CHAPTER 1
General Principles

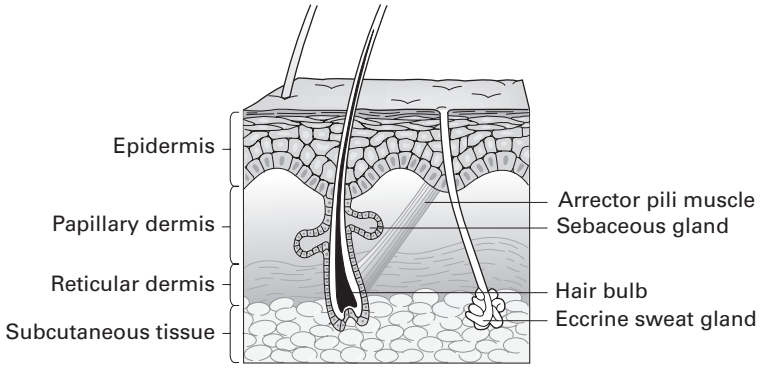
CHAPTER CONTENTS

Embryology, structure and function of the skin

- Skin differentiates from ectoderm and mesoderm during the 4th week.
- Skin gives rise to:
  - Teeth and hair follicles, derived from epidermis and dermis
  - Fingernails and toenails, derived from epidermis only.
- Hair follicles, sebaceous glands, sweat glands, apocrine glands and mammary glands are 'epidermal appendages' because they develop as ingrowths of epidermis into dermis.
- Functions of skin:
  1 Physical protection
  2 Protection against UV light
  3 Protection against microbiological invasion
  4 Prevention of fluid loss

Key Notes on Plastic Surgery, Second Edition. Adrian Richards and Hywel Dafydd.

5 Regulation of body temperature
6 Sensation
7 Immunological surveillance.



The epidermis

- Composed of stratified squamous epithelium.
- Derived from ectoderm.
- Epidermal cells undergo keratinisation – their cytoplasm is replaced with keratin as the cell dies and becomes more superficial.
- Rete ridges are epidermal thickenings that extend downward between dermal papillae.
- Epidermis is composed of these five layers, from deep to superficial:

1 Stratum germinativum
- Also known as the basal layer.
- Cells within this layer have cytoplasmic projections (hemidesmosomes), which firmly link them to the underlying basal lamina.
- The only actively proliferating layer of skin.
- Stratum germinativum also contains melanocytes.

2 Stratum spinosum
- Also known as the prickle cell layer.
- Contains large keratinocytes, which synthesise cytokeratin.
- Cytokeratin accumulates in aggregates called tonofibrils.
- Bundles of tonofibrils converge into numerous desmosomes (prickles), forming strong intercellular contacts.

3 Stratum granulosum
- Contains mature keratinocytes, with cytoplasmic granules of keratohyalin.
- The predominant site of protein synthesis.
- Combination of cytokeratin tonofibrils with keratohyalin produces keratin.

4 Stratum lucidum
- A clear layer, only present in the thick glabrous skin of palms and feet.

5 Stratum corneum
- Contains non-viable keratinised cells, having lost their nuclei and cytoplasm.
- Protects against trauma.
- Insulates against fluid loss.
- Protects against bacterial invasion and mechanical stress.

Cellular composition of the epidermis
- Keratinocytes – the predominant cell type in the epidermis.
- Langerhans cells – antigen-presenting cells (APCs) of the immune system.
- Merkel cells – mechanoreceptors of neural crest origin.
- Melanocytes – neural crest derivatives:
  - Usually located in the stratum germinativum.
  - Produce melanin packaged in melanosomes, which is delivered along dendrites to surrounding keratinocytes.
  - Melanosomes form a cap over the nucleus of keratinocytes, protecting DNA from UV light.

The dermis
- Accounts for 95% of the skin's thickness.
- Derived from mesoderm.
- Papillary dermis is superficial; contains more cells and finer collagen fibres.
- Reticular dermis is deeper; contains fewer cells and coarser collagen fibres.
- It sustains and supports the epidermis.
- Dermis is composed of:

1 Collagen fibres
- Produced by fibroblasts.
- Through cross-linking, are responsible for much of the skin's strength.
- The normal ratio of type 1 to type 3 collagen is 5:1.

2 Elastin fibres
- Secreted by fibroblasts.
- Responsible for elastic recoil of skin.

3 Ground substance
- Consists of glycosaminoglycans (GAGs): hyaluronic acid, dermatan sulphate, chondroitin sulphate.
- GAGs are secreted by fibroblasts and become ground substance when hydrated.

4 Vascular plexus
- Separates the denser reticular dermis from the overlying papillary dermis.

Skin appendages
Hair follicles
- Each hair is composed of a medulla, a cortex and an outer cuticle.
- Hair follicles consist of an inner root sheath (derived from epidermis), and an outer root sheath (derived from dermis).

- Several sebaceous glands drain into each follicle.
  - Drainage of the glands is aided by contraction of arrector pili muscles.
- Vellus hairs are fine and downy; terminal hairs are coarse.
- Hairs are either in anagen (growth), catagen (regressing), or telogen (resting) phase.
  - <90% are in anagen, 1–2% in catagen and 10–14% in telogen at any one time.

Eccrine glands

- These sweat glands secrete odourless hypotonic fluid.
- Present in almost all sites of the body.
- Occur more frequently in the palm, sole and axilla.

Apocrine glands

- Located in axilla and groin.
- Emit a thicker secretion than eccrine glands.
- Responsible for body odour; do not function before puberty.
- Modified apocrine glands are found in the external ear (ceruminous glands) and eyelid (Moll glands).
- The mammary gland is a modified apocrine gland specialised for manufacture of colostrum and milk.
- Hidradenitis suppurativa is a disease of apocrine glands.

Sebaceous glands

- Holocrine glands that drain into the pilosebaceous unit in hair-bearing skin.
- They drain directly onto skin in the labia minora, penis and tarsus (meibomian glands).
- Most prevalent on forehead, nose and cheek; absent from palms and soles.
- Produce sebum, which contains fats and their breakdown products, wax esters and debris of dead fat-producing cells.
  - Sebum is bactericidal to staphylococci and streptococci.
- Sebaceous glands are not the sole cause of so-called sebaceous cysts.
- These cysts are in fact of epidermal origin and contain all substances secreted by skin (predominantly keratin).
  - Some maintain they should therefore be called epidermoid cysts.

Types of secretion from glands

- Eccrine or merocrine glands secrete opened vesicles via exocytosis.
- Apocrine glands secrete by 'membrane budding' – pinching off part of the cytoplasm in vesicles bound by the cell's own plasma membrane.
- Holocrine gland secretions are produced within the cell, followed by rupture of the cell's plasma membrane.

Histological terms

- Acanthosis: epidermal hyperplasia.
- Papillomatosis: increased depth of corrugations at the dermoepidermal junction.
- Hyperkeratosis: increased thickness of the keratin layer.

- Parakeratosis: presence of nucleated cells at the skin surface.
- Pagetoid: when cells invade the upper epidermis from below.
- Palisading: when cells are oriented perpendicular to a surface.

Blood supply to the skin

- Epidermis contains no blood vessels.
- It is dependent on dermis for nutrients, supplied by diffusion.

Anatomy of the circulation

- Blood reaching the skin originates from named deep vessels.
- These feed interconnecting vessels, which supply the vascular plexuses of fascia, subcutaneous tissue and skin.

Deep vessels

- Arise from the aorta and divide to form the main arterial supply to head, neck, trunk and limbs.

Interconnecting vessels

- The interconnecting system is composed of:
  - Fasciocutaneous (or septocutaneous) vessels
    - Reach the skin *directly* by traversing fascial septa.
    - Provide the main arterial supply to skin in the limbs.
- Musculocutaneous vessels
  - Reach the skin *indirectly* via muscular branches from the deep system.
  - These branches enter muscle bellies and divide into multiple perforating branches, which travel up to the skin.
  - Provide the main arterial supply to skin of the torso.

Vascular plexuses of fascia, subcutaneous tissue and skin

1 Subfascial plexus
- Small plexus lying on the undersurface of deep fascia.

2 Prefascial plexus
- Larger plexus superficial to deep fascia; prominent on the limbs.
- Predominantly supplied by fasciocutaneous vessels.

3 Subcutaneous plexus
- At the level of superficial fascia.
- Mainly supplied by musculocutaneous vessels.
- Predominant on the torso.

4 Subdermal plexus
- Receives blood from the underlying plexuses.
- The main plexus supplying blood to skin.
- Accounts for dermal bleeding observed in incised skin.

5 Dermal plexus
   - Mainly composed of arterioles.
   - Plays an important role in thermoregulation.
6 Subepidermal plexus
   - Contains small vessels without muscle in their walls.
   - Predominantly nutritive and thermoregulatory function.

Angiosomes

- An angiosome is a three-dimensional composite block of tissue supplied by a named artery.
- The area of skin supplied by an artery was first studied by Manchot in 1889.
- His work was expanded by Salmon in the 1930s, and more recently by Taylor and Palmer.
- The anatomical territory of an artery is the area into which the vessel ramifies before anastomosing with adjacent vessels.
- The dynamic territory of an artery is the area into which staining extends after intravascular infusion of fluorescein.
- The potential territory of an artery is the area that can be included in a flap if it is delayed.
- Vessels that pass between anatomical territories are called choke vessels.
- The transverse rectus abdominis myocutaneous (TRAM) flap illustrates the angiosome concept well:

Zone 1

- Receives musculocutaneous perforators from the deep inferior epigastric artery (DIEA) and is therefore in its anatomical territory.

Zones 2 and 3

- There is controversy as to which of the following zones is 2 and which is 3.
- Hartrampf's 1982 description has zone 2 across the midline and zone 3 lateral to zone 1.
   - Holm's 2006 study shows the opposite to be true.
- Skin lateral to zone 1 is in the anatomical territory of the superficial circumflex iliac artery (SCIA).
   - Blood has to travel through a set of choke vessels to reach it from the ipsilateral DIEA.
- Skin on the contralateral side of the linea alba is in the anatomical area of the ipsilateral DIEA.
   - It is also within the dynamic territory of the contralateral DIEA.
   - This allows a TRAM flap to be reliably perfused based on either DIEA.

Zone 4

- This lies furthest from the pedicle and is in the anatomical territory of the contralateral SCIA.
- Blood passing from the pedicle to zone 4 has to cross two sets of choke vessels.
- This portion of the TRAM flap has the worst blood supply and is often discarded.

Arterial characteristics

- Taylor made the following observations from his detailed anatomical dissections:
   - Vessels usually travel with nerves.
   - Vessels obey the law of equilibrium – if one is small, its neighbour will tend to be large.

- Vessels travel from fixed to mobile tissue.
- Vessels have a fixed destination but varied origin.
- Vessel size and orientation is a product of growth.

Venous characteristics

- Venous networks consist of linked valvular and avalvular channels that allow equilibrium of flow and pressure.
- Directional veins are valved; typically found in subcutaneous tissues of limbs or as a stellate pattern of collecting veins.
- Oscillating avalvular veins allow free flow between valved channels of adjacent venous territories.
  - They mirror and accompany choke arteries.
  - They define the perimeter of venous territories in the same way choke arteries define arterial territories.
- Superficial veins follow nerves; perforating veins follow perforating arteries.

The microcirculation

- Terminal arterioles are found in reticular dermis.
  - They terminate as they enter the capillary network.
- The precapillary sphincter is the last part of the arterial tree containing muscle within its wall.
  - It is under neural control and regulates blood flow into the capillary network.
- The skin's blood supply far exceeds its nutritive requirements.
- It bypasses capillary beds via arteriovenous anastomoses (AVAs) and has a primarily thermoregulatory function.
  - AVAs connect arterioles to efferent veins.
- AVAs are of two types:
  1. Indirect AVAs – convoluted structures known as glomera (*sing.* glomus)
     - Densely innervated by autonomic nerves.
  2. Direct AVAs – less convoluted with sparser autonomic supply.

Control of blood flow

- The muscular tone of vessels is controlled by:

Pressure of the blood within vessels (myogenic theory)

- Originally described by Bayliss, states that:
  - Increased intraluminal pressure results in constriction of vessels.
  - Decreased intraluminal pressure results in their dilatation.
- Helps keep blood flow constant; accounts for hyperaemia on release of a tourniquet.

Neural innervation

- Arterioles, AVAs and precapillary sphincters are sympathetically innervated.
- Increased arteriolar tone results in decreased cutaneous blood flow.
- Increased precapillary sphincter tone reduces blood flow into capillary networks.
- Decreased AVA tone increases non-nutritive blood flow bypassing the capillary bed.

Humoral factors

- Epinephrine, norepinephrine, serotonin, thromboxane A2 and prostaglandin $F_{2\alpha}$ cause vasoconstriction.
- Histamine, bradykinin and prostaglandin E_1 cause vasodilatation.
- Low O_2 saturation, high CO_2 saturation and acidosis also cause vasodilatation.

Temperature

- Heat causes cutaneous vasodilatation and increased flow, which predominantly bypasses capillary beds via AVAs.

The delay phenomenon

- Delay is any preoperative manoeuvre that results in increased flap survival.
- Historical examples include Tagliacozzi's nasal reconstruction described in the 16th century.
  - Involves elevation of a bipedicled flap with length : breadth ratio of 2:1.
  - The flap can be considered as two 1:1 flaps.
  - Cotton lint is placed under the flap, preventing its reattachment.
  - Two weeks later, one end of the flap is detached from the arm and attached to the nose.
    - A flap of these dimensions transferred without a delay procedure would have a significant chance of distal necrosis.
- Delay is occasionally used for pedicled TRAM breast reconstruction.
  - The DIEA is ligated two weeks prior to flap transfer.
- The mechanism of delay remains incompletely understood.
- These theories have been proposed to explain the delay phenomenon:

Increased axiality of blood flow

- Removal of blood flow from the periphery of a random flap promotes development of an axial blood supply from its base.
- Axial flaps have improved survival compared to random flaps.

Tolerance to ischaemia

- Cells become accustomed to hypoxia after the initial delay procedure.
- Less tissue necrosis therefore occurs after the second operation.

Sympathectomy vasodilatation theory

- Dividing sympathetic fibres at the borders of a flap results in vasodilatation and improved blood supply.
- But why, if sympathectomy is immediate, does the delay phenomenon only begin to appear at 48 hours, and why does it take 2 weeks for maximum effect?

Intraflap shunting hypothesis

- Postulates that sympathectomy dilates AVAs, resulting in an increase in nonnutritive blood flow bypassing the capillary bed.
- A greater length of flap will survive at the second stage as there are fewer sympathetic fibres to cut and therefore less of a reduction in nutritive blood flow.

Hyperadrenergic state

- Surgery results in increased tissue concentrations of vasoconstrictors, such as epinephrine and norepinephrine.
- After the initial delay procedure, the resultant reduction in blood supply is not sufficient to produce tissue necrosis.
  - The level of vasoconstrictor substances returns to normal before the second procedure.
- The second procedure produces another rise in the concentration of vasoconstrictor substances.
  - This rise is said to be smaller than it would be if the flap were elevated without a prior delay.
- The flap is therefore less likely to undergo distal necrosis after a delay procedure.

Unifying theory

- Described by Pearl in 1981; incorporates elements of all these theories.

Classification of flaps

- Flaps can be classified by the five 'C's:
  - **C**irculation
  - **C**omposition
  - **C**ontiguity
  - **C**ontour
  - **C**onditioning.

Circulation

- Can be further subcategorised into:
  - Random
  - Axial (direct, fasciocutaneous, musculocutaneous, or venous).

Random flaps

- No directional blood supply; not based on a named vessel.
- These include most local flaps on the face.
- Should have a maximum length : breadth ratio of 1:1 in the lower extremity, as it has a relatively poor blood supply.
  - Can be up to 6:1 in the face, as it has a good blood supply.

Axial flaps

Direct

- Contain a named artery running in subcutaneous tissue along the axis of the flap.
- Examples include:
  - Groin flap, based on superficial circumflex iliac vessels.
  - Deltopectoral flap, based on perforating vessels of internal mammary artery.
- Both flaps can include a random segment in their distal portions after the artery peters out.

Fasciocutaneous
- Based on vessels running either within or near the fascia.
- The fasciocutaneous system predominates on the limbs.
- Fasciocutaneous flaps are classified by Cormack and Lamberty:

Type A
- Dependent on multiple non-named fasciocutaneous vessels that enter the base of the flap.
- Lower leg 'super flaps' described by Pontén are examples of type A flaps.
  - Their dimensions vastly exceed the 1:1 ratios recommended.

Type B
- Based on a single fasciocutaneous vessel, which runs along the axis of the flap.
- Examples include scapular/parascapular flap, and perforator-based fasciocutaneous flaps of the lower leg.

Type C
- Supplied by multiple small perforating vessels, which reach the flap from a deep artery running along a fascial septum between muscles.
- Examples include radial forearm flap (RFF) and lateral arm flap.

Type C flaps with bone
- Osteofasciocutaneous flaps, originally classified as type D.
- Examples include:
  - RFF raised with a segment of radius; lateral arm flap raised with a segment of humerus.
- The Mathes and Nahai fasciocutaneous flap classification is slightly different:

Type A
- Direct cutaneous pedicle.
- Examples: groin, superficial inferior epigastric and dorsal metacarpal artery flaps.

Type B
- Septocutaneous pedicle.
- Examples: scapular and parascapular, lateral arm, posterior interosseous flap.

Type C
- Musculocutaneous pedicle.
- Examples: median forehead, nasolabial and (usually) anterolateral thigh flap.

Musculocutaneous
- Flaps based on perforators that reach the skin through the muscle.
- The musculocutaneous system predominates on the torso.
- Muscle and musculocutaneous flaps were classified by Mathes and Nahai in 1981:

Type I
- Single vascular pedicle.
- Examples: gastrocnemius, tensor fasciae latae (TFL), abductor digiti minimi.
- Good flaps for transfer – the whole muscle is supplied by a single pedicle.

Type II
- Dominant pedicle(s) and other minor pedicle(s).
- Examples: trapezius, soleus, gracilis.
- Good flaps for transfer – can be based on the dominant pedicle after the minor pedicle(s) are ligated.
- Circulation via minor pedicles alone is not reliable.

Type III
- Two dominant pedicles, each arising from a separate regional artery or opposite sides of the muscle.
- Examples: rectus abdominis, pectoralis minor, gluteus maximus.
- Useful muscles for transfer – can be based on either pedicle.

Type IV
- Multiple segmental pedicles.
- Examples: sartorius, tibialis anterior, long flexors and extensors of the toes.
- Seldom used for transfer – each pedicle supplies only a small portion of muscle.

Type V
- One dominant pedicle and secondary segmental pedicles.
- Examples: latissimus dorsi, pectoralis major.
- Useful flaps – can be based on either the dominant pedicle or secondary segmental pedicles.

Venous
- Based on venous, rather than arterial, pedicles.
- In fact, many venous pedicles have small arteries running alongside them.
- The mechanism of perfusion is not completely understood.
- Example: saphenous flap, based on long saphenous vein.
  - Used to reconstruct defects around the knee.
- Venous flaps are classified by Thatte and Thatte:

Type 1
- Single venous pedicle.

Type 2
- Venous flow-through flaps, supplied by a vein that enters one side of the flap and exits from the other.

Type 3

- Arterialised through a proximal arteriovenous anastomosis and drained by distal veins.

- Venous flaps tend to become congested post-operatively.
- Survival is inconsistent; they have therefore not been universally accepted.
- Modifying the type 3 arterialised venous flap by restricting direct arteriovenous shunting can improve survival rates by redistributing blood to the periphery of the flap.

Composition

- Flaps can be classified by their composition as:
  - Cutaneous
  - Fasciocutaneous
  - Fascial
  - Musculocutaneous
  - Muscle only
  - Osseocutaneous
  - Osseous.

Contiguity

- Flaps can be classified as:
  - Local flaps
    - Composed of tissue adjacent to the defect.
  - Regional flaps
    - Composed of tissue from the same region of the body as the defect, e.g. head and neck, upper limb.
  - Distant flaps
    - Pedicled distant flaps come from a distant part of the body to which they remain attached.
    - Free flaps are completely detached from the body and anastomosed to recipient vessels close to the defect.

Contour

- Flaps can be classified by the way they are transferred into the defect:

Advancement

- Stretching the flap
- Excision of Burow triangles at the flap's base
- V-Y advancement
- Z-plasty at its base
- Careful scoring of the undersurface
- Combinations of the above.

Transposition

- The flap is moved into an adjacent defect, leaving a secondary defect that must be closed by another method.

Rotation
- The flap is rotated into the defect.
- Classically, rotation flaps are designed to allow closure of the donor defect.
- In reality, many flaps have elements of transposition and rotation, and may be best described as pivot flaps.

Interpolation
- The flap is moved into a defect either under or above an intervening bridge of tissue.

Crane principle
- This aims to transform an ungraftable bed into one that will accept a skin graft.
- At the first stage, a flap is placed into the defect.
- After sufficient time to allow vascular ingrowth into the flap from the recipient site, a superficial part of the flap is replaced in its original position.
- This leaves a segment of subcutaneous tissue in the defect, which can now accept a skin graft.

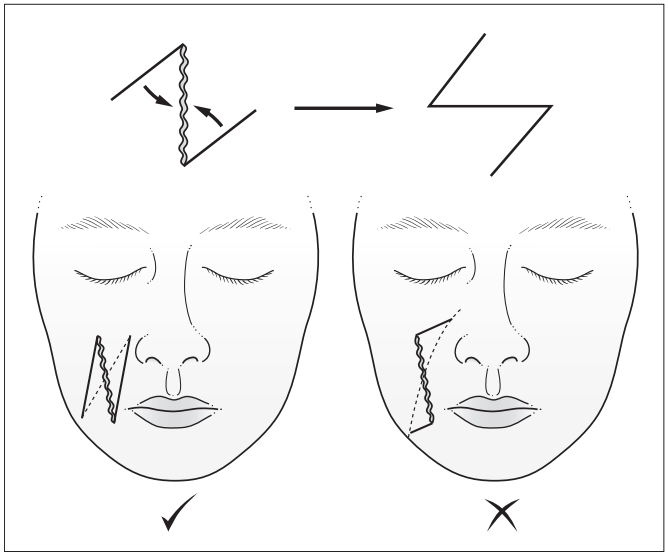
Conditioning
- This involves delaying the flap, discussed in 'Blood supply to the skin'.

Geometry of local flaps

Orientation of elective incisions
- In the 19th century, Langer showed that circular awl wounds produced elliptical defects in cadaver skin.
- He believed this occurred because skin tension along the longitudinal axis of the ellipse exceeded that along the transverse axis.
- Borges has provided over 36 descriptive terms for skin lines, including:
  - Relaxed skin tension lines (RSTLs) – these are parallel to natural skin wrinkles (rhytids) and tend to be perpendicular to the fibres of underlying muscles.
  - Lines of maximum extensibility (LME) – these lie perpendicular to RSTLs and parallel to the fibres of underlying muscles.
- The best orientation of an incision can be judged by a number of methods:
  - Knowledge of the direction of pull of underlying muscles.
  - Making the incision parallel to any rhytids or RSTLs.
  - Making the incision perpendicular to LMEs.
  - Making the incision parallel to the direction of hair growth.
  - 'The pinch test' – if skin either side of the planned incision is pinched, it forms a transverse fold without distortion if it is orientated correctly; if a sigmoid-shaped fold forms, it is orientated incorrectly.

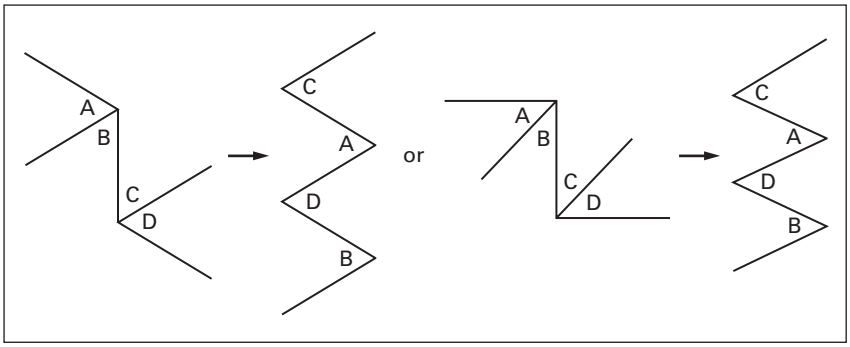
Plasty techniques
Z-plasty
- Involves transposition of two adjacent triangular-shaped flaps.

- Can be used to:
  - Increase the length of an area of tissue or scar
  - Break up a straight-line scar
  - Realign a scar.
- The degree of elongation of the longitudinal axis of the Z-plasty is directly related to the angles of its constituent flaps.
  - 30° → 25% elongation
  - 45° → 50% elongation
  - 60° → 75% elongation
  - 75° → 100% elongation
  - 90° → 125% elongation.
- The amount of elongation can be worked out by starting at 30° and 25% and adding 15° and 25% to each of the figures.
- Gains in length are estimates; true values depend on local tissue elasticity and tension.
- Flaps with 60° angles are most commonly used as they lengthen without undue tension.
- The angles of the two flaps need not be equal and can be designed to suit local tissue requirements.
  - However, all three limbs should be of the same length.
- When designing a Z-plasty to realign a scar:
  1. Mark the desired direction of the new scar.
  2. Draw the central limb of the Z-plasty along the original scar.
  3. Draw the lateral limbs of the Z-plasty from the ends of the central limb, to the line drawn in (1).
  4. Two patterns will be available, one with a wide angle at the apex of the flaps, the other with a narrow angle.
  5. Select the pattern with the narrower angle as these flaps transpose better.



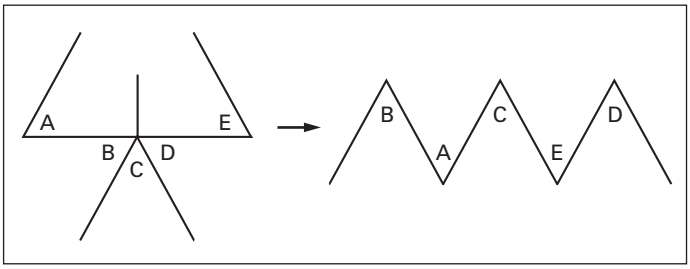
The four-flap plasty

- It is, in effect, two interdependent Z-plasties.
- Can be designed with different angles.
- The two outer flaps become the inner flaps after transposition.
- The two inner flaps become the outer flaps after transposition.
- The flaps, originally in an 'ABCD' configuration, end as 'CADB' (**CADB**ury).



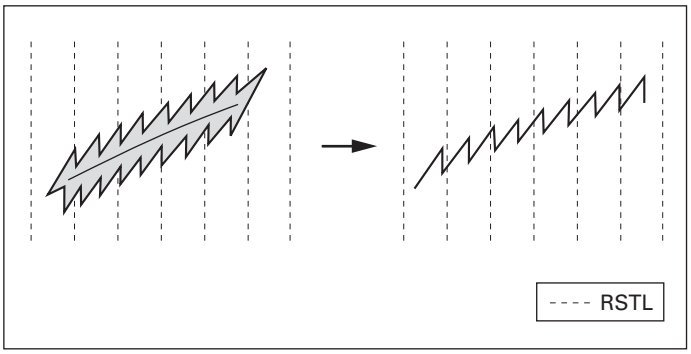
The five-flap plasty

- Because of its appearance, this is also called a jumping-man flap.
- Used to release first web space contractures and epicanthal folds.
- It is, in effect, two opposing Z-plasties with a V-Y advancement in the center.
- The flaps, originally in an 'ABCDE' configuration, end as 'BACED'.



The W-plasty

- Used to break up the line of a scar and improve its aesthetics.
- Unlike the Z-plasty, it does not lengthen tissue.
- If possible, one of the limbs of the W-plasty should lie parallel to the RSTLs so that half of the resultant scar will lie parallel to them.
- Using a template helps ensure each wound edge interdigitates easily.
- The technique discards normal tissue, which may be a disadvantage in certain areas.



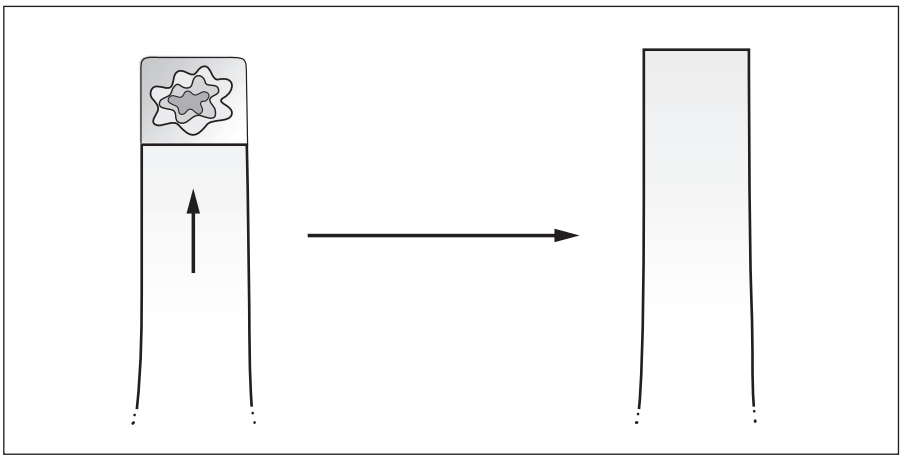
Local flaps

- Advancement flaps (simple, modified, V-Y, keystone, bipedicled).
- Pivot flaps (transposition, interpolation, rotation, bilobed).

Advancement flaps

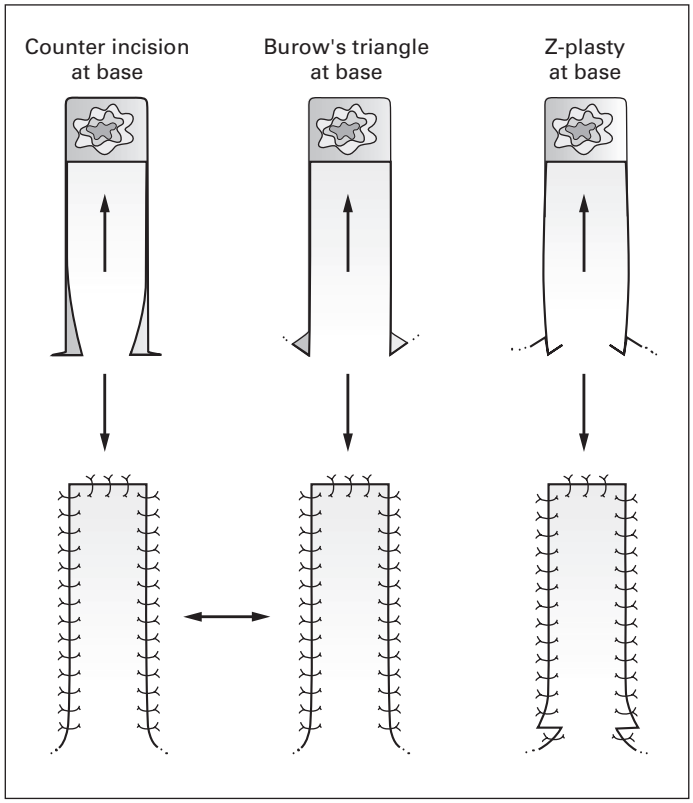
Simple

- Rely on skin elasticity.



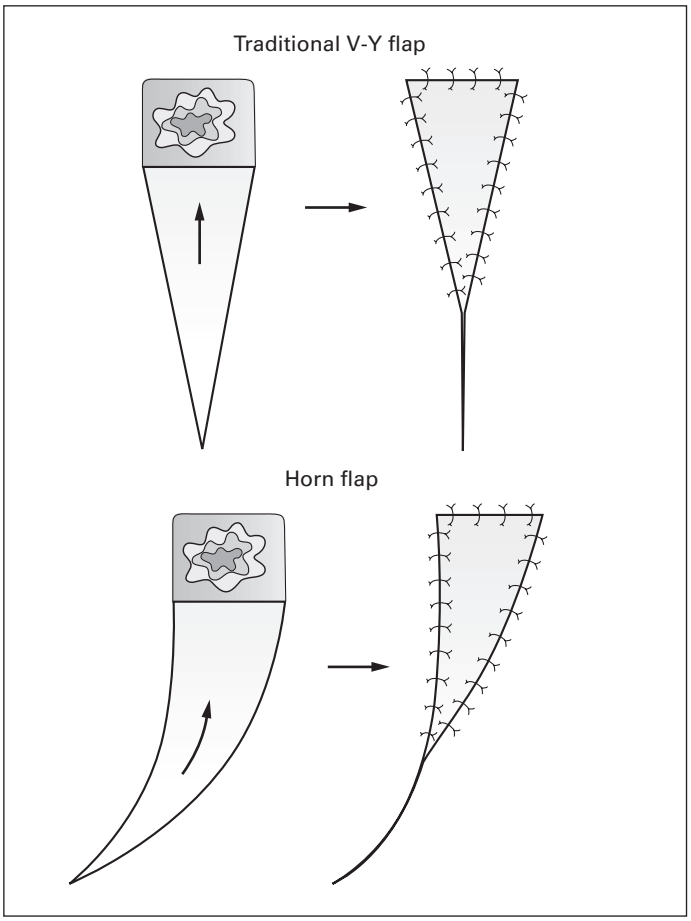
Modified

- Incorporate one of the following at the flap's base to increase advancement:
  - Counter incision
  - Excision of Burow's triangle
  - Z-plasty.



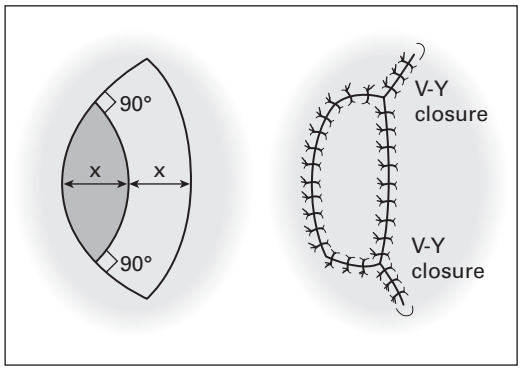
V-Y

- These are incised along their cutaneous borders.
- Their blood supply comes from deep tissue through a subcutaneous pedicle.
- Horn flaps and oblique V-Y flaps are modifications of the original V-Y.



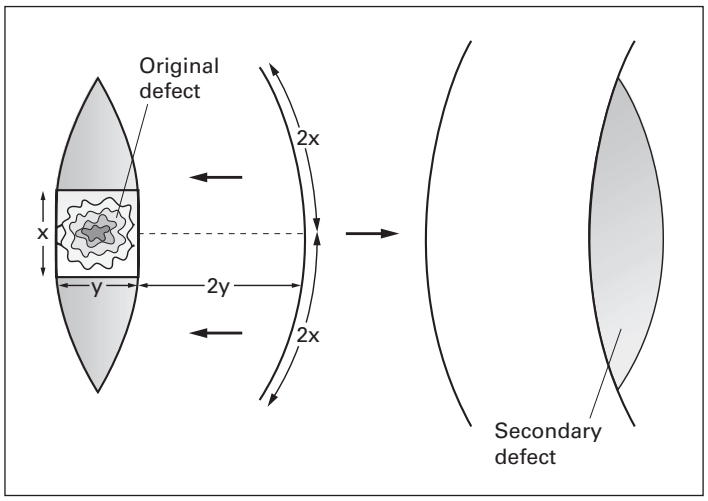
Keystone

- Trapezoidal flaps used to close elliptical defects.
- Essentially two V-Y flaps end-to-side.
- Designed to straddle longitudinal structures, e.g. superficial nerves and veins, which are incorporated into the flap.
- Blunt dissection to deep fascia preserves perforators and subcutaneous veins.
- The lateral deep fascial margin can be incised for increased mobilisation.
- The extremes of the donor site are closed as V-Y advancements, which produces transverse laxity in the flap.



Bipedicled

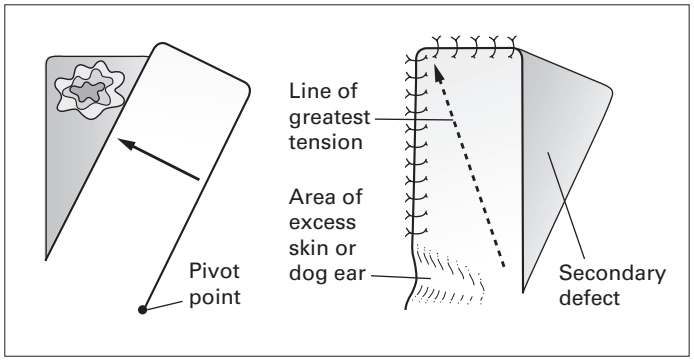
- Receive blood supply from both ends.
- Less prone to necrosis than flaps of similar dimensions attached only at one end.
- Example: von Langenbeck mucoperiosteal flap, used to repair cleft palates.
- Bipedicled flaps are designed to curve parallel with the defect.
  - This permits flap transposition with less tension.



Pivot flaps

Transposition flaps

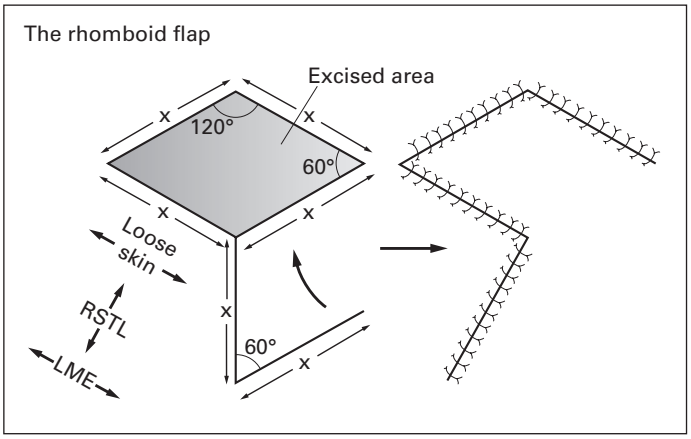
- Transposed into the defect, leaving a donor site that is closed by some other means (often a skin graft).



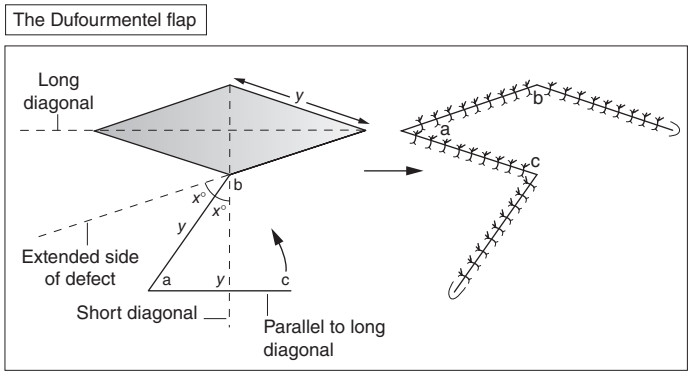
Transposition flaps with direct closure of donor site

- Include the rhomboid flap (Limberg flap) and Dufourmentel flap.
- These are similar in concept but vary in geometry.
- Both are designed to leave the donor site scar parallel to RSTLs.

The rhomboid flap

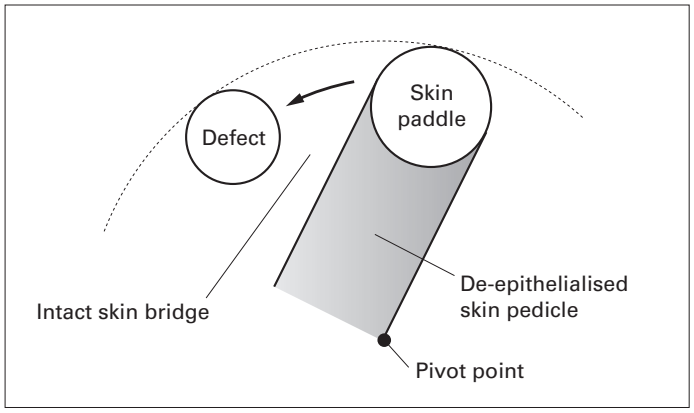


The Dufourmentel flap



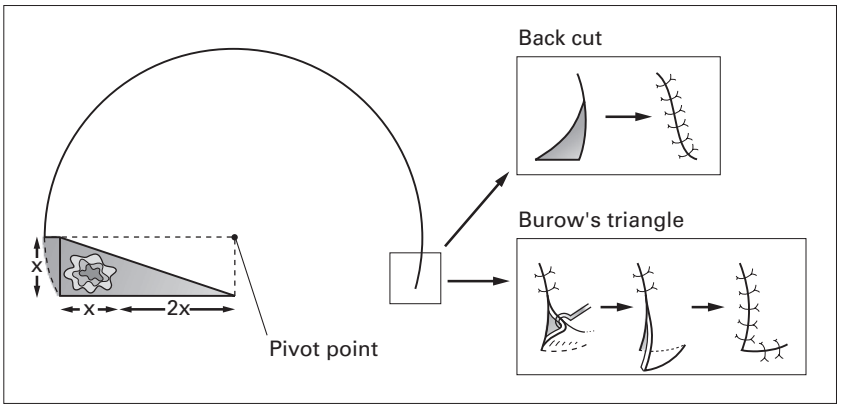
Interpolation flaps

- Flaps raised from local, but not adjacent, skin.
- The pedicle is passed either over or under an intervening skin bridge.



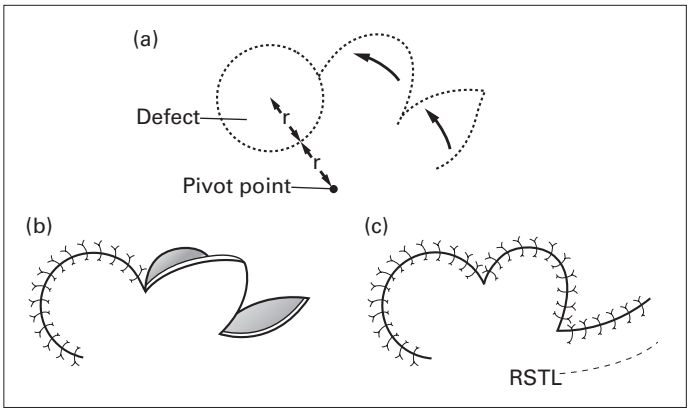
Rotation flaps

- These large flaps rotate tissue into the defect.
- Tissue redistribution usually permits direct closure of the donor site.
- Flap circumference should be 5–8 times the width of the defect.
- These are used on the scalp for hair-bearing reconstruction.
- The back cut at the flap's base can be directed towards or away from the defect.



The bilobed flap

- Various designs have been described.
- Consists of two transposition flaps.
- The first flap is transposed into the original defect.
- The second flap is transposed into the secondary defect – the donor site of the first flap.
- The tertiary defect at the donor site of the second flap closes directly.
  - This suture line is designed to lie parallel to RSTLs.
- Esser, who first described the flap, put the first flap at 90° to the defect and the second flap at 90° to the first flap.
- Zitelli modified these angles to 45° each, resulting in smaller dog ears.



Wound healing and skin grafts

- Healing by primary intention
  - Skin edges are directly opposed.
  - Healing is normally good, with minimal scar formation.

- Healing by secondary intention
  - The wound is left open to heal by a combination of granulation tissue formation, contraction and epithelialisation.
  - More inflammation and proliferation occurs compared to primary healing.
- Healing by tertiary intention
  - Wounds are initially left open, then closed as a secondary procedure.

Phases of wound healing

1 Haemostasis
2 Inflammation
3 Proliferation
4 Remodelling.

Haemostasis

- Vasoconstriction occurs immediately after vessel division due to release of thromboxanes and prostaglandins from damaged cells.
- Platelets bind to exposed collagen, forming a platelet plug.
- Platelet degranulation activates more platelets and increases their affinity to bind fibrinogen.
  - Involves modification of membrane glycoprotein IIb/IIIa (blocked by clopidogrel).
- Platelet activating factor (PAF), von Willebrand factor (vWF) and thromboxane A_2 stimulate conversion of fibrinogen to fibrin.
  - This propagates formation of thrombus.
- Thrombus is initially pale when it contains platelets alone (white thrombus).
- As red blood cells are trapped, the thrombus becomes darker (red thrombus).

Inflammation

- Occurs in the first 2–3 days after injury.
- Stimulated by physical injury, antigen–antibody reaction or infection.
- Platelets release growth factors, e.g. platelet-derived growth factor (PDGF).
  - Also release proinflammatory factors, e.g. serotonin, bradykinin, prostaglandins, thromboxanes and histamine.
  - These increase cell proliferation and migration.
- Endothelial cells swell, causing vasodilatation and allowing egress of polymorphonuclear neutrophils (PMNs) and monocytes into the tissue.
- T lymphocytes migrate into the wound under the influence of interleukin-1.
- Lymphocytes secrete various cytokines, including epidermal growth factor and basic fibroblast growth factor (bFGF).
  - They also play a role in cellular immunity and antibody production.

Proliferation

- Begins on the 2nd or 3rd day and lasts for 2–4 weeks.
- Monocytes mature into macrophages that release PDGF and transforming growth factor-β (TGF-β), which are chemoattractant to fibroblasts.
- Fibroblasts, usually located in perivascular tissue, migrate along fibrin networks into the wound.

- Fibroblasts secrete GAGs to produce ground substance, and then produce collagen and elastin.
  - Initially, type III collagen is produced to increase the strength of the wound.
- Some fibroblasts differentiate into myofibroblasts and effect wound contraction.
- Angiogenesis occurs concurrently to supply oxygen and nutrients to the wound.
  - Endothelial stem cells from blood vessels migrate through extracellular matrix.
  - Attracted to the wound by angiogenic factors, thrombus and local hypoxia.
- Zinc-dependent matrix metalloproteinases aid cell migration through tissues.

Remodelling

- Begins 2–4 weeks after injury and can last a year or longer.
- During remodelling there is no net increase in collagen (collagen homeostasis).
- Type III collagen is replaced by the stronger type I collagen.
- Collagen fibres, initially laid down haphazardly, are arranged in a more organised manner.
- The wound's tensile strength approaches 50% of normal by 3 months; eventually becomes 80% as strong.
- The extensive capillary network is no longer required and is removed by apoptosis, leaving a pale collagen scar.

Abnormal scars

- Classified as either hypertrophic or keloid.
  - Keloids extend beyond the original wound margins.
  - Hypertrophic scars are limited to original wound margins; commoner than keloids.
- Increased numbers of mast cells in abnormal scars may account for the pruritus experienced by some patients.

Hypertrophic scars

- Usually occurs within 8 weeks of wounding.
- Grow rapidly for up to 6 months before gradually regressing to a flat, asymptomatic scar.
  - This may take a few years.
- Typically form at locations under tension, e.g. shoulders, neck, presternal area, knees, ankles.
- Microscopy shows well-organised type III collagen bundles with nodules containing myofibroblasts.

Keloid scars

- Dark-skinned individuals are more prone to keloid scars.
- There is often a family history.
- May develop at any point up to several years after minor injuries.
- Typically persist for long periods of time and do not regress spontaneously.
- Pain and hypersensitivity are associated more with keloids than hypertrophic scars.
- Commonly form on anterior chest, shoulders, earlobes, upper arms and cheeks.
- Excision typically results in recurrence.

- Microscopy shows poorly organised type I and III collagen bundles with few myofibroblasts.
- Expression of proliferating cell nuclear antigen (PCNA) and p53 is upregulated.

Epithelial repair

- If the epidermal basement membrane is not breached, epithelial cells are replaced by upward migration of keratinocytes as in uninjured skin.
- If the basement membrane is breached, re-epithelialisation must occur from the wound margins and, if present and intact, from epidermal appendages.
- Re-establishing epithelial continuity consists of these four phases:

Mobilisation

- Epithelial cells at the wound edges elongate, flatten and form pseudopodia.
- They detach from neighbouring cells and basement membrane.

Migration

- Decreased contact inhibition promotes cell migration.
- Epithelial cells climb over one another to migrate.
- As cells migrate, epithelial cells at the wound edge proliferate to replace them.
- Cells migrate until they meet those from the opposite wound edge.
- At this point, contact inhibition is reinstituted and migration ceases.

Mitosis

- Epithelial cells proliferate once they have covered the wound.
- They secrete proteins to form a new basement membrane.
- Cells reverse the morphological changes required for migration.
- Desmosomes and hemidesmosomes are re-established to anchor themselves to the basement membrane and to each other.
- This new epithelial cell layer forms a stratum germinativum and undergoes mitosis as in normal skin.

Cellular differentiation

- The normal structure of stratified squamous epithelium is re-established.

Collagen

- Constitutes approximately 30% of total body protein.
- Formed by hydroxylation of amino acids lysine and proline by enzymes that require vitamin C as a cofactor.
- Procollagen is initially formed within the cell.
- Procollagen is transformed into tropocollagen after it is excreted from the cell.
- Fully formed collagen has a complex structure.
  - Consists of three polypeptide chains wound in a left-handed helix.
  - These three chains are further wound in a right-handed coil to form the basic tropocollagen unit.

- Collagen formation is inhibited by colchicine, penicillamine, steroids and deficiencies of vitamin C and iron.
- Cortisol stimulates degradation of skin collagen.
- Thus far, 28 types of collagen have been identified.
- Each type shares the same basic structure but differs in the relative composition of hydroxylysine and hydroxyproline, and in the degree of cross-linking between chains.
- The five most common types are:
  - *Type I*: predominant in mature skin, bone and tendon.
  - *Type II*: present in hyaline cartilage and cornea.
  - *Type III*: present in healing tissue, particularly fetal wounds.
  - *Type IV*: predominant constituent of basement membranes.
  - *Type V*: similar to type IV. Also found in hair and placenta.
- The ratio of type I collagen to type III collagen in normal skin is 5:1.
  - Hypertrophic and immature scars contain ratios of 2:1 or less.
- 90% of total body collagen is type I.

The macrophage

- Derived from mononuclear leukocytes.
- Debrides tissue and removes micro-organisms.
- Co-ordinates angiogenesis and fibroblast activity by releasing growth factors:
  - PDGF, FGF 1 and 2, tumour necrosis factor alpha (TNF-α) and TGF-β.
- Essential for normal wound healing.
- Wounds depleted of macrophages heal slowly.

The myofibroblast

- First identified by Gabbiani in 1971.
- Differs from a fibroblast – contains cytoplasmic filaments of α-smooth muscle actin, which are also found in smooth muscle.
- Actin fibres within myofibroblasts are thought to be responsible for wound contraction.
- The number of myofibroblasts within a wound is proportional to its contraction.
- Increased numbers have been found in the fascia of Dupuytren's disease.
  - Thought to be responsible for the abnormal contraction of this tissue.

TGF-β

- Macrophages, fibroblasts, platelets, keratinocytes and endothelial cells secrete this growth factor.
- Believed to play a central role in wound healing:
  - Chemoattraction of fibroblasts and macrophages
  - Induction of angiogenesis
  - Stimulation of extracellular matrix deposition
  - Keratinocyte proliferation.
- Three isoforms have been identified:
  - Types 1 and 2 promote wound healing and scarring; upregulated in keloids.
  - Type 3 decreases wound healing and scarring – may have a role as an antiscarring agent.

- Fetal wounds have higher levels of TGF-β3 than adult wounds.
  - TGF-β3 is thought to antagonise TGF-β1 and 2.
  - May be one factor responsible for decreased inflammation and improved scarring observed in fetal tissue.

Factors affecting healing

- Systemic
  - Congenital
  - Acquired
- Local.

Systemic factors: congenital

Pseudoxanthoma elasticum

- Autosomal recessive.
- Characterised by increased collagen degradation and mineralisation.
- Skin is pebbled and extremely lax.
- Most have premature arteriosclerosis in their 30s.

Ehlers–Danlos syndrome

- Heterogeneous collection of connective tissue disorders.
- Most are autosomal dominant.
- Results from defects in synthesis, structure or cross-linking of collagen.
- Clinical features:
  - Hypermobile fingers
  - Hyperextensible skin
  - Fragile connective tissues.
- Surgery is avoided if possible – wound healing is poor.

Cutis laxa

- Presents in the neonatal period.
- Skin is abnormally lax.
- Patients have inelastic, coarsely textured, drooping skin.

Progeria

- Characterised by premature ageing.
- Clinical features:
  - Growth retardation
  - Wrinkled skin
  - Baldness
  - Atherosclerosis.

Werner syndrome

- Autosomal recessive.
- Skin changes similar to scleroderma.
- Elective surgery avoided whenever possible – healing is poor.

Epidermolysis bullosa

- Heterogeneous collection of separate conditions.
- Skin is very susceptible to mechanical stress.
- Blistering may occur after minor trauma (Nikolsky sign).
- The most severe subtype, dermolytic bullous dermatosis (DBD), results in hand fibrosis and syndactyly – the 'mitten hand' deformity.
- Patients may develop squamous cell carcinoma in areas of chronic erosion.

Systemic factors: acquired

Nutrition

- Vitamin A involved in collagen cross-linking; deficiency delays wound healing.
- Vitamin C required for collagen synthesis.
- Vitamin E acts as a membrane stabiliser; deficiency may inhibit healing.
- Zinc, copper and selenium are important cofactors for many enzymes; administration accelerates healing in deficient states.
- Hypoalbuminaemia is associated with poor healing.

Pharmacological

- Steroids decrease inflammation and subsequent wound healing.
- Cytotoxics damage basal keratinocytes.
- Non-steroidal anti-inflammatory drugs (NSAIDs) decrease collagen synthesis.
- Anti-TNF-α drugs used in rheumatoid may increase post-operative wound complications.

Endocrine abnormalities

- Diabetics often have delayed wound healing; this is multifactorial.
- Untreated hypothyroidism is associated with slow healing.

Age

- Cell multiplication rates decrease with age.
  - All stages of healing are therefore protracted.
- Healed wounds have decreased tensile strength in the elderly.

Smoking

- Nicotine is a sympathomimetic that causes vasoconstriction and consequently decreases tissue perfusion.
- Carbon monoxide in cigarette smoke decreases oxygen-carrying capacity of haemoglobin.
- Hydrogen cyanide in cigarette smoke poisons intracellular oxidative metabolism pathways.

Local factors

Infection

- Subclinical wound infection can impair wound healing.
- Wounds with $>10^5$ organisms per gram of tissue are considered infected and are unlikely to heal without further treatment.

Radiation
- Causes endothelial cell, capillary and arteriole damage.
- Irradiated fibroblasts secrete less collagen and extracellular matrix.
- Lymphatics are also damaged, resulting in oedema and an increased infection risk.

Blood supply
- Decreased tissue perfusion results in decreased wound oxygenation.
- Fibroblasts are oxygen-sensitive and their function is reduced in hypoxic tissue.
- Reduced oxygen delivery results from decreases in:
  - Inspired oxygen concentration
  - Oxygen transfer to haemoglobin
  - Haemoglobin concentration
  - Tissue perfusion.
- Decreased oxygen delivery to tissue reduces:
  - Collagen formation
  - Extracellular matrix deposition
  - Angiogenesis
  - Epithelialisation.
- Hyperbaric oxygen increases inspired oxygen concentration but its effectiveness relies on good tissue perfusion.

Trauma
- The delicate neoepidermis of healing wounds is disrupted by trauma.

Neural supply
- There is evidence that wounds in denervated tissue heal slowly.
- May contribute to delayed healing observed in some pressure sores, and in patients with diabetes and leprosy.
- Mechanisms are poorly understood, but may be related to levels of chemoattractant neuropeptides in the wound.

Fetal wound healing
- Tissue healing in the first 6 months of fetal life occurs by regeneration rather than scarring.
  - Regenerative healing is characterised by absence of scarring.
- Normal dermal structures such as hair follicles form normally.
- Regenerative healing differs from adult healing:
  - Reduced inflammation.
  - Reduced platelet aggregation and degranulation.
  - Reduced angiogenesis.
  - Epithelialisation is more rapid.
  - Virtually no myofibroblasts and no wound contraction.
  - Collagen deposition is rapid, organised and not excessive.
  - More type III than type I collagen is laid down.
  - The wound contains more water and hyaluronic acid.
- Relative proportions of TGF-β isoforms may be responsible for some of these differences.

Skin grafts

- Skin grafts are either full or split thickness.
- Split-skin grafts contain the epidermis and a variable amount of dermis.
  - Usually harvested from thigh or buttock.
- Full-thickness skin grafts contain the entire epidermis and dermis.
  - Usually harvested from areas that allow direct closure of the donor defect.
- Primary contraction is the immediate recoil observed in freshly harvested skin.
  - Due to elastin in the dermis.
- Secondary contracture occurs after the graft has healed.
  - Due to myofibroblast activity.
- The thicker the graft, the greater the degree of primary contraction.
- The thinner the graft, the greater the degree of secondary contracture.

Mechanisms

- Skin grafts heal in four phases:

Adherence

- Fibrin bonds form immediately on applying skin graft to a suitable bed.

Serum imbibition

- Grafts swell in the first 2–4 days after application.
- This results from absorption of fluid (serum imbibition).
- The nutritive value of serum imbibition in maintaining graft viability is debated.

Revascularisation

- After 48–72 hours, capillary buds from the recipient bed have formed a fine vascular network in the fibrin layer between graft and wound.
- Vessel ingrowth into skin grafts begins around the 4th day.
- The mechanism of revascularisation is uncertain and may be via:
  - Inosculation – direct anastomosis between vessels in the graft and those in recipient tissue.
  - Revascularisation – new vessel ingrowth from recipient tissue along the graft's vascular channels.
  - Neovascularisation – new vessel ingrowth from recipient tissue along new channels in the graft.

Remodelling

- The histological architecture of the graft returns to that of normal skin.

Reasons for graft failure

Haematoma

- Most common cause of graft failure.

- Risk of haematoma formation is minimised by:
  - Meticulous haemostasis
  - Use of meshed skin graft, which allows blood to escape
  - Application of a firm dressing.

Infection
- Generally, skin grafts will not take if the bacterial count of the recipient site exceeds 10^5 organisms per gram.
- Group A β-haemolytic *Streptococcus* can destroy grafts when present in much fewer numbers.
  - This ability is attributed to secretion of proteases, such as streptokinase and hyaluronidase, which prevent adhesion.

Seroma
- Fluid collection under the graft reduces the likelihood of successful take.

Shear
- Lateral force applied to a graft.
- Results in disruption of the delicate connections between graft and bed.

Inappropriate bed
- Skin grafts will not survive on bare cartilage, tendon and endochondral bone denuded of periosteum.
- Membranous bone, found in some areas of the skull, will accept a skin graft.
- Grafts on previously irradiated wound beds are prone to failure.

Technical error
- An assortment of technical errors can result in graft failure.
- Examples: upside down graft placement, graft desiccation.

Bone healing and bone grafts

- Bones are derived from mesenchyme.
- Composed of organic matrix (osteoid), which is mineralised by hydroxyapatite (a calcium salt).
- Embryologically, bones form by one of two mechanisms.

1 Intramembranous ossification
- Occurs by deposition of bone within a vascularised membranous template.
- Examples: flat bones of the face, calvarium and ribs.

2 Endochondral ossification
- Develops from a cartilage precursor, or anlage.
  - In German, *Anlage* means primordium, plan or template.
- Examples: all long bones and the iliac crest.

Bone structure

- All bones have an outer cortical layer and an inner cancellous layer.
  - The cancellous part of membranous bone is in the diploic space.
- Cancellous bone consists of loosely woven trabeculae of organic and inorganic bone.
- Cortical bone consists of:
  - Multiple columnar bone units (osteons), composed of a central longitudinal canal (Haversian canal) that contains a central blood vessel.
  - Transverse nutrient canals (Volkmann canals) connecting adjacent osteons.
- Bone is laid down in concentric layers around each Haversian canal.
- Osteocytes are scattered throughout osteons, each within its own space (lacuna).

Blood supply to bone

1 Periosteal vessels at the sites of muscle attachment.
2 Apophyseal vessels at the sites of tendon and ligament attachment.
3 Nutrient arteries supplying the medullary cavity (endosteal supply).
4 Epiphyseal vessels supplying growth plates.

Bone healing

- The phases of bone healing are similar to those of wound healing.
  1 Haematoma formation
  2 Inflammation
    – Fracture haematoma is gradually replaced by granulation tissue.
    – Osteoclasts remove necrotic bone.
  3 Cellular proliferation
    – Stem cell recruitment.
    – Periosteal proliferation occurs on the outer aspect of the cortex.
    – Endosteal proliferation occurs on the inner aspect of the cortex.
  4 Callus formation
    – Callus consists of immature woven bone produced by osteoblasts and hyaline cartilage produced by chondroblasts.
    – This soft callus (osteoid) is mineralised with hydroxyapatite to form hard callus (mature woven bone).
  5 Remodelling
    – Woven bone is slowly replaced by lamellar bone.
    – This lasts until cortical structure and medullary cavity are restored.
- Osteoblasts form new bone by producing osteoid.
  - Derived from osteoprogenitor cells, under the influence of bone morphogenetic proteins (BMPs).
  - They produce alkaline phosphatase, which has a role in bone mineralisation.
- Osteoclasts are responsible for bone resorption.
  - Derived from monocyte stem cells, similar to macrophages.
  - They are large, multinucleate cells capable of phagocytosis.
- Osteocytes are osteoblasts that have become trapped within lacunae in bone matrix.
  - They maintain bone matrix and contribute to calcium homeostasis.

- Osteoid is the unmineralised, organic component of bone.
  - Consists of proteins and ground substance made by osteoblasts.
  - Type I collagen is the main protein; ground substance comprises chondroitin sulphate and osteocalcin.

Primary bone healing

- This is healing without callus formation.
- Occurs if bone ends are directly apposed and fixed with absolute stability.
- Fracture haematoma is removed during surgery.
- The bone is 'tricked' into thinking it was never fractured.
- Inflammatory and proliferative phases of healing do not occur.
- Rather, it is a process of osteonal bone remodelling:
  - Osteoclasts 'drill' across the fracture site from one cortex to the other.
  - The tunnel allows blood vessels and osteoblasts to cross the fracture.
  - This establishes new Haversian systems and normal bone architecture.

Secondary bone healing

- This is healing by callus formation.
- Occurs if fragments are not rigidly fixed, or if a gap exists between bone ends.
- It cannot occur if there is no fracture haematoma.

Complications of fractures

- Delayed union
- Non-union
- Malunion – rotation, angulation, shortening
- Infection
- Avascular necrosis (AVN)
- Damage to adjacent structures.

Bone graft healing

- Bone graft materials may be:
  - Biological
    - Autograft, allograft, xenograft
  - Engineered biological
    - Growth factors, recombinant BMPs, stem cells, platelet-rich plasma concentrate (PRPC)
  - Synthetic
    - Metals, ceramics, polymers.
- Gold standard is autologous bone graft, usually harvested from iliac crest.
- Autologous bone grafts heal by these mechanisms:

Incorporation

- This is adherence of the graft to the host tissue.
- Incorporation is maximised in immobilised, well-vascularised tissue.

Osseoconduction
- Bone graft acts as a scaffold along which vessels and osteoprogenitor cells travel.
- Old bone is resorbed as new is deposited.
- Also known as creeping substitution.

Osseoinduction
- This is differentiation of mesenchymal cells within local tissue into osteocytes.
- Osteoclasts, osteoblasts and osteocytes within bone graft are not capable of mitosis.
- Increased numbers of these cells within bone graft are derived from the recipient site.
- Osseoinduction is controlled by BMPs.

Osteogenesis
- This is formation of new bone by surviving cells within the bone graft.
- It is how most new bone is formed in vascularised bone grafts (bone flaps).
- Vascularised bone grafts incorporate more rapidly this way, without creeping substitution.
- Not much osteogenesis occurs in non-vascularised bone grafts.

Survival of bone grafts
- Factors influencing survival of bone grafts include:
  1 Systemic factors
  2 Intrinsic graft factors
  3 Factors relating to the placement of the graft.

Systemic factors
- Age
- Nutrition
- Immunosuppression
- Drugs
- Diabetes
- Smoking
- Obesity.

Intrinsic graft factors
- Grafts with periosteum included undergo less resorption than those without.
- Membranous bone undergoes less resorption than endochondral bone when used as onlay grafts in the face.
- Cancellous grafts are more easily revascularised than cortical grafts.

Graft placement factors
Orthotopic or heterotopic placement
- Orthotopic – graft is placed into a position normally occupied by bone.
- Heterotopic – graft is placed into a position not normally occupied by bone.
- Grafts in an orthotopic position are less prone to resorption.

Quality of the recipient bed
- Radiotherapy, scarring and infection adversely affect graft survival.

Graft fixation
- Rigidly fixed grafts survive better than mobile ones.

Site of graft placement
- Grafts survive better in areas in which bone is normally laid down (depository sites).
  - Includes areas such as zygoma and mandible in children.

Cartilage healing and cartilage grafts

Cartilage structure
- Derived from condensed mesenchyme.
- Differentiates into chondroblasts that secrete extracellular matrix.
- Chondroblasts eventually get trapped in lacunae within the matrix and become chondrocytes.
- The matrix contains type II collagen, elastin and ground substance (GAGs).
- Cartilage is classified according to the relative proportions of these three matrix components into:
  1 Hyaline cartilage
  2 Fibrocartilage
  3 Elastic cartilage.
- Its molecular structure confers tensile strength and elasticity.
- This facilitates absorption and distribution of mechanical loads.
- Large amounts of water within the matrix help maintain its three-dimensional structure.
- Its viscoelastic properties allow it to resume its original shape after deformation.

Cartilage nutrition
- Cartilage has no intrinsic blood, nerve, or lymph supply.
- Its water content is important because it relies on diffusion of nutrients and oxygen through the matrix.

Cartilage healing
- Chondrocytes show little reparative ability; healing is typically fibrous.
- Lack of blood supply makes healing very slow.

Cartilage grafts
1 Autografts
2 Allografts
3 Xenografts.

Autografts

- These are the gold standard.
- Used for nose, ear and craniofacial reconstruction.
- Donor sites include:
  - Ear conchal bowl
  - Nasal septum
  - Costal cartilage.
- Most cartilage grows from the deep layer of perichondrial connective tissue.
  - Inclusion of perichondrium is therefore thought to be important for continued growth of cartilage after grafting.
- Cartilage has a low metabolic rate; it is resistant to the ischaemia associated with grafting.
- Compared with bone graft, it is more easily shaped and undergoes less resorption.
- One major drawback is warping.
  - This is a tendency to deform under mechanical stress over several days.
- Gillies in 1920 noted that cartilage carved on one side would curve towards the opposite side.
- This was originally thought to be due to tension in the perichondrium, but its removal did nothing to prevent warping.
- Experiments subsequently showed the outer layer of cartilage acted as a 'taut skin', preventing it from expanding on the intact side.
  - This phenomenon, known as Gibson's principle, has practical use in prominent ear correction by the anterior scoring method.
- Warping is most noticeable in the nasal dorsum due to thin overlying skin.
- The naturally straight segment of the 10th or 11th rib shows minimal tendency to warp.
- Most warping of cartilage grafts occurs within 60 minutes of transplantation, and continues for at least 4 weeks.
- For this reason, delaying implantation for at least 30 minutes after harvest is advocated.
  - This allows the cartilage to assume its eventual curvature prior to fixation.

Allografts

- Cartilage allografts are generally unsuccessful in plastic surgery.
- The matrix is non-immunogenic and protects chondrocytes from circulating lymphocytes.
- However, once the matrix breaks down, chondrocytes are exposed and undergo rejection.
- This explains the slow but steady resorption of cartilage allografts.

Xenografts

- These remain immunogenic even after processing.
- They are therefore unsuitable for human implantation.

Nerve healing and nerve grafts

Nerve anatomy and function

- Nerve cells (neurons) consist of a cell body from which nerve fibres project.
- Outgoing impulses are carried by nerve fibres called axons.

- Impulses are received either on the cell body or nerve fibres called dendrites.
- Endoneurium surrounds individual nerve fibres or axons.
- Perineurium surrounds groups of nerve fibres (fascicles).
- Intraneural epineurium contains blood vessels and surrounds perineurium.
- The outer epineurium surrounds groups of fascicles to form a peripheral nerve.
- Schwann cells produce the multilaminated myelin sheath of myelinated nerves.
- Unmyelinated nerves are ensheathed by a Schwann cell-derived double basement membrane.
- Schwann cells of myelinated nerves abut at nodes of Ranvier.
- Nerve conduction involves passage of an action potential along a nerve.
- The impulse in myelinated nerves jumps between adjacent nodes of Ranvier.
  - Known as saltatory conduction.
- Nerve fibres are classified based on their diameter:

Group A

- Myelinated, large-diameter, high-conduction velocity nerves.
  - Group A-α fibres: motor and proprioception.
  - Group A-β fibres: pressure and proprioception.
  - Group A-γ fibres: motor to muscle spindles.
  - Group A-δ fibres: pain, touch, temperature.

Group B

- Myelinated, small-diameter, low-velocity fibres.
- Found in preganglionic autonomic nerves.

Group C

- Unmyelinated, small-diameter, low-velocity fibres, found in:
  - Postganglionic autonomic nerves
- Dorsal root nerves for pain, temperature, touch, pressure and itch.

Medical Research Council grading of nerve function

- The MRC have recommended the following grading of nerve function:

Motor function		Sensory function	
M0	No contraction	S0	No sensation
M1	Flicker	S1	Pain (deep)
M2	Movement with gravity eliminated	S1+	Pain (superficial)
M3	Movement against gravity	S2	Pain and some touch
M4	Movement against resistance	S2+	S2 with over-response
M5	Normal	S3	S2 without over-response
		S3+	Imperfect two-point discrimination
		S4	Normal

Injury

- After nerve transection, degeneration occurs proximally to the nearest node of Ranvier.
- Distally, nerves undergo Wallerian degeneration.
- This process was described by Waller in 1850 and consists of:
  - Degeneration of axons and myelin.
    - Phagocytosed by macrophages and Schwann cells.
  - Remaining basement membranes form endoneurial tubes that have a bandlike appearance on electron microscopy.
    - Known as bands of Büngner.
    - Important for guiding regenerating axons to their targets.
- Neurotropism is selective, directional growth of fibres towards end organs.
  - Mediated by nerve growth factors and cell–cell interactions:
    1. The proximal axon sprouts many new daughter axons, forming a growth cone.
    2. Fibres growing in an inappropriate direction atrophy.
    3. Those growing in the correct direction survive.
- Neurotrophism is non-selective, non-directional growth of nerve fibres.
- Neurotrophic factors are almost all produced by Schwann cells:
  - Growth factors
    - Nerve growth factor, ciliary neurotrophic factor, insulin-like growth factor.
  - Extracellular matrix components
    - Fibronectin, laminin, neural cell adhesion molecule, N-cadherin.

Classification of nerve injury

- Degree of nerve injury has been classified by Seddon and Sunderland.
- Seddon classification:
  1. Neurapraxia
  2. Axonotmesis
  3. Neurotmesis.
- Sunderland expanded this classification:

First-degree injury

- Axon remains in continuity although conduction is impaired.
- Recovery should be complete.

Second-degree injury

- Axonal injury occurs and the segment of nerve distal to the site of damage undergoes Wallerian degeneration.
- All connective tissue layers remain intact and recovery should be good.

Third-degree injury

- Axon and endoneurium are divided.
- Perineurium and epineurium remain intact.
- Recovery should be reasonable.

Fourth-degree injury
- Complete division of all intraneural structures.
- Epineurium remains intact.
- Recovery of some function is expected.
- May result in a neuroma-in-continuity.

Fifth-degree injury
- Nerve trunk completely divided.
- Early surgical repair is mandatory for any recovery.

- Mackinnon added a sixth-degree injury to the classification.
  - This is a mixed pattern nerve injury with segmental damage.
- Seddon's neurapraxia equates to a Sunderland first-degree injury.
- Axonotmesis equates to a second-, third- or fourth-degree injury.
- Neurotmesis equates to a fifth-degree injury.

Nerve repair
- Nerve repair by direct approximation should be performed where possible.
- Nerve ends are trimmed and an epineurial repair under magnification with fine sutures is done.
- Fascicles of nerve trunks should be aligned if possible.
- Repairs should not be under undue tension.
- Some authorities state primary repair should only be performed when a single 9/0 suture is strong enough to appose the nerve ends.
- Clinical studies have not shown clear superiority of fascicular repair over epineurial repair.

Fascicular identification
- The following can aid fascicular matching during nerve repair.

Matching of anatomical structures
- Size and orientation of fascicles
- Distribution of vessels on the nerve's surface.

Electrical stimulation
- Motor nerves respond to stimulation for up to 72 hours after division.
- Stimulation of the distal stump can differentiate motor from sensory fibres.
- Stimulation in a conscious patient can differentiate motor from sensory fibres in the proximal stump:
  - Stimulation of sensory fibres produces sharp pain.
  - Stimulation of motor fibres feels like a dull ache.

Knowledge of internal nerve topography
- The fascicular layout of many nerves is known and can be used to aid accurate repair.
- Ulnar nerve motor fascicles lie centrally between volar sensory branches from the palm and dorsal sensory branches from the dorsal hand.

Nerve grafts

- Required if primary repair not possible without undue tension.
- For large nerves, multiple cables of smaller donor nerves may be required to bridge the defect.
- Tension across the repair can be reduced by mobilising the nerve proximally and distally, and:
  - Anterior transposition of the ulnar nerve at the elbow.
  - Intratemporal dissection of the facial nerve.
- Nerve gaps can be bridged by autografts, allografts, or synthetic materials.
  - Autologous nerve is the gold standard.

Composition

- Autologous tissues used to bridge nerve gaps include:
  - Fresh nerve
  - Freeze–thawed muscle
  - Segments of vein.
- Allograft nerves require systemic immunosuppression to prevent rejection.
- Immunosuppression is withdrawn after Tinel's sign has progressed into the distal nerve.
- Tacrolimus is the immunosuppressant of choice due to its neuroregenerative properties.
- Absorbable synthetic nerve tubes of polyglycolic acid have been trialled.

Autologous grafts

- Common sources of autologous grafts:

Sural nerve

- Passes behind lateral malleolus.
- Proximally, it divides into medial sural and peroneal communicating branches.
- Lengths up to 30–40 cm are available in adults.
- Can be harvested endoscopically.

Lateral antebrachial cutaneous nerve

- Lies adjacent to cephalic vein alongside ulnar border of brachioradialis.
- Lengths up to 8 cm are available.
- Harvest results in limited loss of sensation due to territory overlap with adjacent nerves.

Medial antebrachial cutaneous nerve

- Found in the groove between triceps and biceps, alongside basilic vein.
- Distally, divides into anterior and posterior branches.
- Posterior branch preserved if possible – supplies the resting part of elbow and forearm.
- Lengths up to 20 cm are available.

The terminal branch of the posterior interosseous nerve

- Useful for bridging small defects in small-diameter nerves.
- Located in the base of the fourth extensor compartment of the wrist.
- Only a relatively short length of nerve graft is available.

Principles
- Both nerve ends are trimmed back to healthy tissue.
- Grafts are reversed to funnel regenerating axons distally.
- Place grafts on a healthy vascular bed, or transfer as a vascularised graft.
- Avoid tension on the graft.
- Stagger the level of repair between separate cables.
- Separate cables from each another as they bridge the defect.
- Proper sensory and motor alignment should be restored.

Tendon healing

Anatomy
- Tendons are composed of dense, metabolically active connective tissue.
- Collagen bundles are arranged in a regular spiralling fashion.
  - Collagen is predominantly type I, with small amounts of types III and IV.
- Tendons contain few cells; those that are present include:
  - Tenocytes
  - Synovial cells
  - Fibroblasts.
- Endotendon encloses tendon bundles.
  - Continuous with perimysium proximally and periosteum distally.
- Epitenon is the outer layer of synovial tendons.
- Paratenon is a loose adventitial layer that surrounds extra-synovial tendons.
  - These layers contain blood vessels.
- Flexor tendons receive blood supply from:
  1. Musculotendinous junction
  2. Bony insertion
  3. Mesenteric vincular vessels.
- An avascular zone exists on the volar (frictional) surface of the tendon.
- Extensor tendon blood supply is similar, except that:
  1. A long mesotenon exists within the synovial-lined extensor retinaculum.
  2. There is no vincular supply.
- Over the dorsal wrist, extensor tendons are arranged into six synovial-lined compartments:
  - 1st compartment: abductor pollicis longus, extensor pollicis brevis.
  - 2nd compartment: extensor carpi radialis longus and brevis.
  - 3rd compartment: extensor pollicis longus.
  - 4th compartment: extensor indicis and extensor digitorum.
  - 5th compartment: extensor digiti minimi.
  - 6th compartment: extensor carpi ulnaris.

Mechanisms of tendon healing
Extrinsic healing
- Dependent on fibrous attachments forming between tendon sheath and tendon.

- Historically believed to be the sole mechanism of tendon healing.
- Led to development of post-operative protocols that immobilised tendons in the mistaken belief that this maximised tendon healing.

Intrinsic healing

- Dependent on:
  - Blood flow through long and short vinculae.
  - Diffusion of nutrients from synovial fluid.
- Lunborg showed tendons heal when wrapped in a semipermeable membrane and placed in the knee joint of a rabbit.
  - Enclosing the tendons in semipermeable membrane stimulates intrinsic healing as it permits passage of nutrients, but not cells.
- Discovery of intrinsic healing led to early post-operative mobilisation (see Chapter 5, 'Hand trauma').

Phases of tendon healing

- Similar to those of wound healing.

Inflammation

- Inflammatory cells infiltrate the wound.
- Secrete growth factors that attract fibroblasts.

Proliferation

- Fibroblasts are responsible for tissue proliferation.
- They secrete type III collagen and GAGs.
- Collagen is initially arranged randomly; consequently, the tendon lacks strength.

Remodelling

- Begins approximately 3 weeks following tendon injury.
- Type III collagen is replaced by type I.
- The tendon remodels into an organised structure.
- Early motion limits fibrous attachments between tendon and sheath.
  - It therefore promotes intrinsic healing at the expense of extrinsic healing.
  - Mobilised tendons are stronger than immobilised tendons.

Transplantation

- Transplantation is transfer of tissue from one body location to another.
  - Orthotopic transfers are transplants into an anatomically similar site.
  - Heterotopic transfers are transplants into an anatomically different site.
- Transplant tissue types are classified as follows:

1 Autografts

  - Transplantation within the same individual.
  - Includes all flaps and grafts.
  - Flaps carry intrinsic blood supply with them; grafts do not.

2 Isografts
- Transplantation between genetically identical individuals.

3 Allografts
- Transplantation between different individuals of the same species.
- Also called homografts.
- Large burns can be temporarily covered with allograft skin.

4 Xenografts
- Transplantation from one species to another.
- Previously called heterografts.
- Porcine skin grafts can be used as temporary cover for burns.
- Implantable materials, e.g. Permacol and Strattice, are modified porcine xenografts.

Transplant immunology

History

- Gibson and Medawar were pioneers of transplant immunology in the 1940s and 1950s.
- They described the second set phenomenon, defined as 'accelerated rejection of allogenic tissue due to the presence of humoral antibodies from prior exposure to the same allogenic source'.
- The first set reaction occurs when skin allograft is applied to an individual for the first time.
- The first set reaction is characterised by:
  1. During the first 1–3 days, allograft behaves in a fashion similar to autograft in that it develops dilated capillaries with no blood flow.
  2. Between 4 and 7 days, leukocytes and thrombi infiltrate the graft; punctate haemorrhages appear within its vessels.
  3. Between 7 and 8 days, blood flow ceases and the skin graft necroses.
- The second set reaction occurs in patients who have been previously grafted with the same allograft material.
- The second set reaction is characterised by:
  1. Immediate hyperacute rejection.
  2. The graft never undergoes any revascularisation, termed a 'white graft'.

Immunology

- Rejection occurs when the host immune system recognises foreign antigens.
- ABO blood group antigens are potent barriers to transplantation.
  - ABO matching is easily achieved but other antigens also mediate rejection.
- These antigens are encoded in the major histocompatibility complex (MHC).
  - In humans, these are known as human leukocyte antigens (HLAs).
- HLAs of significance are six closely linked genes on the short arm of chromosome 6 and are divided into two classes:
  - Class I: HLA-A, -B and -C; found on all nucleated cells and platelets.
  - Class II: HLA-DP, -DQ and -DR; found on APCs.
    - APCs include monocytes, macrophages, dendritic cells (called Langerhans cells in skin), B lymphocytes and activated T cells.
- HLA-A, -B and -DR are the most important mediators of tissue rejection.

- HLAs on APCs can be recognised by T cells via two separate pathways:
  1. Direct pathway
     - Unique to transplantation.
     - Recipient T cells recognise HLAs on donor APCs within transplanted tissue.
     - Initiates a strong immune response.
     - Thought to be the major route for initiating acute rejection.
  2. Indirect pathway
     - Physiological pathway activated in response to non-self antigens, e.g. viruses.
     - Recipient T cells recognise donor HLAs after processing by recipient APCs.
- Host immune response is co-ordinated by T helper (T_h) cells.
  - Activation of T_h cells by direct or indirect pathways induces them to differentiate along the T_h1 (cell-mediated response) or T_h2 (humoral response) route.
    - Release of IL-12 from APCs favours T_h1 differentiation; IL-4 favours T_h2 differentiation.
- T_h1 cells release the cytokines IL-2, IFN-γ, TNF-α and TNF-β.
  - These activate macrophages and natural killer (NK) cells that cause direct graft cell lysis.
    - Known as delayed type hypersensitivity (DTH) reaction.
  - Cytotoxic CD8 T cells are also stimulated to destroy allograft cells by inducing apoptosis (Fas activation) and releasing lytic enzymes.
- T_h2 cells release interleukins, particularly IL-4.
  - Stimulate B cells to mature into antibody-producing plasma cells.
  - These antibodies stimulate tissue destruction by complement fixation, or by targeting neutrophils, eosinophils, macrophages and NK cells to the graft.
- A combination of T_h1 and T_h2 responses occurs in most immune reactions.
- IL-2 is the principal T-cell growth factor.
  - An important target for immunosuppressive drugs.

Hyperacute rejection

- Occurs within minutes.
- Pre-existing antibodies to the donor, e.g. anti-ABO blood group antibodies, activate complement.
- The allograft must be removed immediately to prevent systemic inflammatory response.
- Seen with some xenografts:
  - Discordant transplantation occurs when natural antibodies between species are present, e.g. pig to human.
  - Concordant transplantation occurs when natural antibodies are not present, e.g. primate to human.

Acute rejection

- Occurs after 1 week due to the delay in T-cell activation.
- May occur years after transplantation.
- Usually treated with a short course of high-dose corticosteroids.
- Recurrent episodes may lead to chronic rejection.

Chronic rejection
- Poorly understood chronic inflammatory and immune response.
- Irreversible; treatments, other than re-transplantation, are ineffective.

Immunosuppression
- Subdivided into non-specific and specific modalities.
- Non-specific techniques of immunosuppresion:

Radiation
- Whole-body radiation removes mature lymphocytes; not used in humans.
- Localised lymphoid tissue irradiation is specifically targeted, e.g. thymus.
- Graft irradiation reduces antigenicity by destroying Langerhans cells in skin.

Drugs
- Three main groups of immunosuppressants:
  1. Steroids, e.g. prednisolone
     - Anti-inflammatory and immunosuppressive.
     - Usually used in combination with other agents.
  2. Cytotoxics, e.g. cyclophosphamide, methotrexate, mycophenolate mofetil, azathioprine.
     - Interfere with DNA replication; kill proliferating lymphocytes.
  3. Fungal or bacterial products, e.g. ciclosporin, tacrolimus, sirolimus.
     - Ciclosporin and tacrolimus block calcineurin activation.
       - Decrease production of IL-2 and subsequent T-cell activation.
     - Sirolimus (or rapamycin) is a newer drug that blocks lymphocyte proliferation and differentiation.
       - It inhibits mammalian target of rapamycin (mTOR) protein.

Biological agents
- Anti-lymphocyte serum is made by injecting another species with lymphoid tissue from the recipient.
- The resulting polyclonal anti-thymoglobulin (ATG) and anti-lymphocyte sera (ALS) deplete recipient T cells.
- Specific techniques of immunosuppression involve monoclonal antibodies directed towards specific antigens.
  - Basiliximab prevents IL-2-mediated clonal expansion of activated lymphocytes.
  - This is an area of intense research as new antibody targets are discovered.

Immunological tolerance
- Transplant research is focused on development of immunological tolerance.
- Tolerance is the state of immunologic acceptance or unresponsiveness of a recipient to donor allograft or xenograft.
- Induction of tolerance allows transplantation without need for immunosuppression.

Vascularised composite allotransplantation (VCA)

- VCA involves transplantation of various tissues such as skin, nerve, blood vessel, muscle and bone from one human to another.
- Previously known as composite tissue allotransplantation (CTA).
- Examples pertinent to plastic surgery include limb and face transplantation.

History

- A hand transplant was performed in Ecuador in 1963, but was acutely rejected within a few weeks.
- In 1997, the International Symposium on CTA was held in Louisville, Kentucky, to discuss possible human hand allotransplantation.
  - Concluded that it was appropriate to consider undertaking the procedure.
- The first successful hand transplant was performed in 1998 by an international surgical team assembled in Lyon, France.
  - This was repeated in 1999 by units in Louisville, USA and Guangzhou, China.
- Thus it became clear that modern immunosuppressive drugs could allow skin, muscle and bone allotransplants to survive and function.
- This stimulated interest in face transplantation.
- Facial transplantation was shown to be technically possible by a microsurgical team in India led by Abraham Thomas.
  - In 1994 they reattached the face and scalp of a 9 year-old girl after it was avulsed by a machine.
- In 2002, Peter Butler discussed the potential for face transplantation at the BAPS Winter Meeting.
- A working party set up by the Royal College of Surgeons of England examined all aspects of the proposed procedure.
  - They reported in 2003 that further research was required before facial transplantation could be performed.
- The Comité Consultatif National d'Ethique (CCNE) in France produced a report in 2004.
  - They concluded that a partial face transplant involving the mouth–nose triangle could be performed.
- The first successful partial face transplant was done in 2005 by a team based in Amiens, France.
- The first full face transplant was done in Barcelona by a Spanish team in 2010.
- At the time of writing, the most extensive face transplant was performed in 2012 at the R Adams Cowley Shock Trauma Center in Baltimore, Maryland.
  - The transplant replaced almost everything from the coronal plane of the scalp to the clavicles.
- The first British VCA was a right hand transplant performed by the UK Hand Transplant Programme in Leeds on 27th December 2012.

Technical considerations

- Routine techniques of microsurgery and organ harvest, refined over many years.

Biological considerations
- High rejection rates were anticipated due to the perceived high antigenicity of skin.
- This is not borne out in practice:
  - Immunosuppressant regimes for VCAs are virtually identical to those for solid organ transplantations.
  - Most employ either basiliximab or ATG for induction therapy, and triple maintenance therapy with tacrolimus, mycophenolate mofetil and prednisolone.

Ethical considerations
- Although VCAs enhance quality of life, they are not essential for life.
- Quality of life is a subjective judgement that varies between VCA recipients.

Psychological considerations
- These are at the forefront of VCA research.
- Transplantation may have unpredictable psychological effects:
  - Anxiety
    - Regarding the transplant, rejection, side effects of medication.
  - Identity
    - Integration of the VCA into body image, self-recognition.
  - Adjustment
    - Ability to adjust is not well predicted by the severity of disfigurement.

Consent
- Must be completed well in advance of a transplant.
  - There is insufficient time once a suitable donor is identified.

Patient selection
- A comprehensive and coherent protocol is used to select suitable patients.
- Should address physical, psychological and social attributes of the recipient.

Tissue engineering
- Langer and Vacanti, considered the fathers of tissue engineering, define this term as 'an interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain, or improve tissue function or a whole organ'.
- The first tissue-engineered implant was a chondrocyte-seeded synthetic scaffold shaped into a sternum.
  - Used to treat a case of Poland's syndrome in 1991.
- Engineered constructs made of patients' own cells do not require immunosuppression.
- Constructs may be created *in vitro* or *in vivo*.
- They use cells cultured from mature cells or adult-derived stem cells.
- Constructs can be pre-laminated with different cell types, e.g. skin, cartilage.

- Intrinsic blood supply can be provided by embedding engineered capillaries.
- A reliable extrinsic blood supply allows free vascularised transfer.
  - This would minimise risks of tissue necrosis and resorption.
- A method of achieving this *in vivo* is to use the capsule that forms around implanted foreign bodies.
  - Transposing a vascular pedicle onto a silicone mould will form a fibrous capsule that incorporates the pedicle vessels.
- The capsule provides:
  1 A closed compartment for cultured cells.
  2 Nutrients for cells via the capsule's blood supply.
  3 A bridge between intrinsic blood supply and incorporated vascular pedicle.
- After 2–3 weeks the capsule can be elevated on its pedicle and transferred to the recipient site.
- The silicone mould is removed and cultured cells are implanted into the capsule.
- Engineered autogenous tissue can then form.
- Neumeister famously achieved this in 2006 using an ear-shaped silicone block in a rat.
- Pairing an engineered intrinsic vascular supply with an engineered extrinsic vascular pedicle could potentially allow 'spare parts' to be completely manufactured *ex vivo*.

Alloplastic implantation

- The ideal implant should be:
  1 Non-allergenic, causing minimal soft tissue reaction.
  2 Strong and fatigue resistant, but easy to shape and mould.
  3 Resistant to absorption, corrosion or deformation.
  4 Non-carcinogenic.
  5 Non-supportive of growth of micro-organisms.
  6 Sterilisable.
  7 Radiolucent.
  8 Inexpensive.
  9 Readily available.

Indications

- Stabilisation of fractures.
- Reconstruction or augmentation of soft tissue and bony defects.

Relative contraindications

- Implantation within a radiotherapy field.
- Poor surrounding blood supply.
- Tenuous soft tissue coverage.
- Infection.

Classification

- Implants can be classified into:

- Liquids (silicone, collagen preparations, hyaluronic acid preparations)
- Solids (metals, polymers, ceramics).

Liquids

Silicone

- Silicon is an element.
- Silica is silicone dioxide, commonly found as sand or quartz.
- Silicone consists of a monomer backbone of silicon and oxygen with methyl, vinyl, or phenol side groups in a varying number of repeating units.
- In medical terms, 'silicone' usually refers to polydimethylsiloxane.
- Short polymer chains produce a viscous liquid.
- Long polymer chains produce a firmer, cohesive gel.
- Cross-linking of the chains produces solid silicone.
- Silicone is biologically inert but elicits a mild foreign body reaction with subsequent capsule formation.
- Synovitis can occur when silicone prostheses are used in joint arthroplasty.
- Bioplastique™ consists of textured silicone-rubber microparticles mixed with water in a hydrogel carrier.
- The 'silicone controversy' is discussed in Chapter 4, 'Breast augmentation'.

Collagen preparations

Zyderm® 1 and 2

- Made from sterilised, fibrillar bovine dermal collagen.
- Composed of 95% type I collagen and 5% type III collagen.
- Forearm skin testing is required 4 weeks prior to treatment to exclude allergy.
- Effects last up to 6 months, until the body degrades the collagen.
- Collagen concentration in Zyderm 1 is 35 mg/ml, and 65 mg/ml in Zyderm 2.
- Administered by intradermal injection; used for superficial wrinkles.
- Absorption of the water carrier reduces the injected volume by 30%.
  - Defects should therefore be overcorrected initially.

Zyplast®

- Formed by cross-linking collagen with glutaraldehyde.
- Firmer than Zyderm 1 or Zyderm 2.
- Used to treat deep dermal defects and coarse rhytids.
- Little absorption occurs; overcorrection is not recommended.

Autologen™

- Harvested from autologous collagen.
- Autologous skin is obtained from skin biopsy or from excised skin after facelift or abdominoplasty.
- Skin is processed into a collagen suspension at concentrations of 25–100 mg/ml.
- It has two advantages over bovine collagen:
  1. Allergic reactions should not occur.
  2. Contains intact dermal collagen fibres that are more resistant to degradation.

Hyaluronic acid preparations

- A number of preparations composed of synthetic hyaluronic acid are available.
  - Examples: Restylane®, Perlane®, Juvéderm®.
- Average absorption rates are 20–50% of the original volume by 6 months.
- Do not tend to cause allergic reactions.
- Typically injected superficially, to treat wrinkles or increase lip definition.

Solids

Metals

Stainless steel

- Alloy of iron, chromium and nickel.
- Relatively high incidence of corrosion and implant failure.
- Galvanic currents between screws and plates can result in corrosion.

Vitallium

- Alloy of chromium, cobalt and molybdenum.
- Does not corrode like stainless steel.
- Higher tensile strength than stainless steel and titanium.

Titanium

- An element, not an alloy.
- Tensile strength similar to vitallium.
- May be alloyed with aluminium and vanadium for plates and screws.
- More malleable and less prone to corrosion than stainless steel or vitallium.
- Less likely to produce artefact on MRI or CT scanning.
- Titanium implants are synonymous with osseointegration.

Gold

- Resistant to corrosion but low tensile strength.
- Used primarily as an upper eyelid weight in facial palsy.

Polymers

Polyurethane

- Induces intense foreign body reaction, followed by tissue adhesion.
- Breast implants covered with polyurethane foam have a low rate of capsular contracture.
- Initial concerns about carcinogenesis from a polyurethane breakdown product (2,4 toluene diamine, TDA) in humans led to the withdrawal of these breast implants in 1991.
- However:
  - 2,4 TDA has not been found in the blood of patients with polyurethane implants.
  - 2,4 TDA found in urine was an artefact of the assay, which used strong hydrochloric acid boiled for an hour at 105 °C.
    - This cleaved 2,4 TDA from harmless polyurethane breakdown oligomers.

- The UK Committee on Carcinogenicity concluded that the carcinogenic risk of these implants is small and unquantifiable.
- They were reintroduced in the United Kingdom in 2005, but are not FDA approved in the United States at this time.

Fluorocarbons
- Bonding between fluorine and carbon results in an extremely stable biomaterial.
- No human enzyme can break the bond between these two elements.
- The most common fluorocarbon in surgery is polytetrafluoroethylene (PTFE).
  - Marketed as Teflon® by DuPont™.

Proplast® I
- A black composite of PTFE and carbon.
- Historically used for facial bony augmentation.

Proplast® II
- A white composite of PTFE and aluminium oxide.
- Historically used for more superficial augmentation.
- High complication rates (infection, extrusion, etc.) with Proplast temporomandibular joint implants resulted in its withdrawal from US markets.
- The manufacturer went into liquidation; these products are no longer available.

Gore-Tex®
- A sheet of expanded PTFE.
- Soft but strong and allows some tissue ingrowth.
- Available as sheets and blocks.
- Used for vascular prostheses since 1971.
- Approved for facial augmentation in the United States since 1994.

Polyethylene
- Has a simple carbon chain structure and does not contain fluorine.
- Available in three grades:
  1. Low density
  2. High density
  3. Ultra-high molecular weight.
- Medpor® is high-density, porous polyethylene.
  - Commonly used for augmenting the facial skeleton.
  - Elicits little foreign body reaction.
  - Some soft tissue ingrowth does occur, which stabilises the implant.
  - Implants are available in a variety of preformed shapes.
- Ultra-high molecular weight polyethylene used in load-bearing orthopaedic implants.

Polyester

- Dacron® is made from high-density fibres of polyethylene terephthalate (PET).
  - Preferred polymer for arterial prostheses.
- Biodegradable polyesters include polyglycolic acid and poly-L-lactic acid.
  - Degraded by hydrolysis over several months.
  - Available as miniplates, screws and distraction devices for craniofacial surgery.
- An absorbable injectable filler of poly-L-lactic acid microparticles is marketed as Sculptra®.

Polypropylene

- Structure similar to polyethylene.
- Has a methyl group instead of hydrogen atom in each monomer unit.
- Marlex® polypropylene mesh has high tensile strength and allows tissue ingrowth.

Polymethylmethacrylate (PMMA)

- Self-curing acrylic resin, used for:
  - Securing artificial joint components
  - Craniofacial bone augmentation
  - Fabrication of gentamicin-impregnated beads.
- Available in two forms:
  1. A paste that cures, forming a solid block
  2. Preformed implants.
- Methylmethacrylate elicits an exothermic reaction during curing.
- When used for calvarial remodelling, it should be cooled to avoid soft-tissue burns – temperatures up to 70 °C have been recorded.
- Artecoll® and Artefill® are permanent injectable fillers composed of PMMA microspheres suspended in 3.5% bovine collagen.
  - Injected subdermally and massaged to prevent clumping.
  - The collagen is absorbed but the PMMA is encapsulated.
  - 64% of patients reported lasting effects at 2-year follow-up.

Cyanoacrylate

- Main constituent of adhesives such as Super Glue®.
- Strong, biodegradable tissue adhesive.
- The adhesives polymerise on contact with water in an exothermic reaction.
- Clinically used for:
  - Opposing skin edges
  - Securing skin grafts
  - Securing nails to nailbeds.
- Useful for simple lacerations in children, as it avoids the pain of suturing.
- Examples: Histacryl®, Dermabond®, LiquiBand®.

Calcium ceramics

- Three main types:
  1. Calcium sulphate
  2. Calcium carbonate
  3. Calcium phosphate.

Calcium sulphate
- Commercially available as Osteoset®.
  - Dissolves in body fluids faster than bony ingrowth.
- More commonly used as plaster of Paris.

Calcium carbonate
- Found in some corals.
- Not used as calcium carbonate – hydrothermally converted to hydroxyapatite.
- Commercially available as Biocoral®.

Calcium phosphate
- The major inorganic constituent of bone.
- Available in two forms:
  1. Tricalcium phosphate
     - This is remodelled and resorbed in an osteogenic environment.
     - Examples: ChronOS™, Vitoss®, Biosorb®.
  2. Apatite
     - Remodels slowly.
     - Hydroxyapatites, e.g. ApaPore®, Allogran®, are regarded as non-absorbable.
     - Carbonated apatites, e.g. Norian®, BoneSource®, Calcibon®, resorb in an osteogenic environment.
     - Available as a mixture of chips, blocks and injectable cement.
     - Clinically, calcium phosphates are used for:
       - Filling bone tumour and cyst defects.
       - Filling bone voids following open fracture surgery.
       - Augmenting available autologous bone graft.
       - Back-fill for iliac crest after autologous bone graft harvest.
       - Augmentation of the facial skeleton.
       - Calvarial remodelling:
         - Inlay remodelling is replacement of full thickness skull.
         - Onlay remodelling is replacement of part of the outer skull.
     - Radiesse® is an injectable filler composed of calcium hydroxyapatite particles in a gel carrier.
     - Given its low solubility it can theoretically persist for years.
     - Appears radiopaque on X-rays.

Wound dressings

- There is little concrete evidence that any one dressing is better than another.
- The ideal wound dressing should:
  1. Protect the wound physically and microbiologically.
  2. Be non-toxic and non-allergenic.
  3. Maintain high wound humidity while removing excess exudate.
  4. Allow gaseous exchange.
  5. Remove necrotic material.
  6. Promote epithelialisation.

7 Promote granulation.
8 Ensure atraumatic application and removal.
9 Be inexpensive with long shelf life.

Classification

Low-adherent dressings

- Allow exudate to pass through into a secondary dressing.
- Further classified as:
  - Tulles
    - Open-weave cloths soaked in soft paraffin (Jelonet®) with or without chlorhexidine (Bactigras®)
  - Textiles – Atrauman®, NA Ultra®, Mepitel®
  - Perforated multilayered plastic films – Telfa™, Melolin™.

Semipermeable films

- Permeable to gases and vapour.
- Impermeable to liquids and bacteria.
  - Omiderm™ is a polyurethane film without adhesive backing.
  - Opsite® and Tegaderm™ are adhesive polyurethane films.

Hydrogels

- Composed of insoluble polymers with up to 96% water content.
- Donate water to the wound surface and maintain a moist environment.
  - Wound rehydration facilitates natural autolysis of non-viable tissue.
- Not used on gangrene – usually kept dry to reduce infection risk.
- Examples: Aquaform®, Intrasite™, GranuGel®.

Hydrocolloids

- Main components include sodium carboxymethylcellulose, gelatin, elastomers.
- Forms a gel on the wound surface, maintaining a moist environment.
  - Examples: Granuflex®, DuoDERM®.
- Hydrocolloid fibres are now available, referred to as Hydrofiber® dressings.
- Wound exudate converts the dry fibres to a soft coherent gel sheet.
  - Examples: Aquacel®, Versiva®.

Alginates

- Derived from a brown seaweed.
- Some also contain calcium, which activates the clotting cascade.
- They are absorbent and become gelatinous after absorbing moisture.
- Tend to adhere to non-exudating wounds, causing pain on removal.
- Examples: Sorbsan®, Kaltostat®.

Synthetic foams

- Manufactured from either polyurethane or silicone.

- Usually used in deep wounds.
- Conform to cavities, obliterate dead space.
- Suitable for heavily exudating wounds.
- Examples: Lyofoam®, Allevyn®, Cavi-Care®.

Negative pressure wound therapy (NPWT)

- Reports claim that application of suction improves wound-healing rates.
  - There are no randomised controlled trials to support these reports.
- Possible mechanisms of action include:
  - Direct suction effect, pulling the wound inward.
  - Increased rate of angiogenesis and granulation tissue formation.
  - Reduced concentration of tissue metalloproteinases.
  - Decreased bacterial contamination.
  - Decreased interstitial fluid content of the wound.
- Suction is applied to the wound in the following manner:
  1. The wound is covered with an open-cell sponge or open-weave gauze dressing, containing the end of a suction tube.
  2. The wound is sealed with a semipermeable, adhesive film.
  3. Suction is applied to the wound from a specifically designed machine.
- Suction pressures are usually set around 120 mmHg for acute wounds; 50–70 mmHg for chronic wounds.
- Intermittent suction (e.g. 5 minutes on, 2 minutes off) has been shown to increase the rate of granulation tissue formation.
- NPWT has been used to improve skin graft take.

Contraindications

- Malignancy within the wound
- Untreated osteomyelitis
- Unexplored fistulae
- Where there is necrotic tissue or eschar – this should be debrided first.
- Use on ischaemic wounds may increase the zone of necrosis.

Sutures and suturing

Suturing

- Skin edges should be everted.
- This results in:
  - Better dermal apposition
  - Improved healing
  - A finer final scar.
- Most wounds are closed by first opposing skin edges with dermal sutures.
  - Reduces tension on subsequent cutaneous sutures.
  - Limits stretching of the wound.

Suture materials

- Absorbable or non-absorbable
- Synthetic or natural
- Braided or monofilament.

Absorbable sutures

Catgut

- Derived from either bovine serosal or ovine submucosal intestinal layers.
- Elicits significant inflammatory response.
- Absorption is unpredictable:
  - Loses strength by 8–9 days.
  - Absorbed by 2–3 months.
  - Absorption rate decreases if the suture is chromatised (chromic catgut).
- Not used frequently in the UK nowadays, but worldwide it is used for:
  - Mucosal suture
  - Dermal suture in the face
  - Skin suture in children.

Polyglycolic acid

- Dexon™ is a synthetic suture of polyglycolic acid.
- Degraded by hydrolysis.
- Loses strength by 21 days; absorbed by 90 days.

Polyglactin 910

- Vicryl® is a braided synthetic suture of polyglactin 910.
- Loses strength by 21 days; absorbed by 90 days.
- Its braided nature may make it more prone to bacterial colonisation than monofilament alternatives.
- Can provoke a significant inflammatory reaction.
- Vicryl *Rapide* is related to Vicryl, but loses its strength after 7–10 days.
- Vicryl Plus is coated with Triclosan, an antibacterial and antifungal.

Poliglecaprone 25

- Monocryl® is a monofilament synthetic suture composed of poliglecaprone 25.
- Absorption characteristics similar to Vicryl.
- Its monofilament composition may make it less prone to bacterial colonisation.
- Monocryl Plus is coated with Triclosan.

Polydioxanone sulphate (PDS)

- PDS® II is a monofilament synthetic suture.
- Absorbed more slowly than Vicryl, Monocryl, or Dexon.
- Within 6 weeks of insertion:
  - 3-0 PDS loses 40% of its tensile strength.
  - 4-0 PDS loses 65% of its tensile strength.
- Absorbed by 6 months.

- Primarily used as a dermal suture in areas prone to stretched scars.
- Also available as PDS Plus with Triclosan.

Non-absorbable sutures

- Non-absorbable sutures are generally used as:
  - Cutaneous stitches, which require removal.
  - Deep stitches to provide permanent tissue fixation.
- Non-absorbable sutures can be natural or synthetic.

Natural

- Silk
- Cotton

Synthetic

- Polyamide – Nylon
- Polypropylene – Prolene®
- Polyester – Ethibond®, Novafil®
- PTFE – Gore-Tex
- Stainless steel.

Tissue expansion

- Tissue expansion, by techniques such as neck lengthening, has been practised since ancient times.
- In 1957, Neuman described tissue expansion for therapeutic purposes.
- Since then, it has been popularised by authors such as Radovan and Austad.

Mechanisms

- 70% of tissue gain is due to stretch (mechanical creep) and 30% due to growth (biological creep).
- Tissue subjected to constant strain relaxes – less force is required to keep it stretched.
  - This is known as stress relaxation.
- Creep is the time-dependent plastic deformation of any material in response to constant stress.
- Mechanisms of tissue creep:
  - Disruption of elastin fibres
  - Re-alignment of collagen
  - Fluid displacement
  - Migration of local tissue.

Changes

- Tissue-expanded skin is characterised by these changes:

Epidermis

- Thickness usually increases but can remain the same as unexpanded skin.
- Mitotic rate of the basal layer is increased, suggesting new tissue is generated.

Dermis
- Thickness decreases.
- Collagen fibres realign along the lines of tension.

Skin appendages and nerves
- Become increasingly separated from one another.
- Hair density is therefore reduced.

Subcutaneous tissue, muscle and bone
- Pressure effects of the expander may cause localised atrophy of tissue.

Blood supply
- Vascularity of expanded flaps is superior to non-expanded controls.
  - Mechanical force improves vascularity of expander capsule and dermis.
  - Perfusion studies show increased axiality and total capillary blood flow.
- Including the expander capsule in the flap harnesses this enhanced blood supply.
- Improvement in flap length survival is at least equivalent to, if not better than, that achieved with conventional delay techniques.
- Expanded flaps are therefore considered to be delayed.

Microscopic appearance of the expander capsule
- Pasyk describes four zones of a silicone expander capsule:
  1. Inner zone: fibrin layer containing macrophages.
  2. Central zone: elongated fibroblasts and myofibroblasts, pressed between thick bundles of collagen fibres oriented parallel to the expander surface.
  3. Transitional zone: loose collagen fibres and a few blood vessels.
  4. Outer zone: an established vascular layer and loose collagen fibres.

Advantages
- Reconstruction with tissue of colour and texture similar to that of the defect.
- Reconstruction with sensate skin containing skin appendages.
- Limited donor-site deformity.

Insertion and placement of expanders
- Can be inserted through a variety of incisions.
  - These may be local or remote.
- A remote, radially orientated incision has the lowest complication rate.
- Can be placed above or below the fascia.
  - Subcutaneous placement is usually preferred in the face and trunk.
  - Subfascial placement is usually preferred in the forehead and scalp.
- Complication rates in the limb are reportedly higher than in non-limb sites.

- If placed in soft, mobile tissue such as the abdomen, the filling port should be placed over firm tissue such as rib or iliac crest to facilitate filling.

Contraindications

- Ideally, tissue expanders should not be inserted:
  - In the vicinity of an immature scar
  - In the presence of infection
  - In irradiated tissue
  - Under skin grafts.

Design of expanders

- Expandable, saline-filled silicone bags.
- They differ from one another in the following ways:

Shape

- Oval
- Rectangular
- Round
- Square
- Crescentic (croissant-shaped)
  - May result in shorter donor defects with minimal dog ears.
  - Expansion principally occurs over the central portion of the expander.
- Custom made.

Size

- Base dimensions
- Projection when inflated.

Location of the port

- Integrated ports form part of the shell of the expander.
- Remote ports are attached to the expander by a filling tube.
  - Can be placed subcutaneously or externally.

Envelope composition

- The shell of an expander can have a smooth or textured surface.
- The shell is usually of uniform thickness and compliance.
  - Variations in thickness and compliance produce preferential expansion in certain directions.
    - Isotropic expanders expand in all directions.
    - Anisotropic expanders expand in certain controlled directions.
- Expanders may or may not have a stiff backing bonded onto their shell.

Self-inflating expanders

- Have no port; attractive to use in children because they avoid repeated needling.
- Contain a hypertonic compound; they gradually fill through osmosis.
- Early expanders were filled with hypertonic saline.
  - Expansion was uncontrolled and caused widespread tissue necrosis.
- Newer generation expanders, e.g. Osmed®, contain a hydrogel of vinylpyrrolidone and methylmethacrylate.
  - The size and number of holes in the shell control expansion rate.
  - Despite this, high complication rates have been reported.

Timing and length of expansion

Intra-operative expansion

- Sustained traction applied to tissue by skin hooks or other instruments.
- Tissue expansion with a Foley catheter.
- Sure-Closure™ skin stretching devices.

Rapid expansion

- Rationale: most tissue creep and growth occurs in the first 2 days.
- Some therefore recommend expander inflation every 2–3 days.

Conventional expansion

- Most expanders are inflated weekly.
- Allows sufficient time for tissues to stabilise between expansions.
- Expansion is stopped when the amount of tissue gained is sufficient for reconstruction.
- This can be estimated by:
  - Recording the dimensions of tissue over the expander from fixed points before it is inflated.
  - Comparing these measurements to the dimensions after inflation.
  - Comparing the tissue gain to the dimensions of the defect.

Complications

- Minor complications do not result in termination of the procedure.
- Major complications do result in termination of the procedure.
- Complications include:
  - Haematoma
  - Infection
  - Exposure of the expander
  - Extrusion of the expander
  - Pain
  - Neurapraxia
  - Pressure effects on surrounding tissue

- Accidental perforation by missing an integrated filling port
- Flipping of a remote filling port, making filling impossible.

Lasers

- Acronym of **L**ight **A**mplification by **S**timulated **E**mission of **R**adiation.

Laser physics

Radiation

- The visible part of the electromagnetic spectrum consists of light with wavelengths from 400 nm (blue) to 700 nm (red).
- Invisible wavelengths sit either side of the visible spectrum:
  - Shorter wavelengths (higher energy) – ultraviolet, X-rays, γ-rays.
  - Longer wavelengths (lower energy) – infrared, microwaves, radio waves.
- Different lasers use light of different wavelengths to mediate their effects.

Stimulated emission

- A molecule or atom in its resting state is composed of a nucleus and circulating electrons in their ground state.
- Adding energy to an atom causes the electrons to shift into a higher energy, unstable orbit.
- As an excited electron falls back to its more stable ground state, it releases the excess energy as a photon of light.
  - The photon has a wavelength specific to that atom or molecule.
- If that photon collides with another excited electron, that electron returns to its ground state, releasing another photon.
- The original photon is not absorbed, so there are now two photons of the same frequency.
- Importantly, these photons are in phase: their waveforms reinforce each other.
- This process is stimulated emission.

Light amplification

- As photons hit other excited electrons, more photons are released and the light energy increases.
- For the laser to work, a population inversion is necessary.
- Population inversion occurs when the majority of the molecules in the laser exist in an excited state.

Structure of a basic laser

- Laser requires three things:
  1 An external power source, e.g. flash lamp, diode, radio frequency emission.

2 A lasing medium, which can be:
   – Solid, e.g. ruby crystal, Neodymium:YAG, Erbium:YAG, KTP.
   – Gas, e.g. CO_2, argon.
   – Liquid, used in dye lasers.
3 Reflective mirrors at each end of a laser tube.
   – Only photons that hit the mirrors directly are reflected back into the lasing medium.
   – This creates an increasing number of photons that travel back and forth between the mirrors, parallel to the tube.
   – To allow light to escape from the tube, one mirror is only partially reflecting.
   – The resulting light is the output beam of the laser, which can be focused with a lens.

Q-switching

- Q-switching is an important exception to this basic model.
- Rather than a partially reflecting mirror, a Q-switched laser uses two fully reflective mirrors.
- High power is generated because of a large population inversion, and the fact that stimulated emission of light cannot escape.
- The Q-switch dumps the entire contents of the chamber, producing a short pulse of high intensity.
  - A normal laser releases its energy in the same way as water escapes from a bath through the plughole.
  - A Q-switched laser releases its energy in the same way as if one could suddenly remove the bottom of the bath, dumping all the water at once.

Properties of laser light

1 Collimated: laser light diverges very little as it travels.
2 Monochromatic: laser light has only one wavelength.
3 Coherent: the peaks and troughs of laser light waves are in phase.
- These properties make laser light intense and powerful.

Laser interaction with tissue

- Lasers react with tissues through their thermal, chemical, or photoacoustic effects.
- When laser light hits tissue it can be:
  - Reflected
  - Scattered
  - Absorbed
  - Transmitted.
- It is the absorbed light that causes biological effects, both desirable and undesirable.
- A specific wavelength of laser light will be preferentially absorbed by a target chromophore within tissue.
  - Common biological chromophores: water, haemoglobin, melanin.

Thermal effects

- Occur by three different mechanisms:
  1. Coagulation
     - Light absorbed by a target chromophore is converted to heat.
     - Coagulation occurs when tissue containing the chromophore reaches 60 °C.
  2. Vaporisation
     - Tissue heated to 100 °C will vaporise.
  3. Selective photothermolysis
     - Thermal damage is induced in a tissue target that absorbs light of a specific wavelength.
     - Selectivity occurs when the exposure time of the tissue to laser light is shorter than the cooling time, or thermal relaxation time (TRT).
     - TRT is defined as the time taken by a specific volume of tissue to dissipate 51% of the energy absorbed.
     - Heat energy dissipated to surrounding non-target tissues can cause collateral effects.
     - Once the TRT has elapsed, another pulse can be delivered to the target without generating thermal damage to surrounding non-target tissue.

Cooling

- Cooling protects superficial non-target tissue, such as epidermis, from collateral thermal damage.
- Allows higher energy levels to be used.
- Four basic methods of skin cooling:
  1. Bulk pre-cooling – epidermis and dermis cooled prior to pulse delivery.
  2. Dynamic pre-cooling – epidermis cooled prior to pulse delivery.
  3. Parallel cooling – epidermis cooled during pulse delivery.
  4. Post-cooling – epidermis and dermis cooled after pulse delivery.
- Examples: cryogen spray, gliding window handpiece, cold handpiece, cold air, cooling gel.

Laser variables

- Lasers are controlled by four variables:
  1. Wavelength
     - Measured in nanometres (nm); specific to the lasing medium.
  2. Power
     - Measured in Watts (W) or Joules per second (J/s).
  3. Spot size
     - Measured in cm^2. Depends on focal length of the lens.
     - Larger spot sizes show less scatter and penetrate deeper.
  4. Duration of action.
     - Also called pulse width; measured in fractions of a second.

- The latter three variables are used to calculate two further values:
  - Power density: the energy delivered per unit area of incident tissue (W/cm^2).
  - Fluence: the product of power density and exposure time (J/cm^2).

Clinical applications of laser

Indication	Chromophore	Laser	Wavelength (nm)
Vascular lesions	Oxyhaemoglobin	Pulsed Yellow Dye Laser	585
		KTP	532
		Nd:YAG	1064
		IPL*	N/A
Skin resurfacing	Water	Er:YAG	2940
		CO_2	10,600
Pigmented lesions	Melanin	Diode	800
		Ruby	694
		IPL*	N/A
Hair removal	Melanin	Alexandrite	755
		Diode	800
		Nd:YAG	1064
		Ruby	694
		IPL*	N/A
Tattoo removal	Black/blue/green	Q-switched ruby	694
	Black/blue/green	Q-switched alexandrite	755
	Black	Q-switched Nd:YAG	1064
	Red/orange/brown	Q-switched Nd:YAG	532

*IPL, intense pulsed light (not laser light) – Xenon flashlamps generate multiwavelength non-coherent light that is modulated by a series of filters.
KTP, potassium titanyl phosphate; YAG, yttrium aluminium garnet; Nd, neodymium; Er, erbium.

Laser safety

- In the United Kingdom, this is legally enshrined in the Control of Artificial Optical Radiation at Work Regulations 2010.
  - Based on requirements of the International Electrotechnical Commission.
- Laser misuse can cause unintended severe and irreversible damage to the retina.
  - This damage may go unnoticed because wavelengths outside the visible spectrum will not invoke a blink reflex.
- Lasers can also cause cutaneous burns; some represent a fire hazard.
- Lasers are classified from Class 1 to 4 based on wavelength and maximum power output.
  - Medical lasers are Class 4 (severe hazard for eyes and skin).
- Main facets of laser safety:
  - Risk awareness through risk assessment.
  - Watches, jewellery and other reflective surfaces should be covered.

- Eye protection should be worn by everyone in the room.
- The laser key should be stored away from the laser machine.
- Treatment around the eyes may require corneal eye shields.
- A laser-safe endotracheal tube should be used when using CO_2 laser.
- Lasers that create a significant laser plume, such as the CO_2 laser, should be used with a plume evacuator to prevent potential transmission of live virus particles into the airway of treating personnel.

Local anaesthesia

- Local anaesthetics produce reversible loss of sensation in a circumscribed area of the body.
- They prevent generation and conduction of nerve impulses by blocking voltage-gated sodium channels.

Classification

- Local anaesthetics are classified by their molecular structure:
  1. Amides
     - Tend to have an 'i' in the first half of their generic name.
     - Examples: lignocaine, bupivacaine, prilocaine.
     - Metabolised in the liver; rarely cause anaphylaxis.
  2. Esters
     - Tend not to have an 'i' in the first half of their name.
     - Examples: procaine, tetracaine, chloroprocaine, amethocaine.
     - Degraded in plasma by pseudocholinesterase.
     - More likely to cause anaphylaxis because they are metabolised to para-amino benzoic acid (PABA), which is highly allergenic.

Pharmacokinetics

- Local anaesthetic binds to voltage-gated sodium channels in its ionised state.
- Acidifying local anaesthetic solutions to produce more ionised molecules does not increase the degree of nerve block as expected.
  - This is because charged ions cannot cross cell membranes of the epineurium and perineurium.
  - The proportion of local anaesthetic in its non-ionised state is what determines rate of diffusion across nerve cell membranes, and therefore the speed of onset of anaesthesia.
- The pK_a (acid dissociation constant) is the pH at which the ionised and non-ionised forms of an acid are in equilibrium.
  - The pK_a value is constant for any given compound.
- This explains why local anaesthetics with a pK_a close to that of human tissue pH (7.4) have a rapid onset, such as lidocaine, pK_a 7.6.
- By comparison, the slower acting bupivacaine has a pK_a of 8.1.
- Local anaesthetics fail in the presence of infection or inflammation because localised hypoxia produces an acidic tissue environment.
- Alkalinisation of local anaesthetic solution with sodium bicarbonate has been shown to speed onset and enhance its effect.

- Speed of onset is also related to diffusability of local anaesthetic through non-neural tissue.
- More lipid soluble molecules, e.g. bupivacaine, have higher affinity for axons, and therefore slower onset and longer duration of action than more hydrophilic molecules, e.g. lidocaine.
- Duration of action is influenced by the degree of vasodilatation caused by the local anaesthetic.
  - All local anaesthetics except cocaine are vasodilators.
- Quoted maximum safe doses are not universally accepted because:
  - Patients vary both in body habitus and metabolism.
  - Rates of absorption vary in different tissues, depending on the blood flow.
  - Body weight gives no indication of lean tissue mass.

Epinephrine

- Epinephrine is added to local anaesthetics to cause vasoconstriction.
- Reduces local anaesthetic absorption, therefore prolonging block duration and reducing toxicity.
- Maximum safe dose of epinephrine is controversial.
  - A safe guideline amount is 4 μg/kg.
- Commonly used in combination with local anaesthetics at concentrations of 1:200,000.
  - In fact, doses as low as 1:1,000,000 are probably just as effective.
- The maximum dose should be reduced in cases of serious ischaemic heart disease, thyrotoxicosis and hypertension.
- There is no evidence that using concentrations of epinephrine up to 1:100,000 in digital nerve blocks causes digital infarction.

Common local anaesthetics

Lidocaine

- Also called lignocaine or xylocaine.
- Used in clinical practice for almost 60 years.
- Rapid onset; relatively short duration.
- Available as 1% and 2% solutions.
- Maximum safe dose: 3 mg/kg plain; 7 mg/kg with epinephrine, but see Chapter 9, 'Liposuction'.

Bupivacaine

- Used in clinical practice for more than 40 years.
- Long duration of action (up to 24 hours in some cases).
- Adding epinephrine decreases toxicity by delaying drug absorption, but has minimal effect on block duration.
- It is particularly cardiotoxic; should never be used in Biers blocks.
- Available as 0.25% and 0.5% solutions.
- Maximum safe dose: 2 mg/kg plain; 2 mg/kg with epinephrine.

Levobupivacaine
- Relatively new agent; essentially the same as bupivacaine.
  - Bupivacaine is a racemic mixture of R and S enantiomers.
  - Levobupivacaine contains the S enantiomer only.
- It is less cardiotoxic than bupivacaine.
- Available as 2.5 mg/ml and 5 mg/ml solutions.
  - For spinal anaesthesia, 7.5 mg/ml preparations may be used.
- Maximum safe dose: 3 mg/kg plain. There is little data to support this.

Prilocaine
- Closely related to lidocaine.
- More rapidly metabolised and hence less toxic.
- Can cause methaemoglobinaemia in high doses (>600 mg).
  - Blue skin discolouration and false pulse oximeter readings.
  - Usually benign and resolves within a couple of hours.
  - Treatment is methylene blue 1 mg/kg, given IV over 5 minutes.
- Prilocaine is the drug of choice for Biers block.
- Available as a 1% solution.
- Maximum safe dose: 6 mg/kg plain; 9 mg/kg with epinephrine.

Topical anaesthesia
- Used to minimise discomfort prior to venesection or superficial skin treatment.

Ametop®
- Contains 4% tetracaine.
- Takes 30–45 minutes to take effect.

EMLA®
- Acronym for Eutetic Mixture of Local Anaesthetic.
- Consists of 2.5% lidocaine and 2.5% prilocaine.
- Takes 1–5 hours to take effect.

LMX 4®
- Contains 4% lidocaine.
- Takes 30 minutes to take effect.

Dose calculation
- Local anaesthetic concentration is usually expressed as a percentage.
- In contrast, maximum safe dose is expressed as milligram per kilogram.
- It is therefore helpful to convert percentage to milligram per millilitre.
- To do this for local anaesthetics, multiply the percentage by 10.
  - Example: lignocaine 1% is 10 mg/ml; bupivacaine 0.25% is 2.5 mg/ml.

- Epinephrine concentrations are expressed as ratios, such as 1:1000.
- To calculate milligram per millilitre from a ratio, first convert the ratio to a percentage:
  - If 1:100 is 1%, then 1:1000 is 0.1%.
- Once you have a percentage, you can multiply this by 10 to get milligram per millilitre.
- Therefore, 1:1000 epinephrine is 1 mg/ml.

Toxicity

- Rare, but may occur due to:
  - Accidental intravascular administration
  - Administration of an excessive dose.
- Toxicity can manifest several hours after administration.
- Primarily affects central nervous system (CNS) and cardiovascular system (CVS).

CNS toxicity

- Symptoms:
  - Dizziness and light-headedness
  - Disorientation
  - Circumoral paraesthesia
  - Difficulty focusing with the eyes
  - Tinnitus.
- Signs:
  - Shivering/muscle twitching, progressing to
  - Generalised tonic clonic seizures, progressing to
  - Coma.

CVS toxicity

- Occurs at higher doses than CNS toxicity:
  - Sinus bradycardia due to blockade of the spontaneous pacemaker.
  - Can progress to sinus arrest.
  - Depression of cardiac contractility.
- Low level toxicity causes vasoconstriction.
- Higher level toxicity causes vasodilatation.
- Bupivacaine can cause refractory ventricular fibrillation.

Management

- The Association of Anaesthetists of Great Britain & Ireland published guidelines in 2010.
- Immediate actions:
  - Stop injecting local anaesthetic.
  - Call for help.
  - ABCs with 100% oxygen.
  - Control seizures by conventional means.
- If there is circulatory arrest, commence CPR and treat arrythmias conventionally (but not with lidocaine).

- Give 1000 ml of 20% lipid emulsion, such as Intralipid®.
  - Using propofol, which is supplied as a lipid emulsion, is not a safe substitute for Intralipid due to the significant cardiovascular depression it causes.
- Recovery from local anaesthetic-induced cardiac arrest may take over an hour.

Microsurgery

History

- Alexis Carrel described the triangulation technique of blood vessel repair in 1902.
  - He was awarded a Nobel Prize in 1912.
- Ronald Malt and Charles McKann described the first successful arm replantation in 1962.
- Nakayama, a Japanese cardiothoracic surgeon, reported the first true series of microsurgical free tissue transfers using vascularised intestinal segments for oesophageal reconstruction in 1964.
- Komatsu and Tamai reported the first successful digital replant in 1968.
- Cobbett first reported free toe-to-hand transfer, performed at the Queen Victoria Hospital, in 1968.
- Daniel & Taylor and O'Brien & associates independently reported use of the free groin flap for leg reconstruction in 1973.

Pathophysiology of vessel healing

Vessel healing following anastomosis

- A thin layer of platelets forms at the anastomosis site immediately after repair.
- These platelet aggregations disappear between 24 and 72 hours.
- Pseudo-intima forms at the anastomosis site within 5 days.
- New endothelium covers the anastomosis site within 1–2 weeks.
- Factors contributing to intimal damage and anastomotic thrombosis:
  - Rough vessel dissection
  - Desiccation of the vessels
  - Diathermy close to the vessel
  - Prolonged vasospasm
  - Application of vascular clamps with closing pressures >30 g/mm^2
  - Use of large needles
  - Repeated needle stabs
  - Partial-thickness suture bites
  - Unequal spacing of sutures
  - Loose sutures
  - Excessively tight sutures
  - Too many sutures
  - Tension across the suture line.

Thrombus formation

- Platelets do not normally adhere to intact endothelium.

- Collagen exposure within the media and adventitia of vessels triggers platelet aggregation and degranulation.

Drugs that limit thrombus formation

Heparin

- A single dose of IV heparin may be given at the time of anastomosis.
- Some argue that the risk of bleeding outweighs any potential benefit.

Dextran

- A polysaccharide available in molecular weights of:
  - 40 kDa (Dextran 40)
  - 70 kDa (Dextran 70)
- Dextran was initially used as a volume expander.
- Subsequently, it was noted to have antiplatelet and antifibrin properties.
- Animal studies show improved anastomotic patency with dextran.
- Side effects include anaphylactoid reactions and renal impairment.

Aspirin

- Inhibits platelet aggregation.

Proteolytic enzymes

- Used to dissolve thrombus:
  - Streptokinase
  - Urokinase
  - Tissue plasminogen activator (t-PA).
- Routine use of anticoagulants or fibrinolytic agents is controversial.
- If thrombosis occurs, the anastomosis should be explored.
  - These patients should probably receive anticoagulant or fibrinolytic therapy.
- For salvage of repeated thrombosis, fibrinolytic therapy should be instituted.

Reperfusion injury

- Free radicals are used against bacteria in normal circumstances.
  - Examples: superoxide anion radical O_2^-, hydroxyl radical ·HO.
- Free radicals accumulate when a flap is devascularised.
- When a flap is 'reperfused' after a period of ischaemia, the following occur:
  - Endothelial cell damage
  - Endothelial swelling
  - Increased capillary permeability.
- Skin and subcutaneous tissue tolerate:
  - Warm ischaemia of 6 hours
  - Cold ischaemia of 12 hours.
- Muscle is intolerant of ischaemia and develops irreversible changes after:
  - 3 hours of warm ischaemia time
  - 8 hours of cold ischaemia time.
- Bowel is extremely intolerant of ischaemia.

The no-reflow phenomenon

- Characterised by failure of tissue perfusion despite adequate arterial input and venous drainage.
- Believed to occur due to:
  - Swelling of vascular endothelium
  - Platelet aggregation
  - Leakage of intravascular fluid into the interstitial space.
- Can be treated with:
  - Fibrinolytic drugs
  - Lidocaine
  - Heparin
  - NSAIDs, which act by inhibiting cyclooxygenase (COX).

Equipment

Magnification

- Some prefer loupe magnification to repair larger vessels.
- Small vessels are best repaired with an operating microscope.
- The microscope should be able to magnify between ×6 and ×40.

Instruments

- Forceps – four pairs of jeweller's forceps
- Vessel dilators
- Microdissecting scissors
- Needle holders
- Single and double microvascular clamps of varying sizes.
  - They should have a closing pressure of $<30\,g/mm^2$.

Irrigating solutions

- Heparin dissolved in Hartmann's or saline to a concentration of 100 units/ml.
- Topical papaverine, verapamil, or lidocaine to relieve vessel spasm.

Sutures

- Monofilament 8, 9, 10 and 11-0 nylon.
- Half-circle or compound-curve atraumatic needles of 50–130 μm diameter.

Coupling devices

- Commercially available devices that may save time over hand-sewing.
- Mostly used for end-to-end venous anastomosis.

Technique

- Acland described five factors that influence microvascular patency:
  1 Surgical precision
  2 Vessel diameter
  3 Blood flow into the anastomosis

4 Tension of the anastomosis
5 Use of anticoagulants or thrombolytic agents.

- Key steps for successful microvascular free tissue transfer:
  1 Obtain adequate access.
    - Do not operate down a hole.
  2 Operate in a dry field.
  3 Position and secure the flap before starting the anastomosis.
    - The flap should be tacked into position before starting the anastomosis.
    - Position the pedicle with care, ensuring it is:
      - The correct length to lie at the anastomosis site without tension
      - Not twisted or kinked
      - Not compressed.
  4 Prepare the vessels for anastomosis by stripping the adventitia.
  5 Flush the vessel with heparin solution.
    - Excessively powerful irrigation can cause intimal trauma.
  6 Limit vessel distension with the dilating forceps.
    - Excessive dilatation causes intimal tears or vessel spasm.
  7 Perform a forward-flow test prior to anastomosis:
    - Proximal arterial flow is tested by releasing the clamps on the artery.
  8 Never start the anastomosis until you are happy with the setup.
- Points of technique:
  - The needle should be held halfway along its length.
  - The most difficult sutures are generally inserted first.
  - The needle should be accessible within the visual field when tying knots.
    - This facilitates its retrieval for the next stitch.
  - Triangulation, bisecting and posterior wall first techniques can be used.
  - Interrupted or continuous sutures can be used.
  - Airborne tying techniques avoid suture ends getting stuck to surrounding tissues.
  - The suture should not be tied if it may have caught the posterior wall.
  - Limit vessel handling after anastomosis as this can result in spasm.

Post-operative management

- Patients should be 'warm, wet and comfortable':
  - A warm room, often with a warming blanket during surgery and transfer.
  - Well perfused with good urine output and normal blood pressure.
    - Thresholds for blood transfusion should be set.
    - Anaemia in the early post-operative period may be dilutional.
  - Analgesia, often with regional anaesthetic blocks or patient-controlled analgesia.

Post-operative monitoring

Clinical parameters

- Colour
- Temperature
- Tissue turgor

- Capillary return
- Bleeding on pinprick.

Doppler recordings
- Commonly used.
- Can record arterial or venous flow.
- May give false-positive readings by detecting flow in deep vessels.
- Implantable venous Doppler probes are available:
  - An ultrasonic probe is mounted on a silicone cuff and wrapped around the venous pedicle.

Laser Doppler
- Records blood flow in a small area.
- Scans blood flow over a large area.
- Measures changes in the Doppler shift of light.
  - Produced by movement of macromolecules within vessels.
- Depth of penetration is limited to 1.5 mm.

Near-infrared spectroscopy
- Similar to laser Doppler.
- Uses longer wavelength of light; consequently penetrates deeper.

Temperature measurement
- The flap's temperature can be measured accurately with a probe.
- Temperature difference >2 °C between flap and body core indicates possible ischaemia.
- Useful for monitoring digital replants.

Pulse oximetry
- Measures oxygenation of haemoglobin.
- Useful for monitoring digital replants.

Impedance monitoring
- Measures impedance between two electrodes placed on the flap.

Plethysmography
- Measures changes in flap volume.
- Increased readings indicate flap congestion.

Intravenous fluorescein infusion
- Demonstrates blood flow within the flap.
- A test dose is given intravenously, followed by a dose of 15 mg/kg.
- The flow of fluorescein can be observed under a Wood's lamp.

Management of a non-flowing anastomosis
- A common question in plastic surgery examinations.

- Absence of flow through a technically sound anastomosis is managed as follows:
  - Apply lidocaine to the anastomosis and place a warm, wet gauze over it.
  - Ask the anaesthetist to haemodynamically optimise the patient by ensuring:
    - They are warm and well hydrated.
    - They are not receiving vasoconstricting drugs.
    - The blood pressure is raised.
- Do not disturb the anastomosis for at least 15 minutes.
- If flap perfusion remains inadequate, inspect the pedicle for twisting or compression.
- If the anastomosis is not patent or has thrombosed, redo the anastomosis.
- A Fogarty catheter can be carefully used for thrombectomy of recipient vessels.
  - Avoid excessive manipulation of a thrombosed anastomosis.
    - This may send showers of emboli into the flap.
- If the anastomosis repeatedly thromboses, consider thrombolytic treatment:
  - Streptokinase can be administered as Streptase®
  - Give 250,000 international units (IUs) of Streptase dissolved in normal saline as a loading dose over 30 minutes.
  - This is followed by a maintenance dose of 100,000 IUs per hour.
- Contraindications to streptokinase treatment include:
  - Administration of streptokinase within the previous 6 months
  - Previous stroke
  - Mitral valve disease
  - Active bleeding.
- Given the risk of systemic complications, administration of Streptase can be limited to the flap by injecting directly into the pedicle artery and allowing the venous side to bleed out.

Leech therapy

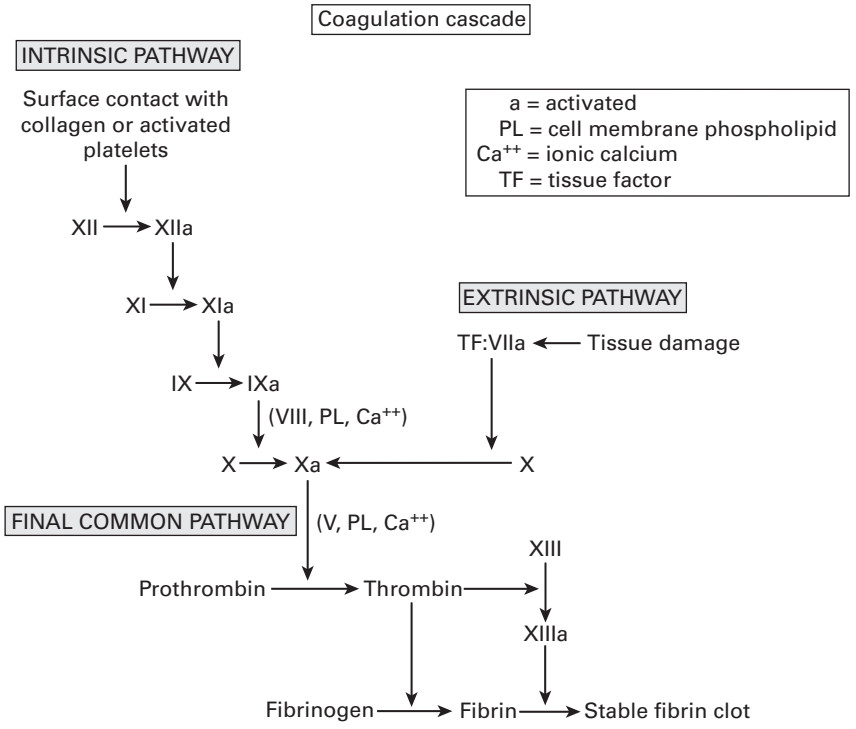
- The leech species *Hirudo medicinalis* can be used to improve venous drainage from congested flaps.
- Once latched on, leeches feed for 30–60 minutes; can consume up to 10 times their body weight.
- Leeches detach themselves when feeding is complete, leaving a characteristic 'Mercedes-Benz'-shaped bite mark.
  - Do not pull them off or their teeth will be left behind, causing infection.
  - Forceful removal can also cause regurgitation of gut flora, causing infection.
- Once fed, leeches are destroyed humanely in alcohol and never reused.
- Prolonged bleeding may occur due to the anticoagulant action of hirudin in leech saliva.
  - This can be controlled with simple pressure.
  - Blood loss should be monitored for the duration of treatment.
- Leech bites may be contaminated with *Aeromonas hydrophila* – an oral commensal.
  - Antibiotic prophylaxis with a quinolone such as ciprofloxacin is recommended.

Haemostasis and thrombosis

- Haemophilia is a tendency to bleeding.
- Thrombophilia is a tendency to thrombosis.
- Both may be inherited or acquired.

The coagulation cascade

- Two pathways culminating in fibrin formation – the basis of clot and thrombus.
- The cascade is not linear as shown here – there are many feedback loops.
  - Activation of one factor can activate many other factors.



Intrinsic pathway

- Triggered by collagen or activated platelets, which activate factor XII.
- Activation cascades eventually convert factor X into activated factor X (Xa).
- Evaluated by the activated partial thromboplastin time (APTT).

Extrinsic pathway

- The primary pathway for initiation of coagulation.
- Tissue damage activates factor VII, which converts factor X into Xa.
- Evaluated by the prothrombin time (PT).

Final common pathway

1 Conversion of prothrombin to thrombin by Xa.
2 Conversion of fibrinogen to fibrin by thrombin.
3 Thrombin also activates factor XIII, which converts fibrin monomers into stable polymers.

Anticoagulants

- Used to prevent thrombus formation in the venous circulation.
- In slower circulations, thrombi predominantly consist of platelets and red cells enmeshed in fibrin.

Heparin

- Naturally occurring GAG produced by mast cells.
- It (indirectly) has anti-thrombin and anti-Xa activity.
- Used to achieve immediate anticoagulation.
- Treatment is monitored by the APTT ratio, aiming for 2–2.5× normal.
- Stopped 6 hours prior to surgery; restarted 6–12 hours after surgery.
- Reversal with protamine sulphate is rarely required.
- Use for 4 days or more is associated with heparin-induced thrombocytopenia (HIT) in some patients.

Low-molecular-weight heparins (LMWH)

- Examples: dalteparin, enoxaparin, tinzaparin.
- Used for prophylaxis and treatment of venous thromboembolism and unstable coronary disease.
- More convenient to administer and has less risk of HIT than unfractionated heparin.
- Monitoring of its anti-factor Xa activity is not routinely required.

Warfarin

- Coumarin derivative; inhibits vitamin K epoxide reductase.
- This depletes intrahepatic vitamin K, which is a necessary cofactor for synthesis of clotting factors II, VII, IX and X.
- Monitored using the International Normalised Ratio (INR), based on the PT.
- Warfarin is stopped pre-operatively unless the risk of thromboembolism is high.
  - Partial reversal usually occurs after 3 days; complete reversal after 5 days.

Platelets

- Platelets survive for 7–10 days.
- They are activated by a myriad of agonists, including:
  - Collagen
  - Tissue factor
  - ADP
  - vWF.
- These converge on activation of a fibrinogen receptor: glycoprotein IIb/IIIa.
- Breakdown of arachidonic acid by COX-1 produces thromboxane A_2.
  - Thromboxane A_2 activates other platelets to aggregate.

Antiplatelet drugs

- Inhibit thrombus formation in the arterial circulation.
- In faster flowing vessels, thrombi predominantly contain platelets with little fibrin.

Non-steroidal anti-inflammatory drugs (NSAIDs)

- Produce reversible inhibition of both COX isoforms.
- Duration of antiplatelet action depends on the specific drug's pharmacokinetics.
  - Ranges from 8 hours to 3 days.
- Selective COX-2 inhibitors, e.g. celecoxib, have no antiplatelet activity.

Aspirin

- A salicylate and NSAID.
- It differs from other NSAIDs by causing *irreversible* inhibition of COX-1.
- This inhibits generation of thromboxanes, required for platelet binding.
- Reversal occurs over 7–10 days as the body replaces the suppressed platelets.

Clopidogrel (Plavix®)

- A thienopyridine; irreversibly inhibits $P2Y_{12}$ ADP receptors on platelets.
  - This receptor is essential for activation of the glycoprotein IIb/IIIa pathway.
- Does not inhibit COX; can be used in patients intolerant of aspirin.
- Used in combination with aspirin following coronary stenting.
- Effects persist until a new platelet population is manufactured (7–10 days).

Dipyridamole

- A phosphodiesterase (PDE) inhibitor.
- This elevates platelet levels of cAMP by inhibiting its breakdown.
- High cAMP levels reduce intracellular calcium.
- Low calcium inhibits events leading to platelet degranulation.
- By the same mechanism, it causes vasodilatation.
- Usually given in combination with aspirin due to its modest antiplatelet activity.

Glycoprotein IIb/IIIa antagonists

- Examples: abciximab, eptifibatide, tirofiban.
- Monoclonal antibodies (or their peptide derivatives) raised against the glycoprotein IIb/IIIa receptor.
- Given parenterally by cardiologists to treat acute coronary syndromes.
- Contraindicated within 4–6 weeks of trauma or major surgery.

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