

Third edition

Notes & Notes

For MRCP part 1 & 2

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Dermatology

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Epidermis

Epidermis - 5 layers - bottom layer = stratum germinativum which gives rise to keratinocytes and contains melanocytes

- The epidermis is the outermost layer of the skin and is composed of a stratified squamous epithelium with an underlying basal lamina
- It may be divided into five layers:

Layer	Description
Stratum corneum	Flat, dead, scale-like cells filled with keratin Continually shed
Stratum lucidum	Clear layer - present in thick skin only
Stratum granulosum	Cells form links with neighbours
Stratum spinosum	Squamous cells begin keratin synthesis Thickest layer of epidermis
Stratum germinativum	The basement membrane - single layer of columnar epithelial cells Gives rise to keratinocytes Contains melanocytes

Definitions

- Plaque** is a descriptive term for a skin lesion that is raised and greater than 1 cm in diameter.
- Macule** is an area of altered skin colour irrespective of the size.
- Papule** is a raised lesion less than 1 cm in diameter.
- Ulcer** is a discontinuity of the skin with complete loss of the epidermis and often portions of the dermis and subcutaneous fat.
- Vesicle** is a fluid-filled, well-circumscribed raised lesion.
- Pustule** are small elevation of the skin containing cloudy or purulent material, usually consisting of necrotic inflammatory cells.
- Bulla** are large vesicle containing serous fluid.
- Fissure** are cracks in the skin that are narrow but deep.
- Telangiectasia** are collection of enlarged capillaries visible on the skin or mucous membranes.
- Lichenification of the skin** is due to epidermal thickening characterised by visible and palpable thickening of the skin with accentuation of skin markings.
- Atrophy** of the skin may be due to loss of epidermis, dermis or subcutaneous tissue. Thinning of the epidermis presents as skin that appears thin and translucent. Thinning of the dermis and subcutaneous tissue leads to a depression in the skin.

Acanthosis nigricans

Overview

- Describes symmetrical, brown, velvety plaques that are often found on the neck, axilla and groin
- presents as a dark **thickened** area of the skin of the back of the neck or the armpit,
- Obesity** is the most common cause
- Classically acanthosis nigricans associated with malignancy appears abruptly, and it can precede diagnosis of malignancy.
- Diabetes causes acanthosis nigricans due to stimulation of **insulin-like growth factor receptor-1**.

Causes

- paraneoplastic phenomenon (usually tumours of the GI tract, especially **adenocarcinoma of the stomach** and **Endometrial carcinoma**)
- diabetes mellitus
- obesity
- polycystic ovarian syndrome
- acromegaly
- Cushing's disease
- hypothyroidism
- familial (autosomal dominant)
- Prader-Willi syndrome
- drugs: oral contraceptive pill, **nicotinic acid (Niacin)**



Management

- first line is **treatment of the underlying cause**.
- In persistent acanthosis nigricans despite treatment of the underlying cause, topical **retinoids** can be tried.

Acne rosacea

is a chronic skin disease of unknown aetiology

Features

- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

Management

Acne rosacea treatment:

- mild/moderate: topical metronidazole
- severe/resistant: oral tetracycline
- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

Acne vulgaris

- Acne vulgaris is a common skin disorder which usually occurs in adolescence.
- It typically affects the face, neck and upper trunk
- characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Epidemiology

- Affects around 80-90% of teenagers
- **Age of onset:** typically by 11–12 years, with symptoms usually disappearing around 20–30 years of age
 - ⇒ Acne presenting at beyond aged 20 years should always prompt investigation of a possible secondary cause.
- **Sex:** more common in males during adolescence, but more common in women during adulthood

Aetiology & Pathophysiology

- **Hormonal factors**
 - ⇒ ↑ Androgens during puberty → increased production of sebum by sebaceous glands
 - ⇒ In women: menstrual cycle
- **Follicular hyperkeratosis:** Follicular epidermal hyperproliferation → formation of a keratin plug → obstruction of pilosebaceous follicle. Higher keratinocyte activity and decreased keratinocyte shedding in pilosebaceous units leads to the formation of comedones.
- **Bacterial colonisation** with **Cutibacterium acnes**; inflammatory reactions with formation of papules, nodules, pustules, and/or cysts

Features

- **Localisation:** common in areas with sebaceous glands (predilection sites: face, shoulders, upper chest, and back)
- **Primary lesions**

- ⇒ Non-inflammatory: comedonal acne
 - Closed comedones ("whiteheads"): closed small round lesions that contain whitish material
 - Open comedones ("blackheads"): dark, open portion of sebaceous material
- ⇒ Inflammatory: affected areas are red and can be painful
 - papules, pustules that arise from comedones
 - Nodular acne (> 5 mm in diameter): Commonly the back and neck
- **Secondary lesions:** hyperpigmentation, and scarring

Management

- A simple step-up management scheme often used in the treatment of acne is as follows:
 - ⇒ Single topical therapy (topical retinoids, benzyl peroxide)
 - ⇒ Topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
 - ⇒ Oral antibiotics: e.g. Oxytetracycline, doxycycline.
 - Improvement may not be seen for 3-4 months.
 - Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation.
 - Gram negative folliculitis may occur as a complication of long-term antibiotic use . high-dose oral trimethoprim is effective if this occurs
 - ⇒ **Oral erythromycin may be used for acne in pregnancy.** The other drugs are contraindicated
- Oral isotretinoin: only under specialist supervision
- Ethinylestradiol with cyproterone acetate (Dianette) is useful in some female patients with acne unresponsive to standard treatment.
- **There is no role for dietary modification in patients with acne**

Weight loss is the most important intervention.

Isotretinoin

Retinoid (isotretinoin) therapy should be discontinued at the latest one month before

Overview

- Isotretinoin is an oral retinoid used in the treatment of severe acne. Two-thirds of patients have a long-term remission or cure following a course of oral isotretinoin

Indication

- Moderate to severe acne

Contraindications

- Pregnancy, women of childbearing age without contraception: strong teratogenic effects
- Liver disease
- Precautions (in all females of childbearing potential)
- A serum/urine pregnancy test

Side effects

- Teratogenicity
 - ⇒ females should ideally be using two forms of contraception (e.g. Combined oral contraceptive pill and condoms)
 - ⇒ should be discontinued at the latest one month before
- Dry skin, eyes and lips: **the most common side-effect of isotretinoin**
- Low mood
- Raised triglycerides
- Hair thinning

- Nose bleeds (caused by dryness of the nasal mucosa)
- Benign intracranial hypertension: isotretinoin treatment should not be combined with tetracyclines for this reason
- Photosensitivity
- Laboratory test abnormalities: ↑ Triglycerides, ↓ HDL, ↑ glucose

Alopecia

Divided into scarring (destruction of hair follicle) and non-scarring (preservation of hair follicle)

Scarring alopecia

- trauma, burns
- radiotherapy
- lichen planus
- discoid lupus
- tinea capitis (scarring may develop in untreated tinea capitis if a kerion develops)

Non-scarring alopecia

- male-pattern baldness
- drugs: cytotoxic drugs, carbimazole, heparin, oral contraceptive pill, colchicine
- nutritional: iron and zinc deficiency
- autoimmune: alopecia areata
- telogen effluvium (hair loss following stressful period e.g. surgery)
- trichotillomania
 - ⇒ psychological disorder where patients are compelled to pull their own hair, resulting in alopecia.
 - ⇒ It is typically encountered in teenage females and children

Cicatricial alopecia (also known as scarring alopecia)

- inflammation injures hair follicles resulting in permanent bald patches with no visible follicles.
 - ⇒ inflammation can be seen as redness, scaling and crusting.
- Common causes include:
 - ⇒ discoid lupus erythematosus, and
 - ⇒ lichen planopilaris (a variant of lichen planus).
- Treatment is dependent on the underlying causes but often requires topical corticosteroids.

Alopecia areata

- Alopecia areata is a presumed autoimmune condition causing localised, well demarcated patches of hair loss.

Feature

- localised patches of non-scarring hair loss.
- Remaining hairs have a characteristic 'exclamation mark' appearance, and are tapered towards the base.
 - ⇒ small, broken hairs at the edge of the hair loss
- More severe involvement may present as alopecia totalis (total loss of scalp hair) or alopecia universalis (total loss of all body hair).

Treatment

- Hair will regrow in 50% of patients by 1 year, and in 80-90% eventually. Careful explanation is therefore sufficient in many patients.
- **Other treatment options include:**

- ⇒ topical or intralesional corticosteroids
 - **the most appropriate treatment for area of hair loss → Intra-lesional triamcinolone**
- ⇒ topical minoxidil
- ⇒ phototherapy
- ⇒ dithranol
- ⇒ contact immunotherapy
- ⇒ wigs

Differential diagnosis

- **Androgenetic alopecia**
 - ⇒ presents after puberty as a more diffuse slow hair loss with characteristic loss over the temporal regions and vertex in males.
- **Discoid lupus erythematosus (DLE)**
 - ⇒ presents as scarring alopecia.
 - ⇒ Areas of alopecia are usually atrophic with visible loss of hair follicles.
 - ⇒ Patients may have DLE lesions elsewhere.
 - ⇒ If not treated early, hair loss is usually irreversible.
- **Telogen effluvium**
 - ⇒ presents with diffuse hair loss and usually presents one to three months after a stressful episode, for example, viral illness, surgery, childbirth, emotional stress.
 - ⇒ Hair loss is never complete and usually stops after three to five months.
 - ⇒ Subsequent hair regrowth is usually complete.
- **Trichotillomania**
 - ⇒ more commonly seen in children compared to adults.
 - ⇒ Patients also present with localised hair loss but in a bizarre pattern.
 - ⇒ Hairs of differing lengths are usually seen within and at the edges of the patches.
 - ⇒ Patients may or may not volunteer a history of hair pulling.

Pemphigus vulgaris

Blisters/bullae

- no mucosal involvement: bullous pemphigoid
- mucosal involvement: pemphigus vulgaris

Overview

- Pemphigus vulgaris is an autoimmune disease caused by antibodies (**IgG**) directed against **desmoglein 3**, a cadherin-type epithelial cell adhesion molecule.
- The binding of autoantibodies results in a loss of cell-to-cell adhesion, a process termed acantholysis.
- It is more common in the Ashkenazi Jewish population
- seen predominantly in patients ages 50-60, but can affect many ages.

Features

- **mucosal ulceration is common and often the presenting symptom.** Oral involvement is seen in 50-70% of patients
- skin blistering - flaccid, easily ruptured vesicles and bullae.
 - ⇒ Blisters are thin-walled and rupture easily (intact blisters are rarely seen).
- Lesions are typically painful but not itchy. These may develop months after the initial mucosal symptoms.
- Nikolsky's describes the spread of bullae following application of horizontal, tangential pressure to the skin

- Immunofluorescent staining of a biopsy sample shows deposition of immunoglobulin (IgG) directed against to keratinocyte desmosomes and to desmosome-free areas of the keratinocyte cell membrane, resulting in a 'chicken wire' appearance.
- acantholysis on biopsy



Mucosal ulceration is common with pemphigus

**Management**

- steroids
- immunosuppressants

Bullous pemphigoid**Overview**

- Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin.
- This is secondary to the development of **antibodies against hemidesmosomal proteins BP180 and BP230**
 - ⇒ caused by (IgG) autoantibodies against components of the basement membrane.

Epidemiology

- Pemphigoid, erythema multiforme, and herpes are the commonest causes of a blistering rash.
- Bullous pemphigoid is more common in elderly patients (over 60 years).
 - ⇒ **Remember, this is a disease of the elderly (uncommon under the age of 60).**

Features

- Include
- itchy, tense blisters typically around flexures
- the blisters usually heal without scarring
- mouth is usually spared*
 - ⇒ *in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

Investigations

- **Skin biopsy:**
 - ⇒ **Perilesional skin biopsy for examination by direct immunofluorescence**
 - ⇒ immunofluorescence shows IgG and C3 at the dermo-epidermal junction

Differential diagnosis

- Blistering in pemphigoid occurs at the sub-epidermal level - deeper than the blisters of pemphigus vulgaris (which occur at the dermal-epidermal junction); hence the tense blisters seen in pemphigoid. Blisters are thin-walled and fragile in pemphigus - few intact blisters are ever seen.

- ⇒ In pemphigus vulgaris, mucous membrane involvement is more common, and intact bullae are rare. Skin biopsy for routine and direct immunofluorescence is needed to differentiate from bullous pemphigoid.

Management

- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used
 - ⇒ Topical corticosteroids may be attempted in patients with mild, localised bullous pemphigoid.



	Pemphigus vulgaris	Bullous pemphigoid
Appearance		
Age	Younger	Older
Mucous membrane involvement	Yes	Rare
Autoantibodies	Against desmoglein 3	Against hemidesmosomes
Blister location	Intraepidermal (superficial)	Subepidermal (deep)
Blister quality	Flaccid, rupture easily	Tense and firm
Nikolsky's sign	Nikolsky positive	Nikolsky negative
Prognosis	Poor	Favorable

Dermatitis herpetiformis (DH)

Dermatitis herpetiformis is associated with HLA-DR3

Dermatitis herpetiformis - caused by IgA deposition in the dermis

Overview

- autoimmune blistering skin disorder **associated with coeliac disease** and gluten sensitivity.
- caused by deposition of IgA in the dermis.
- associated with HLA-DR3.
- Virtually all patients with DH carry the HLA DQ2 or HLA DQ8 haplotype.

Features

- itchy, vesicular skin lesions on the extensor surfaces (e.g. elbows, knees, buttocks)

Association

- increased risk for the development of other autoimmune diseases.
 - ⇒ Thyroid disease is the most common autoimmune disorder associated with DH.
- increased risk for lymphoma.

Diagnosis

- skin biopsy: direct immunofluorescence (The gold standard test for diagnosis) shows:
 - ⇒ Subepidermal **deposition of IgA**
 - in a **granular pattern** in the upper **dermis** (in the **dermal papillae**) (Granular IgA deposits at the basement membrane zone)
 - ⇒ **neutrophilic** dermal infiltrates in the superficial dermis
 - **Neutrophils** are the immune cell that is involved in the blistering skin lesion DH.
- Serology
 - ⇒ blood test showing the presence of IgA antibodies against tissue transglutaminase.

Management

- gluten-free diet
- dapsone



Dermatitis herpetiformis

Discoid lupus erythematosus

Pathology

- it is a chronic type of Cutaneous lupus erythematosus (CLE)
- **characterised by follicular keratin plugs**
- characterised by a well-demarcated macular rash with erythema, scales, and plaques that often results in scarring and atrophy.

Aetiology

- thought to be **autoimmune** in aetiology

Association

- may occur in the absence or in association with systemic SLE.
 ⇒ Approximately 10% of patients may have signs of SLE.

Epidemiology

- generally seen in younger females.
- occurs 2-3 times more frequently in women than in men
- more common in African-Caribbean female.

Features

- erythematous, raised rash, sometimes scaly
- may be photosensitive
- more common on face, neck, ears and scalp
- lesions heal with atrophy, scarring (may cause scarring alopecia), and pigmentation

Diagnosis

- made by biopsy of the lesion.

Management

Discoid lupus erythematosus - topical steroids → oral hydroxychloroquine

- **1st line:** topical potent steroid cream
- **2nd line:** oral antimalarials e.g. hydroxychloroquine
 ⇒ other options
 - Topical calcineurin inhibitors
 - Intralesional corticosteroids
 - Oral corticosteroids.
- Avoid sun exposure

Prognosis

- **The risk of progression to SLE** in patients with DLE was demonstrated to be higher than previously reported (**16.7% progression within 3 years of diagnosis**, as compared with previous data indicating that <5-10% of patients with DLE progress to SLE).
- **children** with DLE seem to have a higher early rate of progression to SLE (up to **25%**) indicating that the **age at onset might influence disease severity**

According to a recent epidemiologic study, approximately **16%** of patients with discoid lupus erythematosus (DLE) may develop systemic involvement within 3 years of diagnosis.



Discoid lupus erythematosus affecting the scalp



Discoid lupus erythematosus affecting the face

Contact dermatitis

Types

- There are two main types of contact dermatitis
 - ⇒ **Irritant contact dermatitis:**
 - common
 - non-allergic reaction due to weak acids or alkalis (e.g. detergents).
 - Often seen on the hands.
 - Erythema is typical, crusting and vesicles are rare
 - ⇒ **Allergic contact dermatitis:**
 - type IV hypersensitivity reaction.
 - Uncommon
 - often seen on the head following hair dyes.
 - Presents as an acute weeping eczema, which predominately affects the margins of the hairline rather than the hairy scalp itself.
 - Topical treatment with a potent steroid is indicated

The main difference between allergic contact dermatitis and irritant contact dermatitis:

- ⇒ The rash caused by **allergic contact dermatitis** **confined to contacted area**, whereas in **irritant contact dermatitis**, the rash is more **widespread**.
- ⇒ In **allergic contact dermatitis** the rash usually appears **after a day or two** after exposure to the allergen, unlike **irritant contact dermatitis** that appears **immediately** after the contact with the trigger.

Pruritus

Causes

The table below lists the main characteristics of the most important causes of pruritus

Liver disease	History of alcohol excess Stigmata of chronic liver disease: spider naevi, bruising, palmar erythema, gynaecomastia etc Evidence of decompensation: ascites, jaundice, encephalopathy
Iron deficiency anaemia	Pallor Other signs: koilonychia, atrophic glossitis, post-cricoid webs, angular stomatitis
Polycythaemia	Pruritus particularly after warm bath 'Ruddy complexion' Gout Peptic ulcer disease
Chronic kidney disease	Lethargy & pallor Oedema & weight gain Hypertension
Lymphoma	Night sweats Lymphadenopathy Splenomegaly, hepatomegaly Fatigue
Other causes	<ul style="list-style-type: none"> • hyper- and hypothyroidism • diabetes • pregnancy • 'senile' pruritus • skin disorders: eczema, scabies, psoriasis, pityriasis rosea • Idiopathic urticaria: Up to 50% of cases are idiopathic

Eczema herpeticum

- Eczema herpeticum describes a severe primary infection of the skin by herpes simplex virus 1 or 2.

Features

- It is more commonly seen in children with atopic eczema.
- **Typically, the child has a high fever for seven days,** and recurrent attacks can occur.
- It may affect any site but is most often seen on face and neck.

Treatment

- Eczema herpeticum is considered as one of the few dermatological emergencies.
- As it is potentially life threatening children should be admitted for IV acyclovir

Complications

- Death can result from physiological disturbances (loss of fluid electrolytes and protein through the skin) or dissemination of the virus to brain and other organs or from secondary bacterial sepsis.
- may be further complicated by secondary staphylococcal infection. This is treated by adding oral antibiotics, for example, flucloxacillin 500 mg q.i.d.

Eczema: topical steroids

Topical steroids

- moderate: Clobetasone butyrate 0.05%
- potent: Betamethasone valerate 0.1%
- very potent: Clobetasol propionate 0.05%

Use weakest steroid cream which controls patients symptoms

The table below shows topical steroids by potency

Mild	Moderate	Potent	Very potent
Hydrocortisone 0.5-2.5%	Betamethasone valerate 0.025% (Betnovate RD) Clobetasone butyrate 0.05% (Eumovate)	Fluticasone propionate 0.05% (Cutivate) Betamethasone valerate 0.1% (Betnovate)	Clobetasol propionate 0.05% (Dermovate)

Finger tip rule

- 1 finger tip unit (FTU) = 0.5 g, sufficient to treat a skin area about twice that of the flat of an adult hand

Topical steroid doses for eczema in adults

Area of skin	Fingertip units per dose
Hand and fingers (front and back)	1.0
A foot (all over)	2.0
Front of chest and abdomen	7.0
Back and buttocks	7.0
Face and neck	2.5
An entire arm and hand	4.0
An entire leg and foot	8.0

The BNF makes recommendation on the quantity of topical steroids that should be prescribed for an adult for a single daily application for 2 weeks:

Area	Amount
Face and neck	15 to 30 g
Both hands	15 to 30 g
Scalp	15 to 30 g
Both arms	30 to 60 g
Both legs	100 g
Trunk	100 g
Groin and genitalia	15 to 30 g

Pompholyx

Pompholyx is a type of eczema which affects both the hands (cheiropompholyx) and the feet (pedopompholyx). It is also known as dyshidrotic eczema

Features

- small blisters on the palms and soles
- pruritic, sometimes burning sensation
- once blisters burst skin may become dry and crack

Management

- cool compresses
- emollients
- topical steroids

Erythema ab igne

- Erythema ab igne is a skin disorder caused by over exposure to infrared radiation.
- It classically presents on the front of the legs due to the patient sitting too close to a fire or heater. It may also arise as a response to chronic hot water bottle use.
- Characteristic features include reticulated, erythematous patches with hyperpigmentation and telangiectasia.
- A typical history would be an elderly women who always sits next to an open fire.
- Hypothyroidism can make patients feel cold and hence more likely to sit next a heater / fire.
- If the cause is not treated then patients may go on to develop squamous cell skin cancer.



Erythema ab igne



Erythema ab igne

Erythema multiforme

Pathophysiology

- Type IV hypersensitivity reaction; triggered by the following
 - ⇒ Infections: herpes simplex virus (HSV - **the most common cause**), Mycoplasma pneumoniae.
 - ⇒ Drugs: phenytoin; beta-lactam antibiotics (e.g., penicillins); sulfonamides

Classification

- **Erythema multiforme minor** (typical targets or raised oedematous papules, with acral distribution, without involvement of mucosal sites, and involving <10% total body surface area)
- **Erythema multiforme major** (typical targets or raised oedematous papules, with acral distribution, plus involvement of 1 or more mucosal sites, and involving <10% total body surface area)

Features

- Erythematous , maculopapular rash (many forms), hence the 'multiforme' in the name.
- **Target lesions** (also called iris lesion): an inner dark red/brown zone, surrounded by a pale zone, and an outer erythematous ring.
- Distribution: Symmetrical and affects backs of hands and feet first → spreads proximally and can affect the entire body.

Treatment

- Supportive: treat the underlying infection or stop the offending drug .

Prognosis

- usually mild and self-limiting disease with the lesions healing within 2 to 3 weeks without scarring.



Erythema multiforme



Erythema multiforme

Differential diagnosis

- Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are the same entity but differ in terms of disease severity (based on surface area of skin involved).
 - ⇒ < 10% – SJS
 - ⇒ 10–30% – SJS/TEN overlap
 - ⇒ 30% – Toxic epidermal necrolysis (severe SJS)

Erythema multiforme VS Stevens-Johnson syndrome

	Erythema multiforme (EM)	Stevens-Johnson syndrome (SJS)
Causes	usually triggered by infections, most commonly herpes simplex virus (HSV). Medications are uncommon cause (<10%)	Most commonly triggered by drugs (~ 80%).
Lesions distribution	Lesions begin on the extremities	Lesions typically begin on the face and trunk.
Target lesions	Typical target lesions	No typical target lesions.
Mucosal membranes	Mucosal membranes may be involved, but usually not	Mucosal membranes almost always involved
Swelling	No associated swelling of face, hands or feet	Associated swelling of face, hands or feet
Systemic symptoms	Systemic symptoms such as fever and malaise, are absent or mild	Systemic symptoms such as fever and malaise, are prominent
Histology	high density of cell infiltrate rich in T-lymphocytes. (more dermal inflammation and individual keratinocyte necrosis)	poor infiltrate of macrophages and dendrocytes with tumor necrosis factor (TNF) (minimal inflammation and sheets of epidermal necrosis.)
Severity	Usually mild	Shock may develop
Treatment	Treat underline cause	need urgent supportive care , fluid resuscitation similar to that of burns and Wound management
Prognosis	Self-limiting	High mortality rate (SJS: ~ 25%, TEN: ~ 50%)

Erythema multiforme (EM):

- a type IV hypersensitivity reaction of the skin.
- can be triggered by certain infections (e.g., HSV, Mycoplasma pneumonia) and medications (e.g., beta-lactam antibiotics, sulfonamides, phenytoin).

Erythema multiforme (EM):

- EM is characterized by lesions of varying morphology (e.g., macules, papules, vesicles) that typically progress to target lesions and spread proximally from the backs of the hands and feet.

Herpes simplex virus (HSV) infection is the commonest cause of Erythema multiforme

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)

Definition

- Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe mucocutaneous reactions, most commonly triggered by medications, characterized by extensive necrosis and detachment of the epidermis
- SJS and TEN are the same entity but differ in terms of disease severity (based on surface area of skin involved).
 - ⇒ < 10% – SJS
 - ⇒ 10–30% – SJS/TEN overlap
 - ⇒ ≥ 30% – Toxic epidermal necrolysis (severe SJS)

Pathophysiology

- Delayed hypersensitivity reaction (type IV)

Causes

- Most commonly triggered by medications, ~ 80% of cases
 - ⇒ Antibiotics: sulfonamides (e.g., TMP/SMX), aminopenicillins
 - ⇒ Antiepileptics: phenytoin, phenobarbital, lamotrigine, valproic acid, carbamazepine,
 - ⇒ Sulfasalazine
 - ⇒ Nonsteroidal anti-inflammatory drugs (NSAIDs)

Features

- Begins with a prodrome of fever and influenza-like symptoms one to three days before the development of mucocutaneous and skin lesions.
- Extensive, full-thickness epidermal necrosis and sloughing (resembling large superficial burns)
- Mucosal membranes: almost always involved ~ 90% of cases
- Systemically unwell e.g. pyrexia, tachycardic, shock may develop
- Positive Nikolsky's sign (the epidermis separates with mild lateral pressure)
- Skin biopsy
 - ⇒ Keratinocyte necrosis with apparent subepidermal split
 - ⇒ Eosinophilic infiltration with minimal infiltration of lymphocytes and histiocytes around blood vessels

Treatment

- Stop precipitating factor **is most likely to improve prognosis**
- Supportive care, often in intensive care unit
- Wound management: similar to that of burns



Stevens-Johnson syndrome (SJS)

Erythema nodosum

Always do a chest x-ray on a patient with erythema nodosum, to exclude sarcoidosis

Overview

- inflammation of subcutaneous fat
- Histology of these lesions shows a vasculitis of small venules and panniculitis.
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks**
- lesions heal without scarring

Causes

- infection: streptococci, TB, brucellosis
 - ⇒ **The commonest cause is streptococcal infection.**
- systemic disease: sarcoidosis, inflammatory bowel disease (**ulcerative colitis**), Behcet's, SLE
- malignancy/lymphoma
- Drugs (oral contraceptive, sulfonamides, penicillins, antipyretics, montelukast, Hep B vaccination, omeprazole).
- pregnancy



Erythema induratum (EI)

- EI is a form of panniculitis characterised by chronic, recurrent, tender, subcutaneous, and sometimes ulcerated nodules on the lower legs that may also appear elsewhere.
 - ⇒ (Erythema nodosum also commonly associated with TB but do not ulcerate)
- Females are more frequently affected, with a female: male ratio of 7:1 and it is more frequent in younger females.
- It is found in association with tuberculosis.

Erythrasma

- Erythrasma is a generally asymptomatic, flat, slightly scaly, pink or brown rash usually found in the groin or axillae.
- It is caused by an overgrowth of the diphtheroid *Corynebacterium minutissimum*
- Examination with Wood's light reveals a coral-red fluorescence.
- Topical miconazole or antibacterial are usually effective. Oral erythromycin may be used for more extensive infection

Erythroderma

- Erythroderma is a term used when more than 95% of the skin is involved in a rash of any kind
- **Mechanism**
 - ⇒ The mechanism behind erythroderma is most likely from cutaneous thermal dysregulation.
 - **Increased blood flow to the skin** leads to heat and fluid loss, and increased rate of skin cell turnover and skin sloughing.
- **Causes** of erythroderma
 - ⇒ Eczema (40%)
 - ⇒ Psoriasis (25%)
 - ⇒ drugs e.g. gold
 - ⇒ lymphoma, leukaemia
 - ⇒ pityriasis rubra pilaris
 - ⇒ idiopathic
- often accompanied with fever, shivering and malaise.
- **Erythrodermic psoriasis**
 - ⇒ may result from progression of chronic disease to an exfoliative phase with plaques covering most of the body. Associated with mild systemic upset
 - ⇒ more serious form is an acute deterioration. This may be triggered by a variety of factors such as withdrawal of systemic steroids. Patients need to be admitted to hospital for management



This image shows the generalised erythematous rash seen in patients with erythroderma, sometimes referred to as 'red man syndrome'



Note the extensive exfoliation seen in this patient

Fungal nail infections

Onychomycosis is fungal infection of the nails. This may be caused by

- dermatophytes - mainly *Trichophyton rubrum*, accounts for 90% of cases
- yeasts - such as *Candida*
- non-dermatophyte moulds

Features

- 'unsightly' nails are a common reason for presentation
- thickened, rough, opaque nails are the most common finding

Investigation

- nail clippings
- scrapings of the affected nail
- **Wood's lamp**
 - ⇒ **useful, rapid and easy way to confirm the diagnosis**
 - ⇒ Yellow to yellow-green fluorescence is characteristic of fine scales taken from active fungal lesions
 - ⇒ the sensitivity of this procedure is reduced when patients have taken a recent shower

Management

Dermatophyte nail infections - use oral terbinafine

- treatment is successful in around 50-80% of people
- diagnosis should be confirmed by microbiology before starting treatment
- dermatophyte infection:
 - ⇒ **first-line: oral terbinafine**
 - ⇒ alternative: oral itraconazole.
 - ⇒ Treatment duration:
 - for fingernail infections → 6 weeks - 3 months
 - for toenails → 3 - 6 months
- *Candida* infection: mild disease should be treated with topical antifungals (e.g. Amorolfine) whilst more severe infections should be treated with oral itraconazole for a period of 12 weeks

Beau's lines

- Beau's lines is a benign nail condition that presents as a jagged transverse groove on the nail plate corresponding to an episode of nail growth arrest, which can **occur during an episode of severe medical illness**. It usually affects several nails.



Beau's lines

Nail conditions

- **Fungal nail infections** present with thickening and discolouration of the nail plate with prominent subungual debris. It usually only affects one or several nails.
- **Nail psoriasis** presents with pitting, onycholysis, subungual debris and yellowish nail discolouration.

Granuloma annulare

Basics

- Granuloma annulare is a benign inflammatory condition of unknown aetiology
- characterised by dermal papules which can coalesce to form annular plaques.
- papular lesions that are often slightly hyperpigmented and depressed centrally
- typically occur on the dorsal surfaces of the hands and feet, and on the extensor aspects of the arms and legs
- Histology reveals foci of degenerative collagen surrounded by areas of granulomatous inflammation.
- A number of associations have been proposed to conditions such as diabetes mellitus but there is only weak evidence for this
- **Treatment → Observation** (The eruption should disappear spontaneously.)
- Locally delivered steroids are effective in resolving the condition.



Granuloma annulare

Herpes simplex virus

Overview

- There are two strains of the herpes simplex virus (HSV) in humans: HSV-1 and HSV-2. Whilst it was previously thought HSV-1 accounted for oral lesions (cold sores) and HSV-2 for genital herpes it is now known there is considerable overlap

Features

- primary infection: may present with a severe gingivostomatitis
- cold sores
- painful genital ulceration

Management

- gingivostomatitis: oral aciclovir, chlorhexidine mouthwash
- cold sores: topical aciclovir although the evidence base for this is modest
- genital herpes: oral aciclovir. Some patients with frequent exacerbations may benefit from longer term aciclovir

Pregnancy

- elective caesarean section at term is advised if a primary attack of herpes occurs during pregnancy at greater than 28 weeks gestation

Molluscum contagiosum

Definition: A common skin infection caused by molluscum contagiosum virus (MCV), DNA poxvirus

Transmission: Direct skin contact (contact sports, sexually transmitted), autoinoculation or indirectly via fomites (contaminated surfaces) such as shared towels and flannels.

Risk factors:

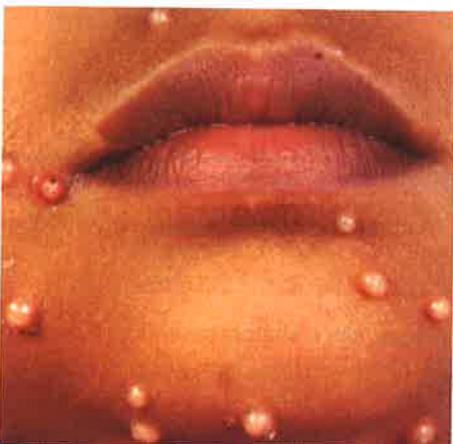
- Most common in children (often in children with atopic eczema)
- Immunosuppression → **HIV testing** if lesions in adults and/or widespread

Presentation

- dome-shaped, smooth, pinkish or pearly white papules with a central umbilication, which are up to 5 mm in diameter. commonly seen on the trunk and in flexures.

Treatment

- Usually self-limiting condition → **Watchful waiting** (especially in children)
- Self-care advice: avoid direct contact and sharing towels . Exclusion from school, gym, or swimming is not necessary.
- For cosmetic or lesions in the genital area:
 - ⇒ Cryotherapy is the first-line treatment
 - ⇒ Topical cantharidin



Molluscum contagiosum

Impetigo

Impetigo - topical fusidic acid → oral flucloxacillin / topical retapamulin

Impetigo is a superficial bacterial skin infection usually caused by either *Staphylococcus aureus* or *Streptococcus pyogenes*.

Features

- 'golden', crusted skin lesions typically found around the mouth
- very contagious

Management

- Limited, localised disease
 - ⇒ **topical fusidic acid is first-line**
 - ⇒ topical retapamulin is used second-line if fusidic acid has been ineffective or is not tolerated
 - ⇒ MRSA is not susceptible to either fusidic acid or retapamulin. Topical mupirocin (Bactroban) should therefore be used in this situation
- Extensive disease
 - ⇒ oral flucloxacillin
 - ⇒ oral erythromycin if penicillin allergic



Erysipelas

- Erysipelas is a *Streptococcus pyogenes* (a group A streptococcal bacterium) infection of the deep dermis and subcutis.

Feature

- It is a tender, intensely erythematous, indurated plaque with a sharply demarcated border.
- Its well-defined margin can help differentiate it from other skin infections (eg, cellulitis).

Treatment

- IV antibiotics such as benzylpenicillin and erythromycin.
- In a penicillin allergic patient a macrolide is the drug of choice**. There is a 10% cross allergy between cephalosporins and penicillins.

Complications

- sepsis
- cerebral abscess
- venous sinus thrombosis.



Well-demarcated, erythematous plaque of erysipelas.

Koebner phenomenon

Describes skin lesions which appear at the site of injury. It is seen in:

- psoriasis
- vitiligo
- warts
- lichen planus
- lichen sclerosus
- molluscum contagiosum

Lichen planus

Lichen

- planus: purple, pruritic, papular, polygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- sclerosus: itchy white spots typically seen on the vulva of elderly women

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated.

Features

- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon may be seen (new skin lesions appearing at the site of trauma)
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging
- **Fibrin deposits at the basement membrane zone** are found in cases of lichen planus , although immunofluorescence studies are uncommonly done to diagnose it.



Lichen planus

Lichenoid drug eruptions - causes:

- gold
- quinine
- thiazides

Management

- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

Lichen sclerosus

- Lichen sclerosus was previously termed lichen sclerosus et atrophicus.
- It is an inflammatory condition which usually **affects the genitalia and is more common in elderly females.**
- Lichen sclerosus leads to atrophy of the epidermis with white plaques forming

Features

- itch is prominent

Diagnosis

- usually made on clinical grounds but a biopsy may be performed if atypical features are present*

Management

- topical steroids and emollients

Follow-up

- increased risk of vulval cancer

*the RCOG advise the following

- *Skin biopsy is not necessary when a diagnosis can be made on clinical examination. Biopsy is required if the woman fails to respond to treatment or there is clinical suspicion of VIN or cancer.*

and the British Association of Dermatologists state the following:

- A confirmatory biopsy, although ideal, is not always practical, particularly in children. It is not always essential when the clinical features are typical. However, histological examination is advisable if there are atypical features or diagnostic uncertainty and is mandatory if there is any suspicion of neoplastic change.
- **Patients under routine follow-up will need a biopsy if:**
 - (i) there is a suspicion of neoplastic change, i.e. a persistent area of hyperkeratosis, erosion or erythema, or new warty or papular lesions;
 - (ii) the disease fails to respond to adequate treatment;
 - (iii) there is extragenital LS, with features suggesting an overlap with morphea;
 - (iv) there are pigmented areas, in order to exclude an abnormal melanocytic proliferation;
 - (v) second-line therapy is to be used.

Lichen simplex chronicus (LSC)

- LSC presents with hyperpigmented, scaly, lichenified plaques.
- Patients may volunteer a history of chronic scratching or manipulation, especially during times of stress.
- The ankles are common sites for LSC.



Lichen amyloidosis

- Lichen amyloidosis is a primary, localised cutaneous amyloidosis (amyloid deposition in the skin).
- It results in intensely itchy shiny or hyperkeratotic, pigmented macules and occurs most commonly in South East Asia.
- It appears that itching drives further amyloid deposition, and treatments are therefore directed at reducing the sensation of itching - for example, with the use of antihistamines and intra-lesional/topical corticosteroids.



Lichen amyloidosis

Onycholysis

Onycholysis describes the separation of the nail plate from the nail bed

Causes

- idiopathic
- trauma e.g. Excessive manicuring
- infection: especially fungal
- skin disease: psoriasis, eczema, dermatitis
- impaired peripheral circulation e.g. Raynaud's
- systemic disease: hyper- and hypothyroidism
- **Tetracycline**

Parvovirus B19

Parvovirus B19 is a DNA virus which causes a variety of clinical presentations. It was identified in the 1980's as the cause of erythema infectiosum

Erythema infectiosum (also known as fifth disease or 'slapped-cheek syndrome')

- most common presenting illness
- systemic symptoms: lethargy, fever, headache
- 'slapped-cheek' rash spreading to proximal arms and extensor surfaces

Other presentations

- asymptomatic
- pancytopenia in immunosuppressed patients
- aplastic crises e.g. in sickle-cell disease (parvovirus B19 suppresses erythropoiesis for about a week so aplastic anaemia is rare unless there is a chronic haemolytic anaemia)

Pityriasis rosea

- describes an acute, self-limiting rash which tends to affect young adults. occurs most commonly in people between the ages of 10 and 35 years.
- The aetiology is not fully understood but is thought that herpes hominis virus 7 (HHV-7) may play a role. does not appear to be contagious;
- aetiology is unknown

Features

- herald patch (usually on trunk)
- followed by **erythematous, oval, scaly patches** which follow a characteristic distribution with the longitudinal diameters of the oval lesions running parallel to the line of Langer. This may produce a 'fir-tree' appearance
- can be pruritic or asymptomatic

Management

- self-limiting, usually disappears after 4-12 weeks
- moisturisers can help the pruritus



On the left a typical herald patch is seen. After a few days a more generalised 'fir-tree' rash appears

Pityriasis versicolor

also called tinea versicolor, is a superficial cutaneous fungal infection caused by *Malassezia furfur* (formerly termed *Pityrosporum ovale*)

Features

- most commonly affects trunk
- patches may be hypopigmented, pink or brown (hence versicolor)
- scale is common
- mild pruritus

Predisposing factors

- occurs in healthy individuals
- immunosuppression
- malnutrition
- Cushing's

Management

- topical antifungal. NICE Clinical Knowledge Summaries advise ketoconazole shampoo as this is more cost effective for large areas
- **Topical selenium sulphide**
- if extensive disease or failure to respond to topical treatment then consider oral itraconazole 200 mg once a day for seven days.

Psoriasis

Definition

- Psoriasis is a chronic relapsing inflammatory skin disorder most commonly characterised by erythematous, sharply demarcated papules and rounded plaques covered by silvery scales.

Epidemiology

- prevalence around 2%.
- there are two peaks of incidence at 16-22 years and 57-60 years.
- Males and females are equally affected.

Pathophysiology

- multifactorial and not yet fully understood
 - ⇒ genetic:
 - polygenic inheritance

- associated HLA-B13, -B17, and -Cw6.
- European populations are commonly affected,
- Strong concordance (70%) in identical twins
- ⇒ immunological:
 - abnormal T cell activity stimulates keratinocyte proliferation.
 - ❖ may be mediated by T helper cells producing **IL-17**.
 - ❖ IL-17 is a pro-inflammatory cytokine which is expressed at high levels in psoriasis lesions.
 - ❖ Ixekizumab is an **anti-IL-17 antibody** which binds to IL-17, it is effective in treating active psoriasis and in reducing the risk of recurrence.
- ⇒ environmental:
 - psoriasis may be worsened (e.g. Skin trauma, stress), triggered (e.g. Streptococcal infection) or improved (e.g. Sunlight) by environmental factors
- increase in mitotic activity of the cells in the malpighian layer of the epidermis
 - ⇒ The Malpighian layer of the skin is generally defined as both the stratum basalis and stratum spinosum as a unit.

Recognised subtypes of psoriasis

- **plaque psoriasis:** the most common sub-type resulting in the typical well demarcated red, scaly patches affecting the extensor surfaces, sacrum and scalp
- **flexural psoriasis:** in contrast to plaque psoriasis the skin is smooth
- **guttate psoriasis:** transient psoriatic rash frequently triggered by a streptococcal infection. Multiple red, teardrop lesions appear on the body
- **pustular psoriasis:** commonly occurs on the palms and soles



Features

- **Salmon colored skin plaques with silvery scales**
- Psoriasis may occur in **hidden sites**, such as the scalp (where psoriasis frequently is mistaken for dandruff), perineum, intergluteal cleft, and umbilicus
 - ⇒ The scalp is often involved in psoriasis. Most commonly, it causes a telogen effluvium, that is, the hair follicles are forced into the telogen resting stage.

Other features

- nail signs: pitting, onycholysis
- arthritis
- New lesions often appear at sites of injury or trauma (**Koebner phenomenon**), which typically occurs one to two weeks after the skin has been damaged.
- Auspitz sign: small bleeding spots when psoriasis scales are scraped off.
- Psoriasis can be associated with an anterior uveitis

Complications

- **psoriatic arthropathy** (around 10%)
 - ⇒ This can range from mild distal interphalangeal joint involvement with nail pitting to severe arthritis mutilans.

- increased incidence of metabolic syndrome
- **increased incidence of cardiovascular disease**
- increased incidence of venous thromboembolism
- psychological distress

Diagnosis

- usually clinical
- skin biopsy is rarely required to confirm psoriasis.
 - ⇒ Hyperkeratosis (described as an increased thickness of the stratum corneum),
 - ⇒ Parakeratosis, defined as hyperkeratosis with retention of nuclei in the stratum corneum,
 - ⇒ **Munro's microabscess** (or neutrophils) in the stratum corneum of the epidermis are a cardinal sign

Exacerbating factors

Psoriasis: common triggers are beta-blockers and lithium

- trauma
- alcohol
- drugs:
 - ⇒ **beta blockers**,
 - ⇒ **lithium**,
 - ⇒ **antimalarials (chloroquine and hydroxychloroquine)**,
 - ⇒ gold salts,
 - ⇒ NSAIDs,
 - ⇒ ACE inhibitors,
 - ⇒ infliximab
 - ⇒ antibiotics such as tetracycline and penicillin
- withdrawal of systemic steroids
- **Notes**
 - ⇒ Reactions may occur from less than one month to one year after the medication is initiated.
 - ⇒ the effect of antimalarials on trans-glutaminase activity leads to stimulation of epidermal proliferation
 - ⇒ **beta blockers** is more common than ACEi

Management

Topical potent corticosteroid + vitamin D analogue is first-line for chronic plaque psoriasis

Management of chronic plaque psoriasis

- regular emollients may help to reduce scale loss and reduce pruritus
- **First-line:**
 - ⇒ **potent corticosteroid applied once daily plus vitamin D analogue applied once daily** (applied separately, one in the morning and the other in the evening) for up to 4 weeks as initial treatment
- **Second-line:**
 - ⇒ if no improvement after 8 weeks then offer a **vitamin D analogue twice daily**
- **Third-line:**
 - ⇒ if no improvement after 8-12 weeks then offer either: a potent **corticosteroid applied twice daily** for up to 4 weeks or a coal tar preparation applied once or twice daily

- short-acting dithranol can also be used

Using topical steroids in psoriasis

- as we know topical corticosteroid therapy may lead to skin atrophy, striae and rebound symptoms
- systemic side-effects may be seen when potent corticosteroids are used on large areas e.g. > 10% of the body surface area
- NICE recommend that we aim for a 4 week break before starting another course of topical corticosteroids
- they also recommend using potent corticosteroids for no longer than 8 weeks at a time and very potent corticosteroids for no longer than 4 weeks at a time

What should I know about vitamin D analogues?

- examples of vitamin D analogues include calcipotriol (Dovonex), calcitriol and tacalcitol
- they work by reducing cell division and differentiation
- adverse effects are uncommon
- unlike corticosteroids they may be used long-term
- unlike coal tar and dithranol they do not smell or stain
- they tend to reduce the scale and thickness of plaques but not the erythema
- they should be avoided in pregnancy
- the maximum weekly amount for adults is 100g



- A 'before and after' image showing the effect of 6 weeks of calcipotriol therapy on a large plaque. Note how the scale has improved but the erythema remains

Steroids in psoriasis

- topical steroids are commonly used in flexural psoriasis and there is also a role for mild steroids in facial psoriasis. If steroids are ineffective for these conditions vitamin D analogues or tacrolimus ointment should be used second line
- patients should have 4 week breaks between course of topical steroids
- very potent steroids should not be used for longer than 4 weeks at a time. Potent steroids can be used for up to 8 weeks at a time
- the scalp, face and flexures are particularly prone to steroid atrophy so topical steroids should not be used for more than 1-2 weeks/month

Scalp psoriasis

Scalp psoriasis - first-line treatment is topical potent corticosteroids

- First line
 - ⇒ potent topical corticosteroids used once daily for 4 weeks
 - ⇒ if no improvement after 4 weeks go to second line
- Second line
 - ⇒ use different formulation of the potent corticosteroid (for example, a shampoo or mousse) **and/or**
 - ⇒ topical agents to remove adherent scale (for example, agents containing salicylic acid, emollients and oils) before application of the potent corticosteroid

Face, flexural and genital psoriasis

Flexural psoriasis - topical steroid

- mild or moderate potency corticosteroid applied once or twice daily for a maximum of 2 weeks
eg: clobetasone butyrate once a day

Secondary care management

Phototherapy

- narrow band ultraviolet B-light is now the treatment of choice. If possible this should be given 3 times a week
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy

• Indications

- ⇒ topical are not effective **and**
- ⇒ person is impacted physically, psychologically, or socially by the problem **and**
- ⇒ one or more of the following apply:
 - extensive psoriasis (eg, > 10% of body surface area affected or a PASI score of > 10) **or**
 - localised psoriasis and associated with significant functional impairment and/or high levels of distress (for example severe nail disease or involvement at high-impact sites) **or**
 - phototherapy has been ineffective, cannot be used or has resulted in rapid relapse (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months).

- **Methotrexate**
 - ⇒ **Oral methotrexate is used first-line.** It is particularly useful if there is associated joint disease
- **Ciclosporin**
 - ⇒ Offer ciclosporin as the first choice in patients who need rapid or short-term disease control (for example a
 - psoriasis flare
 - palmoplantar pustulosis
 - or considering conception (both men and women) and systemic therapy cannot be avoided.
 - ⇒ Consider changing from methotrexate to ciclosporin (or vice-versa) when response to the first-choice systemic treatment is inadequate.
- **Systemic retinoids (acitretin)**
 - ⇒ if methotrexate and ciclosporin are not appropriate or have failed or
 - ⇒ for people with pustular forms of psoriasis.
- **biological agents:** infliximab, etanercept and adalimumab
 - ⇒ **In situation with uncontrolled psoriasis and psoriatic arthritis,** early instigation of a biological is recommended.
 - ⇒ TNF alpha is a pro-inflammatory cytokine closely linked to the severity of psoriasis, and **etanercept, a TNF alpha antagonist is the most appropriate intervention.**
 - ⇒ Tuberculosis and viral hepatitis should be ruled out prior to starting therapy.
 - ⇒ Brodalumab is an anti-IL17 monoclonal antibody which has completed registration trials for psoriasis. It's likely to be reserved however for patients who fail to gain control on other interventions.
- **ustekinumab** (IL-12 and IL-23 blocker) is showing promise in early trials
 - ⇒ it is not an anti- TNF agent (so did not reactivate TB)
 - ⇒ side effects:
 - **common → dental infection**
 - uncommon → depression and injection site reaction

Mechanism of action of commonly used drugs:

- coal tar; probably inhibit DNA synthesis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Contra-indication:

- Oral steroids are contraindicated in psoriasis and although one may see an initial improvement, a very serious rebound effect may be seen.

Question:

An elderly man with learning difficulties, is admitted to hospital with an acute exacerbation of congestive cardiac failure and severe raised plaques of psoriasis covering his chest, elbows, knees and scalp. he has been treating it with topical creams for years but has seen no improvement. What treatment would you recommend for his psoriasis?

→ **Refer for PUVA**

- The safest treatment - that which produces the best clinical effect with minimal side effects in this patient - would be psoralen and ultraviolet light (PUVA).
- Emollients, baths and use of methotrexate require a fair amount of input from the patient in order to be effective and safe, which may not be the best option in this man.

MRCPUK-part-1-sep 2017: Which medication is of most concern with respect to worsening of psoriasis?

⇒ **Atenolol**

Psoriasis: guttate

- Guttate psoriasis is more common in children and adolescents.
- It may be precipitated by a streptococcal infection 2-4 weeks prior to the lesions appearing

Features

- tear drop 'drop-like' papules on the trunk and limbs



Management

- if lesions are not widespread (<10% body surface area) and the person is not impacted physically, psychologically, or socially by the problem:**
 - ⇒ **No treatment required**
 - most cases resolve spontaneously within 2-3 months
- If the lesions are not widespread (<10% body surface area) and treatment is desired:
 - ⇒ topical agents as per psoriasis.
- If lesions are widespread ($>10\%$ body surface area):
 - ⇒ **refer urgently to a dermatologist** as phototherapy (UVB phototherapy) can be considered.
- with recurrent episodes → referral to ENT should be considered → tonsillectomy may be necessary**
- Although guttate psoriasis can be triggered by an acute sore throat, it is not recommended to treat guttate psoriasis with anti-streptococcal antibiotics.

Differentiating guttate psoriasis and pityriasis rosea

	Guttate psoriasis	Pityriasis rosea
Prodrome	Classically preceded by a streptococcal sore throat 2-4 weeks	Many patients report recent respiratory tract infections but this is not common in questions
Appearance	'Tear drop', scaly papules on the trunk and limbs	Herald patch followed 1-2 weeks later by multiple erythematous, slightly raised oval lesions with a fine scale confined to the outer aspects of the lesions. May follow a characteristic distribution with the longitudinal diameters of the oval lesions running parallel to the line of Langer. This may produce a 'fir-tree' appearance
Treatment / natural history	Most cases resolve spontaneously within 2-3 months Topical agents as per psoriasis UVB phototherapy	Self-limiting, resolves after around 6 weeks



Guttate psoriasis

- A 46-year-old man presents with an extensive pruritic rash shown in picture A.
- Two weeks previously he had a sore throat with the appearance shown in picture B.

Pyoderma gangrenosum



Overview

- Pyoderma gangrenosum typically is an expanding ulcer with a polycyclic or serpiginous outline and a characteristic undermined bluish edge.
- The pathogenesis is unknown, and is presumed to be immunological.

Features

- typically on the lower limbs
 - It is most common on the lower limb and in scars or sites of previous trauma.
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

Causes

- idiopathic in 50%
- inflammatory bowel disease: **ulcerative colitis**, Crohn's
 - Estimates of the prevalence in inflammatory bowel disease (IBD) range between 2% and 5%.
 - It tends to be associated with colonic involvement and is perhaps **slightly more common in patients with UC**.
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

Management

- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

Scabies



- Scabies is caused by the mite *Sarcoptes scabiei* and is spread by prolonged skin contact.
- It typically affects children and young adults.
- The scabies mite burrows into the skin, laying its eggs in the stratum corneum.
- The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

Features

- widespread pruritus
 - ⇒ **Scabies can present with an itchy dermatitic-looking rash on the body, but the clues are at certain sites (soles, genitalia, buttocks)**
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
 - ⇒ **Burrows (linear crusted lesions of a few millimetres in length) are pathognomonic**
 - ⇒ **It has a predilection for the web-spaces and around the nipples.**
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

Management

- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication

Patient guidance on treatment (from Clinical Knowledge Summaries)

- permethrin cream doesn't have any direct effect on the pruritis itself but helps to settle symptoms indirectly by killing the mite, which is the root cause.
- You should counsel your patients that it may take longer for the itching to settle as the allergic reaction to the mite abates
- the cream should be applied everywhere below the neck, not merely where there is rash present.
- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic
- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation.

Patients should be given the following instructions:

- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8-12 hours for permethrin, or for 24 hours for malathion, before washing off

- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

Crusted (Norwegian) scabies

- Crusted scabies is seen in patients with suppressed immunity, especially HIV.
- The crusted skin will be teeming with hundreds of thousands of organisms.
- Ivermectin is the treatment of choice and isolation is essential

Seborrhoeic dermatitis

- Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called **Malassezia furfur** (formerly known as *Pityrosporum ovale*).
- It is common, affecting around **2% of the general population**

Features

- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

Associated conditions

- **HIV**
 - ⇒ **in patients with HIV the prevalence of seborrhoeic dermatitis may be as high as 80%.**
 - ⇒ **the most useful next step → HIV testing**
- Parkinson's disease

Scalp disease management

- Dandruff is an uninflamed form of seborrhoeic dermatitis and presents as scaly patches scattered within hair-bearing areas of the scalp.
- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

Face and body management

Seborrhoeic dermatitis - first-line treatment is topical ketoconazole

- topical antifungals: e.g. Ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

Skin disorder in pregnancy

Polymorphic eruption of pregnancy

Polymorphic eruption of pregnancy is not associated with blistering

- also known as Pruritic Urticarial Papules and Plaques of Pregnancy (PUPPP)
- pruritic condition associated with last trimester
- lesions often first appear in abdominal striae
- management depends on severity: emollients, mild potency topical steroids and oral steroids may be used



Polymorphic eruption of pregnancy



Polymorphic eruption of pregnancy

Pemphigoid gestationis

- **Definition**
 - ⇒ bullous disorder that typically develops in the second or third trimester, beginning with urticarial lesions and blisters on the anterior abdominal wall surrounding the umbilicus.
- **Features**
 - ⇒ pruritic blistering lesions
 - ⇒ often develop in peri-umbilical region, later spreading to the trunk, back, buttocks and arms
 - ⇒ usually presents 2nd or 3rd trimester and is rarely seen in the first pregnancy
- **Diagnosis**
 - ⇒ A perilesional skin biopsy demonstrating linear C3 deposition at the dermoepidermal junction would confirm the diagnosis.
- **Treatment**
 - ⇒ oral corticosteroids are usually required



Pemphigoid gestationis



Pemphigoid gestationis

Melasma

- Melasma is a benign but relatively common skin condition which can appear in pregnancy.
- it may resolve a few months after delivery.

Chloasma

- **Overview**
 - ⇒ Chloasma is a hormonally stimulated increase in melanogenesis that mainly appears on the face.
 - ⇒ The pigment is augmented by sunlight
 - ⇒ On testing, levels of melanocyte-stimulating hormone are normal
 - ⇒ more likely to occur in women with darker skin tones
- **Causes**
 - ⇒ **Pregnancy**
 - ⇒ combined oral contraceptive pill
- **Treatment**
 - ⇒ The pigmentation may take many months to resolve after parturition or pill discontinuation
 - ⇒ avoid prolonged sunlight exposure or to use a sunblock

Skin disorders associated with tuberculosis

Possible skin disorders

- ***lupus vulgaris* (accounts for 50% of cases)**
- erythema nodosum
- scarring alopecia
- scrofuloderma: breakdown of skin overlying a tuberculous focus
- verrucosa cutis
- gumma

Lupus vulgaris

- the most common form of cutaneous TB seen in the Indian subcontinent.
- Cutaneous TB usually occurs due to spread from an endogenous source
- It generally occurs on the face and is common around the nose and mouth.
 - ⇒ more than 80% of cases occur on the face and neck.
- The initial lesion is an erythematous flat plaque which gradually becomes elevated and may ulcerate later

- Diagnosis: On diascopy, it shows characteristic "apple-jelly" color. Biopsy will reveal tuberculoid granuloma with few bacilli. Mantoux test is positive.
- Treated with combination of drugs used for tuberculosis, such as Rifampicin, Isoniazid and Pyrazinamide (with either streptomycin or ethambutol)

Spider nevi

- most common on the face and upper chest.
- typically asymptomatic
- usually resolve spontaneously.
- Causes
 - ⇒ chronic liver disease
 - the presence of more than five lesions is likely to be due to chronic liver disease.
 - may resolve when liver function increases or when a liver transplant is performed.
 - **the cause of the spider nevi → patients cannot metabolize circulating estrogen**
 - ⇒ pregnancy
 - may resolve after childbirth.
 - ⇒ oral contraceptives,
 - may resolve after stopping the contraceptives.



forehead lesion (spider nevus (nevus araneus))

Tinea

- Tinea is a term given to dermatophyte fungal infections.
- Three main types of infection are described depending on what part of the body is infected
 1. tinea capitis - scalp
 2. tinea corporis - trunk, legs or arms
 3. tinea pedis - feet

Tinea capitis (scalp ringworm)

- a cause of scarring alopecia mainly seen in children
- if untreated a raised, pustular, spongy/boggy mass called a kerion may form
- Causes
 - ⇒ **most common cause is *Trichophyton tonsurans*** in the UK and the USA (>90% of cases)
 - ⇒ may also be caused by *Microsporum canis* acquired from cats or dogs
- Diagnosis:

- ⇒ the most useful investigation is scalp scrapings
- ⇒ lesions due to *Microsporum canis* green fluorescence under Wood's lamp (but do not fluoresce if caused by *Trichophyton tonsurans*). lesions due to *Trichophyton* species do not readily fluoresce under Wood's lamp
- **Management** (based on CKS guidelines): oral antifungals:
 - ⇒ **Terbinafine** for *Trichophyton tonsurans* infections
 - Although not licensed in young children, a **four-week** course of the **fungicidal** drug terbinafine is often preferred.
 - ⇒ **griseofulvin** for *Microsporum* infections.
 - Griseofulvin is **fungistatic**, so a prolonged course of **2-4 months** is required.
 - ⇒ Topical ketoconazole shampoo should be given for the first two weeks to reduce transmission



Image showing a kerion

griseofulvin

The enzyme that is most likely induced by griseofulvin requires which of the following cofactors?

⇒ **Vitamin B₆**

- Griseofulvin is a microtubule poison that is used to treat skin and nail dermatophytoses
- strong inducer of cytochrome P450 enzymes.
- CYP450 enzymes require heme for proper function, and thus inducers of CYP450 increase heme synthesis.

Tinea corporis (ringworm)

- causes include *Trichophyton rubrum* and *Trichophyton verrucosum* (e.g. From contact with cattle)
- well-defined annular, erythematous lesions with pustules and papules
- may be treated with oral fluconazole



Image showing tinea corporis



Image showing tinea corporis. Note the well defined border

Tinea pedis (athlete's foot)

- characterised by itchy, peeling skin between the toes
- common in adolescence

Tinea incognito

- **What is the cause for tinea incognito?**
⇒ Inappropriate treatment with steroid cream
- Tinea incognito is the name given to tinea when the clinical appearance has been altered by inappropriate treatment, usually a topical steroid cream
- The result is that the original infection slowly extends Often the patient and/or their doctor believe they have a dermatitis, hence the use of a topical steroid cream
- The steroid cream dampens down inflammation so the condition feels less irritable But when the cream is stopped for a few days the itch gets worse, so the steroid cream is promptly used again
- The more steroid applied, the more extensive the fungal infection becomes

Vitiligo

Definition

- Vitiligo is an autoimmune condition which results in the loss of melanocytes and consequent depigmentation of the skin.

Epidemiology

- It is thought to affect around 1% of the population
- symptoms typically develop by the age of 20-30 years.

Features

- well demarcated patches of depigmented skin
- the peripheries tend to be most affected
- trauma may precipitate new lesions (Koebner phenomenon)

Associated conditions

- type 1 diabetes mellitus
- Addison's disease
- autoimmune thyroid disorders
- pernicious anaemia
- alopecia areata

Diagnosis

- Diagnosis is made clinically
- anti-melanocyte antibodies
- can be confirmed using a skin biopsy.

Management

- sun block for affected areas of skin
- camouflage make-up
- topical corticosteroids may reverse the changes if applied early
- there may also be a role for topical tacrolimus and phototherapy, although caution needs to be exercised with light-skinned patients



Vitiligo

Angular stomatitis

- Angular stomatitis describes erythema and fissuring of the skin adjacent to the angle of the mouth.
- The most common cause is *Candida* infection
- also associated with:
 - ⇒ allergy,
 - ⇒ seborrhoeic dermatitis,
 - ⇒ vitamin B deficiencies,
 - ⇒ iron deficiency.

Venous ulceration

- Venous ulcers are secondary to venous stasis and chronic stretching of the walls of the superficial veins. These eventually become thinner and ulcerate.
- **typically seen above the medial malleolus**

The incidence of venous leg ulceration is higher in:

- obese patients
- history of varicose veins
- **history of deep vein thrombosis**

Ulcers occur owing to:

- venous stasis
- secondary increase in capillary pressure
- fibrosis
- poorly nourished skin particularly over areas such as the medial malleolus

Investigations

- **ankle-brachial pressure index (ABPI)** is important in non-healing ulcers to assess for poor arterial flow which could impair healing
 - ⇒ a 'normal' ABPI may be regarded as between 0.9 - 1.2.
 - ⇒ Values below 0.9 indicate arterial disease.
 - ⇒ Interestingly, values above 1.3 may also indicate arterial disease, in the form of false-negative results secondary to arterial calcification (e.g. In diabetics)

Management

Management of venous ulceration - compression bandaging

- compression bandaging, usually four layer (**only treatment shown to be of real benefit**)
- **The mainstay of treatment of venous ulceration is compression therapy**, which aims to improve venous return and thereby reduce venous hypertension.
- The patient should always have their Doppler's and ABPI (ankle brachial pressure index) prior to compression. The ABPI should be greater than 1 before compression bandaging is used (this excludes significant arterial disease).
- oral pentoxifylline, a peripheral vasodilator, improves healing rate
- small evidence base supporting use of flavonoids
- little evidence to suggest benefit from hydrocolloid dressings, topical growth factors, ultrasound therapy and intermittent pneumatic compression

Pressure ulcers

Waterlow score - used to identify patients at risk of pressure sores

Overview

- Pressure ulcers develop in patients who are unable to move parts of their body due to illness, paralysis or advancing age.
- They typically develop over bony prominences such as the sacrum or heel. The following factors predispose to the development of pressure ulcers:
 - ⇒ malnourishment
 - ⇒ incontinence
 - ⇒ lack of mobility
 - ⇒ pain (leads to a reduction in mobility)
- The **Waterlow score** is widely used to screen for patients who are at risk of developing pressure areas. It includes a number of factors including body mass index, nutritional status, skin type, mobility and continence.

Grading of pressure ulcers

the following is taken from the European Pressure Ulcer Advisory Panel classification system.

Grade	Findings
Grade 1	Non-blanchable erythema of intact skin. Discolouration of the skin, warmth, oedema, induration or hardness may also be used as indicators, particularly on individuals with darker skin
Grade 2	Partial thickness skin loss involving epidermis or dermis, or both. The ulcer is superficial and presents clinically as an abrasion or blister
Grade 3	Full thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia.
Grade 4	Extensive destruction, tissue necrosis, or damage to muscle, bone or supporting structures with or without full thickness skin loss

Management

- a moist wound environment encourages ulcer healing. Hydrocolloid dressings and hydrogels may help facilitate this. The use of soap should be discouraged to avoid drying the wound
- wound swabs should not be done routinely as the vast majority of pressure ulcers are colonised with bacteria. The decision to use systemic antibiotics should be taken on a clinical basis (e.g. Evidence of surrounding cellulitis)
- consider referral to the tissue viability nurse
- surgical debridement may be beneficial for selected wounds

Keloid scars

Keloid scars are most common on the sternum

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

Predisposing factors

Keloid scars - more common in young, black, male adults

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk
- Keloid scars are less likely if incisions are made along relaxed skin tension lines*
 - ⇒ *Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

Treatment

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

Increased skin fragility

- Increased skin fragility is seen in a number of disorders and is used as a clinical test in bullous disorders (**Nikolsky's sign**).
- Other causes include:
 - ⇒ pemphigus vulgaris
 - ⇒ porphyria cutanea tarda
 - ⇒ drug reactions (especially pseudoporphyria).
- Other causes of increased skin fragility (not associated with bullae) include:
 - ⇒ long term corticosteroid therapy,
 - ⇒ Ehlers-Danlos syndrome
 - ⇒ curvy (vitamin C deficiency).

Basal cell carcinoma (BCC)

Overview

- Basal-cell carcinomas are the most common malignant skin tumour and are related to excessive sun exposure
 - ⇒ most commonly occurs in elderly patients with sun-damaged skin.
- Lesions are also known as rodent ulcers
- characterised by slow-growth and **local invasion**. Metastases are extremely rare.
- **BCC is the most common type of cancer in the Western world.**
- BCC is more commonly seen on the upper lip.

Genetics

- environmental and genetic factors are believed to predispose patients to BCC
- Basal cell carcinoma is associated with mutations in the Hedgehog signalling pathway.
- Up to 70% of people with sporadic BCC without Gorlin syndrome have patched **PTCH1** gene mutations as a result of UV radiation exposure.

Features

- many types of BCC are described. The most common type is nodular BCC.
- sun-exposed sites, especially the head and neck account for the majority of lesions
- initially a pearly, flesh-coloured papule with telangiectasia
- may later ulcerate leaving a central 'crater'
- characterized histologically by **palisading nuclei**.
 - ⇒ Palisading nuclei consist of parallel rows of elongated nuclei.

Management

- surgical removal
 - ⇒ Mohs surgery for is useful for minimizing the amount of safety margin excised.
- curettage
- cryotherapy
- topical cream: imiquimod, **5- fluorouracil**
- radiotherapy



BCC VS SCC

Basal cell carcinoma	Squamous cell carcinoma
Most common	2 nd most common
Present in upper part of face	Present in lower part of face (appear most often on the lower lip, ear, and nose.)
Does not metastasize and kill by local invasion(rodent ulcer)	Can metastasize
presents as a “pearly” papule or nodule that grows slowly with shiny appearance with telangiectasias and an umbilicated center or ulcer	usually hyperkeratotic scaly lesion with crusting and ulceration. often well-defined, superficial, discrete, and hard lesions arising from an indurated, rounded, and elevated base

Squamous cell carcinoma (SCC)

Overview

- SCC is the second most common non-melanoma skin cancer worldwide (after basal cell cancer).
- SCC is the most common oral cancer.
- More common in elderly males.
- It is possible to get SCC on any part of the body, including the inside of the mouth, lips, and genitals.
- Women frequently get SCC on their lower legs.

Precursor and variants of SCC:

- **Actinic keratoses** presents as hyperkeratotic grey-white plaques and is a precursor lesion to squamous cell carcinoma of the skin.
 - ⇒ Precursor lesions for SCCs are called actinic (or sun-damage) keratoses

- **Keratoacanthoma** is a cup-shaped form of squamous cell carcinoma of the skin that develops rapidly and resolves spontaneously.

Risk factors

- photo-exposed skin such as face and lower lips.
 - ⇒ often caused by **ultraviolet B-light**, which can mutate DNA via the formation of pyrimidine dimers.
 - ⇒ exposure to ultraviolet radiation (UV), especially UVB → **Mutations in the p53 tumour suppression gene**
 - ⇒ commonly affects the lower lip.
- The incidence of skin cancer has been increasing among Caucasians but remains relatively low in people of color.
 - ⇒ Light-skinner, non-Hispanic white populations experience higher rates of SCC than darker people of color.
 - ⇒ Low incidence in darker skins due to photo-protection provided by increased epidermal melanin, which filters twice as much ultraviolet (UV) radiation
 - ⇒ When skin cancer occurs in **people of color**, patients often present with an advanced stage, and thus, **worse prognosis** in comparison to Caucasian patients
- Chronic immunosuppression
 - ⇒ more common in patients who have received an **organ transplant**.
- **old scars** or burns
 - ⇒ may arise from areas of Bowen's disease and sometimes in the margin of a chronic leg ulcer.
 - ⇒ (SCC) arising on a scar is termed a **Marjolin ulcer**.
 - **Marjolin ulcer is typically aggressive** and associated with a poor prognosis.
- **arsenic exposure**
- ionizing radiation
- HPV infection
- chronic infections, particularly those associated with chronically draining sinuses.
- actinic keratoses and Bowen's disease
- Inherited syndromes: eg: xeroderma pigmentosum and albinism
- smoking

Features

- usually appears as a **scaly** or crusty area of skin, with a red, inflamed base.

Diagnosis

- Excision biopsy is essential for accurate diagnosis.
 - ⇒ shows keratin pearl appearance.
 - ⇒ The presence of **keratin pearls** indicates that the tumor is well-differentiated and **carries a better prognosis**.
 - undifferentiated tumor would contain almost entirely atypical cells that have lost their keratin producing function and thus keratin pearls would be absent.

Treatment

- Treatments include non-surgical destruction (e.g., using cryotherapy), topical chemotherapy, traditional surgical excision, and Mohs micrographic surgery.
- Surgical excision with 4mm margins if lesion <20mm in diameter. If tumour >20mm then margins should be 6mm.
- Mohs surgery is the best surgical treatment to minimize the loss of normal tissue.
- Radiotherapy is the treatment of choice in patients who are poor surgical candidates.
- Chemotherapy is used as adjuvant therapy in high risk patients

Prevention

- Sunscreen is used to minimize risk of developing SCC.

Prognosis

Good Prognosis	Poor prognosis
Well differentiated tumours	Poorly differentiated tumours
<20mm diameter	>20mm in diameter
<2mm deep	>4mm deep
No associated diseases	Immunosuppression for whatever reason

Keratoacanthoma (KA)



Overview

- Keratoacanthoma (KA) is a relatively common low-grade malignancy that originates in the pilosebaceous glands and resembles squamous cell carcinoma (SCC) pathologically.
- Some experts support classifying KA as a variant of invasive SCC.
- Keratoacanthoma is a benign epithelial tumour.
- It is believed to develop from the hair follicle,
- more common in males.
- They are more frequent in middle age and do not become more common in old age (unlike basal cell and squamous cell carcinoma)
- KA is characterised by rapid growth over a few weeks to months, followed by spontaneous resolution over four to six months in most cases.
- Lesions typically are solitary and begin as firm, roundish, skin-coloured or reddish papules that rapidly progress to dome-shaped nodules with a smooth shiny surface and a central crateriform ulceration or keratin plug that may project like a horn.

Features - said to look like a volcano or crater

- initially a smooth dome-shaped papule
- rapidly grows to become a crater centrally-filled with keratin

Treatment

- **The most suitable management → Urgent referral to dermatology**
- Spontaneous regression of keratoacanthoma within 3 months is common, often resulting in a scar.
- Should be urgently excised as it is difficult clinically to exclude squamous cell carcinoma. Removal also may prevent scarring.

Actinic keratoses

Overview

- Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure
- Less than 10% of actinic keratoses progress to invasive squamous cell carcinoma.

Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

Management

- prevention of further risk: e.g. sun avoidance, sun cream
- **fluorouracil cream:** typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

Malignant melanoma

Overview

- **Melanocytes are positioned in the basal layer of the epidermis**
- Melanoma is the third most common skin cancer, but is the most common cause of skin cancer-related death.
- Up to 20% of patients develop metastatic disease.

The mnemonic of ABCDE regarding characteristics of a melanoma are as follows:

- **A** - Asymmetry - one half of the lesion does not match the other half
- **B** - Border irregularity
- **C** - Colour variegation - pigmentation is not uniform
- **D** - Diameter- a diameter 7 mm warrants investigation although changes in size are also important
- **E** - Evolution - evolving size or changes in characteristics such as nodules.

Prognostic factors

Melanoma: the invasion depth of the tumour is the single most important prognostic factor

The invasion depth of a tumour (Breslow depth) is the single most important factor in determining prognosis of patients with malignant melanoma

Breslow Thickness	Approximate 5 year survival
< 1 mm	95-100%
1 - 2 mm	80-96%
2.1 - 4 mm	60-75%
> 4 mm	50%

Treatment

- Vemurafenib is a small molecule inhibitor of *BRAF* oncogene that can be found in melanoma. As such, Vemurafenib is used to treat metastatic melanoma.

Lentigo maligna

- Lentigo maligna is a type of melanoma in-situ.
- It typically progresses slowly but may at some stage become invasive causing lentigo maligna melanoma.
- Lentigo maligna melanoma occurs on the sun-exposed skin areas (usually the face) of elderly patients

Acral lentiginous melanoma

- The acral lentiginous melanoma is normally seen on the sole of the foot, and occasionally on the palm of the hand
- It is characterised by a raised darker area surrounded by a paler macular (lentiginous) area that may extend for several centimetres around the raised area
- There are two clinical clues that lead us to suspect this diagnosis: the patient's race and the location of the lesion.
 - Acral lentiginous melanoma is more common in African-Americans and Asians than other forms of melanoma.
 - the lesion is located in an area not exposed to sunlight (the sole of the foot is the most common place for this type of melanoma).

Other notes

- Patients with a **strong family history of melanoma** are more likely to harbor a mutation in the cyclin-dependent kinase inhibitor 2A tumor-suppressor gene (**CDKN2A mutation**) that codes for p16, which prevents progression through G1.
- Periungual melanomas occur in the area of the nailbed
- Hutchinson's sign (brown pigmentation on the nailfold) is an important pointer to malignant melanoma
- Superficial spreading melanoma is the commonest type, consisting of an irregular brown, black or blue-black lesion with some intermingled inflammation
- Nodular melanoma:**
 - the most rapidly growing and aggressive variant and may contain relatively little melanin pigment
 - associated with higher rates of metastasis and poorer outcomes than classic melanoma.

Moles

- Uniform pigmentation is not in itself a suspicious feature of a mole, but colour variegation and irregular border are two of many suspicious features.

Systemic mastocytosis

Results from a neoplastic proliferation of mast cells

Features

- urticaria pigmentosa - produces a wheal on rubbing (Darier's sign)
- flushing
- abdominal pain
- monocytosis on the blood film

Diagnosis

- raised serum tryptase levels
- urinary histamine

Angiosarcoma

- Angiosarcomas are malignant vascular tumours most commonly seen in elderly men.
- most commonly occur on the scalp and forehead.
- present an infiltrative vascular patch or plaque with super-imposed nodules which may bleed with minor trauma.
- poor prognosis.
- Angiosarcomas can also occur in areas of chronic lymphoedema.



Pyogenic granuloma



Overview

- relatively common benign skin lesion
- benign vascular lesion of the skin and mucosa.
- The name is a double misnomer - the lesion is neither pyogenic nor a granuloma.
- There are multiple alternative names but perhaps 'eruptive haemangioma' is the most useful.
- Pathologically, it is an inflammatory lesion composed of granulation tissue and chronic inflammatory cells.

Etiology

- unknown
- associated with trauma and pregnancy

Epidemiology

- more common in women and young adults

Features

- initially soft, round, bright red spot
- usually solitary lesions,
- Lesions often grow rapidly (**over weeks**),
- **tender and bled easily when touched.**

Localization

- The most common location are:
 - ⇒ fingers (**commonly involve the digits**)
 - ⇒ mucosal surfaces of the mouth
 - ⇒ inner surfaces of the nose.

Treatment

- lesions associated with pregnancy often resolve spontaneously post-partum
- other lesions usually persist.
- surgical excision
 - ⇒ Removal methods include curettage and cauterisation, cryotherapy, excision



Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	Associated malignancies
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Ovarian and lung cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bulous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

Acrokeratosis paraneoplastica

A widespread psoriatic-type rash involving the ears is suggestive of acrokeratosis paraneoplastica.

- Most acrokeratosis paraneoplastica cases are **associated with squamous cell carcinoma** of the upper one third of the respiratory or GI tract, i.e. the oropharynx, larynx, lungs or oesophagus.
 - ⇒ The symptoms of indigestion and food sticking fit best with a diagnosis of oesophageal carcinoma.

Otitis externa

Otitis externa is a common reason for primary care attendance in the UK.

Causes of otitis externa include:

- infection: bacterial (*Staphylococcus aureus*, *Pseudomonas aeruginosa*) or fungal
- seborrhoeic dermatitis
- contact dermatitis (allergic and irritant)

Features

- ear pain, itch, discharge
- otoscopy: red, swollen, or eczematous canal

Management

- **Initial management**
 - ⇒ topical antibiotic or a combined topical antibiotic with steroid
 - ⇒ if the tympanic membrane is perforated aminoglycosides are traditionally not used. many ENT doctors disagree with this and feel that concerns about ototoxicity are unfounded
 - ⇒ if there is canal debris then consider removal
 - ⇒ if the canal is extensively swollen then an ear wick is sometimes inserted
- **Second line options include**
 - ⇒ consider contact dermatitis secondary to neomycin
 - ⇒ oral antibiotics if the infection is spreading
 - ⇒ taking a swab inside the ear canal
 - ⇒ empirical use of an antifungal agent
- **Malignant otitis externa**
 - ⇒ more common in elderly diabetics.
 - ⇒ In this condition there is extension of infection into the bony ear canal and the soft tissues deep to the bony canal.
 - ⇒ Intravenous antibiotics may be required.

Livedo reticularis (LR)

Definition

- A vascular syndrome that can be caused by either benign autonomic dysregulation of cutaneous perfusion or pathological obstruction of blood vessels.

Pathophysiology

- Physiological livedo (idiopathic livedo): primary livedo

- ⇒ Autonomic dysregulation (functional disturbance) causing slowed cutaneous perfusion in response to external factors (i.e., cold). **Triggered by cold, regresses after application of warmth.**
- Pathological livedo (livedo racemosa): secondary livedo
 - ⇒ Localized obstructions slow the blood flow (organic disturbance). Persists after warming the skin.

Features

- Patchy, reticulated, vascular network with a red-blue or violaceous discolouration of the skin.
- A "**fish-net like**" **mottling of the skin**
- Occur more in women than in men and usually in the 3rd decade of life.
- Occurs most often in the lower extremities



Causes

It is mainly idiopathic (primary livedo reticularis is the most common cause)

Causes Secondary livedo reticularis:

- **Obstruction / vasculopathy**
 - ⇒ Antiphospholipid syndrome
 - Livedo racemosa is the most common dermatologic presentation in patients with antiphospholipid syndrome (APS), presenting in 25% of patients with primary APS and in 70% of patients with SLE-associated APS.
 - ⇒ Cryoglobulinaemia
 - ⇒ Polycythaemia rubra vera
 - ⇒ Multiple myeloma
 - ⇒ Cold agglutinin disease
 - ⇒ Protein C and S deficiency
 - ⇒ Antithrombin III deficiency
 - ⇒ Disseminated intravascular coagulation
 - ⇒ Haemolytic uraemic syndrome
 - ⇒ Emboli (DVT , cholesterol emboli and septic emboli)
 - ⇒ Hypercalcaemia (calcium deposits)
 - ⇒ Infections (syphilis, tuberculosis, Lyme disease)
- **Autoimmune / vasculitis / connective tissue disease**
 - ⇒ Small, medium and large vessel vasculitis.
 - ⇒ SLE
 - ⇒ Dermatomyositis
 - ⇒ Rheumatoid arthritis
 - ⇒ Polyarteritis nodosa

- **Drugs**
 - ⇒ **Amantadine** (dopamine agonist used to treat Parkinson disease) causes livedo through arteriolar vasospasm provoked by catecholamines.
 - ⇒ **Minocycline**
- **Associations**
 - ⇒ LR preceded the onset of repeated attacks of pancreatitis in a patient with chronic pancreatitis.
 - ⇒ Primary fibromyalgia
 - ⇒ Congenital hypogammaglobulinemia.

Treatment

- Physiological : warmth. bath PUVA is a therapeutic option with the possibility of some success.
- Pathological : treat underline cause

Livedo reticularis that does not regress after application of warmth is indicative of an underlying vascular disease and requires treatment.

Hyperhidrosis describes the excessive production of sweat

Management

- topical aluminium chloride preparations are first-line. Main side effect is skin irritation
- iontophoresis: particularly useful for patients with palmar, plantar and axillary hyperhidrosis
- botulinum toxin: currently licensed for axillary symptoms
- surgery: e.g. Endoscopic transthoracic sympathectomy. Patients should be made aware of the risk of compensatory sweating

Seborrheic keratosis

- Seborrheic keratoses are the most common benign tumor in older individuals.
- and they develop from the proliferation of epidermal cells.
- No specific etiologic factors have been identified.
- Typical features include a warty and waxy surface with surface crypts and a stuck on appearance.
- They typically have an appearance of being stuck on the skin surface.
- Because they begin at a later age and can have a wart-like appearance, seborrheic keratoses are often called the "barnacles of aging."
- Most commonly they are several
- Can growths anywhere on the skin, except the palms and soles. Most often on the chest, back, head, or neck.
- Commonly used treatments include Curettage and cautery (C&C), and cryotherapy (for thinner lesions).



multiple seborrheic keratoses in an autosomally dominant mode of inheritance.

Solar keratosis

- hyperkeratotic lesion with underlying erythema.
- bleed when scratched
- Progression of these lesions to squamous cell skin cancer is slow
- **Topical 5-FU cream** used twice a day for 3–4 weeks usually achieves clearance of the lesion.
- Diclofenac gel requires a more prolonged treatment period (up to 12 weeks), meaning that it is the second-choice option for compliance reasons. It is useful where coverage of a larger area of skin is required.



solar keratosis (on scalp of elderly)

Telogen phase

- The telogen phase is the resting phase of the hair follicle.
- Due to extreme stress → shedding of hair leading to loss of thickness → loss of hair.
- **It occurs as a normal phenomenon one to three months after pregnancy.**
- No treatment is required (**only reassurance**) and hair thickness eventually recovers without further intervention.