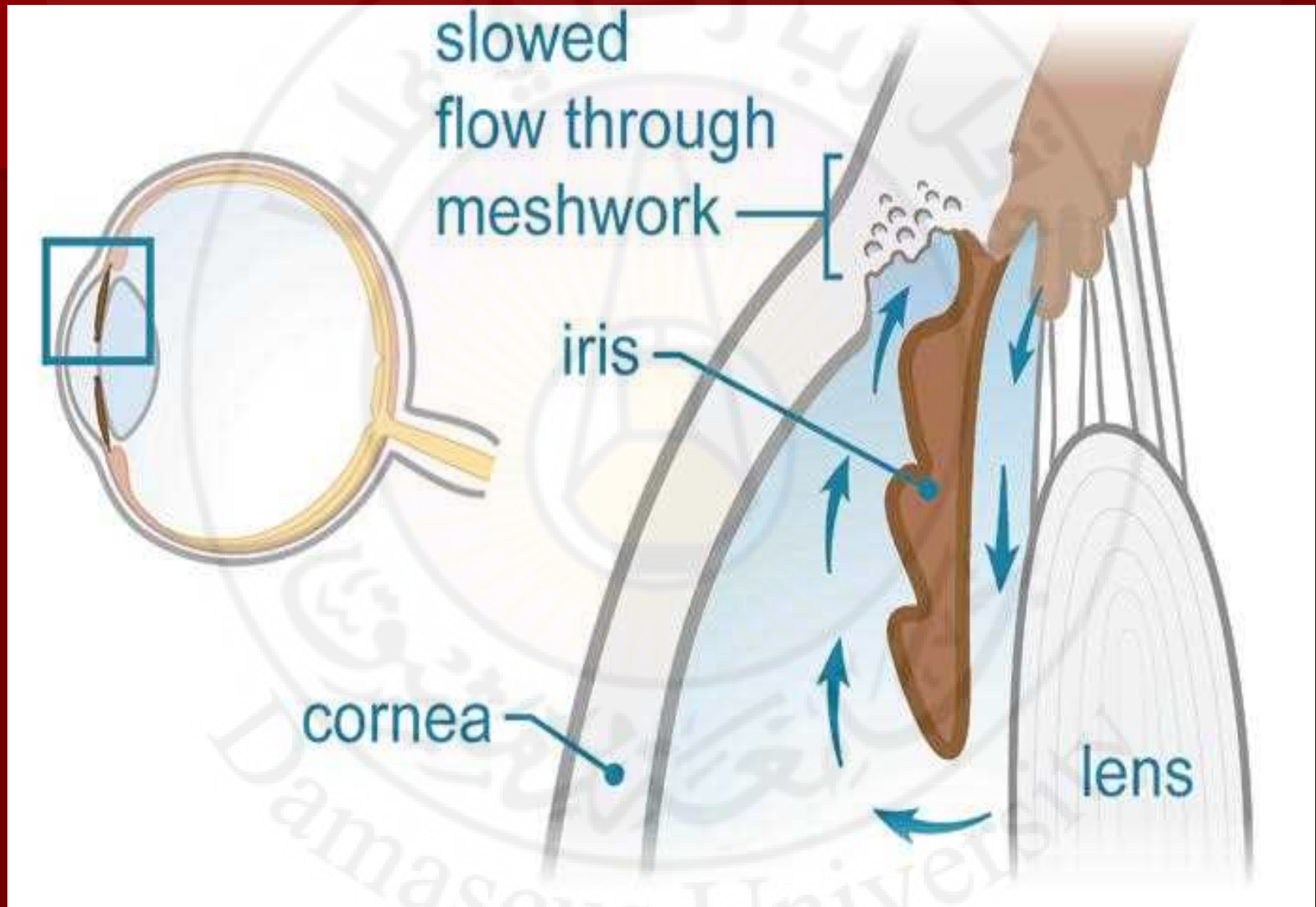
Trabecular meshwork = الشبكة الصلبة



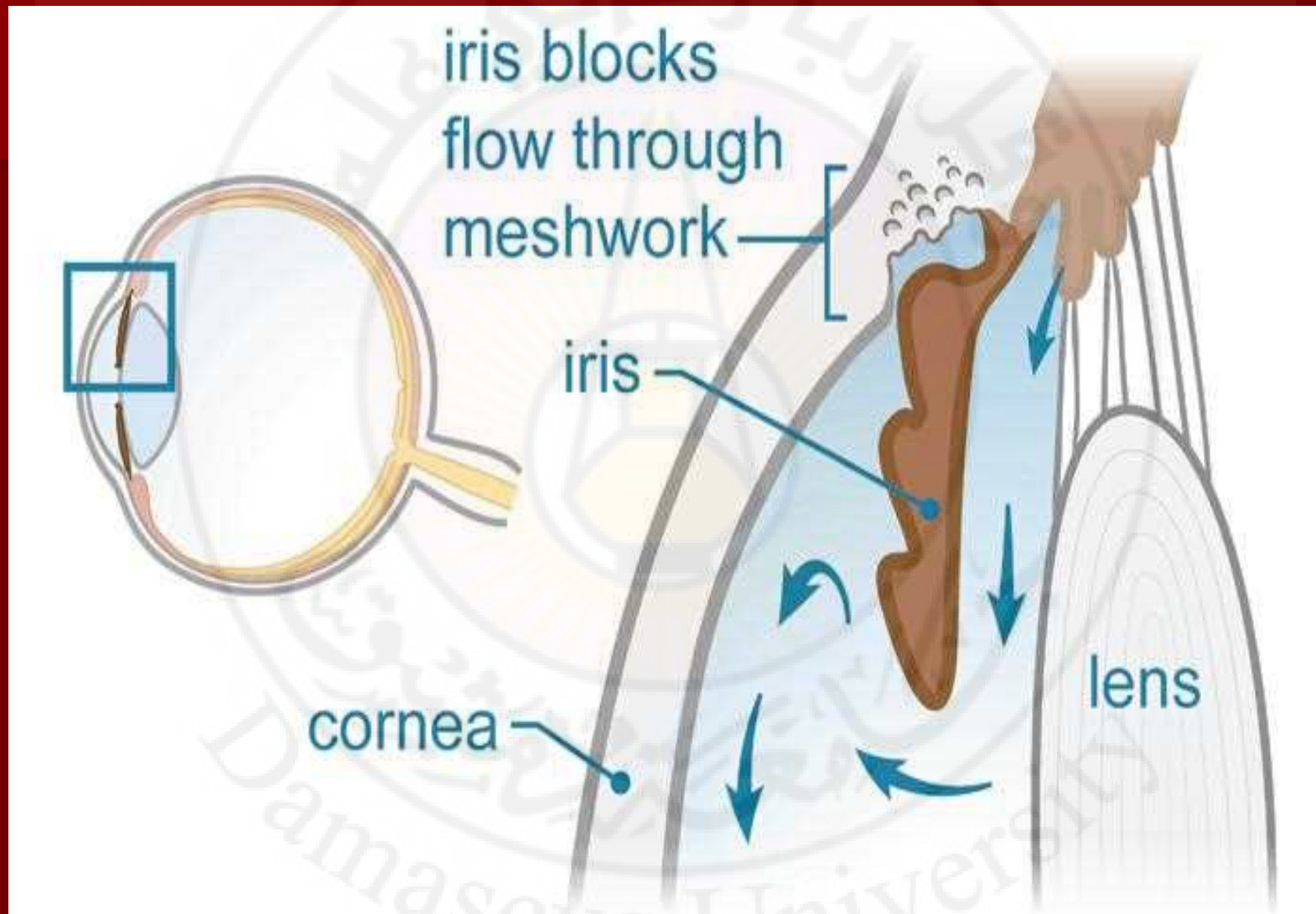
Anatomy of glaucoma



Open-angle glaucoma



Closed-angle glaucoma



Glaucoma symptoms



normal vision



vision with glaucoma



Damascus University

■ **PATHOPHYSIOLOGY**

■ **Types of Glaucoma**

- There are two **main** types of glaucoma:
- • **Open-angle glaucoma** often has no signs until it reaches an advanced stage.
- The pressure **slowly** damages the optic nerve over time. This affects both eyes but you may have signs in one eye first.
- • **Angle-closure glaucoma** has a **very fast rise** in pressure and sudden signs.
- **Permanent vision loss can occur within one day.**
- **Congenital glaucoma and Secondary glaucoma .**

■ Risk Factors

■ You are at risk for developing glaucoma if you :

- • Have a family member with glaucoma;
- • Have diabetes, high blood pressure, heart disease or hypothyroidism;
- • Are nearsighted قصر (حسر) البصر ;
- • Have had an injury to the eye, certain eye surgeries **or chronic eye inflammation**

- • Have been taking **steroids** for long periods of time;
- • Are over age 60;
- • *Are African-American or Mexican-American*
- • *Are of **Asian-American** descent – this puts you at increased risk for **angle closure glaucoma.***

■ Signs

■ Glaucoma may have no signs until there is vision loss. Other signs you may have :

- • Blurred vision = رؤية ضبابي
- • Halos around lights
- • Loss of peripheral or side vision
- • Tunnel vision
- • Red eyes
- • Severe eye pain
- • Nausea and vomiting

- **Many drugs can increase IOP** (Table 1-1).
- The potential to induce or worsen glaucoma depends on the type of glaucoma and on whether it is adequately controlled.
- **Closed-angle glaucoma occurs** when the iris mechanically blocks the trabecular meshwork, resulting in increased IOP.



■ **TABLE 1-1. Drugs That May Induce or Potentiate Increased Intraocular Pressure**

■ **Open-angle glaucoma**

Ophthalmic corticosteroids (high risk)

Systemic corticosteroids

Nasal/inhaled corticosteroids

Fenoldopam (hp, A, D1 ago)

Ophthalmic anticholinergics

Succinylcholine

Vasodilators (low risk)

Cimetidine (low risk)

■ **Closed-angle glaucoma**

Topical and Systemic anticholinergics;

Topical sympathomimetics;

Heterocyclic antidepressants;

Low-potency phenothiazines (Schiz);

Antihistamines;

Ipratropium;

Benzodiazepines (low risk);

Theophylline (low risk);

Central nervous system stimulants (low risk);

- Serotonin selective reuptake inhibitors, Imipramine;
- Tetracyclines (low risk);
- Monoamine oxidase inhibitors (low risk) and
- Topical cholinergics (low risk).



■ Treatment

- Your eye doctor may do tests to check your :
 - • Eye pressure, • Optic nerve, • Vision.
- Glaucoma cannot be cured and damage cannot be reversed. But with treatment, eye pressure can be decreased and further vision loss can be prevented. Eye drops are the most common early treatment for glaucoma.

Other treatments may include oral medicines, laser treatment or surgery. When you have glaucoma, it must be treated for the rest of your life.

■ **TREATMENT OF OCULAR HYPERTENSION AND OPEN - ANGLE GLAUCOMA**

- Treatment is indicated for ocular hypertension if the patient has a significant risk factor such as **IOP greater than 25 mm Hg.**
- Treatment is indicated for all patients with elevated IOP and visual field defects.



- Drug therapy is the most common initial treatment and is initiated in a stepwise manner, **starting with a single well tolerated topical agent** (Table 1-2).
Historically :

- **1) β^2 blockers were the treatment of choice** and continue to be used if there are no contraindications to potential β^2 blockade caused by systemic absorption. β^2 blockers have the advantage of low cost owing to generic formulations.

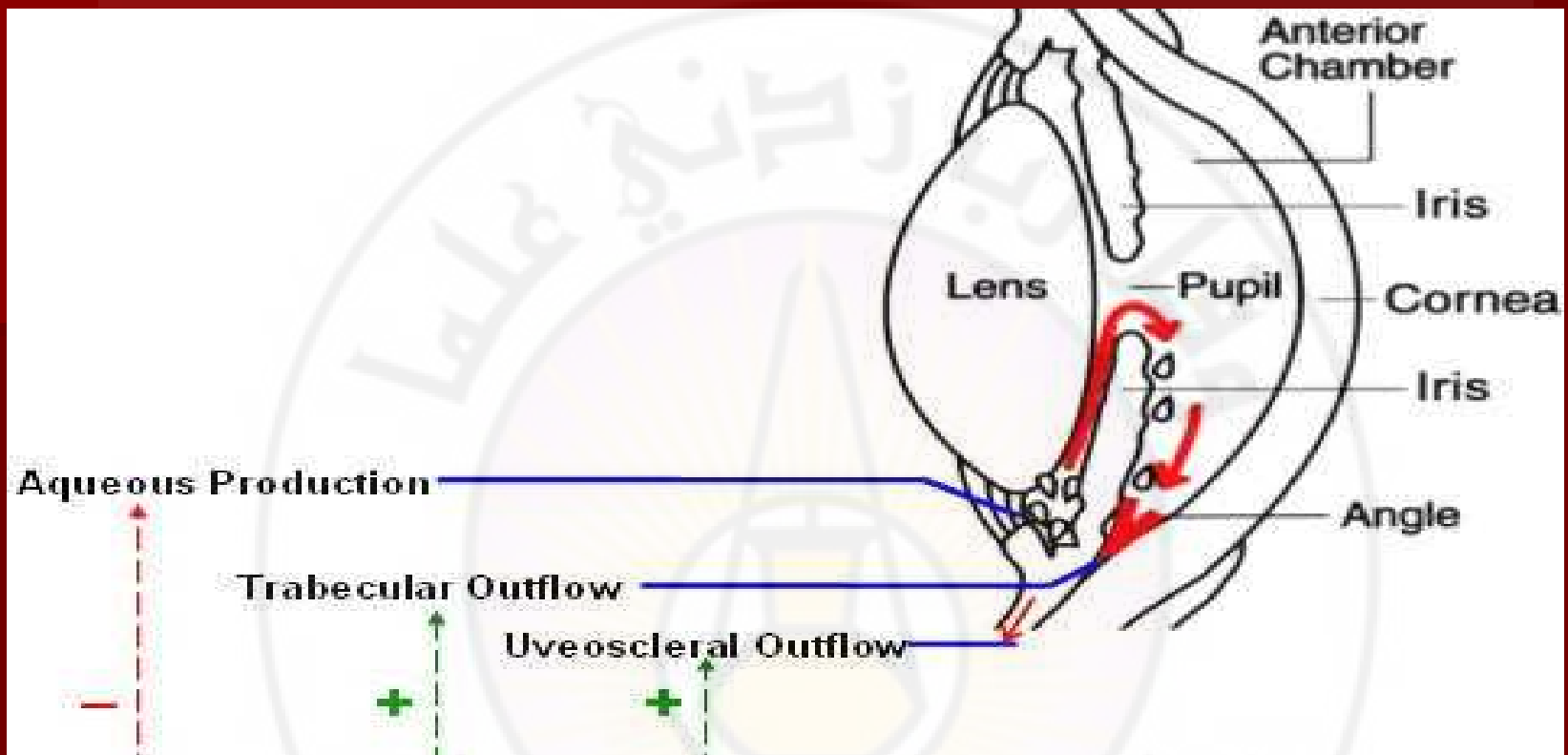
- **Newer agents are also suitable for first-line therapy.**
- **2) Prostaglandin analogues have the advantage of :**
 - *strong potency,*
 - *unique mechanism suitable for combination therapy,*
 - *good safety profile, and*
 - *once-a-day dosing.*

- **3) Topical Carbonic Anhydrase Inhibitors (CAIs)** are also suitable for first-line therapy.
- **4) Pilocarpine and epinephrine**
(or dipivefrin= **Nonspecific adrenergic agonists**)
are used as third-line therapies because of adverse events or reduced efficacy.
- **5) Topical cholinesterase inhibitors**
Carbachol, and **oral CAIs** (Table 1-3) are used as last-resort options after failure of less toxic options.

■ **TREATMENT OF CLOSED-ANGLE GLAUCOMA**

- Acute closed-angle glaucoma with high IOP requires rapid reduction of IOP. **Iridectomy** is the definitive treatment, which produces a hole in the iris that permits aqueous flow to move directly from the posterior to the anterior chamber.
- **Drug therapy of an acute attack typically consists of an osmotic agent and secretory inhibitor** (e.g., β^2 blocker, α_2 agonist, Prostaglandin analogues = latanoprost (xalatan) or CAI).

- **Osmotic agents are used because they rapidly decrease IOP.** Examples include glycerin, 1 to 2 g/kg orally, and *mannitol*, 1 to 2 g/kg *intravenously*.
- **Topical corticosteroids** can be used to **reduce** ocular inflammation and **synechiae** **التَصاقَاتُ القُزَحِيَّة**.



β_2 blockers

α_1 -Adrenergic Agonists

Prostaglandin
analogues

Damascus University

TABLE 1-2. Topical Drugs Used in the Treatment of Glaucoma

Drug	Dose Form	Strength %	Usual Dose	Mechanism of Action
β^2-Adrenergic blocking agents				
Betaxolol	Solution	0.5	1 drop b.i.d.	Reduce aqueous production by the ciliary body
Carteolol	Solution	1	1 drop b.i.d.	
Levobunolol	Solution	0.25, 0.5	1 drop b.i.d.	

TABLE 1-2. Topical Drugs Used in the Treatment of Glaucoma

Drug	Dose Form	Strength %	Usual Dose	Mechanism of Action
β²-Adrenergic blocking agents				
Metipranolol	Solution	0.3	1 drop b.i.d.	Reduce aqueous production by the ciliary body
Timolol	Solution	0.25, 0.5	1 drop b.i.d.	

TABLE 1-2. Topical Drugs Used in the Treatment of Glaucoma

Drug	Dose Form	Strength %	Usual Dose	Mechanism of Action
Nonspecific adrenergic agonists				
Dipivefrin	Solution	0.1	1 drop b.i.d.	Increase aqueous humor outflow

TABLE 1-2. Topical Drugs Used in the Treatment of Glaucoma

Drug	Dose Form	Strength %	Usual Dose	Mechanism of Action
Cholinergic agonists Direct-acting				
Carbachol	Solution	0.75, 1.5, 2.25, 3	1 drop b.i.d.	Increase aqueous humor outflow through trabecular meshwork
Pilocarpine	Solution Gel	0.25, 0.5, 1, 2, 4, 6, 8, 10	1 drop b.i.d.	

TABLE 1-2. Topical Drugs Used in the Treatment of Glaucoma

Drug	Dose Form	Strength %	Usual Dose	Mechanism of Action
Carbonic Anhydrase Inhibitors (CAI)				
Brinzolamide	Suspension	1	1 drop b.i.d.	Reduce aqueous humor production by the ciliary body
Dorzolamide	Solution	2	1 drop b.i.d.	

TABLE 1-2. Topical Drugs Used in the Treatment of Glaucoma

Drug	Dose Form	Strength %	Usual Dose	Mechanism of Action
Prostaglandin analogues				
Latanoprost	Solution	0.005	1 drop q.h.s.	Increase aqueous uveoscleral outflow and, to a lesser extent, trabecular outflow
Bimatoprost	Solution	0.03	1 drop q.h.s.	
Travoprost	Solution	0.004	1 drop q.h.s.	

TABLE 1-3. Systemic Carbonic Anhydrase Inhibitors Used in the Treatment of Glaucoma

Drug	Dose Form	Strength %	Usual Dose
Acetazolamide	Tablet	125 mg, 250 mg	125 â 250 mg 2 â 4 times a day
	Injection	500 mg/vial	250 â 500 mg
	Capsule	500 mg	500 mg twice a day
Dichlorphenamide	Tablet	50 mg	25 â 50 mg 1 â 3 times a day
Methazolamide	Tablet	25 mg, 50 mg	25 â 50 mg 2 â 3 times a day

- **EVALUATION OF THERAPEUTIC OUTCOMES**
- Successful outcomes require identifying an : effective, well tolerated regimen; closely monitoring therapy; and patient adherence. Whenever possible, therapy for open-angle.
- glaucoma should be started **as a single agent in one eye to facilitate evaluation of drug efficacy and tolerance.**
- Many drugs or **combinations** may need to be tried before the optimal regimen is identified.

- Monitoring therapy for open-angle glaucoma should be individualized. **IOP response** is assessed every **4 to 6 weeks** initially, every **3 to 4 months** after IOPs become acceptable, and more frequently after therapy is changed.

- Patients should be monitored for tachyphylaxis, especially with **β^2 blockers or (apraclonidine = α_2 agonist)**. Treatment can be temporarily discontinued to monitor its benefit.
- There is no specific target IOP because the correlation between IOP and optic nerve damage is poor. Typically, a 25% to 30% reduction is desired.

- **Using more than one drop** per dose **increases the risk of adverse events and cost, but not efficacy.**
- Patients should be educated about possible adverse effects and methods for preventing them.

- Patients should be taught how to administer topical therapy. With a forefinger pulling down the lower eyelid to form a pocket, the patient should place the dropper over the eye, look at the tip of the bottle, and then look up and place a single drop in the eye. To maximize topical activity and minimize systemic absorption, the patient should close the lid for 1 to 3 minutes after instillation and place the index finger over the nasolacrimal drainage system in the inner corner of the eye.

- If **more than one** topical **drug** is required, instillation **should be separated by 5 to 10 minutes** to provide optimal ocular contact.
- Adherence to drug therapy should be monitored because it is commonly inadequate and a cause of therapy failure.



Cure and treatment



■ Oral Contraceptives

- Ortho Tri-Cyclen is FDA-approved for moderate acne in women unresponsive to topical medications.
- This triphasic product contains a fixed dose of ethinyl estradiol, 0.035 mg, and increasing doses of norgestimate, 0.180, 0.215, and 0.250 mg.
- The combination increases sex hormone-binding globulin (SHBG), causing a decrease in unbound, biologically active testosterone.

■ PHARYNGITIS

- Pharyngitis is an acute infection of the oropharynx or nasopharynx.

- While viral pharyngitis is a common condition,

- group A β -hemolytic streptococcus, or streptococcus pyogenes, is the primary bacterial cause.

- Viruses cause most of the cases of acute pharyngitis. Specific etiologic agents include:

rhinovirus, coronavirus, adenovirus,

influenza, parainfluenza, and Epstein-

Barr virus.

- Out of all of the bacterial causes, **group A streptococcus is the most common** and it is the only commonly occurring form of acute pharyngitis **for which antimicrobial therapy is indicated**

- **Non suppurative complications** such as acute rheumatic fever, acute glomerulonephritis, and reactive arthritis may occur as a result of pharyngitis with group A streptococcus.

TAB 2-3 Clinical Presentation and Diagnosis of Group A Streptococcal Pharyngitis

Signs and Symptoms

Sore throat.

Pain on swallowing.

Fever, Headache, nausea, vomiting, and abdominal pain (especially children).

Red swollen uvula, petechiae on the soft palate, and a scarlatiniform rash.

Severe symptoms that are not suggestive of group A streptococcal infection include cough, conjunctivitis, coryza, and diarrhea.

■ CLINICAL PRESENTATION

- Is presented in Table 2-3.
- Testing for group A streptococcus be done in all patients with signs and symptoms. *Only those with a positive test for group A Streptococcus require antibiotic treatment.*

■ TREATMENT

- The goals of treatment of pharyngitis are to improve clinical signs and symptoms, minimize adverse drug reactions, prevent transmission to close contacts, and prevent acute rheumatic fever and suppurative complications such as peritonsillar abscess, cervical lymphadenitis

- Antimicrobial therapy should be limited for Group A streptococcal pharyngitis with a positive laboratory test.
- Analgesics such as acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) aid in pain relief. **Isbstrongly recommended**
- Either systemic or topical analgesics can be used, as well as antipyretics and other supportive care including rest, fluids, lozenges, and salt water gargles.

- **Antimicrobial treatment** should be for group A streptococcal pharyngitis (Table 2-4).
- Table 2-5 presents dosing guidelines for recurrent infections.

TAB 2-4 Antibiotic Guidelines for Pharyngitis

Drug	Adult Dosage	Pediatric Dosage	Duration
Penicillin V-K	250 mg 3 times daily or 4 times daily or 500 mg twice daily	50 mg/kg/day divided in 3 doses	10 days
Penicillin benzathine	1.2 million units intramuscularly	0.6 million units. For under 27 kg (50,000 units/kg)	1 dose
Amoxicillin	500 mg 3 times daily	40-50 mg/kg/day divided in 3 doses	10 days
Cephalexin	250-500 mg orally 4 times daily	25-50 mg/kg/day divided in 4 doses	10 days

TAB 2-11 Intracranial Infection: Intravenous Antibiotic Dosage for Children

Drug	Adult Dosage	Pediatric Dosage
Clindamycin	600 mg orally divided in 2- 4 doses	20 mg/kg/day in 3 divided doses (max: 1.8 g/day)
Amoxicillin-clavulanate	500 mg twice daily	40 mg/kg/day in 3 divided doses
Penicillin benzathine	1.2 million units intramuscularly for 1 dose	0.6 million units. For under 27 kg (50,000 units/kg)
Penicillin benzathine with rifampin	As above 20 mg/kg/day orally in 2 divided doses — last 4 days of treatment with penicillin	As above Rifampin dose same as adults

- In patients allergic to penicillin, a macrolide such as erythromycin or a first-generation cephalosporin such as cephalexin can be used.
- Newer macrolides such as azithromycin and clarithromycin are as effective and cause fewer gastrointestinal adverse effects.
- If patients are unable to take oral medications, intramuscular benzathine penicillin can be given.

■ EVALUATION OF THERAPEUTIC OUTCOMES

- Most cases of pharyngitis are self-limited; however, antimicrobial therapy will hasten resolution when given early to proven cases of group A streptococcus. Fever generally resolves by 3 to 5 days, and most other acute symptoms by 1 week. Tonsils and lymph nodes may take a few weeks to return to baseline. Children should be kept home from daycare or school until afebrile and for the first 24 hours after antimicrobial treatment is initiated, after which time transmission is unlikely.

Respiratory system disease



Respiratory tract anatomy

- The **pulmonary and circulatory systems** are designed to provide the body with a continuous supply of oxygen and quick removal of carbon dioxide. **The pulmonary system controls the exchange of gases between the atmosphere and blood,** while the **circulatory system transports these gases between the lungs and the cells.** A dysfunction in either system disrupts homeostasis, can cause anoxia (an inadequate level of oxygen) and even cell death.

- The organs used in the exchange of gases between the atmosphere and the blood are:

nose, pharynx البلعوم , **larynx** الحنجرة ,
trachea الرغامى , **bronchi** القصبات , and
lungs الرئة .

- **The Upper Airways including :**

- **nose,**

- **mouth,**

- **nasopharynx,** البلعوم الأنفي

- **oropharynx,** البلعوم الفموي

- **laryngopharynx,** البلعوم الحنجري and the
larynx الحنجرة .

Lower respiratory tract :

Trachea الرغامى, **and bronchi** القصبات
lungs الرئة



■ **Respiratory Tract Infections, Lower**

- **Lower respiratory tract infections include :**
- infectious processes of the lungs ,
- bronchitis التهاب قصبات ,
- Bronchiolitis التهاب قصيبات ,
- Pneumonia ذات رئة ,
- and lung abscess خراجات رئوية .

■ PNEUMONIA

- **Pneumonia** is the most common infectious *cause of death*.
- It occurs in persons of **all ages**, although the clinical manifestations are most **severe** in the **very young**, the **elderly**, and the **chronically ill**.

TAB 1-4. Clinical Presentation of Pneumonia

Signs and Symptoms

Abrupt onset of fever, chills, dyspnea, and productive cough, Rust-colored sputum or hemoptysis, Pleuritic chest pain.

ظهور مفاجئ للحمى ، قشعريرة ، ضيق في التنفس ، سعال منتج ، بلغم
بلون الصدأ أو نفث دم و ألم في الصدر الجنبى.

■ **PATHOPHYSIOLOGY**

- Microorganisms gain access to the lower respiratory tract by **three routes**:

- 1) they may be inhaled as aerosolized particles;*
- 2) they may enter the lung via the bloodstream from an extrapulmonary site of infection;*
- 3) aspiration of oropharyngeal contents may occur.*

- The **vast majority of pneumonia** cases are due to :

- **S. pneumoniae (pneumococcus)** or **M. pneumoniae (Mycoplasma pneumonia)**, **C. pneumonia (Chlamydia pneumoniae)**.

- Other common bacterial causes include **Legionella**.

■ **PATHOPHYSIOLOGY**

- **Community-acquired pneumonias** caused by **Staphylococcus aureus** and **gram-negative rods** are observed primarily in the elderly, especially those residing in nursing homes, and in association with alcoholism and other debilitating conditions.

- **Gram-negative aerobic bacilli and S. aureus** are also the leading causative agents in *hospital-acquired pneumonia*.
- **Anaerobic bacteria** are the most common etiologic agents in pneumonia that follows the gross **aspiration of gastric or oropharyngeal contents**.
- *In the pediatric age group*, most pneumonias are due to *viruses*, especially **respiratory syncytial virus (RSV), parainfluenza, and adenovirus**.
- **Pneumococcus is the most common bacterial cause.**

■ DESIRED OUTCOME

- Associated morbidity should be minimized (e.g., renal, pulmonary, or hepatic dysfunction).

■ TREATMENT

- The **first priority** on assessing the patient with pneumonia **is to evaluate the adequacy of respiratory function** and to **determine whether there are signs of systemic illness, specifically dehydration or sepsis with resulting circulatory collapse.**

- The **supportive care** of the patient with pneumonia **includes** :

Use of humidified oxygen for hypoxemia;

Fluid resuscitation;

Administration of bronchodilators when bronchospasm is present.

- **Important therapeutic adjuncts include:**
adequate hydration (by IV route if necessary),
optimal nutritional support, and fever control.

- The **treatment of bacterial pneumonia** is shown in TABLE 1-1 for adults and children.



TAB 1-1. Antibiotic Doses for the Treatment of Bacterial Pneumonia

Antibiotic Class	Antibiotic	Pediatric (mg/kg/day)	Adult (total dose/day)
Macrolide	Clarithromycin	15	0.5-1 g
	Erythromycin	30-50	1-2 g
Azalide	Azithromycin	10 mg/kg — 1 day, then 5 mg/kg/day — 4 days	500 mg day 1 then 250 mg/day — 4 days

TAB 1-1. Antibiotic Doses for the Treatment of Bacterial Pneumonia

Antibiotic Class	Antibiotic	Pediatric (mg/kg/day)	Adult (total dose/day)
Tetracycline	Tetracycline HCL	25-50	1-2 g
	Oxytetracycline	15-25	0.25-0.3 g
Penicillin	Ampicillin	100-200	2-6 g
	Amoxicillin/ amoxicillin-clavulanate	40-90	0.75-1 g

TAB 1-1. Antibiotic Doses for the Treatment of Bacterial Pneumonia

Antibiotic Class	Antibiotic	Pediatric (mg/kg/day)	Adult (total dose/day)
Extended-spectrum cephalosporins	Ceftriaxone	50-75	1-2 g
	Ceftazidime	150	2-6 g
Fluoroquinolones	Gatifloxacin	10-20	0.4 g
	Ciprofloxacin	20-30	0.5-1.5 g
Aminoglycosides	Gentamicin	7.5	3-6 mg/kg
	Tobramycin	7.5	3-6 mg/kg

- Antibiotic concentrations in respiratory secretions in excess of the pathogen minimum inhibitory concentration (MIC) are necessary for successful treatment of pulmonary infections.
- Drugs recommended for **empiric** treatment of community-acquired pneumonia are presented in Table 1-2.
- Prevention of pneumonia is possible through the use of vaccines against **S. pneumoniae** and **H. influenzae type b**. In addition, **amantadine** may be administered for **prevention of influenza A** infection, beginning as soon as possible after exposure and continuing for at least 10 days.

TAB 1-2. Guidelines for the Empirical Treatment of Community-Acquired Pneumonia

Clinical Setting	Empirical Therapy
Outpatients	Macrolide/azalide, doxycycline, or fluoroquinolone
Inpatients, general medical ward	Extended-spectrum cephalosporin + macrolide/azalide OR β -lactamase inhibitor + macrolide/azalide or fluoroquinolone
Inpatients, intensive care unit	Extended-spectrum cephalosporin or β -lactamase inhibitor + fluoroquinolone or macrolide/azalide

■ **EVALUATION OF THERAPEUTIC OUTCOMES**

- With community-acquired pneumonia, *time for resolution of cough, sputum production, and presence of constitutional symptoms* (e.g., malaise, nausea or vomiting, lethargy) should be assessed.
- Progress should be noted in the first 2 days, with complete resolution in 5 to 7 days.
- With nosocomial pneumonia, the above parameters should be assessed along with WBC counts, chest radiograph, and blood gas determinations.

Types of fluoroquinolones

ciprofloxacin; ciprofloxacin extended-release

levofloxacin ;

gatifloxacin ;

moxifloxacin ;

ofloxacin ;

Norfloxacin and

gemifloxacin

■ Psoriasis

■ DEFINITION

- Psoriasis is a common **chronic inflammatory disease** characterized by **recurrent exacerbations** and **remissions** هجوع of thickened, erythematous حماميات, and scaling plaques لويحات قشرية .



■ Risk Factors:

- Climate, stress, alcohol, smoking, infection, trauma الرضوض, and drugs may aggravate psoriasis. Warm seasons and sunlight improve psoriasis in 80% of patients, whereas 90% of patients worsen in cold weather. Psoriatic lesions may develop at the site of injury (e.g., rubbing, venipuncture, bites, surgery) on normal-appearing skin. **Lithium carbonate, β -adrenergic blockers, some antimalarials, nonsteroidal anti-inflammatory drugs, ACE inhibitors, tetracyclines, and interferons have been reported to exacerbate psoriasis.**

■ Types of Psoriasis:

■ There are five main types of psoriasis :

- 1) plaque لويحي,
- 2) guttate نقطي,
- 3) inverse معكوس,
- 4) pustular بَنَرِيّ, and
- 5) erythrodermic مُحَمَّرَةٌ لِلْجُد

■ Pathophysiology :

- Skin cells are replaced every **3-5 days in psoriasis** rather than the **usual 28-30 days**. These changes are believed to stem from the premature maturation of **keratinocytes** induced by an inflammatory cascade in the **dermis involving:**
 - **dendritic cells ,**
 - **macrophages, and**
 - **T cells**
- These immune cells secrete inflammatory chemical signals (cytokines) such as **TNF α , interleukin –1 β , interleukin –6, and interleukin –23**. These secreted inflammatory signals are believed to stimulate skin cells (keratinocytes) to proliferate.

■ Pathophysiology :

- One hypothesis is that psoriasis involves a defect in *regulatory T cells*, and in the *regulatory cytokine* interleukin -10.
- Psoriatic T cells move from the dermis into the epidermis and secrete **interferon- γ** and **interleukin -23**.
- **Interleukin-23** is known to induce the production of **interleukin-17** and **interleukin-22**.
Interleukin-22 works in combination with interleukin-17 to induce keratinocytes to secrete neutrophil-attracting cytokines.

■ CLINICAL PRESENTATION

- Psoriatic lesions are relatively **asymptomatic**, but about **25%** of patients **complain of pruritus** الحكة.
- Lesions are characterized by **sharply demarcated, erythematous papules** بثرات حمامية مُحمرّة and **plaques often covered with silver-white fine scales**. Initial lesions are usually small papules that enlarge over time and coalesce into plaques. If the fine scale is removed, **a salmon-pink lesion** is exposed, perhaps with punctate bleeding from prominent dermal capillaries (Auspitz sign).

- **Scalp psoriasis** ranges from diffuse scaling on an erythematous scalp to thickened plaques with **exudation, micro abscess, and fissures**. **Trunk, back, arm, and leg** lesions may be **generalized, scattered** متناثر, **discrete منفصل**, **droplike lesions** or **large plaques**. Palms, soles, face, and genitalia may also be involved. Affected nails are often pitted and associated with subungual keratotic material. **Yellowing under the nail plate may be seen.**

■ **DIAGNOSIS**

- The diagnosis is based on **physical examination** findings of the characteristic lesions of psoriasis.
- **The medical history** of a patient with psoriasis **should include information about** the onset and duration of lesions, family history of psoriasis, presence of exacerbating factors, previous history of antipsoriatic treatment (if any) along with efficacy and adverse effect data, exposure to chemicals and toxins, and allergies (food, drugs, and environmental).
- **Skin biopsy** of lesional skin is useful in confirming the diagnosis.

■ **TREATMENT**

■ **NONPHARMACOLOGIC THERAPY**

- **Emollients** (moisturizers) hydrate the stratum corneum and minimize water evaporation. They may enhance desquamation **توسف**, eliminate scaling, and decrease pruritus. The lotions, creams, or ointments often need to be applied up to 4 times a day to achieve a beneficial response. Adverse effects include folliculitis and allergic or irritant contact dermatitis.
- **Balneotherapy** (and climatotherapy) involves bathing in waters containing certain salts, often combined with natural sun exposure. The salts in certain waters (e.g., the Dead Sea) reduce activated T cells in skin and may be remittive for psoriasis.

- **Ultraviolet B** (UV-B) light exposure (280 to 320 nm) is a beneficial intervention. Use of a narrow-band (NB) light sources, in which 83% of the UV-B emission is at **310 to 313 nm**, focuses treatment within the most effective wavelength. **NB-UVB has been demonstrated to be effective in plaque-type psoriasis. Many topical and systemic therapies are used adjunctively to hasten and improve the response to UV-B phototherapy** (e.g., short-contact **anthralin** with UV-B, addition of **topical calcipotriene**, or adding **systemic methotrexate or retinoids**). **Emollients enhance efficacy of UV-B and may be applied just prior to UV-B treatments.**

- **FIRST-LINE TOPICAL PHARMACOTHERAPY**
- **Keratolytics**
- **Salicylic acid** is one of the most commonly used keratolytics. It causes a **disruption** in **corneocyte-to-corneocyte cohesion** in the abnormal horny layer of psoriatic skin. **This serves to remove scales, smooth the skin, and decrease hyperkeratosis.** The keratolytic effect enhances penetration and efficacy of some other topical agents such as **corticosteroids**.
- **It is applied as a 2% to 10% gel or lotion 2 or 3 times a day.**
- Salicylic acid produces local irritation. Application to large, inflamed areas may induce **salicylism** with symptoms of **nausea, vomiting, tinnitus, or hyperventilation.**

■ Corticosteroids

- Topical corticosteroids may **halte synthesis and mitosis of DNA** in epidermal cells and appear to **inhibit phospholipase A**, **lowering the amounts of arachidonic acid, prostaglandins, and leukotrienes in the skin.** *These effects*, **coupled with local vasoconstriction**, **reduce** erythema, pruritus, and scaling. As antipsoriatic agents, they are best used adjunctively with a product that specifically functions to normalize epidermal hyper proliferation.

- **Low-potency products** (e.g., hydrocortisone 1%, Dexamethasone 0.1) have a weak anti-inflammatory effect and **are safest for long-term application**, for use on the face, for use with occlusion, and for use in infants and young children.
- **Medium-potency products** (Desoximetasone 0.05, Betamethasone valerate 0.01) are used in moderate inflammatory dermatoses. **They may be used on the face and inter triginous areas for a limited time.**

- **High-potency preparations** (Diflorasone diacetate 0.05) are used primarily as alternatives to systemic corticosteroids when local therapy is feasible.
- **Very high potency products** (Halobetasol propionate 0.05) may be used for thick, chronic psoriatic lesions but for only short periods of time and on relatively small surface areas.

- **Ointments** are the most effective formulations for psoriasis because they have an occlusive oily phase that conveys a hydrating effect and enhances penetration of the corticosteroid into the dermis. They are not suited for use in the axilla, groin, or other inter triginous areas where maceration and folliculitis may develop secondary to the occlusive effect.
- **Creams** are more cosmetically desirable for some patients. They may be used in inter triginous areas even though their lower oil content makes them more drying than ointments.

- Topical corticosteroids are applied 2 to 4 times daily during long-term therapy.
- **Adverse effects include** local tissue atrophy, skin degeneration, and striae. If detected early, these effects may be reversible with discontinuation. **Masking of symptoms of bacterial or fungal skin infections have been reported.** **Systemic consequences include** hyperglycemia, and development of cushingoid features. Tachyphylaxis and rebound flare of psoriasis after abrupt cessation of therapy can also occur.

- **Vitamin D Analogs**
- **Vitamin D** and its analogs inhibit keratinocyte differentiation and proliferation and **have anti-inflammatory** effects by **reducing IL-8 and IL-2**. Use of **vitamin D** **itself is limited** by its propensity to cause **hypercalcemia**.
- **Calcipotriene** (Dovonex) **is a synthetic vitamin D analog** used for mild to moderate plaque psoriasis. Improvement is usually seen within 2 weeks of treatment, and approximately 70% of patients demonstrate marked improvement after 8 weeks.

- **Adverse effects** occur in about 10% of patients and **include** *lesional and perilesional burning and stinging*.
Calcipotriene 0.005% cream, ointment, or solution is applied 1 or 2 times a day (no more than 100 g/wk).
- **Calcitriol, Calcipotriol, Maxacalcitol and tacalcitol** are other vitamin D derivatives that have been studied for treatment of psoriasis.

■ Vitamin A analogs, Tazarotene

- Tazarotene (Tazorac) is a **synthetic retinoid** that is **hydrolyzed to its active metabolite, tazarotenic acid**, which modulates keratinocyte proliferation and differentiation.
- It is available as a **0.05% or 0.1% gel** and **cream** and is **applied once daily** (usually in the evening) for mild to moderate plaque psoriasis. **The 0.1% gel is somewhat more effective, but the 0.05% gel causes less irritation.**

- **Adverse effects** are dose- and frequency-related and **include** mild to moderate **pruritus, burning, stinging, and erythema.**
- Application of the **gel** to **eczematous** skin or to **more than 20% of body surface** area **is not recommended** because this may lead to extensive systemic absorption.
- **Tazarotene** is often used **with topical corticosteroids** to decrease local adverse effects and increase efficacy.

■ **SECOND-LINE TOPICAL PHARMACOTHERAPY**

■ **Coal Tar**

- Coal tar contains numerous hydrocarbon compounds formed from distillation of bituminous coal.

Ultraviolet B (UV-B) light-activated coal tar photoadducts with epidermal DNA and inhibits DNA synthesis. This normalized epidermal replication rate reduces plaque elevation.

- Coal tar preparations of **2% to 5%** tar are available in **lotions, creams, shampoos, ointments, gels, and solutions.** It is usually applied directly to lesions in the **evening** and allowed to remain in skin contact through the night. **It may also be used in bath water.**

- Coal tar is an effective treatment, but it is time-consuming, causes local irritation, has an unpleasant odor, stains skin and clothing, and increases sensitivity to UV light (including the sun).
- The **risk of carcinogenicity** is **low** but there are cases indicating a higher rate of nonmyeloma skin cancers in patients chronically exposed to coal tar and UV light.

■ Anthralin

- Anthralin possesses antiproliferative activity on keratinocytes, inhibiting DNA synthesis by intercalation between DNA strands.
- Because anthralin exerts its clinical effects at low cellular concentrations, **therapy usually starts with low concentrations (0.1% to 0.25%) with gradual increases to higher concentrations (0.5% to 1% or 5%).** Cream and ointment formulations are usually applied in the evening and allowed to remain overnight.

■ Anthralin

- Alternatively, short-contact anthralin therapy (**SCAT**) with application for 10 to 20 minutes of higher concentrations (1% to 5%) in water-soluble vehicles is effective with decreased local adverse effects.

- Anthralin products must be applied only to affected areas because contact with uninvolved skin may result in excessive irritation and staining, which usually disappears within 1 to 2 weeks of discontinuation.
- Inflammation, irritation, and staining of skin and clothing are often therapy-limiting effects.

■ FIRST-LINE

■ SYSTEMIC PHARMACOTHERAPY

■ Acitretin

- Acitretin (Soriatane) is a retinoic acid derivative ***and the active metabolite of etretinate.*** *It is indicated for* severe psoriasis, including erythrodermic and generalized pustular types. However, it is more useful as an adjunct in the treatment of plaque psoriasis.

- **Acitretin**
- it has shown good results when combined with other therapies, including **PUVA** and **UV-B**, **cyclosporine**, and **methotrexate**.
- The **initial recommended dose is 25 or 50 mg**; therapy is continued until lesions have resolved.
- **Acitretin is a teratogen** and is **contraindicated** in females who are pregnant or who **plan pregnancy within 3 years after drug discontinuation.**

■ SECOND-LINE

■ SYSTEMIC PHARMACOTHERAPY

- **Cyclosporine** demonstrates immunosuppressive activity by **inhibiting the first phase of T-cell activation. It also inhibits release of inflammatory mediators from mast cells, basophils, and polymorphonuclear cells.** Cumulative treatment for more than 2 years may increase the risk of malignancy, including skin cancers and lymphoproliferative disorders.

- **Methotrexate**, an **antimetabolite**, is indicated for **moderate to severe psoriasis**. It is particularly beneficial for **psoriatic arthritis**. It is also indicated for patients refractory to topical or ultraviolet therapy. Methotrexate can be administered orally, subcutaneously, or intramuscularly. ***Nausea and macrocytic anemia can be ameliorated by giving oral folic acid 1 to 5 mg/day.***

- **Methotrexate should be avoided in patients with active infections and in those with liver disease.**
- ***It is contraindicated in pregnancy because it is teratogenic.***



- **Tacrolimus**, an immunosuppressant that inhibits T-cell activation, is a useful alternative in severe recalcitrant psoriasis.
- **Mycophenolate mofetil** (CellCept) inhibits DNA and RNA synthesis and has been shown to have a specific lymphocyte antiproliferative effect. It is used as part of combination therapy in moderate to severe psoriasis and other autoimmune dermatoses.

- **Sulfasalazine** is an anti-inflammatory agent that *inhibits 5-lipoxygenase*. It is used selectively as an *alternative treatment*, particularly in patients with concurrent psoriatic arthritis. **When used alone, it is not as effective as methotrexate, PUVA, or acitretin.** However, it has a relatively high margin of safety.

- **6-Thioguanine** is a purine analog that has been used as an alternative treatment for psoriasis when conventional therapies have failed. It may be less hepatotoxic and therefore more useful than methotrexate in hepatically compromised patients with severe psoriasis.

- **PHOTOCHEMOTHERAPY**
- **UV-A combined with oral methoxsalen (PUVA)** is a photochemotherapeutic approach for selected patients. Candidates for PUVA therapy usually have moderate to severe, incapacitating psoriasis unresponsive to conventional topical and systemic therapies.

- **Systemic PUVA consists of** oral ingestion of a potent photosensitizer such as methoxsalen (8-methoxypsoralen) at a constant dose (0.6 to 0.8 mg/kg) and variable doses of ultraviolet A (UV-A) depending on patient skin type and history of previous response to UV radiation. **Two hours** after ingesting **psoralen**, the **patient is exposed to UV-A light.** **Photochemotherapy is performed 2 or 3 times a week.** Partial clearing occurs in most patients by the twenty-fifth treatment.

- **Another method** that may have less carcinogenic potential is to **topically deliver the photosensitizer (methoxsalen) to the skin by adding it to bath water (bath PUVA) instead of through systemic administration.**
Advantages of this approach include :

- Minimal risk of systemic effects,
- Overall reduction of PUVA dose to one-fourth of that required with conventional PUVA, and
- Reduction in the risk of nonmelanoma skin cancer.

■ COMBINATIONAL, ROTATIONAL, AND SEQUENTIAL THERAPY

- If monotherapy with a systemic agent does not provide optimal outcomes, combining systemic therapies with other modalities may enhance benefit. The dose of each agent may often be reduced, resulting in lower toxicity.
- Combinations include:
 - Acitretin + UV-B
 - Acitretin + photochemotherapy using UV-A light (PUVA)
 - Methotrexate + UV-B
 - PUVA + UV-B
 - Methotrexate + cyclosporine

- **EVALUATION OF THERAPEUTIC OUTCOMES**
- Patients should understand the general concepts of therapy and the importance of adherence.
- Monitoring for disease resolution and side effects is critical to a successful therapy.
- A positive response is noted with the normalization of involved areas of skin, as measured by reduced erythema and scaling, as well as reduction of plaque elevation.

- Achievement of efficacy by any therapeutic regimen requires days to weeks.
- Initial dramatic response may be achieved with some agents such as corticosteroids; however, sustained benefit with pharmacologically specific antipsoriatic therapy may require 2 to 8 weeks or longer for clinically meaningful response.



■ Ultraviolet C, short wave, or germicidal UVC
100 – 280 nm

■ Ultraviolet B, or medium wave UVB
280 – 315nm

Ultraviolet A, long wave, or black light UVA
315 – 400 nm

