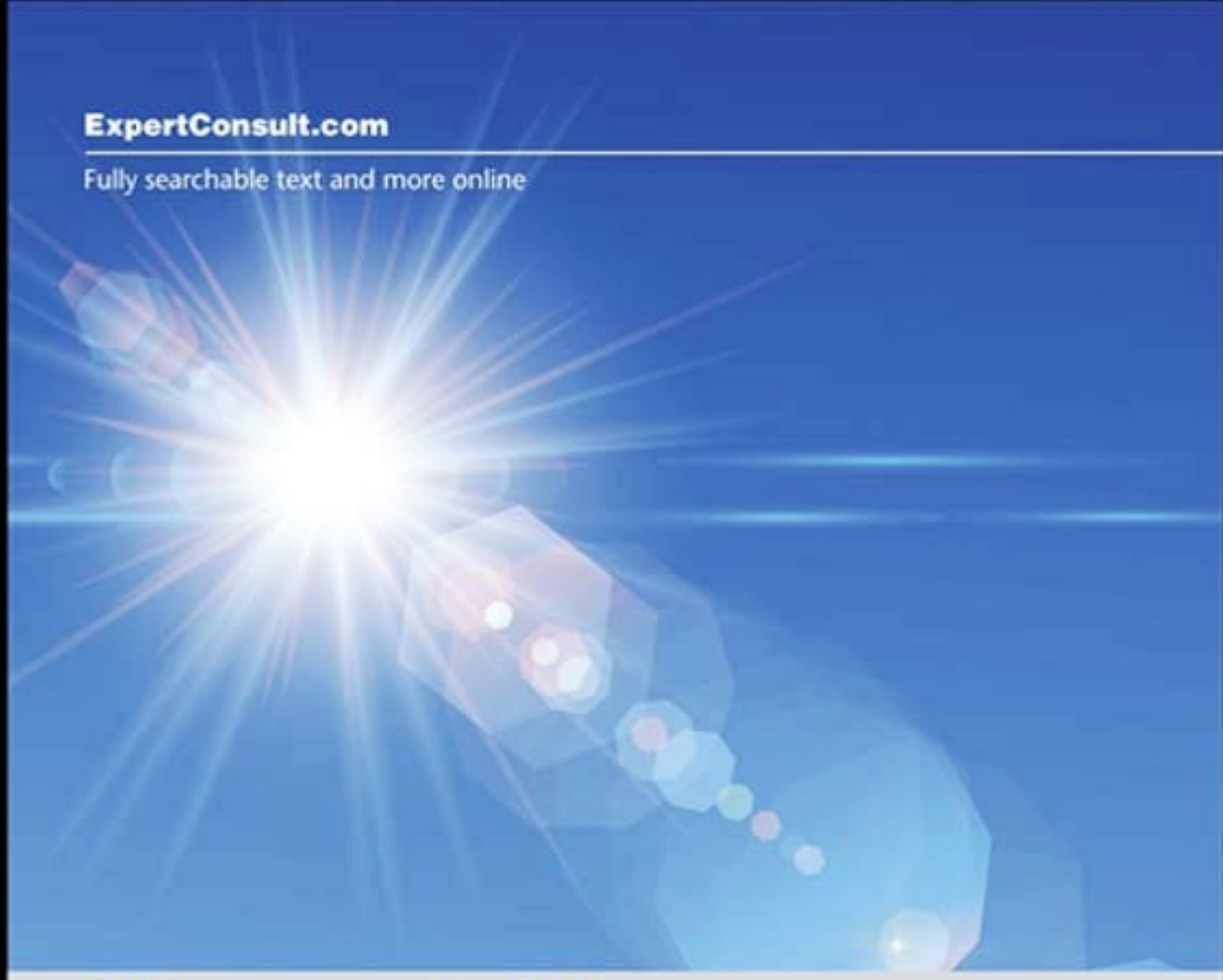

Kanski's Clinical Ophthalmology

A SYSTEMATIC APPROACH

EIGHTH EDITION

Brad Bowling

ELSEVIER

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Kanski's Clinical Ophthalmology

A SYSTEMATIC APPROACH

Dedication

To Jack Kanski, an exceptional teacher and inspirational mentor

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A SYSTEMATIC APPROACH

EIGHTH EDITION

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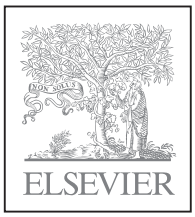

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Contents

Preface to the Eighth Edition

I first met Jack Kanski when I rotated to The Prince Charles Eye Unit in Windsor as part of the Oxford Deanery ophthalmology residency programme. Jack had actually just retired from clinical practice, but continued to attend the unit's weekly education meetings. As the senior registrar, I was responsible for the organization of these sessions, to which Jack brought the same qualities that have facilitated his amazing success as a medical author – his encyclopaedic knowledge of ophthalmology and unerring ability to isolate the critical issues in a topic, not to mention his incisive wit, made the meetings extraordinarily effective as well as hugely enjoyable.

Jack was aware that I had done some textbook writing previously, and after one of the teaching sessions asked me whether I would be interested in writing a basic interactive text with him for medical students and novice ophthalmologists. I was a little daunted at first – Jack had written more than thirty ophthalmology textbooks by this time – but duly proceeded; we worked together extremely well, the book was written to deadline, was critically popular and sold lots of copies.

After I left Windsor, Jack and I worked with each other again on one or two projects and kept in touch socially, and a couple of years later he raised the possibility of collaboration on the next edition of *Clinical Ophthalmology*. I was thrilled. I recall vividly when, just prior to my first ophthalmology post, I contacted two registrars independently to enquire about initial textbook choice, receiving a curt single-word response from both: 'Kanski', with the implication that there was no need to ask. Big shoes to fill.

I have striven to maintain Jack Kanski's approach of presenting core clinical knowledge in a systematic and succinct form; the extent of subject coverage by the later editions of the book is easily underestimated, and it is intended that a thorough acquaintance with its contents will provide a comprehensive basis for general ophthalmic practice. In the present edition every attempt has been made to completely update each chapter, with inclusion of the latest practical evidence-based diagnostic and treatment approaches, and replacement and upgrading of images as appropriate, such as where novel imaging modalities offer an enhanced perspective. The index for this edition has been written by the author to ensure its ease of use and clinical applicability.

I am incredibly indebted to Jack Kanski for the opportunity to contribute to *Clinical Ophthalmology* and other books, and for his ongoing mentoring and support. I have received invaluable help with the eighth edition from colleagues; Simon Chen generously furnished a large number of photographic and other images and gave his time to advise in depth on various posterior segment topics, Chris Barry also kindly provided and edited very numerous images, and many other ophthalmologists, optometrists, ophthalmic photographers and other eyecare professionals contributed one or a small number of figures and are acknowledged in individual legends. Philip Spork was good enough to review the section on macular antioxidant supplements. I am also indebted to the numerous colleagues who contacted Jack Kanski or myself with helpful comments on particular points in the seventh edition. Many individuals have helped substantially with the previous editions of *Clinical Ophthalmology*, the core of which has been brought forward into the present book; Ken Nischal and Andy Pearson both carried out detailed reviews of sections in the seventh edition, Jay Menon made a major contribution to the fifth edition, Anne Bolton and Irina Gout provided photographic expertise over many years and, of course, Terry Tarrant supplied a large number of amazingly authentic ocular paintings. My wife, Suzanne, and sons, Edward and Oliver, supported me unreservedly during the extended revision of the book, tolerating my absence over the course of many months without complaint. Finally, I would like to acknowledge the cheerful and expert support and commitment of the staff at Elsevier, especially Russell Gabbedy, Louise Cook, John Leonard, Anne Collett and Marcela Holmes.

It would be impossible for me to replicate Jack Kanski's style precisely, but I have tried to retain the essence of his approach as faithfully as possible, and hope that this book will prompt in the reader at least some of the enthusiasm for the subject that the second edition of *Clinical Ophthalmology* engendered in me.

B.B.
2015

Abbreviations

AAION	arteritic anterior ischaemic optic neuropathy
AAU	acute anterior uveitis
AC	anterior chamber
AC/A ratio	accommodative convergence/accommodation ratio
AD	autosomal dominant
AF	autofluorescence
AHP	abnormal head posture
AI	accommodative insufficiency
AIBSE	acute idiopathic blind spot enlargement syndrome
AIDS	acquired immune deficiency syndrome
AIM	(unilateral) acute idiopathic maculopathy
AION	anterior ischaemic optic neuropathy
AIR	autoimmune retinopathies
AKC	atopic keratoconjunctivitis
ALT	argon laser trabeculoplasty
AMD	age-related macular degeneration
AMN	acute macular neuroretinopathy
ANA	antinuclear antibody
ANCA	antineutrophil cytoplasmic antibodies
APD	afferent pupillary defect
APMPPE	acute posterior multifocal placoid pigment epitheliopathy
AR	autosomal recessive
AREDS	Age-Related Eye Disease Study
ARN	acute retinal necrosis
ARPE	acute retinal pigment epitheliitis
AZOOR	acute zonal occult outer retinopathy
AZOR	acute zonal outer retinopathy
BCC	basal cell carcinoma
BCVA	best-corrected visual acuity
BIO	binocular indirect ophthalmoscopy
BP	blood pressure
BRAO	branch retinal artery occlusion
BRVO	branch retinal vein occlusion
BSV	binocular single vision
BUT	breakup time
CAI	carbonic anhydrase inhibitor
CCDD	congenital cranial dysinnervation disorders
CCT	central corneal thickness
CDCR	canaliculodacryocystorhinostomy
CF	counts (or counting) fingers
CHED	congenital hereditary endothelial dystrophy
CHP	compensatory head posture
CHRPE	congenital hypertrophy of the retinal pigment epithelium
CI	convergence insufficiency
CMO	cystoid macular oedema (US = CME)
CNS	central nervous system
CNV	choroidal neovascularization
CNVM	choroidal neovascular membrane
COX-2	cyclo-oxygenase-2
CPEO	chronic progressive external ophthalmoplegia
CRAO	central retinal artery occlusion
CRP	C-reactive protein
CRVO	central retinal vein occlusion
CSC	central serous chorioretinopathy
CSMO	clinically significant macular oedema (US = CSME)
CSC/CSCR	central serous chorioretinopathy
CSR	central serous chorioretinopathy
CSS	central suppression scotoma
CT	computed tomography
DCR	dacryocystorhinostomy
DMO	diabetic macular oedema (US = DME)
DR	diabetic retinopathy
DVD	dissociated vertical deviation
ECG	electrocardiogram
EDTA	ethylenediaminetetraacetic acid
EKC	epidemic keratoconjunctivitis
EOG	electro-oculography/gram
ERG	electroretinography/gram
ESR	erythrocyte sedimentation rate
ETDRS	Early Treatment Diabetic Retinopathy Study
FA	fluorescein angiography (also FFA)
FAF	fundus autofluorescence
FAP	familial adenomatous polyposis
FAZ	foveal avascular zone
FBA	frosted branch angiitis
FBC	full blood count
FFM	fundus flavimaculatus
GA	geographic atrophy
GAT	Goldmann applanation tonometry
GCA	giant cell arteritis
GPC	giant papillary conjunctivitis
HAART	highly active antiretroviral therapy
HIV	human immunodeficiency virus
HM	hand movements
HRT	Heidelberg retinal tomography
HSV-1	herpes simplex virus type 1
HSV-2	herpes simplex virus type 2
HZO	herpes zoster ophthalmicus
ICG	indocyanine green
ICGA	indocyanine green angiography
Ig	immunoglobulin
IK	interstitial keratitis
ILM	internal limiting membrane
INO	internuclear ophthalmoplegia
IOFB	intraocular foreign body

IOID	idiopathic orbital inflammatory disease
IOL	intraocular lens
IOP	intraocular pressure
IRMA	intraretinal microvascular abnormality
IRVAN	idiopathic retinal vasculitis, aneurysms and neuroretinitis syndrome
ITC	iridotrabecular contact
IU	intermediate uveitis
JIA	juvenile idiopathic arthritis
KC	keratoconus
KCS	keratoconjunctivitis sicca
KP	keratic precipitate
LA	local anaesthetic
LASEK	laser (also laser-assisted) epithelial keratomileusis
LASIK	laser-assisted *in situ* keratomileusis
LN	latent nystagmus
MCP	multifocal choroiditis and panuveitis
MEWDS	multiple evanescent white dot syndrome
MFC	multifocal choroiditis and panuveitis
MLF	medial longitudinal fasciculus
MRI	magnetic resonance imaging
MS	multiple sclerosis
NF1	neurofibromatosis type I
NF2	neurofibromatosis type II
NPDR	non-proliferative diabetic retinopathy
NRR	neuroretinal rim
NSAID	non-steroidal anti-inflammatory drug
NSR	neurosensory retina
NTG	normal-tension glaucoma
NVD	new vessels on the disc
NVE	new vessels elsewhere
OCT	optical coherence tomography/gram
OHT	ocular hypertension
OKN	optokinetic nystagmus
PAC	primary angle closure
PACG	primary angle-closure glaucoma
PACS	primary angle-closure suspect
PAM	primary acquired melanosis
PAN	polyarteritis nodosa
PAS	peripheral anterior synechiae
PC	posterior chamber
PCO	posterior capsular opacification
PCR	polymerase chain reaction
PCV	polypoidal choroidal vasculopathy
PDR	proliferative diabetic retinopathy
PDS	pigment dispersion syndrome
PDT	photodynamic therapy
PED	pigment epithelial detachment
PIC	punctate inner choroidopathy
PIOL	primary intraocular lymphoma
PION	posterior ischaemic optic neuropathy
PKP	penetrating keratoplasty
POAG	primary open-angle glaucoma
POHS	presumed ocular histoplasmosis syndrome
PP	pars planitis
PPCD	posterior polymorphous corneal dystrophy
PPDR	preproliferative diabetic retinopathy
PPM	persistent placoid maculopathy
PPRF	paramedian pontine reticular formation
PRK	photorefractive keratectomy
PRP	panretinal photocoagulation
PS	posterior synechiae
PUK	peripheral ulcerative keratitis
PVD	posterior vitreous detachment
PVR	proliferative vitreoretinopathy
PXF	pseudoexfoliation
RAO	retinal artery occlusion
RAPD	relative afferent pupillary defect
RD	retinal detachment
RNFL	retinal nerve fibre layer
ROP	retinopathy of prematurity
RP	retinitis pigmentosa
RPC	relentless placoid chorioretinitis
RPE	retinal pigment epithelium
RRD	rhegmatogenous retinal detachment
RVO	retinal vein occlusion
SAP	standard automated perimetry
SCC	squamous cell carcinoma
SD-OCT	spectral domain optical coherence tomography
SF	short-term fluctuation
SFU	progressive subretinal fibrosis and uveitis syndrome
SIC	solitary idiopathic choroiditis
SJS	Stevens–Johnson syndrome
SLK	superior limbic keratoconjunctivitis
SLT	selective laser trabeculoplasty
SRF	subretinal fluid
SS	Sjögren syndrome
STIR	short T1 inversion recovery
TAL	total axial length
TB	tuberculosis
TEN	toxic epidermal necrolysis
TGF	transforming growth factor
TIA	transient ischaemic attack
TTT	transpupillary thermotherapy
TM	trabecular meshwork
TRD	tractional retinal detachment
UBM	ultrasonic biomicroscopy
US	ultrasonography
VA	visual acuity
VEGF	vascular endothelial growth factor
VEP	visual(ly) evoked potential(s)
VFI	visual field index
VHL	von Hippel–Lindau syndrome
VKC	vernal keratoconjunctivitis
VKH	Vogt–Koyanagi–Harada syndrome
VZV	varicella zoster virus
XL	X-linked

Chapter

1 Eyelids

INTRODUCTION

Anatomy

The skin (Fig. 1.1A) consists of the epidermis, dermis and related structures (adnexa).

Epidermis

The epidermis is comprised of four layers of keratin-producing cells (keratinocytes). It also contains melanocytes, Langerhans cells and Merkel cells. The layers of the epidermis around the eye are described below; cells migrate superficially, undergoing maturation and differentiation through successive layers.

- **Keratin layer** (stratum corneum or horny layer) consists of flat cells devoid of nuclei.
- **Granular cell layer** (stratum granulosum) typically consists of one or two layers of flattened cells containing keratohyaline granules.
- **Prickle cell layer** (stratum spinosum) is approximately five cells deep. The cells are polygonal in cross-section and have abundant eosinophilic cytoplasm. Their free borders are united by spiny-appearing desmosomes (cellular junctions).
- **Basal cell layer** (stratum basale) comprises a single row of columnar-shaped proliferating cells containing melanin derived from adjacent melanocytes.

Dermis

The dermis is much thicker than the epidermis. It is composed of connective tissue and contains blood vessels, lymphatics and nerve

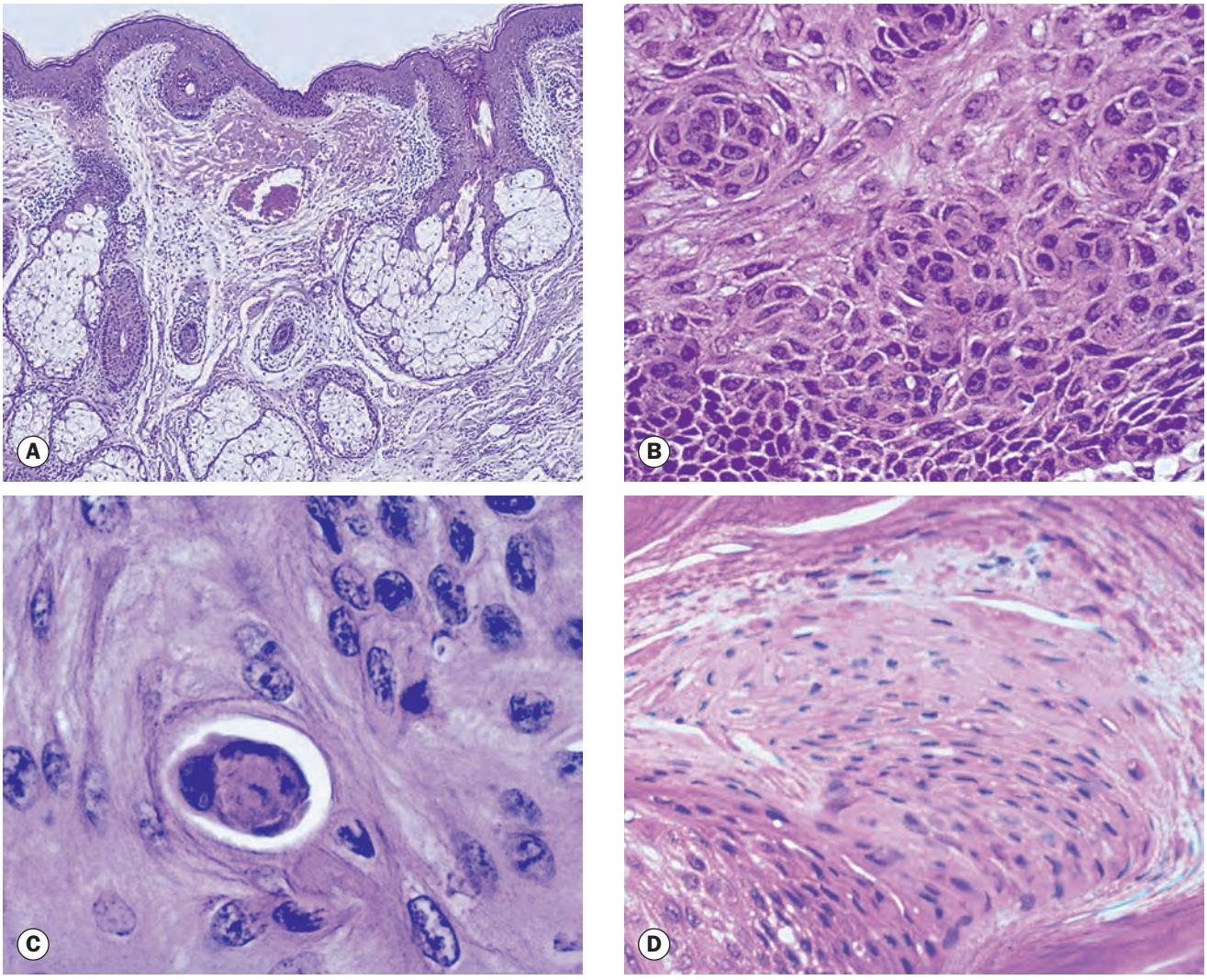


Fig. 1.1 Eyelid skin. **(A)** Normal skin is composed of keratinized stratified epithelium that covers the surface; pilosebaceous elements are conspicuous in the dermis and a few blood vessels and sweat glands are also seen; **(B)** dysplasia with loss of cell polarity; **(C)** dyskeratosis – a non-surface epithelial cell producing keratin; **(D)** parakeratosis – retention of cell nuclei into the surface keratin layer

(Courtesy of J Harry – fig. A; J Harry and G Misson, from Clinical Ophthalmic Pathology, *Butterworth-Heinemann, 2001 – figs B–D)*

fibres in addition to fibroblasts, macrophages and mast cells; upward dermal extensions (papillae) interdigitate with downward epidermal projections (rete ridges). In the eyelid the dermis lies on the orbicularis muscle. Adnexa lie deep in the dermis or within the tarsal plates.

- **Sebaceous glands** are located in the caruncle and within eyebrow hairs. Tiny sebaceous glands are associated with the thin (vellus) hairs covering periocular skin.
- **Meibomian glands** are modified sebaceous glands found in the tarsal plates. They empty through a single row of 20–30 orifices on each lid. A gland consists of a central duct with multiple acini, the cells of which synthesize lipids (meibum) that form the outer layer of the tear film.
- **Glands of Zeis** are modified sebaceous glands associated with lash follicles.
- **Glands of Moll** are modified apocrine sweat glands opening either into a lash follicle or directly onto the anterior lid margin between lashes; they are more numerous in the lower lid.
- **Eccrine sweat glands** are distributed throughout eyelid skin and are not confined to the lid margin, in contrast to glands of Moll.
- **Pilosebaceous units** comprise hair follicles and their sebaceous glands (see Fig. 1.1A).

Terminology

Clinical

- **Macule.** Localized area of colour change without infiltration, depression or elevation, less than 1 cm in diameter.
- **Papule.** A solid elevation less than 1 cm in diameter.
- **Vesicle.** Circumscribed lesion containing serous fluid; less than 0.5 cm across.
- **Bulla.** A large (more than 0.5 cm) serous fluid-filled lesion; plural – bullae.
- **Pustule.** A pus-filled elevation less than 1 cm in diameter.
- **Crust.** Solidified serous or purulent exudate.
- **Nodule.** A palpable solid area measuring more than 1 cm.
- **Cyst.** A nodule consisting of an epithelial-lined cavity filled with fluid or semi-solid material.
- **Plaque.** A solid elevation of the skin, greater than 1 cm in diameter.
- **Scale.** Readily detached fragments of shed keratin layer.
- **Papilloma.** A benign neoplastic warty or tag-like projection of the skin or mucous membrane.
- **Ulcer.** A circumscribed area of epithelial loss; in skin an ulcer extends through the epidermis into the dermis.

Histological

- **Tumour** strictly refers only to a swelling, though is commonly used to denote a neoplasm.
- **Neoplasia.** Abnormal tissue growth, either benign (localized, non-invasive and non-spreading) or malignant (progressive growth with the potential for distant spread).
- **Atypia** refers to an abnormal appearance of individual cells, e.g. abnormal mitotic figures.
- **Dysplasia** is an alteration of the size, morphology and organization of cellular components of a tissue. There is disturbance of normally structured and recognized layers of tissue (e.g. loss of cell polarity – Fig. 1.1B).
- **Carcinoma *in situ*** (intraepidermal carcinoma, Bowen disease) exhibits dysplastic changes throughout the thickness of the epidermis.
- **Hyperkeratosis.** An increase in thickness of the keratin layer that appears clinically as scaling. Hyperkeratosis can be a feature of benign or malignant epithelial tumours.
- **Acanthosis.** Thickening of the prickle cell layer.
- **Dyskeratosis** is keratinization other than on the epithelial surface (Fig. 1.1C).
- **Parakeratosis** is the retention of nuclei into the keratin layer (Fig. 1.1D).

General considerations

- **Classification.** Epidermal, adnexal or dermal.
- **Diagnosis.** The clinical characteristics of benign lesions are a tendency to a lack of induration and ulceration, uniform colour, limited growth, regular outline and preservation of normal lid margin structures. Biopsy may be required if the appearance is suspicious.
  - Incisional biopsy involves removal of a portion of a lesion for histopathology.
  - Excision biopsy is performed on small tumours and fulfils both diagnostic and treatment objectives.
- **Treatment** options include:
  - Excision of the entire lesion and a small surrounding portion of normal tissue.
  - Marsupialization involves the removal of the top of a cyst allowing drainage of its contents and subsequent epithelialization.
  - Ablation with laser or cryotherapy.

NON-NEOPLASTIC LESIONS

Chalazion

Pathogenesis

A chalazion (meibomian cyst) is a sterile chronic granulomatous inflammatory lesion (lipogranuloma) of the meibomian, or sometimes Zeis, glands caused by retained sebaceous secretions. Histopathology shows a lipogranulomatous chronic inflammatory picture with extracellular fat deposits surrounded by lipid-laden epithelioid cells, multinucleated giant cells and lymphocytes (Fig. 1.2A). Blepharitis is commonly present; rosacea can be associated with multiple and recurrent chalazia. A recurrent chalazion should be biopsied to exclude malignancy.

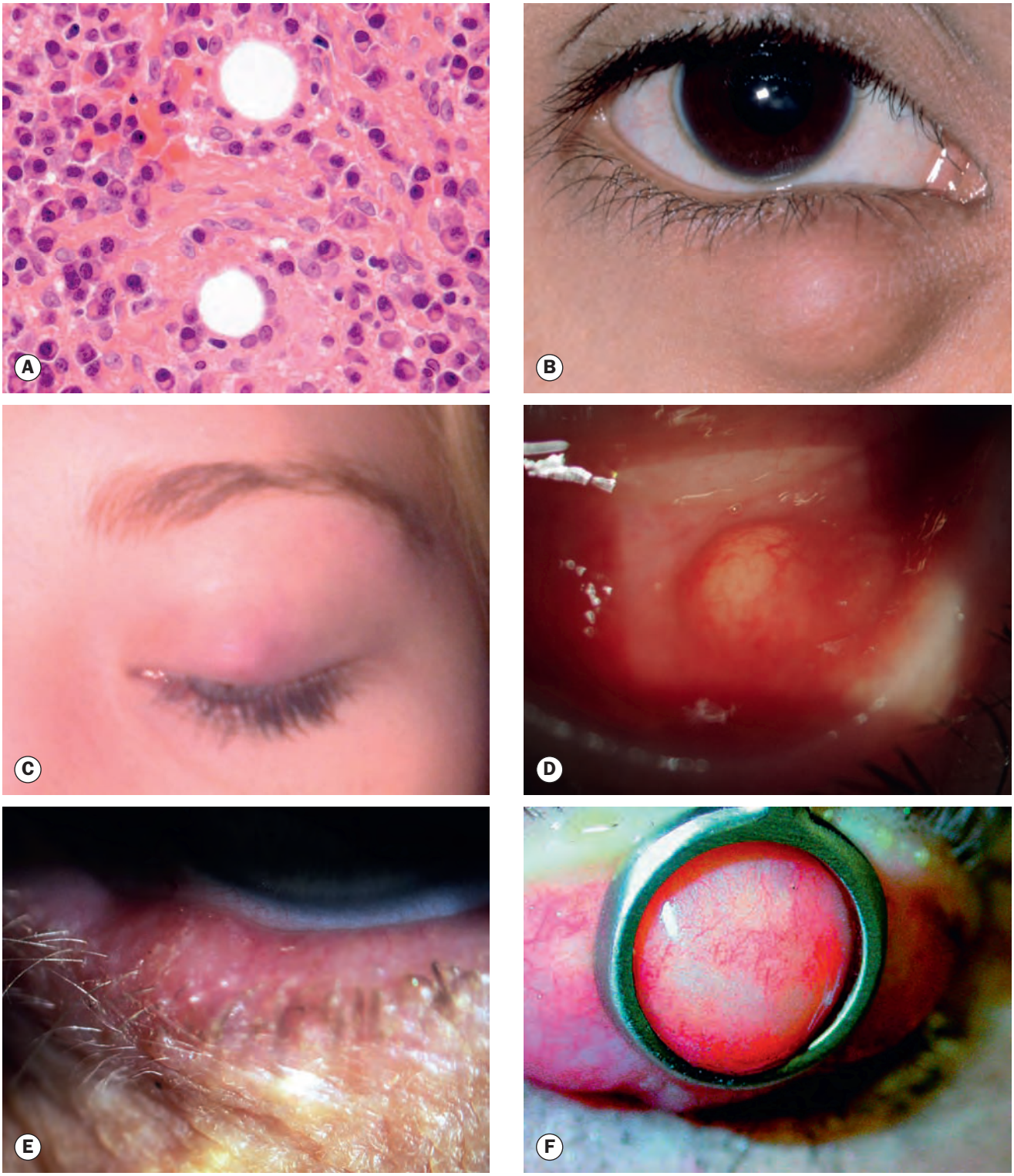


Fig. 1.2 Chalazion. **(A)** Histopathology shows a lipogranuloma; the large pale cells are epithelioid cells and the well-demarcated empty space contained fat dissolved out during processing; **(B)** uninflamed chalazion; **(C)** acutely inflamed lesion; **(D)** conjunctival granuloma; **(E)** marginal chalazion; **(F)** conjunctival view of chalazion clamp in place prior to incision and curettage

(Courtesy of J Harry and G Misson, from Clinical Ophthalmic Pathology, *Butterworth-Heinemann 2001 – fig. A; J Nerad, K Carter and M Alford, from 'Oculoplastic and Reconstructive Surgery', in* Rapid Diagnosis in Ophthalmology, *Mosby 2008 – fig. F)*

Diagnosis

- **Symptoms**
  - Subacute/chronic: gradually enlarging painless rounded nodule (Fig. 1.2B).
  - Acute: sterile inflammation or bacterial infection with localized cellulitis (Fig. 1.2C); differentiation may be difficult. A secondarily infected meibomian gland is referred to as an internal hordeolum.
- **Signs**
  - A nodule within the tarsal plate, sometimes with associated inflammation.
  - Bulging inspissated secretions may be visible at the orifice of the involved gland.
  - There may be an associated conjunctival granuloma (Fig. 1.2D).
  - A lesion at the anterior lid margin – a marginal chalazion (Fig. 1.2E) – may be connected to a typical chalazion deeper in the lid or be due to isolated involvement of a gland of Zeis.

Treatment

- **Oral antibiotics** are required for significant bacterial infection, but not for sterile inflammation.
- **Conservative.** At least a third of chalazia resolve spontaneously so observation may be appropriate, especially if the lesion is showing signs of improvement, though early definitive treatment has been reported to lead to higher patient satisfaction.
- **Hot compress** application several times daily may aid resolution, particularly in early lesions.
- **Expression.** Compression between two cotton-tipped applicators is sometimes effective in expressing the contents of a fresh lesion near the lid margin.
- **Steroid injection** into or around the lesion has been reported to give similar resolution rates to incision and curettage (see below). It may be preferred for marginal lesions or lesions close to structures such as the lacrimal punctum because of the risk of surgical damage.
  - Reported regimens include 0.2–2 ml of triamcinolone acetonide aqueous suspension diluted with lidocaine to a concentration of 5 mg/ml, and 0.1–0.2 ml of 40 mg/ml, injected with a 27- or 30-gauge needle.
  - The success rate following one injection is about 80%; a second can be given 1–2 weeks later.
  - Local skin depigmentation and fat atrophy are potential but uncommon complications, the risk of which may be reduced by avoidance of infiltration immediately subcutaneously or by utilizing a conjunctival approach.
  - Retinal vascular occlusion has been described as a complication, probably due to intravascular injection with subsequent embolization.
- **Surgery**
  - Following local anaesthesia infiltration, the eyelid is everted with a specialized clamp (Fig. 1.2F), the cyst is incised vertically through the tarsal plate and its contents curetted.
  - Limited excision of solid inflammatory material (sent for histopathology) with fine scissors may be helpful in some cases, especially if there is no focus of secretions.
  - A suture should not be used.
  - Topical antibiotic ointment is used three times daily for 5–7 days following curettage.
- **Marginal lesions** can be managed by steroid injection, by curettage of an associated deeper chalazion, by shave curettage or by incision and curettage via a horizontal incision on the conjunctival surface or vertically through the grey line.
- **Prophylaxis**
  - Treatment of blepharitis, e.g. daily lid hygiene regimen.
  - Systemic tetracycline may be required as prophylaxis in patients with recurrent chalazia, particularly if associated with acne rosacea.

Other eyelid cysts

- **Cyst of Zeis** is a small, non-translucent cyst on the anterior lid margin arising from obstructed sebaceous glands associated with the eyelash follicle (Fig. 1.3A).
- **Cyst of Moll** (apocrine hidrocystoma) is a small retention cyst of the lid margin apocrine glands. It appears as a round, non-tender, translucent fluid-filled lesion on the anterior lid margin (Fig. 1.3B).
- **Sebaceous (pilar)** cyst is caused by a blocked pilosebaceous follicle and contains sebaceous secretions; the gland orifice will often be visible (Fig. 1.3C). It is only rarely found on the eyelid although it may occasionally occur at the inner canthus.
- **Comedones** are plugs of keratin and sebum within the dilated orifice of hair follicles that often occur in patients with acne vulgaris. They may be either open (blackheads) containing a darkened plug of oxidized material (Fig. 1.3D), or closed (whiteheads).
- **Milia** are caused by occlusion of pilosebaceous units resulting in retention of keratin. They are tiny, white, round, superficial papules that tend to occur in crops (Fig. 1.3E).
- **Epidermal inclusion** cyst is usually caused by implantation of epidermis into the dermis following trauma or surgery. It is a slow-growing, round, firm, superficial or subcutaneous lesion containing keratin (Fig. 1.3F).
- **Epidermoid** cyst is uncommon and usually developmental, occurring along embryonic lines of closure. It is similar in appearance to an epidermal inclusion cyst.
- **Dermoid** cyst is usually subcutaneous or deeper and is typically attached to the periosteum at the lateral end of the brow (Fig. 1.3G). It is caused by skin sequestered during embryonic development.
- **Eccrine hidrocystoma** is less common but similar in appearance to a cyst of Moll except that it is usually located along the medial or lateral aspects of the lid, and is close to but does not involve the lid margin itself (Fig. 1.3H).

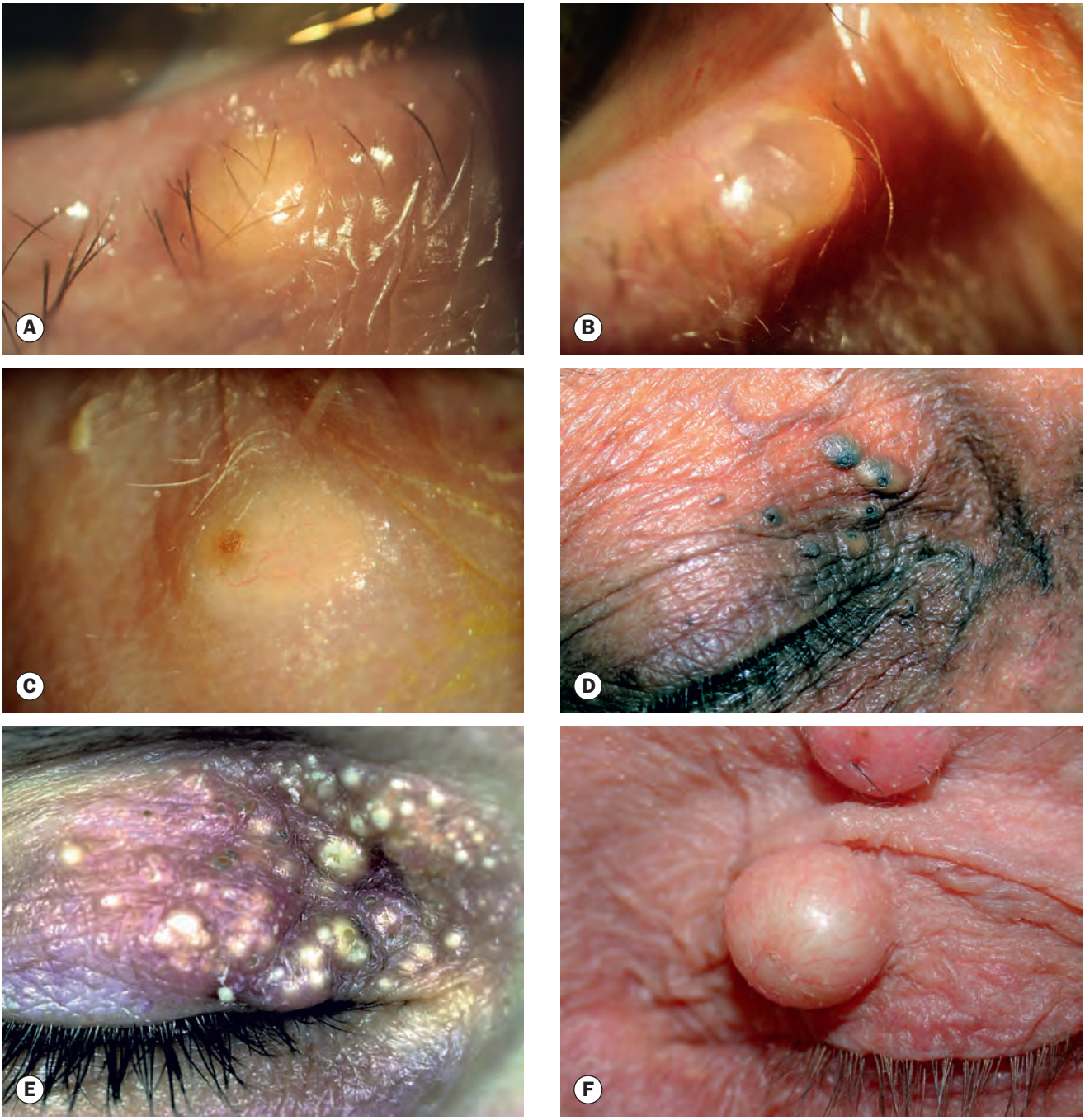


Fig. 1.3 Eyelid cysts. **(A)** Cyst of Zeis; **(B)** cyst of Moll; **(C)** sebaceous cyst; **(D)** comedones – blackheads; **(E)** milia; **(F)** epidermal inclusion cyst;

Xanthelasma

Introduction

Xanthelasma (plural – xanthelasmata) is a common, frequently bilateral condition typically affecting middle-aged and elderly individuals. It is a subtype of xanthoma. Hyperlipidaemia is found in about one-third of patients, in whom corneal arcus may also be present. In contrast to chalazion, fat in xanthelasmata is mainly intracellular, with lipid-laden histiocytes (foam cells) in the dermis (Fig. 1.4A).

Diagnosis

Xanthelasmata are yellowish subcutaneous plaques, usually in the medial aspects of the eyelids (Fig. 1.4B), commonly bilateral and are multiple (Fig. 1.4C).

Fig. 1.3, Continued **(G)** dermoid cyst; **(H)** eccrine hidrocystomas
(Courtesy of A Pearson – figs D, F and H)

Treatment

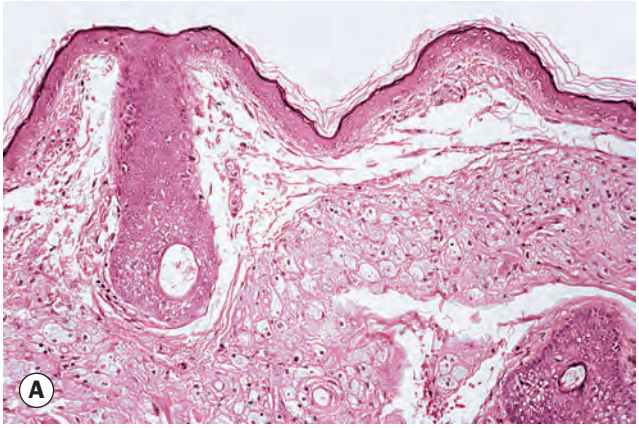
This is principally for cosmesis. Recurrence occurs in up to 50%, and is most common in patients with hypercholesterolaemia.

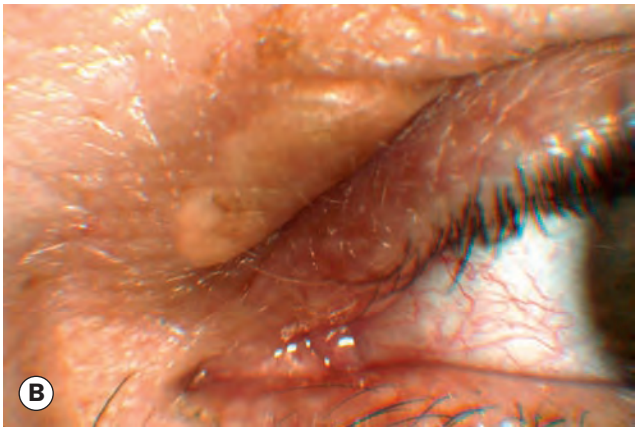
- **Simple excision** is commonly performed where adequate excess skin is present.
- **Microdissection.** Larger lesions can be raised in a flap, the fatty deposits dissected from overlying skin under a surgical microscope using microscissors, and the skin replaced.
- **Other methods.** Good results can be obtained using chemical peeling with bi- or trichloroacetic acid. Laser ablation and cryotherapy have advantages but may be more prone to scarring, including pigmentary changes.

BENIGN EPIDERMAL TUMOURS

Squamous cell papilloma

Squamous cell papilloma is a very common benign epithelial tumour with a variable clinical appearance, including narrow-based (pedunculated or 'skin tag' – Fig. 1.5A), pink broad-based





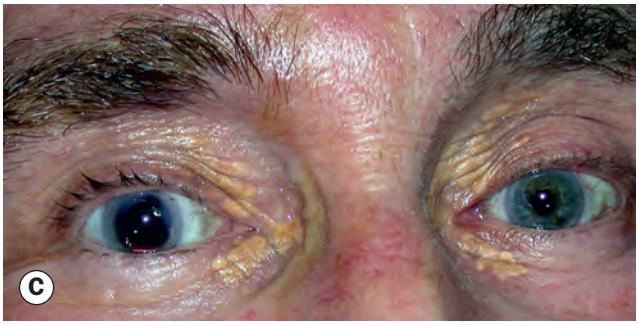


Fig. 1.4 Xanthelasma. **(A)** Histopathology showing foamy histiocytes within the dermis; **(B)** large isolated lesion; **(C)** multiple bilateral smaller lesions
(Courtesy of J Harry – fig. A; S Chen – fig. C)

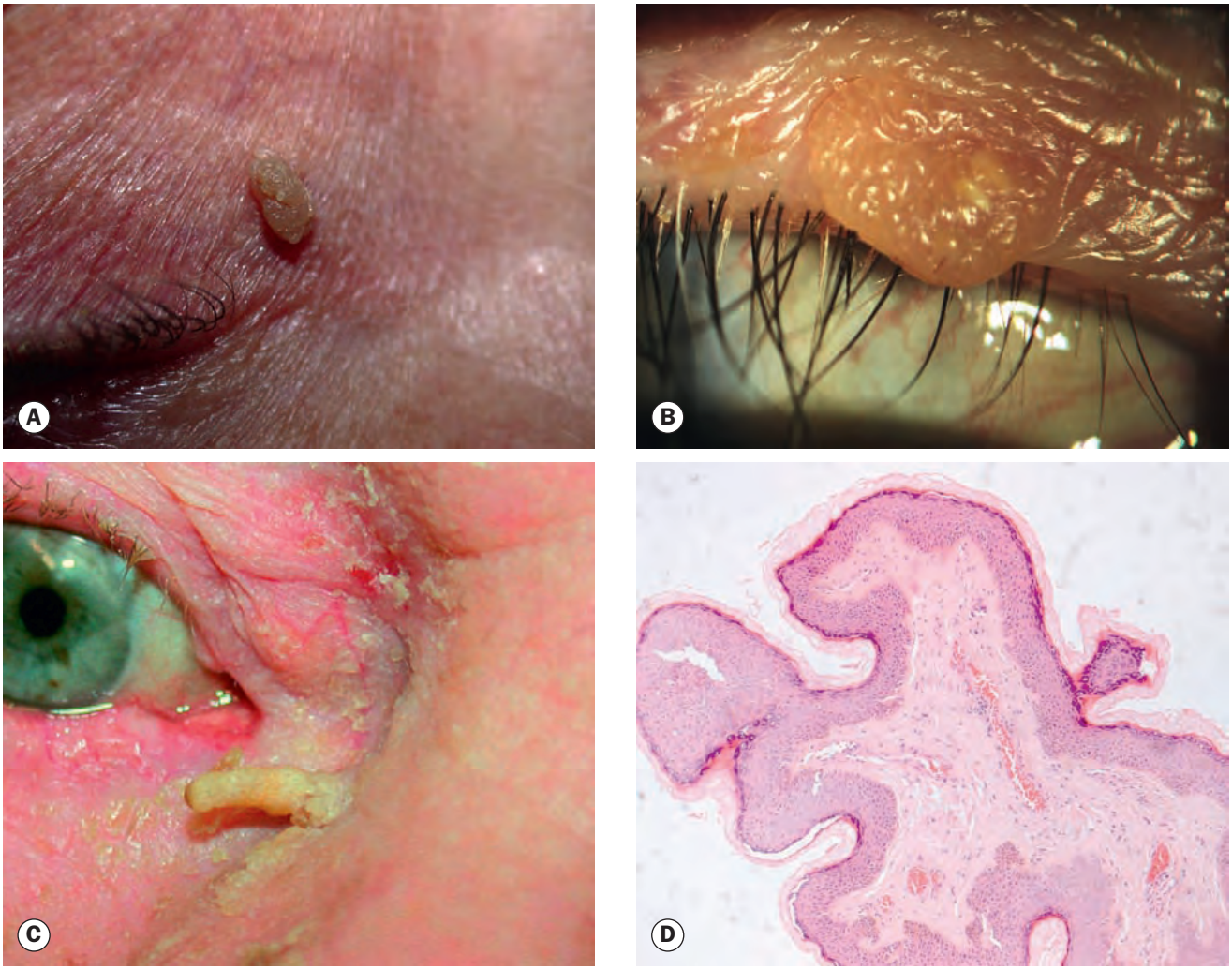


Fig. 1.5 Squamous cell papilloma. **(A)** Pedunculated 'skin tag'; **(B)** sessile lesion; **(C)** hyperkeratotic filiform lesion; **(D)** histopathology shows finger-like projections of fibrovascular connective tissue covered by irregular acanthotic and hyperkeratotic squamous epithelium
(Courtesy of A Pearson – fig. C; J Harry – fig. D)

(sessile – Fig. 1.5B) and whitish thread-like (filiform) hyperkeratotic lesions similar to a cutaneous horn (Fig. 1.5C). Histopathology in all clinical types is similar, showing finger-like projections of fibrovascular connective tissue covered by irregular acanthotic and hyperkeratotic squamous epithelium (Fig. 1.5D). The incidence increases with age; at least some cases result from human papilloma virus infection. Treatment usually involves simple excision, but other options include cryotherapy and laser or chemical ablation.

Seborrhoeic keratosis

Seborrhoeic keratosis (basal cell papilloma) is an extremely common slowly growing lesion found on the face, trunk and extremities of elderly individuals as a discrete light- to dark-brown plaque with a friable, greasy, verrucous surface and a 'stuck-on' appearance (Fig. 1.6A). They are frequently numerous. The differential diagnosis includes pigmented basal cell carcinoma, naevus and melanoma. Histopathology shows expansion of the squamous epithelium of the epidermis by proliferating basal cells, sometimes with keratin-filled horns or cystic inclusions (Fig. 1.6B). Treatment involves shave biopsy (occasionally simple excision), electrodesiccation with curettage, laser ablation, cryotherapy with liquid nitrogen, and chemical peeling.

Actinic keratosis

Actinic (solar, senile) keratosis is a common slowly growing lesion that rarely develops on the eyelids. It typically affects elderly, fair-skinned individuals on areas of sun-damaged skin such as the forehead and backs of the hands, and appears as a hyperkeratotic plaque with distinct borders and a scaly surface that may become fissured (Fig. 1.7A). Occasionally the lesion is nodular or wart-like and may give rise to a cutaneous horn. Histopathology shows irregular dysplastic epidermis with hyperkeratosis, parakeratosis and cutaneous horn formation (Fig. 1.7B). It has potential, though

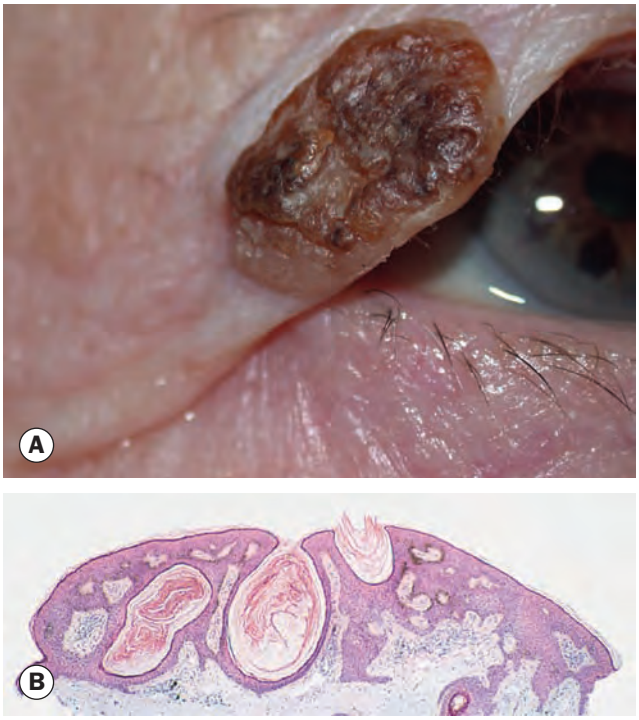


Fig. 1.6 Basal cell papilloma. **(A)** Typical 'stuck-on' appearance; **(B)** histopathology showing an elevated expansion of the epidermis with proliferation from basal cells – horn cysts and pseudohorn cysts are present
(Courtesy of A Pearson – fig. A; J Harry – fig. B)

low, for transformation into squamous cell carcinoma. Treatment involves biopsy followed by excision or cryotherapy.

BENIGN PIGMENTED LESIONS

Freckle

A freckle (ephelis, plural ephelides) is a small (generally 1–5 mm) brown macule due to increased melanin in the epidermal basal layer, typically in sun-exposed skin (Fig. 1.8); numbers vary with the level of sun exposure and can sometimes regress completely. Histopathology shows hyperpigmentation of the basal layer of the epidermis, with a normal melanocyte population.

Congenital melanocytic naevus

Congenital naevi are uncommon and histologically resemble their acquired counterparts (see below). They are usually small and of uniform colour. Rare variants include a 'kissing' or split naevus that involves the upper and lower eyelid (Fig. 1.9A) and may occasionally contain numerous hairs (Fig. 1.9B), and a very large lesion covering an extensive area of the body ('giant hairy naevus' – Fig. 1.9C). Large lesions have the potential for malignant transformation (up to 15%). Treatment, if necessary, involves complete surgical excision.

Acquired melanocytic naevus

Diagnosis

The clinical appearance and potential for malignant transformation of naevi are determined by their histological location within the skin.

- **Junctional** naevus occurs in young individuals as a uniformly brown macule or plaque (Fig. 1.10A). The naevus cells are located at the junction of the epidermis and dermis and have a low potential for malignant transformation (Fig. 1.10B).
- **Compound** naevus occurs in middle age as a raised papular lesion. The shade of pigment varies from light tan to dark

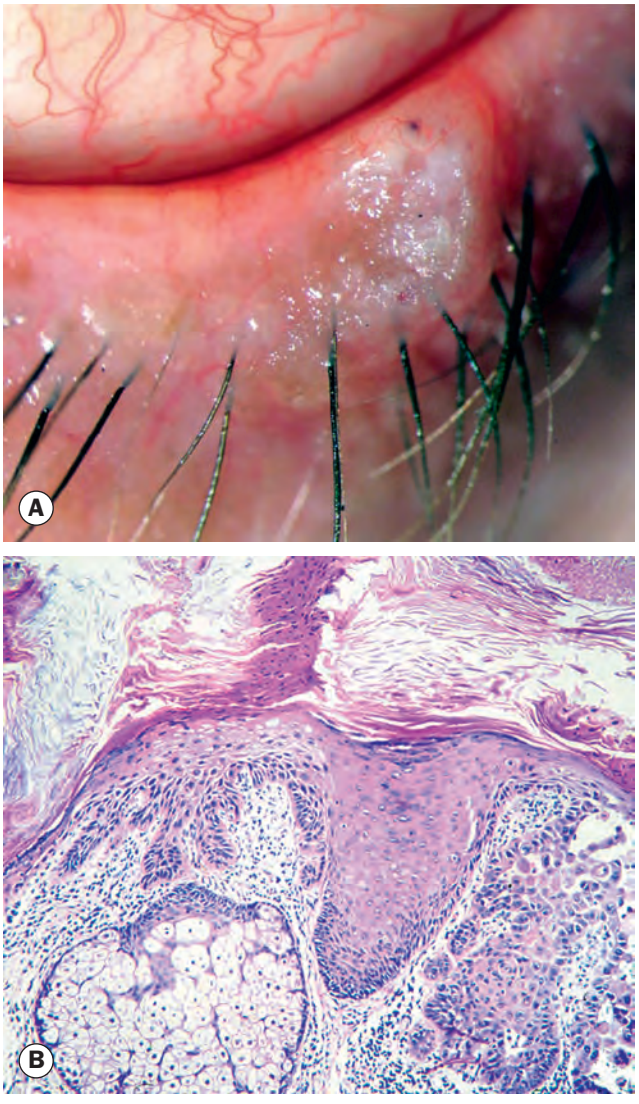


Fig. 1.7 Actinic keratosis. **(A)** Clinical appearance; **(B)** histopathology shows irregular dysplastic epidermis with hyperkeratosis, parakeratosis and cutaneous horn formation
(Courtesy of M Jager – fig. A; J Harry and G Misson, from Clinical Ophthalmic Pathology*, Butterworth-Heinemann 2001 – fig. B)*

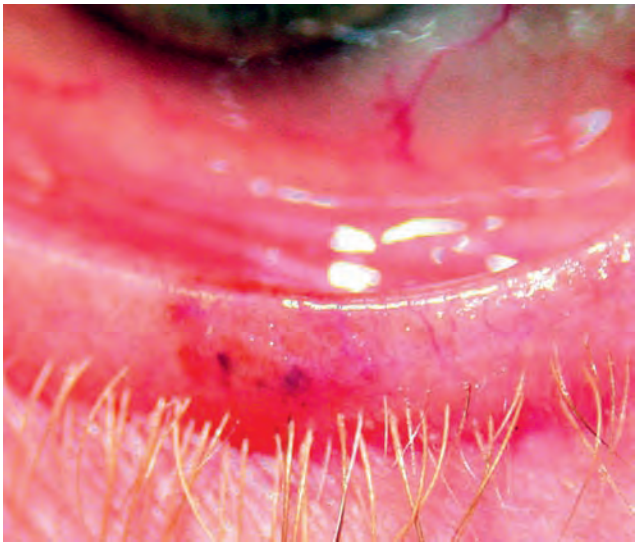


Fig. 1.8 Freckle (ephelis)

brown but tends to be relatively uniform throughout (Fig. 1.10C). The naevus cells extend from the epidermis into the dermis (Fig. 1.10D). It has a low malignant potential related to the junctional component.

- **Intradermal** naevus, the most common, typically occurs in older patients. It is a papillomatous lesion, with little or no pigmentation (Fig. 1.10E). Histologically, naevus cells are confined to the dermis and have essentially no malignant potential (Fig. 1.10F).
- **Variants** of naevi include balloon cell naevi, halo naevi, Spitz naevi (juvenile melanomas) and dysplastic naevi (atypical moles). Multiple dysplastic naevi constitute the dysplastic naevus syndrome (atypical mole syndrome – AMS). Individuals with AMS are at increased risk of developing conjunctival and uveal naevi and cutaneous, conjunctival and uveal melanomas.

Treatment

Treatment is indicated for cosmesis or for concern about malignancy. Excision should be complete in most cases, with at least a 3 mm margin if melanoma is strongly suspected.

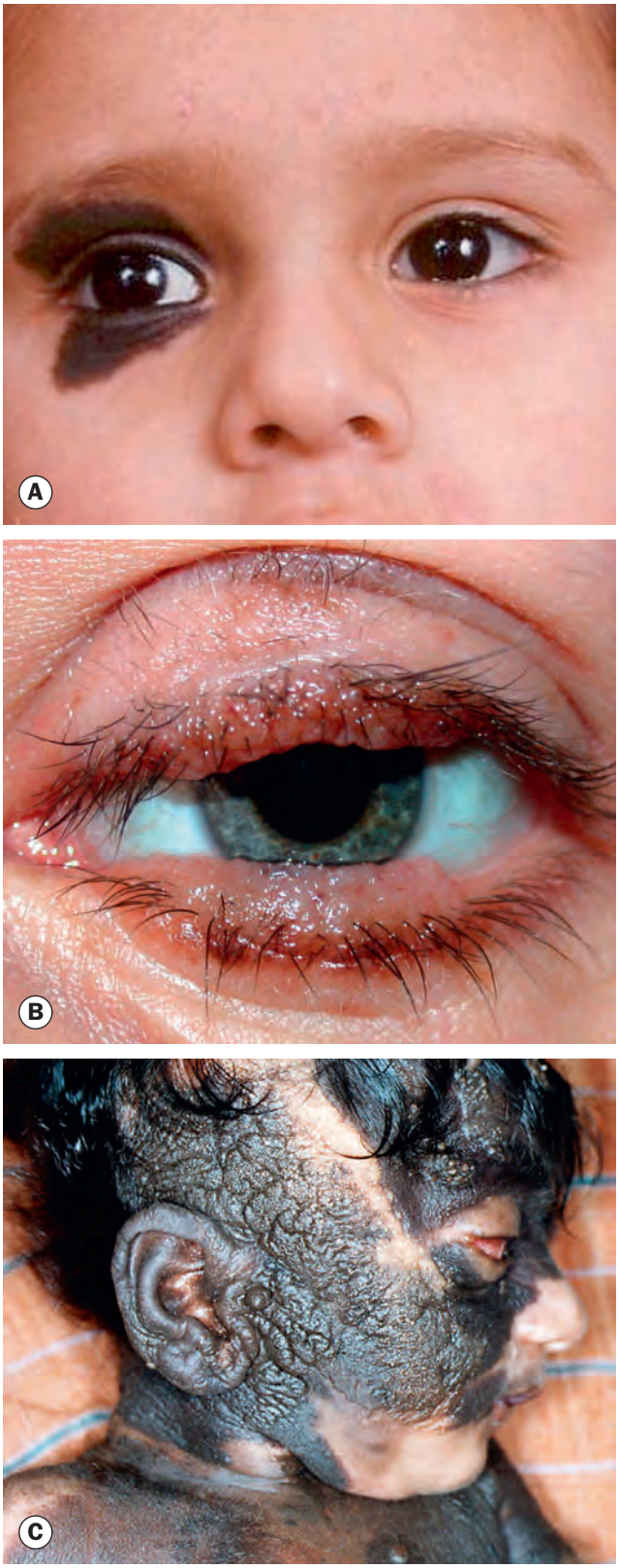


Fig. 1.9 Congenital melanocytic naevus. **(A)** Split naevus; **(B)** split naevus containing hair; **(C)** extensive cutaneous involvement

(Courtesy of A Pearson – fig. B; U Raina – fig. C)

BENIGN ADNEXAL TUMOURS

Syringoma

Syringomas are benign proliferations arising from eccrine sweat glands. They are characterized by small papules that are often multiple and bilateral (Fig. 1.11).

Pilomatricoma

Pilomatricoma (pilomatrixoma, calcifying epithelioma of Malherbe) is derived from the germinal matrix cells of the hair bulb and is the commonest hair follicle proliferation seen by

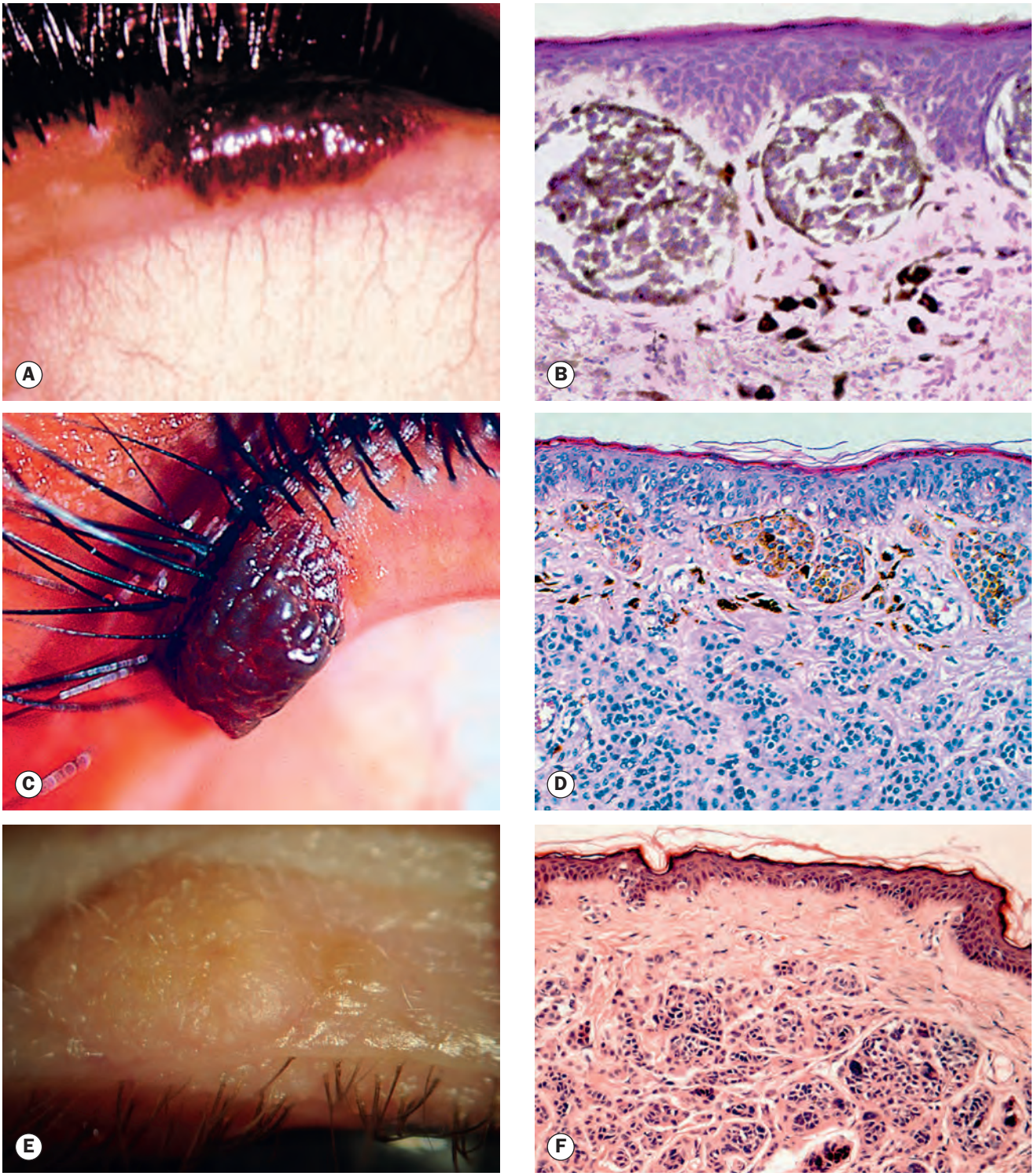


Fig. 1.10 Acquired melanocytic naevus. **(A)** Junctional naevus; **(B)** histopathology shows heavily pigmented naevus cells at the epidermal/dermal junction; **(C)** compound naevus; **(D)** histopathology shows naevus cells both at the epidermal/dermal junction and within the dermis; **(E)** intradermal naevus; **(F)** histopathology shows naevus cells within the dermis separated from the epidermis by a clear zone

(Courtesy of J Harry – figs B, D and F)

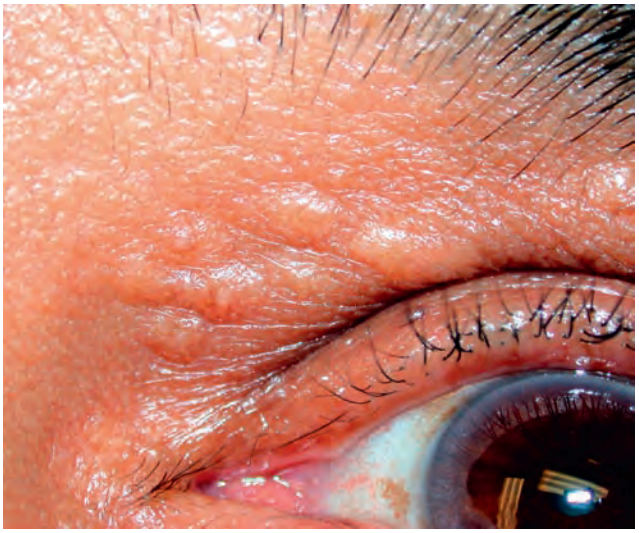


Fig. 1.11 Syringomas
(Courtesy of A Pearson)

ophthalmologists. It affects children and young adults and is more common in females. Clinically it appears as a mobile purplish dermal nodule that may have a hard consistency due to calcification (Fig. 1.12A). Histopathology shows irregular epithelial islands exhibiting viable basophilic cells at the periphery and degenerate 'shadow' cells more centrally (Fig. 1.12B). Calcification is frequently present and there is often a foreign body giant cell reaction. Treatment involves excision. Malignant change is rare. Other, less common, hair follicle proliferations include trichofolliculoma, trichoepithelioma and trichilemmoma.

MISCELLANEOUS BENIGN TUMOURS

Capillary haemangioma

Capillary haemangioma (strawberry naevus) is one of the most common tumours of infancy; it is three times as common in boys as girls. It presents shortly after birth as a unilateral, raised bright red lesion (Fig. 1.13A), usually in the upper lid; a deeper lesion appears purplish (Fig. 1.13B and see also Fig. 3.31). Ptosis is frequent. The lesion blanches on pressure and may swell on crying. There may be orbital extension (see Ch. 3). Occasionally the lesion may involve the skin of the face and some patients have strawberry naevi on other parts of the body. Histopathology shows proliferation of varying-sized vascular channels in the dermis and subcutaneous tissue (Fig. 1.13C). It is important to be aware of an association between multiple cutaneous lesions and visceral haemangiomas, and to consider systemic assessment in appropriate cases. Treatment is described in Ch. 3.

Port-wine stain

Introduction

Port-wine stain (naevus flammeus) is a congenital malformation of vessels within the superficial dermis, consisting histopathologically of vascular spaces of varying calibre separated by thin fibrous septa (Fig. 1.14A). About 10% have associated ocular or CNS involvement, including Sturge–Weber (see below) and other defined syndromes.

Diagnosis

Port-wine stain manifests clinically as a sharply demarcated soft pink patch that does not blanch with pressure, most frequently located on the face. It is usually unilateral and tends to be aligned with the skin area supplied by one or more divisions of the trigeminal nerve (Figs 1.14B and C). Darkening to red or purple takes place with age, and there is commonly associated soft tissue hypertrophy (Figs 1.14D–F). Bleeding may occur from focal overlying lobulations (pyogenic granulomas – see below).

Treatment

Treatment with laser (e.g. pulsed-dye) is effective in decreasing skin discoloration; cosmetically superior results are usually

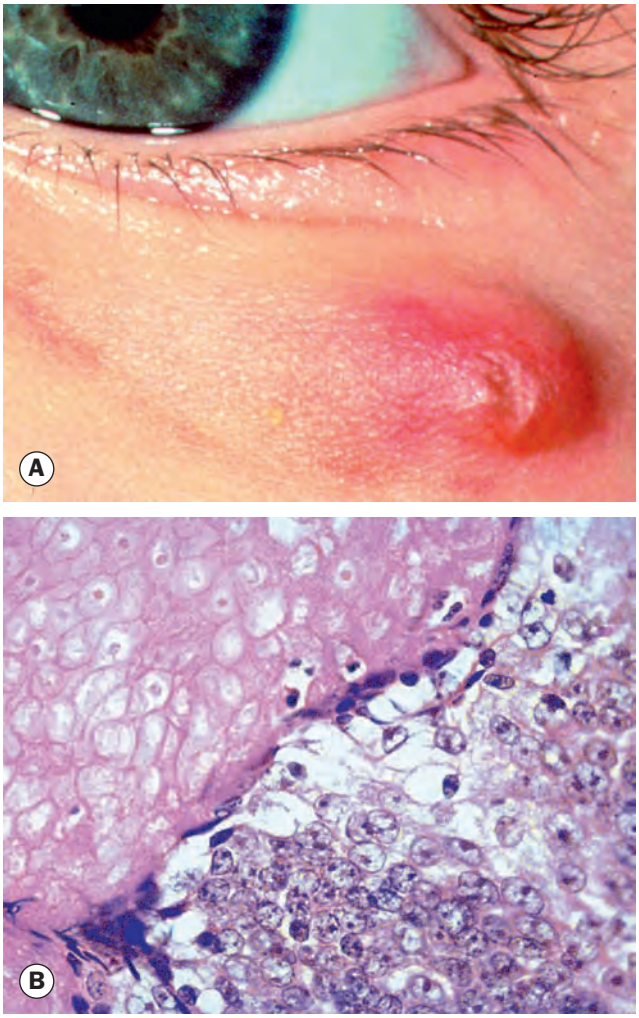


Fig. 1.12 Pilomatricoma. **(A)** Clinical appearance; **(B)** histopathology shows viable basophilic cells to the right and degenerate 'shadow' cells to the left
(Courtesy of J Krachmer, M Mannis and E Holland, from Cornea, *Elsevier 2005 – fig. A; J Harry and G Misson, from* Clinical Ophthalmic Pathology, *Butterworth-Heinemann 2001 – fig. B)*

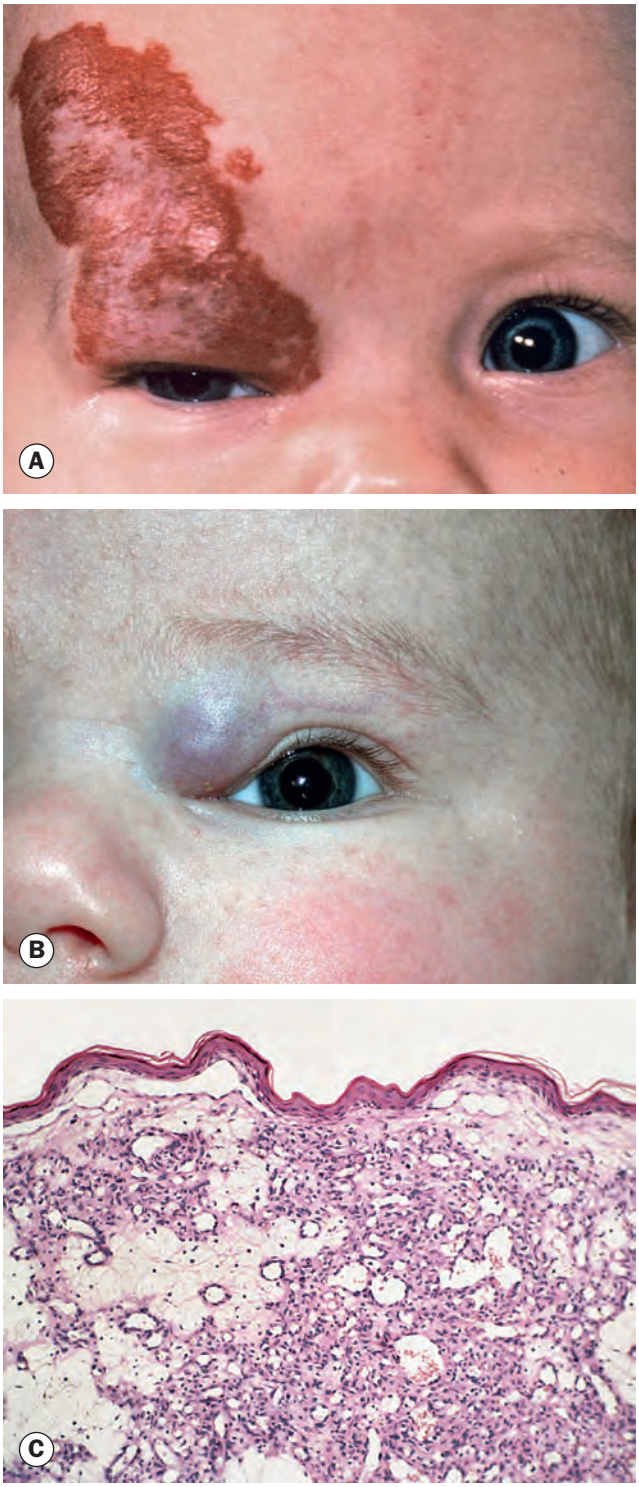


Fig. 1.13 Capillary haemangioma. **(A)** Medium-sized haemangioma; **(B)** mechanical ptosis due to a large lesion; **(C)** histopathology shows vascular channels of varying size within the dermis and subcutaneous tissue
(Courtesy of S Chen – fig. A; J Harry – fig. C)

achieved by early treatment. Topical preparations such as imiquimod and rapamycin, alone or with adjuvant laser, show promise. Soft tissue debulking is used in a small number of cases. Screening for glaucoma should begin in infancy. Systemic investigation is considered in some patients, particularly those with a lesion of the lumbar area.

Sturge–Weber syndrome

Sturge–Weber syndrome (encephalotrigeminal angiomatosis) is a congenital, sporadic phacomatosis.

- **Port-wine stain**, extending over the area corresponding to the distribution of one or more branches of the trigeminal nerve.
- **Leptomeningeal haemangioma** involving the ipsilateral parietal or occipital region may cause contralateral focal or generalized seizures, hemiparesis or hemianopia.
- **Ocular** features may include ipsilateral glaucoma, episcleral haemangioma, iris heterochromia and diffuse choroidal haemangioma (see Ch. 12).

Pyogenic granuloma

Pyogenic granuloma is a rapidly growing vascularized proliferation of granulation tissue that is usually antedated by surgery, trauma or infection, although some cases are idiopathic. Clinically there is a painful, rapidly growing, vascular granulating polypoidal lesion (Fig. 1.15) that may bleed following relatively trivial trauma. Treatment of cutaneous lesions involves excision; conjunctival pyogenic granuloma is discussed in Ch. 5.

Neurofibroma

Cutaneous neurofibromas are benign nerve tumours, usually nodular or pedunculated, that can be found anywhere on the skin. Isolated neurofibromas are common in normal individuals, but if multiple lesions are present neurofibromatosis (see Ch. 19) should be excluded. Plexiform neurofibromas typically present in childhood as a manifestation of neurofibromatosis type 1 with a characteristic S-shaped deformity of the upper eyelid (Fig. 1.16). Treatment of solitary lesions involves simple excision but removal of the more diffuse plexiform lesions may be difficult.

MALIGNANT TUMOURS

The treatment of malignant eyelid tumours in general is discussed at the end of this section.

Rare predisposing conditions

Young patients who suffer from one of the following conditions may develop eyelid malignancies.

- **Xeroderma pigmentosum** is characterized by skin damage on exposure to sunlight, leading to progressive cutaneous abnormalities (Fig. 1.17A). It is inherited in an autosomal recessive (AR) fashion. Affected patients have a bird-like facies and a great propensity to the development of basal cell carcinoma (BCC), squamous cell carcinoma (SCC)

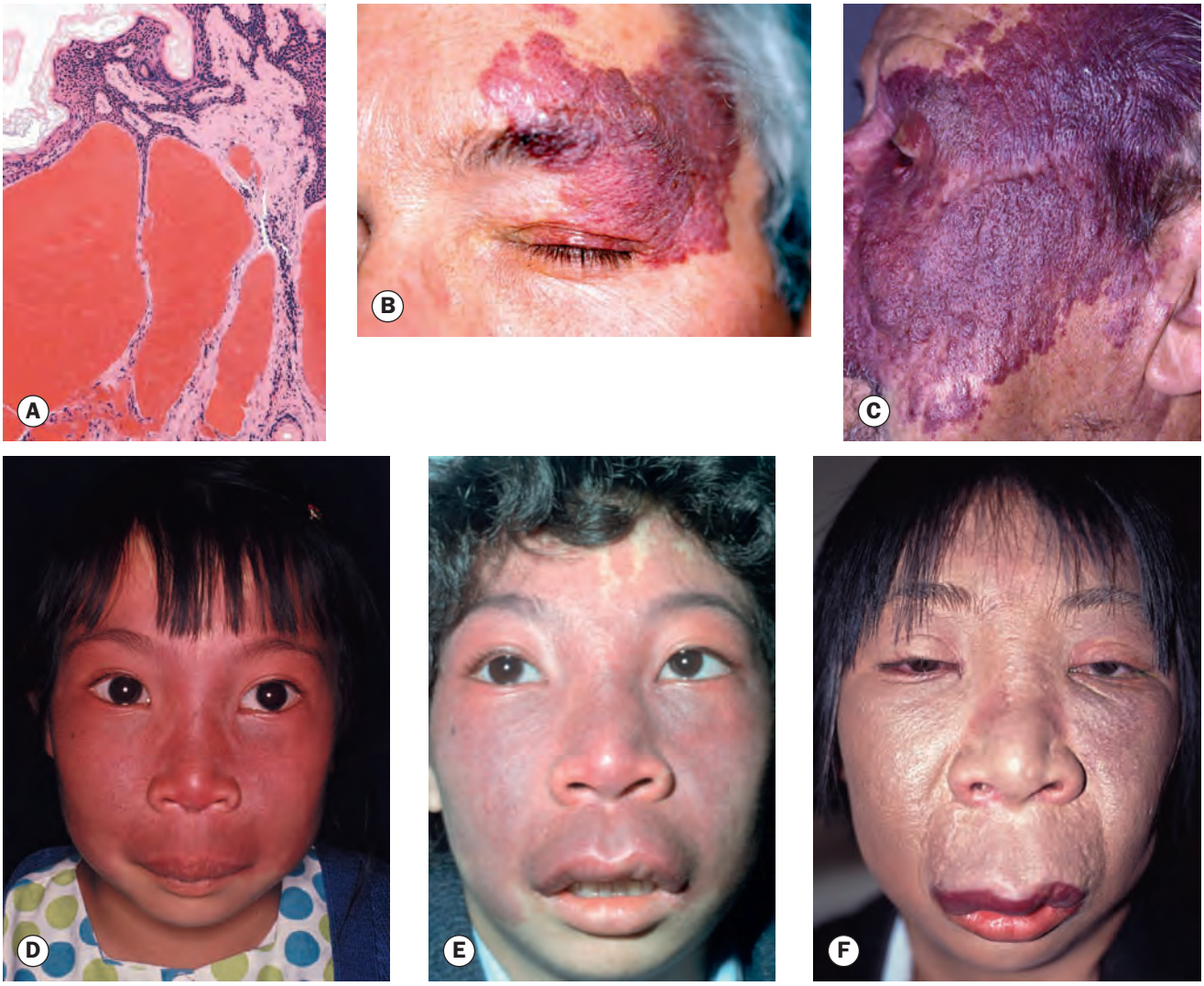


Fig. 1.14 Port-wine stain. **(A)** Histopathology shows widely dilated blood-filled spaces separated by fibrous septa; **(B)** and **(C)** clinical appearance; (**D–F**) progression of port-wine stain over time, with associated underlying soft tissue hypertrophy
(Courtesy of L Horton – fig. A)

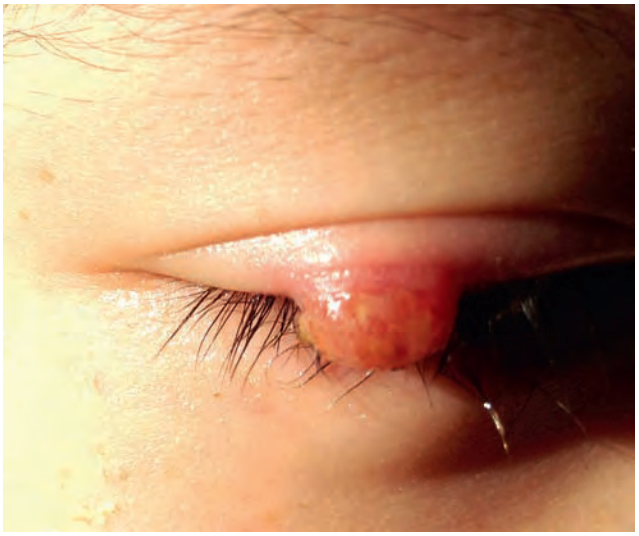


Fig. 1.15 Pyogenic granuloma

Fig. 1.16 Plexiform neurofibroma – characteristic S-shaped upper lid
(Courtesy of J Harry)

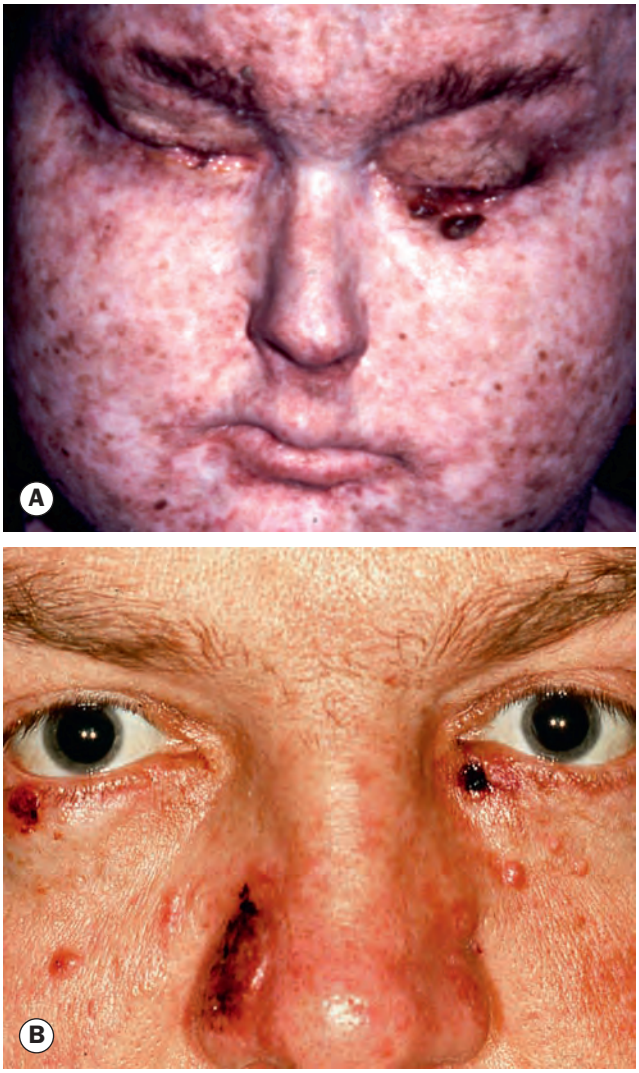


Fig. 1.17 Predispositions to eyelid malignancies. **(A)** Xeroderma pigmentosum; **(B)** Gorlin–Goltz syndrome
(Courtesy of J Krachmer, M Mannis and E Holland, from Cornea, *Mosby 2005 – fig. B)*

and melanoma, which are commonly multiple. Conjunctival malignancies have also been reported.

- **Gorlin–Goltz syndrome** (naevoid basal cell carcinoma syndrome) is a rare autosomal dominant (AD) disorder characterized by extensive congenital deformities of the eye, face, bone and central nervous system. Many patients develop multiple small BCC during the second decade of life (Fig. 1.17B) and are also predisposed to medulloblastoma, breast carcinoma and Hodgkin lymphoma.
- **Muir–Torre syndrome** is a rare AD condition that predisposes to cutaneous and internal malignancies. Cutaneous tumours include BCC, sebaceous gland carcinoma and keratoacanthoma. Colorectal and genitourinary carcinomas are the most common systemic tumours.
- **Bazex syndrome** can be used to describe two distinct conditions: (i) Bazex–Dupré–Christol syndrome, an X-linked dominant condition characterized by multiple BCCs, commonly facial including the eyelids, associated with skin changes including follicular indentations without hairs on extensor surfaces (follicular atrophoderma), hypohidrosis and hypotrichosis; (ii) acrokeratosis paraneoplastica of Bazex, in which eczema-like and psoriatiform lesions are associated with an underlying malignancy of the upper respiratory or digestive tract.
- **Other predispositions** include immunosuppression, prior retinoblastoma and albinism.

Basal cell carcinoma

Introduction

BCC is the most common human malignancy and typically affects older age groups. The most important risk factors are fair skin, inability to tan and chronic exposure to sunlight. Ninety per cent of cases occur in the head and neck and about 10% of these involve the eyelid. BCC is by far the most common malignant eyelid tumour, accounting for 90% of all cases. It most frequently arises from the lower eyelid, followed in relative frequency by the medial canthus, upper eyelid and lateral canthus. The tumour is slowly growing and locally invasive but non-metastasizing. Tumours located near the medial canthus are more prone to invade the orbit and sinuses, are more difficult to manage than those arising elsewhere and carry the greatest risk of recurrence. Tumours that recur following incomplete treatment tend to be more aggressive.

Histopathology

The tumour arises from the cells that form the basal layer of the epidermis. The cells proliferate downwards (Fig. 1.18A) and characteristically exhibit palisading at the periphery of a tumour lobule of cells (Fig. 1.18B). Squamous differentiation with the production of keratin results in a hyperkeratotic type of BCC. There can also be sebaceous and adenoid differentiation while the growth of elongated strands and islands of cells embedded in a dense fibrous stroma results in a sclerosing (morphoeic) type of tumour.

Clinical features

Eyelid BCC generally conforms to one of the morphological patterns below.

- **Nodular BCC** is a shiny, firm, pearly nodule with small overlying dilated blood vessels. Initially, growth is slow and it may take the tumour 1–2 years to reach a diameter of 0.5 cm (Figs 1.19A and B).
- **Noduloulcerative BCC (rodent ulcer)** is centrally ulcerated with pearly raised rolled edges and dilated and irregular blood vessels (telangiectasis) over its lateral margins (Fig. 1.19C); with time it may erode a large portion of the eyelid (Fig. 1.19D).
- **Sclerosing (morphoeic) BCC** is less common and may be difficult to diagnose because it infiltrates laterally beneath

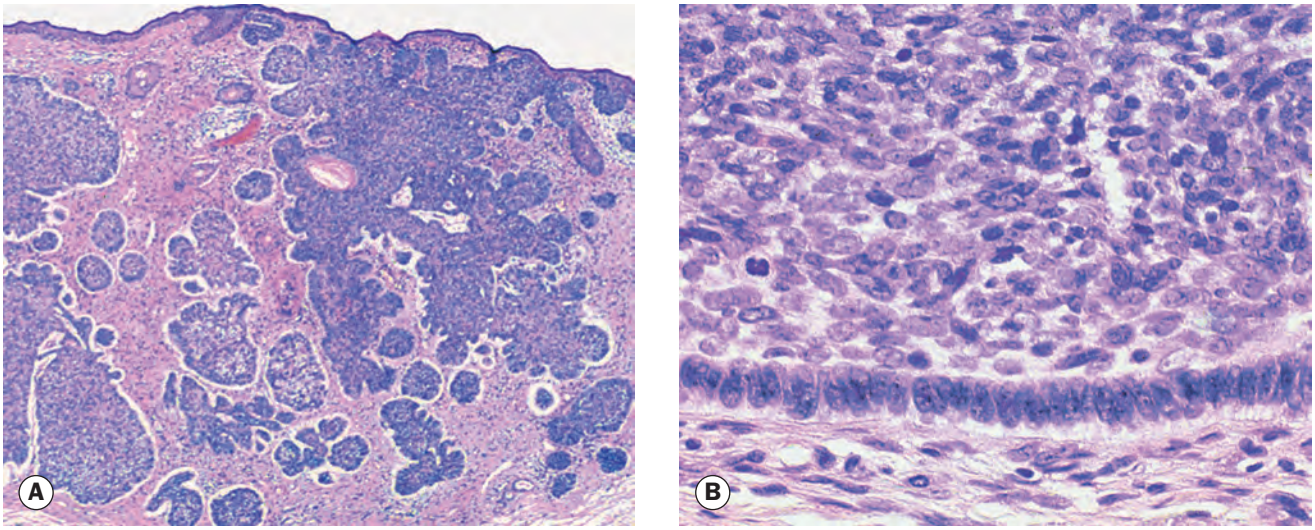


Fig. 1.18 Histopathology of basal cell carcinoma. **(A)** Histopathology shows downward proliferation of lobules of basophilic (purple) cells; **(B)** palisading of cells at the periphery of a tumour lobule
(Courtesy of J Harry)

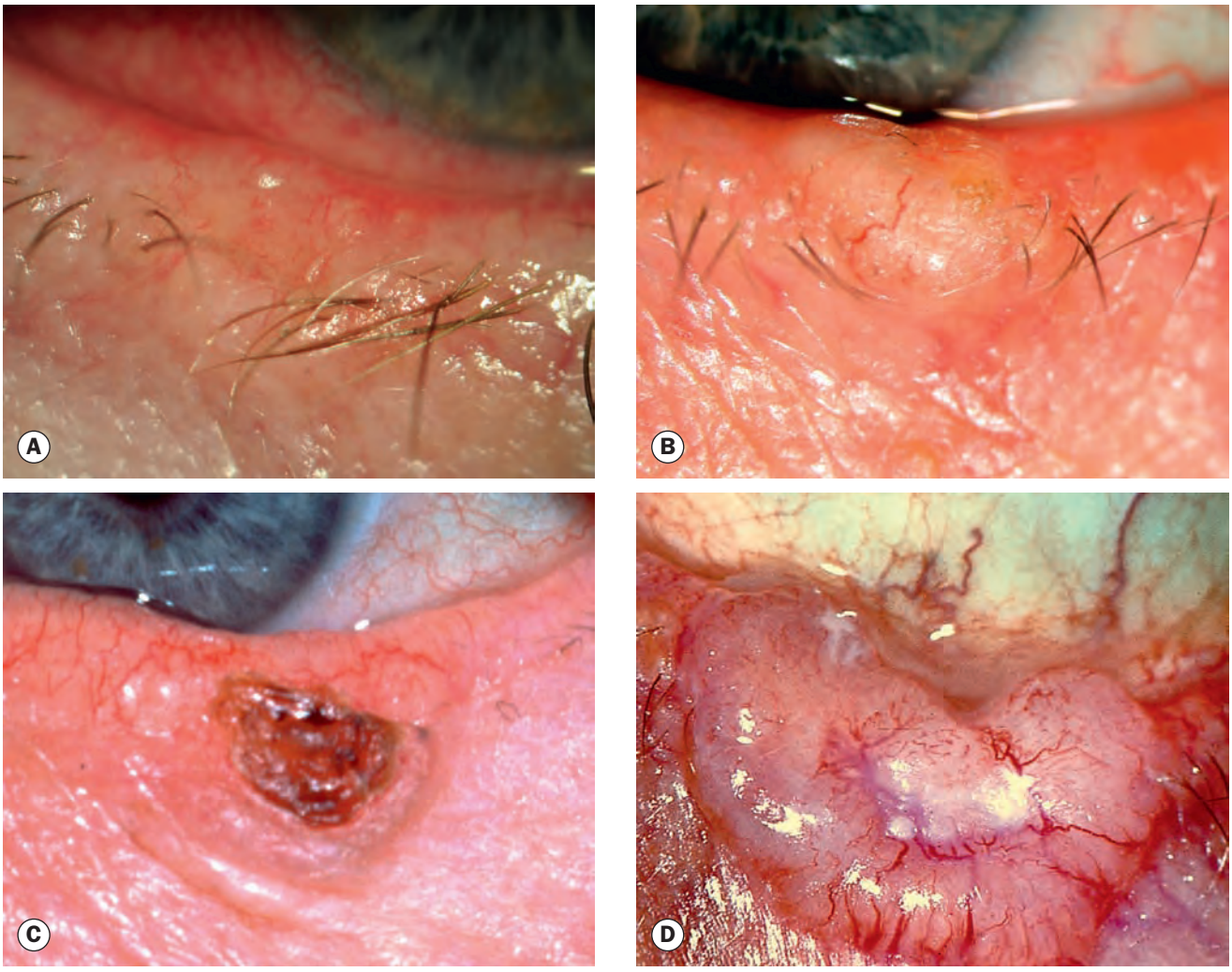


Fig. 1.19 Clinical appearance of basal cell carcinoma. **(A)** Early nodular lesion; **(B)** larger nodular tumour; **(C)** rodent ulcer; **(D)** large rodent ulcer;

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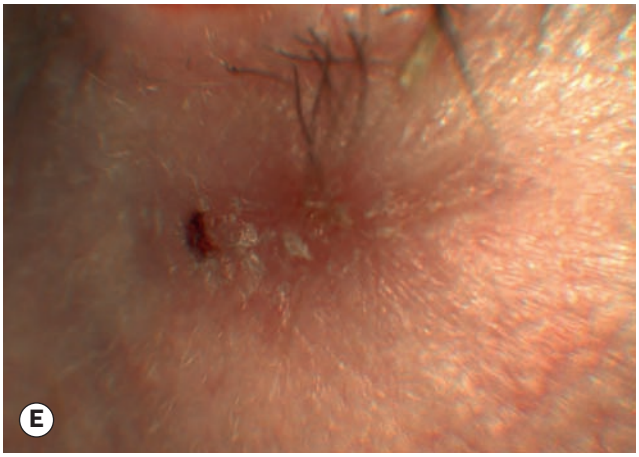


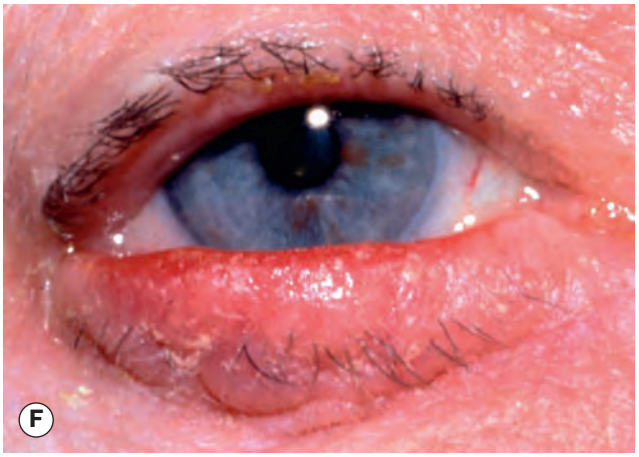


Fig. 1.19, Continued **(E)** sclerosing tumour; **(F)** extensive sclerosing tumour

the epidermis as an indurated plaque (Figs 1.19E and F). The margins of the tumour may be impossible to delineate clinically and the lesion tends to be much more extensive on palpation than inspection. On cursory examination a sclerosing BCC may simulate a localized area of chronic blepharitis.

- **Other types** not usually found on the lid are cystic, adenoid, pigmented and multiple superficial.

Squamous cell carcinoma

Introduction

SCC is a much less common, but typically more aggressive tumour than BCC with metastasis to regional lymph nodes in about 20% of cases. Careful surveillance of regional lymph nodes is therefore an important aspect of initial management. The tumour may also exhibit perineural spread to the intracranial cavity via the orbit. SCC accounts for 5–10% of eyelid malignancies and may arise *de novo* or from pre-existing actinic keratosis or carcinoma *in situ* (Bowen disease, intraepidermal carcinoma – Fig. 1.20). Immunocompromised patients, such as those with acquired immunodeficiency syndrome (AIDS) or following renal transplantation are at increased risk, as are those with a predisposing syndrome such as xeroderma pigmentosum. The tumour has a predilection for the lower eyelid and the lid margin. It occurs most commonly in older individuals with a fair complexion and a history of chronic sun exposure. The diagnosis of SCC may be difficult because certain ostensibly benign lesions such as keratoacanthoma and cutaneous horn may reveal histological evidence of invasive SCC at deeper levels of sectioning.

Histopathology

The tumour arises from the squamous cell layer of the epidermis. It is composed of variably sized groups of atypical epithelial cells with prominent nuclei and abundant eosinophilic cytoplasm within the dermis (Fig. 1.21A). Well-differentiated tumours may show characteristic keratin 'pearls' and intercellular bridges (desmosomes).

Clinical features

The clinical types are variable and there are no pathognomonic characteristics. The tumour may be indistinguishable clinically from a BCC but surface vascularization is usually absent, growth is more rapid and hyperkeratosis is more common.

- **Nodular SCC** is characterized by a hyperkeratotic nodule that may develop crusting, erosions and fissures (Fig. 1.21B).
- **Ulcerating SCC** has a red base and sharply defined, indurated and everted borders, but pearly margins and telangiectasia are not usually present (Fig. 1.21C).
- **Cutaneous horn** with underlying invasive SCC (Fig. 1.21D).

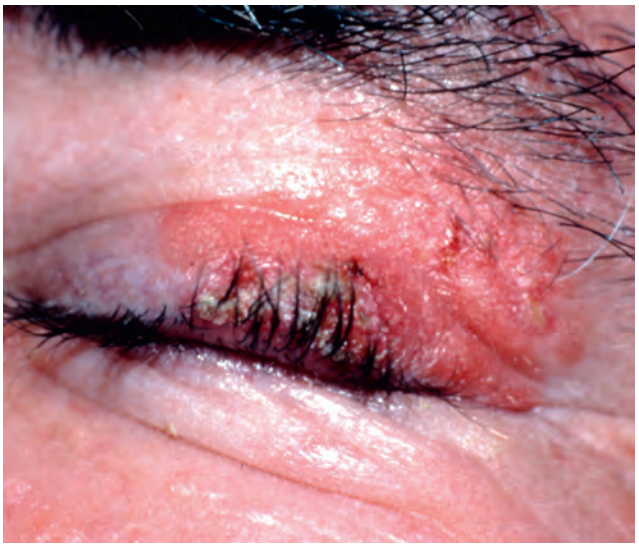


Fig. 1.20 Carcinoma *in situ*
(Courtesy of H Frank)

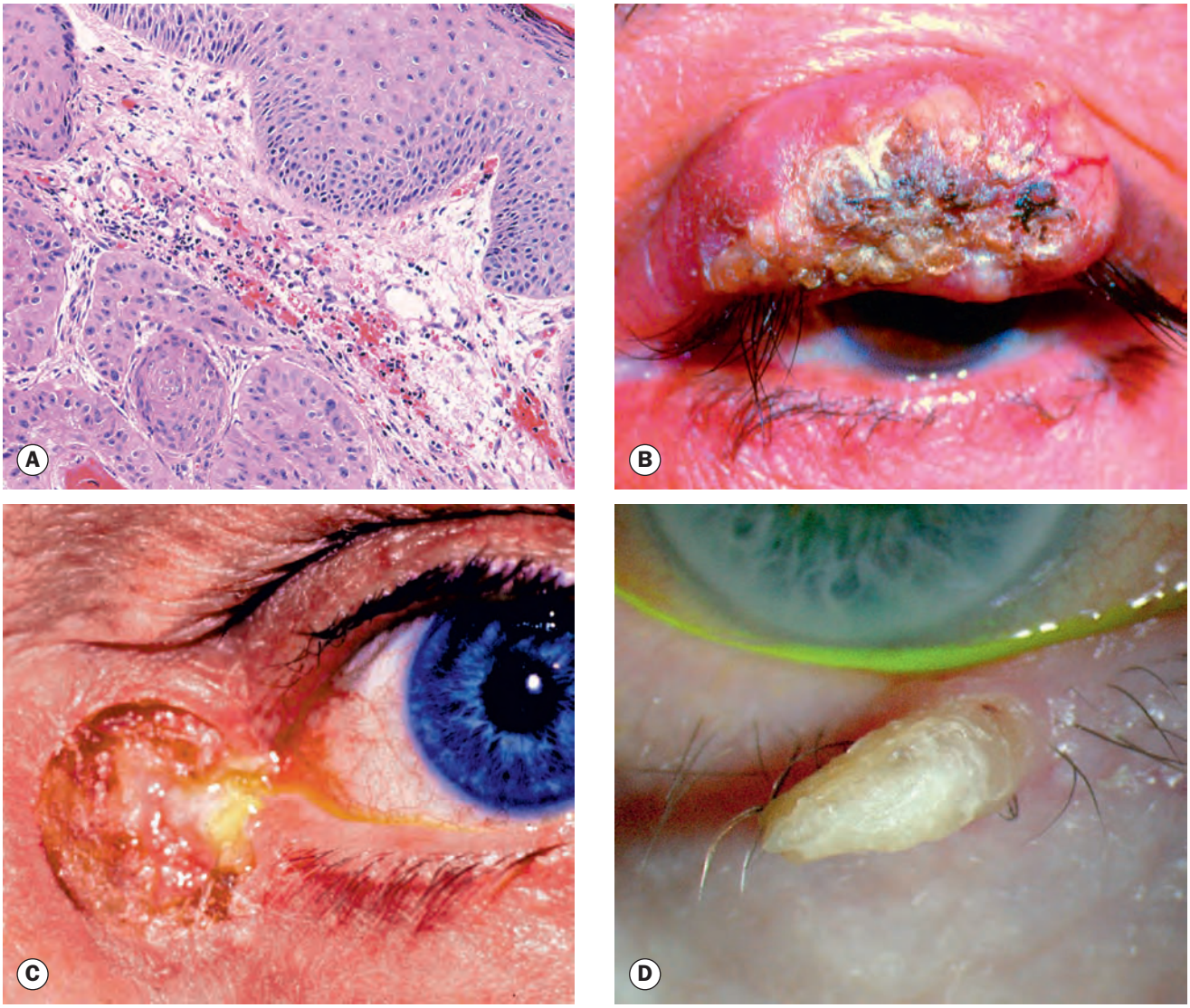


Fig. 1.21 Squamous cell carcinoma. **(A)** Histopathology shows acanthotic squamous epithelium and eosinophilic (pink) islands of dysplastic squamous epithelium within the dermis; **(B)** nodular tumour with surface keratosis; **(C)** ulcerating tumour; **(D)** cutaneous horn

(Courtesy of L Horton – fig. A; A Singh, from Clinical Ophthalmic Oncology, *Saunders 2007 – fig. B; H Frank – fig. C; S Farley, T Cole and L Rimmer – fig. D)*

Keratoacanthoma

Introduction

Keratoacanthoma is a rare, rapidly growing but subsequently regressing tumour that usually occurs in fair-skinned individuals with a history of chronic sun exposure. Immunosuppressive therapy is also a predisposing factor. It is regarded as falling within the spectrum of SCC, and although invasion and metastasis are rare, definitive treatment is usually indicated. Histopathologically, irregular thickened epidermis is surrounded by acanthotic squamous epithelium; a sharp transition from the thickened involved area to normal adjacent epidermis is referred to as shoulder formation (Fig. 1.22A); a keratin-filled crater may be seen.

Diagnosis

A pink dome-shaped hyperkeratotic lesion develops, often on the lower lid (Fig. 1.22B), and may double or treble in size within weeks (Fig. 1.22C). Growth then ceases for 2–3 months, after which spontaneous involution occurs, when a keratin-filled crater may develop (Fig. 1.22D). Complete involution may take up to a year and usually leaves an unsightly scar.

Treatment

Treatment generally involves complete surgical excision with a margin of at least 3 mm, or utilizing Mohs surgery; radiotherapy, cryotherapy or local chemotherapy are sometimes used. Observation is now regarded as inappropriate.

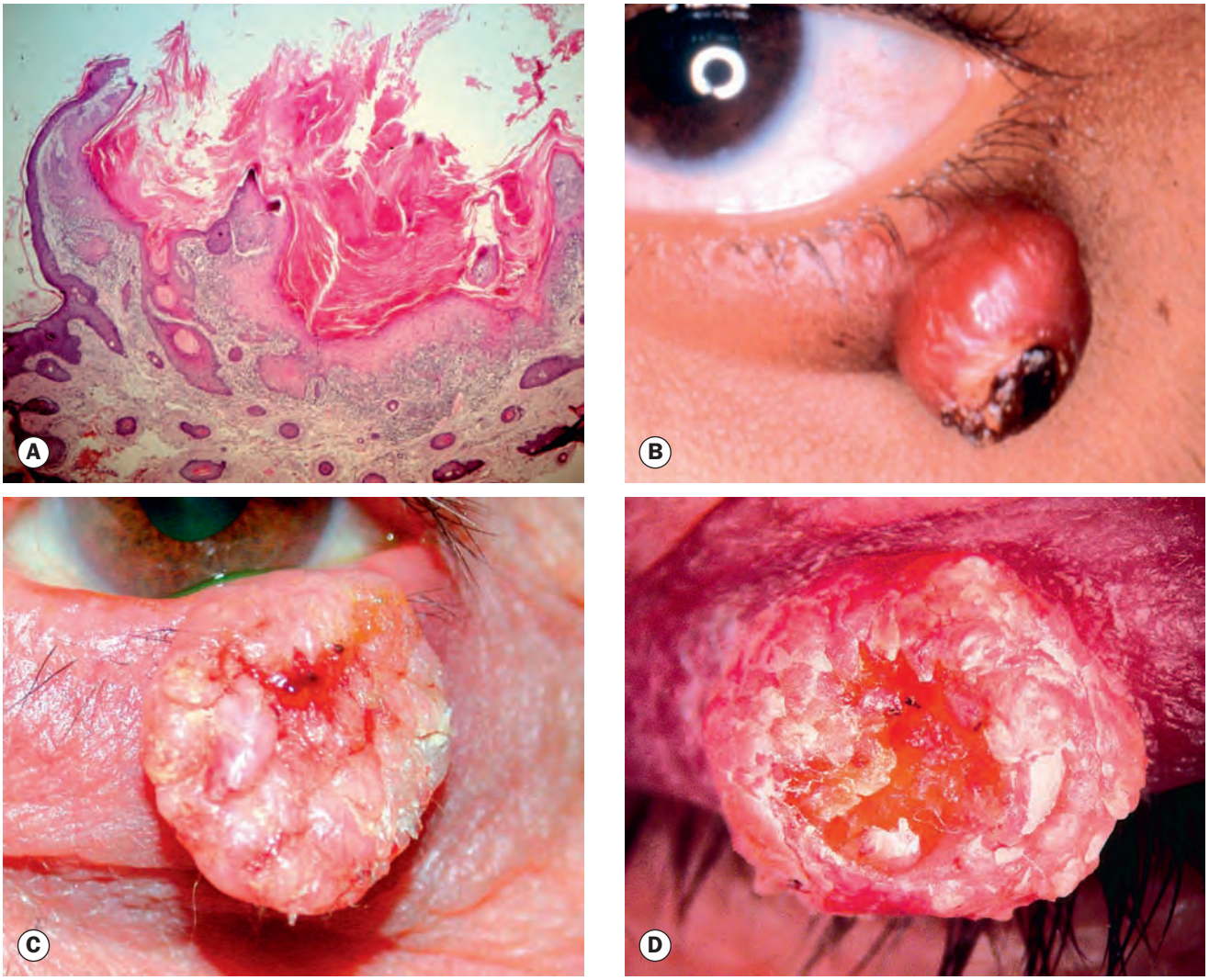


Fig. 1.22 Keratoacanthoma. **(A)** Histopathology shows irregularly thickened eosinophilic epidermis with a keratin-containing cup and well-marked shoulder formation; **(B)** hyperkeratotic nodule; **(C)** large tumour; **(D)** keratin-filled crater during involution

Sebaceous gland carcinoma

Introduction

Sebaceous gland carcinoma (SGC) is a very rare, slowly growing tumour that most frequently affects the elderly, with a predisposition for females. It usually arises from the meibomian glands, although on occasion it may arise from the glands of Zeis or elsewhere. The tumour consists histopathologically of lobules of cells with pale foamy vacuolated lipid-containing cytoplasm and large hyperchromatic nuclei (Fig. 1.23A). Pagetoid spread refers to extension of a tumour within the epithelium, and is not uncommon. Overall mortality is 5–10%; adverse prognostic features include upper lid involvement, tumour size of 10 mm or more and duration of symptoms of more than 6 months.

Clinical features

In contrast to BCC and SCC, SGC occurs more commonly on the upper eyelid where meibomian glands are more numerous; there may be simultaneous involvement of both lids on one side (5%).

- **Yellowish material** within the tumour is highly suggestive of SGC.
- **Nodular SGC** presents as a discrete, hard nodule, most commonly within the upper tarsal plate (Fig. 1.23B), and may exhibit yellow discoloration due to the presence of lipid; it can be mistaken for a chalazion.
- **Spreading SGC** infiltrates into the dermis and causes a diffuse thickening of the lid margin (Fig. 1.23C) often with eyelash distortion and loss, and can be mistaken for blepharitis.

Lentigo maligna and melanoma

Introduction

Melanoma rarely develops on the eyelids but is potentially lethal. Although pigmentation is a hallmark of skin melanomas, half of

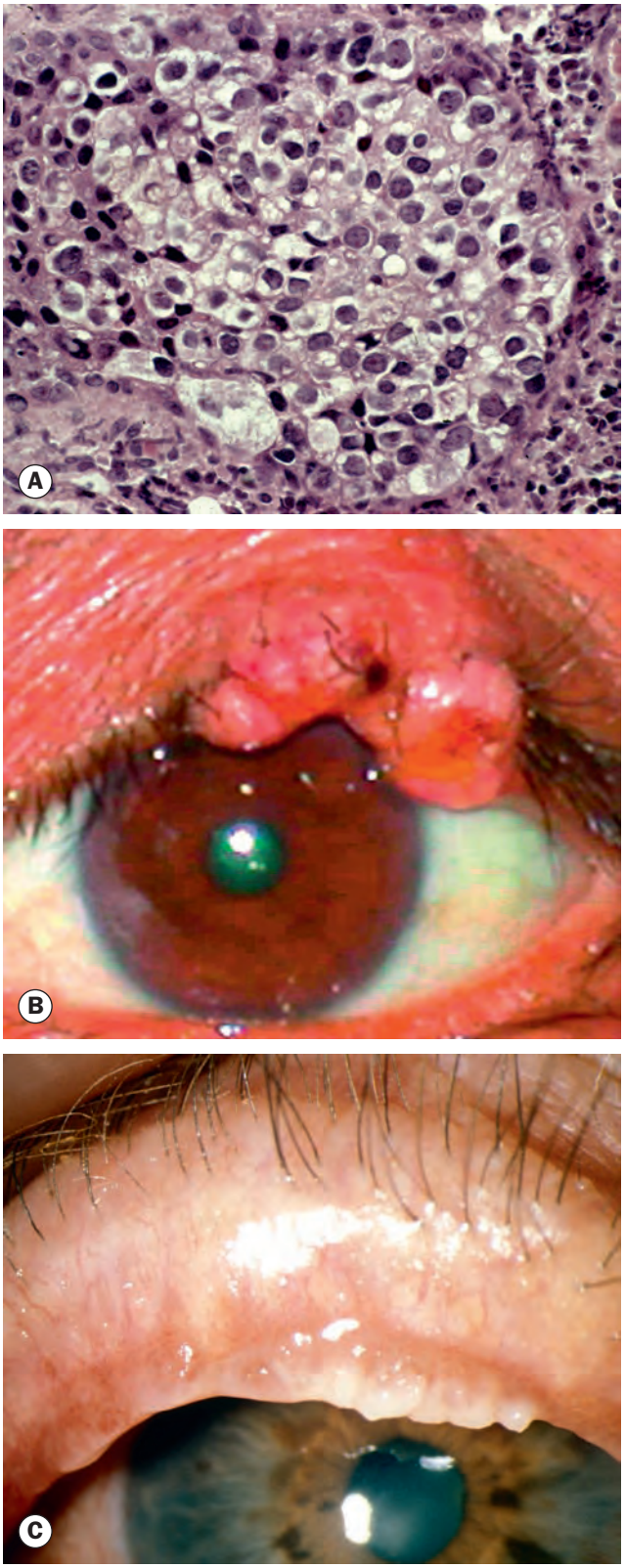


Fig. 1.23 Sebaceous gland carcinoma. **(A)** Histopathology shows cells with large hyperchromatic nuclei and vacuolated cytoplasm; **(B)** nodular tumour; **(C)** spreading tumour

(Courtesy of A Garner – fig. A; A Singh, from Clinical Ophthalmic Oncology, *Saunders 2007 – fig. B; S Tuft – fig. C)*

lid melanomas are non-pigmented and this may give rise to diagnostic difficulty. Features suggestive of melanoma include recent onset of a pigmented lesion, change in an existing pigmented lesion, irregular margins, asymmetrical shape, colour change or presence of multiple colours, and diameter greater than 6 mm.

Lentigo maligna

Lentigo maligna (melanoma *in situ*, intraepidermal melanoma, Hutchinson freckle) is an uncommon condition that develops in sun-damaged skin in elderly individuals. Malignant change may occur, with infiltration of the dermis. Histopathology shows intraepidermal proliferation of spindle-shaped atypical melanocytes replacing the basal layer of the epidermis (Fig. 1.24A). Clinically lentigo maligna presents as a slowly expanding pigmented macule with an irregular border (Fig. 1.24B). Treatment is usually by excision. Nodular thickening and areas of irregular pigmentation are highly suggestive of malignant transformation (Fig. 1.24C).

Melanoma

Histopathology shows large atypical melanocytes invading the dermis (Fig. 1.25A). Superficial spreading melanoma is characterized by a plaque with an irregular outline and variable pigmentation (Fig. 1.25B). Nodular melanoma is typically a blue – black nodule surrounded by normal skin (Fig. 1.25C). Treatment is usually by wide excision and may include local lymph node removal. Radiotherapy, chemotherapy, biological and 'targeted' therapy may also be used, generally as adjuvants.

Merkel cell carcinoma

Merkel cells are a form of sensory receptor concerned with light touch. Merkel cell carcinoma is a rapidly growing, highly malignant tumour that typically affects older adults. Its rarity may lead to difficulty in diagnosis and delay in treatment, and 50% of patients have metastatic spread by presentation. A violaceous, well-demarcated nodule with intact overlying skin is seen, most frequently involving the upper eyelid (Fig. 1.26). Treatment is by excision, often with adjuvant therapy.

Kaposi sarcoma

Kaposi sarcoma is a vascular tumour that typically affects patients with AIDS. Many patients have advanced systemic disease although in some instances the tumour may be the only clinical manifestation of human immunodeficiency virus (HIV) infection. Histopathology shows proliferating spindle cells, vascular channels and inflammatory cells within the dermis (Fig. 1.27A). Clinically a pink, red-violet to brown lesion (Fig. 1.27B) develops, which may be mistaken for a haematoma or naevus. Treatment is by radiotherapy or excision, and by optimal control of AIDS where relevant.

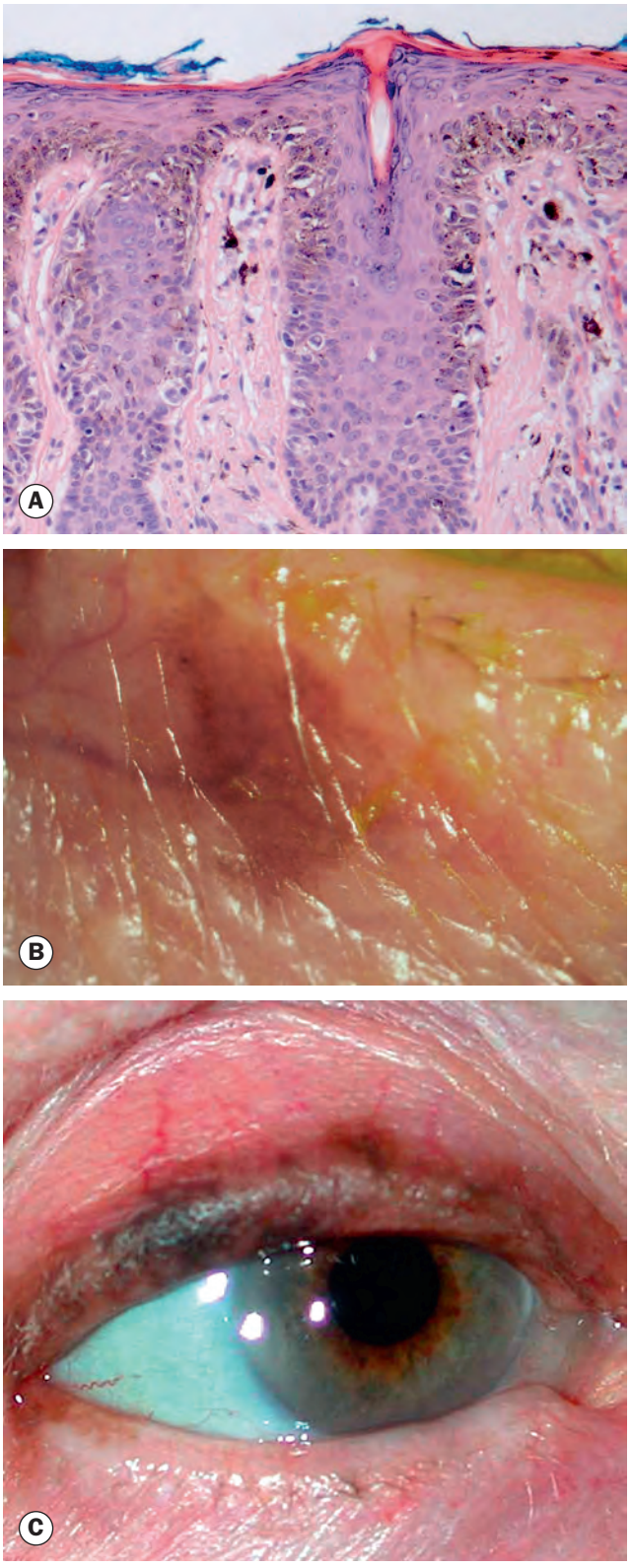


Fig. 1.24 Lentigo maligna of the eyelid. **(A)** Histopathology shows melanoma cells proliferating within the basal layers of the epidermis; **(B)** early lentigo maligna; **(C)** melanoma arising from lentigo maligna

(Courtesy of L Horton – fig. A; S Delva – fig. C)

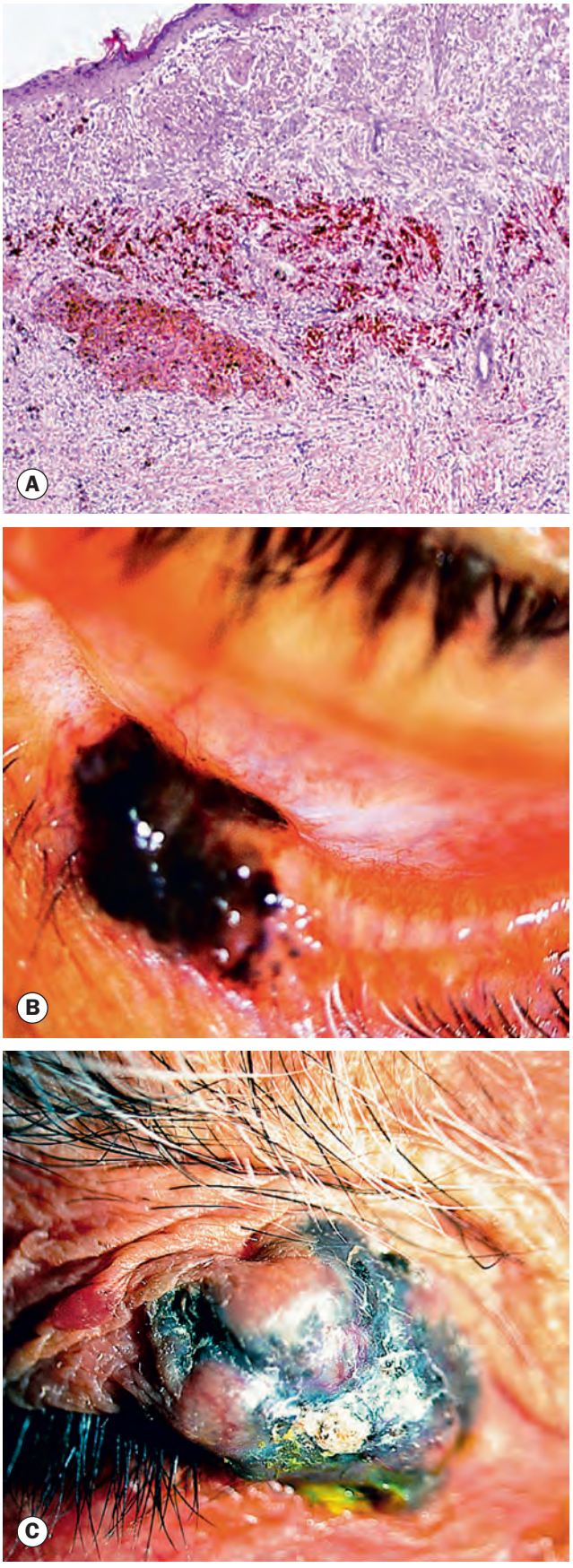


Fig. 1.25 Melanoma. **(A)** Histopathology shows melanoma cells within the dermis; **(B)** superficial spreading melanoma; **(C)** nodular melanoma

(Courtesy of J Harry – fig. A)

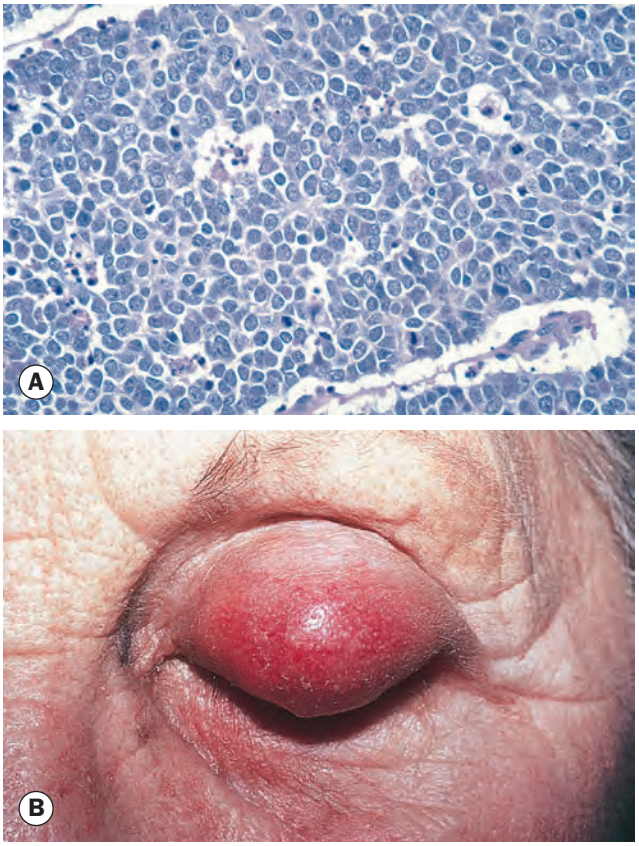


Fig. 1.26 Merkel cell carcinoma. **(A)** Histopathology shows a sheet of Merkel cells; **(B)** clinical appearance

(Courtesy of J Harry and G Misson, from Clinical Ophthalmic Pathology, *Butterworth-Heinemann 2001 – fig. A)*

Treatment of malignant tumours

Biopsy

Biopsy can be (i) *incisional*, using a blade or a biopsy punch, in which only part of the lesion is removed for histological diagnosis, or (ii) *excisional*, in which the entire lesion is removed; the latter may consist of shave excision using a blade to remove shallow epithelial tumours, such as papillomas and seborrhoeic keratosis, or full-thickness skin excision for tumours that are not confined to the epidermis.

Surgical excision

Surgical excision aims to remove the entire tumour with preservation of as much normal tissue as possible. Smaller tumours can be removed via an excision biopsy and the defect closed directly, whilst awaiting histological confirmation of complete clearance. Most small BCCs can be cured by excision of the tumour together with a 2–4 mm margin of clinically normal tissue. More radical surgical excision is required for large BCCs and aggressive tumours such as SCC, SGC and melanoma. It may not be possible to close all defects at the time of initial removal, but it is necessary to ensure complete clearance of tumour prior to undertaking any reconstruction. There are several options for the coordination of histopathological diagnosis and tumour clearance with excision.

- **Conventional paraffin-embedded specimen.** Rapid processing can reduce the interval to confirmation of histological clearance but still requires that reconstruction be performed as a separate procedure. Faster confirmation can be achieved using either frozen-section control or micrographic surgery (see next), and reconstruction can then take place on the same day.
- **Standard frozen section** involves histological examination of the margins of the excised specimen at the time of surgery to ensure they are tumour-free. If no tumour cells are detected, the eyelid is reconstructed on the same day; if residual tumour is present, further excision is performed at the appropriate edge of the surgical site until no tumour is detected.
- **Mohs micrographic surgery** involves layered excision of the tumour; specimens are usually examined frozen. Processing of each layer enables a map of the edges of the tumour to be

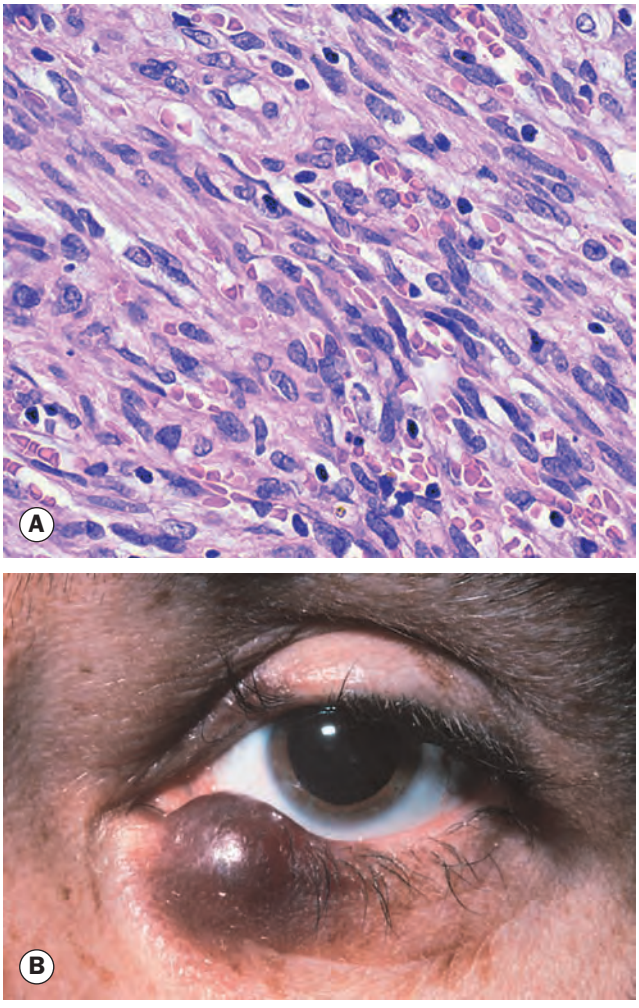


Fig. 1.27 Kaposi sarcoma. **(A)** Histopathology shows a proliferation of predominantly spindle-shaped cells; vascular channels are evident; **(B)** clinical appearance

(Courtesy of J Harry – fig. A)

developed. Further tissue is taken in any area where tumour is still present until clearance is achieved. Although time-consuming, this technique maximizes the chances of total tumour excision whilst minimizing sacrifice of normal tissue. This is a particularly useful technique for tumours that grow diffusely and have indefinite margins with finger-like extensions, such as sclerosing BCC, SCC, recurrent tumours and those involving the medial or lateral canthi. The irregular contours around the eyelids and extension of tumours into orbital fat can make interpretation difficult.

Reconstruction

The technique of reconstruction depends on the extent of tissue removed. It is important to reconstruct both anterior and posterior lamellae, each of which must be reconstructed with similar tissue. Anterior lamellar defects may be closed directly or with a local flap or skin graft. Options for the repair of full-thickness defects are set out below.

- **Small defects** involving less than one-third of the eyelid can usually be closed directly, provided the surrounding tissue is sufficiently elastic to allow approximation of the cut edges (Fig. 1.28). If necessary, a lateral cantholysis can be performed for increased mobilization.
- **Moderate size defects** involving up to half of the eyelid may require a flap (e.g. Tenzel semicircular) for closure (Fig. 1.29).
- **Large defects** involving over half of the eyelid may be closed by one of the following techniques:
  - Posterior lamellar reconstruction may involve an upper lid free tarsal graft, buccal mucous membrane or hard palate graft, or a Hughes tarsoconjunctival flap from the upper lid, which is left attached for 4–6 weeks before transection (Fig. 1.30).
  - Anterior lamellar reconstruction may involve skin advancement, a local skin flap or a free skin graft (Fig. 1.31); the patient must be made aware that grafted skin is unlikely to be a perfect match. At least one reconstructed lamella requires its own blood supply to maximize the viability of a free graft component.

Laissez-faire

Full reconstruction of the defect created by tumour removal may not always be required. In the *laissez-faire* approach the wound edges are approximated as far as possible and the defect is allowed to granulate and heal by secondary intention. Even large defects can often achieve a satisfactory outcome with time.

Radiotherapy

The recurrence rate following irradiation alone is higher than after surgery, and radiotherapy does not allow histological confirmation of tumour eradication. Recurrences following radiotherapy are difficult to treat surgically because of the poor healing properties of irradiated tissue. However, it still has utility in some circumstances.

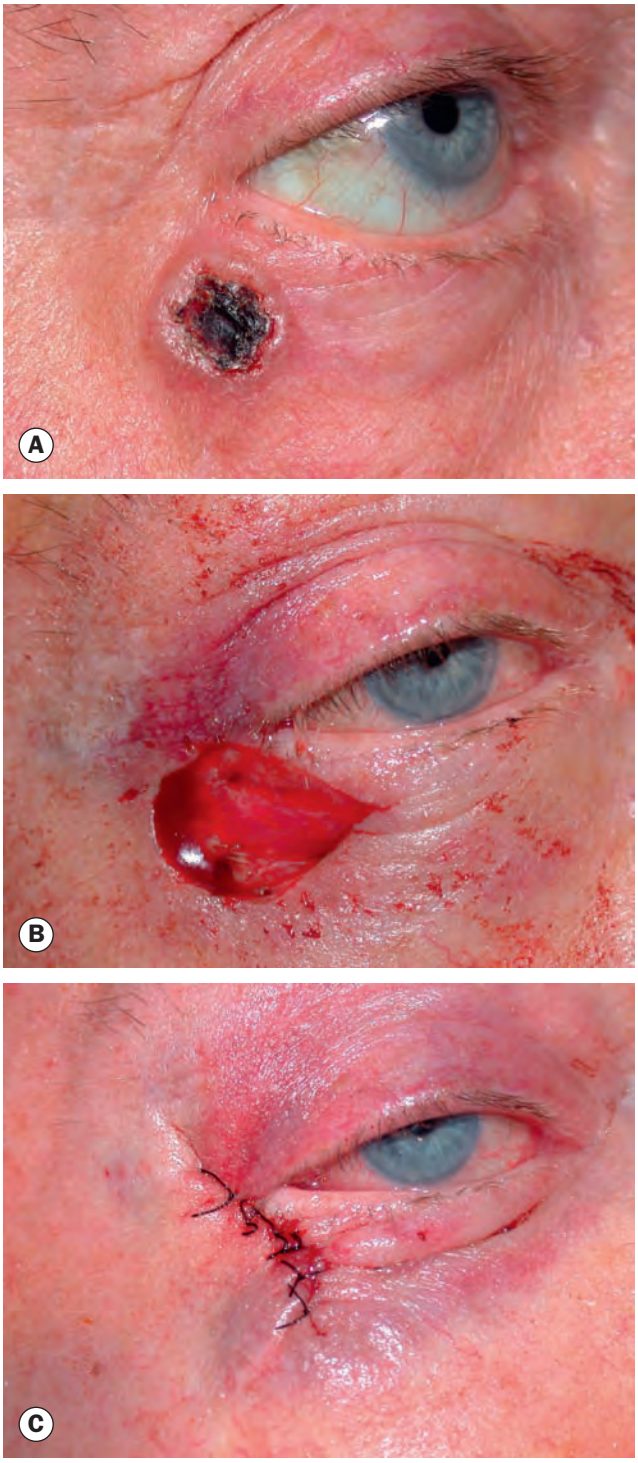
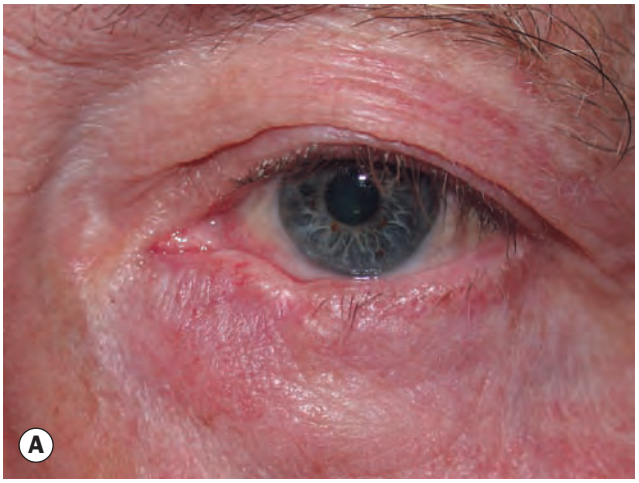
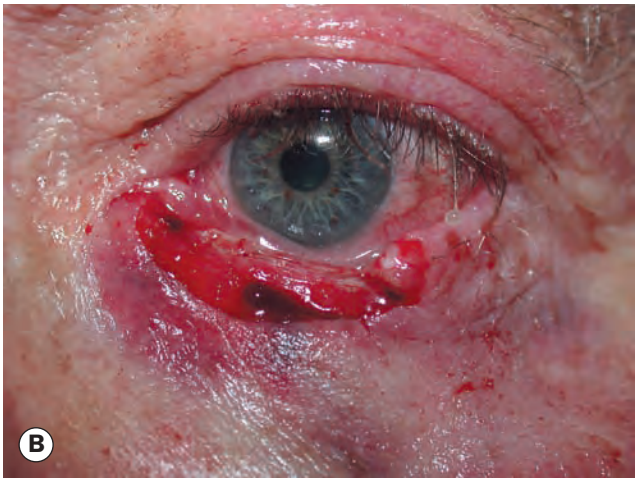


Fig. 1.28 Direct closure. **(A)** Preoperative appearance of a basal cell carcinoma; **(B)** appearance following excision; **(C)** direct closure of defect
(Courtesy of A Pearson)

- **Indications**
  - Patients who are either unsuitable for or refuse surgery.
  - Highly radiosensitive tumours, such as Kaposi sarcoma.
  - Adjunctive therapy in some cases.
  - Palliative treatment.





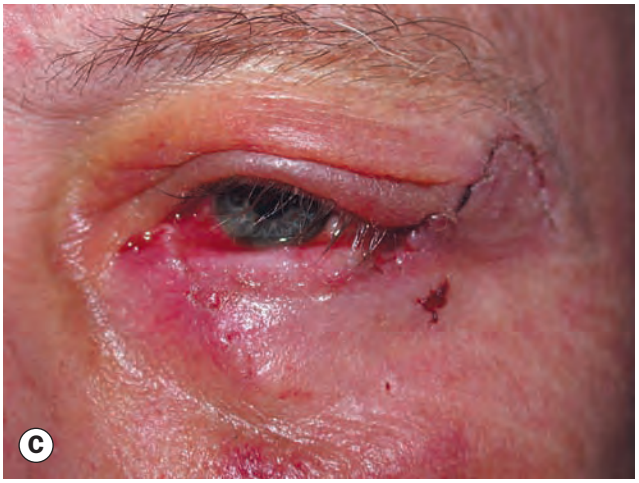
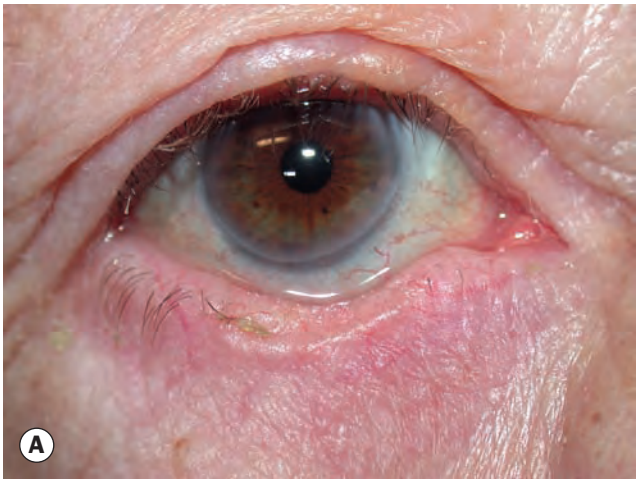


Fig. 1.29 Tenzel flap. **(A)** Preoperative appearance; **(B)** appearance following excision; **(C)** appearance following closure of the flap

(Courtesy of A Pearson)



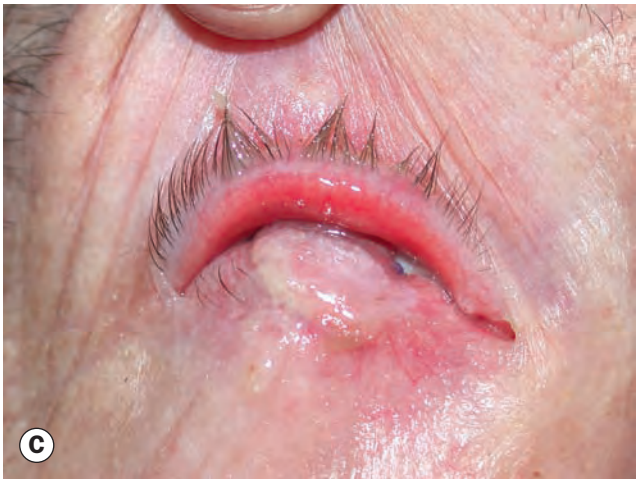


Fig. 1.30 Posterior lamellar reconstruction with a Hughes upper lid flap. **(A)** Preoperative appearance; **(B)** appearance following excision; **(C)** postoperative appearance with the flap yet to be divided

(Courtesy of A Pearson)

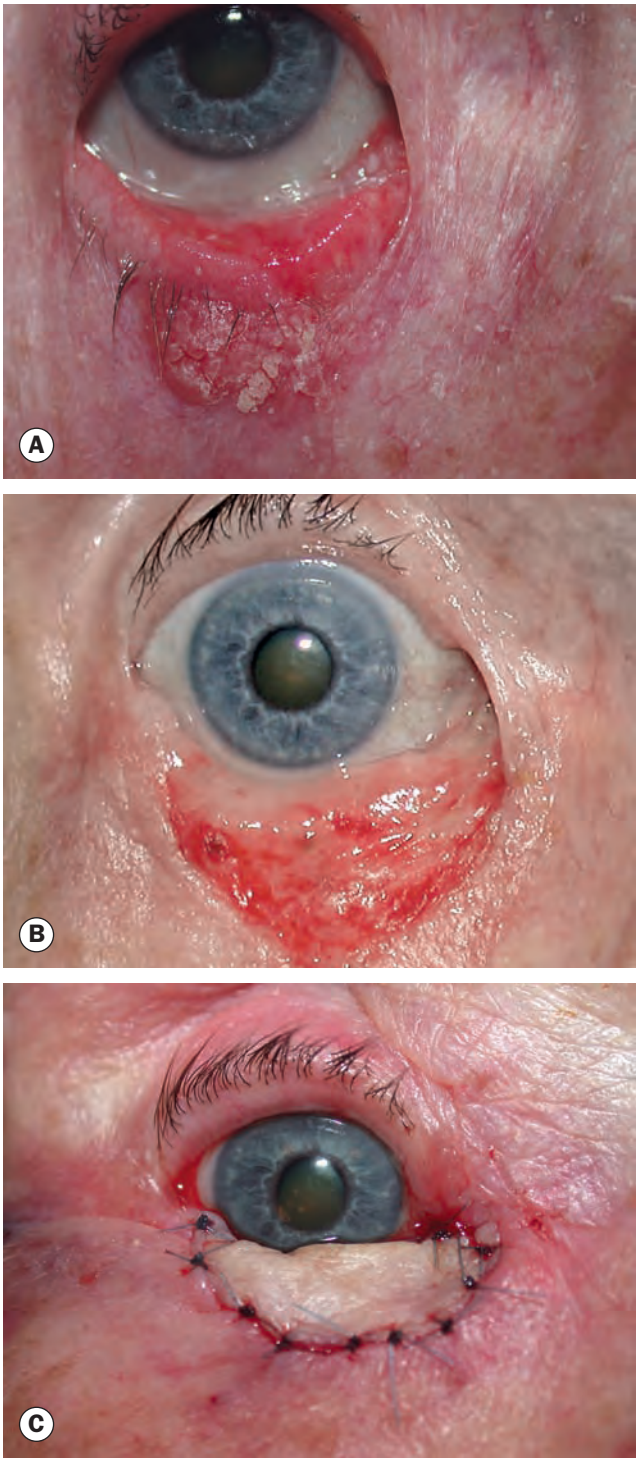


Fig. 1.31 Anterior lamellar reconstruction with a free skin graft. **(A)** Preoperative appearance; **(B)** appearance following excision; **(C)** skin graft in place
(Courtesy of A Pearson)

- **Relative contraindications**
  - Medial canthal lesions due to the high probability of lacrimal canalicular damage.
  - Upper eyelid tumours – conjunctival keratinization is common and difficult to manage.
  - Aggressive tumours such as SGC are relatively radioresistant, but higher-dose treatment may be effective.
- **Complications.** Many of these can be minimized by appropriate shielding.
  - Skin damage and madarosis (eyelash loss).
  - Nasolacrimal duct stenosis following irradiation to the medial canthal area.
  - Conjunctival keratinization, dry eye, keratopathy and cataract.
  - Retinopathy and optic neuropathy.

Cryotherapy

Cryotherapy may be considered for small superficial BCCs; it can be a useful adjunct to surgery in some patients. Complications include skin depigmentation, madarosis and conjunctival overgrowth.

DISORDERS OF THE EYELASHES

Misdirected lashes

Introduction

The roots of the eyelashes (cilia) lie against the anterior surface of the tarsal plate. The cilia pass between the main part of the orbicularis oculi and its more superficial part (Riolan muscle), exiting the skin at the anterior lid margin and curving away from the globe. It is particularly important to be familiar with the normal anatomical appearance of the lid margin in order to be able to identify the cause of eyelash misdirection. From anterior to posterior:

- **Eyelashes** (cilia).
- **The grey line**, by definition the border between the anterior (lashes, skin and orbicularis) and posterior (tarsal plate and conjunctiva) lamellae.
- **The meibomian gland orifices** are located just anterior to the mucocutaneous junction. The edge of the tarsal plate is deep to the gland orifices; the glands themselves run vertically within the plate.
- **The mucocutaneous junction** is where keratinized epithelium of the skin merges with conjunctival mucous membrane.
- **Conjunctiva** lines the posterior margin of the lid.

Clinical features

Trauma to the corneal epithelium may cause punctate epithelial erosions, with ocular irritation often worsened by blinking. Corneal ulceration and pannus formation may occur in severe cases. The clinical appearance varies with the cause.

- **Trichiasis** refers to misdirection of growth from individual follicles (Fig. 1.32A), rather than a more extensive inversion of the lid or lid margin. The follicles are at anatomically normal sites. It is commonly due to inflammation such as chronic blepharitis or herpes zoster ophthalmicus, but can

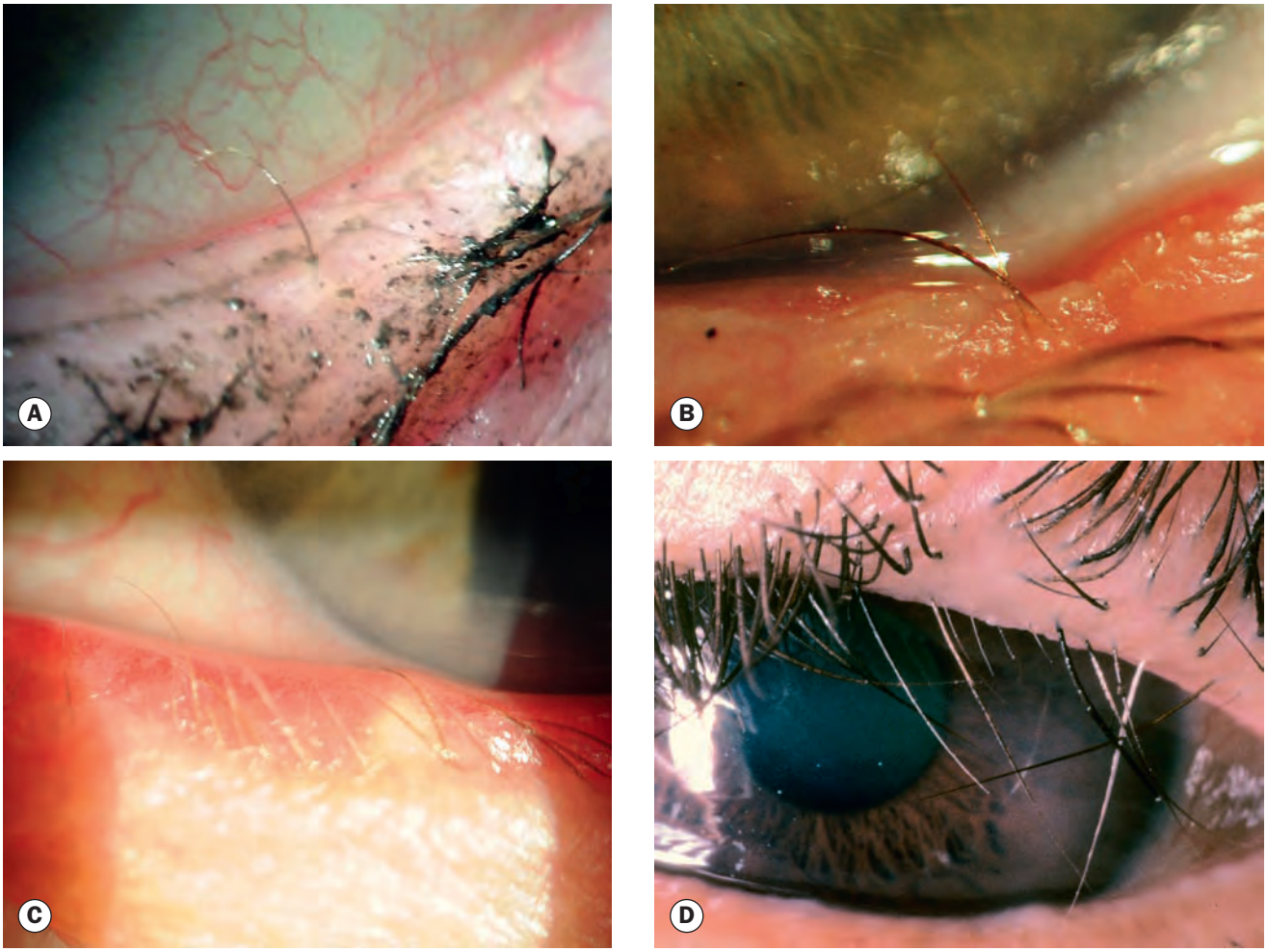


Fig. 1.32 Misdirected lashes. **(A)** Single trichiatic lash; **(B)** trichiasis associated with a lid notch following chalazion surgery; **(C)** marginal entropion showing rows of misdirected lashes, anterior migration of the mucocutaneous junction, and a rounded posterior lid margin; **(D)** acquired distichiasis
(Courtesy of S Chen – fig. A; R Bates – fig. D)

also be caused by trauma, including surgery such as incision and curettage of a chalazion (Fig. 1.32B).

- **Marginal entropion** has increasingly been recognized as a very common cause of eyelash misdirection, the mechanism of which is thought to be subtle cicatricial posterior lamellar shortening that rotates a segment of the lid margin towards the eye. The mucocutaneous junction migrates anteriorly and the posterior lid margin becomes rounded rather than physiologically square. Typically, numerous aligned lashes are involved (Fig. 1.32C).
- **Congenital distichiasis** is a rare condition that occurs when a primary epithelial germ cell destined to differentiate into a meibomian gland develops instead into a complete pilosebaceous unit. The condition is frequently inherited in an autosomal dominant manner with high penetrance but variable expressivity. The majority of patients also manifest primary lymphoedema of the legs (lymphoedema–distichiasis syndrome). A partial or complete second row of lashes is seen to emerge at or slightly behind the meibomian gland orifices. The aberrant lashes tend to be thinner and shorter than normal cilia and are often directed posteriorly. They are usually well tolerated during infancy and may not become symptomatic until the age of about 5 years.
- **Acquired distichiasis** is caused by metaplasia of the meibomian glands into hair follicles such that a variable number of lashes grow from meibomian gland openings. The most important cause is intense conjunctival inflammation (e.g. chemical injury, Stevens–Johnson syndrome, ocular cicatricial pemphigoid). In contrast to congenital distichiasis, the cilia tend to be non-pigmented and stunted (Fig. 1.32D), and are usually symptomatic.
- **Epiblepharon** – see later.
- **Entropion.** In contrast to marginal entropion, profound inversion of a substantial width of the lid is readily identified – see later.

Treatment

- **Epilation** with forceps is simple and effective but recurrence within a few weeks is essentially invariable. It can be used as

a temporizing measure or in the occasional patient who refuses or cannot tolerate surgery.

- **Electrolysis** or electrocautery (hyfrecation) are broadly similar electrosurgical techniques in which, under local anaesthesia, a fine wire is passed down the hair follicle to ablate the lash. It is generally useful for a limited number of lashes; scarring can occur. Frequently multiple treatments are required to obtain a satisfactory result.
- **Laser ablation** is also useful for the treatment of limited aberrant eyelashes, and is performed using a spot size of 50 µm, duration of 0.1–0.2 s and power of 800–1000 mW. The base of the lash is targeted and shots are applied to create a crater that follows the axis of the follicle (Fig. 1.33). Success is broadly comparable to that achieved with electrosurgery.
- **Surgery**
  - Tarsal facture (transverse tarsotomy) is performed for marginal entropion. After placing a 4-0 traction suture, a horizontal incision is made through the tarsal plate via the conjunctiva, at least halfway down the plate, along the affected length of the lid and extended to 2–3 mm either side of the involved region. Depending on the extent of lid involvement, either two or three double-armed absorbable sutures are passed through the upper edge of the lower section of the tarsal plate to emerge just anterior to the lashes, leaving the lid margin very slightly everted (Fig. 1.34). The sutures are left in place following the surgery; occasionally short-term use of a bandage contact lens is required to prevent corneal abrading.
  - A full-thickness eyelid pentagon resection can be used for a focal group of aberrant lashes, typically after trauma, or for localized marginal entropion.
  - Other options include lid splitting (see next) with follicle excision, and anterior lamellar rotation surgery.
- **Cryotherapy** applied externally to the skin just inferior to the base of the abnormal lashes or – especially in distichiasis – to the internal aspect of the anterior lamella of the lid following splitting of the margin at the grey line (Fig. 1.35), can be used for numerous lashes. A double freeze–thaw cycle at −20 °C is applied under local anaesthesia (including adrenaline) with a plastic eye protector in place; suturing of the lid margin is not usually necessary following limited splitting. The method is effective but carries a high rate of local adverse effects, and is less commonly performed than previously.

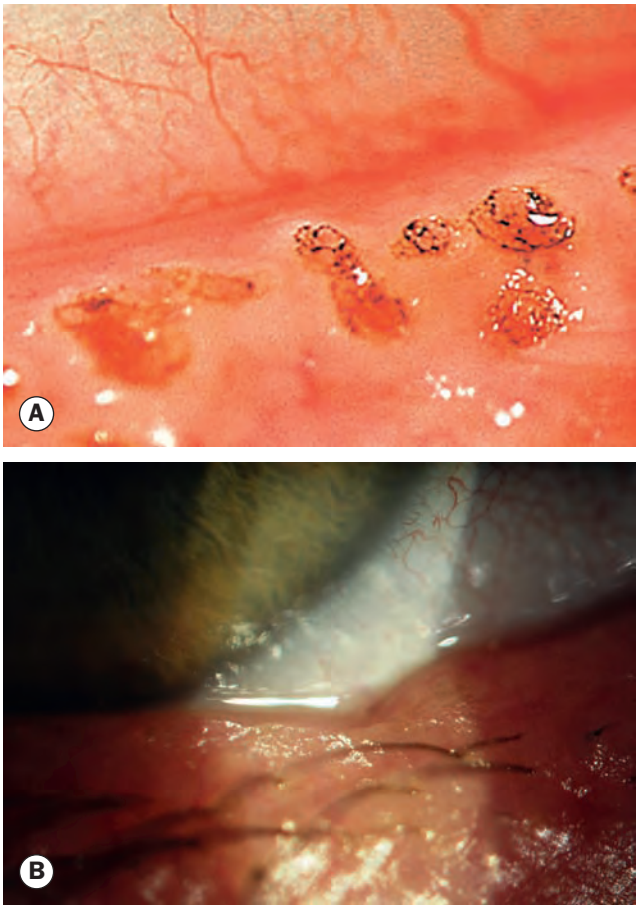


Fig. 1.33 Laser for trichiasis. **(A)** Appearance following ablation of multiple lashes; **(B)** the eye in Fig. 1.32B 6 weeks after laser ablation

Eyelash ptosis

Eyelash ptosis refers to a downward sagging of the upper lid lashes (Fig. 1.36A). The condition may be idiopathic or associated with floppy eyelid syndrome, dermatochalasis with anterior lamellar slip or long-standing facial palsy.

Trichomegaly

Trichomegaly is excessive eyelash growth (Fig. 1.36B); the main causes are listed in Table 1.1.

Madarosis

Madarosis is the term used for the loss of lashes (Fig. 1.36C). The main causes are shown in Table 1.2.

Poliosis

Poliosis is a premature localized whitening of hair, which may involve the lashes and eyebrows (Fig. 1.36D); the main causes are shown in Table 1.3.

Table 1.1 Causes of trichomegaly

Drug-induced – topical prostaglandin analogues, phenytoin and ciclosporin
Malnutrition
AIDS
Porphyria
Hypothyroidism
Familial
Congenital: Oliver–McFarlane, Cornelia de Lange, Goldstein–Hutt, Hermansky–Pudlak syndromes

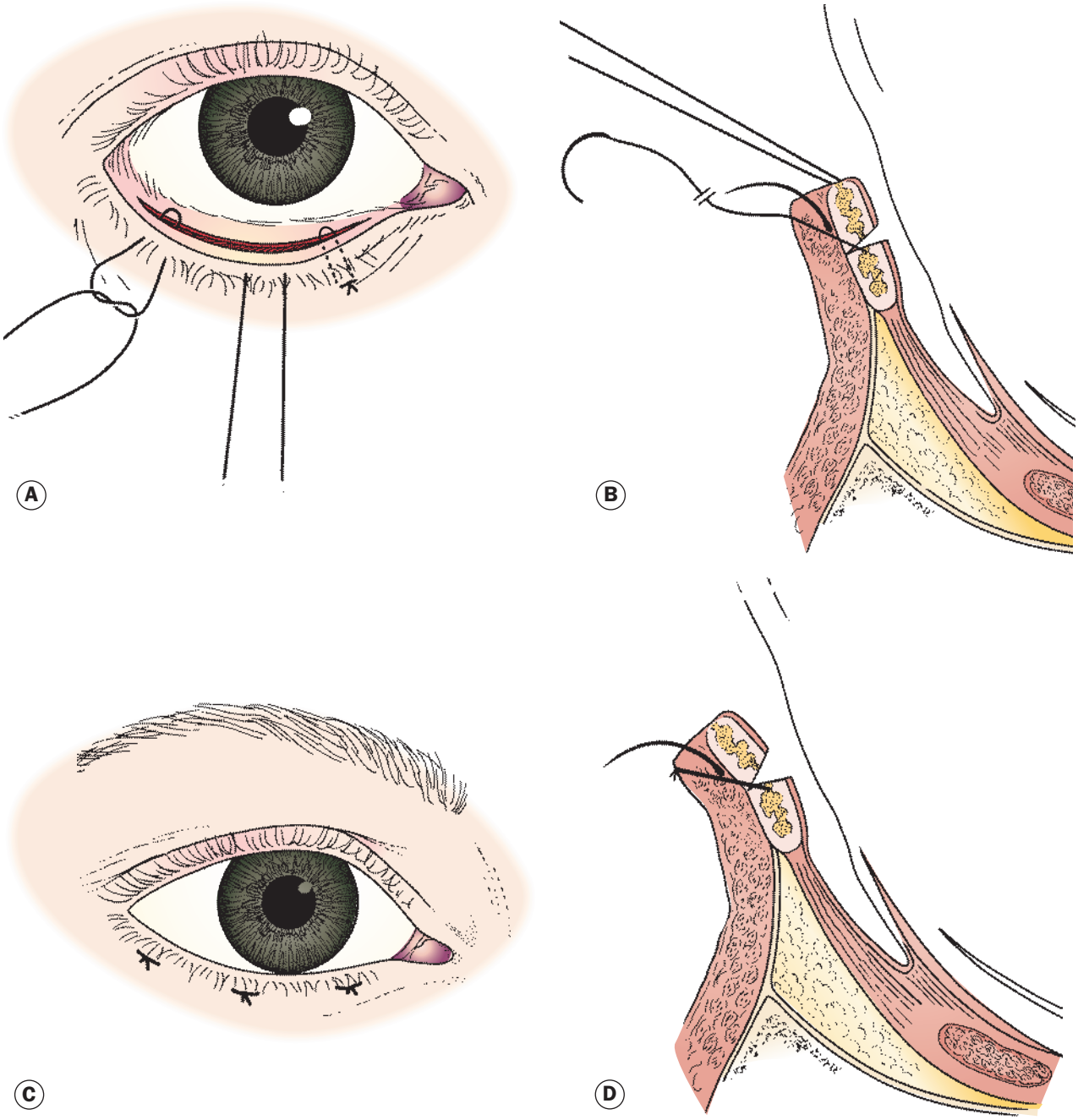


Fig. 1.34 Tarsal fracture for repair of marginal entropion. **(A)** and **(B)** insertion of everting sutures following traction suture emplacement and horizontal tarsal plate incision; **(C)** and **(D)** everting sutures in place
(Courtesy of JA Nerad, from Techniques in Ophthalmic Plastic Surgery, *Saunders 2010)*

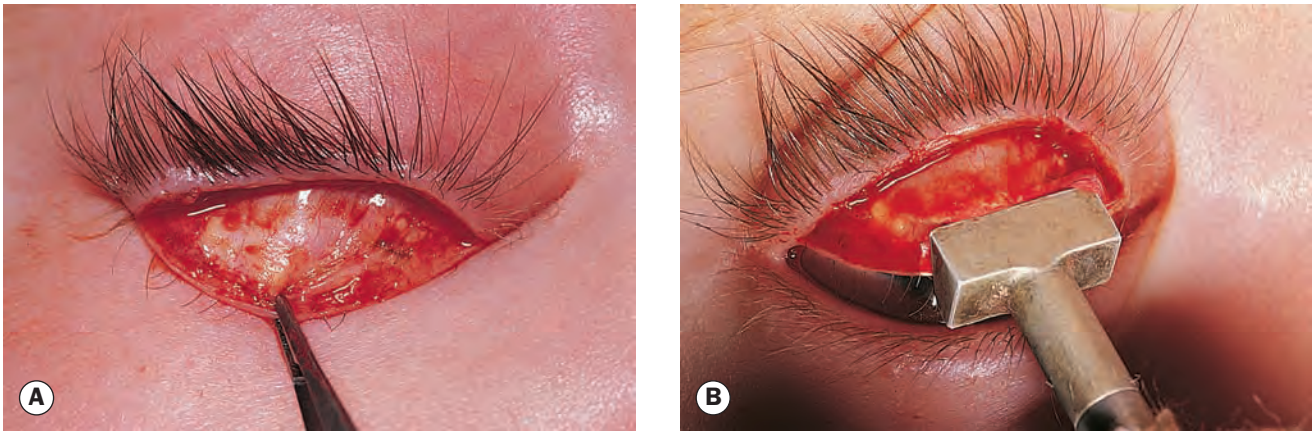


Fig. 1.35 Cryotherapy to the eyelid in distichiasis. **(A)** Separation of the anterior and posterior lamellae; **(B)** application of cryoprobe to the posterior lamella

(Courtesy of AG Tyers and JRO Collin, from Colour Atlas of Ophthalmic Plastic Surgery, *Butterworth-Heinemann 2001)*

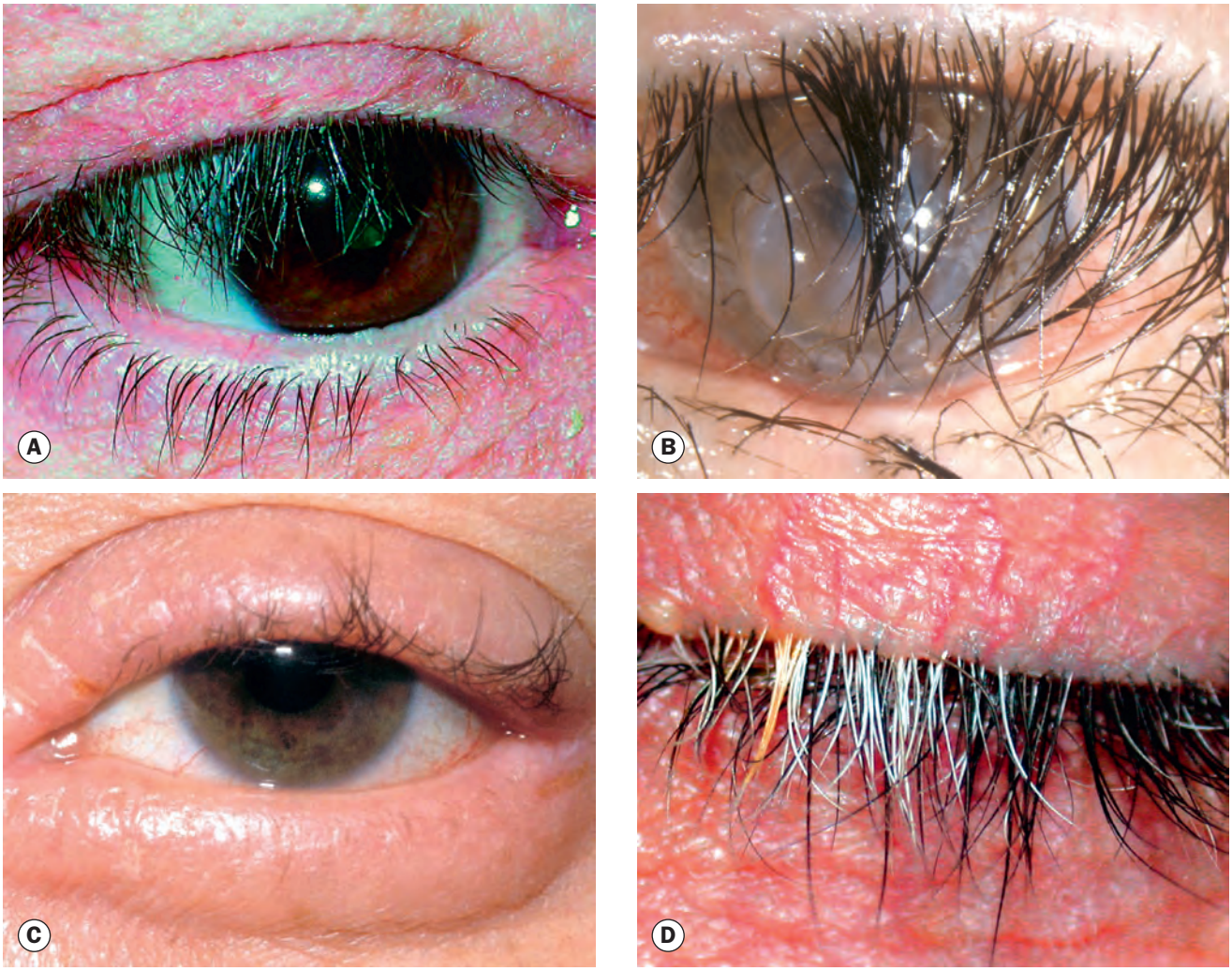


Fig. 1.36 Miscellaneous eyelash disorders. **(A)** Eyelash ptosis; **(B)** trichomegaly; **(C)** madarosis; **(D)** poliosis

(Courtesy of A Pearson – fig. A; L Merin – fig. B; S Tuft – fig. C)

Table 1.2 Cause of madarosis

1. Local
Chronic anterior lid margin disease
Infiltrating lid tumours
Burns
Radiotherapy or cryotherapy of lid tumours
2. Skin disorders
Generalized alopecia
Psoriasis
3. Systemic diseases
Myxoedema
Systemic lupus erythematosus
Acquired syphilis
Lepromatous leprosy
4. Following removal
Procedures for trichiasis
Trichotillomania – psychiatric disorder of hair removal

Table 1.3 Causes of poliosis

1. Ocular
Chronic anterior blepharitis
Sympathetic ophthalmitis
Idiopathic uveitis
2. Systemic
Vogt–Koyanagi–Harada syndrome
Waardenburg syndrome
Vitiligo
Marfan syndrome
Tuberous sclerosis

ALLERGIC DISORDERS

Acute allergic oedema

Acute allergic oedema is usually caused by exposure to pollen or by insect bites, and manifests with the sudden onset of bilateral boggy periocular oedema (Fig. 1.37A), often accompanied by conjunctival swelling (chemosis – see Ch. 5). Treatment is often unnecessary, but systemic antihistamines are sometimes given.

Contact dermatitis

Contact dermatitis is an inflammatory response that usually follows exposure to a medication such as eye drops (often preservative-containing), cosmetics or metals. An irritant can also cause a non-allergic toxic dermatitis. The individual is sensitized on first exposure and develops an immune reaction on further exposure; the mediating reaction is type IV (delayed type) hypersensitivity. Signs consist of lid skin scaling, angular fissuring, oedema and tightness (Fig. 1.37B); there may be chemosis, redness and papillary conjunctivitis. Corneal involvement is usually limited to punctate epithelial erosions. Treatment consists primarily of avoidance of allergen exposure, provided it can be identified. Cold compresses provide symptomatic relief. Topical steroids and oral antihistamines can be used, but are rarely required.

Atopic dermatitis

Atopic dermatitis (eczema) is a very common idiopathic condition, typically occurring in patients who also suffer from asthma and hay fever. Eyelid involvement is relatively infrequent but when present is invariably associated with generalized dermatitis. Thickening, crusting and fissuring of the lids (Fig. 1.37C) is typical, and staphylococcal blepharitis, vernal or atopic keratoconjunctivitis are also commonly present. Herpetic blepharitis and keratoconjunctivitis is more common and more severe in patients with atopy (eczema herpeticum). Treatment of the lid features is with emollients to hydrate the skin and the judicious use of mild topical steroid such as hydrocortisone 1%. Uncommon ocular associations include keratoconus, cataract and retinal detachment (see also Ch. 5).

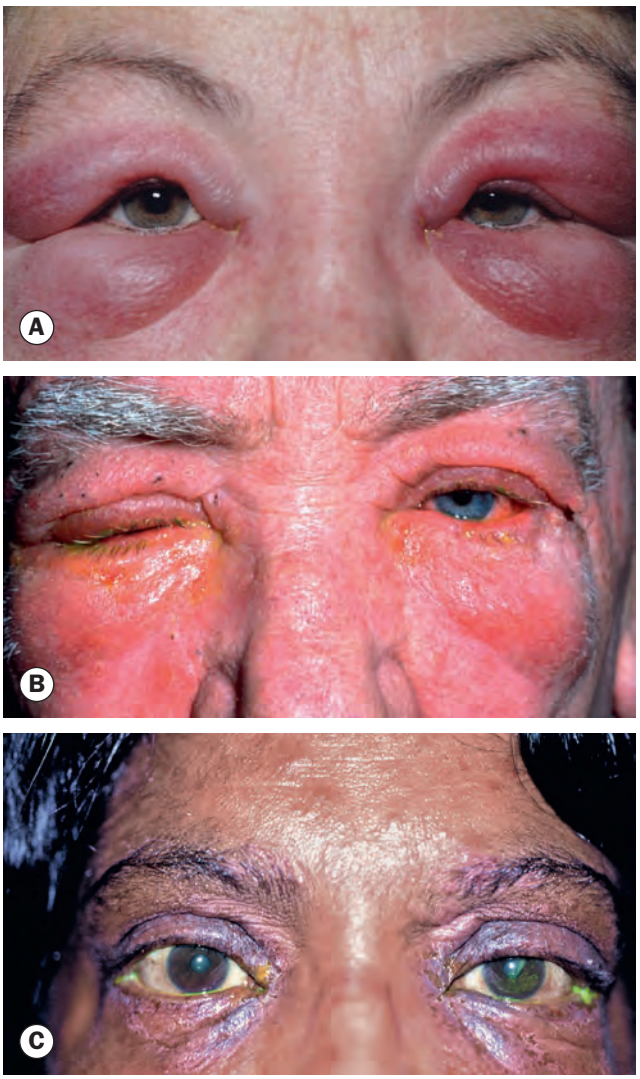


Fig. 1.37 Allergic disorders. **(A)** Acute allergic oedema; **(B)** contact dermatitis; **(C)** atopic dermatitis