CHAPTER

16

Diseases of the Skin

Q. Enumerate and define the terms used to describe skin lesions.

- *Primary skin lesions:* Primary lesions are those that occur de novo on a normal skin.

TABLE 16.1: Primary skin lesions

Term	Description	Examples
Macule	A small flat area of altered color <2 cm in diameter	Tinea versicolor, measles
Patch	Flat area of altered color >2 cm in diameter. This differs from a macule only in size.	Vitiligo
Papule	Solid lesions raised above the surface of the skin, generally <1 cm in size. Larger papules are called nodules.	Acne, warts
Plaque	A large (>1 cm), flat-topped, raised lesion.	Psoriasis
Vesicle	A small, fluid-filled lesion, <0.5 cm in diameter, raised above the surface of skin. Fluid is often visible, and the lesions are translucent.	Herpes simplex, chickenpox
Pustule	Similar to vesicle but filled with pus.	Folliculitis
Bulla	A fluid-filled, raised, often translucent lesion >0.5 cm in diameter.	Impetigo, pemphigus, pemphigoid, toxic epidermal necrolysis
Wheal	A raised, erythematous, edematous papule or plaque, usually due to short-lived vasodilatation and vasopermeability.	Urticaria
Telangiectasia	A dilated, superficial blood vessel.	Rosacea
Petechiae, purpura and ecchymosis	Petechiae are small pinhead-sized (1–3 mm) hemorrhages in the dermis and are not palpable. Purpura are similar to petechiae, but larger (3–10 mm) and may be palpable. Ecchymosis ('bruise') is bleeding into deeper structures and is more than 10 mm.	Thrombocytopenia

- *Secondary skin lesions:* These occur on pre-existing primary lesions and modify them or follow as a consequence of the primary lesions.

TABLE 16.2: Secondary skin lesions

Lichenification	Thickening of the skin characterized by accentuated skin-fold markings.
Scale	Excessive accumulation of stratum corneum.
Crust	Dried exudate of body fluids that may be yellow (serous crust) or red (hemorrhagic crust).
Erosion	Loss of epidermis without an associated loss of dermis.
Ulcer	Loss of epidermis and at least a portion of the underlying dermis.
Excoriation	Linear, angular erosions caused by scratching.
Atrophy	Loss of substance due to diminution of the epidermis, dermis or subcutaneous fat.
Scar	Replacement of normal structure by fibrous tissue.

Q. Discuss the etiology, clinical features, diagnosis and management of scabies.

Q. Norwegian or crusted scabies.

- Scabies is due to infestation of the skin by the mite Sarcoptes scabiei resulting in an intensely pruritic eruption.
- Crowded conditions increase the prevalence of scabies in the population.

Transmission

- It spreads from person to person by direct contact.
- It also spreads by wearing or handling contaminated clothing, or by sleeping in an unchanged bed recently occupied by an infested individual.

Etiologic Agent

- Sarcoptes scabiei, is a whitish-brown eight-legged mite which looks like a turtle. Its small size (0.4 × 0.3 mm) and burrowing habits prevent it from being observed by patients.
- The female mite burrows into the epidermis, lays eggs and dies in place after one to two months. Larvae hatch, leave the burrow for the surface, copulate, and continue the cycle.

Clinical Features

- The prominent clinical feature is itching. It is worse at night. Itching is due to delayed type IV hypersensitivity reaction to the mite, mite feces, and mite eggs.
- Small, erythematous papules, often excoriated may be seen. Miniature wheals, vesicles, pustules, and rarely bullae may also be present.
- The pathognomonic sign of scabies is burrow. It appears as a thin, grayish, reddish, or brownish line 2 to 15 mm long. Burrows may be absent or obscured by excoriation or secondary infection.
- The distribution of scabies usually involves web spaces of fingers, flexor aspects of the wrists, axillae, waist, genitalia, knees, buttocks and adjacent thighs. Head is spared except in very young children. In young children involvement of the palms, soles and head is common.
- Secondary infection with Staphylococcus or Streptococcus can occur.

Crusted or Norwegian Scabies

- Norwegian scabies (so called because it was first described in Norwegian patients with leprosy) occurs in AIDS, leprosy, lymphoma, and other conditions where cellular immunity is compromised. Normally, cellular immunity prevents multiplication of scabies mites and when it is reduced, there can be unrestricted multiplication of mites. It may also be seen in patients with Down syndrome.
- Norwegian scabies begins as erythematous patches which quickly develop a prominent scale. Any area may be affected, but the scalp, hands and feet are prominently involved. If untreated, it spreads extensively and may involve the entire body. Scales and crusts appear. The lesions are malodorous. Crusts and scales contain hundreds of thousands of mites. Nails may be discolored and dystrophic. Itching may be minimal or absent.

Diagnosis

- Diagnosis can be made from history and the distribution of lesions.
- Other members of the family are also affected.
- Presence of burrows.
- Diagnosis is confirmed by finding the mite or eggs on microscopic examination of scrapings from burrows or papules.

Treatment

Eradication of Mites

- Topical agents—permethrin cream (5%) is commonly used and is safe even in infants. Permethrin is applied to the entire body including head in infants and washed after 8 hours. A repeat application is required after 1 week. Other topical agents are benzyl benzoate, crotamiton, lindane, malathion, and sulfur in petrolatum.
- Ivermectin—this is an oral anthelmintic. A single dose of ivermectin 200 µg/kg with a repeat dose two weeks later is as effective as permethrin cream. This is very easy to administer and compliance is very good compared to topical agents. However, it is not recommended in pregnant or lactating women and safety has not been established in children with less than 15 kg weight.
- For Norwegian scabies, two doses of ivermectin two weeks apart should be given along with topical permethrin at the same time. Permethrin should be continued weekly until all scales and crusts are gone.

Control of Itching

- Antihistamines, such as diphenhydramine or cetirizine can be used. Severe itching can be controlled by topical or oral steroids.

Secondary Infection

- This is treated with appropriate systemic antibiotics.

Control of Transmission

- All family members should be treated at the same time to avoid reinfestation.
- Clothing and linen should be bagged for several days, machine washed, and then dried in a hot dryer to kill mites.
- Patients with Norwegian scabies should be isolated and treated.

Q. What are the common dermatophytoses? How do you diagnose and treat them?

- Dermatophytoses, also known as ringworm or tinea, are superficial fungal skin infections caused by dermatophytes.
- Dermatophytes belong to three genera: Microsporum, trichophyton, and epidermophyton. They can originate from the soil (geophilic), animals (zoophilic), or be confined to human skin (anthropophilic).
- These infections differ from candidiasis in that they are rarely if ever invasive.

Types

Depending on the site of infection, dermatophytoses are classified as follows:

- *Tinea corporis*—involvement of the body. Waist is a common site especially in obese women. Lesions are erythematous, annular and scaly, with a well-defined edge and often central clearing. They may be single or multiple and are usually asymmetrical.
- *Tinea capitis*—involvement of the scalp and associated hair. There may be alopecia of the area involved. A soft, boggy mass with loose, easily detachable hairs may be seen (kerion). Tinea capitis is common in children.
- *Tinea barbae*—involvement of the beard and moustache area. It presents with perifollicular pustules, erythema, crusting, seropurulent discharge and local loss of hairs.
- *Tinea cruris*—involvement of the groins. Features are similar to those of tinea corporis.
- *Tinea pedis* (athlete's foot)—involvement of the foot, usually interdigital spaces. It usually presents with fissuring, scaling or maceration in the interdigital areas or as scaly areas all over the soles.
- *Tinea unguium (onychomycosis)*—involvement of nails. It presents as white discolored nails and chalky crumbling nails. There may be subungual hyperkeratosis and partial separation of nail plate. Risk factors for onychomycosis are diabetes mellitus, nail trauma, occlusive footwear, and immunosuppression.

Clinical Features

- Distribution and morphology of lesions is as described above. Lesions are scaly, have slightly raised border with central clearing.
- Patients complain of itching in the lesions which is often worse at night.
- Secondary bacterial infection of the skin lesion may occur producing pustules.

Diagnosis

- Based on history and clinical findings.
- Potassium hydroxide (KOH 10%) mount of skin scrapings—fungi are seen as long, branched and septate hyphae.
- Skin or nail biopsy
- *Culture:* On Sabouraud's medium.
- *Wood's lamp examination:* Lesions of tinea versicolor and certain types of tinea capitis fluoresce when examined under Wood's lamp, emitting ultraviolet rays.

Treatment

- Topical preparations of clotrimazole, miconazole, terbinafine or ketoconazole can be applied twice daily for 4 weeks. Topical therapy is not effective for nail infections.
- For tinea capitis and barbae, ketoconazole shampoo can be used as additional therapy.
- For severe and unresponsive lesions, oral antifungal agents can be used. These are griseofulvin, ketoconazole, fluconazole, itraconazole and terbinafine. Duration of therapy is 4–8 weeks. For tinea unguium, duration of therapy is 3 months.

Q. Tinea versicolor (pityriasis versicolor).

- This is an opportunistic fungal infection caused by *Pityrosporum orbiculare (Malassezia furfur)*, which affects mainly the stratum corneum.

Clinical Features

- Lesions are discrete hypo- or hyperpigmented oval macules with fine scaling. Versicolor refers to the variety of colors of lesions.
- Lesions are most common on the upper trunk and extremities, and less common on the face. Seborrhoeic areas are the sites of predilection as sebum facilitates proliferation of *P. orbiculare*. Lesions may coalesce to form large patches.
- Most patients are asymptomatic, but some may complain of mild pruritus. It is mildly contagious, and other family members may be affected.

Diagnosis

- Diagnosis can be confirmed by examination of scrapings from lesions with 10 percent potassium hydroxide (KOH). Both hyphae and budding cells are seen in a pattern described as "spaghetti and meatballs".
- A Wood light examination reveals golden-white fluorescence.

Treatment

- Topical preparations of clotrimazole, miconazole, terbinafine or ketoconazole are effective.
- Selenium sulphide shampoo applied thrice weekly 10–30 minutes before bath for about 15 applications or ketoconazole 2% shampoo once daily for three days is also effective.
- Oral therapy is more convenient for patients with extensive disease. Two convenient regimens are a single 400-mg dose of ketoconazole or fluconazole 150 mg/wk for 2 to 4 wk.

Q. Enumerate various types of dermatitis (eczema). Discuss the clinical features and management of dermatitis.

- Dermatitis is superficial inflammation of the skin induced by external or internal factors. The terms 'eczema' and 'dermatitis' are synonymous.

General Features of Dermatitis

- Redness and swelling.
- Itching.
- Papules, vesicles and, rarely, large blisters.
- Oozing and crusting.
- Fissures and scratch marks.
- Pigmentation changes (hypo and hyper).
- Scaling.
- Lichenification, secondary to rubbing and scratching.

Classification and Types of Dermatitis

Exogenous
- Irritant contact dermatitis
- Allergic contact dermatitis
- Photoallergic dermatitis

Endogenous
- Atopic
- Seborrhoeic
- Discoid eczema
- Dyshydrotic (pompholyx)
- Asteatotic eczema
- Gravitational (stasis) dermatitis

- *Irritant contact dermatitis*—this occurs due to contact of skin with irritants. Dermatitis is due to direct damage caused by non-immune mechanisms as opposed to allergic contact dermatitis. Examples of irritants are cleansers, soaps, detergents, organic solvents, alkalies, and vegetables like chillies.
- *Allergic contact dermatitis*—this occurs due to delayed hypersensitivity reaction mediated by T-lymphocytes against certain chemicals (allergens) on coming in contact with the skin. Most contact allergens are haptens (incomplete allergens) which become complete allergens after combining with epidermal proteins. Examples are hair dye, shampoos, cement, etc.
- *Photoallergic dermatitis*—this occurs when the skin is exposed to sunlight following application of the chemicals to the skin of a sensitized person.
- *Atopic dermatitis*—this is due to genetic predisposition to form excessive IgE antibodies to antigens. There may be family history of atopy. Clinical features include a low threshold for itching, skin lichenification and raised serum IgE levels. In infants, the lesions are distributed on the face, scalp and front of the knees and legs. In children and adults, lesions are mainly in the cubital and popliteal fossae, sides of the neck, wrists and ankles.
- *Seborrheic dermatitis*—this is a chronic dermatitis characterized by greasy scales overlying erythematous patches or plaques. It mainly involves areas rich in sebaceous glands such as scalp, retroauricular and nasolabial folds, eyelids, trunks and axillae. It is probable due to overgrowth of malassezia furfur or its yeast form *Pityrosporum ovale,* which is normally present on the skin. The disorder is more common in AIDS due to increased susceptibility to yeast infections.
- *Discoid (nummular eczema)*—this is characterized by pruritic circular or oval lesions with closely set papulovesicles on an erythematous base. It is seen most often on the limbs of elderly males.
- *Dyshydrotic eczema (pompholyx)*—this is a type of vesicular eczema with chronic and recurrent lesions affecting palms, soles and sides of the fingers.
- *Asteatotic eczema*—this is seen in hospitalized elderly, often in the lower limbs. Dry skin, low humidity, over-washing and diuretics are contributory factors.
- *Gravitational (stasis) dermatitis*—this is seen in the lower limbs due to venous insufficiency.

Investigations of Dermatitis

- Patch tests—useful in suspected cases of allergic contact dermatitis.
- IgE levels—are useful in atopic dermatitis.
- Bacterial and viral swabs for microscopy and culture in suspected secondary infection.

General Management of Dermatitis

- Explanation and reassurance.
- Avoidance of contact with irritants.
- Avoidance of dryness by regular use of emollients.
- Topical corticosteroids.
- Seborrhoeic eczema is treated with antipityrosporal agents such as ketoconazole shampoo and creams, supplemented with weak corticosteroids.

Q. Contact dermatitis.

- Contact dermatitis (CD) is acute inflammation of the skin caused by irritants (irritant contact dermatitis) or allergens (allergic contact dermatitis).

Etiology

- Irritant contact dermatitis (ICD) accounts for 80% of all cases of contact dermatitis. It is caused by agents which directly cause irritation and inflammation of the skin. Immune system is not involved here. Agents include:
  - Chemicals (e.g. acids, alkalis, solvents, metal salts)
  - Soaps (e.g. abrasives, detergents)
  - Plants (e.g. parthenium, peppers)
  - Body fluids (e.g. urine, saliva)

- Allergic contact dermatitis (ACD) is a type IV cell-mediated hypersensitivity reaction to antigens. Some of the antigens triggering ACD are ragweed pollen, hair dye, cosmetics, poison ivy, latex rubber, etc.

Clinical Features

- ICD is more painful than pruritic. Skin changes include erythema, crusting, erosion, pustules, bullae, and edema.
- In ACD, the primary symptom is intense pruritus. Skin changes are same as those of ICD. Skin changes often occur at the site of contact with allergen, but later may spread due to scratching. Hands are commonly involved due to handling of allergens.

Diagnosis

- Clinical history and examination.
- Sometimes patch testing. Here, standard contact allergens are applied to the upper back using adhesive-mounted patches containing minute amounts of allergens.

Treatment

- Avoidance of allergens.
- Symptomatic treatment: Dressings for excoriation and ulceration, antihistamines for itching.
- Topical corticosteroids.

Q. Discuss the etiology, clinical features and management of psoriasis.

- Psoriasis is a chronic inflammatory disease of the skin, characterized by well-defined erythematous plaques with silvery scale.
- It is more common in European community and less common in African and Asian communities.
- It affects men and women equally. Although psoriasis can begin at any age, there seem to be two peaks in onset: One between ages 20 and 30 and another between 50 and 60.

Etiology

- Psoriasis is considered to be an autoimmune disease with a genetic basis. It has a strong genetic predilection in the form of polygenic autosomal dominant inheritance with variable penetrance. Certain genes and HLA antigens (Cw6, B13, B17) are implicated in psoriasis.
- Precipitating and aggravating factors include hormonal changes of puberty and pregnancy, infections, physical trauma (including sunlight), obesity, smoking, alcohol consumption and mental stress. Drugs like beta-blockers, antimalarials, NSAIDs, lithium, etc. are known to cause psoriasiform drug reactions and also to precipitate the disease.
- Patients with HIV and AIDS can have severe and resistant disease at a young age.

Pathology

There are two main abnormalities noted in psoriatic plaques:

- Inflammatory cell infiltrate in the skin.
- Hyperproliferation of keratinocytes with a grossly increased mitotic index.

Clinical Features

- Psoriasis is characterized by well demarcated plaques, which may vary from few millimeters to several centimeters in diameter. The lesions are red, with a silvery-white scale.
- Extensor aspects such as elbows, knees and lower back are commonly affected. Other sites of predilection include scalp, nails, flexures and palms.
- Nails may show pitting, onycholysis (separation of the nail from the nail bed), and subungual hyperkeratosis.
- Some patients may have seronegative arthritis (psoriatic arthropathy) involving spine and/or peripheral joints.

Investigations

- Diagnosis is made clinically.
- Rarely skin biopsy or scraping may be required to rule out other disorders.
- X-rays and MRI may be needed if there is arthritis.

Management

- Explanation and reassurance.

Topical Therapy

- *Anthralin*—it is a topical antiproliferative, anti-inflammatory agent. It can cause burning sensation of skin with pain and erythema. It can also cause brown staining of the skin.
- *Coal tar*—coal tar has anti-mitotic effects and is effective in the treatment of psoriasis. Coal tar bath followed by exposure to ultraviolet light is the method commonly used. Staining of clothes and development of allergic and irritant dermatitis are its side effects.
- *Calcipotriene*—this is a vitamin D agonist. It has cytostatic and cytotoxic effects on proliferating keratinocytes. It also suppresses the underlying inflammation. It reduces the thickness and scaling of the psoriatic plaque, but does not clear the plaque. It is applied once or twice daily. Calcipotriene has almost replaced anthralin and coal tar for topical therapy.
- *Corticosteroids*—these are useful for many sites, particularly the flexures where tar and dithranol may be too irritant. Main side effects are local skin atrophy. Psoriasis tends to return when steroids are stopped.

PUVA Therapy

- Psoralen along with ultraviolet A (PUVA) is very effective for treatment of psoriasis. Psoralens are natural photosensitisers found in plants. Psoralen is given orally and is distributed all over the body. It gets activated only in those sites that are exposed to UVA. PUVA is as effective as intensive dithranol therapy. It is given 2 to 5 times a week and clearance occurs in the majority within 8 weeks. Main concern is increased risk of skin cancers. NBUVB (Narrow-band UVB light) is equally effective without the side effects of psoralen like gastrointestinal upset, cataract formation, and carcinogenic effect. It can safely be given to children, pregnant and lactating females and even elderly.

Systemic Therapy

- *Methotrexate* is highly effective for psoriasis and is the drug of choice. It can be given as long as the disease remains active. It acts by suppressing the immune system.
- *Oral retinoids* such as acitretin, etretinate are also effective in some patients with psoriasis. Retinoids are teratogens, hence pregnancy should be avoided for at least 2 years following their use.
- *Cyclosporine* can be used to induce a clinical response but its use should be intermittent.
- Biological agents such as infliximab, etanercept, efaluzimab have varying degrees of activity against psoriasis. They are expensive and may be considered when other treatment agents have failed.

Q. Pityriasis rosea.

- Pityriasis rosea is a self-limited, inflammatory disease characterized by diffuse, scaling papules or plaques.
- The cause may be viral infection (human herpesviruses 6, 7, and 8). Drugs may cause a similar eruption.

Clinical Features

- Affects mainly children and young adults. It affects women more often.
- Characterized by sudden appearance of oval, papulosquamous, pink or salmon colored lesions on the trunk and proximal limbs. The eruption usually begins with a "herald" or "mother" patch, a single oval pink or salmon-colored lesion on the chest, neck, or back. It is 2 to 5 cm in diameter with cigarette paper-like scales at the edges.
- A few days or weeks later oval lesions similar to the herald patch, but smaller, appear on the trunk and proximal areas of the limbs. The long axes of these oval lesions tend to be arranged along the cleavage lines of the skin. This arrangement of lesions on the back parallel to ribs gives rise to "Christmas tree pattern".
- Mild to moderate pruritus may be present.
- The rash subsides within 6–8 weeks without significant consequences.
- Differential diagnosis includes secondary syphilis, psoriasis, lichen planus and drug reactions.

Treatment

- Generally requires no treatment.
- Topical or oral steroids and antihistamines may be required to relieve itching.
- Ultraviolet light B (UVB) is helpful to reduce post-inflammatory hypopigmentation.
- Erythromycin has shown benefit in some trials. Benefit is probably due to its anti-inflammatory and immune modulating effects.

Q. What is pemphigus? Write briefly about pemphigus vulgaris.

Q. Nikolsky's sign.

- Pemphigus is a group of rare, chronic, autoimmune blistering disease affecting skin and mucus membranes (Greek *pemphix* = bubble).
- There are three major types of pemphigus:
  - Pemphigus vulgaris.
  - Pemphigus foliaceus.
  - Paraneoplastic pemphigus.

Etiology

- It is an autoimmune disease characterized by the presence of IgG antibodies directed against desmoglein an adhesion molecule on the surface of keratinocytes. Blister formation occurs in the epidermis due to loss of cohesion between epidermal cells, a process known as acantholysis.
- It can also occur due to drugs such as penicillins, sulphonamides, captopril, piroxicam, and antiepileptics.

Clinical Features

Pemphigus Vulgaris

- Most common form of pemphigus ("vulgar" means "common").
- Blisters are flaccid, nonpruritic, and easily breakdown, leaving behind erosions. Any area of the skin can be affected.
- Mucus membrane of oral cavity is commonly involved. Blisters are often found in areas subjected to friction such as cheek mucosa, tongue, palate and lower lip. Pharynx and larynx may be affected leading to pain on eating, and hoarseness of voice.

Pemphigus Foliaceous

- Blisters are more superficial than pemphigus vulgaris, which easily rupture. Hence, erosions, rather than blisters, are the presenting feature.
- Lesions first appear on the face and scalp and later on the chest and back.

- There may be associated scaling, and crusting.
- Unlike pemphigus vulgaris, mucous membrane is not affected.

Paraneoplastic Pemphigus

- Associated with malignancies, such as non-Hodgkin's lymphoma, CLL, and thymoma. Both skin and mucous membrane are affected.

Diagnosis

- The characteristic sign is Nikolsky's sign. It is elicited by applying lateral pressure to normal-looking skin at the periphery of active lesions, causing a shearing away of the epidermis leading to formation of new blisters.
- Biopsy of skin lesions—it shows intraepithelial acantholysis without disruption of the basement membrane. Direct immunofluorescence shows deposits of IgG between epidermal cells.

Differential Diagnosis

- In case of predominant mucus membrane lesions, herpes simplex, aphthous ulcers, lichen planus, and erythema multiforme have to be ruled out. In case of widespread erosions, pyoderma, impetigo, bullous pemphigoid, and bullous drug eruptions should be ruled out.

Treatment

- Without treatment pemphigus has high morbidity and mortality.
- High-dose systemic corticosteroids (e.g. prednisone 1 mg/kg/day) are the mainstay of therapy. Mild pemphigus may be treated with local steroids.
- Azathioprine and cyclophosphamide are used as additional immunosuppressive agents. They reduce steroid requirement, decrease steroid side-effects and improve remission rate.
- Rituximab, alone or in combination with intravenous immunoglobulin (IVIG), is the treatment of choice in severe pemphigus refractory to above therapies.
- Silver sulphadiazine may be used to prevent secondary infection.

Q. Bullous pemphigoid or pemphigoid.

- Bullous pemphigoid is a subepidermal blistering disease usually seen in the elderly (>60 years of age). It is less aggressive than pemphigus vulgaris and usually not life-threatening.

Etiology

- It is an autoimmune disease characterized by linear deposits of IgG at the epidermal basement membrane. The antibodies are directed against hemidesmosomes which attach epithelial cells to the basement membrane). Hence there is a split between the epidermis and dermis. (Note that in pemphigus the split is within the epidermis.)
- Drug-induced bullous pemphigoid develops due to penicillamine, furosemide, captopril, and antibiotics such as penicillin and nalidixic acid.
- It can be associated with systemic malignancies.

Clinical Features

- Blisters are large and tense, arising on a normal or erythematous skin. They occur anywhere on the body but common in flexural areas, groin, and axillae.
- Mucous membranes are not involved.
- Blisters are associated with marked itching. They may contain hemorrhagic fluid.
- Nikolsky's sign is negative.
- Blisters heal without scarring.
- Some patients go into spontaneous remission.

Diagnosis

- Direct immunofluorescence shows linear deposits of IgG and complement at the epidermal basement membrane.

Treatment

- Systemic steroids (e.g. prednisolone, 1 mg/kg per day).
- Azathioprine or cyclophosphamide can be used as additional immunosuppressive and steroid sparing agents.

Q. Discuss the causes, clinical features, investigations and management of Stevens-Johnson syndrome.

Or

Q. Toxic epidermal necrolysis.

- Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe, idiosyncratic reactions, characterized by fever and mucocutaneous lesions that culminate in epidermal necrosis and sloughing.
- SJS and TEN are similar except for the amount of area involved. Involvement of <10% of body surface area is called SJS and >30% of body surface area is called TEN; involvement of 10 to 30% of body surface area is considered SJS/TEN overlap.

Causes

Drugs
- *Anti-gout agents:* Allopurinol
- *Antibiotics:* Sulfonamides (cotrimoxazole, sulfasalazine), penicillins, cephalosporins, flouroquinolones
- *Antipsychotics and antiepileptics:* Carbamazepine, phenytoin, valproate, lamotrigine, and phenobarbital
- *NSAIDs:* Ibuprofen, piroxicam

Infections
- *Mycoplasma pneumoniae*

Rare
- Vaccinations, systemic diseases, chemical exposure, herbal medicines, and foods

Clinical Features

Stevens-Johnson Syndrome

- This is less severe condition with involvement of less than 10 percent of the body surface.
- History of drug intake prior to the onset of rash.
- Prodrome of malaise and fever, followed by the onset of erythematous or purpuric macules and plaques.
- Lesions are symmetrically distributed, and start first on the face and thorax before spreading to other areas.
- Skin lesions progress to epidermal necrosis and sloughing.
- Target lesions may be present.
- Mucosal membranes (ocular, oral, and genital) are involved in most patients. Oral and esophageal involvement causes difficulty and pain while swallowing. Genitourinary involvement causes dysuria and difficulty to void. Bronchial epithelium may also slough, causing cough, dyspnea, pneumonia, pulmonary edema, and hypoxemia.
- Glomerulonephritis and hepatitis may develop.

Toxic Epidermal Necrolysis

- This is a more severe condition with involvement of more than 30 percent of the body surface area.
- Other features are same as SJS.

Investigations

- Anemia and neutropenia may be present.
- AST and ALT may be elevated.
- Skin biopsy may be required.

Differential Diagnosis

- Erythema multiforme.
- Viral exanthems.
- Drug rashes.
- Toxic shock syndrome.
- Exfoliative erythroderma (usually spares mucous membranes).
- Paraneoplastic pemphigus.

Management

- Treatment of underlying cause (e.g. withdrawal of causative agent).
- Maintenance of fluid and electrolyte balance.
- Antihistamines and local steroids are enough for mild cases.
- Silver-impregnated nanocrystalline gauze for topical wound care.
- Systemic corticosteroids are indicated in severe cases. Prednisolone, 1 to 3 mg/kg daily or an equivalent amount of other steroids can be used.
- IV immunoglobulin (1 gm/kg daily for three consecutive days) is also useful in severe cases of SJS and TEN.
- Sepsis is the major cause of death. Systemic antibiotics should be given at the first sign of wound infection.

Q. Erythema multiforme.

- Erythema multiforme is an acute inflammatory skin disease characterized by target or iris skin leisons.
- Earlier, erythema multiforme major was being equated with Stevens-Johnson syndrome. But now most authorities think that these two entities are different.

Etiology

- Majority of cases are caused by herpes simplex virus (HSV) infection (HSV-1 more so than HSV-2).
- Some cases are caused by drugs (sulfonamides, NSAIDs, and anticonvulsants), vaccines, other viral diseases (especially hepatitis C), and SLE.

Clinical Features

- Classic manifestation is target lesion, consisting of three concentric zones of color change. Center and periphery of the lesion is red and in between there is pale area. Such classic lesions are found in herpes simplex infection. They are most often found on the hands and feet. Wheals, vesicles, and bullae can also be seen.

Figure 16.1 Erythema multiforme

Differential Diagnosis

- Urticaria.
- Drug eruptions.
- Paraneoplastic pemphigus.

Treatment

- Withdrawal of offending agent.
- Treatment of infection.
- Systemic steroids in severe cases.

Q. Discuss the etiopathogenesis, clinical features and management of acne vulgaris.

- *Acne vulgaris* is a chronic skin condition involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland).
- Acne is seen in most teenagers. Peak severity is in the late teenage years but acne may persist into the third decade and beyond, particularly in females.

Etiopathogenesis

- Acne occurs through the interplay of 4 major factors: Increased sebum production, follicular plugging with sebum and keratinocytes, colonization of follicles by *Propionibacterium acnes,* and release of multiple inflammatory mediators.
- *Increased sebum production:* With the onset of puberty, sebaceous glands enlarge and sebum production increases. There is a clear relation between severity of acne and sebum production. In the complete absence of sebum, acne does not occur. Androgens are mainly responsible for increased sebum production.
- *Follicular plugging with sebum and keratinocytes:* Blockage of pilosebaceous duct due to retention of keratinous material and sebum leads to formation of small cysts, called *comedones.*
- Colonization and activity of bacteria (*Propionibacterium acnes*) within the comedones releases free fatty acids from sebum, causes inflammation within the cyst and rupture.
- Rupture of the cyst releases oily and keratinous debris leading to an inflammatory foreign body reaction in the skin.

Clinical Features

- The clinical hallmark of acne vulgaris is the comedone, which may be closed (whitehead) or open (blackhead).
- Closed comedones appear as 1–2 mm white papules. Open comedones have a large follicular orifice and are filled with oxidized, darkened, oily debris.
- Inflammatory papules, nodules and cysts occur and healing may lead to scarring.
- Lesions are maximum on the face, but may also occur on shoulders, upper chest and back.

Management

- Treatment of acne vulgaris is directed toward elimination of comedones by normalization of follicular keratinization, decreasing sebum production, decreasing the population of *P. acnes*, and decreasing inflammation.

Local Measures

- Enough for mild to moderate acne.
- Regular washing with soap and water.
- Topical keratolytic agents—retinoic acid, benzoyl peroxide, or salicylic acid. They alter the pattern of epidermal desquamation and prevent the formation of comedones.
- Topical antibacterial agents—azelaic acid, topical erythromycin, or clindamycin. They inhibit *Proprionobacterium acnes*.
- Incision and drainage of cysts.
- Intraleisonal injection of triamcinolone acetonide reduces inflammation and hastens the resolution of cysts.
- Dermabrasion and excision of scars to improve skin appearance.

Systemic Measures

- Useful in severe acne with prominent inflammatory component.
- Antibiotics—tetracycline (250–500 mg bid), or doxycycline (100 mg bid). These antibiotics have anti-inflammatory effect in addition to their antibacterial effect. Oral antibiotics should be given for at least 6 months. Other antibiotics such as amoxicillin, erythromycin, and trimethoprim/sulfamethoxazole are sometimes used.
- Systemic retinoids (isotretinoin) are useful in severe acne unresponsive to other therapies. Retinoids have significant adverse effects including teratogenicity.
- Estrogens (oral contraceptives) also improve acne in women.

Q. Miliaria (heat rash).

- The main cause of miliaria is obstruction of the eccrine sweat glands or ducts. This can be due to cutaneous debris or bacteria such as *Staphylococcus epidermidis* with its formation of biofilms.
- It occurs in hot and humid weather.

Clinical Features

- Lesions are small, superficial, red, thin-walled, discrete but closely aggregated vesicles, papules, pustules or vesicopustules. Itching and burning is usually present.
- Miliaria occurs most commonly on the covered areas of skin such as trunk and intertriginous areas. In hospitalized patients, it occurs commonly on the back.

Treatment

- Patient should keep cool and wear loose and light clothing.
- Local application of triamcinolone acetonide, or a mid-potency corticosteroid in a lotion or cream base.
- Antibiotics for secondary infections (clindamycin).
- Anticholinergic drugs may be helpful in severe cases (glycopyrrolate, 1 mg twice daily). They help by decreasing sweating.

Q. Warts.

- Warts are mucocutaneous manifestation of human papillomavirus (HPV) infection.
- Viral warts are extremely common and most people suffer from one or more at some point during their life. HPV spreads by direct or sexual contact.

Clinical Features

- Common warts (verruca vulgaris) have smooth surface initially, but as they enlarge, their surface becomes irregular and hyperkeratotic, producing the typical warty appearance. They are most common on the hands but may also be seen on the face, genitalia, arm and leg. They are usually multiple.
- Plane warts (verruca plana) are smooth, flat-top papules seen most commonly on the face and backs of hands.
- Plantar warts (verruca plantaris) have a rough surface, surrounded by a horny collar. Plantar warts may be painful and disabling.
- Other types of wart are mosaic warts (mosaic-like plaques of tightly packed individual warts), facial warts (often filiform), and genital warts, which may be papillomatous and protuberant.

Treatment

- Wait and watch—spontaneous regression occurs in two-thirds of warts within two years. However, it is better to treat to avoid the risk of spread.
- Warts can be destroyed by local application of liquid nitrogen, salicylic acid, CO_2 laser, bichloroacetic acid, or cantharidin. Surgical excision and electrocautery are other options.
- Bleomycin injection into warts has a high cure rate for plantar and common warts.
- Podophyllum resin and the immunomodulator imiquimod are useful in anogenital warts.

Q. Erythema nodosum.

- Erythema nodosum (EN) is a specific form of panniculitis (inflammation of subcutaneous fat) characterized by tender, red or violet, palpable, subcutaneous nodules.
- Most likely represents a delayed hypersensitivity reaction to antigens associated with the various infectious agents, drugs, and other diseases.

Causes

- Idiopathic (most common cause)
- Streptococcal pharyngitis (most common known cause)
- Tuberculosis
- Leprosy
- Other infections (HIV, syphilis, systemic fungal infections, yersiniosis)
- Sarcoidosis
- Inflammatory bowel disease
- SLE
- Behcet's disease
- Hodgkin lymphoma
- Pregnancy
- Drugs (oral contraceptives, sulfa drugs)

Clinical Features

- EN primarily affects people in their 20s and 30s but can occur at any age; women are more often affected.
- The lesions are deep nodules, 1–10 cm in diameter, red or violet in color and tender.
- They are most often located on the anterior surfaces of the legs below the knees (shin) but may rarely occur on the arms, trunk, and face.
- Fever, malaise, and arthralgia usually accompany the lesions.
- Lesions last about 6 weeks and heal without scarring.
- Recurrence may occur.

Diagnosis

- Diagnosis is mainly based on clinical features.
- WBC, ESR and CRP are elevated.
- Appropriate tests to identify the underlying cause (chest X-ray, montoux test, ANA, ASO titer, etc.).
- Biopsy may be required in atypical cases.

Treatment

- Usually self-limited.
- Underlying cause should be identified and treated.
- Pain, arthralgia and fever can be treated by NSAIDs.
- Potassium iodide solution, 5–15 drops orally three times daily, results in prompt involution in many cases. Exact mechanism of action of potassium iodide is unknown.
- Oral corticosteroids in severe, extensive disease unless contraindicated by associated infection.

Q. Vitiligo.

- Vitiligo is skin depigmentation due to selective destruction of skin melanocytes.

Etiology

- In vitiligo there are focal areas of melanocyte loss which is considered to be due to cell-mediated autoimmune attack. Some patients have antibodies to melanin. It may be associated with other autoimmune diseases such as diabetes, Addison's disease and pernicious anemia.
- Genetic factors may play a role; 20 to 30 percent of patients may have a family history of vitiligo.
- Extrinsic factors also may play a role. Trauma, certain chemicals and sunburn may precipitate the appearance of vitiligo.

Clinical Features

- Lesions may start at any age, but generally in early adolescence or adult life.
- Segmental vitiligo is restricted to one part of the body.

- Generalized vitiligo is characterized by many widespread macules, often symmetrical and frequently involves the hands, wrists, knees and neck as well as the area around the body orifices.
- The patches of depigmentation are sharply demarcated.
- Sensation in the depigmented patches is normal unlike leprosy.
- Course is static or slowly progressive. Some patients may experience spontaneous repigmentation.

Differential Diagnosis

- Postinflammatory hypopigmentation.
- Piebaldism (a rare autosomal dominant disorder; depigmented patches surrounded by hyperpigmented areas).
- Morphea (localized scleroderma).
- Leprosy (lesions are usually hypoesthetic).
- Lichen sclerosus.
- Pityriasis alba.
- Chemical leukoderma.
- Leukoderma due to melanoma.

Management

- *Corticosteroids:* Topical corticosteroids are the first choice for patients with limited disease. Topical preparations of fluticasone propionate or mometasone, once a day for four to six months has to be applied. Oral corticosteroids may be helpful in progressive disease.
- *Calcineurin inhibitors:* Topical calcineurin inhibitors (e.g. tacrolimus) are also effective.
- *Ultraviolet light:* Topical or oral psoralens plus ultraviolet A radiation (PUVA), or ultraviolet B (UVB) radiation (phototherapy) is used in patients with extensive vitiligo. A total of 75 to 150 treatments (e.g. three times/week for 6 to 12 months) may be necessary.
- *Surgery:* Split-skin grafts and blister roof grafts, can be used to cover vitiligo patches.
- *Depigmentation therapy:* If there is extensive vitiligo with only small areas of normal skin, these normal skin areas can be depigmented (by using hydroquinone) to make the skin look uniform.
- Patients should be advised to avoid excessive sun exposure and to use sunscreens to reduce the risk of skin cancer in the long run.
- Camouflage cosmetics may also be helpful to mask the patches.

Q. Melanocytic nevi (moles).

- Melanocytic nevi (moles) are localized benign proliferations of melanocytes. Moles are a usual feature of most human beings. They are used as identification marks.
- They probably occur due to abnormalities of the normal migratory pattern of the melanocytes during development.

Clinical Features

Congenital Nevi

- These are present at birth or appear shortly after.

Acquired Nevi

- These appear in early childhood, at adolescence, and during pregnancy or oestrogen therapy. They can be divided into 3 types based on the location of clumps of melanocytes.
  - *Junctional nevi:* These are present in the dermal-epidermal junction. They are common on the acral surfaces but may occur anywhere. They appear as flat, pigmented macules.
  - *Compound nevi:* These are present in the dermo-epidermal junction as well as dermis. They are often raised, and may be papillomatous.
  - *Dermal nevi:* These are present in the dermis only. They are typically flesh colored.

Significance of Moles

- Most moles are benign and do not cause any problems. Rarely there may be malignant transformation. Malignant change is most likely in large congenital melanocytic nevi.

Danger signs indicating malignant transformation of moles

- Itching
- Increase in size
- Change in color
- Change in shape
- Bleeding
- Irregular margin or surface
- Inflammation
- Ulceration

Management

- Most nevi do not require any treatment.
- Excision may be considered if malignancy is suspected or when they repeatedly become inflamed or traumatized or for cosmetic reasons.

Q. Alopecia (baldness).

- Alopecia refers to loss of hair from the body. It is a sign rather than a diagnosis.
- The hair cycle consists of three phases: The growth phase, which is called anagen, the resting phase, which is called catagen, and the shedding phase, which is the telogen phase. Different hairs will be at different phase at any given time.

- Anagen is long growing phase which lasts from 2 to 6 years. Catagen is a brief transitional phase where the hair follicle shrinks in size. Telogen is a short resting phase lasting 1 to 4 months. At the end of the resting phase, the hair falls out (exogen) and new hair starts growing in the follicle, beginning the cycle again.
- Alopecia can be broadly classified into scarring and non-scarring types. It can be localized or diffuse.
- Scarring alopecia refers to hair loss associated with fibrosis that replaces and often permanently destroys the hair follicle.
- Nonscarring alopecia refers to hair loss without permanent destruction of the hair follicle.

Causes of Alopecia

Scarring alopecia

- Herpes zoster
- Chemical or physical trauma
- Discoid lupus erythematosus
- Scleroderma
- Severe folliculitis
- Lichen planopilaris
- Dissecting cellulitis
- Tumors
- Radiotherapy
- Idiopathic

Nonscarring alopecia

- Androgenetic alopecia (most common cause)
- Tinea capitis
- Alopecia areata
- Traumatic (trichotillomania, traction)
- Syphilis
- Telogen effluvium
- Hypo- and hyperthyroidism
- Hypopituitarism
- Diabetes mellitus
- HIV
- Nutritional deficiency (e.g. iron)
- Liver disease
- Postpartum
- Drugs (anticancer drugs, antithyroid drugs, oral contraceptives, allopurinol, gentamicin, and levodopa).

Clinical Features

- Note the onset and duration of hair loss, whether hair shedding is increased, and whether hair loss is localized or diffuse. Hair loss can be local or diffuse depending on the cause. Both scalp and body hair loss are seen in alopecia universalis. Loss of up to 100 hairs per day is normal. More than this is significant.
- History of recent exposures to noxious agents (e.g. drugs, toxins, radiation) and stressors (e.g. surgery, chronic illness, fever, psychologic stressors) suggests toxic or stress-induced hair loss.
- History of weight gain, fatigue and cold intolerance suggests hypothyroidism. History of virilization in women (hirsutism, deepening of the voice, and increased libido) suggests adrenal disorder or polycystic ovary syndrome. History of gynecologic/obstetric complaints in women may suggest hormonal problems.
- A family history of hair loss should be recorded.
- Alopecia areata appears as sharply demarcated bald patches, with pathognomonic 'exclamation mark' hairs (broken-off hairs 3–4 mm long, which taper off towards the scalp). The hair usually regrows in small bald patches, but may be incomplete in larger patches.
- Androgenetic alopecia or male pattern baldness is physiological in men over 20 years old. Hair loss usually occurs in an M-shaped pattern (bitemporal recession and then crown involvement) in the frontal hair line. It also occurs in females, usually after menopause, but hair loss is often diffuse.
- Hair loss associated with pruritus, erythema, and scaling is seen in chronic cutaneous lupus and tinea capitis.
- Asymmetric, bizarre, irregular hair loss pattern is seen in trichotillomania.

Investigations

- Serum testosterone, DHEA.
- Iron, total iron binding capacity.
- Urea, creatinine, electrolytes, LFT.
- Thyroid function tests.
- ANA.
- HIV, VDRL and TPHA.
- Fungal stain in localized hair loss with scaling.
- Scalp biopsy, with direct immunofluorescence, if lichen planus or discoid lupus erythematosus is suspected.

Management

- Support and reassurance.
- Treatment of underlying cause.
- Alopecia areata sometimes responds to topical or intralesional corticosteroids such as triamcinolone.
- Systemic finasteride or topical 2% minoxidil solution are useful in severe androgenetic alopecia. In females, antiandrogen therapy such as cyproterone acetate can be used.
- Scalp reduction surgery and autologous hair transplantation are also options in irreversible alopecia.
- Wig may be useful for irreversible extensive alopecia.

Q. Discuss briefly the common skin malignancies.

Basal Cell Carcinoma (BCC) (Rodent Ulcer)

- This is the most common skin cancer. It arises from the basal layer of epidermis and its appendages.

- Both environmental and genetic factors contribute to the development of BCC. Chronic exposure to ultraviolet (UV) radiation in sunlight is the most important risk factor. Other risk factors are chronic arsenic exposure, therapeutic radiation, immunosuppression, and the basal cell nevus syndrome.
- It is common in Europeans and at least 3 times more common than squamous cell carcinoma.
- It is more common in men than in women probably due to more exposure to sun.
- Incidence increases with age.

Clinical Features

- Most BCCs occur on the face.
- Most common type is noduloulcerative form. The earliest lesion is a small papule, with fine telangiectatic vessels on the surface, which slowly enlarges. Central necrosis may occur, leaving an ulcer surrounded by a rolled pearly edge.
- The tumor invades locally but rarely metastasizes.
- The superficial (multifocal) variant is seen most often on the trunk; it appears as a slowly enlarging pink or brown scaly plaque.

Management

- Since metastasis is extremely rare, most BCCs can be treated by local destruction.
- Treatment options include surgery, cryotherapy, radiotherapy, photodynamic therapy or the topical immunostimulant imiquimod. Surgery is usually the first choice, as it allows histological assessment of the tumor and examination of tumor margins.

Squamous Cell Carcinoma (SCC)

- SCC is the second most common skin cancer after BCC.
- Risk factors for SCC are similar to BCC. Additional risk factors are chronic cutaneous ulcer, genetic disorders such as dystrophic epidermolysis bullosa and xeroderma pigmentosum, human papilloma virus infection, and smoking.

Clinical Features

- SCC arises most commonly in areas frequently exposed to the sun, such as the head and neck (most common site), dorsum of the hands and forearms, and legs.
- Varying clinical presentations include nodules, plaques, infiltrating tumors and ulcers.
- Histological grade varies from well-differentiated to anaplastic. SCCs of the lip behave more aggressively and show a greater frequency of metastasis.

Management

- Surgical excision is the preferred option because of the definite risk of metastasis.
- Other options are cryotherapy, electrosurgery (i.e. curettage and electrodessication), topical treatment (5-fluorouracil, or imiquimod) and radiotherapy.

Malignant Melanoma

- Incidence of malignant melanoma has increased in recent decades. There is no effective treatment for metastatic melanoma and hence, the main focus is on primary prevention and early detection.
- Malignant melanoma has very poor prognosis with a case fatality rate of approximately 20–25%.
- The main risk factors for melanoma are ultraviolet rays exposure, pale skin, melanocytic naevi, immunosuppression, and family history of melanoma. About 30–50% of melanomas develop in a pre-existing melanocytic naevus. Development of any danger sign in a naevus should raise the suspicion of malignant transformation.

Clinical Features

- *Superficial spreading:* This is characterized by superficial and radially expanding, pigmented macule or plaque. Its margin is usually irregular.
- *Lentigo maligna:* This is the *in situ* phase of superficial spreading melanoma. It occurs most often on the exposed skin of the elderly. Lentigo maligna may have been present for many years before invasive melanoma develops from it.
- *Nodular:* Appears as a pigmented nodule.
- *Acral lentiginous:* It occurs on the palms and soles.
- In amelanotic melanomas, pigmentation is minimal or absent.
- Subungual melanomas present as painless, expanding areas of pigmentation under a nail.
- *Clinical stages of malignant melanoma:*
  - Stage I—primary lesion only
  - Stage II—involvement of regional lymph nodes
  - Stage III—distant metastases (nodal or visceral).

Management

- Surgical excision is the treatment choice. Palpable local nodes in stage II patients should be removed by block dissection.
- Chemotherapy is rarely curative but can be palliative in stage III disease or earlier.
- Alpha-interferon may reduce recurrences in patients with high-risk melanomas.

Q. Skin manifestations of internal disease.

- Many systemic diseases manifest as skin diseases which can serve as a clue to systemic disease. The type of lesion typically relates to a specific disease or type of disease.

TABLE 16.3: Skin manifestations of internal disease

- ***Erythema nodosum:*** TB, leprosy, syphilis, sarcoidosis, inflammatory bowel disease, SLE.
- ***Acanthosis nigricans:*** Internal malignancy, insulin resistance.
- ***Pyoderma gangrenosum:*** Inflammatory bowel disease.
- ***Hyperpigmentation:*** Hemochromatosis, Addison disease, ectopic ACTH syndrome, vitamin B_{12} deficiency, pellagra.
- ***Hypopigmentation:*** Oculocutaneous albinism, Chediak-Higashi syndrome, phenylketonuria, systemic sclerosis (scleroderma), leprosy, tuberous sclerosis.
- ***Xanthomas and xanthelasma:*** Elevated serum triglycerides.
- ***Acanthosis nigricans, necrobiosis lipoidica, and scleredema:*** Diabetes mellitus.
- ***Thick and dry skin:*** Hypothyroidism.
- ***Striae and skin fragility:*** Cushing disease.
- ***Skin ulcers:*** Vasculitis, sickle cell anemia, cryoglobulinemia, diabetes mellitus.
- ***Vesicles/bullae:*** Paraneoplastic pemphigus, porphyrias.
- ***Purpura:*** Thrombocytopenia, clotting factor defects, Ehlers-Danlos syndrome, scurvy, DIC, APLA, thrombotic thrombocytopenic purpura, cholesterol and fat emboli, systemic vasculitis, acute meningococcemia.
- ***Alopecia:*** SLE, secondary syphilis, hypothyroidism, hyperthyroidism, deficiencies of protein, biotin, zinc, and iron.
- ***Urticaria:*** Urticarial vasculitis, hepatitis B or C infection, serum sickness.
- ***Acneiform eruptions:*** Cushing's disease, congenital adrenal hyperplasia, polycystic ovary syndrome.
- ***Telangiectasias:*** Carcinoid syndrome, ataxia-telangiectasia, hereditary hemorrhagic telangiectasia.
- ***Spider angioma:*** Cirrhosis.
- ***Pruritus:*** Occult cancer, often lymphoma.