Dermatology Summary & Notes

- Skin layers
- Terms:
- Primary lesion:
- Secondary lesion:

Psoriasis

- Genetically determined inflammatory systemic autoimmune disease mediated by the dysregulation of **T-helper lymphocytes** (Th1/Th17).

- **Pathophysiology**: plaques of psoriasis are highly infiltrated with **CD3+ T-cells and CD11c+ dendritic** cells → produce pro-inflammatory cytokines including TNF-α, INF-γ and IL-17, IL-22/23/12/1β → activate keratinocytes and other skin cells → hyperkeratosis + parakeratosis (3-5 days turnover, usually 23 days) → defective keratinocytes that are poorly adherent → reveals BVs when scraped off (Auspitz sign) // In addition, neutrophils infiltrate the epidermis leading to swelling, erythema, and inflammation forming sterile pustules.

- **Psoriatic nails:** subungual hyperkeratosis → onycholysis, pitting (losing parakeratotic cells), Beau's lines, splinter hemorrhage

- Plaques are well-defined, raised, with silvery scaling / erythema / pustules

- If pustules develop around the periphery of chronic plaques of psoriasis or sheets of monomorphic pustules appear more generally in the context of psoriasis, this is a sign of unstable disease – a dermatological emergency.

- **Typical patient:** median age is 28Y, FHx, trigger (infection, alcohol, drugs, trauma or childbirth), at site of skin trauma (Koebner's phenomenon), can improve in the sun, mildly itchy, and arthropathy (1/3) // in areas of minor trauma (elbows and knees) and scalp // annular

  1- **Guttate psoriasis:** widespread small plaques on trunk and limbs, adolescents with a preceding sore throat (group A β-haemolytic streptococcus)

  2- **Palmo-plantar pustular psoriasis:** multiple sterile pustules on the palms and soles // smokers // appear as yellow monomorphic lesions that later on turn brown.

  3- **Acute generalised pustular psoriasis:** uncommon, severe, skin is erythematous and tender with sheets of monomorphic sterile pustules developing acutely // precipitated by taking systemic steroids, or using potent topical steroids // pustules at the peripheral margin

4- **Flexural psoriasis:** well-defined erythematous areas in the axillae, groin, natal cleft, beneath the breasts and in skin folds. Scaling is minimal or absent

5- **Erythrodermic psoriasis:** life threatening condition with erythema affecting nearly all of the skin // scaling of psoriasis is absent // Triggers include withdrawal of systemic steroids, infections, excessive alcohol intake, antimalarials, lithium and low calcium.

- **Psoriatic arthritis:**
  - The distal interphalangeal (DIP) joints are most commonly affected (metacarpophalangeal joints are spared) → distinguish PA from rheumatoid arthritis.
  - The arthropathy is usually asymmetrical oligoarthritis.
  - There is male predominance in the spondylitic form and female predominance in the rheumatoid form.
  - Arthritis mutilans is a rarer form where there is considerable bone resorption leading to 'telescoping' of the fingers

Five types of psoriatic arthropathy:

- *DIP joints* (80% have associated nail changes)
- *Asymmetrical oligoarticular* arthropathy (hands and feet, 'sausage-shaped' digits)
- *Symmetrical polyarthritis* (hands, wrists, ankles, 'rheumatoid pattern')
- *Arthritis mutilans* (digits, resorption of bone, resultant 'telescoping' of redundant skin)
- *Spondylitis* (asymmetrical vertebral involvement, male preponderance) HLA-B27 associated

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Psoriasis Management

- Management depends on the severity (PASI) and impact on life quality (DALQI)
- Patients may start initially using simple topical therapy and/or ultraviolet treatment before switching to the stronger systemic agents if their disease is poorly controlled. Biological agents can be considered first-line if affordable or when 2-3 systemic treatments failed.
- Scalp psoriasis (50%) → products are rubbed into the affected scalp skin and left on overnight (combinations of tar, salicylic acid, sulphur and emollient are used).

Management of psoriasis

Type of psoriasis	Standard therapy	Alternatives
Localised stable plaques	Tar preparations Vitamin D analogues Salicylic acid preparations Topical steroids	Dithranol/ ichthammol TL01 (UVB)
Extensive stable plaques	TL01 (UVB) PUVA Acitretin PUVA + Acitretin	Methotrexate Ciclosporin A Hydroxyurea Biological agents
Widespread small plaque	TL01 (UVB)	Steroid with LPC
Guttate psoriasis	Moderate-potency topical steroids TL01 (UVB)	Steroid with LPC
Facial psoriasis	Mild-moderate potency topical steroid	Steroid with LPC
Flexural psoriasis	Mild-moderate potency topical steroid + antifungal	Methotrexate
Pustular psoriasis of hands and feet	Moderate-potency topical steroids Potent topical steroid + propylene glycol +/− occlusion	Acitretin Methotrexate Hand and foot PUVA
Acute erythrodermic, unstable/ generalised pustular psoriasis	In-patient management Short-term mild topical steroids	Methotrexate Ciclosporin Biological therapy

- **<u>Phototherapy</u>**: reduces the antigen-presenting capacity of dendritic cells, induces apoptosis of immune cells and inhibits synthesis and release of pro-inflammatory cytokines + reduction in dermal inflammation and epidermal cell turnover.
  - ***C/i:*** a history of previous skin malignancy and photosensitive diseases such as lupus, porphyria, albinism and xeroderma pigmentosum.
  - ***Risks***: risk of cutaneous malignancy, premature ageing of the skin and multiple lentigenes can result.
  - *UVB phototherapy* has advantages over PUVA as it can be used in children.

- Psoriasis is a T-cell mediated disease and cytokines such as tumor necrosis factor alpha (TNF-α) and interferon gamma (INF-γ) play a role.

- **<u>Biological agents:</u>** expensive and can result in chronic immunosuppression leading to fatal infections or tumors

Topical			
Emollients	Barrier to cutaneous fluid loss, relieve itching and help replace water and lipids and therefore restore the barrier function of dry skin.		
Coal tar	Keratoplastic (normalises keratinocyte growth patterns), antipruritic (reduces itch) and antimicrobial.		For stable chronic plaques
Ichthammol (ammonium bituminosulfonate)	For unstable or inflamed psoriasis.		
Calcipotriol and tacalcitol	Vitamin D analogues that are calmodulin inhibitors	For mild or moderate plaque psoriasis	Risk of hypercalcemia
Corticosteroids	Mild/moderate topical steroids are safe to use on the face and flexural skin, and in erythrodermic disease. Moderate or potent preparations can be used on chronic stable plaques on the body.		
Phototherapy			
UVB	Short wavelength	Administered three times weekly, (20–30 treatments)	For widespread psoriasis
UVA	Long wavelength	Given in combination with oral or topical psoralen (PUVA) twice weekly (20–30 treatments)	For recalcitrant widespread thick plaque psoriasis.
Systemic			
Methotrexate	Reduces epidermal cell turnover by the inhibition of folic acid synthesis	▪ Hepatotoxic, teratogenic, myelosuppression, renal impairment. ▪ Teratogenic (3 months)	For unstable erythrodermic/pustular psoriasis in the acute setting as well as maintenance for chronic plaque disease and psoriatic arthritis.
Acitretin	A vitamin A derivative A synergistic effect has been observed with concomitant PUVA, when patients require less UV exposure to clear their psoriasis.	▪ Drying of the mucous membranes, crusting in the nose, itching, thinning of the hair, and erythema of the palms and nail folds. ▪ Hepatotoxicity < raised lipid concentrations. ▪ Teratogenic (3 years)	Chronic plaque psoriasis

Cyclosporin A	Immunosuppressant widely used following organ transplantation.	Renal impairment and hypertension	Inflammatory types
Mycophenolate mofetil (MMF)	Selectively inhibits activated lymphocytes	Gastrointestinal upset and myelosuppression, hematological malignancies and opportunistic infections	Usually used as a second line systemic agent for treating psoriasis and psoriatic arthritis
Biological Therapy			
Etanercept	Anti-sTNF	(For all): risk of infections, particularly latent TB and hepatitis B and septicaemia, gastrointestinal symptoms, hypersensitivity and injection site reactions, blood disorders and a lupus-like antibody driven syndrome.	
Infliximab	Anti-TNF human-murine monoclonal antibody for the treatment of severe psoriasis/psoriatic arthritis.	+ Chest pain, dyspnoea, arrhythmias, demyelinating disorders, sleep disturbance, skin pigmentation, gastrointestinal haemorrhage, seizures andtransversemyelitishavebeenreported, amongothers.	
Adalimumab	Human anti-TNF monoclonal antibody used to treat severe psoriasis and psoriatic arthritis	+ Stomatitis, cough, paraesthesia, rash/pruritus, arrhythmias, chest pain, flushing, flu-like symptoms, sleep disturbance, electrolyte disturbances, alopecia and demyelinating disorders among others.	
Ustekinumab	Human monoclonal antibody that targets the p40 subunit of interleukin-12 (IL-12) and IL-23, which prevents them from binding to T-cells and therefore impairs the inflammatory cascade in psoriasis	+ Allergic reactions (urticarial, angiooedema, difficulty breathing), infections, mouth ulcers, haematuria, gastrointestinal symptoms, cough, chest pains, seizures and visual disturbance.	

Eczema

- Genetic predisposition is common in patients with atopic dermatitis.
- Filaggrin gene defects lead to impaired skin barrier function
- There is an *abnormality* in the balance of T-helper lymphocytes (Th-2 cells > Th-1 and Th-17; whereas psoriasis is the opposite)
- **Clinical features**:
  - ⇨ Acute eruptions: erythema, vesicular/bullous lesions and exudates. Secondary bacterial infection (staphylococcus and streptococcus) heralded by golden crusting may exacerbate acute eczema.
  - ⇨ Chronic eczema: increased scaling, xerosis (dryness) and lichenification (thickening of the skin where surface markings become more prominent and linear).
  - ⇨ It is characteristically itchy and subsequent scratching may also modify the clinical appearance leading to excoriation marks, loss of skin surface, secondary infection, exudates and ultimately marked lichenification.
  - ⇨ Inflammation in the skin can result in disruption of skin pigmentation causing post-inflammatory hyper/ hypopigmentation.
- **Histopathology**:
  - ⇨ Edema in the epidermis leading to spongiosis (separation of keratinocytes) and vesicle formation.
  - ⇨ The epidermis is hyperkeratotic (thickened) with dilated blood vessels and an inflammatory (eosinophil) cell infiltrate in the dermis.
  - ⇨ Stratum corneum is usually scraped off due to scratching.
- **Investigations**:
  - ⇨ Skin swabs should be taken from the skin if secondary bacterial or viral infection is suspected.
  - ⇨ Nasal swabs should be performed in older children and adults with persistent facial eczema to check for nasal Staphylococcus carriage.
  - ⇨ If a secondary fungal infection is suspected then scrapings or brushings can be taken for mycological analysis.
  - ⇨ Beware unilateral eczema of the areola, which could be Paget's disease of the nipple
  - ⇨ Varicose eczema (leg ulcer) patients should have their ABPI (ankle brachial pressure index) measured before compressing their legs with bandages (c/I when arterial).
- **Types**:
  - ⇨ Eczema is classified broadly into endogenous (constitutional) and exogenous (induced by an external factor).

Endogenous (constitutional) eczema	Exogenous (contact) eczema	Secondary changes
Atopic	1) Irritant	Lichen simplex
Discoid	2) Allergic	Asteatotic
Pompholyx	3) Photodermatitis	Pompholyx
Varicose		Infection
Seborrhoeic (discussed later)		

Endogenous eczema	
Atopic dermatitis	▪ Typically presents in infancy or early childhood, initially with facial (Figure 4.3) and subsequently flexural limb involvement. It is intensely itchy. ▪ Pattern is one of flare-ups followed by remissions. Exacerbations being associated with inter-current infections, stress, teething, and food allergies. ▪ In older children or adults, AD may become chronic and widespread and is frequently exacerbated by stress. ▪ 90% of the patients spontaneously remit by puberty.
Pityriasis alba	▪ Pale patches of hypopigmentation develop on the face of children
Juvenile plantar dermatosis	▪ Dry cracked skin on the forefoot in children
Eczema herpeticum	▪ Herpes simplex viral infection superimposed onto the skin affected by eczema. ▪ Multiple small 'punched-out' looking ulcers, especially around the neck and eyes. ▪ Early intervention with systemic acyclovir
Lichen simplex	▪ Localized area of lichenification produced by rubbing
Asteatotic eczema	▪ In older people with dry skin, particularly on the lower legs. The pattern on the skin resembles a dry riverbed or 'crazy-paving'
Discoid eczema	▪ Intensely pruritic coin shaped lesions most commonly on the limbs. ▪ Lesions may be vesicular and are frequently colonized by Staphylococcus aureus. ▪ Males are more frequently affected than females.
Pompholyx eczema	▪ Itching vesicles on the fingers, palms and soles. Blisters are small, firm, intensely itchy and occasionally painful. The condition is more common in patients with nickel allergy.
Venous (stasis) eczema	▪ Occurs on the lower legs of patients with venous insufficiency. ▪ In the early stages, there is brown hemosiderin pigmentation of the skin, especially on the medial ankle, but as the disease progresses skin changes can extend up to the knee. ▪ Patients typically have peripheral edema, and ulceration may result. The mainstay of management is compression
Exogenous eczema	
Contact dermatitis	An acute allergic reaction tends to be intensely itchy and results in erythema, oedema and vesicles. The more chronic lesions are often lichenified Box 4.1 **Common contact allergens** • Nickel/cobalt (jewellery, clothing, wristwatch, scissors and cooking utensils). • Potassium dichromate (chemical used to tan leather; Figure 4.17). • Perfumes, myroxylon pereirae (balsam of Peru, fragrances; Figure 4.20). • Formaldehyde, parabens, quaternium, methylchloroisothiazolinone, methylisothiazolinone (MCI/MI) (preservatives). • PPD (permanent hair dyes, temporary tattoos and textiles; Figure 4.22). • Ethylenediamine (adhesives and medications). • Chromates (cement and leather). • Mercaptobenzothiazole, thiurams (rubber gloves and shoes). • Neomycin, benzocaine (medicated ointments; Figure 4.21). • Lanolin (wool alcohol, emollients and mediated ointments).
1. Allergic contact dermatitis	▪ Previous exposure to the substance concerned. ▪ 48–96 h between contact and the development of changes in the skin. ▪ Allergic dermatitis results from a type IV delayed hypersensitivity reaction in the skin
2. Irritant contact dermatitis	▪ No predictable time interval between contact and the appearance of the rash. ▪ Previous contact is not required
Photodermatitis	▪ Interaction of light and chemicals absorbed by the skin. It can result from (a) drugs taken internally, such as sulphonamides, phenothiazines, tetracycline and voriconazole or (b) substances in contact with the skin, such as topical antihistamines, local anaesthetics, cosmetics and antibacterials ▪ Phytophotodermatitis is due to contact with plant material, often containing forms of psoralens (poisonoak,commonrue,lime juice and celery) and sunlight causing an allergic contact dermatitis ▪ Chronic actinic dermatitis (chronic eczema on sun-exposed skin)
Occupational dermatitis	▪ Contact urticaria is an immediate-type sensitivity reaction that can occur to certain food proteins and latex glove allergy.

Eczema Management

- Treatments usually start with simple emollients and mild topical steroids but with increasingly recalcitrant disease stronger therapies such as systemic immunosuppressants may be needed.

1- **Emollients** help to restore barrier function and reduce itching.

2- **Aqueous cream** and emulsifying ointments are useful soap substitutes. Antibacterial moisturizing washes have been shown to be very useful in those prone to infected eczema.

3- **Topical steroids** continue to be the mainstay of treatment for active eczema. They should be used twice daily on the affected skin.
   - ⇨ Very low potency steroids such as hydrocortisone may be purchased over the counter and used to treat mild eczema. For moderate to severe disease, the current approach is to prescribe potent topical steroids (mometasone, betamethasone and fluocinolone acetonide) for short periods followed by steroid 'holidays' rather than using daily low potency steroids, which rarely clear the eczema
   - ⇨ Lower potency topical steroids should be used on the face and groin areas (hydrocortisone and clobetasone butyrate).

4- **Immunomodulators** to control mild eczema Tacrolimus and pimecrolimus are applied twice daily to the affected skin.
   - ⇨ Their use should be limited to those who have failed to respond adequately to first-line treatment (topical steroids)
   - ⇨ It is recommended that their use be for short periods rather than continuous use.

5- **Occlusion:** Covering topical therapy with bandages, body suits, 'wet-wraps' and dressings can be very helpful in the management of chronic eczema
   - ⇨ Prior to occlusion, the practitioner should ensure the eczema is not infected
   - ⇨ The potency of topical steroids is enhanced 100-fold by occlusion; therefore, only very low potency steroids should be used under occlusion.

6- **Antibiotics** to treat infected eczema; they may be given topically or systemically.
   - ⇨ Topical antibiotics used include fusidic acid, silver sulfadiazine, polymyxins, neomycin and mupirocin. It is recommended that topical antibiotics should be used for a maximum of 2weeks continuously to try to reduce the risk of developing resistant bacteria.

7- **Phototherapy**. Light treatment with narrow-band UVB (TL-01) or PUVA (psoralen with UVA) can be highly effective for generalized eczema

8- **Systemic therapy**: severe widespread disease not controlled with topical therapy may require systemic immunosuppressants. Azathioprine, ciclosporin, mycophenolate mofetil and methotrexate can be used for long-term management.

Pruritis

- Pruritus may be localized/generalized and may be associated with skin changes or with normal skin.

Abnormal Skin	
Generalized pruritis	Wide spread eczema/psoriasis, scabies, allergic drug eruptions (antibiotics and anticonvulsants), graft versus host disease (following bone marrow transplantation), pre-bullous pemphigoid (dermatitic eruption before blisters appear), cutaneous lymphoma (may start over the buttocks as more localized disease), parasitophobia (belief that there are parasites under the skin, excoriations are seen), body lice or pubic lice (body lice live in the clothing), viral exanthems (rashes associated with systemic viral illness), urticaria (generalized 'hives') and xerosis (dry skin, especially in the elderly).
Localized pruritis	Eczema, psoriasis, lichen planus (flat-topped itchy papules of unknown cause), dermatitis herpetiformis (gluten allergy with rash, characteristically on elbows and buttocks), insect bites/stings, (nodular prurigo may develop after insect bites and is characterized by persistent itching, lichenified papules and nodules), head lice, contact dermatitis, polymorphic light eruption (an acute allergy to sunlight on sun-exposed skin), urticaria or angioedema ('hives' with swelling, especially of the face), fungal infections (particularly tinea pedis of the feet), pruritus ani (perianal itching, a common condition that may result from anal leakage, skin tags, hemorrhoids, thread worms, excessive washing, the use of medicated wipes or allergy to hemorrhoids creams containing Balsam of Peru) and pruritus vulvae (intense itching may result from lichen sclerosus et atrophicus, Candida infections or eczema).
Normal skin	
Generalized pruritus and normal skin as itching may be the first symptom of a systemic disorder such as Hodgkin's disease, chronic renal failure and diabetes, or may be a side effect of mediation.	• Endocrine – diabetes, myxoedema, hyperthyroidism, menopause and pregnancy. • Metabolic – hepatic failure, biliary obstruction and chronic renal failure. • Haematological – polycythaemia and iron deficiency anaemia. • Malignancy – lymphoma, leukaemia, myeloma and carcino-matosis. • Neurological/psychological – neuropathic pruritus, multiple sclerosis and anxiety. • Infection – filariasis, hookworm and HIV. • Drugs – opioids.

Pruritis Management

- Topical and systemic antihistamines can provide relief from itching. Cetirizine, levocetirizine, desloratadine and fexofenadine during the day and hydroxyzine at night.

Scabies (Sarcoptes scabiei)

- Intense itching that characteristically keeps those affected awake at night.
- Transmission occurs because of close personal contact (at least 15 min of skin-to-skin contact).
- The first symptoms of itching occur 2 weeks later when the immune system reacts to the proteins in the mites, eggs and faeces in the skin.
- **Dx**: burrows can be seen, especially in the finger-web spaces and on the genitals // widespread papular rash.
- **Features in children**: erythematous cutaneous papules and nodules in the axillae and on the soles of the feet. It is not unusual for the lesions to blister. **Classic burrows are rarely seen in this age group.**
- **Crusted scabies:** Patients are usually immunosuppressed or elderly and do not complain of itching. Patients have a crusted fine scaling on the skin which is superficial with **very little erythema** (unlike psoriasis and eczema)
- **Management:**
  - ⇨ First-line treatment for scabies is 5% **permethrin**
  - ⇨ Second line is 0.5% **malathion** lotion left on overnight
  - ⇨ **Ivermectin**, can be given to immunocompromised patients and those with crusted scabies (avoid in patients <15 kg and in pregnancy).
  - ⇨ Pruritus can be alleviated with **menthol** in aqueous cream

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Hair Lice

- Lice are transmitted by head-to-head contact, and on combs, brushes and hats. Girls are more commonly affected than boys; this is thought to be due to their close contact with others during play. Mild itching may be the only symptom of head lice.
- **Tx**: Only treat individuals with live lice visible on the scalp. Fine-toothed nit-combs can be used to comb out lice and eggs over a basin (‘bug-busting’). First-line treatment is **permethrin** 1–5% crème rinse applied to dry hair and left on overnight. This should be repeated after 7days.

Body Lice

- Body lice are the vectors of several human pathogens including Bartonella quintana (agent of **trench fever, bacillary angiomatosis and endocarditis**) and Rickettsia prowazekii (agent of **typhus**).
- Widespread papular eruption with excoriations
- **Tx**: Treat the skin reactions with a moderately potent topical steroid, plus topical antibiotic if secondarily infected with bacteria.

Pubic Lice

- On the skin such as the pubic, axillary and eyelash areas. The so-called crab lice are slow-moving and are spread by close personal contact.

- **Tx:** Use topical permethrin 5% cream or 0.5% malathion to the skin from the neck downwards, left on overnight.
- If the eyelashes are involved use petrolatum only, as insecticides can damage the eyes.

Urticaria and Angioedema

- Urticaria describes transient pruritic swellings of the skin, often referred to as wheals, hives or nettle rash by the patient. Urticaria results from oedema in the superficial layers of the skin causing well-demarcated erythematous lesions. It may be associated with allergic reactions, infections or physical stimuli, but in most patients no cause can be found.
- Urticaria can be chronic (>6 weeks) or acute // ordinary, contact allergic, cholinergic, physical, or urticarial vasculitis.

Urticaria	Angio-edema
Itchy spots or rashes	Painful, well-demarcated
<24hrs	May last hours or days.
Resolve leaving no marks on the skin.	Resolves with bruising
	▪ Laryngeal oedema is the most serious complication and can be life threatening. Hereditary angio-oedema is a rare form with recurrent severe episodes of subcutaneous oedema, swelling of the mucous membranes and systemic symptoms. Can be caused by a deficiency in C1 (esterase) inhibitor. Serum complement C4 levels are low following attacks. ▪ ACEI, NSAIDs, bupropion, statins or PPI may be the cause ▪ **Tx**: Danazol can be used to reduce the frequency and severity of attacks and fresh frozen plasma can be used before elective surgery.

Cholinergic urticaria	▪ Aged 10–30 years ▪ Urticaria following a warm shower/bath, or after exercise. Patients report erythema and burning pruritus followed by extensive urticaria. ▪ Deficiency in α1-antitrypsin may predispose to urticaria ▪ Avoidance of heat usually helps
Pressure urticaria	▪ Urticarial wheals occur at the site of pressure on the skin ▪ The urticarial rash may occur immediately but a delay of up to 6 h can occur, and lesions resolve over several days. ▪ **Dx**: Pressure challenge testing ▪ **Tx**: Patients are less likely to respond to antihistamines // may respond to dapsone or montelukast.
Solar urticaria	▪ Sunlight causes an acute urticarial eruption. ▪ Patients complain of stinging, burning and itching at exposed skin sites within 30min. ▪ Lesions resolve rapidly (minutes to hours) when light exposure ceases. ▪ **DDx**: porphyria (lesions resolve with scarring) and polymorphic light eruption (lesions take days to weeks to resolve).
Ordinary urticaria	▪ Intermittent fleeting wheals at any skin site, with or without angiooedema (Figures 5.2 and 5.5). Lesions may be papular, annular (Figure 5.6) and even serpiginous. ▪ No underlying cause is found. Possible triggers of acute urticaria include infections, vaccinations, medications and food.

- Urticaria can be chronic (>6 weeks) or acute // ordinary, contact allergic, cholinergic, physical, or urticarial vasculitis.

Diagnosis

- Dermatographism (exaggerated release of histamine causing wheal and flare) is usually positive in physical urticaria.
- Skin biopsy can be useful if urticarial vasculitis is suspected; plain lidocaine should be used for the local anaesthetic (as adrenaline causes release of histamine from mast cells). In urticarial vasculitis, there is a cellular infiltrate of lymphocytes, polymorphs and histiocytes.
- Patch testing to identify contact urticaria.
- Suspect hereditary angio-oedema → check the complement C3 level and C1 esterase which are usually low.

Box 5.1 **Causes of non-physical urticaria**

- Food allergies: fish, eggs, dairy products, nuts and strawberries.
- Food additives: tartrazine dyes and sodium benzoates
- Salicylates: medication and foods.
- Infections: viral, bacterial and protozoal.
- Systemic disorders: autoimmune, connective tissue disease and carcinoma.
- Contact urticaria: meat, fish, vegetables and plants.
- Papular urticaria: persistent urticaria often secondary to insect bites.
- Aeroallergens: pollens, house dust mite and animal dander.

Box 5.2 **Causes of physical urticaria**

- Heat.
- Sunlight.
- Cold.
- Pressure.
- Water.

Management

- Oral antihistamines are the mainstay of treatment/prevention of urticaria and angio-oedema.
- Oral corticosteroids may be indicated in very severe eruptions, particularly those associated with urticarial vasculitis.

Acne

- The main changes in acne include:
  - ⇨ Thickening of the keratin lining and subsequent obstruction of the sebaceous duct resulting in closed comedones (‘whiteheads’) or open comedones (‘blackheads’ whose color is due to melanin, not dirt)
  - ⇨ Increase in sebum secretion
  - ⇨ Increase in Propionibacterium acnes bacteria within the duct.
  - ⇨ Inflammation around the sebaceous gland.

- **Infantile acne** occurs in the first few months of life. It can rarely be caused by **congenital adrenal hyperplasia** or **virilizing tumors** but is most commonly due to **transplacental stimulation** of the adrenal gland by maternal hormones causing increased adrenal androgens.

- Corticosteroids, both topical and systemic, can cause increased keratinization of the pilosebaceous duct resulting in acne. Some patients develop perioral dermatitis (no comedones) after application of topical steroids to the face → topical steroid should be stopped, and then treat with oral tetracycline or erythromycin for 6weeks.

- **Causes**: hormones, fluid retention, stress, diet, seasons, oils (acnegenic substances include coal tar, dicophane (DDT), cutting oils and halogenated hydrocarbons), iatrogenic (steroids, OCPs, anti-epileptics)

Box 12.1 **Factors causing acne**

Intrinsic factors

Hormones

- Polycystic ovary syndrome.
- Virilising tumours.
- Congenital adrenal hyperplasia.
- Increased cortisol (Cushing's syndrome).
- Increased growth hormone (acromegaly).

Medications

- Topical and systemic steroids.
- Oral contraceptive pill (higher androgen content).
- Phenytoin.
- Barbiturates.
- Isoniazid.
- Ciclosporin.
- Lithium.

Extrinsic factors

- Oils/pomades.
- Coal and tar.
- Chlorinated phenols.
- DDT and weed killers.

- **<u>Types:</u>**

1- Acne vulgaris:

- The common type of acne, occurs during puberty and affects the comedogenic areas of the face, back and chest // more in boys
- Acne keloidalis is a type of scarring acne seen particularly on the neck in men
- Resolving lesions leave post-inflammatory pigment changes and scarring. Scars maybe atrophic and pitted, deep, ('ice pick'), rolling and boxcar or they may be more hypertrophic or even keloid. Scars may also be hyper/hypopigmented and erythematous.
  - ⇨ Superficial procedures are used to improve the appearance of shallow acne scars (chemical peel, dermabrasion and fillers) // deeper scars may require more aggressive therapy (dermaroller, punch excision, spot fractional resurfacing, fraxel and intense pulsed light).

2- Acne excoriée:

- The patient picks at the skin producing disfiguring erosions

3- Infantile acne

- Localized acne lesions occur on the face in the first few months
- May require topical or systemic therapy as although it will resolve spontaneously it may last up to 5 years and can cause scarring

4- Acne conglobata/fulminans

- Severe form of acne, more common in boys and in tropical climates
- Extensive, nodulocystic acne and abscess formation affecting particularly the trunk, face and limbs
- Acne fulminans is similarly severe but is associated with systemic symptoms of malaise, fever and joint pains // associated with a hypersensitivity to Propionibacterium acnes.

Table 12.1 Treatment of acne.

Treatment	Comedones	Inflammatory papules/pustules	Mixed picture	Nodulocystic
First line	Topical retinoid Azelaic acid Salicylic acid	Benzoyl peroxide	Topical retinoid ± topical antibiotic ± benzoyl peroxide Combination of all three	Oral antibiotic + topical retinoid
Second line	Physical comedone extraction	Oral antibiotic Oral contraceptive pill (high oestrogen, low androgen, e.g. Yasmin®)	Azelaic acid + benzoyl peroxide ± topical antibiotic	Oral isotretinoin A short course of systemic steroids may be given initially with the isotretinoin
Third line		Anti-androgens e.g. co-cypindiol (Dianette®) Different oral antibiotic	Hormone therapy Oral antibiotic Oral isotretinoin	Triamcinolone injections to unresponsive lesions

Topical	
Benzoyl peroxide	Bacteriostatic & comedolytic
Salicylic acid	Desquamation of follicular epithelium and therefore inhibits the formation of comedones
Azelaic acid	Anti-keratinizing and antibacterial effects // can cause depigmentation of the skin
Topical retinoids	Can cause photosensitivity // an initial acne flare may occur
Topical antibiotics	**Erythromycin** and **clindamycin** either alone or in combination with other agents such as zinc or benzoyl peroxide.
Phototherapy	When unresponsive to or unable to tolerate conventional treatments.
Systemic	
Hormones	OCPs that have higher estrogen and lower androgen potential (such as Yasmin)
Oral retinoids	▪ Usually reserved for resistant disease unresponsive to other oral therapies. ▪ Teratogenic, increase liver enzymes and lipids, dryness, depression
Oral antibiotics	▪ Tetracyclines remain the mainstay of treatment ▪ in those over the age of 12 years (below this age, they may cause dental hypoplasia and staining of teeth) // + doxycycline // Tetracyclines should be avoided in pregnancy/breastfeeding and children<12 years. Erythromycin and trimethoprim are good alternatives
▪ Residual lesions, keloid scars, cysts and persistent nodules can be treated by injection with triamcinolone ▪ For severe atrophic boxcar and 'ice-pick' scarring → punch biopsies and pinch grafts (harvested from behind the ear). When healing is complete dermabrasion can then be used for resurfacing. ▪ For milder scarring → chemical peels or dermaroller treatments.	

Rosacea

- Facial flushing, persistent erythema, telangiectasia, inflammatory papules, pustules and edema // changes may be localized to one cheek or the nose.
- In chronic rosacea the nasal skin can become coarse in texture, eventually resulting in gross thickening and hypertrophy → **rhinophyma**
- Conjunctivitis, blepharitis and eyelid oedema may be associated

- **Management:**
  - Trigger factors should be identified and ideally avoided
  - Topical metronidazole, 15% azelaic acid
  - α-adrenoreceptor agonists for diffuse facial erythema
  - Oral antibiotics including tetracycline, doxycycline, erythromycin and minocycline
  - Use of low-dose oral isotretinoin between 3-9months in those with refractory disease
  - Laser ablation of dilated telangiectatic vessels can be undertaken once the inflammatory component has been treated.
  - Intense pulsed light (IPL) can also be effective for reducing erythema, telangiectasia and papules.
  - Carbon dioxide laser or shave removal with a scalpel blade of excess skin from the nose can significantly improve the appearance of **rhinophyma**.

Bullous diseases

- Blisters may result from **destruction of epidermal cells** (a burn or a herpes virus infection). **Loss of adhesion between the cells** may occur within the epidermis (pemphigus) or at the **basement membrane** (pemphigoid). In eczema there is **oedema between the epidermal cells**, resulting in spongiosis.
- **Triggers**: drugs (rifampicin, captopril and D-penicillamine), certain foods (garlic, onions and leeks), viral infections, hormones, UV radiation and X-rays.
- **Investigation**: direct immunofluorescent analysis of perilesional skin (gold standard)
- **Management**: non-adherent dressings or a bodysuit can be used to cover painful cutaneous erosions. Liquid paraffin for eroded areas to help retain fluid and prevent secondary infection / immunosuppressive treatments / In elderly: intensive potent topical steroids to affected skin and maintained on azathioprine or minocycline

Bullous pemphigoid	▪ IgG autoantibodies that target the basement membrane cells (hemidesmosome) → subepidermal split leads to tense bullae formation. ▪ >65Y, tense blister, background of dermatitis or normal , flexure sites on the limbs and trunks, no scarring ▪ **Triggers**: vaccinations, drugs (NSAIDs, furosemide, ACE (angiotensin converting enzyme) inhibitors and antibiotics), UV radiationand X-rays. ▪ In children: follows vaccination on the face, palms, and soles.
Pemphigus vulgaris	▪ Auto-antibodies directed against desmosomal cadherin desmoglein 3 (Dsg3) → flaccid intraepidermal blister formation ▪ Oral lesions in chronic progressive pemphigus vulgaris ▪ Painful flaccid blisters and erosions arising on normal skin ▪ Rubbing apparently normal skin causes the superficial epidermis to slough off (Nikolsky sign positive). ▪ **Triggers**: rifampicin, ACE inhibitors and penicillamine ▪ **Associated with**: non-Hodgkin's lymphoma or chronic lymphocytic leukaemia. ▪ **Tx**: rituximab
Pemphigus foliaceus	▪ Rare autoimmune skin disease characterized by sub corneal blistering and IgG antibodies directed against desmoglein 1 (Dsg1) usually manifested at UV-irradiated skin sites. ▪ Affect patients in middle age ▪ Flaccid small bullae on the trunk, face and scalp that rapidly erode and crust. ▪ **Triggers**: penicillamine, nifedipine, captopril and NSAIDs.
Dermatitis Herpetiform	▪ IgA deposits in the papillary dermis which results from chronic exposure of the gut to dietary gluten → IgA antibodies develop against gluten-tissue transglutaminase → cutaneous blistering ▪ Intensely pruritic autoimmune blistering disorder ▪ Affects young/middle-aged adults and is associated with an underlying gluten-sensitive enteropathy. ▪ Affect the buttocks, knees and elbows. May experience bloating and diarrhoea. Low ferritin and folate can result from malabsorption. ▪ **Tx**: Dapsone and sulphapyridine
Pemphigoid gestationis	▪ Autoimmune disorder usually occurs in the second/third trimester of pregnancy ▪ Acute-onset intensely pruritic papules from the periumbilical area outwards ▪ Usually resolves within weeks after birth, but may flare immediately postpartum. ▪ **Tx**: high doses of systemic corticosteroids
Mucous membrane pemphigoid	▪ Painful sores in their mouth, nasal and genital mucosae, and may complain of a gritty feeling in their eyes. ▪ Tense blisters may be haemorrhagic and heal with scarring / scarring alopecia

(cicatricial pemphigoid)	▪ Symblepharon (tethering of conjunctival epithelium), synechiae (adhesion of iris to cornea) and fibrosis of the lacrimal duct (dry eyes) resulting in opacification, fixed globe and eventually blindness. ▪ **Tx**: Oral disease may respond to topical steroids and tetracycline mouthwashes. Topical steroid drops and mitomycin may be useful for ophthalmic disease, but usually systemic immunosuppression such as mycophenolate mofetil is required.
Linear IgA	▪ Acute onset of blistering to insidious pruritus before chronic tense bullae. ▪ In children, the blisters tend to affect the lower abdomen and perineum, whereas in adults the limbs and trunk are most affected. ▪ Blisters are usually intact and are classically seen around the periphery of annular lesions ('string of beads sign') or in clusters ('jewel sign'). ▪ **Triggers**: vancomycin, ampicillin and amiodarone. ▪ **Tx**: dapsone and sulphapyridine.
DDx	
Development	▪ At birth → genodermatoses, cutaneous infections. ▪ Preceding systemic symptoms → infectious cause such as chicken pox or hand, foot and mouth disease. ▪ Tingling sensation → herpes simplex ▪ Pain → herpes zoster. ▪ Pruritic → DH or pompholyx eczema. ▪ Preceding eczema → bullous pemphigoid.
Duration	▪ Arise rapidly → allergic reactions, impetigo, erythema multiforme and pemphigus ▪ Gradual onset and follow a chronic course →DH, pityriasis lichenoides, porphyria cutanea tarda and bullous pemphigoid
Durability	▪ Subepidermal blisters → bullous pemphigoid, linear IgA and erythema multiforme. ▪ Superficial blisters → pemphigus vulgaris, porphyria, Stevens–Johnson syndrome, toxic epidermal necrolysis, staphylococcal scalded skin and herpes viruses.
Distribution	Box 8.1 **Widespread blistering eruptions** • Bullous pemphigoid. • Pemphigus vulgaris. • DH (or localised). • Erythema multiforme. • Drug rashes: Stevens–Johnson syndrome, toxic epidermal necrolysis. • Chicken pox. Box 8.2 **Localised blistering eruptions** • DH (knees, elbows and buttocks). • Pemphigus gestationis (abdomen). • PF (upper trunk, face and scalp). • Porphyria (sun-exposed sites). • Pompholyx eczema (hands and feet). • Contact dermatitis. • Fixed drug eruption. • Insect bite reactions (often in clusters or linear patterns). • Infections: herpes simplex, herpes zoster and staphylococcus (impetigo).

Immunobullous disorder	Typical patient	Distribution of rash	Morphology of lesions	Mucous membrane involvement	Associated conditions
Bullous pemphigoid	Elderly	Generalised	Intact blisters	Common	None
Mucous membrane pemphigoid	Middle aged or older	Varied	Erosions, flaccid blisters, scarring	Severe and extensive	Autoimmune disease
Pemphigoid gestationis	Pregnant	Periumbilical	Intact blisters, urticated lesions	Rare	Thyroid disease
Pemphigus vulgaris	Middle aged	Flexures, head	Flaccid blisters, erosions	Common	Autoimmune disease
Dermatitis herpetiformis	Young adults	Elbows, knees, buttocks	Vesicles, papules, excoriations	Rare	Small bowel enteropathy (gluten-sensitive), lymphoma
Linear IgA	Children and adults	Face and perineum (children) Trunk and limbs (adults)	Annular urticated plaques with peripheral vesicles	Common	Lymphoproliferative disorders

Slides: CTDs, infections, STDs, systemic disease

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