

45 Skin and subcutaneous tissue

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Acquired

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Kaposi's sarcoma Kaposi's sarcoma is a malignant, proliferative tumour of vascular endothelial cells, which was first described in elderly Jewish men but is now most commonly associated with immune compromise after transplantation or HIV infection (Figure 45.50). There appears to be a causal link with infection by human herpesvirus 8. Kaposi's sarcoma usually starts as a red-brown, indurated, plaque-like skin lesion that becomes nodular and then ulcerates. Treatment is with radiotherapy .

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Pressure sores These begin with tissue necrosis at a pressure point and develop into a cone-shaped volume of necrotic loss. As many as 10% of acute hospital inpatients will have some degree of pressure sore. The majority affect the elderly and patients with spinal injury or decreased sensibility; 80% of paraplegics will get a pressure sore and 8% die as a result. The pathogenesis of pressure sores revolves around unrelieved pressure: an increase in local tissue pressure above that of perfusion pressure produces ischaemic necrosis that is directly proportional to the duration and degree of pressure and inversely proportional to the area over which it is applied. Muscle and fat are more susceptible to pressure than skin. In a patient who has no predisposing factors management is aimed at debridement and repair of the defect, on the assumption that recurrence will not occur once normal function and sensibility returns. In the paraplegic patient, recurrence is likely so management should involve a multidisciplinary approach. Primary treatment involves relieving pressure (special mattress, nursing care, relief of muscle spasm and contractures), optimising nutrition, correcting anaemia and preventing infection. Surgery involves thorough debridement to promote healing and plastic surgery to reconstruct the defect.

Ulcers An ulcer is a discontinuity of an epithelial surface. It is characterised by destruction of the surface epithelium and a granulating base. Ulcers can be classified as non-specific, specific and malignant (Figure 45.51).

Sinus A sinus is a blind-ending tract connecting a cavity lined with granulation tissue (often an abscess cavity) to an epithelial surface (a) (b) (c) (d) (e) Burrill Bernard Crohn , 1884–1983, gastroenterologist, Mount Sinai Hospital, New York, NY , USA, described regional ileitis in 1932. - surface (Figure 45.52a). Sinuses may be congenital or acquired. Congenital sinuses arise from the remnants of persistent embryonic ducts. Acquired sinuses can result from: a retained foreign body (ingrown hair or suture material); chronic infection (tuberculosis, osteomyelitis or actinomycosis); chronic inflammation (Crohn's disease); malignancy; or inadequate surgical drainage of a cavity .

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Anomalies of skin metabolism

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Skin has the potential for a blood supply 20–100 times greater than its metabolic and thermoregulatory requirements. This apparent excess enables restitution of mechanical integrity after the myriad of trivial injuries (scratching, stretching, compressing, thermal) to which skin is subjected; however, blood supply is inadequate to support full-thickness wound healing, which requires primary closure or granulation tissue. Skin functions optimally at temperatures below body core temperature and can tolerate long periods of ischaemia, allowing it to be both grafted and/or expanded for use in reconstruction. Anomalies of skin metabolism

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Atypical (dysplastic) naevus

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To be 'atypical naevi', lesions must have three of the following in situ characteristics: variegated pigmentation; ill-defined borders; undulating irregular surfaces; or size >5 mm. Terminology is confused because, although the terms 'dysplastic' and 'atypical' are often used interchangeably, dysplasia is a histological diagnosis with findings of irregular proliferations of melanocytes at the basal layer of the epidermis. In fact, a small proportion of clinically 'atypical naevi' are actually dysplastic when examined microscopically. Atypical naevi can be sporadic or familial (familial atypical multiple mole-melanoma [FAMMM] syndrome). Possession of more than five lesions confers a relative risk of melanoma six times greater than usual; within FAMMM syndrome confer a 100% risk of malignant melanoma and patients with FAMMM syndrome should be screened for melanoma 6-monthly, lifelong (Figure 45.29). Data from the World Health Organization suggest that both non-melanoma and melanoma skin cancers continue to increase in incidence, despite educational programmes and wide-ranging changes in uptake of sun protective measures and improvements in sunscreens. Skin cancer is the commonest malignancy in white-skinned people, constituting 33% of all recorded malignancies annually, with 2-3 million new non-melanoma skin cancers and 132 000 new malignant melanomas (4.5% of all new cancers) each year.

Figure 45.28 Giant congenital pigmented naevus (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.29 Dysplastic naevus (courtesy of St John's Institute for Dermatology, London, UK).

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Basal cell carcinoma

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This is usually a slow-growing, locally invasive, malignant tumour of pluripotential epithelial cells arising from basal epidermis and hair follicles; hence, it affects the pilosebaceous skin. Summary box 45.2 Basal cell carcinoma /uni25CF /uni25CF /uni25CF /uni25CF - Epidemiology The strongest predisposing factor to BCC is UVR. It occurs in the elderly or the middle-aged after excessive sun exposure, - with 95% occurring between the ages of 40 and 80 years. The incidence of BCC rises with proximity to the equator, although 33% arise in parts of the body not usually exposed to the sun. Other predisposing factors include exposure to arsenical compounds, coal tar, aromatic hydrocarbons and IR, they and genetic skin cancer syndromes. White-skinned people are almost exclusively affected. BCC is more common in men than in women. Pathogenesis BCCs have no apparent precursor lesions and their development is proportional to the initial dose of the carcinogen, but not duration of exposure. The most likely model of pathological factors as intrinsic genesis for BCCs involves mesoderm promoters coupled with an initiation step. BCCs metastasise extremely rarely. Macroscopic BCCs can be divided into localised (nodular, nodulocystic, cystic, pigmented and naevoid) and generalised (superficial: multifocal and superficial spreading; or infiltrative: morphoeic, ice pick and cicatrising). Nodular and nodulocystic variants account for 90% of BCCs. Microscopic Twenty-six histological subtypes have been described. The characteristic finding is of ovoid cells in nests with a single

Slow growing Risk factor – UVR 90% nodular/nodular cystic High- and low-risk BCC

divide, explaining why tumour growth rates are slower than their cell cycle speed would suggest and why incompletely excised lesions are more aggressive. Morphoeic BCCs synthesise type 4 collagenase and so spread rapidly (Figure 45.30 Frederic E Mohs, 1910–2002, American physician and general surgeon, University of Wisconsin, Madison, WI, USA, developed Mohs' micrographic surgical technique in 1938 for cutaneous malignant lesions. Jean-Nicolas Marjolin, 1780–1850, surgeon, Paris, France, described the development of carcinomatous ulcers in scars in 1828. There are 'high-risk' and 'low-risk' BCCs. High-risk BCCs: are large (>2 cm); are located at sites where direct invasion gives access to the cranium (near the eye, nose and ear); are recurrent tumours; are tumours forming in the presence of immunosuppression; or have micronodular or infiltrating histological subtypes. Management Treatment can be surgical or non-surgical. Tumour and surrounding surgical margins should always be assessed and marked under loupe magnification, the latter varying between 2 and 15 mm depending on the macroscopic variant. Where margins are ill-defined or tissue is at a premium (nose, eyes), either a two-stage surgical approach with subsequent reconstruction after confirmation of clear margins or Mohs' micrographic surgery is advisable. The histological sample must be orientated and marked for pathological examination. Mohs' micrographic surgery is a method used by dermatological surgeons (dermatologists who have undergone extra training in techniques of cutaneous surgery and histopathology) to excise skin cancer under microscopic control. In elderly or infirm patients,

radiotherapy produces similar recurrence rates to surgery, but with the risk of generating further malignancy after one to two decades. Biopsy-proven, superficial tumours can be treated with topical treatments (5-fluorouracil, imiquimod). Unless excision of a BCC is complete, there is a 67% recurrence rate if margins are grossly involved and a 33% recurrence rate within 2 years with microscopic involvement or when reported 'close'. Patients with uncomplicated, completely excised lesions can be discharged. Follow-up is reserved for patients with tumours in high-risk areas; for those with globally sun-damaged skin; for those with syndromes; and for those who decline further surgery after incomplete excisions.

(a) (b) (c) Figure 45.30 (a) A nodulocystic basal carcinoma (BCC). Note the characteristic pearly surface with telangiectasia. (b) An ulcerating BCC on the lower eyelid. (c) A recurrent morphoeic BCC. (courtesy of Mr AR Greenbaum; (c) courtesy of St John's Institute for Dermatology, London, UK.)

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and surrounding surgical margins should always be assessed and marked under loupe magnification, the latter varying between 2 and 15 mm depending on the macroscopic variant. Where margins are ill-defined or tissue is at a premium (nose, eyes), either a two-stage surgical approach with subsequent reconstruction after confirmation of clear margins or Mohs' micrographic surgery is advisable. The histological sample must be orientated and marked for pathological examination. Mohs' micrographic surgery is a method used by dermatological surgeons (dermatologists who have undergone extra training in techniques of cutaneous surgery and histopathology) to excise skin cancer under microscopic control. In elderly or infirm patients, radiotherapy produces similar recurrence rates to surgery, but with the risk of generating further malignancy after one to two decades. Biopsy-proven, superficial tumours can be treated with topical treatments (5-fluorouracil, imiquimod). Unless excision of a BCC is complete, there is a 67% recurrence rate if margins are grossly involved and a 33% recurrence rate within 2 years with microscopic involvement or when reported 'close'. Patients with uncomplicated, completely excised lesions can be discharged. Follow-up is reserved for patients with tumours in high-risk areas; for those with globally sun-damaged skin; for those with syndromes; and for those who decline further surgery after incomplete excisions.

(a) (b) (c) Figure 45.30 (a) A nodulocystic basal carcinoma (BCC). Note the characteristic pearly surface with telangiectasia. (b) An ulcerating BCC on the lower eyelid. (c) A recurrent morphoeic BCC. (courtesy of Mr AR Greenbaum; (c) courtesy of St John's Institute for Dermatology, London, UK.)

Basal cell carcinoma

This is usually a slow-growing, locally invasive, malignant tumour of pluripotential epithelial cells arising from basal epidermis and hair follicles; hence, it affects the pilosebaceous skin. Summary box 45.2 Basal cell carcinoma - Epidemiology The strongest predisposing factor to BCC is UVR. It occurs in the elderly or the middle-aged after excessive sun exposure, with 95% occurring between the ages of 40 and 80 years. The incidence of BCC rises with proximity to the equator, although 33% arise in parts of the body not usually exposed to the sun. Other predisposing factors include exposure to arsenical compounds, coal tar, aromatic hydrocarbons and IR, they and genetic skin cancer syndromes. White-skinned people are almost exclusively affected. BCC is more common in men than in women. Pathogenesis BCCs have no apparent precursor lesions and their development is proportional to the initial dose of the carcinogen, but not duration of exposure. The most likely model of pathological factors as intrinsic genesis for BCCs involves mesoderm promoters coupled with an initiation step. BCCs metastasise extremely rarely. Macroscopic BCCs can be divided into localised (nodular, nodulocystic, cystic, pigmented and naevoid) and generalised (superficial: multifocal and superficial spreading; or infiltrative: morphoeic, ice pick and cicatrising). Nodular and nodulocystic variants account for 90% of BCCs. Microscopic Twenty-six histological subtypes have been described. The characteristic finding is of ovoid cells in nests with a single

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Blood supply of the skin

Blood supply of the skin

The body can be envisaged as three-dimensional segments of tissue called angiosomes, each with an arterial supply and a venous drainage. Blood equilibrates and flows between neighbouring angiosomes via 'choke' vessels, which tend to be situated within muscles. Cutaneous arteries, direct branches of segmental arteries (concentrated at the dorsoventral axes and intermuscular septae), perforate the underlying muscles or run directly within fascial layers to the skin from the deep tissues (Figure 45.2). The blood supply to the skin anastomoses in subfascial, fascial, subdermal, dermal and subepidermal plexi. The epidermis contains no blood vessels so cells there derive nourishment by diffusion.

Sweat gland Subcutaneous fat

Angiosome A Angiosome B

Epidermis Subcutaneous fat

Musculocutaneous perforator

Fasciocutaneous perforator Muscle

Fascia and epimysium Choke

vessels between angiosomes A

and B within muscle Named artery

and Major vein vein Major artery

Figure 45.2 Schematic showing

two neighbouring angiosomes.
Note the choke vessels within the muscle spanning the two cutaneous territories of angiosomes A and B; two common examples of myocu

taneous /f_l aps that utilise this physiology include the rectus abdominis and the latissimus dorsi /f_l aps.

unvalved veins. Unvalved veins allow oscillating flow in the subdermal plexus between cutaneous territories, equilibrating flow and pressure. The valved cutaneous veins drain via plexi to the deep veins. Blood supply of the skin

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Common vascular birthmarks

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Salmon patch A salmon patch is a vascular malformation that presents as a pinkish macule, usually at the nape of neck (Figure 45.42 is caused by an area of persistent fetal dermal circulation that usually disappears at 1 year. **Capillary haemangioma (strawberry naevus)** This is the commonest 'birthmark', occurring most frequently on the head and neck (Figure 45.43). Ninety per cent are present at birth; as a consequence of intravascular thrombosis, fibrosis and mast cell infiltration, 10% resolve each subsequent year, with 70% resolved by 7 years old. White skin is affected most commonly and girls are affected three times more than boys. **Capillary vascular malformations ('port-wine' stains)** Capillary vascular malformations ('port-wine stains' [PWSs]) are 20 times less common than capillary haemangiomata and result from defective maturation of the cutaneous sympathetic innervation during embryogenesis, leading to localised intra dermal capillary vasodilatation (Figure 45.44). They appear Campbell Greig de Morgan , 1811–1876, surgeon, Middlesex Hospital, London, UK. First to propose that cancer started locally and then spread first to lymph nodes and beyond. -). It at birth as flat, smooth, intensely purple-stained areas, most frequently on the head and neck, often within the maxillary and mandibular dermatomes of the trigeminal nerve. Treatment with intense pulsed light and pulsed-dye laser is successful. PWSs may be associated with various syndromes.

Figure 45.42 Salmon patch (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.43 Capillary haemangioma (courtesy of St John's Institute for Dermatology, London, UK).

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Congenital genetic disorders

Congenital/genetic disorders

Neurofibromatosis There are two distinct neurofibromatosis (NF) syndromes, in which Schwann cells form tumours (Figure 45.3). Each is caused by different genes on different chromosomes: 70% are autosomal dominant and 30% arise from sporadic mutations. NF-1 (von Recklinghausen's disease) is the commoner variant, mutation on chromosome 17. Skin manifestations appear in early life, with the development of more than five smooth-surfaced café-au-lait spots, subcutaneous neurofibromata, armpit or groin freckling and Lisch nodules. NF-2 produces multiple central nervous system tumours. **Naevoid basal cell carcinoma (Gorlin's) syndrome** This is an autosomal dominant inherited condition caused by an abnormal tumour suppressor gene on chromosome 9q 22-31 coding the 'patched' protein; 90% of patients develop multiple basal cell carcinomas (BCCs). Patients may exhibit specific phenotypical characteristics, including overdeveloped supraorbital ridges; broad nasal roots; hypertelorism; bifid ribs; scoliosis; brachymetacarpalism; palmar pits; and molar odontogenic cysts; patients are also prone to other tumours. **Xeroderma pigmentosum** This syndrome is caused by an abnormality on the 'patched' gene of chromosome 9q, resulting in aberrant nucleotide repair during cellular DNA maintenance. It confers a >2000-fold increase in skin cancer risk and has autosomal recessive inheritance. Sufferers are intolerant of UVR, leading to premature skin ageing and development of multiple neoplasms. Most affected individuals die in early adulthood from metastatic disease (60% mortality by 20 years of age). **Gardner's syndrome** This syndrome is an autosomal dominant disease variant of familial adenomatous polyposis (FAP), which is caused by gene mutations on chromosome 5q 22. Gardner's syndrome can cause the development of cutaneous pathology, such as multiple epidermoid cysts and lipomata. **Ferguson-Smith syndrome** A rare autosomal dominant inherited abnormality on chromosome 9q in which affected individuals develop multiple self-healing squamous cell carcinomas (SCCs) without relation to sun exposure.

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Cutaneous manifestations of generalised disease

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Many diseases have cutaneous manifestations that present in surgical practice. These include: necrobiosis lipoidica, granu loma annulare in diabetes mellitus and pyoderma gangrenosum in inflammatory bowel disease. Their management should be sought in appropriate texts.

Hyperhidrosis This involves excessive eccrine sweating of the palms, soles of the feet, axillae and groins, causing functional and social Karl Lisch , 1907–1999, ophthalmologist, Wörgl, Austria.

Robert J Gorlin , 1923–2006, American dentist and Professor of Oral Pathology , published over 400 articles on craniofacial syndromes. Eldon John Gardner , 1909–1989, geneticist, The University of Utah, Salt Lake City , UT , USA, described this syndrome in 1950. John Ferguson-Smith , 1888–1978, Glaswegian dermatologist.

- problems. It can be treated with antiperspirants or periodic local injections with botulinum toxin A. More resistant cases are treated by transthoracic endoscopic sympathectomy . **APC Lipodystrophy** Lipodystrophy (lipoatrophy) is a localised or generalised loss of fatty tissue, which can be primary or secondary . It can be a complication of long-term

administration of insulin, following treatment of human immunodeficiency virus (HIV) with protease inhibitors or in transplant recipients. It can be treated in selected cases by autologous fat grafting, injections of poly-L-lactic acid and free tissue transfer. **Inflammatory conditions**

Hidradenitis suppurativa Characterised by follicular occlusion, folliculitis and secondary infection (usually with *Staphylococcus aureus* and *Propionibacterium acnes*), hidradenitis suppurativa culminates in chronic - suppurative, painful skin abscesses, sinus tracts and scarring. It affects apocrine gland-bearing skin in the axillae, groins and, less often, scalp, breast, chest and perineum (Figure 45.4). Affecting four women for every man, it has a genetic predisposition, but variable penetrance, and is strongly associated with obesity , smoking and sex hormones (it starts at puberty and often resolves at menopause).

Figure 45.4 Hidradenitis suppurativa affecting the axilla (courtesy of St John's Institute for Dermatology, London, UK).

weight. Symptoms can be reduced by the use of antiseptic soaps, tea tree oil and wearing non-compressive and aerated underwear. Medical treatments include topical and oral antibiotics and antiandrogen drugs. In selected cases, patients require radical excision of the affected skin and subcutaneous tissue. Reconstruction after excision avoids contracture and functional impairment. **Pyoderma gangrenosum** Characterised by rapid onset and painful cutaneous ulceration with purple undermined edges, pyoderma gangrenosum is secondary to heightened immunological reactivity , usually from another disease process, such as inflammatory bowel disease, rheumatoid arthritis, non-Hodgkin's lymphoma or granulomatosis with polyangiitis (Figure 45.5). Ulcers generally respond to steroids; surgery is rarely indicated and may exacerbate the condition. Cutaneous

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Cutaneous squamous cell carcinoma

Cutaneous squamous cell carcinoma

SCC is a malignant tumour of keratinising cells of the epidermis or its appendages. It arises from the stratum basalis of the epidermis and expresses cytokeratins 1 and 10. Epidemiology Four BCCs occur for every SCC, which is the second most common form of skin cancer. It is strongly related to cumulative sun exposure and damage, especially in white-skinned individuals living nearer the equator. In the northern hemisphere it affects the elderly, whereas it is not uncommon in sun-damaged, middle-aged white people in the southern hemisphere. Everywhere, it is more common in men than in women. SCC is also associated with chronic inflammation (chronic sinus tracts, pre-existing scars, osteomyelitis, burns, vaccination points) and immunosuppression. When a SCC appears in a scar it is known as a Marjolin's ulcer.

(a, b)

Squamous cell carcinoma /uni25CF /uni25CF /uni25CF IR causes SCC, as do chemical carcinogens (arsenicals, tar) and infection with HPV subtypes 5 and 16. There is also evidence that current and previous tobacco use doubles the relative risk of SCC. In the past, actinic (solar) keratoses (AKs), i.e. cutaneous horns and keratoacanthomas, were considered to be premalignant lesions leading to SCC. Current thinking is to classify these lesions on a continuum of lesions, some of which can improve, as with other squamous cell tumours such as cervical intraepithelial neoplasia. AKs are areas of permanent sun damage in which there is dyskeratosis, partial-thickness cellular atypia and subepidermal inflammation, but an intact basement membrane (Figure 45.31). They 'wax and wane' macroscopically between macular and papular, with and without keratinous surfaces. Most improve after moisturisation and remain as erythematous macules; however, up to 20% form SCC. When an AK has a keratinous surface with a height greater than its base diameter, it is termed a keratin horn; 10% will have an underlying SCC (Figure 45.32). Keratoacanthomas are rapidly growing, nodular tumour exhibiting symmetry around a central keratin-filled crater. John T Bowen, 1857–1941, Professor of Dermatology, Harvard University Medical School, Boston, MA, USA, described this condition in 1912. August Queyrat, 1856–1933, dermatologist, Paris, France, described this condition in 1911. - Current thinking is that, rather than being separate pre-malignant entities, they are better considered as self-healing SCCs and, as such, are often reported by pathologists as 'keratoacanthoma-like SCCs' (Figure 45.33). Keratoacanthomas are twice as common in men as in women and are usually found on the face or limbs of chronically sun-damaged 50- to 70-year-old white-skinned individuals. They may be caused by HPV in a hair follicle during the growth phase and are also associated with smoking and chemical carcinogen exposure. Excision is recommended, rather than observation, as the differential diagnosis includes anaplastic SCC and the excision scar is often better than that which remains after

resolution. in situ and often develops as Bowen's disease is SCC full-thickness dysplasia in hypertrophic AKs (Figure 45.34). SCC in situ usually presents as a slowly enlarging erythematous scaly plaque and may occur anywhere on the mucocutaneous surface of the body . On the glans penis, it is called erythroplasia of Queyrat (Figure 45.35). Topical therapy with 5-fluorouracil or imiquimod is an effective treatment. Alternatives include surgical excision with a 4-mm margin or Mohs' micrographic surgery for larger or recurrent lesions.

Associated with UVR, chronic inflammation, immunosuppression and chemical carcinogens High- and low-risk SCC Metastasis in 2% of low-risk and up to 30% of high-risk cases Figure 45.31 Actinic keratosis (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.32 Cutaneous horn (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.33 Keratoacanthoma (courtesy of St John's Institute for Dermatology, London, UK).

Macroscopic The appearance of SCC may vary from smooth nodular, verrucous, papillomatous to ulcerating lesions. All ulcerate eventually as they grow . The ulcers have a characteristic everted edge and are surrounded by inflamed, indurated skin. Differential diagnoses of SCC include: AK; BCC; pyoderma gangrenosum; warts; and lichen simplex chronicus (Figure 45.36). Albert Compton Broders , 1885–1964, American pathologist, MN, USA, and Chairman of the Department of Surgical Pathology MN, USA; for 1 year in 1935 Professor of Surgical Pathology and Director of Cancer Research, University of V graded rectal cancer in the USA in a similar manner to the one that Cuthbert Dukes used to classify it in the UK. A combination of Broders' grading and Dukes' classification gave a more accurate prognosis for rectal carcinoma than either method alone.

Microscopic Characteristic irregular masses of squamous epithelium are noted to proliferate and invade the dermis from the basal layer. The tumour stains positive for cytokeratins 1 and 10. SCC can be graded histologically according to Broders' grading, which describes the proportion of differentiated cells in the tumour. Table 45.1 presents tumour classification and staging. Prognosis There are several independent prognostic variables for SCC: Depth: the deeper the lesion, the worse the prognosis. For SCC <2 mm, metastasis is highly unlikely; if SCC >6 mm, 15% will have metastasised. y, M a y o Clinic, Rochester, irlginia, Charlottesville, V A, USA. Broders also

Figure 45.34 Bowen's disease – squamous cell carcinoma in situ (courtesy of St John's Institute for Dermatology, London, UK). TABLE 45.1 Tumour-node-metastasis (TNM) classification and staging of squamous cell carcinoma. Size Nodes NX TX Nodal involvement cannot be Primary tumour cannot be assessed assessed T0 N0 No evidence of primary tumour No regional nodes N1 Tis Spread to 1 ipsilateral nearby node In situ (con f_i ned to full-thickness that is <3 cm in diameter epidermal) disease T1 N2a Primary <2 cm Spread to 1 ipsilateral nearby node that is 3–6 cm in diameter T2 N2b Primary >2 cm Spread to >1 ipsilateral nearby nodes but none >6 cm in diameter T3 N2c Primary invasion of a facial bone Spread to contralateral node(s) but none are >6 cm in diameter N3 T4 Spread to any node >6 cm in Invasion of muscle, base of skull diameter or other bones Figure 45.35 Erythroplasia of Queyrat – squamous cell carcinoma in situ on the glans penis; also called Paget's disease of the penis (courtesy of St John's Institute for Dermatology, London, UK). Metastases Stages M0 Stage 0 No metastatic disease Tis, N0, M0 M1 Stage I Metastatic disease present T1, N0, M0 Stage II T2, N0, M0 Stage III T3, N0, M0 or T1–T3, N1, M0 Stage IV T1–T3, N2, M0 or any disease that is N3, or T4 or M1

Surface size: lesions >2 cm have a worse prognosis than smaller ones. Histological grade: the higher the Broders' grade, the worse the prognosis. Microscopic invasion of lymphovascular spaces or nerve tissue carries a high risk of metastatic disease. Therefore, as well as information on pathological pattern, cellular morphology and Broders' grade, any histopathology report for SCC should include the depth of invasion, the presence of perineural or lymphovascular invasion and the deep and peripheral margin clearance. Site: SCCs on the lips and ears have higher local recurrence rates than lesions elsewhere, and tumours at the extremities fare worse than those on the trunk. Aetiology: SCCs that arise in burn scars, osteomyelitis skin sinuses, chronic ulcers and areas of skin that have been irradiated have a higher metastatic potential. Immunosuppression: SCCs will invade further in those with impaired immune response. The overall rate of metastasis varies between 2% and 30% for SCC (usually to regional nodes) with a local recurrence rate of 20%. Management SCC is a heterogeneous tumour with a malignant potential that varies between subtypes. Management must address the tumour's tendency for lymphatic metastasis and the possibility of in-transit metastasis. Surgical excision is the only means of providing accurate information on histology and clearance. The margins for primary excision should be tailored to surface size in the first instance. This should ideally be assessed using surgical loupe - magnification. A 4-mm clearance margin should be achieved and a 1-cm clearance if the SCC measures <2 cm across, margin if the SCC measures >2 cm; 95% of local recurrence and regional metastases occur within 5 years, thus follow-up - beyond this period is not indicated. Cutaneous malignant melanoma Melanoma is a cancer of melanocytes and can, therefore, arise in skin, mucosa, retina and the leptomeninges. Epidemiology Observational data suggest that cutaneous melanoma is caused by exposure to UVR, but this general observation, which is a generally reliable fact, may hide some of the nuanced variables that contribute to melanoma formation.

(c) Figure 45.36 (a) A squamous cell carcinoma (SCC) on the face. (c) SCC arising on the dorsum of the hand in a renal transplant recipient on immunosuppressive therapy. who worked outside on a farm. ((a-c) courtesy of Mr AR Greenbaum; (d) (b) A recurrent SCC arising in a previously skin-grafted area of the scalp. (d) SCC arising on the lip of a smoker (d) courtesy of St John's Institute for Dermatology, London, UK.)

recreational activity in the sun and emigration among white-skinned people not suited to sun exposure. Although it accounts for less than 5% of skin malignancy (and 1.6% of all malignancy worldwide), it is responsible for over 75% of skin malignancy-related deaths. It is the commonest cancer in young adults (20–39 years) and the most likely cause of cancer-related death. Distribution between the sexes varies around the world and reflects occupational and recreational exposure to sunlight. Likewise, geographical distribution reflects exposure of white-skinned individuals to sunlight: Australia and New Zealand, countries with a predominantly white-skinned, immigrant population, have an incidence of 33.6 per 100 000. Five per cent of all patients with malignant melanoma will develop a second primary melanoma; 7% of malignant melanomas present as occult metastasis from an unknown primary. What is less clear within data on cutaneous melanoma is the contribution by variables such as serum vitamin D levels and vitamin receptor genotypes, because thinner melanomas and lower recurrence rates have been linked to higher serum vitamin D levels, and why some forms of melanoma seem more attributable to cumulative sun exposure (superficial spreading) than others (nodular). Studies exploring whether there may be benefit from a degree of sun exposure that avoids 'sunbathing' and burning and

whether sun-related vitamin D production in skin, rather than supplemental vitamin D, is beneficial are ongoing, but our best information still bases sun avoidance at the centre of melanoma prevention. Pathophysiology Cumulative UV exposure favours the development of lentigo maligna melanoma (LMM) and later onset of disease, whereas 'flash fry' exposure, typical of rapidly acquired holiday tans, favours the other morphological variants and early onset of disease. A small proportion of malignant melanoma is genetically mediated and develops at an earlier age. People at most risk of developing malignant melanoma include: those with genetic syndromes; those with a past history of malignant melanoma or with a first-degree relative who has malignant melanoma; those who have more than 30 sun-acquired naevi or a history of five significant sunburns before the age of 16; fair-skinned/ red-haired people living close to the equator; anyone with excessive UVR exposure (environmental or salon-delivered); Summary box 45.4 Malignant melanoma

/uni25CF /uni25CF /uni25CF /uni25CF /uni25CF Alexander Breslow, 1928–1980, pathologist, George Washington University, Washington, DC, USA, first reported in 1970 that the prognosis depends upon the thickness of the tumour. Malignant melanoma incidence 20- to 30-fold). Male gender and solitary living are both associated with thicker melanomas at diagnosis. In women, higher socioeconomic status is positively correlated with developing melanoma. Macroscopic Only 10–20% of malignant melanomas form in pre-existing naevi, with the remainder arising de novo in previously normally pigmented skin. The most likely naevi to form malignant melanoma are atypical naevi, atypical junctional lentiginous naevi (usually facial) and giant pigmented congenital naevi. Macroscopic features in a pre-existing naevus that suggest malignant change are listed in Summary box 45.5. There are four common macroscopic variants of malignant melanoma and several other notable, but rarer, forms, as follows. This is the most common presentation (70%); usually arises in a pre-existing naevus after several years of slow change, followed by rapid growth in the months before presentation (Figure 45.37). Nodularity within SSM heralds the onset of the vertical growth phase. NM accounts for 15% of all malignant melanoma and tends to be more aggressive than SSM, with a shorter clinical onset. These lesions often arise de novo in skin and are more common in men than in women, often presenting in middle age and usually on the trunk, head or neck (Figure 45.38). They typically appear as blue/black papules, 1–2 cm in diameter, and because they lack the horizontal growth phase they tend to be sharply demarcated. Up to 5% are amelanotic.

Rising incidence Genetic and acquired risk factors Superficial spreading form the most common Breslow thickness is the most important prognostic indicator Sentinel node biopsy (SNB) is useful for staging Superficial spreading melanoma (SSM). Nodular melanoma (NM). Figure 45.37 Superficial spreading melanoma (courtesy of St John's Institute for Dermatology, London, UK).

LMM was previously also known as Hutchinson's melanotic freckle. This variant presents as a slow-growing, variegated brown macule on the face, neck or hands of the elderly (Figure 45.39). They are positively correlated with prolonged, intense sun exposure and affect women more than men. They account for between 5% and 10% of malignant melanomas. LMMs are thought to have less metastatic potential than other variants as they take longer to enter a vertical growth phase. Nonetheless, when they have entered the vertical growth phase their metastatic potential is the same as any other melanoma. ALM affects the soles and palms. It is rare in white-skinned individuals (2–8% of malignant melanoma) but more common in Afro-Caribbean, Hispanic and Asian populations (35–60%). It usually presents as a flat, irregular macule in later life; 25% are

amelanotic and may mimic a fungal infection or pyogenic granuloma. Sir Jonathan Hutchinson, 1828–1913, surgeon, St Bartholomew's Hospital, London, UK. Malignant melanomas under the fingernail are usually SSM rather than ALM. For finger- or toenail lesions it is vital to biopsy the nail matrix rather than just the pigment on the nail plate. A classical feature of a subungual melanoma is Hutchinson's sign: nail fold pigmentation that widens progressively to produce a triangular pigmented macule with associated nail dystrophy. The differential diagnosis is 'benign racial melanonychia', which produces a linear dark streak under a nail in a dark-skinned individual. Malignancy is unlikely if the nail fold dark-skinned is uninvolved (Figure 45.40). Amelanotic melanoma may present as a flesh-coloured skin lesion; as a metastasis from an unknown skin primary; or in the gastrointestinal tract, with obstruction or intussusception.

Figure 45.38 Nodular melanoma
(courtesy of St John's Institute for Dermatology, London, UK). **Lentigo maligna melanoma. Acral lentiginous melanoma (ALM).** (a) **Figure 45.40 (a) Acral lentiginous melanoma on the sole of the foot.** Note the swelling proximal to the nailfold. (c) **Benign racial melanonychia.** (Institute for Dermatology, London, UK.) **Figure 45.39 Lentigo maligna melanoma**

(courtesy of St John's Insti

tute for Dermatology, London, UK). Miscellaneous (b) (c) (b) Subungual melanoma – probably a super /f_i cial spreading melanoma. (a) courtesy of Mr AR Greenbaum; (b, c) courtesy of St John's

neck region. It has a propensity for perineural infiltration and often recurs locally if not widely excised. It may be amelanotic clinically . Summary box 45.5 Macroscopic features in naevi suggestive of malignant melanoma /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF Microscopic Malignant change occurs in the melanocytes in the basal epidermis, while in situ atypical melanocytes are limited to the dermoepidermal junction and show no evidence of dermal involvement. During the horizontal growth phase, cells spread along the dermoepidermal junction; although they may breach the dermis, their migration is predominantly radial. During the vertical growth phase, the dermis may be invaded. The greater the depth of invasion, the greater the metastatic potential of the tumour. Management History and clinical examination should be directed at discov ering the primary lesion and identification of local, regional or distant spread. An excision biopsy with a 2- to 3-mm margin of skin and a cu ff of subdermal fat is acceptable. Incision biopsy is occasion ally indicated: for instance, in large lesions on the face where an excision biopsy of the whole lesion would be disfiguring. In experienced hands, observation and review every 2 /uni00A0 months may avoid biopsies in equivocal cases, but serial clin ical and dermoscopic photography by a clinician with exper tise in dermoscopy is mandatory when observ ation is chosen, rather than excision biopsy for definitive histopathological diagnosis. Dermoscopy coupled to computers with learning capability may soon outperform clinicians in melanoma diag nosis to the point where screening becomes m uch easier. Biopsy and pathological examination provide the first step towards staging melanoma. The Breslow thickness of a mel anoma (measured to the nearest 0.1 /uni00A0 mm from the granular layer to the base of the tumour) is the most important prog nostic indica tor in the absence of lymph node metastases. The American Joint Committee on Cancer (AJCC) staging system takes lymph node involvement, distant metastases and evidence-based prognostic factors into account; these can then be used to guide optimum care and inclusion in researc studies for adjuvant or other treatments where applicable. The detail of the AJCC melanoma staging system has become too specialised for the ambit of this text; most spe cialists look up its detail as they assign a stage to a patient (Table 45.2). Guidelines for staging are controversial. The author suggests that investigations should be directed towards detecting occult disease, so as to upstage patients and treat them accurately and appropriately , the only cure for malignant melanoma currently being appropriate surgery . Thus, o ff ering SNB to patients with T2a disease and greater is critical and investigations for T3a disease and greater should be directed to individual clinical presentation. Local treatment The treatment for melanoma is surgery . Lentigo maligna (melanoma in situ) should be excised completely in most clin - ical situations because of the risk of it entering the vertical growth phase to become LMM. A complete excision requires no further treatment. For melanoma in situ a wide excision of 5 /uni00A0 mm is su ffi cient; for melanoma <1 /uni00A0 mm deep, a 1-cm margin is su ffi cient; and for deeper lesions, a 2-cm only margin is recommended, as there is no evidence that wider margins make a di ff erence. Regional lymph nodes The likelihood of metastatic spread to regional lymph nodes is proportional to the Breslow thickness of the melanoma. Management of regional lymph nodes has been a contentious topic for well over a century . Some advocated simultaneous elective lymph node clearance at the

time of wide excision of the primary melanoma. Others favoured a therapeutic lymphadenectomy if regional metastases became clinically evident. Ideally, one would like to be able to select for treatment - those patients with the highest risk of metastatic spread. SNB, an investigation based on the fact that lymphatic metastases proceed in an orderly fashion and can be predicted by mapping the lymphatic drainage from a primary tumour to the first or - 'sentinel' node in the regional lymphatic basin, offered that potential, but prospective controlled studies have shown no survival benefit from lymphadenectomy after positive SNB involving micrometastasis <0.2 mm in a single node. This may be because most patients have been treated by removing the - sentinel node, which was the only node involved at that stage. However, completion lymphadenectomy after positive SNB remains, on current evidence, the optimum method for regional control, if patients accept the morbidity associated - with regional lymphadenectomy .

Adjuvant therapy - When mutation locks BRAF protein signalling to 'on', it affects the mitogen-activated protein kinase (MAPK) cellular - pathway, promoting initiation, malignant transformation, tumour progression and metastasis in the 50% of malignant melanomas with BRAF V600 mutations. Targeted therapy in stage IV melanoma using dabrafenib or vemurafenib, which block BRAF action, has shown promising results with h metastatic melanoma. Trametinib has a different action on the MAPK pathway: stopping cell growth and promoting apoptosis. Combined use with dabrafenib to counter acquired - tumour resistance via MAPK pathway reactivation shows promising results in stage IV disease. Also, the selective immune

Change in size Shape Colour Thickness (elevation/nodularity or ulceration) Satellite lesions (pigment spreading into surrounding area) Tingling/itching/serosanguineous discharge (usually late signs)

checkpoint inhibitors ipilimumab and nivolumab demonstrate benefit in metastatic or unresectable melanoma. Over the last 5 years, five randomised prospective trials of adjuvant therapy have reported findings in the treatment of patients with stage II to IV disease. While all five trials showed a significant improvement in relapse-free survival, only two of the trials were mature enough to report on overall survival. Prognosis The Breslow thickness of the primary tumour offers the best correlation with survival in stage I disease. The higher the mitotic index, the poorer the prognosis of the primary tumour. This has greater significance than the presence or absence of ulceration. The presence of lymph node metastases is the single most important prognostic index in melanoma, outweighing both tumour and host factors. The number of affected nodes and the presence of extranodal extension are also significant outcome predictors. Once regional nodes are clinically involved, 70–85% of patients will have occult distant metastases. Merkel cell (dermal mechanoreceptor) tumour This is an aggressive malignant tumour of Merkel cells and usually affects the elderly . It is four times more common in Haig H Kasabach, 1898–1943, radiologist, Presbyterian Hospital, New York, NY, USA. Katharine K Merritt, 1886–1986, pediatrician, Babies Hospital, Columbia University College of Physicians and Surgeons, New York, NY, USA. Kasabach and Merritt described the condition as a joint paper in 1940. women than in men (Figure 45.41). Treatment is with wide local excision, aiming for a 25- to 30-mm margin, followed by radiotherapy .

Primary tumour Regional nodes NX TX Patients in whom nodes cannot be assessed Primary tumour cannot be assessed (has (e.g. previous excision) been curettage or has severely regressed) T0 N0 No evidence of primary tumour No node involvement Tis Melanoma in situ N1 a: <0.8 mm, no ulceration T1 1 node b: 0.8–1.0 mm, no ulceration; or <1.0 mm ulceration; or <1.0 mm

/uni00A0 mm with ulceration a: No ulceration N2 T2 b: With ulceration 2 or 3 nodes 1.01–2.0
 /uni00A0 mm a: No ulceration N3 T3 b: With ulceration 2.01–4.0 /uni00A0 mm a: No ulceration T4
 b: With ulceration

4 /uni00A0 mm Clinical staging of melanoma Stage IIa: T2b or T3a, N0, M0 Stage
 0: Tis, N0, M0 Stage IIb: T3b or T4a, N0, M0 Stage Ia: T1a, N0, M0 Stage IIc: T4b,
 N0, M0 Stage Ib: T1b or T2a, N0, M0 LDH, lactate dehydrogenase; MSI denotes
 the presence of satellite lesions, in-transit lesions or local recurrence. Distant
 metastases M0 No detected distant metastases M1a a: Micrometastasis (no MSI)
 Skin, subcutaneous or distant lymph node b: Macrometastasis (no MSI)
 metastases (normal serum LDH levels) c: MSI present M1b a: Micrometastasis
 (no MSI) Lung metastases (normal serum LDH b: Macrometastasis (no MSI)
 levels) c: MSI present M1c a: Micrometastasis, >3 nodes All other visceral
 metastases or any distant (no MSI) metastases with elevated serum LDH b:
 Micrometastasis, >3 nodes levels or matted or 1 clinical node (no MSI) c: 1
 clinical or occult node with MSI present M1d Brain metastases Stage III: any T,
 >N1, M0 Stage IV: any T, any N1, M1

Cutaneous squamous cell carcinoma

SCC is a malignant tumour of keratinising cells of the epidermis or its appendages. It arises from the stratum basalis of the epidermis and expresses cytokeratins 1 and 10. Epidemiology Four BCCs occur for every SCC, which is the second most common form of skin cancer. It is strongly related to cumulative sun exposure and damage, especially in white-skinned individuals living nearer the equator. In the northern hemisphere it affects the elderly, whereas it is not uncommon in sun-damaged, middle-aged white people in the southern hemisphere. Everywhere, it is more common in men than in women. SCC is also associated with chronic inflammation (chronic sinus tracts, pre-existing scars, osteomyelitis, burns, vaccination points) and immunosuppression. When a SCC appears in a scar it is known as a Marjolin's ulcer.

(a, b)

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recreational activity in the sun and emigration among white-skinned people not suited to sun exposure. Although it accounts for less than 5% of skin malignancy (and 1.6% of all malignancy worldwide), it is responsible for over 75% of skin malignancy-related deaths. It is the commonest

cancer in young adults (20–39 years) and the most likely cause of cancer-related death. Distribution between the sexes varies around the world and reflects occupational and recreational exposure to sunlight. Likewise, geographical distribution reflects exposure of white-skinned individuals to sunlight: Australia and New Zealand, countries with a predominantly white-skinned, immigrant population, have an incidence of 33.6 per 100 000. Five per cent of all patients with malignant melanoma will develop a second primary melanoma; 7% of malignant melanomas present as occult metastasis from an unknown primary. What is less clear within data on cutaneous melanoma is the contribution by variables such as serum vitamin D levels and vitamin receptor genotypes, because thinner melanomas and lower recurrence rates have been linked to higher serum vitamin D levels, and why some forms of melanoma seem more attributable to cumulative sun exposure (superficial spreading) than others (nodular). Studies exploring whether there may be benefit from a degree of sun exposure that avoids ‘sunbathing’ and burning and whether sun-related vitamin D production in skin, rather than supplemental vitamin D, is beneficial are ongoing, but our best information still bases sun avoidance at the centre of melanoma prevention.

Pathophysiology Cumulative UV exposure favours the development of lentigo maligna melanoma (LMM) and later onset of disease, whereas ‘flash fry’ exposure, typical of rapidly acquired holiday tans, favours the other morphological variants and early onset of disease. A small proportion of malignant melanoma is genetically mediated and develops at an earlier age. People at most risk of developing malignant melanoma include: those with genetic syndromes; those with a past history of malignant melanoma or with a first-degree relative who has malignant melanoma; those who have more than 30 sun-acquired naevi or a history of five significant sunburns before the age of 16; fair-skinned/ red-haired people living close to the equator; anyone with excessive UVR exposure (environmental or salon-delivered);

Summary box 45.4 Malignant melanoma Alexander Breslow, 1928–1980, pathologist, George Washington University, Washington, DC, USA, first reported in 1970 that the prognosis depends upon the thickness of the tumour. Malignant melanoma incidence 20- to 30-fold). Male gender and solitary living are both associated with thicker melanomas at diagnosis. In women, higher socioeconomic status is positively correlated with developing melanoma.

Macroscopic Only 10–20% of malignant melanomas form in pre-existing naevi, with the remainder arising de novo in previously normally pigmented skin. The most likely naevi to form malignant melanoma are atypical naevi, atypical junctional lentiginous naevi (usually facial) and giant pigmented congenital naevi. Macroscopic features in a pre-existing naevus that suggest malignant change are listed in Summary box 45.5. There are four common macroscopic variants of malignant melanoma and several other notable, but rarer, forms, as follows. This is the most common presentation (70%); usually arises in a pre-existing naevus after several years of slow change, followed by rapid growth in the months before presentation (Figure 45.37). Nodularity within SSM heralds the onset of the vertical growth phase. NM accounts for 15% of all malignant melanoma and tends to be more aggressive than SSM, with a shorter clinical onset. These lesions often arise de novo in skin and are more common in men than in women, often presenting in middle age and usually on the trunk, head or neck (Figure 45.38). They typically appear as blue/black papules, 1–2 cm in diameter, and because they lack the horizontal growth phase they tend to be sharply demarcated. Up to 5% are amelanotic.

Rising incidence Genetic and acquired risk factors Superficial spreading form the most common Breslow thickness is the most important prognostic indicator Sentinel node biopsy (SNB) is useful for staging Superficial spreading melanoma (SSM). Nodular melanoma (NM). Figure 45.37 Superficial spreading melanoma (SSM). Nodular melanoma (NM).

/f_i cial spreading melanoma (courtesy of St John's Institute for Dermatology, London, UK).

LMM was previously also known as Hutchinson's melanotic freckle. This variant presents as a slow-growing, variegated brown macule on the face, neck or hands of the elderly (Figure 45.39). They are positively correlated with prolonged, intense sun exposure and affect women more than men. They account for between 5% and 10% of malignant melanomas. LMMs are thought to have less metastatic potential than other variants as they take longer to enter a vertical growth phase. Nonetheless, when they have entered the vertical growth phase their metastatic potential is the same as any other melanoma. ALM affects the soles and palms. It is rare in white-skinned individuals (2–8% of malignant melanoma) but more common in Afro-Caribbean, Hispanic and Asian populations (35–60%). It usually presents as a flat, irregular macule in later life; 25% are amelanotic and may mimic a fungal infection or pyogenic granuloma. Sir Jonathan Hutchinson , 1828–1913, surgeon, St Bartholomew's Hospital, London, UK. Malignant melanomas under the fingernail are usually SSM rather than ALM. For finger- or toenail lesions it is vital to biopsy the nail matrix rather than just the pigment on the nail plate. A classical feature of a subungual melanoma is Hutchinson's sign: nail fold pigmentation that widens progressively to produce a triangular pigmented macule with associated nail dystrophy . The differential diagnosis is 'benign racial melanonychia', which produces a linear dark streak under a nail in a individual. Malignancy is unlikely if the nail fold dark-skinned is uninvolved (Figure 45.40). /uni25CF Amelanotic melanoma may present as a flesh-coloured skin lesion; as a metastasis from an unknown skin primary; or in the gastrointestinal tract, with obstruction or intussusception.

Figure 45.38 Nodular melanoma
(courtesy of St John's Institute for Dermatology, London, UK). **Lentigo maligna melanoma. Acral lentiginous melanoma (ALM). (a)**
Figure 45.40 (a) Acral lentiginous melanoma on the sole of the foot. Note the swelling proximal to the

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neck region. It has a propensity for perineural infiltration and often recurs locally if not widely excised. It may be amelanotic clinically . Summary box 45.5 Macroscopic features in naevi suggestive of malignant melanoma /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF Microscopic Malignant change occurs in the melanocytes in the basal epidermis, while in situ atypical melanocytes are limited to the dermoepidermal junction and show no evidence of dermal involvement. During the horizontal growth phase, cells spread along the dermoepidermal junction; although they may breach the dermis, their migration is predominantly radial. During the vertical growth phase, the dermis may be invaded. The greater the depth of invasion, the greater the metastatic potential of the tumour. Management History and clinical examination should be directed at discov ering the primary lesion and identification of local, regional or distant spread. An excision biopsy with a 2- to 3-mm margin of skin and a cu ff of subdermal fat is acceptable. Incision biopsy is occasion ally indicated: for instance, in large lesions on the face where an excision biopsy of the whole lesion would be disfiguring. In experienced hands, observation and review every 2 /uni00A0 months may avoid biopsies in equivocal cases, but serial clin ical and dermoscopic photography by a clinician with exper tise in dermoscopy is mandatory when observ ation is chosen, rather than excision biopsy for definitive histopathological diagnosis. Dermoscopy coupled to computers with learning capability may soon outperform clinicians in melanoma diag nosis to the point where screening becomes m uch easier. Biopsy and pathological examination provide the first step towards staging melanoma. The Breslow thickness of a mel anoma (measured to the nearest 0.1 /uni00A0 mm from the granular layer to the base of the tumour) is the most important prog nostic indica tor in the absence of lymph node metastases. The American Joint Committee on Cancer (AJCC) staging system takes lymph node involvement, distant metastases and evidence-based prognostic factors into account; these can then be used to guide optimum care and inclusion in researc studies for adjuvant or other treatments where applicable. The detail of the AJCC melanoma staging system has become too specialised for the ambit of this text; most spe cialists look up its detail as they assign a stage to a patient (Table 45.2). Guidelines for staging are controversial. The author suggests that investigations should be directed towards detecting occult disease, so as to upstage patients and treat them accurately and appropriately , the only cure for

malignant melanoma currently being appropriate surgery . Thus, offering SNB to patients with T2a disease and greater is critical and investigations for T3a disease and greater should be directed to individual clinical presentation. Local treatment The treatment for melanoma is surgery . Lentigo maligna (melanoma in situ) should be excised completely in most clinical situations because of the risk of it entering the vertical growth phase to become LMM. A complete excision requires no further treatment. For melanoma in situ a wide excision of 5 mm is sufficient; for melanoma <1 mm deep, a 1-cm margin is sufficient; and for deeper lesions, a 2-cm only margin is recommended, as there is no evidence that wider margins make a difference. Regional lymph nodes The likelihood of metastatic spread to regional lymph nodes is proportional to the Breslow thickness of the melanoma. Management of regional lymph nodes has been a contentious topic for well over a century . Some advocated simultaneous elective lymph node clearance at the time of wide excision of the primary melanoma. Others favoured a therapeutic lymphadenectomy if regional metastases became clinically evident. Ideally , one would like to be able to select for treatment - those patients with the highest risk of metastatic spread. SNB, an investigation based on the fact that lymphatic metastases proceed in an orderly fashion and can be predicted by mapping the lymphatic drainage from a primary tumour to the first or - 'sentinel' node in the regional lymphatic basin, offered that potential, but prospective controlled studies have shown no survival benefit from lymphadenectomy after positive SNB involving micrometastasis <0.2 mm in a single node. This may - be because most patients have been treated by removing the - sentinel node, which was the only node involved at that stage. However, completion lymphadenectomy after positive SNB remains, on current evidence, the optimum method for regional control, if patients accept the morbidity associated - with regional lymphadenectomy . Adjuvant therapy - When mutation locks BRAF protein signalling to 'on', it affects the mitogen-activated protein kinase (MAPK) cellular - pathway , promoting initiation, malignant transformation, tumour progression and metastasis in the 50% of malignant melanomas with BRAF V600 mutations. Targeted therapy in stage IV melanoma using dabrafenib or vemurafenib, which block BRAF action, has shown promising results with h metastatic melanoma. Trametinib has a different action on the MAPK pathway: stopping cell growth and promoting apoptosis. Combined use with dabrafenib to counter acquired - tumour resistance via MAPK pathway reactivation shows promising results in stage IV disease. Also, the selective immune

Change in size Shape Colour Thickness (elevation/nodularity or ulceration) Satellite lesions (pigment spreading into surrounding area) Tingling/itching/serosanguineous discharge (usually late signs)

checkpoint inhibitors ipilimumab and nivolumab demonstrate benefit in metastatic or unresectable melanoma. Over the last 5 years, five randomised prospective trials of adjuvant therapy have reported findings in the treatment of patients with stage II to IV disease. While all five trials showed a significant improvement in relapse-free survival, only two of the trials were mature enough to report on overall survival. Prognosis The Breslow thickness of the primary tumour offers the best correlation with survival in stage I disease. The higher the mitotic index, the poorer the prognosis of the primary tumour. This has greater significance than the presence or absence of ulceration. The presence of lymph node metastases is the single most important prognostic index in melanoma, outweighing both tumour and host factors. The number of affected nodes and the presence of extranodal extension are also significant outcome predictors. Once regional nodes are clinically involved, 70-85% of patients will have occult distant metastases. Merkel cell (dermal

mechanoreceptor) tumour This is an aggressive malignant tumour of Merkel cells and usually affects the elderly . It is four times more common in Haig H Kasabach , 1898–1943, radiologist, Presbyterian Hospital, New York, NY , USA. Katharine K Merritt , 1886–1986, pediatrician, Babies Hospital, Columbia University College of Physicians and Surgeons, New York, NY , USA. Kasabach and Merritt described the condition as a joint paper in 1940. women than in men (Figure 45.41). Treatment is with wide local excision, aiming for a 25- to 30-mm margin, followed by radiotherapy .

Primary tumour Regional nodes NX TX Patients in whom nodes cannot be assessed Primary tumour cannot be assessed (has (e.g. previous excision) been curettage or has severely regressed) T0 N0 No evidence of primary tumour No node involvement Tis Melanoma in situ N1 a: <0.8 mm, no ulceration T1 1 node b: 0.8–1.0 mm, no ulceration; or <1.0 mm with ulceration a: No ulceration N2 T2 b: With ulceration 2 or 3 nodes 1.01–2.0 mm a: No ulceration N3 T3 b: With ulceration 2.01–4.0 mm a: No ulceration T4 b: With ulceration

4 mm Clinical staging of melanoma Stage IIa: T2b or T3a, N0, M0 Stage 0: Tis, N0, M0 Stage IIb: T3b or T4a, N0, M0 Stage Ia: T1a, N0, M0 Stage IIc: T4b, N0, M0 Stage Ib: T1b or T2a, N0, M0 LDH, lactate dehydrogenase; MSI denotes the presence of satellite lesions, in-transit lesions or local recurrence. Distant metastases M0 No detected distant metastases M1a a: Micrometastasis (no MSI) Skin, subcutaneous or distant lymph node b: Macrometastasis (no MSI) metastases (normal serum LDH levels) c: MSI present M1b a: Micrometastasis (no MSI) Lung metastases (normal serum LDH b: Macrometastasis (no MSI) levels) c: MSI present M1c a: Micrometastasis, >3 nodes All other visceral metastases or any distant (no MSI) metastases with elevated serum LDH b: Micrometastasis, >3 nodes levels or matted or 1 clinical node (no MSI) c: 1 clinical or occult node with MSI present M1d Brain metastases Stage III: any T, >N1, M0 Stage IV: any T, any N1, M1

Cutaneous squamous cell carcinoma

SCC is a malignant tumour of keratinising cells of the epidermis or its appendages. It arises from the stratum basalis of the epidermis and expresses cytokeratins 1 and 10. Epidemiology Four BCCs occur for every SCC, which is the second most common form of skin cancer. It is strongly related to cumulative sun exposure and damage, especially in white-skinned individuals living nearer the equator. In the northern hemisphere it affects the elderly , whereas it is not uncommon in sun-damaged, middle-aged white people in the southern hemisphere. Everywhere, it is more common in men than in women. SCC is also associated with chronic inflammation (chronic sinus tracts, pre-existing scars, osteomyelitis, burns, vaccination points) and immunosuppression. When a SCC appears in a scar it is known as a Marjolin's ulcer.

(a, b)

Squamous cell carcinoma /uni25CF /uni25CF /uni25CF IR causes SCC, as do chemical carcinogens (arsenicals, tar) and infection with HPV subtypes 5 and 16. There is also evidence that current and previous tobacco use doubles the relative risk of SCC. In the past, actinic (solar) keratoses (AKs), i.e. cutaneous horns and keratoacanthomas, were considered to be pre-malignant lesions leading to SCC. Current thinking is to classify these lesions on a continuum of lesions, some of which can improve, as with other squamous cell tumours such as cervical intraepithelial neoplasia. AKs are areas of permanent sun damage in which there is dyskeratosis, partial-thickness cellular atypia and subepidermal inflammation, but an intact basement membrane (Figure 45.31). They 'wax and wane' macroscopically between macular and papular, with and without keratinous surfaces. Most improve after moisturisation and remain as erythematous macules; however, up to 20% form SCC. When an AK has a keratinous surface with a height greater than its base diameter, it is termed a keratin horn; 10% will have an underlying SCC (Figure 45.32). Keratoacanthomas are rapidly growing, nodular tumour exhibiting symmetry around a central keratin-filled crater. John T Bowen , 1857–1941, Professor of Dermatology , Harvard University Medical School, Boston, MA, USA, described this condition in 1912. August Queyrat , 1856–1933, dermatologist, Paris, France, described this condition in 1911. - Current thinking is that, rather than being separate pre-malignant entities, they are better considered as self-healing - SCCs and, as such, are often reported by pathologists as 'keratoacanthoma-like SCCs' (Figure 45.33). Keratoacanthomas are twice as common in men as in women and are usually found on the face or limbs of chronically sun-damaged 50- to - 70-year-old white-skinned individuals. They may be caused by HPV in a hair follicle during the growth phase and are also associated with smoking and chemical carcinogen exposure. Excision is recommended, rather than observation, as the differential diagnosis includes anaplastic SCC and the excision scar is often better than that which remains after resolution. in situ and often develops as Bowen's disease is SCC full-thickness dysplasia in hypertrophic AKs (Figure 45.34). SCC in situ usually presents as a slowly enlarging erythematous scaly plaque and may occur anywhere on the mucocutaneous surface of the body . On the glans penis, it is called erythroplasia of Queyrat (Figure 45.35). Topical therapy with 5-fluorouracil or imiquimod is an effective treatment. Alternatives include surgical excision with a 4-mm margin or Mohs' micrographic surgery for larger or recurrent lesions.

Associated with UVR, chronic inflammation, immunosuppression and chemical carcinogens High- and low-risk SCC Metastasis in 2% of low-risk and up to 30% of high-risk cases Figure 45.31 Actinic keratosis (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.32 Cutaneous horn (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.33 Keratoacanthoma (courtesy of St John's Institute for Dermatology, London, UK).

Macroscopic The appearance of SCC may vary from smooth nodular, verrucous, papillomatous to ulcerating lesions. All ulcerate eventually as they grow . The ulcers have a characteristic everted edge and are surrounded by inflamed, indurated skin. Differential diagnoses of SCC include: AK; BCC; pyoderma gangrenosum; warts; and lichen simplex chronicus (Figure 45.36). Albert Compton Broders , 1885–1964, American pathologist, MN, USA, and Chairman of the Department of Surgical Pathology MN, USA; for 1 year in 1935 Professor of Surgical Pathology and Director of Cancer Research, University of V graded rectal cancer in the USA in a similar manner to the one that Cuthbert Dukes used to classify it in the UK. A combination of Broders' grading and Dukes' classification gave a more accurate prognosis for rectal carcinoma than either method alone.

Microscopic Characteristic irregular masses of squamous epithelium are noted to proliferate and

invade the dermis from the basal layer. The tumour stains positive for cytokeratins 1 and 10. SCC can be graded histologically according to Broders' grading, which describes the proportion of differentiated cells in the tumour. Table 45.1 presents tumour classification and staging. Prognosis There are several independent prognostic variables for SCC: Depth: the deeper the lesion, the worse the prognosis. For SCC <2 mm, metastasis is highly unlikely; if SCC >6 mm, 15% will have metastasised. y, M a y o Clinic, Rochester, Virginia, Charlottesville, V A, USA. Broders also

Figure 45.34 Bowen's disease – squamous cell carcinoma in situ (courtesy of St John's Institute for Dermatology, London, UK). TABLE 45.1 Tumour-node-metastasis (TNM) classification and staging of squamous cell carcinoma. Size Nodes NX TX Nodal involvement cannot be Primary tumour cannot be assessed assessed T0 N0 No evidence of primary tumour No regional nodes N1 Tis Spread to 1 ipsilateral nearby node In situ (confined to full-thickness that is <3 cm in diameter epidermal) disease T1 N2a Primary <2 cm Spread to 1 ipsilateral nearby node that is 3–6 cm in diameter T2 N2b Primary >2 cm Spread to >1 ipsilateral nearby nodes but none >6 cm in diameter T3 N2c Primary invasion of a facial bone Spread to contralateral node(s) but none are >6 cm in diameter N3 T4 Spread to any node >6 cm in Invasion of muscle, base of skull diameter or other bones Figure 45.35 Erythroplasia of Queyrat – squamous cell carcinoma in situ on the glans penis; also called Paget's disease of the penis (courtesy of St John's Institute for Dermatology, London, UK). Metastases Stages M0 Stage 0 No metastatic disease Tis, N0, M0 M1 Stage I Metastatic disease present T1, N0, M0 Stage II T2, N0, M0 Stage III T3, N0, M0 or T1–T3, N1, M0 Stage IV T1–T3, N2, M0 or any disease that is N3, or T4 or M1

Surface size: lesions >2 cm have a worse prognosis than smaller ones. Histological grade: the higher the Broders' grade, the worse the prognosis. Microscopic invasion of lymphovascular spaces or nerve tissue carries a high risk of metastatic disease. Therefore, as well as information on pathological pattern, cellular morphology and Broders' grade, any histopathology report for SCC should include the depth of invasion, the presence of perineural or lymphovascular invasion and the deep and peripheral margin clearance. Site: SCCs on the lips and ears have higher local recurrence rates than lesions elsewhere, and tumours at the extremities fare worse than those on the trunk. Aetiology: SCCs that arise in burn scars, osteomyelitis skin sinuses, chronic ulcers and areas of skin that have been irradiated have a higher metastatic potential. Immunosuppression: SCCs will invade further in those with impaired immune response. The overall rate of metastasis varies between 2% and 30% for SCC (usually to regional nodes) with a local recurrence rate of 20%. Management SCC is a heterogeneous tumour with a malignant potential that varies between subtypes. Management must address the tumour's tendency for lymphatic metastasis and the possibility of in-transit metastasis. Surgical excision is the only means of providing accurate information on histology and clearance. The margins for primary excision should be tailored to surface size in the first instance. This should ideally be assessed using surgical loupe - magnification. A 4-mm clearance margin should be achieved and a 1-cm clearance if the SCC measures <2 cm across, margin if the SCC measures >2 cm; 95% of local recurrence and regional metastases occur within 5 years, thus follow-up - beyond this period is not indicated. Cutaneous malignant melanoma Melanoma is a cancer of melanocytes and can, therefore, arise in skin, mucosa, retina and the leptomeninges. Epidemiology Observational data suggest that cutaneous melanoma is caused by exposure to UVR, but this

general observation, which is a generally reliable fact, may hide some of the nuanced variables that contribute to melanoma formation.

(c) Figure 45.36 (a) A squamous cell carcinoma (SCC) on the face. (c) SCC arising on the dorsum of the hand in a renal transplant recipient on immunosuppressive therapy, who worked outside on a farm. (a–c) courtesy of Mr AR Greenbaum; (d) (b) A recurrent SCC arising in a previously skin-grafted area of the scalp. (d) SCC arising on the lip of a smoker (d) courtesy of St John's Institute for Dermatology, London, UK.)

recreational activity in the sun and emigration among white-skinned people not suited to sun exposure. Although it accounts for less than 5% of skin malignancy (and 1.6% of all malignancy worldwide), it is responsible for over 75% of skin malignancy-related deaths. It is the commonest cancer in young adults (20–39 years) and the most likely cause of cancer-related death. Distribution between the sexes varies around the world and reflects occupational and recreational exposure to sunlight. Likewise, geographical distribution reflects exposure of white-skinned individuals to sunlight: Australia and New Zealand, countries with a predominantly white-skinned, immigrant population, have an incidence of 33.6 per 100 000. Five per cent of all patients with malignant melanoma will develop a second primary melanoma; 7% of malignant melanomas present as occult metastasis from an unknown primary. What is less clear within data on cutaneous melanoma is the contribution by variables such as serum vitamin D levels and vitamin receptor genotypes, because thinner melanomas and lower recurrence rates have been linked to higher serum vitamin D levels, and why some forms of melanoma seem more attributable to cumulative sun exposure (superficial spreading) than others (nodular). Studies exploring whether there may be benefit from a degree of sun exposure that avoids 'sunbathing' and burning and whether sun-related vitamin D production in skin, rather than supplemental vitamin D, is beneficial are ongoing, but our best information still bases sun avoidance at the centre of melanoma prevention. Pathophysiology Cumulative UV exposure favours the development of lentigo maligna melanoma (LMM) and later onset of disease, whereas 'flash fry' exposure, typical of rapidly acquired holiday tans, favours the other morphological variants and early onset of disease. A small proportion of malignant melanoma is genetically mediated and develops at an earlier age. People at most risk of developing malignant melanoma include: those with genetic syndromes; those with a past history of malignant melanoma or with a first-degree relative who has malignant melanoma; those who have more than 30 sun-acquired naevi or a history of five significant sunburns before the age of 16; fair-skinned/ red-haired people living close to the equator; anyone with excessive UVR exposure (environmental or salon-delivered); Summary box 45.4 Malignant melanoma Alexander Breslow, 1928–1980, pathologist, George Washington University, Washington, DC, USA, first reported in 1970 that the prognosis depends upon the thickness of the tumour. Malignant melanoma incidence 20- to 30-fold). Male gender and solitary living are both associated with thicker melanomas at diagnosis. In women, higher socioeconomic status is positively correlated with developing melanoma. Macroscopic Only 10–20% of malignant melanomas form in pre-existing naevi, with the remainder arising de novo in previously normally pigmented skin. The most likely naevi to form malignant melanoma are atypical naevi, atypical junctional lentiginous naevi (usually facial) and giant pigmented congenital naevi. Macroscopic features in a pre-existing naevus that suggest malignant change are listed in Summary box 45.5. There are four common macroscopic variants of malignant melanoma and several other notable, but rarer, forms, as follows. This is the most common

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Figure 45.38 Nodular melanoma
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the point where screening becomes much easier. Biopsy and pathological examination provide the first step towards staging melanoma. The Breslow thickness of a melanoma (measured to the nearest 0.1 mm from the granular layer to the base of the tumour) is the most important prognostic indicator in the absence of lymph node metastases. The American Joint Committee on Cancer (AJCC) staging system takes lymph node involvement, distant metastases and evidence-based prognostic factors into account; these can then be used to guide optimum care and inclusion in research studies for adjuvant or other treatments where applicable. The detail of the AJCC melanoma staging system has become too specialised for the ambit of this text; most specialists look up its detail as they assign a stage to a patient (Table 45.2). Guidelines for staging are controversial. The author suggests that investigations should be directed towards detecting occult disease, so as to upstage patients and treat them accurately and appropriately , the only cure for malignant melanoma currently being appropriate surgery . Thus, offering SNB to patients with T2a disease and greater is critical and investigations for T3a disease and greater should be directed to individual clinical presentation.

Local treatment The treatment for melanoma is surgery . Lentigo maligna (melanoma in situ) should be excised completely in most clinical situations because of the risk of it entering the vertical growth phase to become LMM. A complete excision requires no further treatment. For melanoma in situ a wide excision of 5 mm is sufficient; for melanoma <1 mm deep, a 1-cm margin is sufficient; and for deeper lesions, a 2-cm only margin is recommended, as there is no evidence that wider margins make a difference. Regional lymph nodes The likelihood of metastatic spread to regional lymph nodes is proportional to the Breslow thickness of the melanoma. Management of regional lymph nodes has been a contentious topic for well over a century . Some advocated simultaneous elective lymph node clearance at the time of wide excision of the primary melanoma. Others favoured a therapeutic lymphadenectomy if regional metastases became clinically evident. Ideally , one would like to be able to select for treatment - those patients with the highest risk of metastatic spread. SNB, an investigation based on the fact that lymphatic metastases proceed in an orderly fashion and can be predicted by mapping the lymphatic drainage from a primary tumour to the first or - 'sentinel' node in the regional lymphatic basin, offered that potential, but prospective controlled studies have shown no survival benefit from lymphadenectomy after positive SNB involving micrometastasis <0.2 mm in a single node. This may - be because most patients have been treated by removing the - sentinel node, which was the only node involved at that stage. However, completion lymphadenectomy after positive SNB remains, on current evidence, the optimum method for regional control, if patients accept the morbidity associated - with regional lymphadenectomy .

Adjuvant therapy - When mutation locks BRAF protein signalling to 'on', it affects the mitogen-activated protein kinase (MAPK) cellular - pathway , promoting initiation, malignant transformation, tumour progression and metastasis in the 50% of malignant melanomas with BRAF V600 mutations. Targeted therapy in stage IV melanoma using dabrafenib or vemurafenib, which block BRAF action, has shown promising results with h metastatic melanoma. Trametinib has a different action on the MAPK pathway: stopping cell growth and promoting apoptosis. Combined use with dabrafenib to counter acquired - tumour resistance via MAPK pathway reactivation shows promising results in stage IV disease. Also, the selective immune

Change in size Shape Colour Thickness (elevation/nodularity or ulceration) Satellite lesions (pigment spreading into surrounding area) Tingling/itching/serosanguineous discharge (usually late signs)

checkpoint inhibitors ipilimumab and nivolumab demonstrate benefit in metastatic or unresectable melanoma. Over the last 5 years, five randomised prospective trials of adjuvant therapy have reported findings in the treatment of patients with stage II to IV disease. While all five trials showed a significant improvement in relapse-free survival, only two of the trials were mature enough to report on overall survival. Prognosis The Breslow thickness of the primary tumour offers the best correlation with survival in stage I disease. The higher the mitotic index, the poorer the prognosis of the primary tumour. This has greater significance than the presence or absence of ulceration. The presence of lymph node metastases is the single most important prognostic index in melanoma, outweighing both tumour and host factors. The number of affected nodes and the presence of extranodal extension are also significant outcome predictors. Once regional nodes are clinically involved, 70–85% of patients will have occult distant metastases. Merkel cell (dermal mechanoreceptor) tumour This is an aggressive malignant tumour of Merkel cells and usually affects the elderly. It is four times more common in women than in men (Figure 45.41). Treatment is with wide local excision, aiming for a 25- to 30-mm margin, followed by radiotherapy.

Primary tumour Regional nodes NX TX Patients in whom nodes cannot be assessed Primary tumour cannot be assessed (has (e.g. previous excision) been curettage or has severely regressed) T0 N0 No evidence of primary tumour No node involvement Tis Melanoma in situ N1 a: <0.8 mm, no ulceration T1 1 node b: 0.8–1.0 mm, no ulceration; or <1.0 mm with ulceration a: No ulceration N2 T2 b: With ulceration 2 or 3 nodes 1.01–2.0 mm a: No ulceration N3 T3 b: With ulceration 2.01–4.0 mm a: No ulceration T4 b: With ulceration

4 Clinical staging of melanoma Stage IIa: T2b or T3a, N0, M0 Stage 0: Tis, N0, M0 Stage IIb: T3b or T4a, N0, M0 Stage Ia: T1a, N0, M0 Stage IIc: T4b, N0, M0 Stage Ib: T1b or T2a, N0, M0 LDH, lactate dehydrogenase; MSI denotes the presence of satellite lesions, in-transit lesions or local recurrence. Distant metastases M0 No detected distant metastases M1a a: Micrometastasis (no MSI) Skin, subcutaneous or distant lymph node b: Macrometastasis (no MSI) metastases (normal serum LDH levels) c: MSI present M1b a: Micrometastasis (no MSI) Lung metastases (normal serum LDH levels) b: Macrometastasis (no MSI) c: MSI present M1c a: Micrometastasis, >3 nodes All other visceral metastases or any distant (no MSI) metastases with elevated serum LDH b: Micrometastasis, >3 nodes levels or matted or 1 clinical node (no MSI) c: 1 clinical or occult node with MSI present M1d Brain metastases Stage III: any T, >N1, M0 Stage IV: any T, any N1, M1

Cylindroma (turban tumour)

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A variant of eccrine spiradenoma that coalesce when multiple on the scalp, forming a 'turban tumour'. Cylindroma (turban tumour)

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Dermis

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The dermis constitutes 95% of the skin and is structurally divided into a superficial papillary layer, which is composed of delicate collagen and elastin fibres in ground substance, into which a capillary and lymphatic network ramifies, and a deeper reticular layer, which is composed of coarse branching collagen, layered parallel to the skin surface (Figure 45.1). - The epidermis and dermis meet at the dermoepidermal junction in a three-dimensional wave-like arrangement in - which epidermal rete ridges project down, inter digitating with the upward-pointing, dermal papillae containing vascular and lymphatic plexi. m - The skin also contains specialised cells such as Langerhans cells, whose role is to engulf antigens and present them to T cells. Merkel cells, and Meissner's and Pacinian corpuscles have roles in mechanosensation. - Dermis

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Epidermis

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The epidermis constitutes 5% of the skin and is composed of five layers of keratinised, stratified squamous epithelium – the strata: basalis (deep), spinosum, granulosum, lucidum and corneum (superficial). Most epidermal cells are keratinocytes arranged in layers. The basal epidermis (stratum basalis) also contains melanocytes. Keratinocytes are classified according to their depth in the epidermis and their degree of differentiation. Keratinocytes grow and are replaced via mitosis in the cells of stratum granulosum as they progress from deep to superficial, losing their nuclei and organelles as they ascend, before forming the stratum corneum. The other keratinocyte layers in the skin (strata lucidum, granulosum and spinosum) are variably thick according to body site; for instance, all three are thick in the glabrous skin of the palms and soles of the feet and almost absent in eyelid skin. Melanocytes are dendritic cells of neural crest origin, usually located in the basal epidermis. Each melanocyte synthesises melanin, a brown-black pigment, which is transferred via membrane processes to the keratinocytes in the strata granulosum and spinosum. Melanin provides protection against ultra violet radiation (UVR). Ethnic differences in skin colour are determined by variations in the amount, combination and distribution of melanin within the keratinocytes, not by differences in the number of melanocytes. The surface of the epidermis is coated with a mixture of secreted molecules and microorganisms and generally has an acid pH, which is protective against harmful flora.

The classification of benign skin tumours • The management of malignant skin tumours •

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FUNCTION OF THE SKIN

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Skin and subcutaneous tissue have several important functions: /uni25CF Barrier to the environment enveloping the body and protecting against trauma, radiation and pathogens. Secreted sebum and sweat mix to form a microscopic acidic film across the epidermis – ‘the acid mantle’ – which is protective against microorganisms and toxic substances. /uni25CF Regulates temperature and water homeostasis. /uni25CF Organ of excretion for urea, sodium chloride, potassium and water, as well as sulphur-containing metabolites from drugs (e.g. dimethyl sulphoxide) or food (garlic, cumin). /uni25CF The skin has significant endocrine and metabolic functions and interactions. Skin cells contain receptors for and respond to peptides, steroid sex hormones, thyroid hormones and neurotransmitters and they both produce (cholecalciferol) and metabolise (androgens) hormones and precursors to activate, potentiate and inactivate their functions. /uni25CF Sensory organ with multiple receptors for pain, pressure and movement.

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FURTHER READING

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Giant congenital pigmented naevus or giant hairy n

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This hamartoma of naevo-melanocytes causes confusion because its definition and management are contentious. It has a similar histology to compound naevi, but with naevus cells distributed variably throughout all skin layers and into the subdermal fat and muscle and with a tendency to dermatomal distribution (Figure 45.28). Giant congenital pigmented naevi (GCPNs) are precursors of melanoma but the magnitude of this risk is unclear, largely because of the lack of well-conducted studies and variable classification of the naevus. A 3–5% lifetime risk of melanoma is quoted. One in three childhood malignant melanomas arise in patients with GCPN, but the risk decreases with age: 15% of malignant melanomas present at birth, 62% present by puberty and 99% by 45 years of age. A multidisciplinary management approach is advocated, with initial investigations examining for neurocutaneous mela - nosis as there may be leptomeningeal involvement. Removal of ed for both aesthetic and oncological GCPN should be consider reasons. Giant congenital pigmented naevus or giant hairy naevus

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Hair follicles

Trichoepithelioma

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Infections

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Skin and soft-tissue infections can be localised or spreading, necrotising or non-necrotising. Localised or spreading non-necrotising infections usually respond to broad-spectrum antibiotics. Localised necrotising infections need surgical debridement as well as antibiotic therapy. Spreading necrotising soft-tissue infection constitutes a life-threatening surgical emergency, requiring immediate resuscitation, intravenous antibiotic therapy and urgent surgical intervention with radical debridement. Impetigo Impetigo is a superficial infection of skin with staphylococci, streptococci or both (Figure 45.6). It is highly infectious and is characterised by blisters that rupture and coalesce to form a honey-coloured crust; it usually affects children. Treatment is directed at washing the affected areas and applying topical antistaphylococcal treatments; broad-spectrum oral antibiotics are required if streptococcal infection is also implicated. Erysipelas Erysipelas is a sharply demarcated streptococcal infection of the superficial lymphatics, usually associated with broken skin on the face (Figure 45.7). The area affected is erythematous and oedematous. The patient may be febrile and have a leukocytosis. Prompt administration of broad-spectrum antibiotics after swabbing the area for culture and sensitivity is usually all that is necessary. Cellulitis/lymphangitis This is a bacterial infection of the skin and subcutaneous tissue that is more generalised than erysipelas. It is usually associated with broken skin or pre-existing ulceration. It is characterised by an expanding area of erythematous, oedematous tissue that is painful, in association with fever, malaise and leukocytosis. Erythema tracking along lymphatics may be visible (lymphangitis) (Figure 45.8). The commonest causative Thomas Hodgkin, 1798–1866, curator of the museum and demonstrator of morbid anatomy, Guy's Hospital, London, UK. - - - Streptococcus pyogenes and S. aureus. Blood and organisms are skin cultures for sensitivity should be taken before prompt administration of broad-spectrum intravenous antibiotics and elevation of the affected extremity.

(b) Figure 45.5 Pyoderma gangrenosum affecting the legs (a) and the breasts (b) (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.6 Impetigo. Note the honey-coloured crust (courtesy of St John's Institute for Dermatology, London, UK).

Figure 45.7 Erysipelas (courtesy of St John's Institute for Dermatology, London, UK).

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Introduction

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Learning objectives

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To understand: The structure and functional properties of skin • The classification of vascular skin lesions • The cutaneous manifestations of generalised disease as related to surgery Learning objectives

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To understand: The structure and functional properties of skin • The classification of vascular skin lesions • The cutaneous manifestations of generalised disease as related to surgery

Necrotising fasciitis

Necrotising fasciitis

Meleney's synergistic gangrene and Fournier's gangrene are variants of a similar disease process. Necrotising fasciitis results from synergistic polymicrobial infection, most commonly a group A β -haemolytic *Streptococcus* in combination with *Staphylococcus*, *Escherichia coli*, *Pseudomonas*, *Proteus*, *Bacteroides* or *Clostridium*; 80% of patients have a history of previous trauma/infection and over 60% of cases commence in the lower extremities. Predisposing conditions include diabetes mellitus, smoking, penetrating trauma, pressure sores, immunosuppression, intravenous drug abuse, perineal infection (perianal abscess, Bartholin's cysts) and skin damage/infection (abrasions, bites, boils). Summary box 45.1 Necrotising fasciitis

Classical clinical signs include oedema stretching beyond visible skin erythema; a woody-hard texture to the subcutaneous tissues; an inability to distinguish fascial planes and muscle. Frank Meleney, 1889–1963, American surgeon in the First World War, then became a Professor at Columbia Medical School in New York, NY, USA. Jean Fournier, 1832–1914, French dermatologist, also described tertiary syphilis. Caspar Bartholin (Secundus), 1655–1709, Professor of Medicine, Anatomy and Physics, Copenhagen, Denmark, described these glands in 1677. groups on palpation; disproportionate pain in relation to the affected area, with associated skin vesicles and soft-tissue crepitation (Figure 45.9). Lymphangitis tends to be absent. Early on, patients may be febrile and tachycardic, with a very rapid progression to septic shock. Radiographs, which should not delay urgent treatment, may demonstrate air in the tissues. Management should commence with urgent fluid resuscitation, monitoring of haemodynamic status and administration of high-dose intravenous broad-spectrum antibiotics. This is a surgical emergency and the diseased area should be debrided as soon as possible until viable, healthy tissue is reached. Early surgical review and further debridement is advisable, together with the use of vacuum-assisted dressings. Early skin grafting in selected cases may minimise protein, hyperbaric oxygen therapy and fluid losses. Where available, hyperbaric oxygen after debridement may be helpful. Mortality of between 30% and 50% can be expected, even with prompt operative intervention.

Surgical emergency Polymicrobial synergistic infection 80% have a history of previous trauma or

infection Rapid progression to septic shock Urgent resuscitation, antibiotics and surgical debridement Mortality 30–50%

Figure 45.8 Cellulitis affecting the left leg (courtesy of St John's Institute for Dermatology, London, UK).

Necrotising fasciitis

Meleney's synergistic gangrene and Fournier's gangrene are variants of a similar disease process. Necrotising fasciitis results from synergistic polymicrobial infection, most commonly a group A β - haemolytic *Streptococcus* in combination with *Staphylococcus*, *Escherichia coli*, *Pseudomonas*, *Proteus*, *Bacteroides* or *Clostridium*; 80% of patients have a history of previous trauma/infection and over 60% of cases commence in the lower extremities. Predisposing conditions include diabetes mellitus, smoking, penetrating trauma, pressure sores, immunosuppression, intravenous drug abuse, perineal infection (perianal abscess, Bartholin's cysts) and skin damage/infection (abrasions, bites, boils). Summary box 45.1 Necrotising fasciitis

Classical clinical signs include oedema stretching beyond visible skin erythema; a woody-hard texture to the subcutaneous tissues; an inability to distinguish fascial planes and muscle. Frank Meleney, 1889–1963, American surgeon in the First World War, then became a Professor at Columbia Medical School in New York, NY, USA. Jean Fournier, 1832–1914, French dermatologist, also described tertiary syphilis. Caspar Bartholin (Secundus), 1655–1709, Professor of Medicine, Anatomy and Physics, Copenhagen, Denmark, described these glands in 1677. groups on palpation; disproportionate pain in relation to the affected area, with associated skin vesicles and soft-tissue crepitation (Figure 45.9). Lymphangitis tends to be absent. Early on, patients may be febrile and tachycardic, with a very rapid progression to septic shock. Radiographs, which should not have delayed urgent treatment, may demonstrate air in the tissues. Management should commence with urgent fluid resuscitation, monitoring of haemodynamic status and administration of high-dose intravenous broad-spectrum antibiotics. This is a surgical emergency and the diseased area should be debrided as soon as possible until viable, healthy tissue is reached. Early surgical review and further debridement is advisable, together with the use of vacuum-assisted dressings. Early skin grafting in selected cases may minimise protein, hyperbaric oxygen therapy and fluid losses. Where available, hyperbaric oxygen therapy may be helpful. Mortality of between 30% and 50% can be expected, even with prompt operative intervention.

Surgical emergency Polymicrobial synergistic infection 80% have a history of previous trauma or infection Rapid progression to septic shock Urgent resuscitation, antibiotics and surgical debridement Mortality 30–50%

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PATHOPHYSIOLOGY OF THE SKIN AND SUBCUTANEOUS TISSU

PATHOPHYSIOLOGY OF THE SKIN AND SUBCUTANEOUS TISSUES Radiation damage

UVR and ionising radiation (IR) damage cellular DNA via the tumour suppressor gene p53 , inhibiting cellular repair and apoptotic mechanisms. There is also evidence that e ff erent immune responses are impaired after skin exposure to UVR, facilitating neoplasia. Friedrich Theodor Schwann , 1810–1882, Professor of Anatomy , successively at Louvain (1839–1848) and Liege, Belgium (1849–1880). Original research before the age of 27 laid the foundation of the physiology of nerve and muscle. The first to deal with problems related to living matter on a purely physical and chemical basis and to recognise the cell as the unit of living matter. Discovered pepsin and the role of living organisms in fermentation. Friedrich Von Recklinghausen , 1833–1910, German Professor of Pathology , also described haemochromatosis. - - Ultraviolet radiation UVR is divisible into A, B and C according to wavelength. UVR, inducing oxidative damage, is the principal cause of skin cancer in all skin types as well as sunburn and skin ageing. UV A and UVB are the principal natural causes of ultraviolet - (UV)-induced damage (UVC is absorbed by the atmosphere, but can be emitted by artificial sources). UV A has a longer wavelength than and less energy per photon than UVB, but - penetrates more deeply . The e ff ects of UVR are attenuated by melanin and there is an inverse relationship between melanin content and skin susceptibility to UV-induced neoplasia. Some protection is a ff orded by the stratum corneum, which reflects and refracts UVR, and by clothing, protective creams, cloud cover, particulate air pollution and buildings. - Ionising radiation The e ff ects of IR are dose, wavelength and time dependent. - The skin, with its rapid cellular turnover, shows signs soon after exposure. High-frequency rays cause electron coupling at the molecular level, damaging proteins, polysaccharides and lipids. Infrared radiation Infrared radiation generates heat; cumulative exposure can cause thermal burns.

Figure 45.3 Neuro /f_i bromatosis (courtesy of St John's Institute for Dermatology, London, UK).

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Pilomatrixoma (calcifying epithelioma of Malherbe)

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These are benign hair matrix cell tumours that often calcify; 40% are found in the under-10 age group. Josef Jadassohn , 1863–1936, dermatologist, Breslau, Germany (now Wrocław , Poland). Desire M Bourneville , 1840–1909, physician, Le Bicêtre, Paris, France. Trichilemmoma (naevus sebaceous of Jadassohn) Trichilemmoma is a congenital hamartoma with the appearance of a linear verrucous naevus; 10% lifetime risk of forming a BCC (Figure 45.24). Adenoma sebaceum (tuberous sclerosis, Bourneville disease) These are facial papules (angiofibromata) that are red-brown depending on skin colour and usually appear on the naso - labial folds, cheek and chin. They usually appear in children before 10 years of age and increase in size and number until adolescence. Cosmetic removal by argon or pulsed-dye lasers Figure 45.25). or scalpel is indicated (Rhinophyma Rhinophyma is the end-stage sequela of nasal acne rosacea (Figure 45.26). It is nasal sebaceous gland hypertrophy and hyperplasia and tends to affect elderly men (male-to-female ratio 12:1). Occult BCCs exist in 3%. Treatment by derm - abrasion or laser resurfacing produces good results.

Figure 45.21 Blue naevus (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.22 Naevus of Ota (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.23 Naevus of Ito (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.24 Naevus sebaceous of Jadassohn (courtesy of St John's Institute for Dermatology, London, UK).

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Premalignant lesions

Extramammary Paget's disease (intraepidermal adenocarcinoma)

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This occurs in cutaneous sites that are rich in apocrine glands such as the axillae and the genital and perianal regions. Approximately 25% are associated with an underlying Sir James Paget , 1814–1899, surgeon, St Bartholomew's Hospital, London, UK. or invasive adenocarcinoma. Early skin changes are subtle and may present as an eczematous lesion or intertrigo. Surgical excision forms the basis of treatment, with up to 20% demonstrating invasive disease after pathology assessment (Figure 45.27).

Figure 45.27 Extramammary Paget's disease involving the perineum (courtesy of St John's Institute for Dermatology, London, UK).

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Purpura fulminans

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This is a relatively rare condition in which intravascular thrombosis produces rapid skin necrosis and haemorrhagic infarction, which progresses rapidly to septic shock and disseminated intravascular coagulation. Usually seen in children, it can occur in adults and may be subdivided into three types based on the aetiological mechanism: 'acute infectious', 'neonatal' and 'idiopathic' purpura fulminans. - Acute infectious is the commonest form. It is associated with multiorgan with a mortality rate of 40–50%, usually from failure, and is secondary to either an acute bacterial (Neisseria meningitidis) or viral infection (varicella). It is most common in children under 7 years, following an upper respiratory tract infection or in asplenia. Endotoxins produce an imbalance in procoagulant and anticoagulant endothelial activity, producing protein C deficiency; this gives the clinical picture of an initial petechial rash developing into confluent ecchymoses and haemorrhagic bullae, which necrose to form well-demarcated lesions that form hard eschars. Extensive tissue loss is common, which often culminates in limb amputation (Figure 45.10)

Figure 45.9 Necrotising fasciitis affecting the left orbit and facial skin (courtesy of St John's Institute for Dermatology, London, UK).

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SKIN TUMOURS Benign lesions

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Basal cell papilloma (seborrheic keratosis, senile keratosis, verruca senilis) Their appearance varies from macular to soft, excrescent, warty lesions – often pigmented and hyperkeratotic – but may be flesh-coloured or pink. They are formed from the basal layer of epidermal cells and contain melanocytes. Papillary wart (verruca vulgaris) This is a benign skin tumour arising from infection with the human papillomavirus (HPV), which is also responsible for plantar warts and condylomata acuminata. Freckle (ephelis) A freckle is an area of skin that contains a normal number of melanocytes, producing an abnormally large number of melanin granules. Lentigo These are small, circumscribed pigmented macules that stem from sun damage and some systemic syndromes. Solar lentigos are commoner in fairer skins. Moles/naevi Melanocytes migrate from the neural crest to the basal epidermis during embryogenesis. When melanocytes aggregate in the dermis or at the dermoepidermal junction, they are called naevus cells. Sophie Spitz, 1910–1956, American dermatopathologist at the Memorial Sloan Kettering Cancer Center, published the first case series of ‘juvenile melanoma’ in 1948. Junctional naevus A junctional naevus is a dermoepidermal proliferation of naevus cells, visible as deeply pigmented macules or papules that occur commonly in childhood or adolescence, usually progressing to form compound or intradermal naevi with advancing age. Benign mucosal lesions tend to be junctional naevi (Figure 45.13). Compound naevus This is a maculopapular, pigmented lesion that becomes most prominent during adolescence (Figure 45.14). It represents a junctional proliferation of naevus cells, with nests and columns in the dermis. Intradermal naevus Intradermal naevi are faintly pigmented papules in adults that show no junctional proliferation; however, they do show a cluster of dermal melanocytes (Figure 45.15). Spitz naevus These are reddish brown (occasionally deeply pigmented) nodules, previously termed ‘juvenile melanoma’ (Figure 45.16). They most commonly occur on the face and legs, growing rapidly initially then remaining static or regressing. The differential diagnosis is melanoma and excision biopsy is warranted if there is doubt as to the diagnosis. Spindle cell naevus Spindle cell naevi are dense black lesions that contain spindle cells and atypical melanocytes at the dermoepidermal junction. They are commonly seen on the thighs and affect women more frequently. They may have malignant potential. Halo naevus The halo of depigmentation around any benign naevus - represents an antibody response to melanocytes. Depigmentation may also be a feature of a malignant melanoma. Halo naevi are associated with vitiligo (Figure 45.17).

Figure 45.13 Junctional naevus (courtesy of St John’s Institute for Dermatology, London, UK).

Café-au-lait spots These are coffee-coloured macules of variable size (from a few millimetres to 10 cm) (Figure 45.18). Multiple lesions are associated with NF-1 and McCune–Albright syndromes. They are more common in dark-skinned people. **Naevus spilus** (speckled lentiginous naevus) These are similar in appearance to café-au-lait spots but with hyperpigmented speckles throughout (Figure 45.19). They are benign lesions that are associated with various cutaneous diseases, but whose speckled appearance can be confused with malignant change. The mainstay of management is observation and serial photography as malignant transformation is rare. **Donovan** James McCune , 1902–1976, American pediatrician. **Fuller Albright** , 1900–1969, physician, Massachusetts General Hospital, Boston, MA, USA. **Masao Ota** , 1885–1945, Japanese dermatologist. **Minoru Ito** , 1892–1986, Professor of Dermatology , Tohoku University , Sendai, Honshu, Japan. **Mongolian spot** A Mongolian spot is a congenital blue-grey macule found on the sacral skin (Figure 45.20). Pigmentation initially deepens and then regresses completely by age 7 years. **Blue naevus** This is a benign skin lesion that is four times more common in children, typically affecting the extremities and face (Figure 45.21). **Naevi of Ota and Ito** A naevus of Ota is a dermal melanocytic hamartoma visible as a blue or grey macule in the trigeminal V1 and V2 dermatomes. It is four times more common in women and most frequently seen in Asian and African people (Figure 45.22). A naevus of Ito is characterised by dermal melanocytosis in the shoulder region and can occur simultaneously in patients with naevus of Ota (Figure 45.23).

Figure 45.14 Compound naevus
(courtesy of St John's Institute for Dermatology, London, UK). **Figure 45.15 Intradermal naevus**
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Albert Hippolyte Malherbe , 1845–1945, Professor of Histology , Anatomy and Surgery , Nantes, France.

(b) Figure 45.18 Café-au-lait spots. Note the two topographical variants: in (a) the spot has a smooth 'coast of California' border, whereas the upper spot in (b) has an irregular 'coast of Maine' border. Multiple smooth-bordered lesions are commonly associated with syndromes (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.19 Naevus spilus (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.20 Mongolian spot (courtesy of St John's Institute for Dermatology, London, UK).

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(b) Figure 45.18 Café-au-lait spots. Note the two topographical variants: in (a) the spot has a smooth 'coast of California' border, whereas the upper spot in (b) has an irregular 'coast of Maine' border. Multiple smooth-bordered lesions are commonly associated with syndromes (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.19 Naevus spilus (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.20 Mongolian spot (courtesy of St John's Institute for Dermatology, London, UK).

SKIN TUMOURS Benign lesions

Basal cell papilloma (seborrheic keratosis, senile keratosis, verruca senilis) Their appearance varies from macular to soft, excrescent, warty lesions – often pigmented and hyperkeratotic – but may be flesh-coloured or pink. They are formed from the basal layer of epidermal cells and contain melanocytes. Papillary wart (verruca vulgaris) This is a benign skin tumour arising from infection with the human papillomavirus (HPV), which is also responsible for plantar warts and condylomata acuminata. Freckle (ephelis) A freckle is an area of skin that contains a normal number of melanocytes, producing an abnormally large number of melanin granules. Lentigo These are small, circumscribed pigmented macules that stem from sun damage and some systemic syndromes. Solar lentigos are commoner in fairer skins. Moles/naevi Melanocytes migrate from the neural crest to the basal epidermis during embryogenesis. When melanocytes aggregate in the dermis or at the dermoepidermal junction, they are called naevus cells. Sophie Spitz , 1910–1956, American dermatopathologist at the Memorial Sloan Kettering Cancer Center, published the first case series of 'juvenile melanoma' in 1948. Junctional naevus A junctional naevus is a dermoepidermal

proliferation of naevus cells, visible as deeply pigmented macules or papules that occur commonly in childhood or adolescence, usually progressing to form compound or intradermal naevi with advancing age. Benign mucosal lesions tend to be junctional naevi (Figure 45.13). Compound naevus This is a maculopapular, pigmented lesion that becomes most prominent during adolescence (Figure 45.14). It represents a junctional proliferation of naevus cells, with nests and columns in the dermis. Intradermal naevus Intradermal naevi are faintly pigmented papules in adults that show no junctional proliferation; however, they do show a cluster of dermal melanocytes (Figure 45.15). Spitz naevus These are reddish brown (occasionally deeply pigmented) nodules, previously termed 'juvenile melanoma' (Figure 45.16). They most commonly occur on the face and legs, growing rapidly initially then remaining static or regressing. The differential diagnosis is melanoma and excision biopsy is warranted if there is doubt as to the diagnosis. Spindle cell naevus Spindle cell naevi are dense black lesions that contain spindle cells and atypical melanocytes at the dermoepidermal junction. They are commonly seen on the thighs and affect women more frequently . They may have malignant potential. Halo naevus The halo of depigmentation around any benign naevus - represents an antibody response to melanocytes. Depigmentation may also be a feature of a malignant melanoma. Halo naevi are associated with vitiligo (Figure 45.17).

Figure 45.13 Junctional naevus (courtesy of St John's Institute for Dermatology, London, UK).

Café-au-lait spots These are coffee-coloured macules of variable size (from a few millimetres to 10 cm) (Figure 45.18). Multiple lesions are associated with NF-1 and McCune-Albright syndromes. They are more common in dark-skinned people. Naevus spilus (speckled lentiginous naevus) These are similar in appearance to café-au-lait spots but with hyperpigmented speckles throughout (Figure 45.19). They are benign lesions that are associated with various cutaneous diseases, but whose speckled appearance can be confused with malignant change. The mainstay of management is observation and serial photography as malignant transformation is rare. Donovan James McCune , 1902–1976, American pediatrician. Fuller Albright , 1900–1969, physician, Massachusetts General Hospital, Boston, MA, USA. Masao Ota , 1885–1945, Japanese dermatologist. Minoru Ito , 1892–1986, Professor of Dermatology , Tohoku University , Sendai, Honshu, Japan. Mongolian spot A Mongolian spot is a congenital blue-grey macule found on the sacral skin (Figure 45.20). Pigmentation initially deepens and then regresses completely by age 7 years. Blue naevus This is a benign skin lesion that is four times more common in children, typically affecting the extremities and face (Figure 45.21). Naevi of Ota and Ito A naevus of Ota is a dermal melanocytic hamartoma visible as a blue or grey macule in the trigeminal V1 and V2 dermatomes. It is four times more common in women and most frequently seen in Asian and African people (Figure 45.22). A naevus of Ito is characterised by dermal melanocytosis in the shoulder region and can occur simultaneously in patients with naevus of Ota (Figure 45.23).

Figure 45.14 Compound naevus (courtesy of St John's Institute for

Dermatology, London, UK). Figure 45.15 Intradermal naevus

(courtesy of St John's Institute for Dermatology, London, UK). Figure 45.16 Spitz naevus (courtesy of St John's Institute for Derma

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Skin adnexa

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- Adnexal structures such as hair follicles, sebaceous glands and sweat glands span both the epidermal and dermal layers and - contain some keratinocytes in their ducts. In injuries where epidermis is lost, re-epithelialisation occurs from these structures as well as from the wound margins. Hair follicles are tubular invaginations of the epidermis, from which grow hair shafts (dead keratinised tissue). Strips of smooth muscle (arrector pili) are inserted into the wall of the hair follicle and elevate it in response to stress and cold. Sebaceous glands are hair follicle appendages situated between the follicle and arrector pili muscle such that muscle contraction compresses the gland and sebum is released (holocrine secretion) along the elevated hair. Simple eccrine and apocrine sweat glands open into pores in hair follicles. Eccrine glands are distributed throughout the entire body surface, except the lips. They secrete sweat in response to emotion or during thermoregulation. Apocrine glands are found in the axillae and groins and become active at puberty. Their secretion, characteristically malodorous after bacterial degradation, is in response to emotion and hormone secretion.

Hair Sweat pore Epidermis Pilus muscle Sebaceous gland Dermis Hair follicle Subcutis Figure 45.1
Three-dimensional diagram of the structural layers of the skin and its adnexal structures.
(Reproduced from Simonsen T, Aarbakke J, Kay I et al. Illustrated pharmacology for nurses .
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Skin and soft-tissue cysts

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Milia Small, hard, keratin retention cysts (Figure 45.11) seen both in babies and, after chronic sun exposure, in the elderly as part of Favre-Racouchot syndrome (solar comedones, pseudocysts and leathery, furrowed sun-damaged skin – heightened by smoking). Epidermal cysts These cysts are lined with true stratified squamous epithelium, derived from hair follicle infundibuli or traumatic inclusion. Commonly known as sebaceous cysts, they can occur anywhere. They are fixed to the skin and usually have a central punctum (Figure 45.12). Albert Ludwig Siegmund Neisser, 1855–1916, Director of the Dermatological Institute, Breslau, Germany (now Wrocław, Poland). Maurice Favre, 1876–1954, French dermatologist. Jean Racouchot, 1908–1994, French dermatologist. Heinrich Meibom (Meibomius), 1638–1700, Professor of Medicine, History and Poetry, Helmstadt, Germany, described these glands in 1666. -). Treatment depends on the clinical state of the cyst. When inflamed or infected, they should be incised and drained initially; they should be removed later once the inflammation and induration has subsided. It is important to excise the cyst in its entirety as failure to do so usually results in recurrence. Meibomian cysts are epidermal cysts found on the free eyelid. Trichilemmal (pilar/pilosebaceous) cysts edge of the eye are derived from the epidermis of the external root sheath of follicle; 90% are found in the scalp and 70% are multilocular. They are usually distinguished from epidermal cysts by pathologists, rather than clinically.

Figure 45.10 Acute infectious purpura fulminans caused by meningococcal septicaemia. Note the sharply demarcated necrotic areas distal to the affected end or

perforating arteries with surrounding nor

mal skin (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.11 Milia (courtesy of St John's Institute for Dermatology, London, UK).

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Skin dimensions

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The skin is a large organ. In an adult it may have an area of 2 1-2 /uni00A0 m and weigh 15-20 /uni00A0 kg. Skin thickness varies with age, location and sun damage, but in any given region it is thinner in children than in adults. The dermis is between 15 and 40 times thicker than the epidermis, but starts to thin during the fourth decade. The epidermis is thickest on the palms, soles, back and buttocks and thinnest on eyelids (0.5-1 /uni00A0 mm on the sole of the foot; 0.05-0.09 /uni00A0 mm on the eyelid). Skin dimensions

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Sweat glands

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Cystadenoma (hydrocystadenomas, hidradenomas) These are 1- to 3-cm translucent blue cystic nodules.

Figure 45.25 Adenoma sebaceum (courtesy of St John's Institute for Dermatology, London, UK).

Figure 45.26 Rhinophyma (courtesy of St John's Institute for Dermatology, London, UK).

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VASCULAR LESIONS

Congenital haemangiomata and vas

VASCULAR LESIONS Congenital: haemangiomata and vascular malformations

These can be subclassified biologically into vascular tumours or vascular malformations based on their endothelial characteristics, or radiologically into haemangiomata, vascular and lymphatic malformations based on their vascular dynamics. Haemangiomata These are benign endothelial tumours that affect three girls for every boy. Thirty per cent have a herald patch at birth, which then grows rapidly in the first year of life and slowly involutes over several years, with 70% having resolved by 7 years of age. Large haemangiomata can trap platelets, leading to thrombocytopenia (Kasabach-Merritt syndrome). Vascular malformations Vascular malformations affect boys and girls equally and are associated with numerous syndromes. They are invariably present at birth but may be missed if deep to the skin. Vascular malformations subsequently grow in proportion to the child's growth (rather than in response to sepsis or hormonal stimulation). Stasis can lead to a localised, consumptive coagulopathy in large venous malformations. Low-flow malformations may cause skeletal hypoplasia, while high-flow malformations can cause hypertrophy.

Figure 45.41 Merkel cell tumour (courtesy of St John's Institute for Dermatology, London, UK).

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WOUNDS Congenital

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Cutis aplasia congenita This is a rare condition characterised by the congenital absence of epidermis, dermis and, in some cases, subcutaneous tissues, with underlying bony defects in 20%. Treatment depends on the severity of the presentation, but usually involves plastic surgery .

Parry-Romberg disease (linear morphoea) A rare variant of scleroderma affecting up to 3:100 /uni00A0 000 children. It is linked to certain HLA subtypes and to a family history of autoimmune disease. It is three times more common in females and often develops after an external physical trigger, such as friction or trauma. Moritz Kaposi , 1837–1902, Austrian dermatologist, described xeroderma pigmentosum in 1874. He also described a rare cutaneous sarcoma in Ashkenazi Jews, now more often an AIDS-defining condition. Caleb Hillier Parry , 1755–1822, physician, The General Hospital, Bath, UK. Moritz Heinrich Romberg , 1795–1873, neurologist, Director of the University Hospital, Berlin, Germany . Parry-Romberg disease is a progressive, hemifacial atrophy of skin, soft tissue and bone. The disease commonly starts in the late twenties but can present in childhood, when the resulting deformity is worse because it is magnified by differential growth elsewhere. The condition is self-limiting, usually by 5–10 years after onset. Once stable, plastic surgery techniques can be employed alone or in combination to reconstruct an aesthetic contour. Coup de sabre is a variant that affects the cranium and scalp and resembles a 'blow from a sabre'. Spina bifida Failure of closure of the caudal neuropore during the fourth week in utero results in incomplete development of some or all of the structural elements posterior to the spinal cord. This can occur anywhere, but is commonest in lumbar vertebrae and presents as gross variants: spina bifida occulta, in which there is a bony defect without neural protrusion, and spina bifida cystica, in which there is herniation of the meninges (meningocele), spinal cord (myelocele) or, most commonly ,

Figure 45.49 Angiosarcoma (courtesy of St John's Institute for Dermatology, London, UK). Figure 45.50 Kaposi's sarcoma (courtesy of St John's Institute for Dermatology, London, UK).

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