Plastic surgery

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Introduction to plastic surgery

- Plastic surgery is divided into:
    - Aesthetic surgery :deals with improving the beauty of clients
    - Reconstructive surgery: deals with return of lost tissue and repair of congenital and acquired defect. In our course, we deal with the basic principles of reconstructive surgery.
- Wound are defined by pathologists as a discontinuity of epithelium. This could be due to trauma or to pathological causes. In the case of a pathological cause, they are called ulcers. The wounds may be of partial thickness or full thickness. Partial thickness wounds usually heal by regeneration; thus, they are treated conservatively.
- Causes of soft tissue defects:
    - Congenital: celft lip and palate, hypospadias, microcia and anocia, syndactely, vascular anomalies, and other soft tissue congenital anomalies.
    - Acquired:
        - Inflammatory: defects that follow soft tissue infections such as abscesses and necrotizing fascitis.
        - Neoplastic: resulting from tumors as in the case of post-mastectomy
        - Metabolic: diabetic foot
        - Ischemic: following peripheral vascular diseases and pressure sores
        - Traumatic: follows burns, frost bites, radiation injury, and soft tissue injury
        - Iatrogenic: extravastion injury.
- Why do we need reconstructive surgery?
    - The body can deal with defects by wound healing. This simply means replacement of lost or discontinued tissue. There are two modes of wound healing:
        - Regeneration: replacement of lost or discontinued tissue by the same type of tissue. This is the ideal mode of healing with maximal functional and cosmetic recovery
        - Fibrosis: replacement of lost or discontinued tissue by fibrous tissues. The fibrous tissue does not have the function and form of the lost tissue. Healing by fibrosis is bad.
    - In humans, unfortunately, the ability to heel by regeneration is limited to simple tissues (epithelium, hepatocytes, and bone). Lower creatures, such as salamanders, can heal organs and limbs. The role of a plastic surgeon is to deal with the defects that would heal by fibrosis. This is done by tissue transfer to avoid fibrosis.
- The role of the plastic surgeon:
    - In wound healing, all lost tissues would ultimately heal. However, in human beings, tissues mostly heal by fibrosis. This is an unfavorable fate. Plastics

surgeons reconstruct the tissues by replacing the lost tissue by transferring tissues from donor sites of the same patient. The donor area will donate tissues to the defected area. By doing this, we try to achieve a result that is better than fibrosis. However, it is less than idea. To be optimal, tissue transfer should achieve the following criteria:

- The transferred tissues should be as similar as possible to the lost tissues
- The tissue transfer should achieve maximum benefit to the recipient area
- Tissue transfer should achieve minimal harmful effect to the donor area. This is referred to as minimal donor site morbidity
- The tissue transfer should be safe to the patient.

Wounds and their management

- Types of wounds:
    - Contusion:
        - It is a bruising injury caused by a blunt trauma
        - Contusions are, sometimes, associated with a hematoma, which can be small or large.
        - A small hematoma is resorbed by itself due to the action of macrophages. This means that there is no need to open and evacuate small hematomas. An exception to this rule is small hematomas in the face. These need to be opened and evacuated because leaving them will cause fibrosis and persistent indurations leading to cosmetic problems. Intracranial hematomas should be evacuated, as well.
        - Large hematomas are managed according to the of presentation by one of the following techniques:
            - Aspiration: this is applicable when the hematoma is acute (<24 hours). At that early stage, the hematoma is still liquid.
            - Incision and drainage: after 24 hours of injury, the hematoma starts to undergo clotting, and it is best managed by incision and drainage.
    - Abrasion:
        - It is the loss of epithelial cells (epidermis), and sometimes the upper dermis.
        - They are managed by dressing to prevent secondary bacterial infections.
    - Puncture wound:
        - This is caused by pointed objects (lead pencils), and is sometimes associated with the implantation of foreign bodies (wood or rust). The depth of the wound and the degree of contamination cannot be predicted in this type of wounds.
        - Management:
            - Tetanus vaccine: puncture wounds provide a suitable environment for the growth of the anaerobic Clostridium tetani
            - Excision of the puncture wound
            - Removal of foreign bodies.
    - Simple lacerations:
        - Lacerations are caused by sharp objects like knives.
        - Management:
            - Cleaning
            - Debridement

                - Suturing: this depends on the degree of contamination. If the wound is clean, it can be closed primarily (immediately). However, in the case of heavily contaminated wounds or wounds more than 6 hours old, delayed closure is indicated. However, lacerations in the face, can be closed after 24 hours of injury.
        - Avulsion flap:
            - An undermined laceration in the dermis and subcutaneous tissue
            - Management:
                - Debridement of the edges
                - Excision of the small avulsion flap: this is recommended to prevent the trap door effect. The trap door effect is the formation of nodules and indurations on the flap due to lymphatic and venous obstruction upon suturing the flap.
                - Suturing
- Methods of soft tissue closure:
    - Direct closure
    - Healing by secondary intention
    - Skin grafting: split thickness or full thickness
    - Flaps: local or distant
    - Prosthesis
- When and how to close a defect?
    - When?
        - If the wound is clean, we close it. This means that the wound should b free of contamination, infection, and dead tissue.
    - How?
        - It depends on the need and the condition of the defect. When there is no tissue loss, or minimal skin loss, the edges of wound can be approximated without tension. Here, we use direct closure. If the tissue loss is great (beyond the ability of direct approximation), a different method must be chosen.
- Management of defects:
    - When?
        - Now: when the wound is clean.
        - Later: when the wound is dirty
    - The cleanness of the wound depends on the mechanism of injury and time elapsed from injury to presentation. Crushing injuries with blunt instruments are associated a high degree of tissue damage and contamination. If the time between injury and presentation is more than 6 hours, it is considered as a contaminated wound. Facial wound are an exception to this rule; primary closure can be done after up to 24 hours after injury.

- Different classification for wounds:
    - Incised wound:
        - Caused by a sharp, relatively clean instrument (kitchen knife).
        - These wounds have minimal necrosis and contamination.
        - If the patient arrives within 6 hours of injury, they can be closed primarily.
    - Lacerated wound:
        - Characterized by jagged edges. They are caused by blunt instrument.
        - Associated with a moderate degree of necrosis and contamination.
        - If the patient arrives within six hours of injury, they can be managed via excision. They are transformed into an incised wound that can be closed primarily.
    - Crushed wound:
        - Seen in industrial and severe road traffic accidents.
        - Associated with heavy contamination and severe tissue devitalization.
        - These wounds are managed by opening, cleaning, irrigation, and adequate debridement. The devitalized tissue should be excised. This procedure is repeated daily until the wound is clean with no dead tissue. This is when you close the wound.
- How to close a wound with tissue loss?
    - Secondary intention: this option is good for small defects, when the area is of no functional or cosmetic value, or when other operative methods like flaps or grafts are risky
    - Skin grafts: in this method, a part of the skin is harvested from a donor area and applied on a defected area.
    - Flaps
- Types of wound healing:
    - Primary healing: when the wound is closed within hours of its creation
    - Delayed primary healing: if the wound is contaminated, we leave it open to prevent wound infection. Then, it is closed after 3-5 days.
    - Secondary healing: open, full thickness wounds are allowed to close by both contraction and epithilization. Wound contractions means a decrease in the wound size due to the contraction of myofibroblasts, which contain filaments.
    - Tertiary healing: when we use a skin graft or flap to cover the defect.
- Overview of wound healing:
    - In the process of healing, the injured tissue, depending on its type, is either regenerated or repaired.
    - Regeneration: the process in which the same type of cells regrows without functional effects. Examples include: regeneration of GI mucosa and vascular endothelium

    - Repair: the process in which the injured cells are replaced by fibrous tissue (Scarring). Examples include: repair of neurons and muscle cells.
- Stages of wound healing:
    - Early stage:
        - Tissue injury
        - Coagulation
        - Inflammation: during the inflammatory phase, polymorphs are recruited during the first 24-48 hours. Macrophages play their role in 48-72 hours. Fibroblasts follow. Macrophages function as phagocytic cells. They are the primary source of growth factors (cytokines), which regulate the whole process of wound healing.
    - Intermediate phase:
        - Mesenchymal cell migration and proliferation
        - Epithelization from the edges of the wound and remaining appendages.
        - Angiogenesis: the formation of new blood vessels
    - Late phase:
        - Matrix formation: collagen synthesis by fibroblasts. Collages fives tissues their strength and integrity.
        - Wound contraction
        - Proteoglycan synthesis: this is more important in the healing of fractured bones.
    - Final phase: this is the stage of wound remodeling. This occcurs by the breakdown and resynthesis of collagen. This stage can continue for 12-18 months.
- The stages of wound healing are not neatly arranged into distinct stages; these stages overlap.
- Abnormal wound healing:
    - The process of wound healing might be inadequate or abnormally extensive.
    - Inadequate wound healing: the causes of inadequate wound healing are either local or systemic:
        - Local:
            - Local tissue hypoxia: fibroblasts and macrophages are sensitive to hypoxia
            - Infection: this will perpetuate the inflammatory (early) phase
            - Presence of a foreign body
        - Systemic:
            - DM: it causes microangiopathy and most importantly atherosclerosis. At the molecular level, it affects inflammation through impairing chemotaxis of macrophages, fibroblast function (even if glucose levels are controlled), and inhibits epithelization, angiogenesis, and wound contracture.

- Vitamin C deficiency: this prevents cross linking of proline and lysine moieties in tissue collagen.
- Drugs (steroids and chemotherapy) : steroids are anti-inflammatory; therefore, they prevent the release of cytokines. This process is counteracted by vitamin A through an unknown mechanism affecting only wound healing.
- Malnutrition: protein balance is affected
- Trace elements deficiency: zinc and copper
- Renal disease: causes hypoalbuminemia due to proteinurea. In addition, it might lead to uremia with the toxic effects of uric acid on the tissues
- Liver diseases causing hypoalbuminemia
- Old age: attributable to slower metabolic rates.

▪ Acute wound healing is governed by macrophages. They release cytokines. Cytokines will cause fibroplasia and cellular proliferation. Proteases and their inhibition are controlled processes, so epithelization is followed by matrix deposition, angiogenesis, and tissue remodeling. This leads to normal wound healing.

▪ If the wound was affected by repeated trauma due to its location, for example, the acute inflammatory phases changes into a chronic inflammatory phase due to the increased activation of macrophages and neutrophilic infiltration. Inflammatory cytokines are released in copious amounts from macrophages. The neutrophils release hydrogen peroxide, a reactive oxygen species, responsible for bacterial killing. Both cytokines and peroxide lead to the activation of matrix degrading proteases and decrease the activation of protease inhibitors leading to excessive ECM degradation. In addition, peroxide will kill surrounding cells impairing epithelization. This leads to more inflammation; therefore, leading to a vicious cycle of chronic inflammation and ulceration.

o Excessive wound healing:

▪ There are two types of abnormally excessive wound healing; hypertrophic scars and keloid scars. These two types are different from normal scars biochemically and histopathologically.

▪ Occurs only in humans. No animal models exist

▪ During the early stages, these two anomalies cannot be differentiated from each other.

▪ Incidence of excessive healing is 5-15% of all wounds.

▪ Common features:

- Raised above the skin
- Erythematous: ongoing inflammation; always reddish

        - Pruritic
        - Near the wound
        - Common in areas of stress and tension (joint over shoulder, upper back, anterior chest, and ear lobe)
    - Hypertrophic scars develop insidiously 6-8 weeks after trauma. They worsen up to 6 months to 2 years. Then, they regress spontaneously or by medications. Keloid scars do not regress
    - Both are more common in darkly pigmented races
    - When excised, they have a tendency to re-occur months after treatment.
    - Keloid scars tend to worsen during puberty and pregnancy.
    - Fetal wound healing doesn't leave any scars.
    - Keloids and hypertrophic scars do not have an increased number of fibroblasts; they have an increased activity of fibroblasts.

Hypertrophic scar	Keloid scar
Improves with time (within 2 years)	Does not improve with time
No genetic predisposition (can occur in caucasians)	Genetic predisposition (blacks with nigroid features). Autosomal dominant with incomplete penetration
Limited ot the borders of the original wound	Extends beyond the margins of the wound.
Less collagen	More collagen
Distinct bundles with fine fibers	Large collagen fibers with closely packed fibrils
Fibers parallel to the dermis	Fibers random in orientation
Less cytokines	More cytokines
Myofibroplasts present (undergo contraction formation)	Absent myofibroplasts (do not undergo contracture formation)

- Pathogenesis of fibroproliverative scars:
    - Increase in the activity of cytokines, especially TGF-beta from platelets, macrophages, T-cells, and fibroblasts.
    - TGF-beta causes an increase in pro-collagen gene expression and reduction in proteolytic enzyme synthesis.
    - It increases the lay down of extracellular matrix (fibronectin and proteoglycans). Fibronectin is the tissue glue secreted by cells into the ECM. It allows for the chemotaxis of inflammatory cells.
    - Angiogenesis is triggered by other cytokines; therefore, the scar appears red.

        - The itching is caused by elevated levels of mast cells when compared to normal scar tissue. The itching can be relieved by antihistamines (systemic or local).
        - TGF-beta affects apoptosis related genes/ it prolongs the lifespan of cells in these scars when compared to normal scars.
- Histopathological differences between hypertrophic scars and keloid scars cannot be appreciated through light microscopy. They can only be differentiated through immunohistochemistry or electron microscopy.
- Treatment:
    - Surgical:
        - If surgery was not coupled with adjuvant therapy, the scar will reoccur. Recurrence rate is 50-80%. The median recurrence time is 13 months.
        - Multimodal therapy should be applied
        - Z-plasty or W-plasty are used for scars occuring against lines of minimal tension to reorient the scar.
        - Steroids are used to suppress the inflammatory process intraoperatively. This technique is used for keloids.
        - Factors to consider during surgical treatment:
            - Tension free closure to prevent ischemia of the edges of the wound
            - Removal of all old scar tissue
            - Avid trauma to surrounding normal skin and tissue
            - Obliterate dead space to prevent hematoma formation
            - Multimodal therapy.
    - Artificial skin (Integra):
        - It is a form of artificial dermis
        - These are used to supplement skin grafts (mainly epidermis) by filling the defect that was occupied by the debrided dermis over which the skin graft is applied.
    - Steroids:
        - Intralesional Triamcenolone acironide: most effective and young scars.
        - 4-8 weeks between injections to prevent systemic side effects (cushinoid features which are reversible). In children, the dose is 40 mg for a 6x10 lesion. In adults, the dose can reach up to 120 mg for a lesion of the same size. Steroids are not given for children less than one year of age as they may affect bone growth.

    - Side effects: hypopigmentation, skin and subcutaneous tissue atrophy (Adipose tissue does not regenerate; therefore, a depression may form permanently), telangiectasias, necrosis and ulceration of the skin, and cushinoid features.
- Pressure therapy:
    - Utilizes custom made pressure garments.
    - It reduces and softens hypertrophic scars. It also reduces the progression in 60-85% of hypertrophic scars. However, a single study reported no significant benefits of the use of this type of therapy.
    - The mechanism is by creating local tissue ischemia that leads to reduced metabolism. This will lead to reduced cell proliferation, which results in decreased collaged synthesis.
    - 24-30 mmHg is the effective pressure range
    - The garments should be utilized 24 hours a day for 12 months.
- Topical silicon:
    - Available as gel and sheets
    - Application of 12 hours a day for 6 months.
    - Mechanism is mainly unknown; however, it may involve an increase in tissue temperature under the silicon (2 degrees). This increase in temperature inhibits fibroblastic enzymes. Therefore, less collagen is synthesized.
    - The silicon that is applied is not absorbed through the skin. It helps reduce water loss. This leads to an increase in the elasticity and cosmetic appearance of the scar without any change in the history of the scar.
- Low dose radiation: superficial radiation is used. Given to resistant cases.
- Lasers: CO_2 and argon lasers are used
- Calcium channel blockers:
    - Trigger ECM degradation
    - Decrease proline entry into ECM
    - Change fibroblast shape; therefore, they disturb its function.
- Interferons:
    - Alpha, beta, and gamma interferons are applied intralesionally.

    - Decrease cell proliferation, inhibit collagen and fibronectin synthesis, increase collagenase, and decrease glycosaminoglycans synthesis.
    - There are expensive and not used in Jordan.
    - Recurrence rate with interferon therapy is low when compared to steroid therapy.
    - Side effects: fever, chills, fatigue, decrease in WBC
- TGF-beta antagonists:
    - Inhibition of TGF-beta by exogenous administration of receptors to scavenge excess TGF-beta.
    - We can use auto-antibodies against TGF-beta
    - We can also use binding proteins (alpha-2-macroglobulins)

Skin grafts and flaps (a detailed discussion)

- Skin grafts:
    - Classification:
        - Split thickness skin grafts: thin grafts formed of epidermis and a thin part of the dermis. The donor site heals by epithelization within two weeks; the same donor area can be reharvested after this period. Any area of the body can be used as donor sire; large areas of skin defects may be covered with a split thickness graft.
        - Full thickness skin grafts: consist of the whole skin (epidermis and dermis). They are taken from areas of loose skin; the donor area is closed by approximation of the edges. Only small areas could be covered by a full thickness skin graft.
    - Graft take: the process by which the graft is integrated into the recipient site. Take passes through two stages:
        - Plasmatic circulation: in the first 2 days, the graft is nourished from the underlying recipient site by the process of imbition or diffusion (plasmatic circulation)
        - Neovascularization: within 2-3 days, the graft's blood vessels are joined with the recipient's site vessels.
    - Signs of graft take:
        - The graft is adherent to the recipient site
        - The graft is pink in color
        - The graft blanches with pressure denoting vascularity
    - Factors affecting take:
        - Vascularity of the recipient site; it is the most important factor. The take is poor in areas of limited vascularity. Such areas include cortical bone bared of its periosteum, cartilage devoid of its perichondrium, tendons cared of their paratendons, and irradiated areas.
        - Infections: strep group A infections
        - Presence of barriers between the graft and recipient area: hematoma, seroma, debris, or foreign bodies.
        - Immobilization: the graft should b fixed to the recipient site. Graft mobility hinders its take.
    - Split thickness Vs. full thickness grafts:
        - When the area to be covered needs good quality skin or durable skin, a full thickness graft is used. However, if the covered area is large, the logical choice is a split thickness graft.
- Flaps:
    - A flap is a piece of tissue that carries its own blood supply and is moved from its original site to cover a defect.

- Flaps vary in their composition to suit the need of the recipient area. They may composed of: skin and subcutaneous tissue (skin flaps), skin and muscle (myocutaneous flaps), muscle alone (muscle flaps), or skin fascia and bone (osseofasciocutaneous flaps)
- Flaps Vs. grafts:
    - Compared to flaps, grafts are thinner. Flaps are formed of bulkier tissues. The complexity of the defect dictates the use of either flap or a graft. Moreover, the type of flap is determined by the nature of the effect. A facial defect due to the excision of BCC, for example, can be closed using a full thickness graft. However, a defect that follows the excision of an infiltrating oral tumor will require a flap.
    - Skin grafts depend on the vascularity of the recipient area for their survival. They cannot be used on vascular beds or over prostheses. On the other hand, we can use flaps in such situations.
- Flaps may be raised locally to cover nearby defects or may be brought from distant sites as free flaps. In the case of free flaps, the flap and its vascular pedicle are taken from the donor area to the recipient area where the artery and vein are connected using microvascular anastamoses.

Ulcers, sinuses, and fistulae

- The body is covered and lined by epithelium. The skin is covered by epidermis formed by keratinized stratified squamous epithelium, which is continuous with the epithelium lining the different internal organs. The epidermis is continuous with the GIT through the mouth and the anal canal, with the respiratory system through the nose, with the genital organs through the vaginal and with the urological system through the urethral meatus.
- The dermis of the skin is made of:
    - Fibers, cells, and ground substances
    - Blood, vessels, nerves, and lymphatics
    - Hair follicles, sebaceous glands, and sweat glands
- The epithelium stops diving via a mechanism called contact inhibition; division stops when the cell is surrounded by epithelial cells from all directions.
- Ulcer:
    - Defined as a pathological discontinuity of an epithelial surface. There are skin ulcers, gastric ulcers, and duodenal ulcers. The difference between a wound and an ulcer is that the ulcer is a wound, but of a pathological origin. The wound is of a traumatic origin.
    - Erosions of the mucosa and abrasions of the skin: Discontinuity of epithelium. Healed by regeneration.
    - Clinical examination: ulcers should be examined systematically. First, by inspection, then by palpation. The medical student should memorize the points to be examined, and record them:
        - Site, size and shape: it is more informative to join these items in one statement: there is an ulcer situated on the (specify the area), circular/oval/irregular in shape, and measures 5x3 cm.
        - Margin: describe the surrounding skin
        - Edge: the transition between the margin and the floor.
            - Sloping: denotes healing
            - Undermined: tuberculous or pressure ulcer
            - Everted: malignant (SCC)
            - Rolled or raised: rodent ulcer (BCC)
        - Floor: what the examiner sees; you should comment on the following:
            - Granulation tissue: healthy or not healthy
            - Necrotic tissue
            - Exposed structures as bone, tendon, or prosthesis
            - Islands of healing or skin grafts if present
            - Discharge.
        - Base: what can be palpated
        - Lymph nodes: lymph nodes draining the ulcer area should be examined.

- Lower limb ulcers:
  - The leg is a common site for different types of ulcers:
    - Arterial (ischemic)
    - Venous
    - Neuropathic
    - Malignant
    - Traumatic
    - Inflammatory
    - Diabetic
  - Every type of these aforementioned ulcers is usually associated with a specific clinical environment or background in the legs. The ulcer is a result of this environment, so upon physical examination, it is important to look for the signs of these environments or chronic diseases. This will help you in diagnosing what type of ulcer there is.
  - Arterial ulcers:
    - Occur on top of chronic arterial insufficiency due to atherosclerosis of the lower limb. The lower limb should be examined for signs of chronic ischemia: coldness, pallor, dryness, venous gutters, and absent pulses.
    - The arterial ulcer itself occurs at the distal parts of the foot or on the pressure areas. It usually lacks the signs of healing (sloping edges and presence of granulation tissue on the floor)
  - Venous ulcers:
    - Occur on top of chronic venous insufficiency. Other names are chronic venous hypertension or post-phlebetic syndrome.
    - This entity is characterized by increased venous pressure of the legs due to destruction of the veins following DVT. The leg is swollen due to venous edema. It is accompanied with induration and hyperpigmentation around the ankle. In addition, varicosity of the veins might be noted.
    - The venous ulcer is characteristically located on the lower third of the leg above the ankle. The most common site is above the medial malleolus. These ulcers usually show signs of healing.
  - Neuropathic or trophic ulcers:
    - Occur on top of an area with a disturbed sensation. The disturbance in sensation might be due to peripheral neuropathy or due to spinal cord pathology (spina bifida). The foot may be deformed due to loss of proprioception. Loss of proprioception leads to continuous trauma that ends as a Charcot joint. Moreover, muscle atrophy might be noted.

        - Mechanism: it was thought that nerves have a nutritional role to tissue. This is why these ulcers were called trophic ulcers. However, it was discovered that sensory nerves have a protective role to the foot. They protect the foot from recurrent trauma. These ulcers occur over pressure areas (heads of the metatarsals or the heels). These areas are areas where soft tissue suffers from repeated pressure and trauma. This results in ischemia, scattered necrosis, and healing by fibrosis. This vicious cycle continues until the area finally breaks down and ulcerates
- Malignant ulcers:
    - Develop on top of chronic unstable scars that were not allowed to fully heal due to repeated trauma (burn scars), pr due to the presence of dead bones (chronic osteomyelitis).
    - These ulcers are squamous cell carcinomas called Marjolin ulcers; they usually need 20-30 years to develop.
- Diabetic ulcers:
    - Diabetic foot is defined as the pathological results of diabetes on the foot of a diabetic patient, namely ischemia, tissue loss, and infection. These changes are the result of three factors:
        - Diabetic peripheral neuropathy: this leads to the loss of or disturbance in the sensation of the feet. The feet will be vulnerable to injury and pressure ischemia.
        - Angiopathy: diabetic patients have both micro-angiopathy and macro-angiopathy.
        - Decreased immunity: different aspects of immunity are affected.
    - These factors contribute to the production of two elements of the diabetic foot: ischemia and tissue loss and infection. In fact, one of these elements leads to the other as follows:
        - Ischemia decreases the immunity of the affected part. This makes it more vulnerable to infection. Dead tissue is a good medium for contamination. On the other hand, infection contributes to ischemia and tissue loss by the following mechanism:
            - Infection cases edema which causes ischemia
            - Infection causes thrombosis of the micro-circulation
            - Infection causes tissue damage.
            - Infection increases the metabolic rate and oxygen requirement of the affected area. This results in relative ischemia.

- Fistula:
    - defined as an abnormal tract connecting two epithelial surfaces. It could be a communication between the epithelium of one viscus to another, or between the epithelium of a viscus and that of the skin.
    - Etiology: fistulae may be congenital or acquired. The latter could be inflammatory, malignant, iatrogenic, or traumatic.
    - Congenital fistulae:
        - Tracheo-esophageal fistula: many types of abnormal communications between the trachea and the esophagus with different clinical presentations.
        - Branchial fistula: it is a pharyngeo-cutaneous fistula formed by the second branchial cleft and pouch due to failure of obliteration of the cervical sinus. The cervical sinus is formed by the down growth of the second pharyngeal arch over the second, third, and fourth pharyngeal clefts. The tract is lined by ciliated columnar epithelium. Its discharge is mucus or muco-pus. The tract passes between the external and internal carotid arteries and opens internally into the pharynx posterior to the tonsil. It opens externally on the skin of the lower neck anterior to the sternocliedomastoid muscle.
        - Umbilical fistula: it is formed due to the presence of a patent vitello-intestinal duct. It communicates the midgut with the umbilicus. The vitello-intestinal duct normally disappears, but it may persist as an umbilical fistula, umbilical sinus, vitelline cyst, a fibrous band, or Meckel's diverticulum.
        - Fistulae associated with anorectal agenesis: with the high type of anorectal agenesis, the anus, the anal canal, and the lower part of the rectum are absent. The rectum ends with a pouch; a fistula connects this pouch with the bladder or urethra in males, and the vagina in females.
        - Differential diagnosis of umbilical discharge:
            - Pilonidal sinus
            - Umbilical fistula
            - Umbilical sinus
            - Patent urachus
            - Sister Mary-Joseph's nodule: a nodule of metastatic carcinoma bulging through the umbilicus causing a seroanguinous discharge.
    - Inflammatory fistulae:
        - Inflammatory bowel disease and diverticultis may be complicated by the formation of cutaneous or internal fistulae. These fistuale connect the colon to the urinary bladder or the vagina

        - In acute cholecystitis, rupture of the inflamed gallbladder into a part of the GIT produces a fistula into that part.
        - Perianal fistulae are the result of infection of the anal glands.
    - Malignant fistulae: malignant disease of one viscus may invade another one and commnicate with it. Examples include: tracheo-esophageal, gastro-colic, and colo-vesical fistulae. Cancers may open to the skin producing a cutaneous fistula.
    - Iatrogenic fistulae: due to dehiscence and leakage of bowel anastomosis.
    - Traumatic fistulae: due to penetrating abdominal trauma with visceral injury.
    - Clinical presentation of a fistula:
        - The bacterial effect: when a viscus with a high bacterial load (colon) communicates with a normally sterile viscus (bladder), it causes an infection. A colo-vesical fistula produces a UTI.
        - The effect of bypassing functional parts of the GIT: in a gastro-colic fistula, the small bowel is bypassed. This produces diarrhea and malabsorption.
        - Loss of water, electrolytes, enzymes and nutrients. Entero-butaneous fistulae are classified into high and low output fistulae depending on their output volume. The more the amount, the more the loss. The more proximal the fistula is, the greater the loss. This means that a duodenal fistula is more dangerous than an ileal one.
        - Effect of fistula content on the skin: upper GI fistulae contain a high amount of digestive enzymes. This produces skin damage and maceration.
        - Vesico-vaginal fistulae are associated with urinary incontinence. Colo-urinary fistulae are associated with passage of feces with urine.

- Sinus:
    - Defined as a blind tract lined by granulation tissue and opens into an epithelial surface.
    - Most sinuses are congenital:
        - Auricular and pre-auricular sinuses: due to incomplete fusion of the nodules originating from the first and second pharyngeal arches. These form the pinna of the ear.
        - Branchial sinus: failure of obliteration of the cervical sinus or due to infection of a branchial cyst.
        - Thyroglossal sinus: due to infection of thyroglossal duct cyst.
        - Umbilical sinus: a remnant of the vitello-intestinal duct
        - The pilonidal sinuses are believed to be of an acquired nature. The most common site is over the coccyx in the anal cleft. They may be seen in the umbilicus, as well.

- Clinical picture of a sinus: sinuses are prone to recurrent infections, so they should be excised completely before an infection that produces fibrosis, adhesions, and secondary tracts. At this stage, complete removal is a difficult task.
- Clinical case: a patient presents with umbilical discharge; what is your differential diagnosis?
    - Vitello-intestinal fistula: the content is feculent
    - Vitello-intestinal sinus: contains mucus
    - Patent urachus: smell of urine
    - Pilonidal sinus: purulent discharge, hair is seen
    - Sister Mary-Joseph's nodule: serosanguinous discharge; rare.

Detailed pathophysiology of different types of ulcers

- Venous ulcer:
    - Chronic venous insufficiency and venous hypertension due to:
        - Incompetent valve
        - DVT
        - Calf muscle dysfunction due to dystrophy or atrophy.
    - Theories that explain venous ulcers:
        - Homan's theory: in 1917, Homan said that venous ulcers result from stasis in the underlying veins.
        - After Homan, they discovered that there is a hyperdynamic circulation in the limb that has a venous ulcer. This means that is a hyperdynamic state rather than stasis that causes the ulceration.
        - Recently, a new theory is becoming wildly accepted. The white-cell theory states that when there is a problem in the veins proteins and cells leak outside the circulation. When these cells (leukocytes) are outside, they will degranulate. Their granules contain enzymes and reactive oxygen species; both of which are damaging materials. Damage to the capillaries will ensue; this will increase the permeability of the capillaries to certain macromolcules (mainly albumin and alpha 2 macroglobulin). These macromolecules will bind the growth factors (cytokines) along with the matrix material making them unavailable for the surrounding tissues. In this case, the cytokines never work because they are trapped in the extravascular space.
        - In the USA, there is a special dressing for those with a venous ulcer. These dressings contain certain digestive (proteolytic) enzymes to digest albumin and alpha-2-macroglobulin.
- Diabetic foot ulcer:
    - Pathogenesis of diabetic ulcer:
        - Neuropathy: it affects the sensory, motor, and autonomic divisions:
            - Sensory: loss of vibrational and proprioceptive sensations.
            - Motor:
                - Flat foot is due to collapse in the medial arch of the foot (muscle weakness)
                - Claw toes (hammer toes): plantar flexion at the distal interphalangial joints of the toes. It follows weakness of both flexors and extensors of the lower limb; however, flexor muscles are stronger than the extensors. This results in plantar flexion
            - Autonomic:

        - Dry skin and poor nutrition
        - AV shunting: in a diabetic patient, you will find weak pulses with pink and warm skin. This is due to AV shunting not because of good circulation.
    - Biochemical bases of diabetic neuropathy:
        - Accumulation of sorbitol inside Schwann cells leads to absorption of water from the extraneuronal tissue to the Schwann cells (hyperosmolar effect). This leads to swelling of Schwann cells, which decreases their conduction velocity. This leads to impaired sensation.
        - Increased concentration of glucose inside the neuron causes inhibition of the entry of myoenositol. Decreased myoenositol entry will lead to abnormal cellular response to receptor stimulation (there is stimulation, but the response is weak), impairment of the Na^+/K^+ ATPase pump which is responsible for nerve conduction, and a decrease in ATP production (decreased energy).
        - Glucose entry to the neurons does not require insulin
- Vascular:
    - In contrast to the classical teaching about microangiopathy of the skin, it has been found out that the only histological change is a thickening of the basement membranes of the muscle of arterioles. This thickening of the basement membrane doesn't impair perfusion of the surrounding tissue. This was proven by measuring the transcutaneous O_2 tension in diabetic foot patients. However, if the patient has peripheral vascular disease in addition to diabetes, it will be a completely different story. This means that there is nothing called microangiopathy of the skin or even of the vasa nervosa in diabetics. There is microangiopathy in the kidneys and retina.
    - Patients with diabetes characteristically have an infrapopliteal macrovascular disease (at the bifurcation of the popliteal artery)
- Infection:
    - There is no evidence that diabetic foot ulcer results primarily from infection; however, it is a contributing factor. If the diabetic ulcer becomes infected, it will make the condition worse. Infection means that there is an abundance of proteolytic enzymes, which will result in more damage to the skin. Moreover, these patients have a decreased immunity.

        - Decreased cellular immunity due to decrease in chemotaxis and phagocytosis
        - Decrease in humoral immunity dye to a decrease in antibody production. This is caused by high levels of glucose (affects lymphocyte function)
    - Note: all chronic wounds are contaminated; however, they are not necessarily infected.
        - Contamination means the presence of bacteria
        - Infection means invasion and multiplication of the microorganism in the bodily tissue with our without systemic manifestations.
    - Each chrnoic ulcer is contaminated. Therefore, if you want to diagnose an infection, you should take a swab of tissue and culture it. A result of more than 10^5 cells per gram of tissue indicates an infection.
    - When taking a swab, always take the sample from a deep part of the ulcer.
- Ischemic ulcer (arterial ulcer):
    - The oxygen molecule is very important for the synthesis and hydroxylation of collagen. Collagen is a weak structure that is strengthened by the hydroxylation of proline and lysine moieties. For this process to happen, O_2 is needed. Therefore, hypoxia is one of the causes of poor wound healing and development of chronic ulcers.
    - Causes of hypoxia:
        - Local causes: peripheral ischemia and vasculitis
        - Systemic cause: heart diseases and chronic pulmonary disease
    - Chronic ulcers are treated using cytokines:
        - You should know that some cytokines are found in acute ulcers more than in chronic ulcers. This is proven by biochemical assays. It was found out that TGF-beta is present in chronic ulcers.
        - Accordingly, TGG-beta has been used to treat chronic ulcers. However, it was found out that some patients improved while others didn't. The reason behind this variation is that cytokines work in a cascade fashion.
        - Nowadays, TGF-beta is given in combination with other cytokines. They are administered in manner similar to the physiological progression of the events.
        - The type of cytokine used to treat a chronic ulcer depends on the phase of wound healing:

- If the chronic wound is caused by a defect in the epithelization (as in venous ulcers), we administer PDGF, which is the most important cytokine in the epithelization process.
- In pressure ulcers, the defect is in fibroplasia (lay down of collagen). In these cases, we give TGF-beta, which is the most important cytokine in the process of fibroplasia.

Pressure sores

- A pressure sore is defined as an ulcer that develops over a bony prominence due to prolonged pressure. They can be called decubitus ulcers or bedsores; however, it is preferable to call them pressure sores as they may develop in a paraplegic patient due to prolonged sitting in a wheelchair.
- Despite countless advances during the last decade, the treatment of pressure sores remains a significant challenge to the medical community. What is particularly disturbing is the enormous number of affected patients.
- Epidemiology:
    - The incidence of pressure sore formation is highly variable; it depends on the population of patients under question
    - Several studies have been performed to determine the incidence of pressure sores in different settings:
        - In general, approximately, 9% of all hospitalized patients develop pressure sores.
        - In acute care settings, 11% (CVD 41%, acute neurological disease 27%, orthopedic injury 15%)
        - In chronic care facilities 30%
        - Acute settings include: ICU, CCU, and NICU.
        - Acute neurological disease includes: spinal cord injury or head injury
- The more significant ulcerations (deeper, more severe, and more in number) tend to occur in acute settings. In these patients, the primary disease process may overshadow other concerns leading to pressure sores to progress unnoticed for greater periods of time.
- In chronic care facilities, the most common sites for pressure sores are ischial (because of sitting on a wheelchair, and sitting on the ischial tuberosity), trochaneric (because of sleeping on one side more than the other, greater troachnter), and sacral regions (because the elderly sleep on their backs).
- Patients at high risk: these patients are at a high risk due to incontinence (stool, urine, or double), bed or wheelchair bound, unable to ambulate without assistance, loss of sensation (DM or multiple sclerosis).
    - Elderly: according to the national pressure ulcer prevalence survey (1994), it was found out that 62% of patients with ulcers were more than 70 years of age.
    - Malnourished (poor wound healing)
    - Alterations in mental abilities (the patient is semi conscious or unconscious; thus, you can’t ask the patient to change position or corporate)
    - Paraplegics and tetraplegics
    - Spastic disorders (multiple sclerosis)
- Contributing factors and pathophysiology:
    - Pressure:
        - It is the single most important etiological factor.

- 96% of all pressure sores occur below the level of the umbilicus.
- 75% of all pressure sores are located around the pelvic girdle.
- In early studies, it was noticed that the pressure caused by an externally applied pressure reaches a maximum in deep tissues at the point of osseous protrusions (occiput, heel, knees, malleoli, sacral areas).
- Landis, in 1930, using a microinjection system, determined that capillary blood pressure in a single capillary ranged from 12 mmHg on the venous end to 32 mmHg on the arterial end.
- The external pressure at which blood flow stops is known as the capillary closing pressure.
- Complete cessation of flow, even in the face of positive arterial pressure, was found to occur at an external pressure of 70 mmHg less than the mean arterial pressure. The difference, known as transmural arterial pressure = MAP-70. However, this effect is not instantaneous; it needs time.
- There is an inverse relationship between the amount of pressure and the length of time required to cause ulceration:
    - Hussain et. Al studied the effects of pressure and time to determine which had the greater impact on ulcer formation. He believed that low pressures maintained for long time induced more tissue damage than did high pressure for short periods of time (proven in animal models); thus, the time factor is more important.
    - It was found that relieving the pressure for as little as five minutes can lessen the damage caused by pressures as high as 450 mmHg.
    - Based on many studies, it was proven that muscle is more susceptible to ischemia than skin. The initial pathology of ulcers occurs in muscle. With increasing magnitude or duration of pressure, the pathology progresses towards the skin. Muscle is especially sensitive, and it begins to degenerate after 4 hours of ischemia. In contrast, skin can withstand ischemia due to its lesser metabolic demands.
    - Due to this sensitivity, pressure sores in areas with a greater deal of muscle tend to take the shape of an inverted cone or flask. What we see is the “tip of the iceberg”.
    - Efforts to map the distribution of pressure on the bodies of supine and seated subjects suggest that pressures experience by the body in supine and prone positions are between 10-50 mmHg. However, on the ischial tuberosity, it ranges from 10-100 mmHg.

- Immobility:
    - It was found that patients with even some ambulation are less likely to develop ulcers. The protective mechanism of ambulation does not only

include relief of pressure, it includes an increase in minute ventilation, cardiac output, venous return, and maintenance of muscle mass.

- Shear (tangential pressure)
  - It is the second ischemic force in pressure ulcer formation. The theory states that a shearing force will weaken the superficial fascial fibers that attach skin to deep underlying fascia. This will lead to deformation and destruction of blood vessels leading to vascular occlusion and tissue destruction
  - In other words, the skin's blood supply comes from a dermal plexus which comes from perforators, which in turn, originate from the fascia of muscles. These perforators perforate fascia and ascend perpendicularly, then they start to branch giving the dermal plexus. Fascia is immobile relative to the skin, so when we apply a shearing force on the skin, it moves. However, the fascia doesn't. This will cause blood vessels to undergo angulations; thus, it augments ischemia.
  - To avoid shearing forces:
    - Mobilize patients as one piece; skin and fascia together.
    - Elevate the patient in linen
  - Although both shear and pressure act to produce stasis, pressure is the primary force in terms of occluding the arteriolar blood flow. Shear's greatest effect is on the reduction of the pressure value needed to stop arteriolar blood flow.
  - Friction is a factor that can contribute to skin ulceration through a non-ischemic mechanism. Friction increases mechanical forces on the epidermis, this leads to loss of stratum (friction is an issue in those patients who cannot lift themselves to change position). Friction occurs between the skin and the underlying liner, but shearing occurs between the skin and fascia.
- Moisture:
  - It leads to skin maceration, which leads to cellulitis (skin napkin rash). This will lead to infections, which will accelerate tissue breakdown increasing friction.
  - Sources of moisture include: perspiration, urine, feces, fistulae, and wound drainage. This is common in patients with incontinence.
- Nutrition:
  - Hypoproteinemia: a drop in either serum albumin or hemoglobin indicates anemia or hypoalbuminurea. Albumin is important for wound healing as it serves as a precursor for cytokines.
  - Ascorbic acid deficiency (vitamin C)
  - Decrease in trace elements: zinc

        - People with malnutrition are more liable for bed sores due to:
            - Decreased cushioning somatic fat mass
            - Decreased mobility
            - Decreased wound healing
- Staging and grading: this system is a clinical system, and it has its limitations. Erythema, for example, is harder to detect in darker people
    - Stage I: skin is intact, but reddened for more than 1 hour after relief of pressure. The muscle is involved, but it is not apparent clinically
    - Stage II (ischemia): blister or other break in dermis with or without an infection. It develops if pressure was continuous for 2-6 hours. In contrast to hyperemia, redness from ischemia requires at least 36 hours to disappear.
    - Stage III (necrosis): subcutaneous destruction into the muscle with or without an infection. Occurs if the pressure last for more than 6 hours. Usually, the skin is blue and firm
    - Stage IV (ulceration): involvement of bone and joint with or without an infection.
- Preoperative care:
    - The treatment of pressure sores is one of the most challenging areas in plastic surgery. Recurrence rates as high as 95% have been reported. Preparing a patient and the family for the long road ahead requires a team approach. The team should include: an internist, endocrinologist, nutritionist, neurologist, urologist, physiotherapist, psychiatrists, and a wound care nurse specialist.
    - All the components of the patient's overall care must be optimized prior to surgery. This increases the chances for a successful closure. These components include:
        - Nutrition:
            - Keeping serum albumin >2 g/dL
            - Protein intake: 1.5-3 g/kg: depends on the size of the ulcer
            - Caloric intake: 25-35 kCal/kg of non-protein calories
            - Vitamins: A, C, Zinc, Ca, Ferrous, copper
            - Patients may need a supplemental diet
        - Infection:
            - You should eradicate any UTI whether it is catheter related or not. Infected urine is a source of bacteremia and septicemia; thus, if you have recent wounds and there are bacteria in the blood, the bacteria will always settle on this fresh wound because it is an area rich in blood supply. Therefore, prior to any surgery, it is important to make sure that the patient doesn't have a septic focus.
            - Decrease the bacterial load inside the pressure sore itself. This is done through systemic and local antibiotics depending on the

tissue culture. Contamination of the pressure sore cannot be totally eliminated because it is a deep contamination.
        - The most common organisms that infect pressure sores include skin flora and enteric bacteria.
    - Pressure relief:
        - Turning the patient at intervals (5 minutes every two hours)
        - Special mattresses: to relieve pressure (foam, static floating, alternating air, low air loss, and air fluidized beds. The purpose of these beds is to evenly distribute the patient's weight. This will minimize the pressure in pressure areas.
    - Spasm relief:
        - Common in patients with spinal cord injury. The more proximal the lesion, the higher the incidence of spasm
        - The patient will be in flexion deformity due to head injury or multiple sclerosis.
        - If the spasm is not eliminated prior to any surgical procedure, the pressure sore will inevitably recur. In addition, it will be difficult for the nurse to take care of the reconstructed area.
        - To relieve the spasm:
            - Medical: diazepam
            - Surgical: this method is used in longstanding flexion deformities in which fibrosis of the tendons occur. Here, we perform tenotomy (cutting the spastic tendon).
    - Contracture (of a joint):
        - Longstanding denervation will lead to joint contracture.
        - Early cases are treated with physiotherapy
        - Late cases are treated with tenotomies.
        - If they are not treated, pressure sores will recur.
- Different methods for treating an ulcer:
    - Non-surgical treatment:
        - It is always prudent to attempt ulcer closure without surgical means.
        - If proper preoperative assessment and preparation are performed, there will be a period of time during which the ulcer can be observed. If the ulcer appears to be healing significantly, continuation of non operative treatment is indicated.
        - Some patients may never be candidates for surgical correction because of significant medical problems. In these patients, conservative treatment may lead to successful closure or at least it may allow for a stable wound that doesn't progress.

        - Local treatment with antibiotics (ointments), recombinant human PDGF and basic FGF (costly, limited, and not applicable for a huge wound), and wound care products.
    - Surgical treatment:
        - Excisional debridement of the ulcer, buria, heterotropic calcification, and the necrotic bone (removal of the whole iceberg)
        - Partial or complete osteoctomy to reduce the bony prominence
        - Closure of the wound with healthy, durable tissue. This depends on the nature of the patient, ulcer, and the need for subsequent procedures. Closure can be:
            - Direct closure: used in small pressure sores
            - Skin grafts: used in superficial ulceration with a success rate of 30% due to the presence of unhealthy underlying tissue
            - Flapps: local tissue flap, fascio-cutaneous, or myocutaneous.
    - Choice of flap: depends on the location, size, depth, previous surgery, and ambulation.
        - Myocutaneous flaps (superior to fascio-cutaneous flaps):
            - Excellent blood supply
            - Provision of bulky padding (cushioning)
            - Ability to readvance or reroatate to treat recurrence
            - Good for infected wounds
            - Can atrophic in elderly and patients with a spinal cord injury
            - It causes functional deformity in ambulatory patients.
            - Sensitive to external pressure
        - Fascio-cutaneous flaps:
            - Adequate blood supply
            - Durable coverage
            - Minimal functional deformity
            - Limited bulk (disadvantage)
    - Examples of flaps:
        - Flaps used to close a pressure sore in the gluteal region:
            - Medially based thigh flap: fascio-cutaneous flap
            - Gluteus maximus muscle flap: cover the pressure sore using this flap and cover the muscle with a skin graft.
            - V-Y hamstring advancement flap
            - Gluteal island flap
            - Gluteus maximus myocutaneous flap: muscle and skin
            - Tensor fascia lata flap: it is a good flap; but you must graft the donor area.

        - Gracilis flap: skin grafting for the donor area.
    - Flaps used to close a sacral pressure sore:
        - Bilateral gluteus maximus myocutaneous flap: it is called a rotation flap because there is an arch of rotation during the procedure.
        - Local flaps (fascio-cutaneous): these are called transposition flaps
        - Gluteus maximus muscle flap: you turn part of the gluteus maximus over the defect, and skin graft the donor area.
        - Myocutaneous flaps.
- Postoperative care:
    - Continuation of preoperative care
    - Leave the drains for a longer period of time.
    - No pressure on the operation site for 2-3 weeks, followed by gradual weight bearing.
    - Complications:
        - Acute, especially when taking a huge flap:
            - Hemorrhage
            - pulmonary and cardiac complications
            - infections.
        - Long term complications:
            - Recurrence (most common complication):
                - Causes of recurrence include underlying medical problems, changed mentation, improper nursing care, presence of spasm and contractures.
            - Marjolin's ulcer: SCC that develops in chronic ulcers (pressure sore is a chronic ulcer). It is aggressive with a poor overall survival (2 year survival rate is 66%). It can develop after as short as 3 years and as long as 25 years. Treated by chemotherapy, radiotherapy, and surgery.

Frost bite and related injuries

- The injuries caused by cold are divided into:
    - Tissue freezing injury (frost bite)
    - Non-tissue freezing injury (French foot, chilblain, pernio)
    - Hypothermia
- Chilblain: the skin is exposed to chronic high humidity and low temperatures without tissue freezing. The body's core temperature remains normal; it occurs to mountain climbers.
- French foot: the extremities are exposed to a damp environment over long period of time at temperatures of 1-10 degrees. Heat is lost because the extremity is wet. The vascular flow is poor because of vasoconstriction. The clinical picture is numbness, tingling, pain and itching. The skin is initially red and edematous, then it gradually becomes bluish-grayish. After a few days, the syndrome resolves; however, the extremity remains sensitive to cold.
- Cold urticaria: urticara and angioedema due to exposure to cold temperatures (seen mainly in aquatic activities). There are two types; familial and acquired. History of cold stimulation confirms the diagnosis.
- Frost bite:
    - The most common type of cold injury
    - Occurs when the temperature fall to -2C. The tissue freezes resulting in the formation of intracellular ice crystals and microvascular occlusions.
    - Pathophysiology:
        - The damage is either direct damage caused by formation of intracellular crystals or indirect due to ischemia caused by microvascular thrombosis and vasoconstriction. The damage occurs due to rewarming changes. When ice crystals melt, they will cause endothelial damage, which promotes edema. This releases reactive oxygen species, which increases tissue damage. Vasoconstriction occurs due to the release of prostaglandins.
    - Predisposing/risk factors:
        - Substance abuse (30-50%) alcohol
        - Psychiatric illness (10-20%)
        - Environmental factors (lack of appropriate clothing)
        - Peripheral vascular disease
        - Age: elderly and very young
        - Race: black more than white
        - Medications: amirophylline, caffeine, and ergot alkaloids.
    - Classification:
        - 1st degree: while/yellow plaque, hyperemia, edema, causalgia and pain (indicates nerve damage). Here, tissue loss and necrosis are rare

        - 2nd degree: blisters containing clear or milky fluid, erythema and edema are common. Characteristic recovery without tissue loss
        - 3rd degree: deep full-thickness skin necrosis. Tissue loss is common
        - 4th degree: cyanosis, gangrene and necrosis. Underlying muscles and bones are affected.
    - Treatment:
        - The most important step is rapid rewarming. Immersion in water heated to 40-42C
        - Pain killers
        - Massage is contraindicated because it increases the damage.
        - Debridement of clear blisters. Hemorrhagic blisters are left intact and aspired only if infected. You shouldn't attempt to debride aggressively during the early phase of a frostbite. Debride after you have a landmark between dead and viable tissue. The only indication for early operative intervention is to ameliorate a constricting eschar in circumferential 3rd or 4th degree frostbites to prevent the occurrence of compartment syndrome. Another indication is to drain a subeschar infection. If the gangrene is well demarcated, amputation is indicated.
        - Elevation of the affected area to decrease edema
        - Apply topical thrbomoxane inhibitors (aloevera) to injured areas
        - Systemic antiprostaglandin agents (NSAIDs)
        - Physiotherapy and mobilization
    - Adjuvant therapy:
        - Alpha blockers: work as pharmacologic sympatholytics
        - Nifedipine (Adalat)
        - Free radical scavengers (dimethylsulfide, vitamin C and E)
    - Diagnostic modalities:
        - Radio-isotope vascular imaging
        - Radio-isotope bone imaging
        - MRI and MRA
    - Sequels of a frostbite:
        - Arthritis
        - Pain at the site
        - Hyperasthesia
        - Hyperhydrosis (increse in sweating)
        - Pigment changes
        - Growth deformities
        - Cold sensitivity

Burns

- The burn wound and surrounding tissues have been classically described as a system of several circumferential zones radiating from primarily burned tissues as follows:
    - Zone of coagulation: a nonviable area of tissue at the epicenter of the burn
    - Zone of ischemia or stasis (injury zone) surrounding tissues (both deep and peripheral to the coagulated necrotic areas), which are not devitalized initially. However, due to microvascular insult, they can progress to irreversible necrosis over several days.
    - Zone of hyperemia: peripheral tissues that undergo vasodilatory changes due to neighboring inflammatory mediator release, but are injured thermally. These tissues remain viable.
- The primary aim of managing any burn is to preserve the tissues in the ischemic areas by:
    - Proper fluid resuscitation to maintain adequate perfusion and proper tissue oxygenation during the initial stages
    - Minimizing tissue edema, which has a negative effect on micro-circulation and tissue perfusion. This is achieved by proper fluid resuscitation (avoid over resuscitation) and by elevation of the injured limbs.
    - Proper burn wound management
- Etiology (types)
    - Thermal burns:
        - Heat causes coagulative necrosis of the tissues. By coagulation of the cellular proteins, this type of necrosis is characterized by preservation of the shape of the tissue involved. The temperature that causes burn is greater than 45 degrees. The depth of the burn depends on the quantity of heat (temperature and duration of exposure). Exposure to relatively lower temperature for long periods may cause more damage than exposure to high temperatures for short periods.
        - Classification:
            - Dry heat: direct flame burn. Direct exposure to fire
            - Moist heat (scald burn): exposure to hot liquids
            - Contact burn: contact with hot metals
            - Friction burns
    - Chemical burns:
        - Caused by acids or alkalis.
        - Characterized by deeper penetration and damage to the tissue due to the longer duration of action of the chemical. The chemical agent will continue its action until it is inactivated by a reaction with the tissues.
        - Contrary to the expectations, acids produce less damage and less penetration than alkalis. Acids usually produce coagulative necrosis

(denaturation of cellular proteins); this forms a barrier limiting the destructive effects of acids on tissue. Alkalis produce liquefaction necrosis allowing for deeper penetration and destruction.
        - The primary management of chemical burns is irrigation of the area affected by water to dilute the chemical agent. This should continue for 2-4 hours in case of alkaline burns, and for 30 minutes in cases of acid burns.
    - Electrical burns:
        - Te severity of the burn depends on the voltage. It is more serious with a high voltage current. High voltage currents can produce arrhythmias, as well.
        - The passage of electrical current through different tissues within the body, and hence the burn's damaging effect, is inversely related to the tissue resistance. This resistance varies among tissues. Nerves, muscles, blood, and blood vessels have low resistance. They are affected the most. Skin, bones, and tendons have the highest resistance; therefore, they are less burned. It is very important to remember this fact because a massively burned patient suffers from a massive hidden muscle burn.
        - Managing electrical burns:
            - Patient should be monitored for cardiac arrhythmias
            - Due to the muscle damage, these patients are liable for acute renal impairment (myoglobinemia and myoglobinurea). Good hydration and alkalization of urine are measures used to prevent this sort of renal impairment.
            - Due to muscle damage, patients are liable for compartment syndrome. It is important to monitor limb vascularity.
            - The severity of the electrical burn is not evident. It cannot be estimated, so fluid management could be based on a calculated formula. Therefore, close clinical observation, urine output, serial hematocrit values, and CVP reading are used for fluid management.
- Assessment of the severity of burn (depth and percentage):
    - The depth of the damage (degree):
        - Determines local management of the burn wounds.
        - In partial thickness burns, the part of the dermis containing skin appendages is preserved. These epithelial elements will make the burn heal by regeneration. This happens within 2 weeks. Here, the local management is conservative
        - In full thickness burns, all the dermis along with its epithelial elements are lost. The burn wound would naturally heal by fibrosis. This process

usually takes a long period and leaves an unstable scar with functional and cosmetic complications. Toa void this unfavorable fate, full thickness burns should be treated by skin grafting (better sooner than later).

- From the previous discussion, it can be concluded that the deeper the burn is, the more the scarring. This means that it will take more time to heal.
- Different classification for the degree of a burn:
    - First degree burns: thermal necrosis is limited to the epidermis. Clinically, there is pain and erythema. It takes 1-6 days to heal and leaves no scars.
    - Second degree burn (partial thickness): necrosis of the epidermis and varying depths of the dermis. It is characterized by pain (due to irritation of the dermal sensory nerves), erythema, blisters (bullae), wet exudates (weeping), blanching (denoting intact dermal vascularity), and preservation of skin elasticity. It takes 1-4 weeks to heal and leaves variable degrees of scarring.
    - Third degree burns (full thickness): necrosis of the whole skin and its skin appendages. Clinically, there is an eschar which is simply the burned necrotic skin. It is insensitive, leathery, hard, inelastic, and may show thrombosed dermal vessels. It takes months to heal, and usually leaves significant scarring. To avoid scarring, skin should be grafted.
- The deeper the burn is, the more dermis is necrotic so:
    - Less pain due to damage of dermal nerves
    - Healing is by fibrosis rather than regeneration. This leaves more post-burn contractures.
    - More loss of skin elasticity (might need escharotomy)

- Surface area involved in the burn
    - It is expressed as a percentage of the total body surface area (TBSA)
    - This determines the prognosis and general management of the burn, especially fluid management.
    - How to estimate TBSA?
        - Rule of nines: the body is divided into 11 nines. Head and neck (9%), upper limbs (9% each), anterior trunk (18%), posterior trunk (18%), lower limbs (18% each), and the remaining 1% is for the genitals.
        - The rule of nines is not accurate in children because the surface area of a child’s head is about 20% of the total body surface area. For children, it is better to follow specifically constructed charts for estimation of the area of the burn.

- For small burns, the palm of the hand equals 1% of the body's surface area.

- Management of the burn:
    - The burn should be looked at as a systemic disease or syndrome affecting all the systems of the body.
    - Regarding the respiratory system, the burn victim may have upper respiratory tract obstruction during the first 24 hours, smoke inhalation syndrome during the first 2-3 days, and later, the patient may develop respiratory infections.
    - The cardiovascular, renal, gastrointestinal, endocrine, and immune systems may be affected burns. Burns increase the body's metabolic rate; this results in negative nitrogen balance and malnutrition.
- Stages of management:
    - Acute or emergency stage
    - Local management of the burn wound
    - Treatment of complications
- Acute management:
    - Like any case of trauma, we follow the ATLS rules. These rules state that life threatening conditions should be treated within the first few minutes (prior to screening and diagnosis of other injuries). Therefore, we follow the ABC rules.
    - Airway:
        - Patients involved in flame burns may suffer from upper airway obstruction due to soft tissue edema of the oropharynx and vocal cords.
        - This results from direct thermal injury to the upper respiratory tract, which is caused by inhalation of the flames and hot gases.
        - This obstruction may not be evident initially. However, it appears during the first 24 hours.
        - Direct inspection of the oropharynx and the vocal cords (by laryngeoscopy or endoscopy) is indicated.
        - Endotracheal intubation should be performed before the obstruction in complete.
        - Signs of an impending obstruction include: tachycardia, progressive hoarseness, and difficulty clearing bronchial secretions.
    - Carbon monoxide poisoning:
        - The oxygen carrying sites are occupies with CO. CO has 210 time higher affinity than oxygen.
        - The condition is diagnosed by the estimation of carboxyhemoglobin levels in the blood. PO_2 levels might be normal.
        - Treatment is administration of 100% oxygen. This is used to displace the tightly bound CO from hemoglobin
    - Fluid management in burn patients:

- In the last decades, the understanding of the pathophysiology of fluid derangement in burn patients and their proper management has decreased the mortality of burn related to shock and its sequels.
- In burns, there is a major shift of fluids from the intravascular compartment, which is responsible for direct tissue perfusion, to the interstitial compartment. The cause of this shift is the increase in capillary permeability or loss of the capillary integrity. The capillary membrane, which is normally semi-permeable and sieves proteins to the circulation to exert oncotic pressure, becomes fully permeable. Proteins will leak to the interstitium dragging the intravascular water with them.
- The shifted fluids are known as "third space losses". They cause edema in the interstitium. Hemodynamically, the depletion of the intra-vascular compartment will cause shock; its severity depends on the percentage of burn. Practically, burn shock is seen in adults with burns greater than 15%. In children, with burns more than 10%.
- The causes of loss of the capillary integrity in the burned tissues are direct thermal damage to the capillaries and the release of vaso-active mediators. However, it is important to mention that non-burned areas will show edema and third space losses. The cause here is the resulting generalized hypo-proteinemic state in addition to the circulating mediators.
- Fluid management in major burns is critical; the following guidelines are important in planning fluid replacement:
    - The lost capillary membrane integrity with increased permeability has two implications. Most of the administered fluids will leak into the interstitium causing more tissue edema. This is harmful to the tissue as it increases tissue hypoxia. Moreover, large amounts of fluids are needed to maintain a functional perfusing intravascular compartment.
    - The amount of fluid given should be just adequate to perfuse the tissue. Overperfusion is at the expense of edema.
    - Although there are many formulas to estimate the amount of fluid needed to resuscitate a burned patient, there is no ideal one that you can apply and go to sleep. This means that the amount of fluid needed varies among patients. The only way to ensure that the optimal amount of fluid is given is by close monitoring:
        - Clinically, by observing the general condition of the patient (vital signs)
        - Urine output: the most sensitive indicator of tissue perfusion. It should be 0.5-1 mL/kg/hour; higher urine

output indicates that extra fluid is being given. This increases tissue edema.
        - Serial PCV readings: high PCV indicated heme-concentration. This indicates that more fluid needs to be administered. On other hand, if the PCV readings are low (heme-dilution), less fluid needs to be administered.
        - Swan-Ganz or CVP lines may be indicated in some patients, especially those with a limited cardiac reserve.
    - Due to the initial leakiness in the capillaries, it is wise to give crystalloids during the first 16-24 hours. Switch to colloids after 24 hours.
    - All formulas are based on the burned percentage and the patient's weight. The Parkland formula:
        - Fluid in the first 24 hours = 4 x weight x % of burn
        - An adult who weights 70 kgs with a 50% burn should receive 4 X 70 X 50 = 14,000 mL of Ringer's lactate during the first 24 hours.
        - Half of the amount is administered during the first 8 hours; the remainder is given over a period of 16 hours.
- Escharotomy:
    - In full thickness burns, the skin, which is normally elastic, is transformed into eschar (dead skin). This is accompanied by loss of elasticity. In circumferential deep burns of the limbs, the eschar would act as a tourniquet. As the burned patient develops edema, the pressure inside the limb increases above the capillary level leading to tissue ischemia. The picture is similar to compartment syndrome.
    - Management of compartment syndrome:
        - Elevation of the affected limbs
        - Observation of the circulation (capillary filling, color, temperature) and signs of ischemia (pain, paresthesia, and paralysis). It is important to mention that the presence of distal pulses does not rule out compartment syndrome.
        - If ischemia is suspected, escharotomy is indicated. This means incising the eschar of the affected limbs and fiber on both, medial and lateral aspects, to release the high pressure inside the limb.
- Antibiotics:
    - They are used to treat infections; not used prophylactically
    - Prophylactic antibiotics are contraindicated in burns for the following reasons:

        - Studies did not prove that prophylactic antibiotics decrease incidence of sepsis.
        - Antibiotics increase the incidence of fungal infection
        - Antibiotics increase the incidence of bacterial resistance.
- Analgesia and sedation:
    - Pain and anxiety relief. It is needed in all burn patients even those with full thickness burns. The following guidelines are to be applied:
        - In patients with low tissue perfusion, the drugs should be administered through the IV route to avoid accumulation of the drug.
        - Given in increments of small doses until the required dose is reached.
        - Head injury, hypoxia, and shock have the same symptoms. These should be ruled out before treating pain.
- Local management of burn wounds:
    - Partial thickness burn: in partial thickness burns, healing occurs within two weeks by regeneration of dermal skin appendages contained in the remaining dermis. The more superficial the burn is, the quicker the healing and the better the results are. Treatment is conservative aiming at providing the optimal conditions for regeneration to occur. We protect the wound from dryness, infection, and trauma. Practically, this means keeping the burn wet, covered with local antibiotics, and changing the dressing as required. Infection of partial thickness burns would damage the epithelial elements and the burn to a full thickness one.
    - Full thickness burns: naturally, this heals by fibrosis, which takes long time and leaves a bad scar. To avoid this fate, these wounds should be skin grafted. The eschar (dead skin) is adherent to the underlying subcutaneous tissue. As time goes by, bacteria invade the eschar and produces enzymes that separate the eschar from the subcutaneous tissue. This process takes 2-3 weeks. By this time, the SC tissue is covered by granulation tissue. A split thickness graft is harvested from unburned areas and applied to the burn wound. The modern treatment of burn evolved in the last decades. Now, the process involves the excision of the eschar early on and covering the burn wounds with a skin graft. The advantages of this approach are:
        - Decrease the hospital stay
        - Decrease the incidence of burn wound sepsis by elimination of the dead tissue and bacteria
        - Helps in early mobilization of the patient decreasing joint contractures.

        - Shortens the catabolic state minimizing the protein break down and malnutrition.
        - Better cosmetic outcome.
- This process does not come without disadvantages:
    - The eschar is adherent to the underlying SC tissue, so surgical excision results in massive blood loss and hypothermia
    - When the burned area is big (>60%), excision would leave a large exposed wound that we cannot cover by the patient's own skin.
- The first problem is solved by better blood banking, better ICU care, hypotensive anesthetics, and staged excision. The second problem is dealt with by temporary coverage of the excised area with a biological dressing. These are either allografts (taken from cadavers), or heterografts (taken from animals).
- After the excision of the eschar, we cover as much as we can of the excised areas with split thickness skin grafts (autografts). The remaining areas are covered, temporarily, with a biological dressing. After around two weeks, when the donor area heals, we take skin grafts again.

Detailed discussion of fluid management in burn patients

- Starling law of fluids:
    - The physiologist Ernest Starling published his theory, now known as the Starling law, in 1896.
    - Normal fluid homeostasis dictates equilibrium between the three fluid compartments. In burn injury, there are many disturbances in the normal homeostatis.:
        - The major event is the loss of the capillary integrity due to direct damage of the capillaries followed by release of inflammatory vaso-active mediators. This leads to increased capillary permeability and flux of water and proteins from the intra-vascular compartment to the interstituium the peak of this third-spacing occurs at some point 6-12 hours after burn injury. After 12 hours, the capillary membranes starts to regain its integrity; however, it remains abnormal for days. This third space loss occurs mainly in burnt tissue and to a lesser extent in the non-burnt areas.
        - Heat induced denaturation of collagen fibers in the interstitium causing a physical expansion of the potential third space with a transient -20 -- -30 mmHg negative pressure gradient favoring extravasion of fluid.
        - In adults with burns approaching 25-30% TBSA, damage to cell membranes also occurs. It is associated with a decrease in transmembrane potential and the accumulation of intracellular sodium and water with resultant swelling at the cellular level (cellular edema).
        - Edema in a burned patient leads to the following:
            - Hypoproteneima occurs from the loss of protein in the edema fluid
            - Tissue hypoxia and increased tissue pressure. This can result in further injury to the already ischemic tissue.
            - With circumferential injuries, increased interstitial pressure in burned soft tissue compartments often requires escharotomy or fasciotomy.
            - Pulmonary edema: increased intra-abdominal pressure. Increased intra-ocular pressure.
    - Who needs intra-venous fluid resuscitation?
        - Adults with TBSA 15-20%
        - Children with TBSA 10-15%.
        - Adults burns of less than 15-20% without inhalational injury are usually nor enough to initiate the systemic inflammatory response. These patients can be rehydrated successfully via the oral route with modest IV fluid supplementation.
    - Dilemma of fluid resuscitation:

        - The major problem of fluid resuscitation in the burnt patient is how to fill the leaky, sieve-like intravascular compartment to treat the shock and perfuse the tissues while minimizing the resultant edema.
        - To achieve this, we need constant monitoring:
            - Clinical monitoring: vital signs; signs of shock; signs of fluid overload.
            - Urine output: as a guide for volume status and end organ perfusion:
                - 0.5-1 mL/kg/hour in adults
                - 1-2 mL/kg/hour in children.
            - The presence of glycosuria can result in an osmotic diuresis and can lead to artificially elevated urine output values.
            - Older patients with longstanding diuretic use may be dependent on diuretics. They may not be able maintain the desired urine output despite what appears to be an adequate resuscitation volume.
            - Serial PCV readings
            - CVP and Swan-Ganz catheters should not be used routinely; however, they can be used with patients who have an underlying cardiac problem.
            - Improving base deficit and maintenance of the cardiac index in those whom invasive monitors are placed.
    - Fluid resuscitation:
        - Fluid resuscitation should start as early as possible. A delay of more than two hours is associated with increased morbidity and mortality.
        - Many formulas have been used (based on weight and percentage of TBSA.
        - The Parkland formula is the most used equation.
    - Crystalloids Vs colloids:
        - They complement each other, but due to the cost and potential risks of colloids, colloids should be given when the capillary integrity improves (6-12 hours after burn injury). To put it simply, start with crystalloids, then use colloids.
        - Due to the high morbidity associated with high volume resuscitations, an interest exists in using various colloid solutions to decrease edema, volume requirements, and blunt myocardial depression phenomenon observed with large burns areas. This is specifically true in patients with a preexisting heart disease, geriatric patients, and those with burns with an inhalational injury.
        - Different types of colloids:
            - Albumin: the largest contributor to intravascular oncotic pressure. When administered IBV as a 5% solution from pooled plasma

products, approximately, half of the volume remains intravascularly. With crystalloid solutions, only 20-30% of the volume stays intravascularly.

- Fresh frozen plasma: has the theoretical advantage of replacing all the lost proteins, not just albumin.
- Dextran: a solution of polymerized, high molecular weight glucose chains with almost twice the oncotic pressure of albumin. An increase in microcirculatory flow is also produced by reducing erythrocyte aggregation. Proponents of dextran point to the reduction of edema in non-burned tissues as a justification for the its use. The edema-reducing properties are maintained as long as the infusion is continued; however, upon withdrawal and subsequent metabolism of glucose, rapid loss of interstitial fluid occurs.
- Hypertonic saline solutions ranging in concentration from 180-300 mEq sodium per liter have many theoretical benefits. These benefits are achieved by the reduction in volume requirements by mobilizing intracellular fluid into the vascular space by the increased osmotic gradient. The intracellular depletion of water that results is a debated concern; however, it appears to be well tolerated. Close monitoring of serum sodium levels is mandatory. Serum sodium levels should not be allowed to increase to greater than 160 mEq/dL. The greatest benefit may ultimately be for those patients with the most limited cardiopulmonary reserves, those with inhalational injury, and those with larger burns approaching 40% of TBSA.

- Certain patient groups require greater resuscitation volumes than those calculated:
    - Patients with inhalational injuries are perhaps the most studied subset with required volumes as much as 30-40% higher than calculated.
    - Delays in initiating resuscitation. Those patients have been shown to need 30% more fluid (due to an increased inflammatory cascade)
    - Patients on home diuretic therapy frequently have a preexisting free water deficit.
    - The presence of an escharotomy or fasciotomy can substantially increase free water loss from the wound, and this must be replaced.

- Patients with electrical burns are often associated with large and underappreciated tissue insult. These require large volume resuscitations.

- Compartment syndrome:
    - Compartment syndrome is a limb-threatening and life-threatening condition observed when perfusion pressure falls below tissue pressure in a closed anatomical space. The current body of knowledge unequivocally reflects that untreated compartment syndrome leads to tissue necrosis, permanent functional impairment, and, if severe, renal failure and death.
    - Pathophysiology: the pathophysiology follows the path of ischemic injury. Intracompartmental structures cannot withstand infinite pressures. If fluid is introduced into a fixed volume, pressure rises. Various osseofascial compartments have a relatively fixed volume; introduction of excess fluid to extraneous constriction increases pressure and decease tissue perfusion, until no oxygen is available for cellular metabolism
    - Elevated perfusion pressure is the physiological response to rising intracompartmental pressure. As intracompartmental pressure rises, autoregulatory mechanisms are overwhelmed and a cascade of injury develops. Tissue perfusion is determined by measuring capillary perfusion pressure minus the interstitial fluid pressure
    - Normal cellular metabolism requires 5-7 mmHg oxygen tension; this easily is maintained with the capillary perfusion pressure averaging 25 mmHG and interstitial pressure 4-6 mmHg. However, rising interstitial pressure overwhelms perfusion pressure
    - Matsen demonstrated that as intracompartmental pressures rises, venous pressure rises. When venous pressure is higher than capillary perfusion pressure, capillaries collapse. The pressure at which this occurs is under debate; however, intracompartmental pressures greater than 30 mmHg are agree to require intervention.
    - At this point, blood flow through the capillaries stops. In the absence of flow, oxygen delivery stops. Hypoxic injury causes cells to release vasoactive substances (eg histamine and serotonin), which increase endothelial permeability .capillaries allow continued fluid loss, which increases tissue pressure and advances injury. Nerve conduction slows, tissue pH falls due to anaerobic metabolism, surrounding tissue suffers further damage, and muscle tissue suffers necrosis, releasing myoglobin, end result is loss of extremity, and, possibly, loss of life.

Post burn complications

- Splanchnic ischemia: ischemia to the splanchnic circulation of 3 major types:
    - Acalculus cholecystitis:
        - It occurs in cases of sepsis, TPN, critically ill patients, and diabetics.
        - It happens in less than 0.5% of burn patients
        - It is more common in patients with major burns (those involving more than 50% of TBSA)
        - It occurs 2-4 weeks post burn
        - If the patient can communicate and talk, he will complain of right upper quadrant pain associated with nausea and vomiting.
        - In the lab investigations, we would have leukocytosis and increase amylase levels.
        - Ultrasound is the diagnostic tool of choice due to its high accuracy (98%).
        - Management: an urgent operation is needed because the gallbladder is distended due to obstruction. The urgent operation may be cholecystectomy or cholecystotomy (drain in the gallbladder to decompress it)
    - Curling ulcer:
        - Gastroduodenal ulcer due to ischemia and hypoperfusion
        - When it occurs in the stomach, they are multiple
        - When it occurs in the duodenum, it is solitary.
        - One third of the patients complain of pain in the form of heart burn and epigastric pain; the rest do not have pain.
        - Patients have hematemesis
        - In 12% of patients, perforation takes place (it is mostly anterior).
        - Prophylaxis is better than treatment. It can be achieved by 3 measures:
            - Resuscitation and fluid management to prevent hypoperfusion.
            - Locally acting drugs:
                - Antacids: like Maalox (magnesium and aluminum hydroxide)
                - PPIs: like omeprazole
                - H_2 blockers: whether the old or the new generations
                - Sucralfate: used for mucosal cytoprotection (since mucosa is the most sensitive to ischemia and ulceration)
                - Bismuth therapy: mechanical barier preventing acid reflux
            - Start enteral nutrition as soon as the clinical status of the patient permits enteral nutrition. (orally or through and NG tube). TPN increases the possibility of curling ulcers, and it is one of the most important causes of bacterial translocation through the GI mucosa

to the circulation. This will lead to sepsis and multi organ failure syndrome.

- Ischemic enterocolitis:
  - Ischemia to the mucosa due to hypoperfusion and hypotension ending in bacterial translocation (mainly gram negative) and it has a very high mortality rate to multiple organ failure syndrome.
  - In order prevent bacterial translocation due to poor circulation, they use a technique called selective digestive tract decompression. The technique is as follows:
    - These patients are given cefotaxime (3^{rd} generation cephalosporin), tobramycin (aminoglycoside), polymyxin, and amphotericin B (since these antibiotics are wide spectrum antibiotics, fungal infections may cause trouble to the patient).
    - This technique prevents bacterial translocation and superimposed fungal infection.
    - This technique could successfully decrease bacteremia and MOFS. However, there is an increase in MRSA infections.

- Hypercatabolic metabolism:
  - Burn patients will pass through 2 phases which are the ebb and the flow phase.
  - What is peculiar to burn patients is that they remain in negative nitrogen balance as long as their burn is not grafted.
  - Once you graft them, or the burn heals with or without scarring, they will approach zero. Then, they proceed into positive nitrogen balance.
  - Since this negative balance and other metabolic changes may persist chronically, these patients will start to lose weight from both, fat and muscle mass. This will have 3 main chronic consequences:
    - Respiratory muscle paralysis; thus, they can't breathe or can't cough. This usually ends with multiple pneumonias.
    - Immune deficiency (lymphocytes and Ig deficiency)
    - Wound healing impairment (fibroblast problems)
  - If these patients have major burns, their B<R will increase by 100-150% the normal BMR.
  - Our job is to minimize the protein deficiency as much as we can. Thus, we give these patients a diet with the following ratios:
    - Carbohydrate: 50%
    - Fat: 30%
    - Protein 20%
  - This diet should be enteral whenever the patient's status permits.

- We have formulas to estimate the energy need in burn patients and these formulas are different between adults and children. Children need more energy for their growth; otherwise, they fail to thrive.
- Setherland's formula:
  - For children: energy = 60 kCal/kg + 35 kCal for % burn
  - For adults: 20 kCal/kg + 70 kCal/kg for % burn
- Now, if after using the formula, the patient was found to need 6000 calories, then we construct a diet in which 3000 calories come from carbohydrates, 1800 calories from fat, and 1200 calories from protein.
- Being the most important part of the diet, we have several formulas for the estimation of protein needs. The most important of which is Davie's formula:
  - For children: 3gm/kg + 1 gm for % burn
  - For adults: 1 gm/kg + 3 gm for % burn
- In general, proteins are not used as a source of energy. This is why we give more carbohydrates and fats. We let the body use them as a source of energy and keep proteins for our vital functions (immunity, wound healing, and muscle mass).
- We prefer to give these patients what they need and only what they need. However, if you give them more than what they need, it will not be a problem except in COPD patients. In these patients, carbohydrates will be metabolized to CO_2 and H_2O. this will increase CO_2 concentration, and these patients end with more CO_2 retention.
- Patients with renal impairment should not receive proteins more than they need. This also applies to hepatic failure patients in whom a higher protein intake is better avoided since amino acids are normally metabolized to urea. These patients have problems in the urea cycle, which takes place in the liver. They might end up with a hepatic coma.

- Suppurative thrombophlebitis:
  - This complication is directly related to the duration of canula usage. In the special units (ICU and CCU), a microfilter is used to filter small bacteria (but not very small viruses).
  - In general, a canula should last no longer than 48 hours except in patients with difficult veins. In these cases, a microfilter must be used.
  - 1/3 of the patients who develop this complication will show clinical signs in the form of fever or tenderness at the insertion site. However, the remaining 2/3 will present with fever of an unknown origin. These usually have a completely normal physical examination. However, if you culture the blood, it will be positive.
  - In non-burn patients, the most common microorganism in canula infections is staph aureus. However, in burn patients the organism is the same as the organism found inside the burn wound.

- Heterotrophic bone formation:
    - This takes place in joints underneath a full thickness burn. If a patient had a full thickness burn over the elbow joint, and the burn was never grafted, abnormal calcifications around the joint will develop and limit the patient's movement.
    - It was found that the aggravating factor for this process is passive aggressive physiotherapy. This form of therapy will cause trauma; this trauma will lead to Ca deposition (deposited as hydroxyapatite).
    - This complication is more common in patients when the burn's surface area exceeds 20%. It occurs 3 weeks – 3 months after the burn injury.
    - In these patients calcium and phosphorus serum levels are normal because it is a local process. However, alkaline phosphatase will be elevated due to new bone formation.
    - Treatment:
        - if patients present early on, NSAIDs will prevent the differentiation of mesenchymal cells into osteoblasts. This will prevent bone formation.
        - If there is early bone lay down, the joint should be closed. This will reverse the process (seen on X-ray).
        - If bone deposition was complete, the wound is left for a year. After a year, an X-ray for the area is taken. If the X-ray shows no "hotspots", this indicates that the process of deposition has stopped. The joint can be operated. However, if bone deposition is still active, you cannot operate. If it was operated, the deposition will recur. A delay in the treatment is associated with a poorer outcome.
        - If treatment was never sought, the joint will become dysfunctional. Moreover, bony alkalosis will develop.
    - This complication has to be differentiated from a similar condition called myositis ossificans. Myositis ossificans is a limb mass that develops secondary to a muscle trauma. After the trauma, a hematoma develops. This hematoma will organize to form a well localized, hard, and rounded mass. An X-ray of this mass will reveal a rounded mass surrounded by a calcified wall. There is no center of inflammation; the disease's name is a misnomer.
- Marjolin's ulcer:
    - SCC that develops over a longstanding chronic ulcer or chronic scar (especially that of a post-burn origin).
    - When compared to SCC de novo, Marjolin's ulcer has a more aggressive systemic and local behaviors.
- Hypopigmentation:
    - Occurs in the head and neck and on the hands of black burned patients.
    - Melanin in the skin is synthesized in melanocytes. Melanocytes are present at the junction between the dermis and epidermis. After its production, melanin is

transported to the keratenocytes in the dermis through the melanosomes that are transported through the dendrites of the melanocytes.
    - Even if the melanocytes are intact, the presence of scar tissue will prevent the transport of meanosomes to the keratenocytes. This will result in permanent hypopigmentation.
    - This phenomenon is known as Koepner's phenomenon. It is different from the Koepner's phenomenon of psoriasis in which psoriatic patches will appear in a previously path free area after an incision.
    - Treatment: dermabrasion (removal of the superficial later which is the rough scar tissue. After the removal of that layer, a skin graft is placed to permit melanosomal transport). Medical tattooing or camouflage are alternatives.
- Post traumatic stress syndrome (PTSS):
    - This is a psychological disorder that burn patients have. It comes in the dorm of depression, insomnia, anxiety, nightmares, and low self esteem.
    - After those patients are discharged from the burn unit, many families report behavioral changes in these patients. Some of these patients will end with psychosis. This is why psychotherapy is an important part of the treatment of such patients.
- Late post-electric burn complications:
    - If elctricity passes through the CNS or the peripheral nerves, it may produce central or peripheral damage.
    - Central damage is apparent after 6 months. It manifests in the form of epilepsy, encephalopathy, and brain stem dysfunction. This might lead to an abnormal breathing pattern, arrhythmias, and vasomotor disturbances. If electricity passes through the spinal cord, it will produce ALS.
    - Peripheral damage is apparent after 6 months of injury. It manifests as peripheral neuropathy that affects the motor part more than any other part. This is due to the heavy myelination of the motor fibers.
    - If electricity passes through the eyes, patients will suffer from permanent cataracts. The lenses will lose their translucency and they will be opaque. This, if you look at the black part of the eye, you will be able to see white spots. The patients will present with a decreased level of vision.

Postoperative pain control

- Postoperative pain control is inadequate for the following reasons:
    - Misbelieves:
        - Addiction
        - Overdose of narcotics which might lead to cardiac and respiratory arrest
    - Psychological causes: the patient thinks that postoperative pain is normal. Most of the time, patients will not admit to pain. Sometimes, the nurses don't provide enough care for such patients
- Answers to the aforementioned problems:
    - Narcotics can cause addiction. However, the dose at which addiction happens is much higher than the dose needed for postoperative pain relief. In burn patients, analgesia can be continued for 2 months without addiction.
    - To give analgesia without complications and to avoid overdosing, it should be given in a controlled manner.
- Why should we provide adequate postoperative analgesia?
    - Humane cause: doctors should control pain and stop the suffering of their patients.
    - Physical causes: inadequate postoperative pain will increase morbidity and mortality.
- Effect on pain on the body:
    - Increase in heart rate, blood pressure and oxygen demand. If the patient has borderline coronary circulation with a decreased cardiac reserve, increased pain can lead to ischemia
    - Decreased GI motility: paralytic ileus.
    - Atelactasis: if the patient has pain, their chest won't be able to move.
    - Pneumonia: inability to expectorate
    - Decreased mobility: increased risk for DVT and PE
- Certain advances that helped ease pain:
    - Laparoscopic surgery: decreased size of incision will decrease postoperative pain
    - Medical treatment for previously surgically treated diseases.
- Route of admission:
    - Minor surgery: oral
    - Major surgery: IM or IV. Due to the unreliable absorption of IM doses, IV is used most of the time.
- Frequency of analgesia:
    - Regular (eg Q4hours): here, doctor guarantees that the pain is controlled. The dose is given every 4 hours regardless of the patient's pain
    - PRN: (eg. Q4hours PRN): this means that the doses are given at least 4 hours apart. It doesn't mean that the patient is given a dose every 4 hours. If the patient doesn't need analgesia after the passage of 4 hours, the dose can be avoided.

- PCA (patient controlled analgesia): you install a pump that gives a baseline dose of analgesia. If the patient is in pain, he/she can press a button that will give an increased dose. Here, the patient doesn't have absolute control as the doctor sets a safety interval. It was found out that patients who had control over their analgesia needed lesser doses

Vascular anomalies

- Vascular anomalies are congenital anomalies caused by abnormal growth of blood vessels leading to masses originating and consisting of blood vessels with variable shapes.
- Classification:
    - According to morphology:
        - Salmon patch
        - Strawberry hemangioma
        - Port-wine stain
        - Cherry
    - According to the diameter of the blood vessel:
        - Thin small channel: capillaries
        - Wide cavernous
        - Mixed: cavernous and capillaries
    - According to the histological features: hemangiomas and vascular malformations
        - Hemangioma: this definition is restricted vascular anomalies caused by endothelial hyperplasia
            - They consist of young endothelial cells that are plump, active with high metabolic activity, high number of mitotic figures indicating division of endothelial cells, and have receptors for cortisone to mediate cellular proliferation.
            - In between the enothelial cells, there are some mast cells
            - They are considered embryonal cells with short doubling time.
            - They two phases; the proliferative phase and involution phase. During the proliferative phase, mast cells will increase in number. They will play a role in neo-angiogenesis. The lesion will expand with a rapid growth pattern. This will last for one year, then the lesion will stabilize. After that, it will start to decrease in size and color. So, it will start as a small lesion at the age of 3-4 months. They will grow and reach their maximum size at the age of one year. Them, they disappear to become fibrofatty skin.
            - These lesions grow and behave like neoplasms forming blood vessels. This is why they were called hemangiomas; they are considered the most common tumors of infancy.
            - More common in females with a ratio of 3:1
            - 80% are solitary; 20% are multiple
            - Most of them are in the head and neck, less in the trunk and extremities.
            - At the age of 5, resolution is complete in 50% of the cases.

- There is no need to treat them; most the time they resolve spontaneously. Treat when complicated.
- Complications:
    - Eyelid growth leading to ambylopia (lazy eye).
    - Bleeding
    - Large hemangiomas entrap platelets leading to thrombocytopenia; Kassbach-Merrit syndrome
    - Skeletal distortion
    - Congestive heart failure due to multiple hemangiomas.
    - Ulceration and infection
- Treatment:
    - Steroids ; first line of treatment. They will induce involution.
    - Laser treatment
    - Operative treatment

- Vascular malformations:
    - Structural anomalies resulting from errors in the morphogenesis of embryonic vessels between the fourth and tenth week of gestation.
    - Sporadic
    - They appear at birth, but not always congenital. They can appear years after birth.
    - The endothelial cells are normal, mature cells with normal turnover rates throughout their natural history.
    - Grow parallel to the child's growth.
    - Have no receptors for cortisone; they contain no mast cells
    - Can be one of two types: high flow or low flow (capillary, venous, lymph, or combines)
    - Do not regress spontaneously
    - May need treatment if complicated
    - Complications:
        - Erosion of bones leading to fractures
        - Stealing of blood from a limb leading to atrophy of distal parts
        - Entrapment of platelets
        - Bleeding
    - Treatment:
        - Surgery
        - Laser
        - Embolization: embolization of the feeding artery

Hemangioma	Vascular malformation
Not seen at birth; usually seen as a small macule after birth	Usually seen at birth, but may appear late
Rapid postnatal growth followed by involution	Grows with the child
Female:male 3:1	Female:male 1:1
Large ones lead to platelet entrapment and thrombocytopenia	Low flow ones might lead to diffuse hyperplasia
Rarely cause any complications	High flow ones can lead to destructive changes

    - Color will not distinguish between hemangiomas and vascular malformations
    - It is important to differentiate between these types of anomalies because hemangiomas tend to regress spontaneously
- Port-wine stain:
    - Capillary vascular malformation; not a hemangioma
    - Usually not evident at birth
    - Facial lesions restricted to one of the three trigeminal sensory areas . some can occur bilaterally, cross the midline, or overlap more than one division.
    - Flat, sharply demarcated, growth with the child, and have a surface studded with nodules.
    - Part of Sturge-Weber syndrome:
        - Vascular malformations of the face, chorroid plexus, and meninges
        - The stain involves the ophthalmic division
        - Local or generalized seizures
        - Intracerebral glaucoma
        - Ipsilateral glaucoma
    - Treated with scarrification, laser, surgical excision, or tattoos
- OSCE cases:
    - Case 1: the patient presents with a skin lesion, what should you do?
        - Color: brown (melanin), RBCs (red or pink). If it was brown, it is usually called a nevus. On average, an individual has 30 nevi.
        - Depending on the color, you should think of two possibilities: nevus or vascular anomaly
    - Case 2: 9 months old patient presented with a neck spot:
        - Nevus or vascular anomaly? Depends on the color; in this cases, it was violet.
        - Vascular malformation or hemangioma? Based on history:
            - Was it present at birth?
            - When did it start
            - Is it increasing in size?

        - It is changing in color?
    - Case 3: 1.5 year old patient; the mom says that he had a spot that started out as a small one, grew larger, then turned white. What should you ask?
        - What is it: vascular anomaly or a nevus?
        - It is a hemangioma or a vascular malformation
        - What is the prognosis?
        - What the indications for treatment?
        - What is the first line of treatment?

Hand infections and trauma

- We are going to deal with hand problems as a separate entity because Man is very dependent on his hand. Without hands, Man would be disabled. In addition, the hand is formed from compartments. This means that hands can suffer from compartment syndrome.
- Hand infections:
    - Paronychia:
        - Infection of the nail fold.
        - The most common infection in the hand
        - It happens due to bad maneuvering of hangnails or due to bad manicure.
        - In paronychia, there is redness around the nail on either or both sides of the nail.
    - Felon
        - It is the layman term for distal pulp space infection
        - The proximal, middle, and distal pulp spaces lie on the palmar aspects of the proximal, middle, and distal phalanges.
        - The pulp space is lined by skin, subcutaneous tissue, and a deep fascia connected to the bone. Skin of the palms and soles is thick due to its adherence to the underlying tissue by fibrous septa. The skin of the dorsum of the hand or foot, on the other hand, slides freely over the underlying tissue.
        - The distal pulp space is formed of fibrofatty tissue and it is considered as a compartment. Infection in that area will remain contained.
        - Each finger receives 2 digital arteries (one at each side of the finger) as part of the neurovascular bundle.
        - The 2 digital arteries anastamose with each other. Upon reaching the distal phalanges, they are considered as end arteries with no anastomosis between them. Thrombosis of the end arteries due to infection and increased pressure can lead to gangrene of the distal pulp space and bone necrosis. This leads to osteomyelitis. In other words, a felon can lead to osteomyelitis.
        - Felon is usually caused by pricking. This means that it affects the index and thumb fingers the most.
    - Tenosynovitis:
        - Anatomy:
            - Each finger receives two tendons; one for flexor digitorum superficialis and the other one for flexor digitorum profundus. FDS is inserted on the middle phalanx and flexes the finger at the proximal interphalangeal joint. FDP is inserted on the proximal

part of the distal phalanx. So it flexes the finer at the distal interphalagneal joint.
- DIP is located at the distal finger crease; the PIP is located at the next finger crease. The MCP is not located at the third crease; it is located more proximally in the palm (at the distal palmar crease)
- Each tendon is surrounded by a synovial shear. Infection in this sheath is called tenosynovitis.
- Since the tendon of FDP is inserted on the proximal part of the distal phalanx, tenosynovitis will not involve the distal pulp space.

- Treatment of hand infections:
  - The most common causative organism of hand infections is staph aureus. The second most common is streptococcus.
  - Strep and staph are gram positive cocci. Staph usually produces abscesses and contained infection due to the production of coagulase. Strep infections usually cause a spreading infection due to the production of hyaluronidase and streptokinase.
  - The initial treatment of hand infections is according to the "good guess" principle. We use oxacillin or amplicillin to combat staph aureus. Them, we take sample and culture them. The treatment is then determined according to the culture.
  - The initial phase of any subcutaneous infection is the cellulitic phase. In staph infections, the infection will be localized to form an abscess. The abscess is treated by incision and drainage.
  - If a patient presents with a staphylococcal abscess and we don't treat it, the abscess will transform into a sterile abscess. This abscess is treated b incision and drainage; there is no need for antibiotics. Usually, patients present at earlier stages where an abscess and a cellulitic focus are both present. These patients are given systemic antibiotics. In other words, if a patient presents with signs of infection he/she is treated with antibiotics. If there was no response, this indicates the presence of a sterile abscess.
  - General rules of management:
    - Antibiotics with incision and drainage
    - Elevation of the upper limb to decrease edema, which improves the circulation. This decreases the pain.
    - Resting the organ to decrease its pain.

- Trauma of the hand:
  - This is complicated issue because we have tendons, soft tissues, blood vessels, and nerves.

        - The most important thing to know is the concept of revascularization of a completely removed finger. We replant the finger by joining its artery to the corresponding artery in the hand. This amputated finger has to be dealt with carefully. While being transported to the hospital, it should not be placed in water nor frozen. On the other hand, has to be kept at 4 degrees in a dry environment.
    - Notes:
        - Acute inflammation Vs. chronic inflammation:
            - The insult forces the body to form an inflammatory reaction, which will subside either when the insult disappears or the body overcomes it by resolution and repair.
            - In the case of chronic inflammation, tissue destruction coincides with tissue repair. This leads to a viscous cycle of insult, inflammation, and healing.
        - Antibioma:
            - It is a hard, edematous swelling containing sterile pus. It is a result of the treatment of an abscess with long term antibiotics rather than by incision and drainage.
            - Treatment involves exploration and drainage of the lump (if it looks suspicious) or by careful observation until spontaneous resolution

Cleft lip and palate

- Embryology:
    - The frontonasal process, which is a proliferation of mesenchyme from the ventral surface of the developing brain, forms the nose, the central part of the upper lip, and the central part of the alveolar process.
    - The first pharyngeal arch gives rise to the maxillay and mandibular processes. From the former develops the lateral parts of the upper lip, the lateral parts of the alveolus, and the palatine shelves which fuse in the midline to form the palate. The mandibular processes fuse to form the lower lip and the mandible.
    - Cleft lip and cleft alveolus result from the failure of fusion of the frontoasal process with either one or both maxillary processes. This results in left, right, or bilateral cleft. Failure of fusion of the palatine shelves results in cleft palate.
- Incidence:
    - The incidence of clip lip or cleft palate is 1:750 live births
    - These constitute 2/3 of all craniofacial anomalies; the incidence of cleft lip is two times that of cleft palate.
    - In cleft lip, 60% of the cases affect the left side, 30% the right side, and 10% are bilateral.
    - Cleft lip is more common in males, while cleft palate is more common in females.
    - Isolated cleft palate is associated with other syndromes in 30% of cases.
- Etiology:
    - Not known. Hereditary factors play a role, but other factors include:
        - Vitamin deficiency in pregnancy (folic acid)
        - Drugs and steroids
        - Gestational viral infections or irradiation
        - Loss of amniotic fluid
- Cleft lip:
    - Cleft lip, which is usually associated a nasal deformity, is a purely aesthetic problem. Although it can be corrected at any age, most surgeons prefer to repair it at 3 months of age.
    - Cleft alveolus might lead to abnormal teething, especially of the lateral incisors and canines. Orthodentic treatment may be needed to correct the alignment of the alveolar arch. Those children need alveolar bone graft at the age of 809 to allow for the eruption of permanent canines.
- Cleft palate:
    - Unlike cleft lip, cleft palate is not an aesthetic problem. It is a functional problem with problems in feeding, speech, and regurgitation of food from the nose.
    - Patients with cleft palate have Eustachian tube dysfunction due to abnormal insertion of muscles. This leads to an obstructed tube; fluids will accumulate in the tube leading to secretory otitis media, which is evident by fluid behind the ear

drum. This condition is treated by an ENT specialist using drugs such as anti-histamines or by surgical drainage of the fluids. Surgical drainage can be done through the insertion of Gromet tubes.

- If secretory otitis media was not treated properly, it will be complicated by bacterial acute otitis media (recurrent ear infections) that may lead to hearing loss.
- Hearing loss in cleft palate patients is NOT congenital. It is acquired through repeated ear infections.
- Functions of the soft palate:
  - The soft palate (velum) is formed of muscles that elevae the soft palate and push it backward to meet the posterior pharyngeal wall to close and separate the nasopharynx from the oropharynx.
  - Velophalyngeal competence is defined as the ability of the soft palate and pharyns to act as a valve between the mouth and those. This valve should open during breathing to allow for air entry. However, it should be closed during swallowing to prevent nasal regurgitation of food. Moreover, normal speech requires the closure of the port between the mouth and the nose. This is done to create a positive pressure inside the oral cavity, which will help in the pronunciation of most consonants.
  - During sucking, the port between the mouth and the nose should be closed to create negative pressure for suckling.
  - Failure of this mechanism is called velopharyngeal incompetence. Among many causes, cleft palate is the most common cause. This failure is attributed to:
    - The mechanical defect of the cleft
    - Hypoplasia of the palate
    - Abnormal insertion of the palatal muscles
  - Surgical correction of cleft palate aims at the closure of the cleft palate to restore the velopharyngeal competence
- Family counseling:
  - The parents of the cleft baby should be counseled. This means reassurance, relief of anxiety, and discussion of the associated problems.
  - The family should be informed about the other functional deficits including nasal regurgitation, speech abnormalities, and the importance of ENT follow up.
  - The family should be introduced to the cleft palate team which consists of a plastic surgeon, pediatrician, ENT surgeon, dentist, orthodentic surgeon, speech therapist, cleft palate nurse, and a social worker.
- Feeding:
  - For normal feeding, the baby should suckle the milk and swallow it. It is important to educate the mothers about the baby's defective suckling.

        - These babies cannot create negative pressure inside their vocal cavity. This makes breast feeding difficult. Although sucking is defective, swallowing is normal.
        - To solve this problem, they invented special nipples designed to close the cleft during feeding to help suckling. A different solution includes passive introduction of the milk through the mouth by widening the opening of the bottle's nipple.
        - The following rules should be applied:
            - The mother is the best nurse; she is the person who should be involved in taking care and feeding her baby
            - Nasogastric feeding should not be used as a permanent mode of feeding
            - The baby should be nursed in semisitting position. He/she should be burped well to get rid of the swallowed air
            - Mothers should realize that feeding a cleft palate baby, at least initially, takes more time than normal babies.
            - Although breastfeeding is difficult in some babies, the mother can still breastfeed her baby by pressing her breast.
    - Speech:
        - Normal speech requires:
            - Passage of air from the lung to vocal cords
            - Collection of air in the oral cavity to create a positive pressure
            - Passage of air through the lips to produce consonants
        - Patients with cleft palate are unable to create this positive intra-oral pressure because air leaks through the nose. This leads to nasal escape, which is referred to as abnormal nasal speech.
        - Surgical correction of cleft palate helps in the restoration of normal speech.
    - Recurrent otitis media and hearing loss:
        - Normally, the Eustachian tube should be patent and aerated. This helps to balance the pressure on the two sides of the tympanic membrane.
        - In cleft palate patients, the tubes are not patent due to abnormal insertion of pharyngeal muscles. Fluid accumulates behind the eardrums leading to recurrent otitis media. If it was not managed properly, it will result in hearing loss.
        - The ENT surgeon is an important member of the cleft palate team as he is able to deal with these problems.
    - Timing of surgical repair:
        - Speech therapists believe that the earlier the repair, the better the speech outcome is. However, facial surgeons think that early surgery interferes

with the facial growth, which leads to retardation of maxillary growth (dish face). The compromise between these two opinions is to operate at 1 year of age.

11

Malignant Skin and Soft Tissue Lesions

Timothy A. Janiga

Melanoma

I. **Biology**
   A. **Epidemiology**
      1. **Eighth most common** cancer diagnosis in the United States.
      2. **Incidence is increasing** faster than any other cancer.
      3. **40,000 new cases** are diagnosed per year in the United States.
      4. **Lifetime risk** in general population is 0.5%.
   B. **Demographic risk factors**
      1. **Phenotypic risk factors** include fair skin (Fitzpatrick I and II) (Table 11-1), freckling, light eye color, and light hair color (stronger risk factor than eye color). Darker skin is protective against melanoma.
      2. **Geographic risk factors:** High altitude and higher latitude. Extreme southern latitudes (Australia, New Zealand) experience additional ultraviolet (UV) exposure from ozone depletion.
      3. **Gender:** Females have lower risk and better prognosis; the lower extremity is the most common site in females (Table 11-2). Males more commonly have lesions on the head and trunk.
      4. **Prognosis is worse for African Americans** (acral lentiginous type leads to delayed diagnosis).
      5. **Higher socioeconomic status** is associated with higher risk.
      6. **History of ultraviolet radiation exposure** (both UVA and UVB), especially a history of blistering sunburns, sunburns in early life, and intermittent exposure to UV light.
   C. **Precursor lesion risk factors**
      1. **Melanoma is caused by multiple processes** leading to malignant transformation of melanocytes.
      2. **A previous melanoma confers a 3% to 5% chance** of developing a second melanoma.
      3. **Congenital nevi**
         a. Malignant potential is more dependent on histology than size.
         b. Giant hairy nevi confer a 5% to 20% lifetime risk of melanoma; most commonly occur on head or pelvic region; prophylactic excision is recommended.
      4. **Acquired melanocytic nevi**
         a. Typically appear at 6 to 12 months of age; usually smaller than 5 mm.
         b. Increase in number through the fourth decade then slowly regress.
         c. The greater the number of nevi (>50), the greater the chance of melanoma.
      5. **Dysplastic or atypical nevi**
         a. Appear near puberty.
         b. Larger than common nevi (5–12 mm).
         c. Commonly found in covered areas.
         d. Most likely represent both a precursor lesion and a marker for patients with increased risk for development of melanoma.

Table 11-1. Fitzpatrick classification of skin type

Class	Skin Phototype	Unexposed Areas	Tanning History
I	Never tan, always burn	Pale/milky white	Red sunburn, painful swelling, skin peels
II	Sometimes tan, usually burn	Very light brown, sometimes freckles	Usually burn; pinkish or red coloring; light brown tan gradually develops
III	Usually tan, sometimes burn	Light tan, brown, olive	Rarely burn, with moderately rapid tanning response
IV	Always tan, rarely burn	Brown, dark brown, or black	Rarely burn, with rapid tanning response

6. **Atypical junctional melanocytic hyperplasia (AJMH)** (also known as lentigo maligna, or Hutchinson freckle)
   - **a.** Thought to represent a melanoma precursor lesion.
   - **b.** Can be present in dysplastic nevi that tend to be more irregular and lighter in color.
   - **c.** Needs to be fully excised; 5-mm margins are recommended, but are typically inadequate.
7. **Spitz nevus**
   - **a.** Most commonly found in children and young adults (formerly called juvenile melanoma).
   - **b.** Easily confused with melanoma, and almost always benign.
   - **c.** Well circumscribed and raised, with variable pigmentation.

D. Genetic risk factors

1. **Family history:** Two or more cases of melanoma in first-degree relatives. Hereditary melanoma shows autosomal dominant transference with variable penetrance.
2. **Suppressor genes and oncogenes**
   - **a.** p16/CDKN2A: Tumor suppressor gene that is mutated or deleted in the majority of melanoma cell lines.
   - **b.** RB1: Tumor suppressor gene expressed in higher levels in certain melanomas. Uncommon mechanism in melanoma development.
   - **c.** CDK4: Oncogene thought to play a role in melanoma progression in a small proportion of familial and sporadic melanomas.
3. **Dysplastic nevus syndrome** (also known as familial atypical mole and melanoma syndrome): Patients have a first- or second-degree relative with malignant melanoma, and typically have at least 50 melanocytic nevi.
4. **Xeroderma pigmentosum (XP):** Typically presents in childhood with early death secondary to metastatic spread of skin tumors. DNA damaged

Table 11-2. Distribution of melanomas with respect to gender

Location	Men (%)	Women (%)
Scalp	7	3
Face	12	9
Neck	5	3
Arm	13	19
Front of trunk	16	8
Back of trunk	**36**	23
Leg	9	**31**
Sole of foot	2	4

by UV light is unrepaired secondary
Restriction from sunlight exposure is mandatory, with aggressive treatment of skin lesions.

II. Clinical diagnosis and classification

A. A dermatologist's physical examination is only 60% to 80% sensitive for diagnosing melanoma. Full-body photography to monitor atypical nevi may increase sensitivity.

B. Common clinical features of melanoma (ABCDE mnemonic)

1. **Asymmetry**
2. **Border irregularity**
3. **Color variation (shades of blue are the most ominous)**
4. **Diameter more than 6 mm**

C. Major types of melanoma

1. **Superficial spreading melanoma**
   - **a.** Most common type: 70% of cases.
   - **b.** Intermediate in malignancy.
   - **c.** Usually arises from preexisting nevus.
   - **d.** Affects both genders equally.
   - **e.** Median age at diagnosis: fifth decade.
   - **f.** Most common sites: Upper back in men and lower legs in women.
   - **g.** Irregular, asymmetric borders with color variegation.
   - **h.** Radial growth phase early; vertical growth phase late.
2. **Nodular melanoma**
   - **a.** Second most common: 15% to 30% of cases.
   - **b.** Most aggressive type.
   - **c.** Typically does not arise from preexisting nevi.
   - **d.** Men are affected twice as frequently as women.
   - **e.** Median age at diagnosis is 50 years.
   - **f.** Bluish-black, with uniform, smooth borders.
   - **g.** Vertical growth phase is a hallmark feature.
   - **h.** Not directly associated with sunlight exposure.
   - **i.** 5% are amelanotic—associated with a poorer prognosis because of delayed diagnosis.
3. **Lentigo maligna melanoma (LMM)**
   - **a.** 10% to 15% of cutaneous melanomas.
   - **b.** LMM is the least aggressive type and the only one clearly associated with sunlight exposure.
   - **c.** Head, neck, and arms of elderly (sun-exposed areas).
   - **d.** Women are affected more frequently than men.
   - **e.** The median age at diagnosis is 70 years.
   - **f.** Usually greater than 3 cm in diameter; irregular, asymmetric with color variegation; areas of regression may appear hypopigmented.
   - **g.** Precursor lesion is lentigo maligna or Hutchinson freckle (histologically equivalent to melanoma *in situ*, or AJMH): radial growth phase only. Transition to vertical growth phase marks development of lentigo maligna melanoma.
   - **h.** Malignant degeneration is characterized by nodular development.
4. **Acral lentiginous melanoma**
   - **a.** 2% to 8% of melanomas in whites and 35% to 60% of melanomas in blacks, Hispanics, and Asians.
   - **b.** Presents in palms, soles, and beneath nail plate (subungual). Note: Melanonychia is a linear pigmented streak in the nail, which is often benign and is more common in black and Asian populations. Due to the risk of melanoma, biopsy of suspect lesions should be performed.
   - **c.** Median age at diagnosis is approximately 60 years.
   - **d.** Irregular pigmentation is common.
   - **e.** Large size (>3 cm).
   - **f.** Majority involve great toe or thumb.
   - **g.** Long radial growth phase; transition to vertical growth phase occurs with high risk of metastasis.

D. **Noncutaneous melanoma**
   1. **Mucosal melanoma**
      a. Mucosal melanomas represent fewer than 2% of melanomas, usual presenting within the genital tract, anorectal region, and head an neck mucosal surfaces.
      b. They are usually large at diagnosis, with poor prognosis.
      c. Radical excision is of questionable benefit.
   2. **Ocular melanoma**
      a. Represent 2% to 5% of melanomas (most common noncutaneous mel noma).
      b. Interference with vision leads to earlier diagnosis.
      c. The eye has no lymphatic drainage; therefore, no nodal metastases ar seen.
      d. The liver is the main site of metastatic disease.
      e. Treatment is by enucleation

E. **Melanoma with an unknown primary**
   1. **Represents 3% of melanomas.**
   2. **Diagnosis is by exclusion.**
   3. **Nodal metastases are the most common presentation.**
   4. **Prognosis is similar to melanomas with a known primary.**

III. **Melanoma staging and prognostic factors**

A. **Major prognostic factors:** Tumor thickness, Nodal status, and Metastases–TNM (Table 11-3)
   1. **Breslow thickness** is reported in millimeters; it is more accurate tha Clark's level and is a better prognostic indicator.
   2. **Clark's level** is based on invasion through the histologic layers of the skin

B. **Other significant prognostic factors**
   1. **Anatomic location:** Trunk lesions generally carry a worse prognosis tha those on the extremities.
   2. **Sex:** For a given melanoma, women tend to have a better prognosis women are also more likely to have extremity melanomas, which have better prognosis.
   3. **Ulceration** is a poor prognostic sign.
   4. **Lymph node involvement** or in-transit metastases are more significar than any other prognostic factors.

C. **The American Joint Committee on Cancer** has developed a staging syster based on TNM classification (Table 11-4).

IV. **Diagnosis and treatment**

A. **Diagnosis of primary melanoma** is made by histologic analysis of full-thickness biopsy specimens.

Table 11-3. Melanoma thickness grading

Skin	5-Year Survival (%)
Clark Level	
I–In situ	100
II–Papillary dermis	88
III–Papillar-reticular dermis	66
IV–Reticular dermis	55
V–Subcutaneous	22
Breslow Depth (mm)	
<1.00	89–95
1.01–2.00	77–89
2.01–4.00	63–79
>4.00	7–67

Thin melanoma. (4)
<.78 mm
Int.
Thick M. >1 mm.

Table 11-4. AJCC Melanoma Staging System (2002)

TNM Definitions

Primary Tumor		*Ulceration status*
Tis	Melanoma in situ	
T1	≤1.0 mm	a: without ulceration and level II/III
		b: with ulceration or level IV/V
T2	1.01–2.0 mm	a: without ulceration
		b: with ulceration
T3	2.01–4 mm	a: without ulceration
		b: with ulceration
T4	>4.0 mm	a: without ulceration
		b: with ulceration
Regional Lymph Node Involvement		*Nodal Metastatic Mass*
N0	Negative	
N1	1 node	a: micrometastasis*
		b: macrometastasis°
N2	2–3 nodes	a: micrometastasis*
		b: macrometastasis°
		c: in-transit met(s)/satellites(s) without metastatic nodes
N3	4 or > metastatic nodes, or matted nodes, or in-transit met(s)/satellite(s) with metastatic node(s)	

*Micrometastases are diagnosed after sentinel or elective lymphadenectomy

°Macrometastases are defined as clinically detectable nodal metastases confirmed by therapeutic lymphadenectomy or when nodal matastasis exhibits gross extracapsular extension

Distant Metastasis		*Serum Lactate Dehydrogenase*
M0	No distinct metastasis	Normal
M1a	Distant skin, subcutaneous, or nodal mets	Normal
M1b	Lung metastases	Normal
M1c	All other visceral metastasis	Elevated
	Any distant metastasis	

Staging

Stge 0	Tis N0 M0
Stage IA	T1a N0 M0
IB	T1b N0 M0, T2a N0 M0
Stage IIA	T2b N0 M0, T3a N0 M0
IIB	T3b N0 M0, T4a N0 M0
IIC	T4b N0 M0
Stage IIIA	T1-4a N1a M0, T1-4a N2a M0
IIIB	T1-4b N1 M0, T1-4b N2a M0, T1-4a N1bM0, T1-4a N2b M0, T1-4a/b N2c M0
IIIC	T1-4b N1b M0, T1-4b N2b M0, any T N3 M0
Stage IV	any T any N M1a, any T any N M1b, any T any N M1c

1. **Excisional biopsy** is preferred for lesions less than 1.5 cm in diameter. If possible, excise lesion with 1- to 2-mm margins.
2. **Incisional biopsy** is appropriate when suspicion is low, the lesion is large (>1.5 cm) or is located in a potentially disfiguring area (face, hands, and feet), or when it is impractical to perform complete excision. Incisional biopsy does not increase risk of metastasis or affect patient survival.
3. **Permanent sectioning** is used to determine tumor thickness.
4. **Avoid shave biopsies,** because they forfeit the ability to stage the lesion based on thickness.
5. **Do not cauterize or freeze** the specimen: Tissue destruction makes it impossible to evaluate thickness and margins.
6. **Wide local excision** for tissue diagnosis can decrease the efficacy of future lymphatic mapping because of disruption of local lymphatics. Biopsy incisions should result in scars parallel to lymphatic drainage.
7. **Orientation of biopsy** incisions should also take definitive surgical therapy into consideration.
   a. Extremity biopsies should use longitudinal incisions.
   b. Transverse incisions are sometimes preferable for preventing contractures over joints.
   c. Head and neck incisions should be placed within relaxed skin tension lines, keeping facial aesthetic units in mind.

B. Definitive management of melanoma

1. **Wide local excision** is the treatment of choice.
2. **Recommended surgical margins** depend on tumor thickness (Table 11-5).
3. **Subungual melanoma** requires amputation proximal to the distal interphalangeal joint for fingers, and proximal to the interphalangeal joint for the thumb.

C. Management of regional lymph nodes

1. **Elective lymph node dissection (ELND)** involves removal of clinically negative lymph nodes from the nodal basin. A survival benefit was demonstrated in retrospective reviews; however, no survival benefit has been seen with prospective trials except for a subgroup with 1- to 2-mm (intermediate-thickness) melanomas.
2. **Sentinel lymph node biopsy (SLNB)**
   a. In the sentinel node theory, a sentinel node will be the first lymph node seeded by tumor cells; therefore, excision of sentinel node(s) alone is adequate to determine nodal status. The morbidity of SLNB is considerably less than ELND. Sentinel node(s) can be detected in more than 90% to 95% of patients. SLNB is now widely considered the standard of care.
   b. SLNB is performed in conjunction with wide local excision of the primary tumor. Lymphatic mapping is performed to determine the first lymph node that drains the primary tumor site (sentinel node).
   c. SLNB-positive patients undergo staged regional lymphadenectomy and may be candidates for adjuvant therapy.
   d. Preoperative nuclear imaging: Radiolabeled colloid solution (technetium 99) is injected intradermally at the primary tumor. Lymphoscintigraphic imaging localizes the sentinel node basin(s) (some tumor sites can drain to multiple basins).

Table 11-5. Recommended surgical margins for melanoma excision

Melanoma Thickness (mm)	Margin (cm)
In situ	0.5
<1	1
1–4	2
>4	2–3 (controversial)

e. In the operating room, blue lymphangiography dye (Lymphazurin) is injected intradermally at the periphery of the primary tumor site prior to excision of the primary tumor.
   (1) Mark edges of the lesion before injection to avoid obscuring them with the dye.
   (2) Potential sentinel nodes will appear blue when exploring the nodal basin, giving secondary confirmation to localization with Geiger counter detection of ^{99}Tc.
   (3) Dye injection may briefly interfere with pulse-oximeter readings; alert anesthesiologist at time of injection.
   (4) Caution: Risk of allergy or anaphylaxis with dye injection.

f. Following excision of the primary tumor, drapes, instruments, gowns, and gloves are changed and the regional lymph node basin(s) identified by lymphoscintigraphy are explored. All radioactive ("hot") and/or blue nodes are excised.

g. Histologic analysis of sentinel node(s) with immunohistochemical staining identifies micrometastases. Permanent sections are required; frozen sections cannot reliably differentiate normal from neoplastic melanocytes.

D. Surveillance and treatment of melanoma recurrence

1. Guidelines vary depending on stage of melanoma.
2. **Asymptomatic patients** should be seen every 3 to 4 months for 2 years, then every 6 months for 3 years, then annually. The most accurate way to detect metastatic disease is to take a thorough history.
3. **Chest x-ray and liver function tests** (LDH and alkaline phosphatase) are usually sufficient; more extensive workups including computed tomographic (CT) scans have not altered outcomes.
4. **Local recurrence** typically occurs within 5 cm of the original lesion, usually within 3 to 5 years after primary excision; most often this represents incomplete excision of the primary tumor.
5. **The most common sites** of recurrence are the skin, subcutaneous tissues, distant lymph nodes, and then other sites (lung, liver, brain, bone, gastrointestinal tract).
6. **Reexcision** is the primary treatment for local, small, isolated lesions.
7. **Surgery is effective for palliation** in patients with isolated recurrences in skin, central nervous system, lung, or gastrointestinal tract.
8. **Chemotherapy:** Complete remission is rare.
   a. Dacarbazine (DTIC), carmustine, cisplatin, and tamoxifen in combination are most frequently used.
   b. Isolated hyperthermic limb perfusion for extensive cutaneous disease (melphalan and tumor necrosis factor) is used at some centers.
9. **Immunotherapy with vaccines and cytokines** is the subject of ongoing clinical trials. FDA-approved regimens include interferon-α (IFN-α) for stage III disease and interleukin 2 (IL-2) for stage IV disease.
10. **The mean survival with disseminated disease** is 6 months. Respiratory failure and central nervous system complications are the most common causes of death.

Nonmelanoma Skin Cancer

Nonmelanoma skin cancers (NMSCs) are the most common malignancies, and their incidence is increasing. Twenty percent of the U.S. population will develop NMSC during their lifetime. The ratio of basal cell carcinoma (BCC) to squamous cell carcinoma (SCC) is 4:1.

I. Basal cell carcinoma

A. Basal cell carcinoma is the most common skin cancer.

B. Risk factors:

1. **Sun exposure** (increased with high latitude, high altitude).
2. **Advancing age.**
3. **Fair complexion.**
4. **Long-term exposure to psoralens and UVA therapy** (i.e., PUVA therapy for psoriasis).
5. **Immunosuppression.**
6. **Nevus sebaceus of Jadassohn** (a superficial skin lesion typically in the head and neck region; presents as an irregular, raised, yellow to pink, nonhairbearing mass). The lesions are usually present at birth or in early childhood, and approximately 15% undergo malignant transformation to BCC.
7. **Arsenic exposure.**

C. Characteristics of BCC

1. **Basal keratinocytes** are the cell of origin, residing in the basal layer of the epidermis at the dermoepidermal junction.
2. **There is no common clinical precursor lesion**, and metastasis is rare.
3. **BCC is most common** in areas with high concentrations of pilosebaceous follicles, and thus more than 90% of lesions are found on the head and neck.
4. **Morbidity** is caused by invasion of the tumor into underlying structures, including the sinuses, orbit, and brain.

D. Types of BCC

1. **Nodular BCC:** The most common type, usually presenting as a single lesion consisting of pearly papules with telangiectasias, pruritus, and occasional bleeding. Lesion breakdown over time leads to noduloulcerative BCC ("rodent ulcer"). Histology demonstrates palisading nuclei.
2. **Superficial spreading BCC:** Slow-growing, erythematous, with minimal induration, and located primarily on the trunk. It is easily confused with other scaly, eczematous dermatoses. The lesions are shallow with a characteristic horizontal growth pattern, and often present in multiples.
3. **Morpheaform (sclerosing, fibrosing) BCC:** Flat, often yellowish or hypopigmented, sometimes resembling scars or normal skin. The true extent of the lesion is usually greater than the clinical appearance. There is a high incidence of recurrence or incomplete excision due to fingerlike extensions. Margins of 1 cm or Mohs extirpation is warranted.
4. **Pigmented BCC:** Similar to nodular BCC; easily confused with melanoma because of its deep pigmentation and nodularity.
5. **Adnexal BCC:** Uncommon and found in older individuals. Tumors arise from sweat glands, and although they exhibit slow growth, they are locally invasive, with a high incidence of local recurrence.

E. Syndromes associated with NMSC

1. **Basal cell nevus syndrome (Gorlin's syndrome).**
   a. Autosomal dominant inheritance.
   b. Multiple nevi/lesions often seen early in childhood, with malignant degeneration more likely by the age of puberty.
   c. Skin pits on palms and soles, jaw cysts (odontogenic keratocysts), rib abnormalities, mental retardation.
2. **Xeroderma pigmentosum (XP):** Patients have increased incidence of BCC, SCC, and malignant melanoma (see "Melanoma").
3. **Albinism.**

II. Squamous cell carcinoma (also see Chapter 14, "Squamous Cell Carcinoma of the Head and Neck")

A. Second most common skin cancer after BCC

B. Etiology and risk factors

1. **Ultraviolet radiation:** Sun exposure and tanning booth use; PUVA therapy for psoriasis.
2. **Chemical exposure:** Including some pesticides, organic hydrocarbons such as coal tar, fuel oil, paraffin oil, and arsenic (in welding materials).
3. **Viral infection:** Some types of human papillomavirus (HPV); herpes simplex virus.
4. **Radiation:** Long latency between exposure and disease.

5. **Marjolin's ulcer:** SCC arising in a chronic wound (e.g., chronic burn scars and pressure sores) secondary to genetic changes caused by chronic inflammation.
6. **Impaired immunity:** Immunosuppression for transplants and from AIDS; ratio of SCC to BCC is 2:1.

C. Characteristics and precursor lesions

1. **Actinic keratosis** (AK, or solar keratosis)
   a. Erythematous macules and papules with coarse, adherent scale.
   b. Histologically resembles early SCC *in situ* (premalignant).
   c. AK is considered a precursor lesion; up to 4% progress to SCC.
2. **Bowen's disease** (SCC *in situ*)
   a. Exhibits full-thickness cytologic atypia of the keratinocytes.
   b. Erythroplasia of Queyrat is SCC *in situ* of the glans penis.
3. **Leukoplakia**
   a. Presents as a white patch on oral or other mucosa.
   b. Malignant transformation occurs in 15% of cases.
4. **Keratoacanthoma**
   a. Typically a benign, self-healing skin tumor that is composed of squamous cells and keratin; may clinically resemble SCC.
   b. Etiology is unknown but thought to originate from hair follicles.
   c. Typically has a rapid 6-week growth phase followed by involution over the next 6 months.
   d. Excision is the treatment of choice; may be difficult to differentiate from SCC histologically.

D. Types of SCC

1. **Verrucous SCC:** Slow-growing, exophytic, and less likely to metastasize.
2. **Ulcerative SCC:** Grows rapidly and is locally invasive.
   a. Ulcerative SCC has very aggressive growth characteristics, raised borders, and central ulceration.
   b. Less than 50% 5-year survival if spread to lymph nodes in head and neck.

III. Other types of nonmelanoma skin cancer

A. Merkel cell carcinoma

1. **Malignant neuroendocrine tumor** arising within the dermis from cells of neural crest origin.
2. **Aggressive, with radial spread,** high local recurrence, and regional and systemic metastasis.
3. **Presents as a purple to red papulonodule or indurated plaque;** 50% involve the head and neck, 40% involve the extremities, and 10% involve the trunk.
4. **Treatment** involves wide (up to 3 cm) margins.
5. **30–50% survival at 5 years.**

B. Microcystic adnexal carcinoma

1. **Follicular and eccrine differentiation.**
2. **Invasive and locally destructive.**
3. **Presents as a white to pink papule-plaque** primarily on the head and neck.

C. Sebaceous gland carcinoma

1. **Malignant tumor** derived from adnexal epithelium of sebaceous glands.
2. **Yellowish to pink,** slowly growing papulonodule on eyelid (resembles chalazion).

IV. Treatment of nonmelanoma skin cancer

A. Standard techniques: 90% to 95% cure rates

1. **Excision**
   a. BCC: 3- to 5-mm margins for nonaggressive types, and 7-mm margins (or Moh's) for morpheaform type.
   b. SCC: 5- to 10-mm margins are usually sufficient.
   c. Frozen sections may be used to confirm negative margins intraoperatively. False negatives are common. Surgeon must have confidence in the pathologist and laboratory to use this modality.

2. **Mohs surgery:** Sequential horizontal excision with frozen-section testing
   a. Indications include recurrent, higher-risk NMSC (morpheaform BCC and high-risk SCC) and lesions in aesthetically sensitive areas (nose, eyelid, lip, etc.).
   b. Advantages are tissue preservation and confirmation of complete excision.
3. **Field therapy**
   a. Curettage and electrodesiccation can be used for BCC less than 1 cm that is *not* recurrent disease or morpheaform type; however, this treatment leads to a widened scar.
   b. Cryotherapy is effective for small BCC over bone or cartilage, tip of nose, or around the eye.
   c. Radiation: Requires multiple visits. High cure rates, but recurrence is relatively common many years (10–15) later.

B. Regional lymphadenectomy

1. **Indicated for clinically positive (palpable) nodes.**
2. **Fine-needle aspiration (FNA):** Confirm spread of SCC to palpable lymph node.
3. **ELND:** Indicated for a tumor extending down to parotid capsule or a large lesion contiguous with a draining nodal basin.
4. **SLNB:** Considered for high-risk SCC without palpable nodes (controversial).

C. Indications for adjuvant radiation therapy

1. **Cutaneous SCC** with high-risk factors.
2. **Aggressive, deeply invasive BCC.**

Soft Tissue Sarcoma

I. Biology and epidemiology

A. Arise from mesoderm-derived tissues: Bone, fat, muscle, nerve, vasculature, synovium, fibrous tissue, and cartilage.

B. Epidemiology

1. **6,000 to 7,000 new cases** are diagnosed annually in the United States.
2. **1% of all malignancies** occur in adults, and 15% in children.
3. **50% are located in the extremities.**
4. In contrast to ectoderm-derived carcinomas, **sarcomas behave in a similar fashion regardless of the cell of origin.**
5. **Paucity of local symptoms** often leads to advanced disease at diagnosis.
6. **A pseudocapsule forms** as the tumor expands and compresses adjacent tissue.
7. **Major fascial planes** typically act as barriers to local invasion.

C. Risk factors and etiology

1. **The majority of sarcomas** have no identifiable predisposing genetic or environmental cause.
2. **Radiation exposure**
   a. Associated with osteosarcomas and malignant fibrous histiocytomas.
   b. Typically, there is a 10- to 20-year latency period after exposure.
   c. Thorium dioxide (Thorotrast), a contrast agent used in the 1940s and 1950s for radiologic procedures, is linked with a high incidence of hepatic angiosarcoma.
3. **Chemical exposure:** Arsenic, vinyl chloride, and dioxin (contained in the Vietnam War-era defoliant Agent Orange).
4. **Genetic factors**
   a. Neurofibromatosis (von Recklinghausen's syndrome): 5% lifetime risk of developing neurofibroma or neurofibrosarcoma.
   b. Mutation in Rb1 tumor suppressor gene: Retinoblastoma (sarcoma of the eye).

c. Mutation in p53 tumor suppressor gene: Li-Fraumeni syndrome (variety of sarcomas).

5. **Lymphedema**
   a. Following surgical procedures, radiation therapy, or parasitic infection; may also arise idiopathically.
   b. 10- to 20-year latency for development of lymphangiosarcoma.
6. **Kaposi's sarcoma:** Strongly associated with human immunodeficiency virus infection.

II. Classification

A. Subtypes are named for the cell of origin (Table 11-6). Fibrosarcoma is the most common sarcoma in adults and the second most common in children.

B. Histologic type has little prognostic significance; histologic grade (including frequency of mitotic figures, cellular atypia, and presence or absence of tumor necrosis) is the best guide for prognosis and therapy.

III. Diagnosis and staging

A. Extremity sarcoma: Generally painless. Delay in diagnosis is common, and patients are often erroneously treated for a hematoma or "pulled muscle."

1. **Suspicious findings include** mass larger than 5 cm, enlarging or symptomatic mass, and mass present for more than 4 weeks.
2. **Magnetic resonance imaging (MRI)** is the best imaging modality.
3. **Pulmonary metastases** are the most common finding with metastatic disease.
4. **The 5-year survival rate is approximately 75%.**

B. Sarcoma of the abdomen or retroperitoneum

1. **Can present with vague abdominal complaints:** Fullness, early satiety, pain, weight loss, nausea, and vomiting.
2. **Metastatic disease:** Most common to liver.
3. **Palpable mass in 80% of patients at the time of presentation.**
4. **Median survival.**
   a. Primary disease: 72 months.
   b. Recurrent disease: 28 months.
   c. Metastatic disease: 10 months.
5. **Imaging**
   a. MRI with gadolinium contrast: Best technique for visualizing tumor and relationship to adjacent structures.
   b. CT scan: Valuable for evaluating chest, abdomen, and pelvis for metastatic disease, and as a staging tool.
   c. Angiography: For surgical planning.
   d. Chest x-ray: Evaluate for pulmonary metastasis.
6. **Biopsy of sarcomas:** Performed for extremity lesions smaller than 5 cm.

C. Staging criteria (Tables 11-7 and 11-8)

1. **Histologic grade is the most important prognostic indicator** (see above). Low-grade tumors have less than a 15% chance of metastasis; high-grade tumors metastasize in more than 50% of cases.

Table 11-6. Tissue classification of soft-tissue sarcomas

Tissue of Origin	Benign Soft Tissue Tumor	Malignant Soft Tissue Tumor
Fat	Lipoma	Liposarcoma
Fibrous tissue	Fibroma	Fibrosarcoma
Smooth muscle	Leiomyoma	Leiomyosarcoma
Skeletal muscle	Rhabdomyoma	Rhabdomyosarcoma
Cartilage	Chondroma	Chondrosarcoma
Bone	Osteoma	Osteosarcoma
Blood vessel	Hemangioma	Angiosarcoma

Table 11-7. AJCC "GTNM" classification of soft tissue sarcomas

Classification	Description
Histologic Grade	
G1	Well differentiated
G2	Moderately well differentiated
G3	Poorly differentiated
G4	Undifferentiated
Primary Tumor Size	
T1	Tumor ≤ 5 cm in greatest diameter
T2	Tumor > 5 cm in greatest diameter
Regional Lymphatic Involvement	
N0	No known metastases to lymph nodes
N1	Verified metastases to lymph nodes
Distant Metastasis	
M0	No known distant metastases
M1	Known distant metastases

AJCC, American Joint Committee on Cancer.

2. **Tumors of larger size are more difficult to grade** and have a greater chance of recurrence and dedifferentiation.
3. **Nodal and distant metastases** are associated with a similar prognosis and are classified as stage IV disease.
4. **Five-year survival** is on the order of 80% for stage I disease, 60% for stage II, 35% for stage III, and less than 10% for stage IV.

IV. Management

A. The extremity (especially the thigh) is the most common site for sarcoma.

1. Surgery

a. Complete resection with negative margins is the mainstay of treatment.

b. The pseudocapsule should not be entered.

c. Wide-local excision (WLE) is the standard of care, with 3- to 5-cm margins of normal tissue proximally and distally. En bloc resection of uninvolved fascial plane with tumor is performed for control of the other margins.

Table 11-8. AJCC stage groupings for soft tissue sarcomas using the "GTNM" classification

Stage	Groupings	5-Year Survival (%)
IA	G1, T1, N0, M0	80
IB	G1, T2, N0, M0	
IIA	G2, T1, N0, M0	60
IIB	G2, T2, N0, M0	
IIIA	G3-4, T1, N0, M0	35
IIIB	G3-4, T2, N0, M0	
IVA	Any G, any T, N1, M0	<10
IVB	Any G, any T, N1, M1	

   d. WLE is performed after excisional biopsy even if the margins are clear.
   e. Major neurovascular structures are generally preserved for low-grade lesions, but are sacrificed and reconstructed as needed for high-grade tumors.
   f. There is no survival benefit of amputation compared with limb-sparing procedures.
2. **Radiation therapy** is not indicated for small (<5 cm) low-grade tumors because of the excellent prognosis with WLE alone. It can be used as primary therapy for patients who cannot tolerate or refuse surgery, and is also useful as combination therapy for sarcomas up to 10 cm.
3. **Chemotherapy** is of undetermined benefit in soft tissue sarcoma.

B. **Retroperitoneal and intraabdominal sarcomas** have a uniformly poor prognosis. Excision with tumor-free margins is curative, but difficult to achieve. Radiation is rarely used because surrounding organs cannot tolerate therapeutic doses.

Pearls

1. **SCC commonly affects the lower lip** and upper eyelid; BCC characteristically affects the upper lip and lower eyelid.
2. **Perform a punch or excisional biopsy of pigmented lesions** rather then shaving or curettage so that the depth of the lesion can be determined if it happens to be melanoma.
3. **Lentigo maligna melanoma** is the only type of melanoma that is clearly associated with sunlight exposure.
4. **Fibrosarcoma** is generally not sensitive to chemotherapy or radiation therapy.

12

Benign Skin Lesions

Anastasia Petro

I. Definitions

- **A. Macules** are flat, circumscribed lesions.
- **B. Papules** are raised lesions, generally less than 0.5 cm in diameter.
- **C. Plaques** are raised lesions in which the surface area is significantly greater than the height.
- **D. Nodules** are raised lesions, typically larger and thicker than papules.

II. Technical considerations of cutaneous biopsy

- **A. Planning:** Orientation of biopsy incisions should result in the scar lying parallel to relaxed skin tension lines (RSTLs, or Langer's lines). Biopsies should be excised to the level of the subcutaneous fat.
- **B. Anesthesia:** Local anesthetics (e.g., lidocaine) are infiltrated after marking the planned lines of excision. Epinephrine is valuable in providing hemostasis, especially for facial biopsies (see Chapter 8, "Local Anesthetics").
- **C. Biopsy techniques:** Each technique can be valuable in certain circumstances.
  1. **Fusiform excision:** Most biopsies are amenable to fusiform excision and closure. A lesion is excised, and the resulting defect is lengthened in a 3:1 ratio to eliminate standing cutaneous deformities ("dog ears") with closure. The long axis of the excision should lie within the RSTL. Closure is performed using layered sutures (see Chapter 2, "Surgical Techniques and Wound Management").
  2. **Punch biopsy:** Specimens measuring 2 to 6 mm can be removed with a circular punch (similar in principle to a cookie cutter); this technique is highly effective for small lesions.
  3. **Shave biopsy:** Lesions with very low malignant potential can be excised in this manner. However, it leaves an open wound, which can lead to unnecessary morbidity.

III. Epidermal lesions

- **A. Epidermal nevus (linear nevus)**
  1. **May be associated with developmental abnormalities** of the ocular, central nervous, skeletal, cardiovascular, and urogenital systems.
  2. **Age of onset:** Birth or early childhood.
  3. **Clinical appearance:** Tan or brown warty papules, usually in a linear array.
  4. **Location:** Extremities most common.
  5. **Treatment:** Excision, laser therapy, dermabrasion, or cryotherapy.
- **B. Inflammatory linear verrucous epidermal nevus**
  1. **Age of onset:** Birth or early childhood.
  2. **Clinical appearance:** Erythematous, rough, scaly papules in a linear array.
  3. **Often extremely pruritic.**
  4. **Location:** Extremities most common.
  5. **Treatment:** Excision.
- **C. Seborrheic keratosis**
  1. **Etiology is unknown.**
  2. **Age of onset:** Middle age.

3. **Clinical appearance:** "Stuck-on" brown, warty papule or plaque.
4. **Typical location:** Trunk.
5. **Treatment:** Cryotherapy, curettage.
6. **No malignant potential.** However, many melanomas are initially misdiagnosed as seborrheic keratoses.
7. **Human papillomavirus (HPV) warts** (sexually transmitted) can mimic seborrheic keratoses in the groin and perineal areas.

D. Actinic keratosis

1. **Induced by excessive sun exposure.**
2. **Approximately 1 in 20** will develop into squamous cell carcinoma (SCC)
3. **Actinic keratosis in transplant patients** (on chronic immunosuppression) should be aggressively treated because of high risk of transformation into SCC.
4. **Age of onset:** Middle age.
5. **Clinical appearance:** Erythematous, rough, or scaly macule or papule
6. **Location:** Sun-exposed areas, including scalp, ears, face, hands.
7. **Treatment:** Cryotherapy, topical 5-fluorouracil (5-FU), imiquimod cream topical tretinoin.

E. Lentigo

1. **Age of onset:** Middle age.
2. **Clinical appearance:** Tan or brown macule with slightly irregular borders.
3. **Location:** Sun-exposed areas, including head, neck, upper trunk, and arms
4. **Treatment:** Cryotherapy, topical tretinoin, hydroquinone cream.

IV. Nevocellular (melanocytic) lesions

A. Nevus of Ota

1. **Age of onset:** Appears at birth.
2. **Typically found in patients of Asian ancestry.**
3. **Clinical appearance:** Large, blue-gray patch.
4. **Location:** Periocular; areas innervated by first and second trigeminal branches.
5. **Treatment:** Laser therapy.

B. Nevus of Ito

1. **Age of onset:** Appears at birth.
2. **Typically found in patients of Asian ancestry.**
3. **Clinical appearance:** Large, blue-gray patch.
4. **Location:** Posterior shoulder; areas innervated by posterior supraclavicular and lateral cutaneous brachial nerves.
5. **Treatment:** Laser therapy.

C. Nevus spilus

1. **Age of onset:** Appears at birth.
2. **Clinical appearance:** Tan patch speckled with hyperpigmented small macules and papules.
3. **Location:** Trunk.
4. **Treatment:** Excision if feasible, although not necessary.
5. **No increased risk of melanoma.**

D. Spitz nevus (benign juvenile melanoma)

1. **Age of onset:** Childhood to early adulthood.
2. **Clinical appearance:** Pink or tan, dome-shaped, smooth papule.
3. **Location:** Face (especially cheek).
4. **Treatment:** Excision with definitive margins to decrease risk recurrence.
5. **May be difficult to distinguish** histopathologically from malignant melanoma.

E. Junctional nevus

1. **Nevus cells are located** at the epidermal-dermal junction.
2. **Age of onset:** Childhood to early adulthood.
3. **Clinical appearance:** Brown, evenly pigmented macule with well-defin borders.

4. **Location:** Trunk.
5. **Treatment:** Excision.
6. **May be difficult to differentiate** from melanoma.

F. **Compound nevus**
1. **Contains both junctional and intradermal components** and is likely a transition between these types.
2. **Age of onset:** Childhood to early adulthood.
3. **Clinical appearance:** Dark brown papule with well-defined regular borders.
4. **Location:** Trunk.
5. **Treatment:** Excision.

G. **Intradermal nevus**
1. **Age of onset:** Second or third decade of life.
2. **Clinical appearance:** Flesh-colored or light tan papule.
3. **Location:** Face or neck.
4. **Treatment:** Excision.

H. **Common blue nevus**
1. **Age of onset:** Adolescence.
2. **Clinical appearance:** Blue or blue-black papule, generally less than 1 cm.
3. **Location:** Head and neck and dorsum of the hands and feet.
4. **Treatment:** Excision.
5. **A cutaneous metastasis of malignant melanoma** can resemble a blue nevus.

I. **Cellular blue nevus**
1. **Age of onset:** Second decade of life or older.
2. **Clinical appearance:** Blue-black papule or plaque.
3. **Location:** Buttocks most common.
4. **Treatment:** Excision.

J. **Atypical (dysplastic) nevus**
1. **Age of onset:** Puberty and later.
2. **Clinical appearance**
   a. Classic lesion: Central brown macule surrounded by an irregular pink rim.
   b. Usually greater than 6 mm.
   c. There is a large clinical spectrum. In general, dysplastic nevi are larger than typical nevi and have more irregular pigmentation and borders compared with typical nevi.
3. **Location:** Trunk most common.
4. **Treatment**
   a. Excision with definitive margins to prevent recurrence.
   b. Total body skin examination (including oral, ocular, and anogenital areas) to rule out synchronous lesions.
   c. Sunscreen use and avoidance of sunburns and tanning should be strongly encouraged.
5. **Patients with dysplastic nevi and a family history of melanoma** in a first-degree relative are at an especially high risk (up to 100% lifetime risk) of melanoma, and warrant regular total body skin examinations.

V. Lesions derived from epidermal appendages

A. **Epidermal appendages** include the sebaceous glands, hair follicles, and eccrine glands.

B. **Pilomatrixoma (calcifying epithelioma of Malherbe)**
1. **Derived from hair follicles,** located in the lower dermis to subcutaneous fat.
2. **Age of onset:** Early childhood.
3. **Clinical appearance.**
   a. Extremely firm, flesh-colored nodule.
   b. Positive "tent" sign: Stretching of the overlying skin reveals multiple peaks.
4. **Location:** Most commonly involves the head, neck, and upper extremities.
5. **Treatment:** Excision

C. **Trichoepithelioma**
   1. **Derived from hair follicles.**
   2. **Age of onset:** Puberty or older.
   3. **Clinical appearance:**
      a. Pink or flesh-colored, shiny papule.
      b. Multiple trichoepitheliomas often coalesce to form plaques.
   4. **Location:** Most commonly involves the face.
   5. **Treatment:** Excision.
   6. **May be difficult to distinguish** clinically and microscopically from basal cell carcinoma.
   7. **Rasmussen syndrome:** Autosomal dominant disorder; triad of multiple trichoepitheliomas, cylindromas, and milia.

D. **Cylindroma ("tomato tumor," "turban tumor")**
   1. **Derived from eccrine gland structures.**
   2. **Age of onset:** Puberty or older.
   3. **Clinical appearance:** Firm, rubbery bluish-pink nodule.
   4. **Location:** Scalp.
   5. **Treatment:** Excision.
   6. **Multiple cylindromas may be present** in autosomal dominant cylindroma syndromes.

E. **Eccrine poroma**
   1. **Derived from eccrine gland structures.**
   2. **Age of onset:** Any age.
   3. **Clinical appearance:** Red, soft nodule, often pedunculated.
   4. **Location:** Sole or lateral surface of foot.
   5. **Treatment:** Excision.

F. **Syringoma**
   1. **Derived from eccrine gland structures.**
   2. **Age of onset:** Early adulthood.
   3. **Clinical appearance:** Small, clear papules.
   4. **Location:** Periocular (eyelids, upper cheek).
   5. **Treatment:** Electrodesiccation, cryotherapy, laser.
   6. Increased incidence with Down syndrome.

G. **Nevus sebaceus (of Jadassohn)**
   1. **Age of onset:** Birth.
   2. **Clinical appearance:**
      a. Before puberty: Yellow-orange, waxy smooth plaque, linear or elongated.
      b. After puberty: Rough, verrucous, orange plaque.
   3. **Location:** Scalp.
   4. **Treatment:** Excision during childhood.
   5. **May give rise to several different invasive neoplasms.**
   6. **After puberty,** approximately 10% to 15% degenerate into basal cell carcinoma.

H. **Sebaceous adenoma**
   1. **Age of onset:** Middle age.
   2. **Clinical appearance:** Yellow nodule.
   3. **Location:** Head or neck.
   4. **Treatment:** Excision.
   5. **Rare.**
   6. **Muir-Torre syndrome:** Autosomal dominant; associated with multiple keratoacanthomas and marked increase in visceral neoplasms, particularly colon carcinoma.

I. **Sebaceous hyperplasia**
   1. **Age of onset:** Middle age.
   2. **Clinical appearance:** Small, shiny, umbilicated, yellow-white papules. May be confused clinically with basal cell carcinoma.
   3. **Location:** Face.
   4. **Treatment:** Cryotherapy, electrodesiccation, or laser therapy.

VI. Cysts
A. Epidermoid cyst (epidermal inclusion cyst)
1. **Age of onset:** Adulthood.
2. **Clinical appearance**
a. Somewhat fluctuant, flesh-colored, well-circumscribed nodule.
b. Often with punctum.
c. Cyst cavity filled with malodorous, keratinous debris. The term "sebaceous cyst" is a misnomer because the tumor is of epidermal and not sebaceous origin.
3. **Location:** Commonly on the face, neck, and trunk.
4. **Treatment:** Excision; if infected, incision and drainage with delayed excision after healing.

B. Dermoid cyst
1. **Age of onset:** Birth, early childhood.
2. **Clinical appearance:** Resembles epidermoid cyst, without punctum.
3. **Lined with all types of epidermal skin appendages,** usually in a vestigial form.
4. **Location:** Supraorbital ridge or lateral brow; sometimes in nasal midline.
5. **Treatment:** Excision.
6. **Differential diagnosis of a midline nasal mass** includes dermoid cyst, glioma, and meningocele. Computed tomography (CT) or magnetic resonance imaging (MRI) should be ordered prior to excision.

C. Trichilemmal cyst (pilar cyst)
1. **Age of onset:** Adulthood.
2. **Clinical appearance:** Same as epidermoid cyst.
3. **Location:** Scalp.
4. **Treatment:** Same as epidermoid cyst.

VII. Dermal lesions
A. Dermatofibroma
1. **Age of onset:** Adulthood.
2. **Clinical appearance:** Brown-red indurated papule or nodule; positive "dimple" sign.
3. **Location:** Lower extremities.
4. **Treatment:** Excision.

B. Lipoma
1. **Age of onset:** Any age.
2. **Clinical appearance:** Soft, flesh-colored nodule.
3. **Location:** Trunk, extremities.
4. **Treatment:** Excision.
5. **Generally painless,** whereas angiolipomas are more likely to be painful.

C. Dermatofibrosarcoma protuberans
1. **Age of onset:** Middle age.
2. **Clinical appearance:** Reddish-brown, firm, nodular plaque.
3. **Location:** Trunk, extremities.
4. **Treatment:** Radical excision, due to locally aggressive, infiltrative nature.
5. **Local recurrence** is common due to poorly defined clinical and histologic margins.
6. **Metastases are rare.**

D. Neurofibroma
1. **Consists of Schwann cells** and endoneurial fibroblasts.
2. **Age of onset:** Any age.
3. **Clinical appearance:** Soft, compressible, flesh-colored or pink nodule; positive "button-hole" sign.
4. **Location:** Trunk or extremities.
5. **Treatment:** Excision.

VIII. Miscellaneous
A. Granuloma annulare
1. **Age of onset:** Childhood.

2. **Clinical appearance:** Annular plaques composed of several flesh-colored or pink firm papules.
3. **Location:** Distal extremities.
4. **Treatment:**
   a. Observation (lesions will often spontaneously resolve).
   b. Intralesional corticosteroids.
   c. Cryotherapy.
   d. Surgical excision.

B. Calciphylaxis

1. **The cutaneous manifestation of metastatic calcification,** which leads to calcification of blood vessels and subsequent necrosis of surrounding tissue.
2. **Usually occurs in the setting of renal failure.**
3. **Age of onset:** Any age.
4. **Clinical appearance:** Hemorrhagic, necrotic ulcerations with accompanying livedo reticularis, which is a red-blue mottling of the skin.
5. **Location:** Most commonly on the trunk and extremities.
6. **Treatment**
   a. Supportive care (patients are often systemically ill).
   b. Phosphate-binding agents.
   c. Parathyroidectomy, if appropriate.
   d. Excision is usually followed by progressive calcification in proximal tissues, creating a vicious cycle.

C. Hidradenitis suppurativa

1. **Description:** Chronic inflammatory process involving cutaneous apocrine glands, often affecting the subcutaneous tissue and fascia.
2. **Age of onset:** Puberty.
3. **Clinical appearance:**
   a. Tender, fluctuant erythematous nodules with purulent, malodorous drainage.
   b. Extensive scarring and sinus tracts.
   c. Pain often intense.
4. **Location:** Axillae, inframammary folds, groin, buttocks, and perineal areas.
5. **Treatment**
   a. Meticulous cleansing with antibacterial soaps.
   b. Topical 2% clindamycin lotion twice a day.
   c. Chronic courses of oral antibiotics such as minocycline.
   d. Referral to dermatologist.
   e. Incision and drainage for localized abscess formation.
   f. Radical surgical excision of affected areas, with interim dressing changes followed by delayed skin grafting.
   g. Electron beam irradiation for severe refractory cases.