Dermatology (with leprosy and STIs)

MBBS Recap: high-yield notes for revision

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Revision notes for the MEC PG entrance: the facts an examiner asks, grouped by the topics of the practice questions.

Skin structure and pigmentation

Epidermal layers (superficial to deep)

- **Corneum, lucidum, granulosum, spinosum, basale.** The **stratum lucidum exists only on thick skin (palms and soles)**; it holds eleidin.
- **Thickest living layer: spinosum** (prickle cells joined by **desmosomes**). **Thinnest of the layers present everywhere: granulosum**, one to three cells thick; keratohyalin granules (profilaggrin) and lamellar (**Odland**) bodies, which release the lipids of the skin barrier, are made here.
- **Basal layer**: dividing stem keratinocytes, **melanocytes** (about 1 in 10 basal cells), **Merkel cells**. Basal plus spinosum is the **Malpighian layer**.
- **The granular layer is lost over psoriatic plaques** and the corneum keeps its nuclei (**parakeratosis**); in **lichen planus** the granular layer is thickened in wedges (**wedge-shaped hypergranulosis**, seen clinically as Wickham's striae) and there is no parakeratosis.
- Terms: **hyperkeratosis** is a thick corneum; **parakeratosis** is nuclei kept in the corneum (psoriasis, eczema, actinic keratosis, seborrhoeic dermatitis, SCC); **acanthosis** is a thick spinosum; **spongiosis** is oedema between keratinocytes (eczema); **acantholysis** is loss of keratinocyte-to-keratinocyte adhesion (pemphigus); **dyskeratosis** is premature single-cell keratinisation (Darier disease).
- **Normal epidermal turnover (basal cell to shedding) is about 4 weeks** (transit through the corneum about 2 weeks); **in psoriasis it falls to 3–4 days**.
- The corneum is thin and the barrier poor in **preterm neonates**: more water loss and more absorption of anything applied.

The four epidermal cells

Cell	Origin	Site	Marker or product
Keratinocyte	Surface ectoderm	All layers	Keratins (K5/K14 basal, K1/K10 suprabasal)
Melanocyte	**Neural crest**	Basal layer	Melanosomes; **S-100, HMB-45, Melan-A, SOX10**
Langerhans cell	**Bone marrow** (monocyte–dendritic lineage)	**Spinosum** (suprabasal)	**Birbeck (tennis-racket) granules**; antigen-presenting; **CD1a, langerin (CD207)**
Merkel cell	Epidermal (keratinocyte) lineage on lineage tracing; older texts say neural crest	Basal layer	Slow-adapting touch receptor, neurosecretory granules; **CK20**

- **Langerhans cell histiocytosis**: Birbeck granules, **CD1a and langerin positive**; **BRAF V600E** in about half (now treated as a myeloid neoplasm; BRAF and MEK inhibitors in refractory disease).

Basement membrane zone (where blisters split)

Level	Component	Disease when it is the target
Basal keratinocyte	**Keratin 5 and 14**	**Epidermolysis bullosa simplex** (intraepidermal split)
Hemidesmosome	**BP180 (collagen XVII)**, BP230	**Bullous pemphigoid**, pemphigoid gestationis, some junctional EB
Lamina lucida	**Laminin 332**	**Junctional EB**; anti-laminin-332 mucous membrane pemphigoid (cancer link)
Lamina densa	Collagen IV	Alport syndrome (not a blistering disease)
Sublamina densa (anchoring fibrils)	**Collagen VII**	**Dystrophic EB**, **epidermolysis bullosa acquisita**, bullous SLE

- **Recessive dystrophic EB** (COL7A1): scarring, mitten hands, oesophageal strictures and **aggressive SCC in early adult life**. Current practice: **beremagene geperpavec** (topical HSV-1 vector carrying COL7A1, FDA 2023) and birch triterpene gel for its wounds.
- **Filaggrin** loss-of-function: **ichthyosis vulgaris** and atopic dermatitis.

Dermis and glands

- Papillary and reticular dermis; **type I collagen** is about 80% of dermal collagen, type III most of the rest.
- **Eccrine** glands: everywhere except lips, nail bed, glans and labia minora; densest on palms, soles and axillae; **sympathetic but cholinergic** (hence anticholinergic anhidrosis and botulinum toxin for hyperhidrosis).
- **Apocrine** glands: axillae, groin, areola, perianal; open into the follicle; active from puberty; adrenergic. Modified apocrine: ceruminous and **Moll's** glands. **Hidradenitis suppurativa** is now regarded as a disease of follicular occlusion, not of apocrine glands (adalimumab, secukinumab and bimekizumab approved, 2015–2024).
- **Sebaceous** glands: **holocrine**, androgen-driven, **absent on palms and soles**; free (not on a hair) as Fordyce spots, Meibomian glands and Montgomery's tubercles.

Pigmentation

- **One melanocyte supplies about 36 keratinocytes** (the epidermal melanin unit).
- **Racial skin colour differs because of melanosome number, size, degree of melanisation and dispersal, not melanocyte number**, which is similar in all races. Dark skin has larger, more melanised melanosomes spread singly; fair skin has

small ones clumped in groups. Eumelanin is brown-black; pheomelanin red-yellow (MC1R variants in red hair).

- Melanin synthesis: tyrosine to DOPA to dopaquinone by **tyrosinase (copper-dependent)**. Absent tyrosinase gives **oculocutaneous albinism type 1**: **melanocytes present in normal number but make no pigment**; high risk of SCC in the tropics.
- **Vitiligo**: **loss of melanocytes**, autoimmune (CD8 T cells, interferon-gamma and CXCL10), **Koebner-positive**, **chalk-white under Wood's lamp**; linked to thyroid disease, alopecia areata, pernicious anaemia, type 1 diabetes. Treatment: topical steroids or calcineurin inhibitors, **NB-UVB (the best for generalised disease)**, grafting for stable segmental disease. Current practice: **ruxolitinib cream** (topical JAK inhibitor, FDA 2022) is the first drug approved for repigmentation.
- **Piebaldism** (KIT): white forelock and patches **present from birth and not progressive**, unlike vitiligo.
- **Melasma**: women, face, pregnancy and the pill, sun; epidermal, dermal or mixed (Wood's lamp accentuates epidermal). Treatment: photoprotection, **triple combination** (hydroquinone, tretinoin, mild steroid); oral **tranexamic acid** is now widely used.
- **Dermal melanocytosis**: **Mongolian spot** (sacral, in most Asian newborns, fades in childhood); **naevus of Ota** (V1 and V2 territory, sclera involved, Asian women, glaucoma risk; Q-switched laser).
- Vitamin D synthesis begins in the basal and spinosum layers (7-dehydrocholesterol, **UVB**).

Hair and nail kinetics

- **Hair cycle: anagen about 3 years (2–6), catagen about 3 weeks, telogen about 3 months.** About 85–90% of scalp hairs are in anagen; **50–100 hairs are shed a day**.
- Scalp hair grows about **0.35 mm a day** (about 1 cm a month); **fingernails about 0.1 mm a day (3 mm a month)**, replaced in about 6 months; toenails a third as fast, replaced in 12–18 months.
- Hair types: lanugo (fetal, shed by birth), vellus, terminal (androgens convert vellus to terminal at puberty).

Leprosy

Basics

- *Mycobacterium leprae* (also *M. lepromatosis*); **cannot be cultured in vitro**, grown in the **mouse footpad** and the **nine-banded armadillo**. Acid-fast with **modified Ziehl–Neelsen (5% sulphuric acid, a weaker decolouriser)**; bacilli lie in **cigarette-pack bundles**, and in **globi** in lepromatous disease. Koch's postulates are not met. Generation time about 12–14 days; incubation usually 3–5 years (longer in lepromatous). Spread mainly by **nasal droplets** from untreated multibacillary patients.
- Elimination as a public-health problem: **prevalence below 1 per 10,000**. **Nepal reached it in 2009–10** (declared January 2010, 0.89 per 10,000; Ministry of Health and Population) but still finds new cases, with transmission continuing in 16 high-burden districts (WHO Nepal, 2026). WHO Global Leprosy Strategy 2021–2030: "Towards zero leprosy".
- Cardinal signs (WHO; one is enough): **definite loss of sensation in a pale or reddish skin patch; a thickened or enlarged peripheral nerve with loss of sensation or weakness; acid-fast bacilli in a slit-skin smear**.
- **Ridley–Jopling spectrum**: tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), lepromatous (LL); indeterminate leprosy is the early unclassified stage. TT has strong cell-mediated immunity (Th1) and few bacilli; **LL has no specific cell-mediated immunity (Th2), the most bacilli and is the most infectious**.
- **Tuberculoid**: one or few well-defined anaesthetic hypopigmented or erythematous plaques, a thickened nerve near the patch; **TT usually affects one nerve, BT several asymmetrically (mononeuritis multiplex)**. **Lepromatous**: many symmetrical ill-defined macules, nodules and infiltration, **leonine facies**, **madarosis** (loss of lateral eyebrows), saddle nose from septal destruction, **foamy (Virchow) lepra cells**, symmetrical glove-and-stocking **polyneuropathy**, testicular atrophy and gynaecomastia. **Pure neuritic** leprosy has nerve damage without skin lesions (relatively common in South Asia).
- **Satellite lesions** around a plaque suggest **borderline tuberculoid** disease. **Histoid leprosy** (shiny nodules, spindle-shaped histiocytes) is a lepromatous variant linked with dapsone resistance or relapse. **Lucio phenomenon**: necrotising vasculitis with stellate ulcers in untreated diffuse lepromatous leprosy (Mexico, Central America).

Slit-skin smear

- **Bacterial index (BI)**: density of bacilli on a **logarithmic scale of 0 to 6+** (Ridley); falls slowly, about 1 log a year on treatment.
- **Morphological index (MI)**: the percentage of **solidly staining (viable) bacilli**; falls within months of effective treatment, so it measures response and drug resistance.

Nerves and sensation

- **Temperature is the first sensation lost** (usually cold before warm); then touch and pain (sources differ on which of the two goes next); pressure and deep sensation last. Small dermal fibres are damaged first.
- **Ulnar nerve is the commonest peripheral nerve involved** (thickened above the elbow, **claw hand**); **facial is the commonest cranial nerve** in classical teaching (lagophthalmos, from the zygomatic branch), with the trigeminal (corneal anaesthesia) next. Others: median, radial cutaneous, **common peroneal (foot drop)**, posterior tibial (anaesthetic sole, plantar ulcers, a major cause of disability), great auricular. **Wartenberg's sign**: the little finger abducted from ulnar palsy. The **testis** is commonly involved in lepromatous men.
- Leprosy is the **commonest treatable peripheral neuropathy** worldwide. An anaesthetic, non-scaly hypopigmented patch suggests indeterminate leprosy (not pityriasis alba, which is scaly and sensate).

Lepromin test

- Not diagnostic; it **classifies and gives prognosis**: **strongly positive in tuberculoid, negative in lepromatous**; negative in most normal infants.
- **Early (Fernandez) reaction at 24–48 hours** shows prior sensitisation (a delayed hypersensitivity response to soluble antigen); **late (Mitsuda) reaction at 21–28 days** is a granulomatous nodule that reflects **cell-mediated immunity**. BCG can turn it positive.

Treatment (WHO)

	Paucibacillary (PB)	Multibacillary (MB)
WHO definition	**1–5 skin lesions and a negative smear**	**More than 5 lesions, or any nerve involvement (pure neuritis, or lesions with neuritis), or a positive smear**
Spectrum (roughly)	TT, BT, indeterminate	BB, BL, LL
Regimen, WHO 2018	**Rifampicin, dapsone, clofazimine** (as MB)	**Rifampicin 600 mg and clofazimine 300 mg monthly supervised; dapsone 100 mg and clofazimine 50 mg daily**
Duration	**6 months**	**12 months**

- **Exam answer (classical)**: PB had two drugs, **rifampicin 600 mg monthly supervised and dapsone 100 mg daily**, for 6 months. **Current practice (WHO 2018): all patients get the three drugs**; PB 6 months, MB 12 months. Some national programmes, India's among them, also counted nerves (one nerve PB, two or more MB); WHO's own definition puts any nerve involvement in MB.
- **Single-lesion ROM** (rifampicin 600 mg, ofloxacin 400 mg, minocycline 100 mg once) was a WHO single-dose option of the late 1990s for one lesion; it is **no longer recommended**.
- Rifampicin is the key bactericidal drug (a single dose kills over 99% of viable bacilli). **Dapsone**: haemolysis (check **G6PD**), methaemoglobinaemia, **dapsone hypersensitivity syndrome** (HLA-B*13:01). **Clofazimine**: red-brown to black **skin pigmentation**, ichthyosis; anti-inflammatory, useful in type 2 reactions.
- **Rifampicin-resistant leprosy** (WHO 2018): clarithromycin or minocycline with a fluoroquinolone and clofazimine, for 24 months.
- **Post-exposure prophylaxis: single-dose rifampicin (SDR-PEP)** for contacts aged 2 years and above, once leprosy and TB are excluded (WHO 2018).

Lepra reactions

	Type 1 (reversal)	Type 2 (ENL)
Spectrum	**Borderline (BT, BB, BL)**, the unstable part of the spectrum	**BL and LL** (high bacillary load)
Mechanism	**Type IV** delayed hypersensitivity, a rise in cell-mediated immunity	**Type III**, immune complexes, neutrophils and **TNF-alpha**
Skin	**Existing lesions turn red and swollen**	**New crops of tender red subcutaneous nodules**
Systemic	Usually none	**Fever**, arthralgia, iritis, orchitis, neuritis, lymphadenitis, nephritis
Nerve	**Severe neuritis, risk of rapid permanent damage**	Variable

- **Treat both with oral prednisolone** (about 40 mg a day, tapered over 3–6 months for neuritis) **and continue MDT**: a reaction is not drug failure or allergy, and stopping MDT is the classic wrong answer.
- **Type 2**: **thalidomide is the most effective drug** (the "gold standard"), but teratogenic and not given to women who could conceive, so **prednisolone is the drug of choice in practice**; high-dose clofazimine (slow, steroid-sparing) for chronic or recurrent ENL; pentoxifylline is an alternative. Chloroquine is older teaching.
- Reactions occur before, during or after MDT; ENL often starts in the first year of treatment.
- **WHO disability grades**: hands and feet: **0** no anaesthesia and no visible deformity; **1** anaesthesia without visible deformity; **2** visible deformity or damage. Eyes: grade 2 is lagophthalmos, iridocyclitis, corneal opacity or vision worse than 6/60. **Grade 2 disability in new cases is the indicator of late detection.**

Bacterial and viral skin infections

Streptococcal versus staphylococcal (an examiner's favourite split)

- ***S. pyogenes* almost exclusively: erysipelas and scarlet fever.** Non-bullous impetigo and cellulitis may be either.
- ***S. aureus*: bullous impetigo, folliculitis, furuncle (a deep follicular abscess), carbuncle (a cluster of furuncles, nape of the neck, diabetics), SSSS, toxic shock, paronychia** (the commonest hand infection; felon, the pulp-space abscess, needs drainage).
- **Erysipelas** (St Anthony's fire): infection of the upper dermis and its lymphatics, **raised sharply demarcated edge**, usually the leg (in the past the face); **Milian's ear sign**: erysipelas spreads onto the ear, while cellulitis, an infection of subcutaneous fat, stops short of it because the ear has almost none. Treat with **penicillin**. Cellulitis is deeper, with ill-defined borders; commonest portal is toe-web tinea or a leg ulcer.
- **Impetigo contagiosa (non-bullous)**: honey-coloured crusts around the nose and mouth; the **commonest bacterial skin infection of children**; *S. aureus* now the commonest cause, *S. pyogenes* alone or with it; post-streptococcal **glomerulonephritis can follow, rheumatic fever does not**. Localised disease: **topical mupirocin or fusidic acid** (exam answer); **current practice (NICE 2020)**: hydrogen peroxide 1% cream first for localised non-bullous impetigo, then fusidic acid (mupirocin if resistant); extensive disease needs oral flucloxacillin (clarithromycin in allergy). **Bullous impetigo**: *S. aureus* exfoliative toxin, **subcorneal** (granular layer) bulla.
- **Scarlet fever**: sandpaper rash a day or two after pharyngitis, circumoral pallor, **strawberry tongue** (white then red), **Pastia's lines** in skin creases, desquamation of hands and feet; **pyrogenic (erythrogenic) exotoxins** from a **bacteriophage-carrying** strain. Dick test (historical).

SSSS and SJS/TEN

- **SSSS (Ritter disease)**: *S. aureus* (phage group II) **exfoliative toxins A and B**, serine proteases that **cleave desmoglein 1 in the stratum granulosum** (**superficial** peeling), mostly in **infants and children under 5** and adults with renal failure (toxin not cleared); the focus may be the umbilicus, nose or conjunctiva; **Nikolsky positive**; **mucosa spared** (mucosa relies on desmoglein 3); low mortality in children with antistaphylococcal antibiotics.
- **SJS and TEN**: drug-induced in most adults (**allopurinol** the commonest in many series, sulfonamides including cotrimoxazole, **carbamazepine, phenytoin, lamotrigine**, phenobarbital, **nevirapine**, oxicam NSAIDs), *Mycoplasma* in children; 4–28 days after starting the drug; split at the **dermo-epidermal junction** with **full-thickness epidermal necrosis** (cytotoxic T cells, **granulysin**); **two or more mucosae** involved. **SJS under 10% BSA detached, overlap 10–30%, TEN over 30%.**

- **HLA-B*15:02** predicts carbamazepine SJS/TEN in Han Chinese, Thai, Malaysian and Indian patients (screen before starting where it is common); **HLA-B*58:01** allopurinol; HLA-A*31:01 carbamazepine DRESS in Europeans and Japanese.
- **SCORTEN** (one point each, day 1): **age over 40, malignancy, heart rate over 120, detached BSA over 10%, urea over 10 mmol/L, glucose over 14 mmol/L, bicarbonate under 20 mmol/L**; 5 or more predicts mortality over 90%.
- Management: **stop the drug** (the most important step), burns or intensive care, fluids, wound and eye care; ciclosporin or etanercept are used (evidence modest); systemic steroids are debated. **Erythema multiforme is now a separate disease** (HSV, typical target lesions, acral), not mild SJS.

Necrotising fasciitis

- **Type 1 polymicrobial** (anaerobes such as *Bacteroides* and *Peptostreptococcus*, with enteric Gram-negatives and streptococci; diabetics, postoperative; **Fournier's gangrene** of the perineum is one); **type 2 monomicrobial *S. pyogenes*** (with or without *S. aureus*, including MRSA), any age after minor trauma; type 3 (some texts) *Vibrio vulnificus* or clostridial.
- **Pain out of proportion**, woody induration beyond the erythema, dusky skin, haemorrhagic bullae, **crepitus**, anaesthesia of the skin, rapid shock. **Urgent surgical debridement with broad-spectrum antibiotics (a carbapenem or piperacillin–tazobactam, plus vancomycin or linezolid) and clindamycin to switch off toxin production**; imaging must not delay the operating theatre. The **finger test** at the bedside (no resistance to blunt dissection, dishwater pus) supports it. **LRINEC score** is a screening aid only (a score of 6 or more raises suspicion).

Viral exanthems and skin viruses

- Numbered diseases: 1st measles, 2nd scarlet fever, 3rd rubella (Forchheimer spots on the palate), 4th Filatov–Dukes (disputed), **5th erythema infectiosum (parvovirus B19, slapped cheek, then lacy rash; aplastic crisis in haemolytic anaemia, hydrops fetalis)**, **6th roseola infantum (HHV-6, also HHV-7): high fever for about 3 days, then rash as the fever falls**; febrile convulsions are its commonest complication.
- Day of the fever on which the rash appears (a common mnemonic): varicella and rubella day 1; scarlet fever day 2; smallpox day 3; measles day 4; typhus day 5; dengue day 6; typhoid day 7. **Koplik spots appear on about day 2 of the fever**, a day or two before the rash, and fade as it spreads.
- **Chickenpox**: HHV-3 (VZV), incubation 10–21 days, **centripetal** lesions in crops at all stages ("dew drop on a rose petal"), infectious from 2 days before the rash until all are crusted; smallpox was centrifugal and all at one stage. **Herpes zoster**: reactivation in a dermatome (thoracic the commonest, then ophthalmic); **Hutchinson's sign** (vesicles on the tip of the nose, nasociliary nerve) predicts eye involvement; **Ramsay Hunt** syndrome is zoster of the geniculate ganglion (facial palsy, ear vesicles); oral aciclovir, valaciclovir or famciclovir within 72 hours; **postherpetic neuralgia** the commonest complication, commoner with age. Current practice: the **recombinant zoster vaccine** (two doses, from 50 years) has replaced the live one.
- **Hand, foot and mouth**: **Coxsackie A16, enterovirus 71** (brainstem encephalitis in Asia), now often Coxsackie A6. **Herpetic whitlow**: HSV on the finger; do not incise. **Tzanck smear** shows multinucleated giant cells (HSV and VZV, not distinguishing them); PCR is the test of choice now. **Eczema herpeticum**: HSV spread over atopic skin, punched-out erosions, an emergency for aciclovir.
- **Molluscum contagiosum**: poxvirus, pearly **umbilicated** papules, **Henderson–Paterson (molluscum) bodies**; extensive or facial in HIV.
- **Warts (HPV)**: common warts types 2 and 4 (also 1); **plantar 1**; **plane warts 3 and 10**; **anogenital warts 6 and 11** (low risk); **16 and 18 are oncogenic** (cervical, anal, oropharyngeal cancer); epidermodysplasia verruciformis 5 and 8.
- **Mpox** (monkeypox): the 2022 global outbreak (clade IIb, mostly sexual spread among men who have sex with men) and the 2024 clade Ib outbreak in Africa (both WHO emergencies of international concern); firm, deep-seated, umbilicated vesiculopustules at one stage, prominent **lymphadenopathy** (unlike smallpox). **Kaposi sarcoma**: HHV-8 (see Tumours).

Cutaneous tuberculosis

- Immunity and route decide the form: **lupus vulgaris** (the **commonest form overall**, including in South Asia; moderate immunity; haematogenous, lymphatic or contiguous; **apple-jelly nodules on diascopy**, scarring, on the buttocks and limbs in South Asia, the face in Europe; SCC can arise in old lesions); **scrofuloderma** (spread from an underlying node or bone, neck; the **commonest form in children** in Indian series; low immunity; undermined ulcers and sinuses); **tuberculosis verrucosa cutis** (**exogenous inoculation in a previously sensitised person**, high immunity, warty plaque on the hands or feet; prosector's wart); **tuberculous chancre** (primary inoculation in the non-immune); miliary and orificial forms in severe immunosuppression.
- **Tuberculides** are hypersensitivity reactions with few or no bacilli: **lichen scrofulosorum**, **papulonecrotic tuberculide**, and **erythema induratum of Bazin** (nodular vasculitis on the calves of women). Treatment of every form is the standard antitubercular regimen.

Fungal infections and scabies

Dermatophytes

- Keratinophilic fungi that live in the corneum, hair and nail. **Trichophyton: skin, hair and nails. Microsporum: skin and hair, not nails (*M. canis* rarely if ever invades nails). Epidermophyton: skin and nails, never hair.**
- **Commonest dermatophyte worldwide: *T. rubrum*** (tinea pedis, cruris, onychomycosis). **Current practice in South Asia**: since about 2015 an epidemic of extensive, recalcitrant tinea corporis and cruris is caused mainly by ***T. indotineae*** (formerly *T. mentagrophytes* ITS genotype VIII), named in 2020 from isolates that included one from a Nepali patient (Kano et al., *Mycopathologia* 2020); many strains are **terbinafine-resistant** (squalene epoxidase, SQLE, mutations), and **itraconazole** is the usual oral choice. Misuse of over-the-counter steroid combination creams drives it.
- **Commonest cause of tinea capitis in South Asia: *T. violaceum*** (*T. tonsurans* in the US and UK; *M. canis* in parts of Europe and from cats).
- **Hair invasion**: **ectothrix** (spores outside the shaft; *Microsporum*, which **fluoresces**); **endothrix** (inside; ***T. tonsurans* and *T. violaceum*, no fluorescence**, black-dot

pattern); **favus** (*T. schoenleinii*, hyphae and air spaces in the shaft, dull green).

- **Tinea capitis** (prepubertal children; rare after puberty because sebum fatty acids are fungistatic): grey patch, black dot, **kerion** (boggy, pustular inflammatory mass; treat the fungus, do not incise; can scar), **favus** (yellow cup-shaped **scutula**, mousy odour, scarring). **Always treat orally**: **terbinafine is preferred for *Trichophyton*, griseofulvin for *Microsporum*** (griseofulvin, taken with fatty food, was the traditional drug of choice overall). **Hair perforation test** is positive in ***T. mentagrophytes*** (negative in *T. rubrum*) and *M. canis*.
- **Tinea incognito**: a topical steroid suppresses inflammation, so the raised scaly active edge is lost while the fungus spreads. **Topical steroids are contraindicated in tinea, acne, rosacea and scabies.**
- **Tinea corporis** (ringworm): annular plaque with a scaly, active edge and **central clearing**. **Majocchi granuloma**: dermatophyte folliculitis after steroid use (oral treatment). Local tinea: topical azoles or terbinafine; extensive disease oral terbinafine or itraconazole.
- **Onychomycosis**: **distal lateral subungual is the commonest type** (*T. rubrum*); **proximal subungual suggests HIV**; white superficial (*T. interdigitale*). Confirm by KOH and culture before treating; **oral terbinafine 250 mg daily, 6 weeks for fingernails and 12 weeks for toenails**, or pulsed itraconazole.
- **Diagnosis: KOH mount** of scrapings (septate branching hyphae); culture on **Sabouraud dextrose agar**.

Other superficial infections

- **Pityriasis versicolor**: ***Malassezia*** (*M. globosa* is the commonest species; *M. furfur* in older texts), a commensal yeast turning to hyphae in heat and humidity; branny (furfuraceous) scale on the upper trunk; **"spaghetti and meatballs"** on KOH; **hypopigmentation from azelaic acid** (dicarboxylic acids that inhibit tyrosinase); **yellow-gold fluorescence**; **scratch sign** (Besnier's, coup d'ongle) brings up scale; linked to Cushing's and steroids; **topical ketoconazole or selenium sulphide**; oral fluconazole or itraconazole for extensive disease (**not oral terbinafine**, which does not reach the skin surface well enough). Pigment returns slowly after cure. *Malassezia* also drives **seborrhoeic dermatitis** and *Malassezia* folliculitis.
- **Erythrasma**: ***Corynebacterium minutissimum***, brown scaly patches in the groin, axillae and toe webs, **coral-red fluorescence** (coproporphyrin III); topical fusidic acid or clindamycin, oral erythromycin or clarithromycin.
- **Pitted keratolysis**: *Kytococcus*, crater-like pits on sweaty soles, malodour.
- **Candidiasis**: intertrigo with **satellite pustules**, angular cheilitis, chronic paronychia (wet work), oral thrush (inhaled steroids, HIV). **Chronic mucocutaneous candidiasis** points to defective IL-17 immunity: **APECED** (AIRE mutation: candidiasis, **hypoparathyroidism**, Addison's disease), STAT1 gain of function.

Wood's lamp (UVA, peak about 365 nm)

Condition	Colour
Erythrasma	**Coral red**
Tinea capitis (*Microsporum*, ectothrix)	**Blue-green**
Favus (*T. schoenleinii*)	Dull green
Pityriasis versicolor	**Yellow-gold**
Vitiligo	**Chalk white** (ash-leaf macules of tuberous sclerosis show off-white)
Porphyria cutanea tarda (urine), congenital erythropoietic porphyria (teeth)	Pink-red, orange-red
Pseudomonas	Yellow-green
Trichophyton endothrix (*T. tonsurans*, *T. violaceum*)	**None**

Subcutaneous mycoses

- **Chromoblastomycosis**: slow, **warty, cauliflower-like plaques on the foot or leg of a barefoot farmer**, after a thorn or splinter injury (*Fonsecaea pedrosoi* commonest); **sclerotic (Medlar) bodies**, brown, thick-walled, septate "copper pennies", on KOH or biopsy; itraconazole with surgery or cryotherapy.
- **Mycetoma** (Madura foot): the triad of **painless swelling, draining sinuses and grains**; **eumycetoma** (fungal, *Madurella mycetomatis*, **black** or white grains; itraconazole with surgery) versus **actinomycetoma** (bacterial, *Nocardia*, *Actinomadura*, *Streptomyces*; white, yellow or **red** grains; the commonest form in India; **Welsh regimen of cotrimoxazole and amikacin**); MRI **"dot-in-circle" sign**. Actinomycetoma responds to drugs; eumycetoma often needs excision.
- **Sporotrichosis**: *Sporothrix schenckii*, thermally dimorphic; a nodule at the site of a thorn with **nodules in a line along the lymphatics** (rose gardener's disease); asteroid bodies (Splendore–Hoeppli phenomenon); **itraconazole**, or saturated potassium iodide.
- **Rhinosporidiosis** (*Rhinosporidium seeberi*, an aquatic protist): strawberry-like nasal polyps, in pond bathers in South Asia; excision.

Scabies

- *Sarcoptes scabiei* var. *hominis*; the fertilised female burrows in the corneum. **First infestation itches after 3–6 weeks** (type IV hypersensitivity to mites and their products), a re-infestation within a day or two. **Classic scabies carries about 10–15 mites; crusted scabies thousands to millions.**
- Burrows in **finger webs**, flexor wrists, elbows, axillary folds, umbilicus, buttocks, **genitals (penile and scrotal nodules)** and nipples; **head and face spared in adults**; **intense nocturnal itch** with household contacts affected. **Infants have palm, sole, face and scalp involvement**, often vesiculopustules. Nodular scabies persists for months after cure. Secondary impetigo with *S. pyogenes* can cause **post-streptococcal glomerulonephritis**. Diagnosis: the burrow, dermoscopy (**delta-wing, "jet with contrail"**), skin scraping for mite, eggs or scybala.
- **Permethrin 5% cream is first line**, including **infants from 2 months, pregnancy and lactation**: neck down in adults (include the scalp and face in infants and the elderly), left on 8–14 hours, repeated after 7 days. **Oral ivermectin** 200 microgram/kg, two doses 1–2 weeks apart (it does not kill eggs); **not for children under 15 kg** or in pregnancy. **Benzyl benzoate 25%** in adults, diluted for children, avoided in infants; **crotamiton 10%** is safe in infants but less effective; **lindane** is neurotoxic (seizures) and avoided in children, pregnancy and on broken skin; sulphur 5–10% ointment is safe in infants and pregnancy. **Treat all close contacts at the same time**; wash clothing and bedding at 60 °C or seal them

for 3 days. Itch can last 2–4 weeks after cure: not treatment failure.

- **Crusted (Norwegian) scabies** in the immunosuppressed (HIV, HTLV-1, steroids), elderly, Down syndrome and leprosy: thick crusts, little itch, highly contagious; **oral ivermectin in several doses plus a topical scabicide and keratolytic**.
- Current practice: WHO added scabies to the **neglected tropical diseases** (2017) and recommends **ivermectin mass drug administration** in communities where prevalence is 10% or more (WHO, from 2020).

Other parasites

- **Pediculosis capitis**: nits cemented to the hair shaft; permethrin 1% or dimeticone, repeated after 7–10 days; ivermectin lotion. *Pediculus humanus corporis* (body louse) transmits epidemic typhus, trench fever and relapsing fever; *Phthirus pubis* (crab louse) is sexually spread, also on eyelashes.
- **Cutaneous leishmaniasis**: sandfly (*Phlebotomus*), a nodule that ulcerates with a raised rim (**"volcano" sign**), on exposed skin. **Post-kala-azar dermal leishmaniasis (PKDL)**: *L. donovani*, months to years after visceral leishmaniasis, hypopigmented macules (mostly, in South Asia) or nodules on the face; a reservoir that matters to the **kala-azar elimination programme of Nepal, India and Bangladesh**; long treatment (miltefosine, or liposomal amphotericin B).

Papulosquamous and bullous disease

Psoriasis

- Chronic immune disease of the **IL-23–Th17 axis** (IL-17, TNF-alpha); **HLA-C*06:02 (HLA-Cw6)** the strongest gene, especially in early-onset disease; prevalence about 1–3%; peaks in the 20s and 50s. Type: chronic plaque (the commonest), guttate (children, after streptococcal throat), inverse (flexural, no scale), erythrodermic, pustular (generalised, **von Zumbusch**; localised palmoplantar).
- Well-defined erythematous plaques with **silvery scale on extensors (elbows, knees), scalp, sacrum and nails**. **Histology: parakeratosis, loss of the granular layer, regular (psoriasiform) acanthosis with clubbed rete ridges, thinned suprapapillary plates, dilated tortuous papillary capillaries, Munro microabscesses (neutrophils in the stratum corneum)** and **spongiform pustules of Kogoj** (neutrophils in the spinosum).
- **Grattage test**: scraping gives candle-grease scale (**candle-grease sign**), then a thin glistening film (**Bulkley membrane**), then **pinpoint bleeding (Auspitz sign)** from the capillaries under the thinned suprapapillary plate. **Woronoff ring**: a pale ring round healing plaques. **Koebner phenomenon (true)**: **psoriasis, lichen planus, vitiligo** and discoid lupus. **Pseudo-Koebner**: inoculation along a scratch (warts, molluscum). **Reverse Koebner**: a lesion clears where injured.
- **Nails** (up to half of patients, most with arthritis): **pitting is the commonest sign** (coarse, deep, irregular; fine regular pits are alopecia areata), **oil-drop (salmon-patch) sign**, regarded as **pathognomonic**, onycholysis with a reddish-yellow border, subungual hyperkeratosis, splinter haemorrhages.
- **Triggers**: cold weather, trauma, streptococcal infection (guttate), stress, alcohol, smoking, **drugs (beta-blockers, lithium, antimalarials such as chloroquine, NSAIDs, interferon, terbinafine, and abrupt withdrawal of systemic steroids, which can precipitate pustular psoriasis)**. Sudden severe psoriasis suggests **HIV**. Severity: **PASI** (Psoriasis Area and Severity Index) and BSA; PASI 75 and 90 are trial end-points.
- **Psoriatic arthritis** (about a quarter of patients; nail disease predicts it): **seronegative**, **distal interphalangeal** involvement, dactylitis, enthesitis, asymmetric oligoarthritis (the commonest pattern), **arthritis mutilans**; X-ray **pencil-in-cup**, **acro-osteolysis (tufting) of distal phalanges**; **CASPAR** criteria. Associations: metabolic syndrome, cardiovascular disease, IBD, depression.
- **Treatment ladder**: emollients, **topical steroids and vitamin D analogues (calcipotriol), the commonest combination**, tar, **dithranol**, salicylic acid for scalp; **phototherapy (NB-UVB first; PUVA)**; systemic: **methotrexate** (weekly, with folic acid; hepatotoxic, marrow suppression, teratogenic in both sexes), **ciclosporin** (rapid; nephrotoxic, hypertension), **acitretin** (good in pustular; **teratogenic, contraception for 3 years after**), apremilast (PDE4), **deucravacitinib** (oral TYK2 inhibitor, FDA 2022), fumarates. **Biologics**: TNF (adalimumab, etanercept, infliximab), **IL-12/23 (ustekinumab)**, **IL-17 (secukinumab, ixekizumab, bimekizumab)**, **IL-23 p19 (guselkumab, risankizumab, tildrakizumab)**; screen for latent TB first. **Generalised pustular psoriasis**: IL36RN mutations; **spesolimab** (anti-IL-36 receptor, FDA 2022) for flares. Systemic steroids are avoided (rebound pustular or erythrodermic flare).

Lichen planus

- **Six Ps: purple, polygonal, pruritic (itch is usually intense; psoriasis classically itches less, though most psoriasis patients report some itch), planar (flat-topped), papules and plaques**, with **Wickham's striae** (fine white lacy lines, from wedge-shaped hypergranulosis); flexor wrists, shins, lower back; **Koebner positive**. **Oral mucosa** in about half (lacy white reticular network on the buccal mucosa; **erosive oral LP has a small risk of SCC**); genital lesions; **nail pterygium** (the characteristic nail sign) and longitudinal ridging; scarring alopecia (**lichen planopilaris**; frontal fibrosing alopecia is a variant). Heals with grey-brown pigmentation (**melanin incontinence**); **lichen planus pigmentosus** on the face and neck is common in South Asian skin.
- **Histology**: compact **hyperkeratosis without parakeratosis**, **wedge-shaped hypergranulosis**, **saw-tooth acanthosis**, **basal-cell (vacuolar) degeneration**, **Civatte (colloid) bodies**, a **band-like lymphocytic infiltrate** hugging the junction, **Max-Joseph spaces** (clefts), melanophages. Direct IF: shaggy fibrinogen at the basement membrane.
- **Associations: hepatitis C** (especially oral LP), other autoimmune disease. **Lichenoid drug eruptions**: gold, antimalarials, ACE inhibitors, thiazides, beta-blockers, checkpoint inhibitors. Treatment: potent topical steroids (in the mouth, a steroid in an adhesive gel, or tacrolimus), intralesional steroid for hypertrophic LP, oral steroids or acitretin for extensive disease; most cutaneous LP clears in 1–2 years.
- **Lichen nitidus**: pin-head, shiny skin-coloured papules on the forearm, penis and abdomen; **"ball in claw" histology**.

Other papulosquamous and eczematous disease

- **Pityriasis rosea**: young adults, spring and autumn; linked to **HHV-6/7** reactivation; a **herald patch** (the largest, oval, on the trunk), then 1–2 weeks later smaller oval lesions with an inward-facing **collarette scale** along skin cleavage lines (**Christmas-tree** pattern on the back), the **hanging-curtain**

sign; palms, soles and face spared; **self-limiting in 6–8 weeks** (up to 12); **check VDRL** if syphilis is possible (secondary syphilis involves palms and soles). **Reassure**, emollients, a mild steroid for itch; aciclovir early in extensive disease has some evidence. Drugs (ACE inhibitors, gold) give a rosea-like eruption. In pregnancy it is linked to miscarriage when it starts early.

- **Pityriasis rubra pilaris**: orange-red (salmon) plaques with **islands of normal skin**, follicular papules on the backs of fingers ("nutmeg grater"), **palmoplantar keratoderma ("keratodermic sandal")**; cephalocaudal spread.
- **Pityriasis alba**: ill-defined scaly hypopigmented patches on the faces of atopic children; benign, sensate, fades.
- **Seborrhoeic dermatitis**: greasy yellow scale on the scalp (dandruff), eyebrows, nasolabial folds, chest; **cradle cap** in infants; *Malassezia*; severe in **HIV** and **Parkinson's disease**; ketoconazole shampoo or cream, mild steroids.
- **Atopic dermatitis**: the commonest chronic skin disease of children; **filaggrin mutations** and a Th2 (IL-4, IL-13, IL-31) bias; **infants: face and extensor surfaces (napkin area spared); children and adults: flexures**; itch is essential. **Hanifin–Rajka** major and minor criteria (UK Working Party criteria simpler); **Dennie–Morgan infraorbital folds**, **white dermatographism**, **Hertoghe's sign**, palmar hyperlinearity, keratosis pilaris, ichthyosis vulgaris; risk about 50% with one atopic parent and about 80% with two; most improve by adolescence, but **it often persists or recurs in adult life**. Complications: *S. aureus* infection, **eczema herpeticum**, cataract (anterior subcapsular). Treatment: **emollients**, topical steroids, **topical calcineurin inhibitors** (tacrolimus, pimecrolimus; for the face), crisaborole, NB-UVB, ciclosporin and methotrexate; **current practice for moderate–severe disease: biologics (dupilumab, anti-IL-4Rα; tralokinumab and lebrikizumab, anti-IL-13; nemolizumab, anti-IL-31 receptor) and oral JAK inhibitors (upadacitinib, abrocitinib, baricitinib)**.
- **Contact dermatitis**: **irritant is the commonest overall** (hand dermatitis of wet work); **allergic is type IV**, **nickel the commonest allergen** (women), also chromate (cement), fragrance, para-phenylenediamine (hair dye); confirmed by **patch testing** (read at 48 and 96 hours). **Parthenium dermatitis** (*Parthenium hysterophorus*, an invasive weed in Nepal and India) is an **airborne contact dermatitis** of exposed sites in farmers; it reaches the upper eyelids, behind the ears and under the chin, the sites a photodermatitis spares.
- Scale by type: **silvery** (psoriasis); **branny or furfuraceous** (pityriasis versicolor); **collarette** (pityriasis rosea); **greasy** (seborrhoeic dermatitis); **fish-like or ichthyosiform** (ichthyosis vulgaris); **mica-like** (pityriasis lichenoides chronica); **trailing**, behind an advancing edge (erythema annulare centrifugum).

Where the blister splits

Level	Diseases
Subcorneal (granular layer)	**SSSS**, **bullous impetigo**, **pemphigus foliaceus**, subcorneal pustular dermatosis, miliaria crystallina
Intraepidermal, spongiotic	Eczema (pompholyx), allergic contact dermatitis
Suprabasal	**Pemphigus vulgaris**, Darier and Hailey–Hailey disease
Basal cell	EB simplex, lichen planus (bullous), erythema multiforme
Subepidermal	**Bullous pemphigoid**, **dermatitis herpetiformis**, **linear IgA disease**, pemphigoid gestationis, mucous membrane pemphigoid, **EB acquisita**, porphyria cutanea tarda, bullous SLE, TEN (full-thickness necrosis at the junction)

Pemphigus vulgaris versus bullous pemphigoid

	Pemphigus vulgaris	Bullous pemphigoid
Split	**Suprabasal (intraepidermal)**, a row of "tombstone" basal cells	**Subepidermal**
Target	**Desmoglein 3 (and 1 when the skin is involved)**	Hemidesmosome **BP180 (collagen XVII) and BP230**
Blister	Flaccid, ruptures into erosions	**Tense**, on urticarial plaques; eosinophils
Mucosa	**Almost always, often first (oral)**	Uncommon
Nikolsky and bulla spread	**Positive**	**Negative** (the roof is the whole epidermis)
Direct IF	**Intercellular IgG and C3 ("fishnet" or "chicken-wire")**	**Linear IgG and C3 along the basement membrane**; on salt-split skin, on the roof
Age	40–60	**Over 70**, intense itch, may precede blisters
Prognosis	Fatal in most before steroids	Better; mortality from age and frailty

- **Pemphigus**: **type II hypersensitivity**; **HLA-DR4 and DR14**, commoner in Ashkenazi Jews and South Asians; **Tzanck smear shows acantholytic (Tzanck) cells**. **Pemphigus foliaceus**: **desmoglein 1 only**, **subcorneal**, crusted scaly erosions in a seborrhoeic distribution, **no mucosal disease** (the **desmoglein compensation** theory: mucosa expresses mostly Dsg3); **pemphigus erythematosus (Senear–Usher)** is its localised variant with lupus features; **fogo selvagem** the endemic form in Brazil. **Pemphigus vegetans** (Neumann, Hallopeau) is a variant of vulgaris in the flexures. **Paraneoplastic pemphigus**: severe stomatitis with **non-Hodgkin lymphoma, CLL or Castleman disease**; antibodies to **envoplakin and periplakin**; bronchiolitis obliterans. **Drug-induced pemphigus**: **thiol drugs (penicillamine, captopril)**. IgA pemphigus: intercellular IgA.
- **Diagnosis**: biopsy of a fresh **lesion's edge** for histology, plus **direct immunofluorescence of perilesional skin (the gold standard)**; indirect IF and **ELISA** for circulating antibodies (titres follow activity in pemphigus).
- **Treatment, pemphigus**: exam answer, **systemic corticosteroids** (with azathioprine or mycophenolate as steroid-sparing agents); **current practice: rituximab (anti-CD20) with short-course prednisolone is first-line for moderate to severe pemphigus** (FDA 2018; EADV guideline 2020); IVIG for refractory disease. Dexamethasone–cyclophosphamide pulse therapy is older Indian practice.
- **Treatment, pemphigoid**: **potent topical clobetasol over the whole body** is as effective as and safer than oral prednisolone; doxycycline as a steroid-sparing start; methotrexate. **DPP-4 inhibitors (gliptins)** trigger it (stop the drug), as do checkpoint inhibitors. **Current practice: dupilumab** (FDA 2025) for moderate to severe bullous pemphigoid.
- **Nikolsky sign** (lateral pressure shears the epidermis off normal-looking skin): **pemphigus vulgaris, pemphigus**

foliaceus, SJS/TEN, SSSS. **Asboe-Hansen (bulla-spread) sign**, called "Nikolsky II" in some books: pressing a bulla spreads it sideways (pemphigus, TEN).

- **Pemphigoid gestationis**: 2nd or 3rd trimester, periumbilical urticarial plaques then tense blisters, anti-BP180 (NC16A), recurs in later pregnancies and with the pill; neonate may be transiently affected. **Mucous membrane (cicatricial) pemphigoid**: scarring of conjunctiva (symblepharon) and mucosae.
- **Dermatitis herpetiformis**: intensely itchy grouped vesicles and excoriations on **elbows, knees, buttocks, scalp**; **granular IgA at the dermal papillary tips** (biopsy perilesional, normal-looking skin); neutrophil microabscesses in the papillae; **autoantigen: epidermal transglutaminase (TG3)**; **HLA-DQ2 (and DQ8)**; nearly all have a gluten-sensitive enteropathy, often silent; **anti-endomysial and tissue transglutaminase IgA**; lymphoma risk falls on the diet. **Dapsone controls itch within days; the gluten-free diet is the long-term treatment** and lets dapsone be withdrawn.
- **Linear IgA disease**: **linear IgA along the basement membrane**; in children (chronic bullous disease of childhood) blisters ring older ones (**"string of pearls" or "cluster of jewels"**); in adults often **drug-induced (vancomycin)**; dapsone.
- **Epidermolysis bullosa acquisita**: autoantibodies to **collagen VII**; trauma-site blisters, scarring and milia; IgG on the floor of salt-split skin.

Syphilis and genital ulcers

Syphilis stages

- *Treponema pallidum* subsp. *pallidum*, a spirochaete that **cannot be cultured in vitro** and **does not take the Gram stain**; seen on **dark-field microscopy**, the **investigation of choice for exudate from a moist primary chancre** (or secondary condylomata; not mouth lesions, where commensal treponemes confuse), or by PCR and silver stain in tissue. Its relatives cause yaws (subsp. *pertenue*), bejel (subsp. *endemicum*) and pinta (*T. carateum*), which serology cannot tell apart.
- **Primary**: incubation **9–90 days, about 3 weeks**; a **single painless, indurated, clean-based (punched-out) ulcer** that does not bleed, with **painless, firm, rubbery, non-suppurative regional nodes**; heals in 3–6 weeks without treatment. Extragenital chancres on the lip or finger.
- **Secondary** (6–8 weeks after the chancre; with condylomata and mucous patches, the **most infectious stage**): a **symmetrical, non-itchy maculopapular rash including palms and soles** (copper-coloured, with a collarette of scale, **Biett's collarette**), **condylomata lata** (moist flat papules in the anogenital area), **mucous patches** and snail-track ulcers, split papules at the mouth's angles, **moth-eaten alopecia**, generalised lymphadenopathy (epitrochlear is suggestive), malaise, hepatitis, **membranous glomerulonephritis**, periostitis, uveitis. **Buschke–Ollendorff sign**: a papule is tender to a blunt probe.
- **Latent**: positive serology without signs; **early latent under 1 year (CDC) or under 2 years (WHO)**.
- **Tertiary** (years later, about a third of the untreated): **gummas** (granulomatous necrosis of skin, bone, liver, palate); **cardiovascular** (**ascending aortitis**, aortic regurgitation, **saccular aneurysm of the ascending arch**, coronary ostial stenosis; tree-bark intima, endarteritis obliterans of the vasa vasorum); **neurosyphilis**: meningovascular, **general paresis** (dementia, personality change), **tabes dorsalis** (dorsal columns and roots: lightning pains, sensory ataxia, positive Romberg, **areflexia**, **Argyll Robertson pupil** that accommodates but does not react to light, Charcot joints of the knee). **Diabetes, not syphilis, is now the commonest cause of Charcot joint overall.** Neurosyphilis can occur at any stage, early in HIV.

Serology

Type	Tests	What to know
Non-treponemal	**VDRL, RPR**	Antigen: **cardiolipin–lecithin–cholesterol**; they **detect antibody to cardiolipin (reagin)**, released from damaged host cells and from treponemes; flocculation tests; screening; **quantitative titre tracks activity and response** (a **fourfold fall**, two dilutions, means success); turn negative with time or treatment
Treponemal	**FTA-ABS, TPHA, TP-PA, MHA-TP, EIA/CLIA, TPI**	Detect antibody to treponemal proteins; confirmatory; **usually stay positive for life**, so they cannot show reinfection or cure; **FTA-ABS becomes positive first** (it is the most sensitive test in primary syphilis); **TPI (Nelson's immobilisation test, live treponemes) is the most specific** in the classical answer, no longer done; **TP-PA is the most specific in routine use**

- **Biological false-positive VDRL**: acute (under 6 months) after viral infections (infectious mononucleosis, hepatitis, measles), malaria, vaccination, **pregnancy**; chronic in **SLE, antiphospholipid syndrome**, **leprosy**, IV drug use, old age, HIV. Treponemal test is negative.
- **VDRL is most sensitive (nearly 100%) in secondary syphilis**; the **prozone phenomenon** gives a false negative at very high titre (dilute the serum). Non-treponemal tests can be negative in early primary and in late syphilis.
- **CSF VDRL is highly specific but insensitive** for neurosyphilis (a positive confirms, a negative does not exclude); CSF lymphocytes and protein help. **IgM FTA-ABS (19S-IgM)** or IgM immunoblot for congenital syphilis, since maternal IgG crosses the placenta.
- Current practice: many laboratories use the **reverse sequence algorithm**, an automated treponemal EIA or CLIA first, then RPR, with TP-PA to settle a discordant pair. **Rapid point-of-care treponemal tests** are used for antenatal screening (WHO). **Serofast**: a low titre that persists after adequate treatment.

Treatment (CDC 2021; WHO 2016)

- **Primary, secondary and early latent: benzathine penicillin G 2.4 million units IM, a single dose. Late latent, unknown duration or tertiary (not neuro): 2.4 million units weekly for 3 weeks.**
- **Neurosyphilis and ocular or otosyphilis: aqueous crystalline penicillin G, 18–24 million units a day IV (3–4 million units every 4 hours) for 10–14 days** (procaine penicillin with probenecid an alternative). Benzathine penicillin does not reach treponemicidal levels in CSF.
- **Penicillin allergy (not pregnant)**: **doxycycline 100 mg twice daily, 14 days for early and 28 days for late disease**; ceftriaxone is an alternative. **Pregnancy: only penicillin reliably treats the fetus**, so allergic women are **desensitised** (CDC); erythromycin and azithromycin do not cross the

placenta well enough. **Azithromycin is not used for syphilis** (resistance, A2058G mutation).

- **Jarisch–Herxheimer reaction**: fever, chills, myalgia and a flare of lesions within 24 hours of the first dose, from released treponemal lipoproteins and cytokines; **commonest in secondary syphilis**; self-limiting, treated with antipyretics; in pregnancy it can cause contractions or fetal distress, but treatment must not be delayed.
- Follow-up: repeat RPR or VDRL at 6 and 12 months; test for HIV. Treat sexual partners of the last 90 days presumptively.
- Current practice: **doxycycline post-exposure prophylaxis (doxy-PEP)**, 200 mg within 72 hours of condomless sex, cuts syphilis, chlamydia and gonorrhoea in men who have sex with men and transgender women with a recent STI (CDC 2024). Benzathine penicillin shortages (2023–24) are a global problem.

Congenital syphilis

- Transmission at any stage of pregnancy, most likely in early (primary and secondary) maternal syphilis; **screen every woman at the first antenatal visit** (WHO target: elimination of mother-to-child transmission of HIV and syphilis). Treatment of the mother at least 30 days before delivery protects the baby.
- **Early (under 2 years)**: **snuffles (haemorrhagic rhinitis, the earliest sign)**, **bullous lesions on palms and soles (syphilitic pemphigus)**, maculopapular rash, hepatosplenomegaly, jaundice, lymphadenopathy, anaemia, **osteochondritis and periostitis** (pseudoparalysis of Parrot; **Wimberger's sign**, bilateral erosion of the medial proximal tibial metaphyses; not Wimberger's ring of scurvy or Wartenberg's sign of leprosy), hydrops.
- **Late (over 2 years)**: **Hutchinson's triad: notched, peg-shaped upper central permanent incisors (Hutchinson's teeth), interstitial keratitis (at 5–20 years) and eighth-nerve deafness**; also **mulberry (Moon's) molars**, **saddle nose**, **sabre shin** (anterior bowing of the tibia), **Clutton's joints** (painless bilateral knee effusions), **Olympian brow** (frontal bossing), **rhagades** (radial scars round the mouth).
- **Diday's law** (and Kassowitz's): **untreated maternal syphilis does less harm in each successive pregnancy** (miscarriage, then stillbirth, then congenital syphilis in a live baby, then a healthy child) as the infection ages.
- Treatment of the infant: **aqueous crystalline penicillin G IV for 10 days** (or procaine penicillin IM).

Genital ulcers

Disease	Organism	Features	Treatment (CDC 2021)
Syphilis (chancre)	*T. pallidum*	Incubation about 3 weeks; **painless, single, indurated, clean base**; painless rubbery nodes	**Benzathine penicillin 2.4 MU** once
Chancroid (soft sore)	*Haemophilus ducreyi*	Incubation 3–7 days; **painful, multiple, soft, ragged undermined edge, purulent base, bleeds**; tender **unilateral bubo that suppurates** (aspirate, do not incise); Gram stain: short Gram-negative rods in **"school of fish" or "railroad track" chains**	**Azithromycin 1 g once** or **ceftriaxone 250 mg IM once** (ciprofloxacin 3 days, erythromycin 7 days)
Genital herpes	**HSV-2**; HSV-1 now causes many first episodes	**Painful grouped vesicles, then shallow erosions**, tender nodes, systemic upset in the first episode; recurrences milder	**Aciclovir or valaciclovir** for 7–10 days; suppressive therapy for frequent recurrences
Lymphogranuloma venereum	*Chlamydia trachomatis* **L1–L3**	Transient **painless** papule or ulcer, then **painful matted inguinal nodes**, **groove sign** (nodes above and below the inguinal ligament), buboes rupture with sinuses; **proctocolitis** in men who have sex with men; late **esthiomene** (genital elephantiasis) and rectal stricture; Gamna–Miyagawa bodies	**Doxycycline 100 mg twice daily for 21 days**
Donovanosis (granuloma inguinale)	*Klebsiella granulomatis* (formerly *Calymmatobacterium*)	**Beefy-red, painless, friable ulcer that bleeds on touch**, slowly spreading; **Donovan bodies** (bipolar "safety-pin" bacilli in macrophages) on crush smear; **pseudobubo** (subcutaneous granuloma), **no true lymphadenopathy**; SCC risk	**Azithromycin 1 g weekly** (or 500 mg daily) **for at least 3 weeks and until healed**; doxycycline

- The old **Frei test** (intradermal LGV antigen) is **obsolete**: insensitive and cross-reactive. Diagnosis of LGV now is **NAAT** with genotyping.
- **Syndromic management (WHO 2021)**: for a genital ulcer, **treat for syphilis and herpes** (by same-day test results, or syndromically and revise when results come), **chancroid only where cases are reported**, and LGV when tests are positive. Herpes is now the commonest cause of genital ulcers worldwide; chancroid has become rare.
- Every patient with a genital ulcer is tested for **HIV** (ulcers raise its transmission several-fold) and for syphilis.

Discharge syndromes (for completeness)

- **Urethritis**: gonococcal (Gram-negative intracellular diplococci, short incubation, purulent) or non-gonococcal (*C. trachomatis* the commonest, *Mycoplasma genitalium*). Gonococci are cultured on **selective chocolate agar (modified Thayer–Martin, with vancomycin, colistin and nystatin) in 5–10% CO_2**, needed for sensitivity testing; NAAT is now the usual diagnostic test. **Gonorrhoea: ceftriaxone 1 g IM once (WHO 2024; CDC 2020 gives 500 mg, 1 g over 150 kg)**; azithromycin is no longer added routinely (CDC). **Chlamydia: doxycycline 100 mg twice daily for 7 days** (preferred; azithromycin 1 g in pregnancy). Complications: epididymitis, PID, infertility, ectopic pregnancy, reactive arthritis (with **keratoderma blennorrhagicum** and circinate balanitis), ophthalmia neonatorum.
- **Vaginal discharge**: **bacterial vaginosis** (the commonest cause; **Amsel's criteria**: thin grey homogeneous discharge, **pH over 4.5**, **positive whiff test** with KOH, **clue cells**; **Nugent score** the gold standard; metronidazole 500 mg twice daily for 7 days); **trichomoniasis** (frothy yellow-green discharge, **strawberry cervix**, motile flagellates; **metronidazole 500 mg twice daily for 7 days in women**, CDC 2021; treat partners);

candidiasis (curdy white, itch, **pH normal under 4.5**; fluconazole 150 mg once or a topical azole).

Hair, nutrition and skin signs of systemic disease

Hair loss

- **Non-scarring** (follicles survive, hair can regrow): **alopecia areata**, **androgenetic alopecia**, **telogen effluvium**, **anagen effluvium (chemotherapy, radiotherapy, thallium)**, traction alopecia, **trichotillomania** (broken hairs of different lengths, black dots, **hamburger sign** and flame hairs on trichoscopy), **secondary syphilis** ("moth-eaten"), ordinary **tinea capitis** (comma and corkscrew hairs).
- **Scarring (cicatricial)**: **lichen planopilaris** and frontal fibrosing alopecia, **discoid lupus** (carpet-tack scale, follicular plugging), **favus and kerion** (the inflammatory forms of tinea capitis), pseudopelade of Brocq, folliculitis decalvans, central centrifugal cicatricial alopecia, **aplasia cutis**, **naevus sebaceus**, burns and radiation, morphoea, tumours (BCC). On examination: loss of follicular openings. Biopsy decides.
- **Telogen effluvium**: diffuse shedding **2–3 months after a stressor** (childbirth, fever, surgery, **COVID-19**, crash dieting, iron deficiency, thyroid disease, drugs); a positive pull test with club (telogen) roots; recovers in 6 months once the cause goes. **Anagen effluvium** follows within days to weeks of chemotherapy, with tapered dystrophic hairs.
- **Alopecia areata**: autoimmune (CD8 T cells against the anagen bulb, loss of immune privilege; interferon-gamma and JAK–STAT signalling); round smooth patches, **exclamation-mark hairs** at the edge (tapered towards the scalp), **Coudability sign**, regrowth white at first; "overnight greying" because pigmented hairs fall first; **fine, regular (geometric) nail pitting** and **trachyonychia**; variants **ophiasis** (band round the occiput, poor prognosis), **totalis** (whole scalp) and **universalis** (whole body). Associations: atopy, thyroid disease, vitiligo, **Down syndrome**. **Treatment: intralesional triamcinolone** for limited patches in adults (first line), potent topical steroids in children, **contact immunotherapy (diphencyprone)** and minoxidil; **current practice for severe disease: oral JAK inhibitors (baricitinib, FDA 2022; ritlecitinib from 12 years, FDA 2023; deuruxolitinib, FDA 2024)**.
- **Androgenetic alopecia**: men, vertex and frontotemporal recession (**Hamilton–Norwood** scale); women, widening central parting with the frontal line kept (**Ludwig** scale); dihydrotestosterone miniaturises follicles. **Topical minoxidil** (both sexes) and **oral finasteride** (men; a 5-alpha-reductase type 2 inhibitor); **current practice: low-dose oral minoxidil** is widely used off-label; hair transplantation.
- **Hirsutism** (male-pattern terminal hair in a woman; **PCOS the commonest cause**; Ferriman–Gallwey score) is distinct from **hypertrichosis** (excess hair anywhere: drugs such as ciclosporin, minoxidil and phenytoin, porphyria, anorexia; **hypertrichosis lanuginosa acquisita** is paraneoplastic).

Nutritional and metabolic

- **Pellagra (niacin, vitamin B3): the 4 Ds, dermatitis, diarrhoea, dementia, death. Photosensitive** symmetrical dermatitis that turns dark and scaly, in a **Casal necklace** (the neck, C3–C4 territory), glove and boot distribution; glossitis. Niacin is made from tryptophan (**60 mg tryptophan gives 1 mg niacin**), a step that needs pyridoxine and riboflavin. Causes: **maize or sorghum (jowar) diets: in maize, niacin is bound as niacytin and tryptophan is low; in sorghum, excess leucine impairs the conversion** (Park; both are combined in the usual exam answer); **isoniazid** (pyridoxine antagonism); **carcinoid syndrome** (tryptophan diverted to serotonin); **Hartnup disease** (neutral amino acid transporter SLC6A19); chronic alcohol use; 6-mercaptopurine. Treat with **nicotinamide**. Lime-treated maize (nixtamalisation, as in Mexico) releases niacin.
- **Acrodermatitis enteropathica**: **zinc deficiency**; the inherited form is **autosomal recessive (SLC39A4, the ZIP4 zinc transporter)**, starting at weaning from breast milk; acquired in malabsorption, parenteral nutrition and premature infants fed low-zinc breast milk. **Periorificial and acral (hands, feet, napkin area) eczematous or bullous dermatitis, diarrhoea and alopecia**, with irritability and secondary candidiasis; **low serum zinc and alkaline phosphatase** (a zinc enzyme); **zinc supplements cure it quickly**.
- **Phrynoderma** ("toad skin", follicular hyperkeratosis on the extensors): vitamin A deficiency, also essential fatty acid and B-complex deficiency. **Riboflavin (B2)**: angular cheilitis, glossitis, seborrhoeic-like dermatitis. **Scurvy (vitamin C)**: **perifollicular haemorrhage, corkscrew hairs**, gum bleeding, poor wound healing. **Kwashiorkor**: flaky-paint dermatosis, **flag sign** of the hair (bands of pale and dark hair). **Biotin**: periorificial dermatitis and alopecia. **Vitamin B12**: hyperpigmentation of the knuckles.

Porphyrias

Porphyria	Enzyme	Skin	Key points
Porphyria cutanea tarda (the **commonest**)	**Uroporphyrinogen decarboxylase**, hepatic (mostly acquired, type 1; familial type 2 AD)	**Blisters, fragility, erosions, milia and scarring on the backs of the hands**, facial **hypertrichosis**, hyperpigmentation, sclerodermoid plaques	Triggers: **hepatitis C**, **alcohol**, **iron overload (HFE haemochromatosis)**, **oestrogens**, HIV; urine **uroporphyrin**, **pink-red fluorescence**; **phlebotomy or low-dose hydroxychloroquine**; avoid triggers

Porphyria	Enzyme	Skin	Key points
Acute intermittent porphyria	**Porphobilinogen deaminase (HMBS), autosomal dominant**	**None** (no porphyrin build-up)	**Neurovisceral attacks**: colicky abdominal pain, vomiting, constipation, tachycardia, hypertension, motor neuropathy, hyponatraemia (SIADH), anxiety or psychosis; **urine darkens to port-wine on standing**; triggered by drugs that induce ALA synthase or CYP450 (**barbiturates**, sulfonamides, griseofulvin, rifampicin, carbamazepine, phenytoin), **oestrogens and progesterone (premenstrual attacks)**, **alcohol**, **fasting**; diagnosis: **raised urinary porphobilinogen (and ALA) during the attack**; treatment: stop triggers, **intravenous haem (haem arginate or haemin)** and carbohydrate loading, opioid analgesia; **current practice: givosiran** (siRNA against hepatic ALAS1, FDA 2019) for recurrent attacks
Erythropoietic protoporphyria	**Ferrochelatase**	**Painful burning photosensitivity within minutes of sun, without blisters**, in childhood	Raised erythrocyte protoporphyrin; gallstones, liver failure; **afamelanotide** implant (FDA 2019)
Congenital erythropoietic porphyria (Günther)	**Uroporphyrinogen III synthase, autosomal recessive**	Severe blistering and mutilating scarring from infancy, hypertrichosis	**Erythrodontia (red teeth, red fluorescence)**, pink urine in nappies, haemolytic anaemia, splenomegaly
Variegate porphyria, hereditary coproporphyria	Protoporphyrinogen oxidase; coproporphyrinogen oxidase (both AD)	**Blistering like PCT plus acute attacks like AIP**	Variegate common in South Africa (founder effect)

- Lead poisoning inhibits **ALA dehydratase and ferrochelatase**. Skin-blistering porphyrias come from porphyrins absorbing light near 400 nm (the Soret band), so **ordinary sunscreens do not protect** (opaque reflectant ones do).

Skin as a window on systemic disease

Sign	Condition
Acanthosis nigricans	**Insulin resistance** (obesity, PCOS, type 2 diabetes, acromegaly, Cushing's); **sudden, extensive, itchy, with mucosal and palmar involvement ("tripe palms") in a thin older adult: gastric adenocarcinoma** (paraneoplastic, tumour TGF-alpha)
Leser–Trélat sign	Sudden eruption of many seborrhoeic keratoses: gastrointestinal (gastric) adenocarcinoma
Gottron's papules, Gottron's sign, **heliotrope rash**, **shawl and V signs**, **holster sign**, mechanic's hands, ragged cuticles	**Dermatomyositis**; in adults look for a **malignancy** (ovary, lung, stomach, colon; **nasopharyngeal carcinoma in East and Southeast Asians, especially southern Chinese**), especially with **anti-TIF1-gamma or anti-NXP2** antibodies; **anti-MDA5**: amyopathic disease with rapidly progressive interstitial lung disease and skin ulcers; **anti-Jo-1**: antisynthetase syndrome
Pyoderma gangrenosum	**IBD (ulcerative colitis)**, **rheumatoid arthritis**, **IgA monoclonal gammopathy, myeloma, myeloid leukaemia**; painful ulcer with an undermined violaceous edge; **pathergy** (worsens with surgery); steroids, ciclosporin, anti-TNF
Sweet syndrome (acute febrile neutrophilic dermatosis)	**Acute myeloid leukaemia**, infection, pregnancy, G-CSF; tender red plaques, fever, neutrophilia; steroids
Necrolytic migratory erythema	**Glucagonoma** (alpha-cell tumour, diabetes, weight loss)
Erythema gyratum repens	Wood-grain pattern: **lung carcinoma**
Acrokeratosis paraneoplastica (Bazex)	Psoriasiform plaques of ears, nose, hands: SCC of the upper aerodigestive tract
Acquired ichthyosis	**Hodgkin lymphoma**; also leprosy, HIV, sarcoid, hypothyroidism
Tylosis (focal palmoplantar keratoderma, Howel-Evans; RHBDF2)	**Oesophageal squamous carcinoma**
Lichen planus, porphyria cutanea tarda, cryoglobulinaemic vasculitis	**Hepatitis C**
Severe seborrhoeic dermatitis, sudden severe psoriasis, eosinophilic folliculitis, extensive molluscum, oral hairy leukoplakia, Kaposi sarcoma	**HIV**
Seborrhoeic dermatitis	Also **Parkinson's disease**
Erythema nodosum	Tender red nodules on the shins, **septal panniculitis without vasculitis**, heals like a bruise, never ulcerates; causes: **streptococcal infection (the commonest identifiable cause in the West)**, **tuberculosis (an important cause in South Asia)**, **sarcoidosis (Löfgren's syndrome: with bilateral hilar lymphadenopathy, fever, arthritis; good prognosis)**, IBD, **drugs (oral contraceptives, sulfonamides)**, pregnancy; **ENL in leprosy is a different reaction**
Lupus pernio	Violaceous plaques on the nose, cheeks and ears: **chronic sarcoidosis** with lung and upper-airway disease
Dermatitis herpetiformis	**Coeliac disease**
Keratoderma blennorrhagicum, circinate balanitis	**Reactive arthritis** (not Behçet's, which has oral and genital ulcers, pathergy and uveitis)
Necrobiosis lipoidica	Yellow-brown shin plaques with telangiectasia: **diabetes**

Sign	Condition
Eruptive xanthomas	Hypertriglyceridaemia (uncontrolled diabetes); tendon xanthomas: familial hypercholesterolaemia
Skin tags	Insulin resistance, pregnancy (perianal: Crohn's)
Café-au-lait macules, **Crowe's sign** (axillary and inguinal freckling), neurofibromas	**Neurofibromatosis 1**: smooth-bordered spots ("coast of California"); **McCune–Albright** has jagged, segmental ones ("coast of Maine") with polyostotic fibrous dysplasia and precocious puberty
Ash-leaf macules (the earliest sign; Wood's lamp), **facial angiofibromas** (adenoma sebaceum), **shagreen patch**, **periungual (Koenen) fibromas**, confetti macules	**Tuberous sclerosis** (TSC1 hamartin, TSC2 tuberin; mTOR overactive); everolimus for SEGA and angiomyolipoma, **topical sirolimus for angiofibromas**
Port-wine stain in the V1 territory	**Sturge–Weber syndrome** (somatic GNAQ mutation; glaucoma, seizures, tram-track calcification)
Malar rash sparing the nasolabial folds, photosensitivity, oral ulcers	**SLE**; **discoid lupus** scars (carpet-tack sign); **subacute cutaneous lupus** anti-Ro, often drug-induced (thiazides, PPIs, terbinafine); **neonatal lupus** (anti-Ro: "raccoon eyes" rash, **congenital heart block**)
Sclerodactyly, digital pits, telangiectasia, calcinosis, Raynaud's	**Systemic sclerosis** (limited: anticentromere; diffuse: anti-Scl-70, anti-RNA polymerase III)

- **NF1 diagnostic criteria** (revised 2021), two or more of: **6 or more café-au-lait macules over 5 mm before puberty or over 15 mm after**; **2 or more neurofibromas or 1 plexiform neurofibroma**; axillary or inguinal freckling; optic glioma; **2 or more Lisch nodules** (iris hamartomas) or choroidal abnormalities; a distinctive bony lesion (sphenoid dysplasia, tibial pseudarthrosis); a pathogenic NF1 variant; an affected parent. **Selumetinib** (MEK inhibitor, FDA 2020) shrinks plexiform neurofibromas.
- **Urticaria**: wheals that each last **under 24 hours** and leave no mark (lasting longer, with bruising, suggests **urticarial vasculitis**: biopsy); **angioedema** in the deeper dermis; **chronic if it lasts over 6 weeks**, usually spontaneous and autoimmune (IgG against IgE or its receptor), rarely allergic. Treatment: **second-generation H1 antihistamine, up-dosed to four times**, then **omalizumab** (anti-IgE), then ciclosporin; dupilumab is also approved for chronic spontaneous urticaria (FDA 2025). **Angioedema without wheals**: think of **ACE inhibitors** and **hereditary angioedema (C1-esterase inhibitor deficiency, low C4)**, which does not respond to antihistamines or adrenaline (C1-inhibitor concentrate, icatibant). **Dermographism** is the commonest physical urticaria; cholinergic urticaria comes with heat and exercise.
- **Erythema multiforme**: **typical target lesions** (three zones) on the **acral** limbs, spreading centripetally; **HSV the commonest trigger** (recurrent EM), then *Mycoplasma*; drugs less often; little or one-site mucosal involvement (EM minor) or more (EM major); suppressive aciclovir for recurrent HSV-associated EM. Distinct from SJS, which has atypical flat targets and widespread mucosal disease from drugs.
- **Other named erythemas**: **erythema migrans (chronicum migrans)**, an expanding annular patch with central clearing at a tick bite, **Lyme disease** (*Borrelia burgdorferi*, *Ixodes* ticks; doxycycline, amoxicillin in pregnancy); **erythema marginatum**, evanescent rings on the trunk, **rheumatic fever**; **erythema infectiosum**, fifth disease; **erythema toxicum neonatorum**, benign blotchy papulopustules with eosinophils in a newborn; **erythema gyratum repens**, internal malignancy (see table).
- **Peutz–Jeghers syndrome**: **mucocutaneous lentigines on the lips, buccal mucosa, hands and feet** from childhood (those on the lips may fade in adult life, the buccal ones persist), with **hamartomatous gastrointestinal polyps**, mostly in the small intestine (intussusception, bleeding), autosomal dominant **STK11 (LKB1)** mutation, and a raised risk of gastrointestinal, breast and pancreatic cancer.
- Other named signs: **Darier's sign** (a lesion urticates when rubbed) in **urticaria pigmentosa (mastocytosis)**; **buttonhole sign** (the lesion invaginates under the finger) in **neurofibromas**; **target (iris) lesion** in erythema multiforme; **volcano sign** in cutaneous leishmaniasis; **Osler's sign** (blue-black scleral pigment near the recti insertions) in **alkaptonuria**; **Hertoghe's (Queen Anne's) sign** (loss of the outer third of the eyebrows) in atopic dermatitis, hypothyroidism and lepromatous leprosy; "breakfast, lunch and dinner" bites in bed bugs; **Groove sign** in LGV; **Chik sign** (brown pigmentation of the nose) after chikungunya.

Primary lesions (sizes)

- **Macule** flat, under 1 cm; **patch** flat, over 1 cm. **Papule** raised and solid, under 1 cm (a 3 mm raised solid lesion is a papule); **plaque** raised, over 1 cm, broader than it is high; **nodule** solid and deeper, over 1 cm. **Vesicle** fluid-filled, under 1 cm; **bulla** over 1 cm. **Pustule**: pus-filled. **Wheal**: transient dermal oedema. These 1 cm limits are Bolognia's and the usual exam answer; Rook and Fitzpatrick put papule, vesicle and nodule at **0.5 cm**, so read the options.
- Bleeding into skin, not blanching on diascopy: **petechiae** pinpoint (up to about 3 mm; some books 4 mm), **purpura** about 3–10 mm, **ecchymosis** over 1 cm. **Palpable purpura** means **small-vessel (leukocytoclastic) vasculitis** (IgA vasculitis, Henoch–Schönlein, in children).

Tumours and therapy

Melanoma

- From melanocytes; risk factors: **intermittent intense sun and sunburn in childhood**, fair skin (Fitzpatrick I–II), many or atypical naevi, a **giant congenital naevus** (over 20 cm), family history (**CDKN2A**), xeroderma pigmentosum, immunosuppression. Recognition: **ABCDE** (asymmetry, border irregularity, colour variation, **diameter over 6 mm**, evolution) and the "ugly duckling" sign; **dermoscopy** improves accuracy. **Excision biopsy with a 1–3 mm margin** is the biopsy of choice (not shave or incision of a suspected melanoma where avoidable).
- Immunohistochemistry: **S-100 (most sensitive), HMB-45 and Melan-A (more specific), SOX10**; PRAME helps tell melanoma from a naevus (modern).
- **Breslow thickness, the vertical depth in millimetres from the top of the granular layer (or the base of an ulcer) to the deepest tumour cell, is the most important prognostic factor in localised (stage I–II) melanoma**; **ulceration** is next (it upstages the tumour); **mitotic rate** also predicts outcome (dropped from T-staging in AJCC 8th but still reported). **Clark level** (anatomical depth, I–V) is older and adds little. Once it has spread, **sentinel node status is the strongest predictor**. AJCC 8th (2017) T-stage: T1 up to 1.0 mm (T1a under 0.8 mm without ulceration), T2 1–2 mm, T3 2–4 mm, T4 over 4 mm.

- **Wide local excision margins** (NCCN, BAD): in situ **0.5–1 cm**; **up to 1 mm: 1 cm**; **1–2 mm: 1–2 cm**; **over 2 mm: 2 cm** (so a **3 mm melanoma needs 2 cm**). Many exam books simplify this to 1 cm below 1 mm and 2 cm above. **Sentinel node biopsy**: discussed from **0.8 mm or any ulceration (T1b)**, offered over 1 mm. Completion lymph node dissection after a positive sentinel node is **no longer routine** (trial evidence, 2017): ultrasound surveillance instead.
- **Types**: **superficial spreading is the commonest in fair skin** (about 70%; long radial growth phase, trunk and legs); **nodular is the most aggressive** (vertical growth from the start, often amelanotic or blue-black, no ABCD warning); **lentigo maligna melanoma** (chronic sun-damaged face of the elderly, from lentigo maligna, the **least aggressive**, slowest growing); **acral lentiginous** (**palms, soles, subungual**; **the commonest type in dark-skinned and Asian people, including South Asia**; not related to sun; often diagnosed late, hence its worse outcome). **Desmoplastic** and mucosal melanomas are rare. Commonest site: **the back in men, the legs in women**. Melanoma is **relatively radioresistant**.
- **Hutchinson's sign** (of the nail): **pigment spreading from a nail streak onto the proximal or lateral nail fold** suggests **subungual melanoma** (the commonest site the big toe or thumb). Not to be confused with Hutchinson's sign of zoster or Hutchinson's teeth.
- **Molecular and modern treatment**: **BRAF V600E** mutation in about half (sun-exposed trunk, young), **NRAS** in about a fifth, **KIT** in acral and mucosal melanoma. **BRAF plus MEK inhibitors (dabrafenib with trametinib; encorafenib with binimetinib)** for BRAF-mutant disease. **Immune checkpoint inhibitors**: **anti-PD-1 (nivolumab, pembrolizumab)**, **anti-CTLA-4 (ipilimumab)**, **anti-LAG-3 (relatlimab with nivolumab, FDA 2022)**; used for metastatic disease and as **adjuvant** therapy after resection of stage IIB–IV disease, and now **neoadjuvant pembrolizumab** before surgery for resectable stage III (2023). Immune-related side effects: colitis, hepatitis, thyroiditis, hypophysitis, pneumonitis, vitiligo-like depigmentation (a good sign).

Non-melanoma skin cancer

- **Basal cell carcinoma (rodent ulcer)**: the **commonest skin cancer** and the commonest cancer in fair-skinned people; **pearly, translucent papule with telangiectasia and a rolled edge**, central ulcer; **face above a line from the angle of the mouth to the ear lobe, inner canthus**; the **commonest eyelid malignancy** (lower lid; in some South Asian series sebaceous carcinoma comes close); **palisading of basal cells at the periphery** with retraction clefts; **locally invasive, almost never metastasises**. Subtypes: **nodular (commonest)**, superficial (trunk), **morphoeic (sclerosing), the most aggressive locally**, pigmented (commoner in Asian skin). Causes: **UV (mostly UVB)**, **arsenic** (in groundwater, documented in parts of Nepal's Terai), radiation, immunosuppression. **Hedgehog pathway: PTCH1 loss**; **Gorlin (naevoid BCC) syndrome**: many BCCs from youth, **odontogenic keratocysts of the jaw, palmar pits**, falx calcification, bifid ribs, medulloblastoma (AD, PTCH1). Treatment: **surgical excision (4 mm margin for small well-defined lesions)**; **Mohs micrographic surgery** for high-risk sites (central face), recurrent and morphoeic BCC; superficial BCC: imiquimod, 5-fluorouracil, photodynamic therapy, cryotherapy; **hedgehog inhibitors (vismodegib, sonidegib)** for advanced or metastatic disease, cemiplimab after them.
- **Squamous cell carcinoma**: the **second commonest skin cancer**, but **the commonest in organ-transplant recipients** (65 to 250 times the usual risk) and in **albinism**; sun-exposed skin (lip, ear, back of hand); arises on **actinic keratosis** (the commonest precursor; flag sign on histology), **Bowen's disease** (SCC in situ; on the glans, **erythroplasia of Queyrat**), chronic ulcers, sinuses and **burn scars (Marjolin's ulcer: slow-growing, painless, no nodes until late)**, lupus vulgaris, **HPV**, arsenic, chronic radiation dermatitis, recessive dystrophic EB; **keratin pearls**, intercellular bridges; **can metastasise** (lip and ear the riskiest). Treatment: excision (4–6 mm margins), Mohs, radiotherapy; **cemiplimab (anti-PD-1, FDA 2018)** for advanced disease.
- **Keratoacanthoma**: a **rapidly growing (weeks), volcano-shaped nodule with a central keratin plug** on sun-exposed skin of the elderly; usually **regresses on its own** within months, but because it cannot be told from SCC reliably it is **regarded as a well-differentiated SCC variant and excised**. Multiple: Ferguson-Smith, Muir–Torre (sebaceous tumours with colorectal cancer, mismatch-repair genes).
- **Seborrhoeic keratosis**: benign, waxy, **"stuck-on"** warty plaque with horn cysts, in the elderly; **dermatosis papulosa nigra** is its small facial form in dark skin.
- **Xeroderma pigmentosum**: **autosomal recessive defect of nucleotide excision repair** (cannot repair UV thymine dimers); freckling and skin cancers (BCC, SCC, melanoma) from childhood, eye damage, some with neurological decline; strict sun avoidance.
- **Merkel cell carcinoma**: aggressive red-violet nodule on the sun-exposed head of the elderly or immunosuppressed; **Merkel cell polyomavirus** in about 80%; **CK20 with a perinuclear dot**; **avelumab** and pembrolizumab (checkpoint inhibitors) for advanced disease.
- **Kaposi sarcoma**: **HHV-8**; violaceous patches, plaques and nodules, spindle cells and slit-like vascular spaces; forms: classic (elderly Mediterranean men, legs), endemic (Africa), **iatrogenic (transplant)**, **AIDS-associated (historically the commonest AIDS-defining cancer; falls with antiretroviral therapy)**.
- **Mycosis fungoides**: the **commonest primary cutaneous lymphoma** (cutaneous T-cell lymphoma, **CD4**), patch, plaque and tumour stages on sun-protected skin (buttocks, trunk); **epidermotropism with Pautrier microabscesses**; **Sézary syndrome**: **erythroderma, lymphadenopathy and circulating cerebriform Sézary cells**. Treatment by stage: topical steroids, phototherapy (NB-UVB, PUVA), radiotherapy, retinoids (bexarotene).

Acne and isotretinoin

- Acne vulgaris: **the commonest skin disease of adolescents** (about 85% at some time); four steps: **androgen-driven sebum excess, follicular hyperkeratinisation, *Cutibacterium (formerly Propionibacterium) acnes* and inflammation**; **comedones (open blackheads, closed whiteheads) are the hallmark lesion**, absent in rosacea. Hormonal clues in women: PCOS. Drug-induced acne (steroids, isoniazid, lithium, phenytoin, anabolic steroids) is monomorphic, without comedones. **Acne fulminans** and acne conglobata are severe forms.
- Ladder: **mild comedonal: topical retinoid (tretinoin, adapalene)**; **mild–moderate inflammatory: topical retinoid with benzoyl peroxide** (which prevents antibiotic resistance), topical clindamycin with benzoyl peroxide, azelaic acid;

moderate: add oral doxycycline or minocycline for up to 3–4 months (never antibiotic alone; never with isotretinoin); women: **combined oral contraceptive or spironolactone**; **severe nodulocystic or scarring acne, or failure of the above: oral isotretinoin** (the most effective treatment, the only one that changes the disease's course).

- **Isotretinoin**: 0.5–1 mg/kg a day to a cumulative 120–150 mg/kg (low-dose regimens are now common), for about 4–6 months. **Highly teratogenic** (craniofacial, cardiac, thymic and CNS defects): **two negative pregnancy tests before starting, two forms of contraception from 1 month before, throughout and for 1 month after**, a monthly pregnancy test (iPLEDGE and similar programmes); no blood donation. Side effects: **cheilitis (the commonest; nearly universal)**, dry skin and eyes, epistaxis, raised triglycerides and liver enzymes (check before and during), myalgia and back pain, photosensitivity, early flare, hyperostosis, mood change and depression (counsel and watch). **Not combined with tetracyclines** (both cause **benign intracranial hypertension**).
- **Rosacea**: adults over 30, flushing, persistent central facial erythema, telangiectasia, papules and pustules **without comedones**, **rhinophyma** (men), **ocular rosacea** (blepharitis, conjunctivitis, keratitis); *Demodex* mites and neurovascular dysregulation; triggers heat, alcohol, spicy food, sun. **Topical steroids worsen it and cause steroid rosacea.** Treatment by phenotype (ROSCO 2017): topical **ivermectin 1%**, metronidazole or azelaic acid; **brimonidine or oxymetazoline** for erythema; oral doxycycline (low dose); isotretinoin for refractory; laser for telangiectasia.

Topical corticosteroids

- **Potency classes** (US: I super-potent to VII least): **clobetasol propionate 0.05% is the most potent** (class I; UK "very potent"); betamethasone valerate 0.1% and mometasone 0.1% potent; clobetasone butyrate moderate; **hydrocortisone 1% the least potent**. Ointments penetrate better than creams; **occlusion raises absorption about tenfold**.
- **Amount: the fingertip unit** (a line from the tip to the first crease of an adult index finger, about **0.5 g**) covers **two adult palms' area**.
- **Used in**: psoriasis, atopic and contact dermatitis, **vitiligo**, lichen planus, discoid lupus, bullous pemphigoid, alopecia areata (intralesional). **Contraindicated or avoided: acne, rosacea, perioral dermatitis, scabies, untreated bacterial, viral or fungal infection (tinea incognito)**, leg ulcers.
- **Avoid potent steroids on the face, flexures, genitals and in infants**: thin skin with a thin corneum, and occluded folds or nappies, absorb far more. **Local effects**: **atrophy (the commonest)**, striae (permanent), telangiectasia, purpura and bruising, **perioral dermatitis and steroid-induced acne or rosacea**, hypopigmentation, **hypertrichosis**, folliculitis, delayed wound healing, masked infection (**tinea incognito**), glaucoma and cataract from eyelid use, contact allergy. **Systemic effects** (large areas, potent agents, occlusion, infants): **HPA-axis suppression**, Cushingoid features, **growth retardation in children**, hyperglycaemia, hypertension, osteoporosis. **Topical steroid misuse** (unprescribed combination creams of a potent steroid with an antifungal and an antibiotic, sold over the counter) is a major problem in South Asia: **topical steroid-damaged face** and steroid-modified chronic tinea.
- **Topical calcineurin inhibitors** (tacrolimus, pimecrolimus) are steroid-sparing for the face and folds: no atrophy; burning at first.

Cutaneous drug reactions

- **Morbilliform (exanthematous) eruption is the commonest**, 4–14 days after starting (aminopenicillins, especially **amoxicillin in infectious mononucleosis**, sulfonamides, anticonvulsants).
- **Fixed drug eruption**: a round dusky-violet plaque or bulla that **recurs at the same site** each time the drug is taken, leaving **grey-brown pigmentation**; lips, genitals, hands; **cotrimoxazole and other sulfonamides, NSAIDs, tetracyclines, fluconazole, paracetamol**; diagnosed by oral or topical provocation after healing.
- **DRESS** (drug reaction with eosinophilia and systemic symptoms): **2–8 weeks** after starting (later than other reactions); **fever, facial oedema, widespread rash, lymphadenopathy, eosinophilia, atypical lymphocytes, hepatitis (the commonest organ; also kidney, lung, heart)**; **anticonvulsants (carbamazepine, phenytoin, lamotrigine), allopurinol, sulfonamides, dapsone, minocycline, vancomycin**; **HHV-6 reactivation**; RegiSCAR scoring; stop the drug, **systemic corticosteroids**; thyroiditis and diabetes may follow months later.
- **AGEP** (acute generalised exanthematous pustulosis): **within 48 hours**, many sterile non-follicular pinhead pustules on oedematous erythema in the folds, fever, neutrophilia; **beta-lactams and macrolides**, hydroxychloroquine, diltiazem; resolves in about 2 weeks once the drug is stopped.
- **SJS/TEN** (see Bacterial and viral skin infections) is the most dangerous: latency 4–28 days. Others: photosensitivity (tetracyclines, especially doxycycline, thiazides, amiodarone with blue-grey pigment, fluoroquinolones, voriconazole), drug-induced lupus, lichenoid eruption, **hand–foot syndrome** (capecitabine, 5-FU), acneiform rash with EGFR inhibitors (a sign of response).

Infections

Revision of the infections an examiner asks across the skin; the full detail of each is in the earlier sections (leprosy, bacterial and viral, fungal, syphilis and genital ulcers).

Fungal and viral organisms

Condition	Organism	Key fact
Pityriasis versicolor	*Malassezia* **(a lipophilic yeast;** *M. globosa* **commonest)**, not a dermatophyte	Scaly hypo- or hyperpigmented macules on the trunk and neck; KOH shows **short hyphae with round spores ("spaghetti and meatballs")**; yellow-gold fluorescence; **topical ketoconazole or selenium sulphide**
Tinea (dermatophytosis)	*Trichophyton, Microsporum, Epidermophyton*	KOH shows branching septate hyphae; terbinafine or itraconazole
Intertrigo, candidiasis	*Candida*	Satellite pustules; pseudohyphae and yeast
Erythrasma	*Corynebacterium minutissimum*	**Coral-red fluorescence** under Wood's lamp; erythromycin

Condition	Organism	Key fact
Molluscum contagiosum	**Poxvirus (family Poxviridae)**	**Pearly, umbilicated papules with a central core**; histology shows **molluscum (Henderson–Paterson) bodies**; self-limiting in children, extensive in HIV; curettage, cryotherapy
Warts	Human papillomavirus	Types 1, 2, 4 common warts; 6 and 11 genital warts; 16 and 18 cancer risk
Hand, foot and mouth	Coxsackie A16, enterovirus 71	Picornavirus
Herpes simplex, chickenpox, zoster	Herpesviruses (HSV, VZV)	Tzanck smear shows multinucleated giant cells

- **Herpes zoster:** reactivation of VZV from a dorsal root or cranial ganglion; **burning pain first (prodrome), then grouped vesicles on an erythematous base confined to one dermatome** (thoracic commonest) and not crossing the midline. **Treatment: oral aciclovir, valaciclovir or famciclovir, ideally within 72 hours of the rash**, which shortens the illness and reduces the risk of **postherpetic neuralgia**; analgesia, and gabapentin or amitriptyline for neuralgia. Steroids are not antiviral; antibiotics only for secondary infection. **Ophthalmic zoster** (Hutchinson sign) and the Ramsay Hunt syndrome need urgent treatment. The **recombinant zoster vaccine** (Shingrix) is the current preventive option for people over 50.
- **Chancroid** (*Haemophilus ducreyi*, Gram-negative coccobacillus): **painful, soft, ragged ulcer with undermined edges and a tender suppurative inguinal bubo**; contrast the painless indurated chancre of syphilis. Treatment: **single-dose azithromycin 1 g or ceftriaxone 250 mg IM**. Donovanosis is *Klebsiella granulomatis*, LGV is *C. trachomatis* L1–L3.
- **Gonorrhoea:** *Neisseria gonorrhoeae*, Gram-negative intracellular diplococci; **culture on selective chocolate agar (modified Thayer–Martin) in a CO_2-rich atmosphere**, nucleic acid amplification tests are now the usual diagnosis; commonest cause of non-gonococcal urethritis is *Chlamydia trachomatis*. Resistance to penicillins, tetracyclines and fluoroquinolones is widespread, so the **first-line drug is a single injection of ceftriaxone** (WHO 2024 recommends 1 g IM; CDC 2020 500 mg), with treatment for chlamydia where it is not excluded; doxycycline alone is unreliable.
- **Leprosy** has its own section and **cutaneous tuberculosis** is under Bacterial and viral skin infections; syphilis is a spirochaete (*Treponema pallidum*), treated with benzathine penicillin.
- **Rose spots** of **enteric (typhoid) fever**: a few pink, blanching macules on the lower chest and abdomen at the end of the first week or in the second, in about a third of patients, each fading in 2–3 days; the fever-day table (typhoid day 7) is under Viral exanthems. **Koplik spots** (measles, buccal mucosa) and **Forchheimer spots** (petechiae on the soft palate, in rubella, though not specific: also in infectious mononucleosis and scarlet fever) are the enanthems to match to disease.
- **Herpes labialis (HSV-1)**: **tingling prodrome, then grouped vesicles on the vermilion border and adjacent skin**, crusting in about a week, recurring after sun, fever or stress; **recurrent aphthous ulcers are round, shallow, grey-based ulcers on non-keratinised mucosa and spare the vermilion border**. Topical or oral aciclovir or valaciclovir early in the prodrome; suppressive therapy for frequent recurrences.

Drug and immunological

Severe cutaneous adverse reactions

Reaction	Skin	Mucosa	Typical culprit
Stevens–Johnson syndrome (SJS)	**Epidermal detachment under 10% of body surface area (BSA)**	Two or more mucosae, usual	Allopurinol, sulfonamides, anticonvulsants
SJS–TEN overlap	**10–30% BSA**	Usual	
Toxic epidermal necrolysis (TEN)	**More than 30% BSA**	Usual	Same drugs; nevirapine, oxicam NSAIDs
DRESS	Morbilliform rash, facial oedema	Rare	Allopurinol, carbamazepine, phenytoin, dapsone, vancomycin; eosinophilia, hepatitis, 2–8 weeks after starting
Acute generalised exanthematous pustulosis (AGEP)	Sheets of sterile pustules, within 48 hours	Rare	Aminopenicillins, macrolides
Fixed drug eruption	**Round dusky plaque recurring at the same site on each re-exposure, leaving brown pigment**	Lips, genitals	**Cotrimoxazole**, tetracyclines, NSAIDs, paracetamol

- **SJS and TEN are a spectrum defined by the body surface area detached; mucosal involvement is usual in all three and does not define the class.** Histology: **full-thickness epidermal necrosis**, with a split at the dermo-epidermal junction mediated by cytotoxic T cells (granulysin). Nikolsky sign is positive. Management: **stop the culprit drug immediately** (the earlier, the better), supportive care in a burns or intensive care setting (fluids, temperature, wound and eye care, nutrition); **SCORTEN** gives prognosis. Current practice: ciclosporin or etanercept are used by some units; high-dose steroids and IV immunoglobulin are not proven. **HLA-B*15:02 predicts carbamazepine SJS/TEN in several Asian populations and HLA-B*58:01 predicts allopurinol reactions**, so genotyping is advised where those alleles are common.
- **Urticaria:** transient itchy wheals each lasting under 24 hours (mast-cell histamine); **angioedema** is deeper swelling of lips, eyelids and airway. Acute causes: food, drugs (penicillins, NSAIDs), infection. **Non-sedating H1 antihistamines are first line**; omalizumab for refractory chronic spontaneous urticaria. **Hereditary angioedema** (C1-esterase inhibitor deficiency) causes swelling without urticaria (bradykinin, not histamine) and responds poorly to adrenaline, antihistamines and steroids; it is treated with C1-esterase inhibitor concentrate or icatibant (a bradykinin B2 receptor blocker). **ACE inhibitors cause angioedema** without wheals.

- **Anaphylaxis:** intramuscular adrenaline 0.5 mg (1:1000, 0.5 mL) in an adult into the anterolateral thigh is the first drug.
- **Erythema multiforme** (typical acral target lesions, HSV the commonest trigger) is distinct from SJS (atypical flat targets, drugs).

Eczema

Atopic dermatitis

- **Pathogenesis:** an **inherited skin barrier defect plus a Th2-skewed immune response. Loss-of-function mutations in the filaggrin gene (FLG)** impair the stratum corneum and the natural moisturising factor, so skin is dry, permeable to allergens and loses water; the same mutations cause **ichthyosis vulgaris**. IL-4, IL-13 and IL-31 drive inflammation and itch; raised serum IgE; the atopic triad is eczema, asthma and allergic rhinitis. Desmoglein 3 (pemphigus vulgaris), type VII collagen (dystrophic epidermolysis bullosa) and uroporphyrinogen decarboxylase (porphyria cutanea tarda) are unrelated genes.
- **Distribution by age: infants: face and extensor surfaces, the napkin area spared**; children and adults: **flexures** (antecubital and popliteal fossae). **Itch is essential.** Signs: **Dennie–Morgan infraorbital folds**, white dermatographism, Hertoghe sign (loss of the outer third of the eyebrows), palmar hyperlinearity, keratosis pilaris, pityriasis alba. Hanifin–Rajka criteria; UK Working Party criteria are simpler.
- **Complications:** secondary *Staphylococcus aureus* infection (impetiginisation), **eczema herpeticum** (HSV, an emergency treated with aciclovir), molluscum, cataract and keratoconus.
- **Treatment ladder:** emollients and bathing care (the base of treatment), **topical corticosteroids** by potency and site, **topical calcineurin inhibitors (tacrolimus, pimecrolimus)** for the face and flexures, wet wraps, phototherapy; for severe disease **dupilumab (anti-IL-4R-alpha, the first biologic)**, tralokinumab, lebrikizumab and **JAK inhibitors (upadacitinib, abrocitinib)**, and ciclosporin or methotrexate. Antihistamines help sleep only.
- **Other eczemas: contact dermatitis** (irritant, the commonest; allergic, type IV hypersensitivity, nickel the commonest allergen, patch test is the test), **seborrhoeic dermatitis** (Malassezia; greasy scale on scalp, nasolabial folds; ketoconazole shampoo; extensive in HIV and Parkinson disease), **nummular (discoid)**, **stasis** (venous insufficiency) and **dyshidrotic (pompholyx)** eczema.

Pigmentary disorders

Hypopigmentation

Feature	Vitiligo	Oculocutaneous albinism	Piebaldism
Cause	**Acquired autoimmune destruction of melanocytes** (CD8 T cells)	**Inherited defect of melanin synthesis (tyrosinase in type 1)**	KIT mutation; melanocytes fail to migrate
Melanocytes in the patch	**Absent**	**Present in normal number but unable to make melanin**	Absent in the patches
Distribution	Acquired depigmented patches, often symmetrical (face, hands, genitals); Koebner phenomenon	**Diffuse, from birth**; pale skin and hair, **visual problems** (nystagmus, photophobia)	Congenital stable patches, white forelock
Under Wood's lamp	**Chalk white**	Pale	Pale
Associations	Thyroid disease, alopecia areata, type 1 diabetes, pernicious anaemia	**High risk of squamous cell carcinoma and sun damage**	Usually none

- **Vitiligo treatment:** topical steroids or calcineurin inhibitors, **NB-UVB** (best for generalised disease), surgical grafting for stable segmental disease, **topical ruxolitinib** (JAK inhibitor, FDA 2022) for repigmentation. Sunscreen protects depigmented skin.
- **Melanin synthesis:** tyrosine to DOPA to dopaquinone by **tyrosinase (copper-dependent)** in the melanosome; skin colour depends on the amount and type of melanin (eumelanin versus pheomelanin) and not on the number of melanocytes, which is roughly equal in all races.
- **Melasma:** symmetrical brown patches on the cheeks, forehead and upper lip in women, driven by **sunlight, hormones (pregnancy, oral contraceptive pill) and genetics**. **Ultraviolet and visible light stimulate melanocytes, so strict photoprotection with broad-spectrum, preferably tinted, sunscreen is the basis of management**; any treatment fails if exposure continues and the disorder relapses. Treatments: **hydroquinone (tyrosinase inhibitor)**, the triple combination (hydroquinone, tretinoin, mild steroid), azelaic acid, **oral tranexamic acid**, chemical peels, and careful lasers. Epidermal melasma shows more in Wood's lamp light than dermal melasma.
- **Hyperpigmentation, other:** post-inflammatory (after eczema, acne, fixed drug eruption), **acanthosis nigricans** (insulin resistance; velvety hyperpigmentation in the neck and axillae), **Addison disease** (ACTH and MSH; buccal and palmar-crease pigment), café-au-lait macules (neurofibromatosis type 1: six or more over 5 mm before puberty), **phytophotodermatitis**, and **drug pigmentation** (amiodarone blue-grey, minocycline, hydroxychloroquine).
- **Incontinentia pigmenti**: **X-linked dominant (IKBKG/NEMO)**, lethal in most males; in girls, four stages along Blaschko's lines (blisters, warty lesions, swirled hyperpigmentation, atrophic hypopigmentation) with possible eye, dental and CNS involvement.
- **Other naevi**: **Becker naevus** (hairy hyperpigmented patch on the shoulder or chest, in male adolescents), **Spitz naevus** (pink dome-shaped papule in children), **naevus of Ito** (shoulder and neck dermal melanocytosis, like Ota).

Sources

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- Curriculum fill (2026-11-26): Rook's Textbook of Dermatology; Fitzpatrick's Dermatology; IADVL and AAD guidance on atopic dermatitis (AAD 2023), melasma and vitiligo; WHO 2024 gonorrhoea update; Bolognia's Dermatology for severe cutaneous adverse reactions.