WOUND HEALING

Anatomy of Skin

Epidermis:

- composed of several thin layers:

  stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, stratum corneum

- the several thin layers of the epidermis contain the following:

  a) melanocytes, which produce melanin, a pigment that gives skin its color and protects it from the damaging effects of ultraviolet radiation.

  b) keratinocytes, which produce keratin, a water Repellent protein that gives the epidermis its tough, Protective quality.

Anatomy of Skin

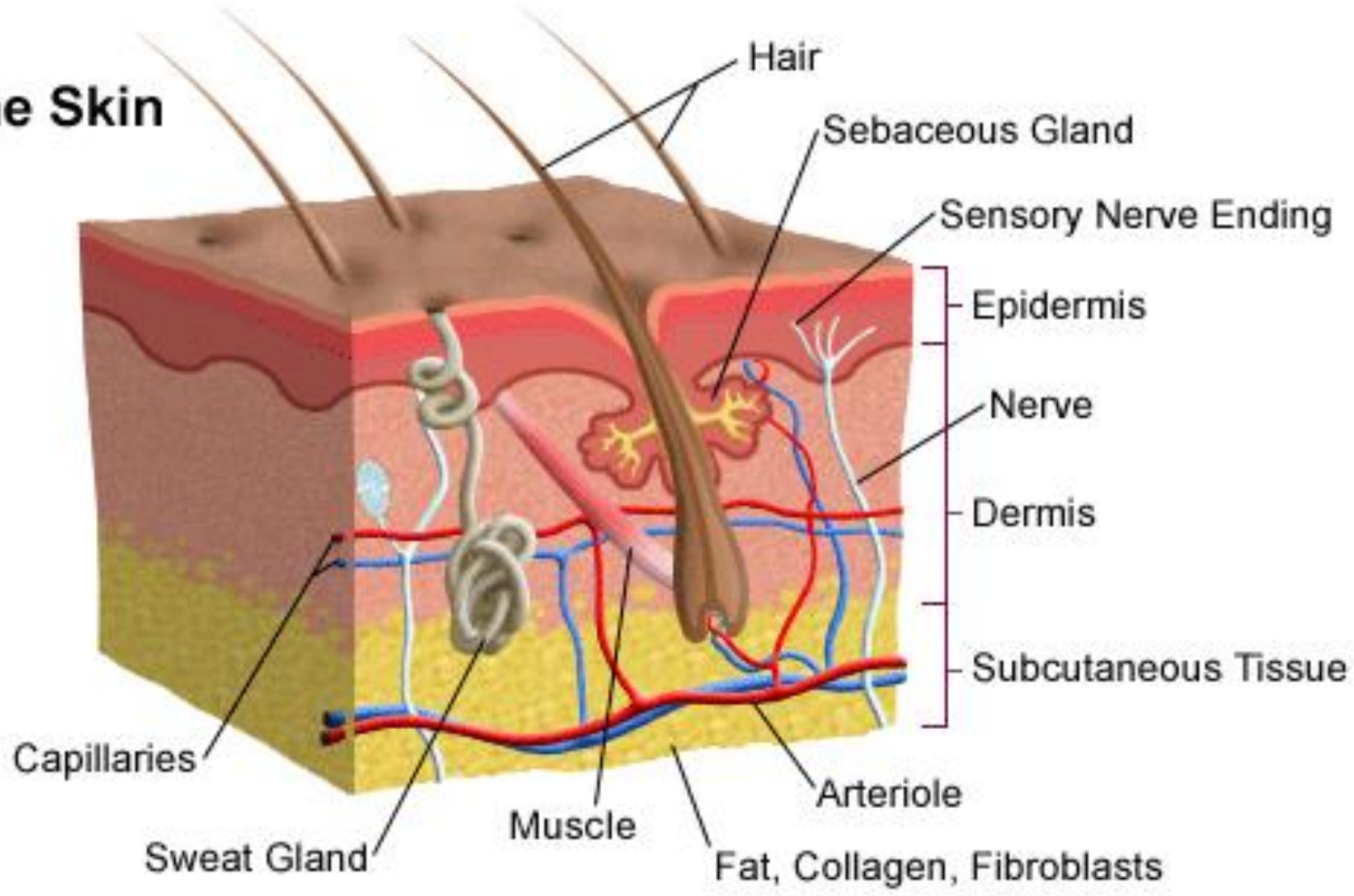
Dermis:

- composed of a thick layer of skin that contains collagen and elastic fibers, nerve fibers, blood vessels, sweat and sebaceous glands, and hair follicles.

Subcutaneous Tissue:

- composed of a fatty layer of skin that contains blood vessels, nerves, lymph, and loose connective tissue filled with fat cells

The Skin


Hair
Sebaceous Gland
Sensory Nerve Ending
Epidermis
Nerve
Dermis
Subcutaneous Tissue
Capillaries
Sweat Gland
Muscle
Arteriole
Fat, Collagen, Fibroblasts

Function of Integument

- **Protection:**
  - intact skin prevents invasion of the body by bacteria
- **Thermoregulation:**
  - intact skin facilitates heat loss and cools the body when necessary through the following processes:
    - production of perspiration which assists in cooling the body through evaporation
    - production of vasodilatation which assists in facilitating heat loss from the body through radiation and conduction
    - production of vasoconstriction which assists in preventing heat loss from the body through radiation and conduction

Function of Integument

- **Fluid and Electrolyte Balance:**
  - intact skin prevents the escape of water and electrolytes from the body
- **Vitamin D Synthesis**
- **Sensation**
- **Psychosocial**

Classification of Wounds

- 1) **Clean Wound:**
  - Operative incisional wounds that follow nonpenetrating (blunt) trauma.
- 2) **Clean/Contaminated Wound:**
  - uninfected wounds in which no inflammation is encountered but the respiratory, gastrointestinal, genital, and/or urinary tract have been entered.
- 3) **Contaminated Wound:**
  - open, traumatic wounds or surgical wounds involving a major break in sterile technique that show evidence of inflammation.
- 4) **Infected Wound:**
  - old, traumatic wounds containing dead tissue and wounds with evidence of a clinical infection (e.g., purulent drainage).

Classification of Wounds Closure

- ## Healing by Primary Intention:
  - All Layers are closed. The incision that heals by first intention does so in a minimum amount of time, with no separation of the wound edges, and with minimal scar formation.
- ## Healing by Secondary Intention:
  - Deep layers are closed but superficial layers are left to heal from the inside out. Healing by second is appropriate in cases of infection, excessive trauma, tissue loss, or imprecise approximation of tissue.
- ## Healing by Tertiary Intention:
  - Also referred to as delayed primary closure.

- Wound healing occurs in three phases:
- (1) inflammatory or substrate phase,
- (2) proliferative phase,
- (3)maturation

- **Primary Hemostasis**
- Primary hemostasis and recruitment of inflammatory cells occurs in the first 1 to 2 hours after injury. The first
- cellular elements to enter the wound are platelets, which come into contact with damaged collagen at the site
- of injury. The platelets release α granules that contain multiple growth factors, including platelet-derived
- growth factor and transforming growth factor-β. Inflammatory cells arrive and release a variety of cytokines
- and growth factors

.

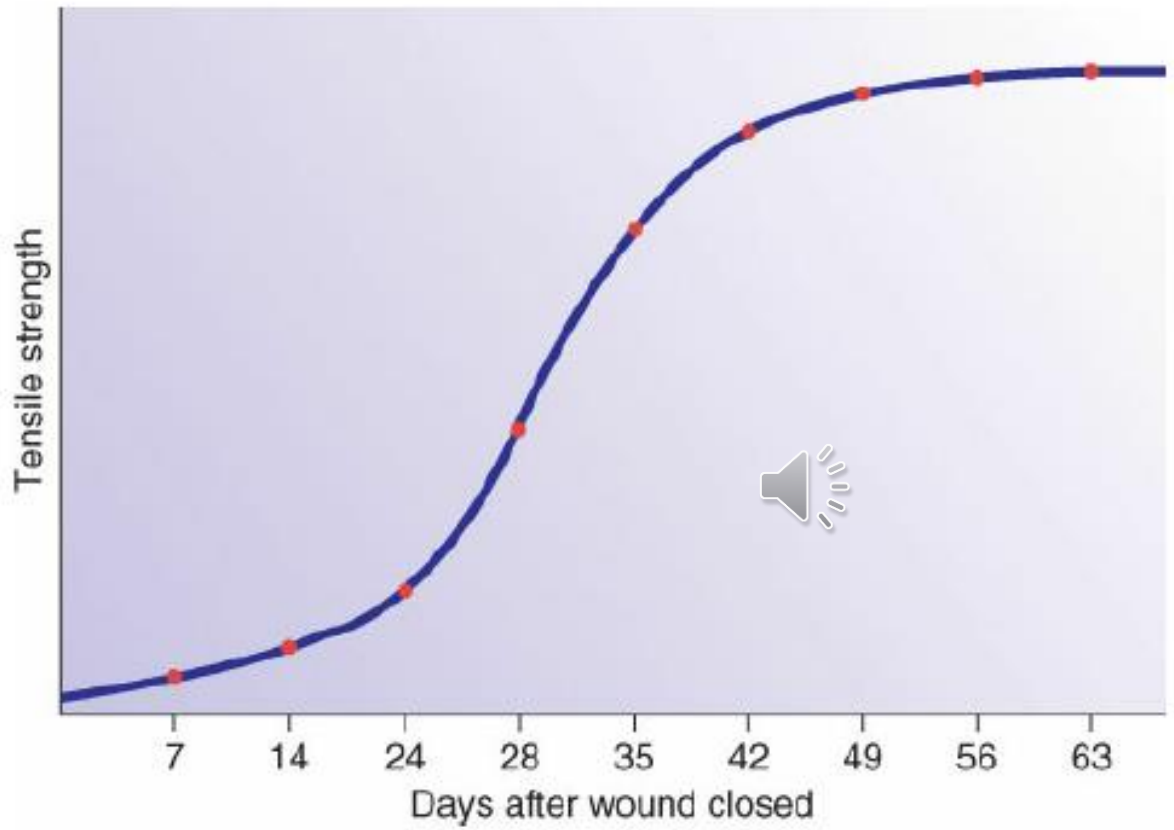
Substrate (Inflammatory) Phase

The substrate/inflammatory phase lasts approximately 3 days. The main cells involved are polymorphonuclear leukocytes (PMNs) and macrophages. PMNs appear first and remain the predominant cell for approximately 48 hours. PMNs are the origin of many inflammatory mediators, such as complement and kallikrein.

Monocytes arrive after the PMNs, reaching maximum numbers approximately 24 hours later. Monocytes evolve into macrophages that debride the wound. Small numbers of bacteria can be neutralized by the macrophages that are present;

- **Proliferative Phase**
- As debris and bacteria are being removed from the wound, substrates for collagen synthesis are being
- assembled. The proliferative phase is the second stage of wound healing; it begins on day 3 and continues for
- approximately 6 weeks. It is characterized by additional cellular migration and proliferation, angiogenesis, and
- the production of collagen in the wound, which results in an increase in wound strength. The primary cell in
- this phase is the fibroblast. Collagen deposition begins between 3 and 5 days after the initial trauma and peaks
- around 4 to 6 weeks

- **Maturation Phase (Remodeling)**
- The third phase is the maturation phase, characterized by the remodeling and strengthening of collagen in the
- wound by intermolecular cross-linking. The wound scar gradually flattens and becomes less prominent and
- more pale and supple. Wound maturation in the adult takes at least 6 and sometimes up to 12 months.


Tensile strength
7
14
24
28
35
42
49
56
63
Days after wound closed

- **Primary Intention**
- The most common method is to primarily close the wound, resulting in *healing by primary intention*. The term
- applies to all surgical incisions and lacerations that are closed with sutures, staples, adhesive
- **Secondary Intention**
- 152
- An alternative to primary closure of a full-thickness wound is to leave it open or let it *heal by secondary*
- *intention*. Classically, these wounds are treated with “wet-to-dry” dressings or negative-pressure wound
- therapy,
- **Delayed Primary Closure**
- In delayed primary closure (DPC), sometimes called *healing by tertiary intention*, the wound is initially
- managed as a secondary intention. After approximately 5 days, when the wound is clean and granulation tissue
- is abundant, the wound edges are actively approximated

- **Skin Grafting**
- For large surface area full-thickness wounds that cannot be closed, an alternative to the lengthy process of
- healing by secondary intention is skin grafting. Split-thickness skin grafts consist of epidermis and a portion
- of the underlying dermis, which are harvested (Figure 7-4). For the first 48 hours, the grafted skin derives its
- nutrients by passive absorption from the recipient bed, a process known as imbibition

TABLE 7-1 Factors That Affect Wound Healing

Local Factors	Systemic Factors
• Infection	• Malnutrition
• Ischemia	• Diabetes mellitus
• Hematoma	• Corticosteroid use
• Seroma	• Chronic illness
• Foreign body	• Cancer
• Hypoxia	• Immune deficiency states
• Radiation	• Smoking
• Obesity	• Old age
• Tension	

- **MANAGEMENT OF CHRONIC WOUNDS**
- A chronic wound is one in which the reparative processes of normal wound healing, as described above, fail to
- occur in an orderly and timely sequence. Most often, chronic wounds are stalled in the inflammatory phase of
- healing and have poor granulation tissue formation, altered cell cycles, and biochemical imbalances. Examples
- include a diabetic foot wound, venous stasis ulcers, fistula-in-ano, and chronic osteomyelitis.

- Advanced Care for Chronic Wounds
- Management of chronic wounds requires a significant investment of resources, and many novel and
- technically sophisticated methods for stimulating wound healing have been devised in recent decades.Advanced Care for Chronic Wounds
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- technically sophisticated methods for stimulating wound healing have been devised in recent decades.

- 1. Intermittent negative-pressure wound therapy
- 2. Topical foams and occlusive dressings to promote a moist wound environment
- 3. Topical growth factors and collagen preparations to promote healing
- 4. Topical broad-spectrum antimicrobial compounds
- 5. Topical enzymatic debridement preparations
- 6. Biologic (cell-based) dressings
- 7. Hyperbaric oxygen therapy

Wound Healing

- **Inflammation** occurs when the damaged endothelial cells release cytokines that increase expression of integrands in circulating lymphocytes.

- Histamine, serotonin, and kinins cause vessel contraction (thromboxane), decrease in blood loss, and act as chemotactic factors for neutrophils, the most abundant cells in the initial 24 hour period.

Wound Healing

- **Proliferative phase** occurs next, after the neutrophils have removed cellular debris and release further cytokines acting as attracting agents for macrophages.
  - Fibroblasts now migrate into the wound, and secrete collagen type III.
  - Angiogenesis occurs by 48 hours.
  - The secretion of collagen, macrophage remodeling and secretion, and angiogenesis continues for up to 3 weeks.
  - The greatest increase in wound strength occurs during this phase.

Wound healing:

"Pathophysiology of Tissue Repair and Transfer" by Edoardo Austoni, Vincenzo Giannoccaro

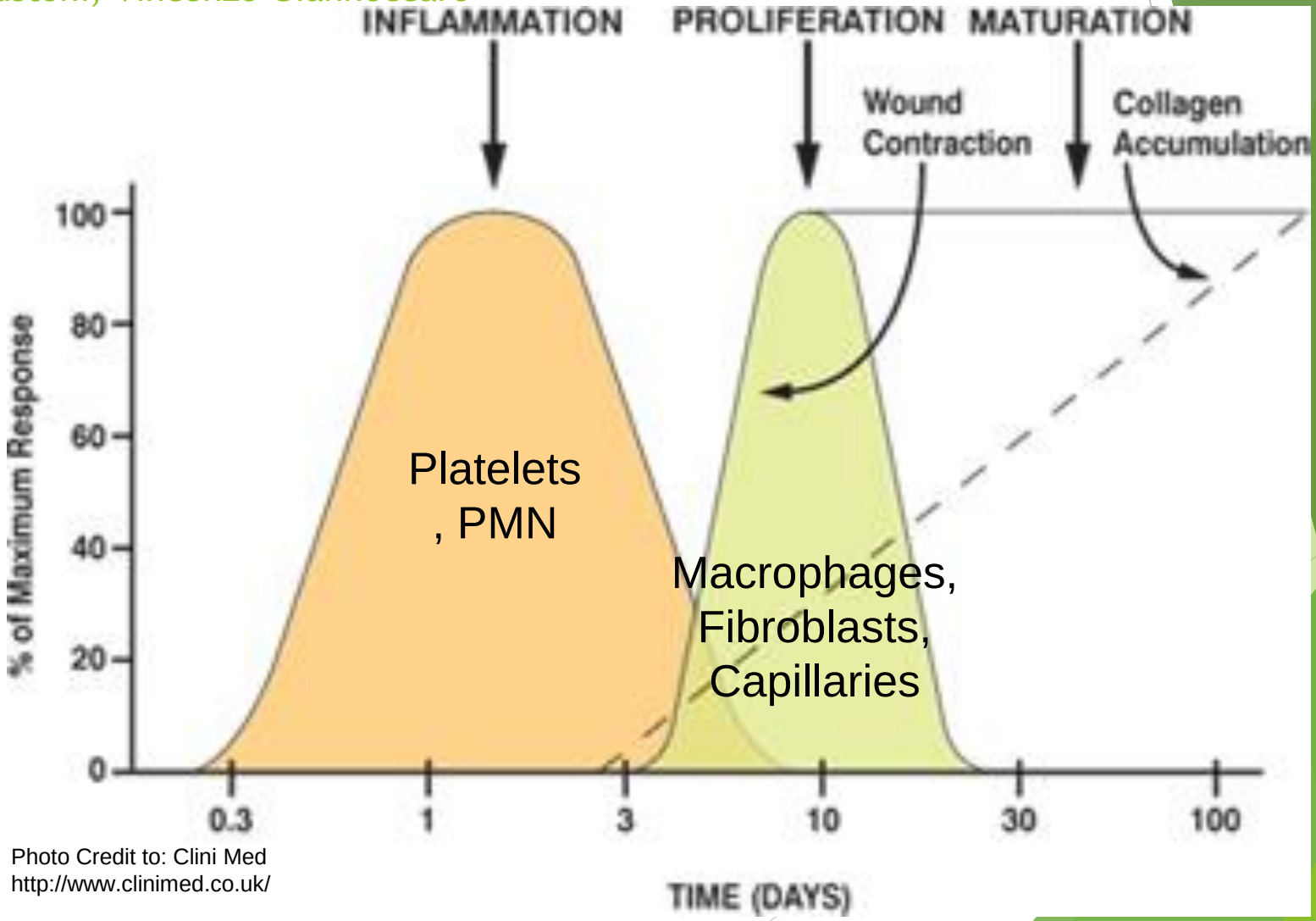


Photo Credit to: Clini Med
http://www.clinimed.co.uk/

Wound healing

overproduction of scar tissue

What is a scar?

- Body's **natural healing mechanism** in response to injury, trauma, etc.
- Tissue formed during healing process

Scar Formation Complications

- Collagen fibers arranged randomly as opposed to linear, parallel formation

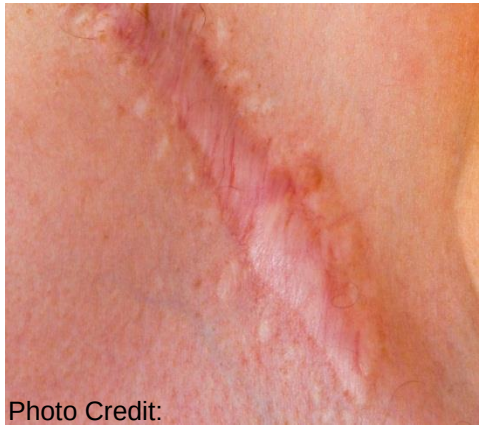


Photo Credit: wiseGEEK.com

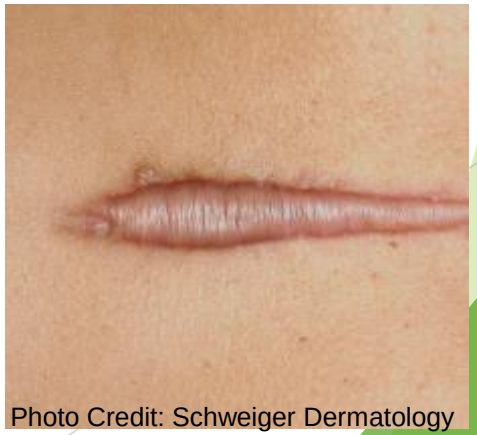


Photo Credit: Schweiger Dermatology

CAUSES Of scar formation complications

Myofibroblast Theory

- Fibroblast differentiation into myofibroblasts
- Myofibroblasts contract with alpha-smooth muscle actin
- Contracts edges of wound to repair
- **Lack of apoptosis** leads to keloid and hypertrophic scar

Fibronectin Theory

- Fibronectin structure precedes wound contraction
- **Provides structure** for fibroblasts

Some current treatments

Corticosteroid Injections

- Reduce collagen synthesis, **inflammatory** mediators, and fibroblast **proliferation**

5-Fluorouracil

- Pyrimidine analogue with antimetabolite activity
- Reduces fibroblastic **proliferation** in tissue culture and postoperative scarring

Tamoxifen

- Nonsteroidal antiestrogen used to treat breast cancer
- Inhibit **proliferation** of keloid fibroblasts and their collagen synthesis

Manipulation

- Physically bending joint to **break** scar tissue

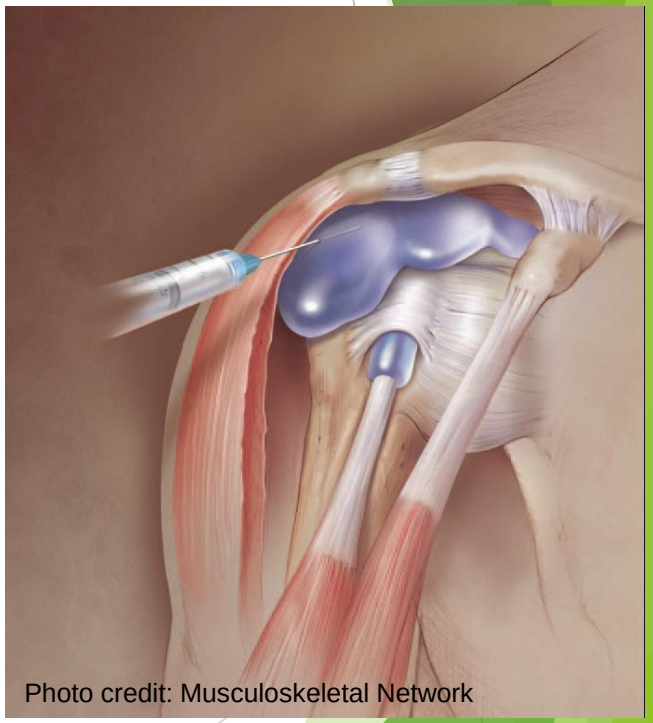


Photo credit: Musculoskeletal Network

Wound Healing

- **Maturation phase** is the final phase and starts from the 3rd week and continues for up to 9-12 months.

- This is where collagen III is converted to collagen I, and the tensile strength continues to increase up to 80% of normal tissue.

Surgical Wound Infection

- Incisional infections identified by purulent or culture positive drainage is isolated from any structure above the fascia in proximity to the initial wound
- Deep infections are characterized by purulent drainage from subfascial drains, wound dehiscence, or abscess formation and involve adjacent sites manipulated during surgery.
- Wound Dehiscence
- Breakdown of the surgical wound

Risk Factors for SWI

- **Patient-related factors:**
- Age > 60, sex (female), weight (obesity)
- Presence of remote infections
- Underlying disease states
- Diabetes, Congestive heart failure (CHF)
- Liver disease, renal failure
- Duration of preoperative stay hospitalization
- > 72 hours, ICU stay
- Immuno-suppression
- ASA (American Society of Anesthesiologists)
- physical status (3,4, or 5)

Risk Factors for SWI

Surgery-related factors:

- Type of procedure, site of surgery, emergent surgery
- Duration of surgery (>60- 120 min)
- Previous surgery
- Timing of antibiotic administration
- Placement of foreign body
- Hip/knee replacement, heart valve insertion, shunt insertion
- Hypotension, hypoxia, dehydration, hypothermia

Risk Factors for SWI

Surgery related factors:

- Patient preparation
- Shaving the operating site
- Preparation of operating site
- Draping the patient
- Surgeon preparation
- Hand washing
- Skin antiseptics
- Gloving

Risk Factors for SWI

Wound-related factors:

- Magnitude of tissue trauma and devitalization
- Blood loss, hematoma
- Wound classification
- Potential bacterial contamination
- Presence of drains, packs, drapes
- Ischemia
- Wound leakage

Antibiotic Use

Characteristics of an optimal antibiotic for surgical prophylaxis:

- Effective against suspected pathogens
- Does not induce bacterial resistance
- Effective tissue penetration
- Minimal toxicity
- Minimal side effects
- Long half-life
- Cost effective

Antibiotic Use

Appropriate antibiotic use for prevention of SWI includes the following:

- Appropriate timing of administered agents and repeated dosing based on length of procedure and antibiotic half-life Consider redosing if procedure > 4 hours
- Appropriate selection based on procedure performed
- Appropriate duration to avoid infection and decrease potential for development of resistance

Antibiotic Use

- **Nose**

S. aureus, pneumococcus, meningococcus

- **Skin**

S. aureus, S. epidermidis

- **Mouth/pharynx**

Streptococci, pneumococcus, e.coli, bacteroides,

fusobacterium, peptostreptococcus

- **Urinary tract**

E.coli, proteus, klebsiella, enterobacter

Antibiotic Use

- **Colon**

E. coli, klebsiella, enterobacter, bacteroides spp, peptostreptococci , clostridia

- **Biliary tract**

E. coli, klebsiella, proteus, clostridia

- **Vagina**

Streptococci, staphylococci, E. coli, Peptostreptococci, bacteroides spp.

- **Upper respiratory tract**

Pneumococcus, H. influenzae

Antibiotic Use

Identify wound infection risk based on

patient's surgical procedure:

- **Clean:** Cefazolin
- **Clean/contaminated:** Cefazolin vs broad spectrum (Cefoxitin or Cefotetan)
- **Contaminated:** Broad spectrum (Cefoxitin or Cefotetan)
- **Dirty:** Therapeutic antibiotics

Fetal Wound Healing

- Fetal wound healing proceeds without fibrosis or scar formation in contrast to adult wound healing. The mechanisms responsible for this remarkable process are mediated in part through a fetal wound extracellular matrix rich in hyaluronic acid (HA).
- Proposed contributing factors to scarless healing in fetal wounds are the presence of fewer neutrophils and more monocytes during the inflammatory period, different concentrations of cytokines, and a greater proportion of type III collagen in contrast to adult wounds.

Fetal Wound Healing

- Transforming growth factor-b (TGF- ß, specifically, low levels of TGF-ß1 and TGF- ß2 and high levels of TGF- ß3—probably has a central role in scar formation, and studies of its role are ongoing.
- Low levels of platelet-derived growth factor (PDGF), a greater amount of epidermal growth factor (a mitogen for epithelialization), a faster rate of wound healing, and a greater amount of hyaluronic acid in the extracellular matrix has been documented and suggests a more efficient process of wound healing in fetal models.

Diabetic foot ulcers

Staging of Pressure Ulcers

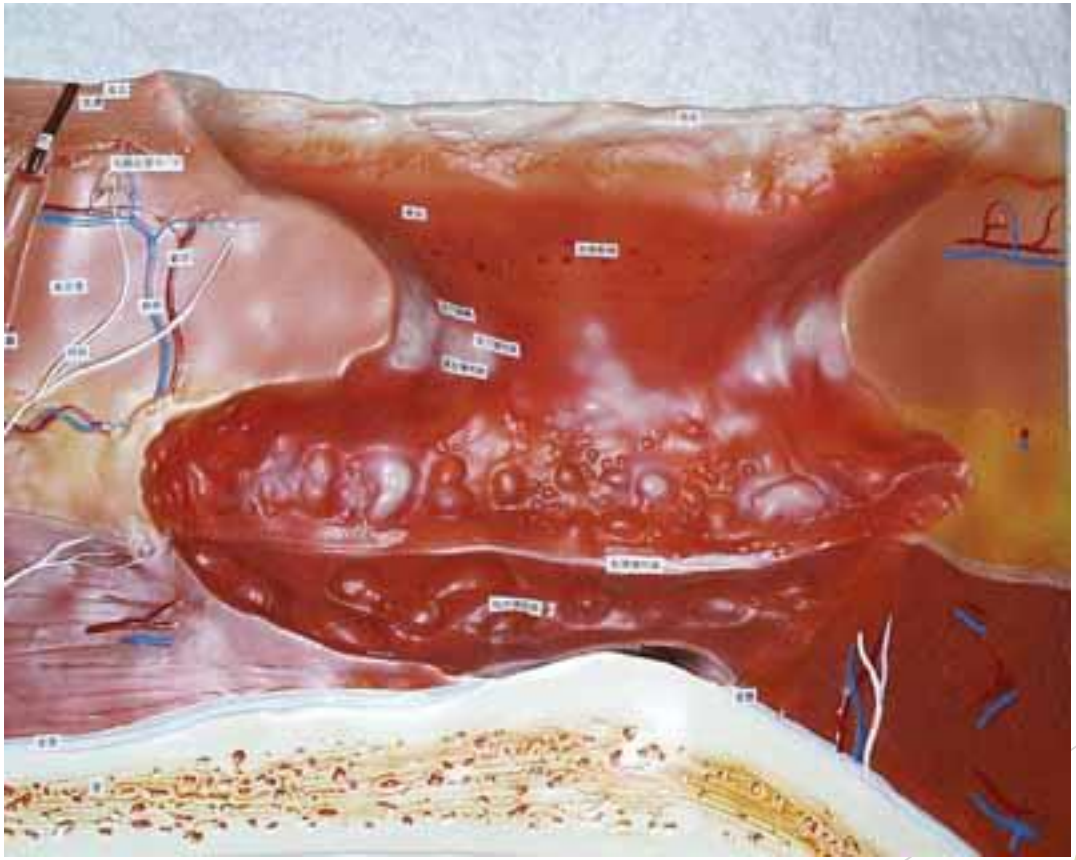
- Stage I: redness and warmth
- Stage II: shallow ulcer with distinct edges
- Stage III: full-thickness loss of skin
- Stage IV: involvement of fascia, connective tissue, muscle and bone
- Stage V: area covered with black eschar (aka scab)

Stage I

Stage II

Stage III

Stage IV



Hypertrophic Scars and Keloids

- The natural response to injury involves several stages of wound healing, migration of macrophages, neutrophils, and fibroblasts and the release of cytokines and collagen in an array to promote wound healing and maturation.

- Hypertrophy and keloid formation are an overactive response to the natural process of wound healing.

Hypertrophic Scars

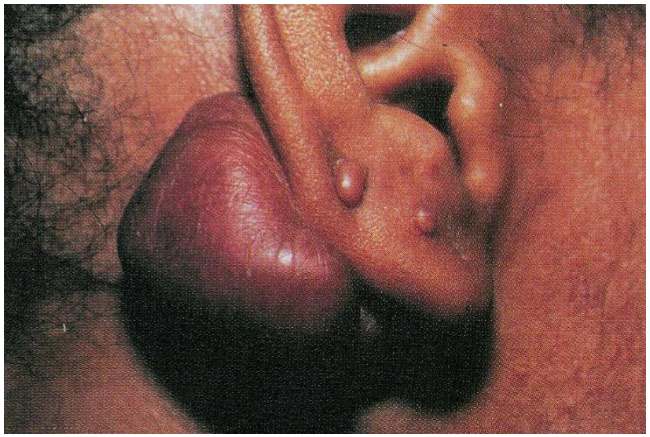
- These lesions are raised and thickened.
- This process does not extend beyond the boundary of the incision/scar.
- This process is exacerbated by tension lines on the area of surgery: incisions over the knee and elbow have a higher incidence of hypertrophic reaction.

Hypertrophic Scars

- NOTE: hypertrophic scars and keloids are indistinguishable by plain H&E staining.
- Treatment: nearly all hypertrophic scars undergo a degree of spontaneous resolvement.
- If still present after six months, surgical excision is indicated.
- Pressure applied early to a lesion is also of benefit.
- Intractable lesions can be injected with triamcinolone.

Keloids

- Raised and thickened. This process extends beyond the boundary of the incision.
  - **Continues weeks to months past the initial insult.**
- Higher incidence in African Americans.
- May have different incidences in different parts of the same person;
  - may not develop a keloid on the arm, yet has a keloid after earring insertion.



Keloids

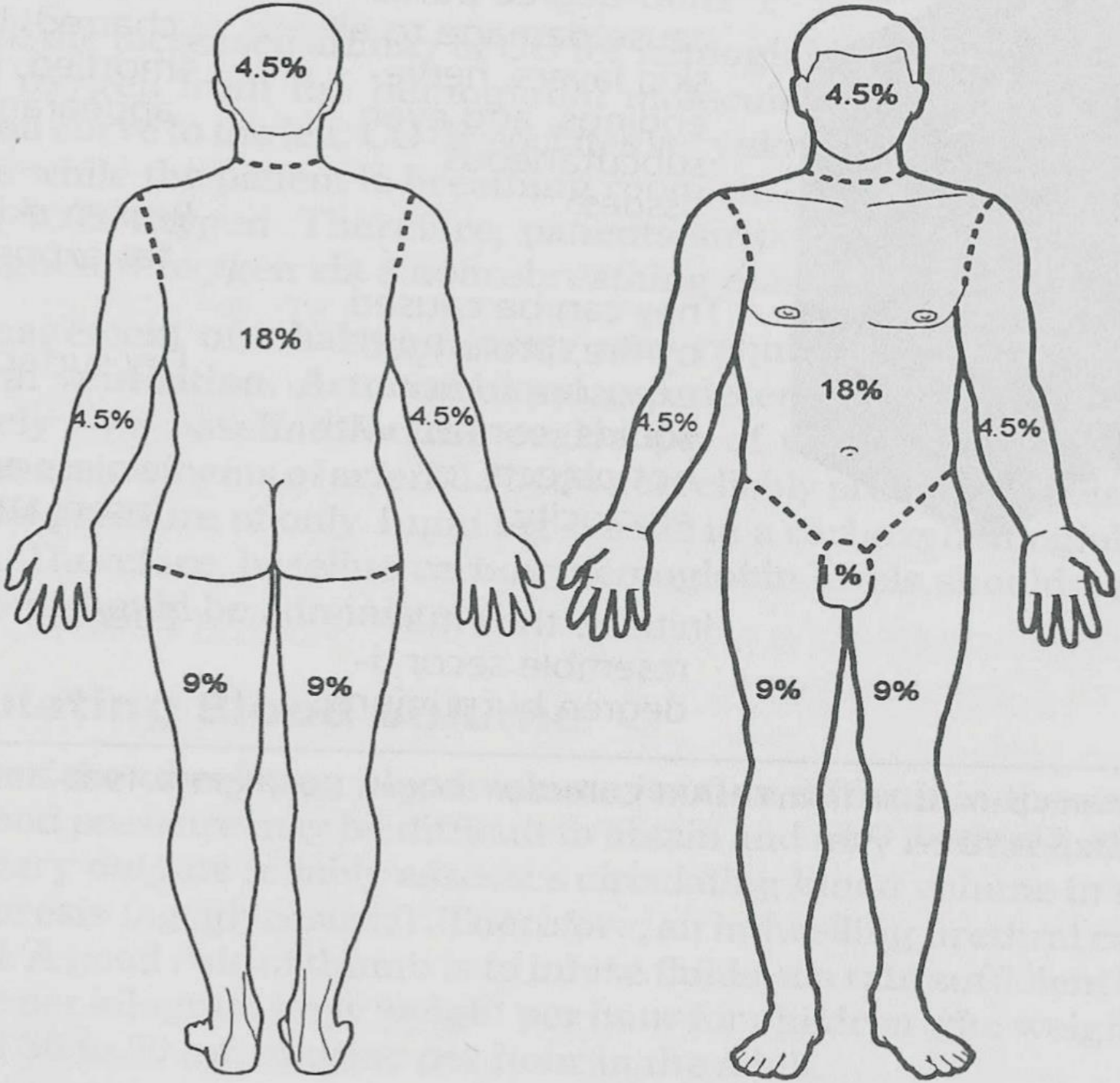
- NOTE: hypertrophic and keloids are indistinguishable by plain H&E staining.
- Treatment: Pressure applied early may decrease the extent of keloid formation.
- Injection of triamcinolone, or corticosteroid injection may be helpful.
- Excision with intramarginal borders is reserved for intractable keloids, and used in conjunction with the above.

Burns

- Are divided by depth of injury. Classically, and in some institutions the burn is organized by "degree:'
- **First-degree:** involve the epidermis and demonstrates erythema and minor microscopic changes. Pain is major complaint. No scar is left. Healing is complete in up to 10 days.
- **Second-degree burns**: involves all the epidermis and part of the dermis. Superficial second-degree burns are characterized by blister formation while deeper burns have a more reddish or non-viable whitish appearance.

Burns

- **Third-degree:** these full thickness burns are characteristically white, non-viable.
- They may demonstrate darkened brown or black adipose tissue.
- Skin is non-sensate, and leathery.
- Muscle injury may also occur.


4.5%
18%
4.5%
4.5%
9%
9%
4.5%
18%
4.5%
4.5%
1%
9%
9%

Burns

- The most important assessment of volume status and adequate volume administration is monitoring of the urine output.
- **Burn Resuscitation**: (**Parkland Formula**) 4x % Burn x Weight in kg for 24 hours, Lactated Ringer's. Give the first half in first 8 hours and the next half in the next 16 hours.
- Urine output is normally 0.5ml/kg, but for burns and trauma patients is at least 1-1.5 ml/kg/hour.
- Initial treatment of the actual burn is first debridement of the denuded skin with moist gauze.
- This additionally aids in estimating volume of burn.
- Coverage with topical antibacterial agents is necessary.

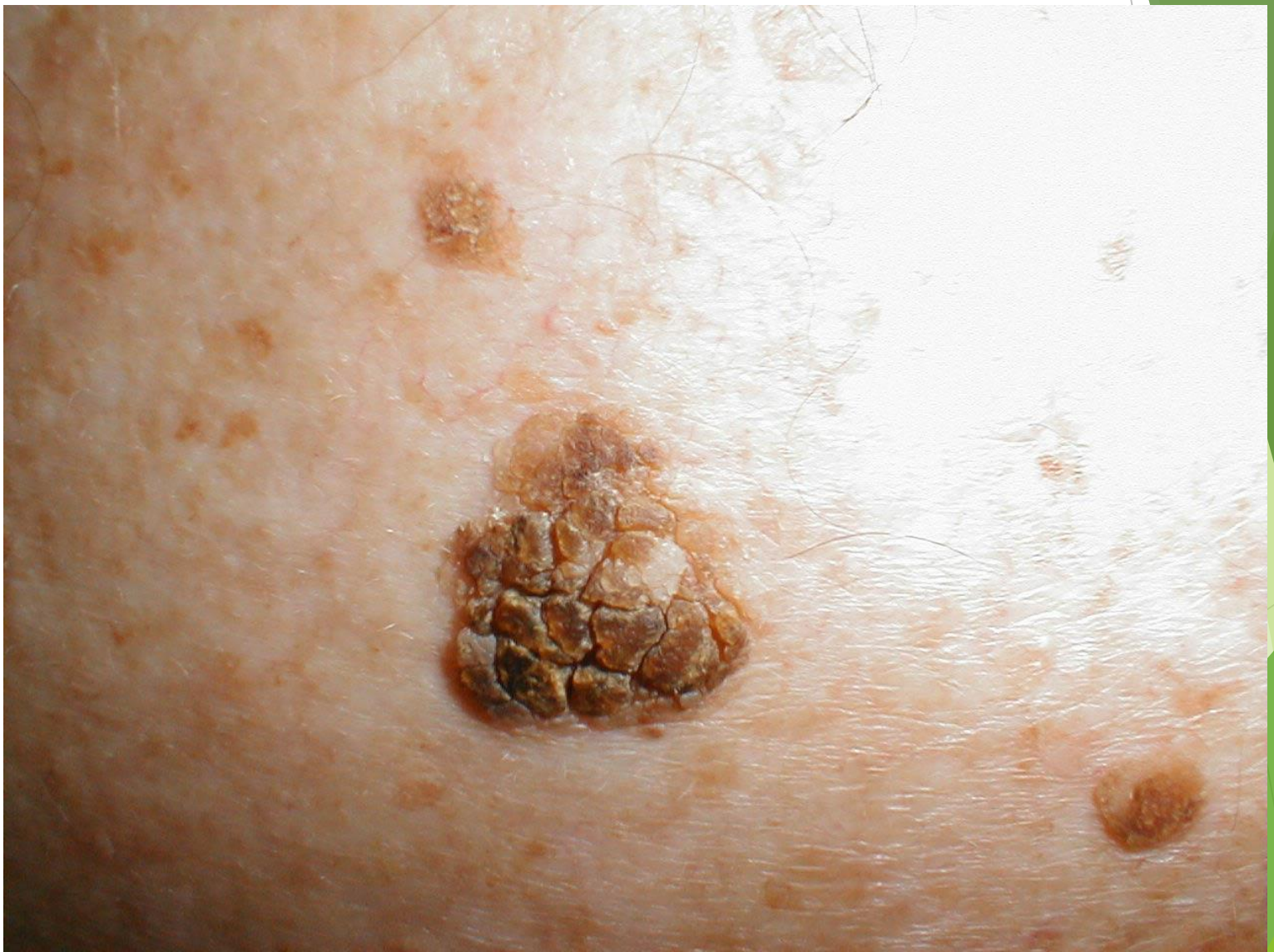
Burns

- Silver sulfadiazine: wide spectrum, moderate eschar penetration. May cause leucopenia
- Silver nitrate: mild spectrum, non-painful. Does not penetrate eschar, causes staining. Sodium, calcium, and potassium wasting.
- Mafenide: wide spectrum penetrates eschar. Painful. Causes metabolic acidosis.
- Initial coverage can include culture skin and skin substitutes. Split thickness skin grafts for burns of small percentage (<25%) can be utilized.

Seborrheic Keratoses

- These lesions are superficial, non-invasive tumors that originate in the epidermis.
- Typically appear in older people as multiple slightly elevated yellowish, brown or brownish-plaque rounded plaques, and are found typically on the shoulders, trunk, scalp, and face.
- Treatment is by shave excision.

Seborrheic Keratoses

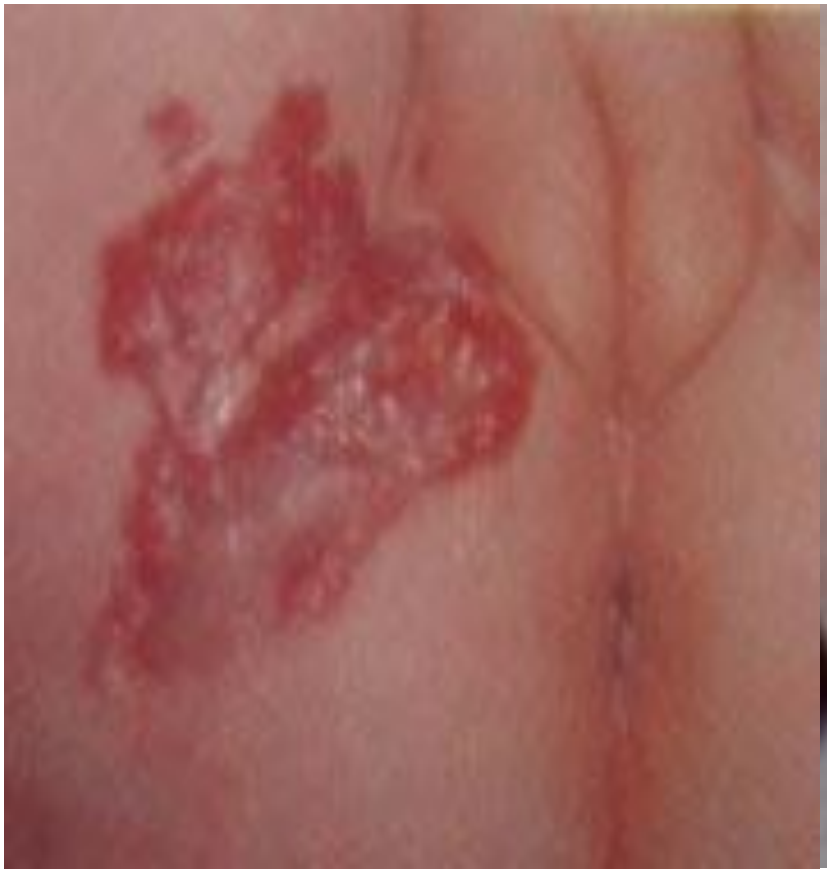


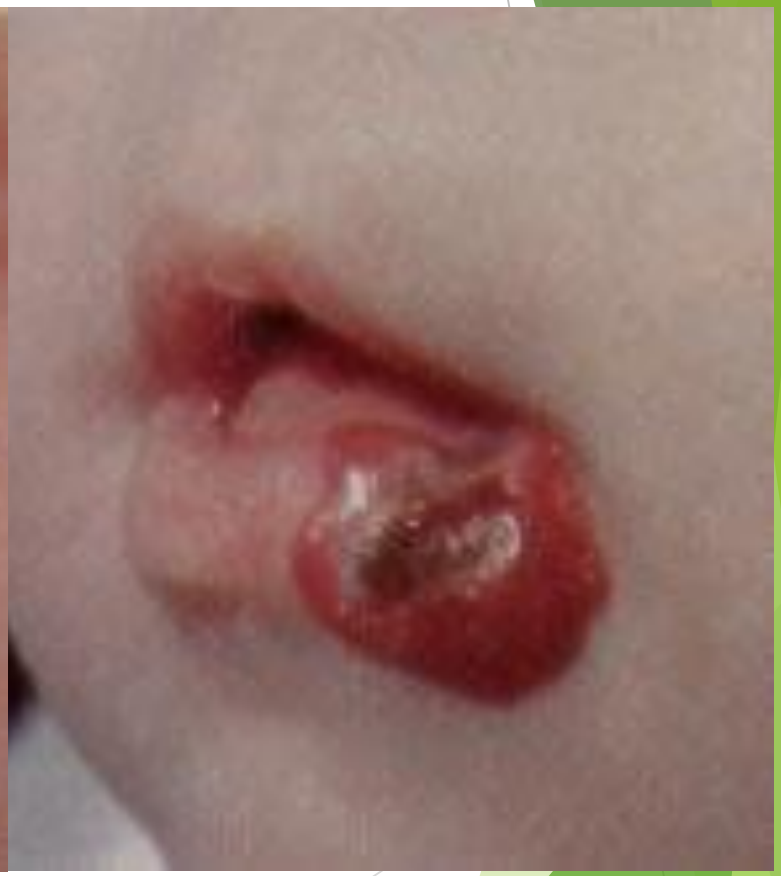
Involuting Hemangiomas

- Most common tumors that occur in childhood, 95% of all hemangiomas that are seen in childhood.

- Typically present at birth or during 2-3 weeks of life, grow at a rapid rate for 4-6 months, then involution begins and is complete by 5-7 years of age.

Involuting Hemangiomas





Involuting Hemangiomas

- These types include strawberry nevus, nevus vasculosus, capillary hemangioma, and cavernous hemangioma.
- Treatment is not usually indicated.
  - Only indicated if the lesions impair vision (eyelid), a condition that can lead to amblyopia.

Noninvoluting Hemangioma

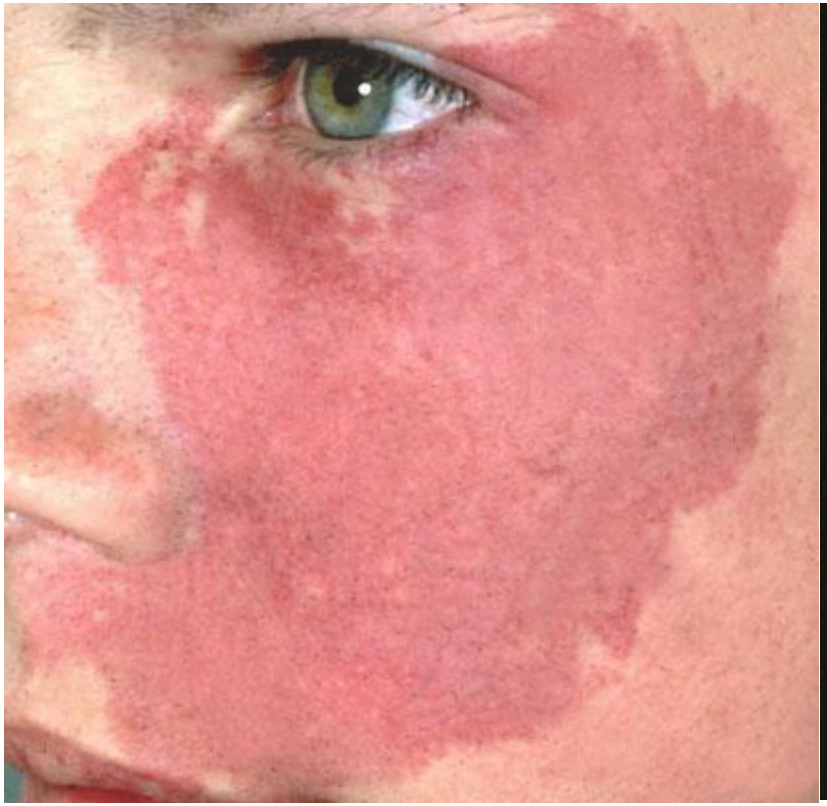
- Most of these lesions are present at birth.
- They grow in proportion to the growth of the infant, and persist into adulthood.
- Unlike involuting, these are not true neoplasms, but malformations of arterial and/or veins

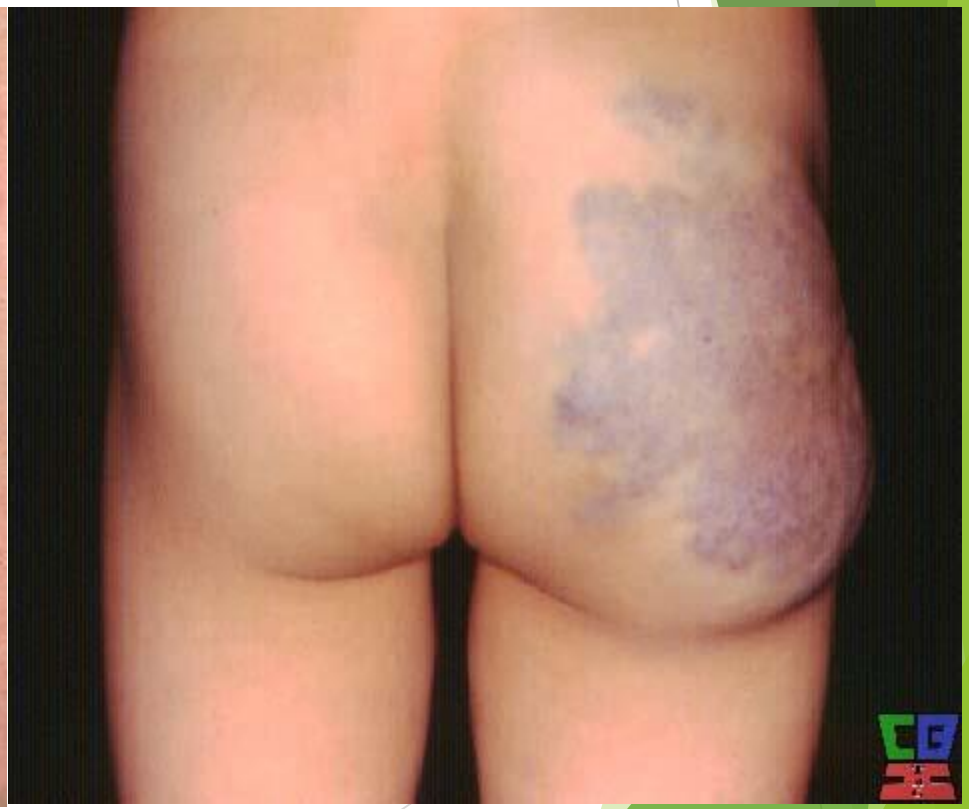
Non-involuting Hemangiomas

- These lesions malformations include:
  - Port wine stains: most common, mainly occur on face or neck. Best to observe, or laser surgery.
  - Cavernous Hemangioma: more common on head and neck. Observation or injection of sclerosing agents.

Non-involuting Hemangiomas

Port Wine Stain Cavernous Hemangioma





Verrucae

- Also known as common warts, these lesions are seen in childhood and in young adults, typically on fingers and hands.
- These lesions appear as round or dome-shaped elevated masses with rough surfaces with multiple villi like keratinized projections.
- They may range from brown to gray to skin colored.

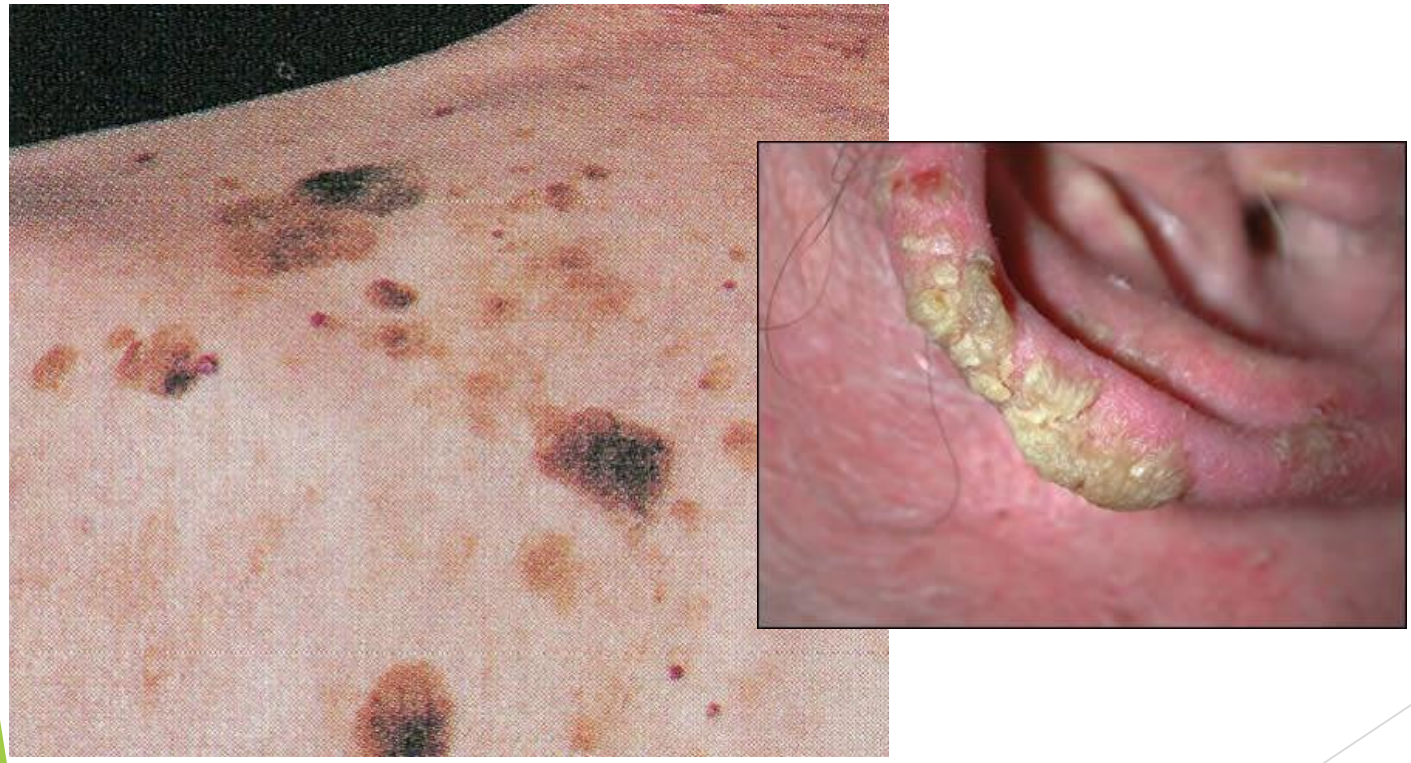
Verrucae

- The etiology is by human papillomaviruses (over 50 different types exist). Types 1, 2, 4, and 7 typically cause verrucae.
- **Treatment:** is by electrodessication or liquid nitrogen.
- Surgical excision is not recommended.
- Most treatment can be delayed by several months because these lesions may spontaneously resolve.
- Duct tape is listed in many current journals as most non-invasive method of treatment.

Actinic Keratoses

- Actinic keratoses are the most common precancerous skin lesions.
- Most commonly appear as single or multiple, slightly elevated, scaly or warty lesions that are red to yellow, brown or black.
- Occur most frequently on the face and backs of hands in fair-skinned Caucasians.
- Approximately 15-20% become malignant, invade the dermis as squamous cell carcinomas.
- Treatment: curettement and electrodessication or 5-FU.

Actinic Keratoses



Melanoma

- Melanocytes are cells of neural crest origin that migrate during fetal development to multiple sites in the body, principally the skin.
- These cells are exposed to carcinogenic stimuli that result in malignant transformation to become melanoma.
- Melanoma accounts for only 4% to 5% of all skin cancers but causes the majority of deaths from skin malignancies. It is the eighth most common cancer in the United States, and the incidence is rising faster than any other type of cancer.

Epidemiology and Etiology

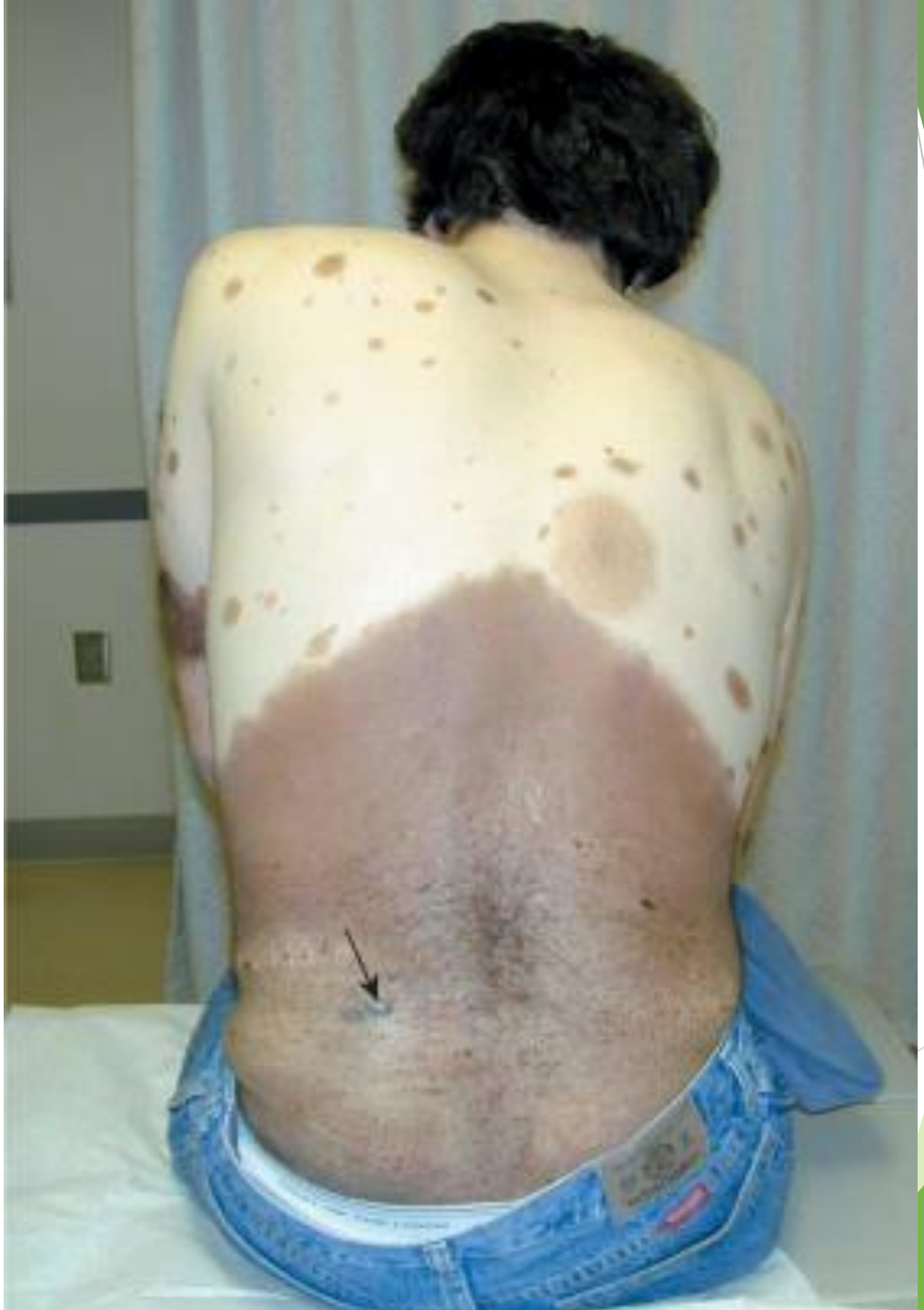
- The incidence and outcome of melanoma are related to multiple factors. Melanoma is principally a disease of whites, particularly those of Celtic ancestry. It is estimated that melanoma occurs 20 times more often in whites than in blacks.
- The median age of diagnosis is in the range of 45 to 55 years. There is a significant incidence in the 3rd and 4th decades of life.

Epidemiology and Etiology

- It is well established that exposure to sunlight increases the risk of developing melanoma in susceptible populations. This is specifically attributed to solar ultraviolet (UVA/UVB) radiation.
- Additional factors that increase the risk for development of melanoma include fair skin, dysplastic nevus (DN) syndrome, xeroderma pigmentosum, a history of non-melanoma skin cancer (NMSC), and a family history of melanoma.

Precursor Lesions and Risk Factors

- Congenital nevi, DNs, Spitz nevi, and familial patterns all raise the risk of developing melanoma. Individuals with congenital nevi have an increased risk that is proportional to the size and number of nevi.
- Giant congenital nevi are rare (1 in 20,000 newborns) and carry an increased risk for development of melanoma within the nevi



Melanoma

- Screening: Any new pigmented nevus should be suspected.
- Approximately one third arise from pigmented nevi.
- **Junctional nevi**: small, circumscribed and are light brown to black.
  - Rarely have hair.
  - Appear on all parts of the body, and mucous membranes, genitalia, palms, and soles.
  - Located on the epidermis and dermal-epidermal junction.

Melanoma

- **Intradermal nevi**: small spots to large extensive areas, variable shape. Often black or brown and slightly elevated, and confined to the dermis.

- **Compound nevi**: combination junctional and intradermal.

Melanoma

- **Blue nevi**: flat or dome-shaped, bluish-black usually on hands arms, or face. May resemble nodular melanoma.
- **Dysplastic nevi**: are larger, up to 5-12 mm, have macular and popular features, varied in color with pink base, and have indistinct, irregular edges. PRECURSOR OF MELANOMA.
- **Congenital nevi**: occur in approximately 1% of newborns. PRECURSOR OF MELANOMA.

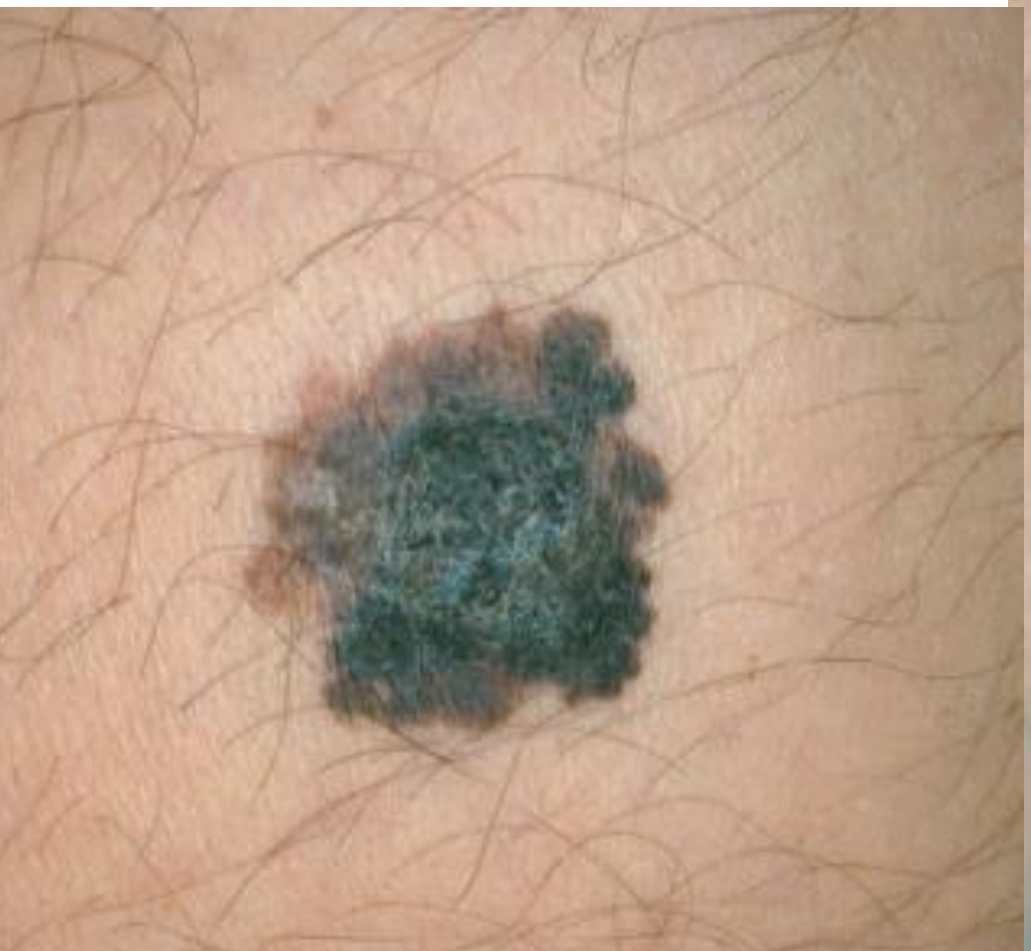
Melanoma

- **Symptoms:** features that are suggestive of melanoma are the following
  - Irregular areas of differentiating color (black to brown to tan with focal discoloration)
  - Rapid enlargement
  - Irregular edges
  - Erosion, bleeding or crust formation
  - Pruritis
  - Location: lesions on back and lower extremities require close motoring.

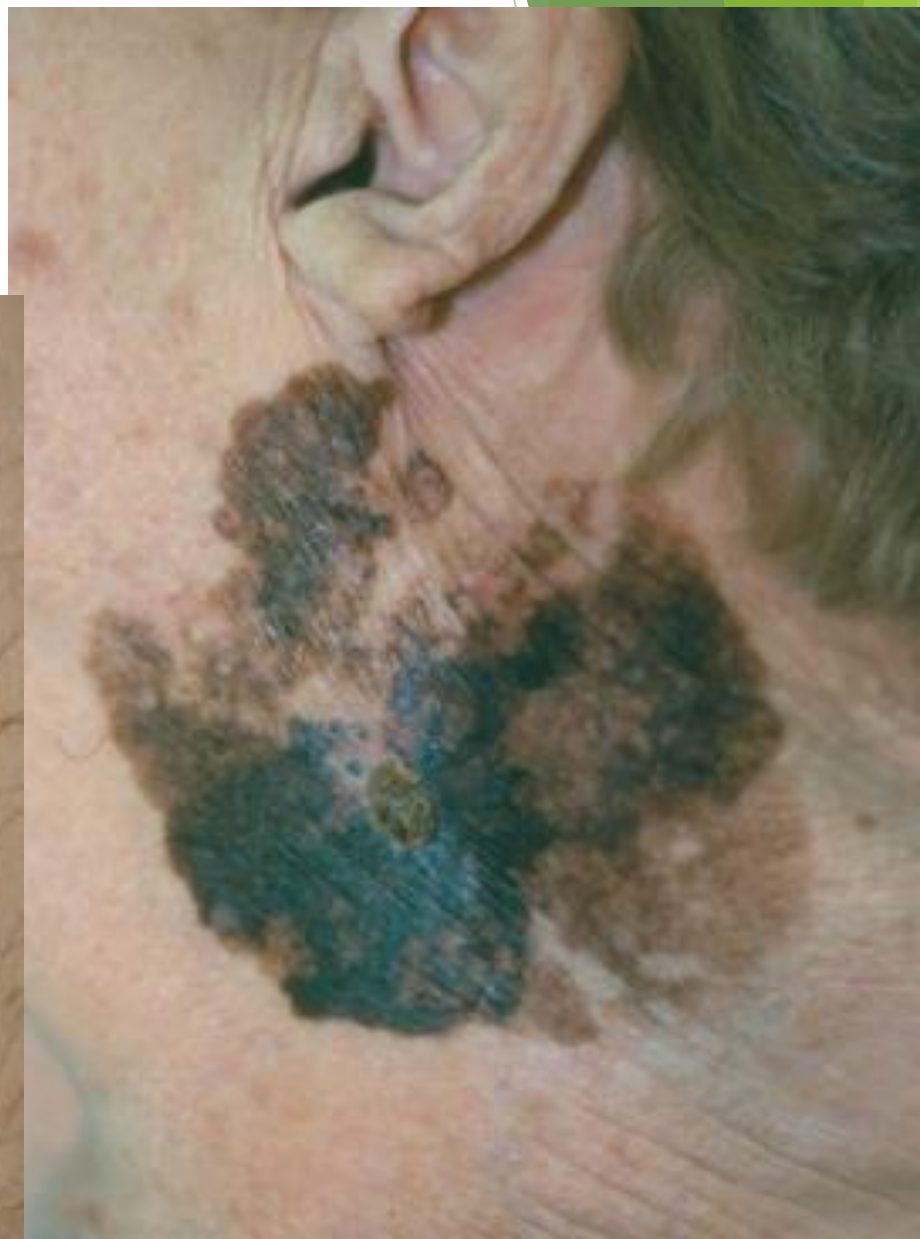
Melanoma

- Several different tumor types exist:
  - **Superficial spreading**: Most common type. Typically appears on back, and may be black, gray blue or pinkish in color.
  - **Nodular**: may develop from a preexisting nevi, and rapidly becomes palpable. May also ulcerate, and is worse prognosis.
  - **Lentigo maligna**: usually occurs in older patients. Seen most often as a large melanotic freckle (Hutchinson's freckle) on the temple or malar region. Grows very slowly, and is the largest of the malignant melanomas.
  - **Acral Lentiginous**: Confined to the subunual areas and glabrous skin of the palms and soles. Most common in black population.

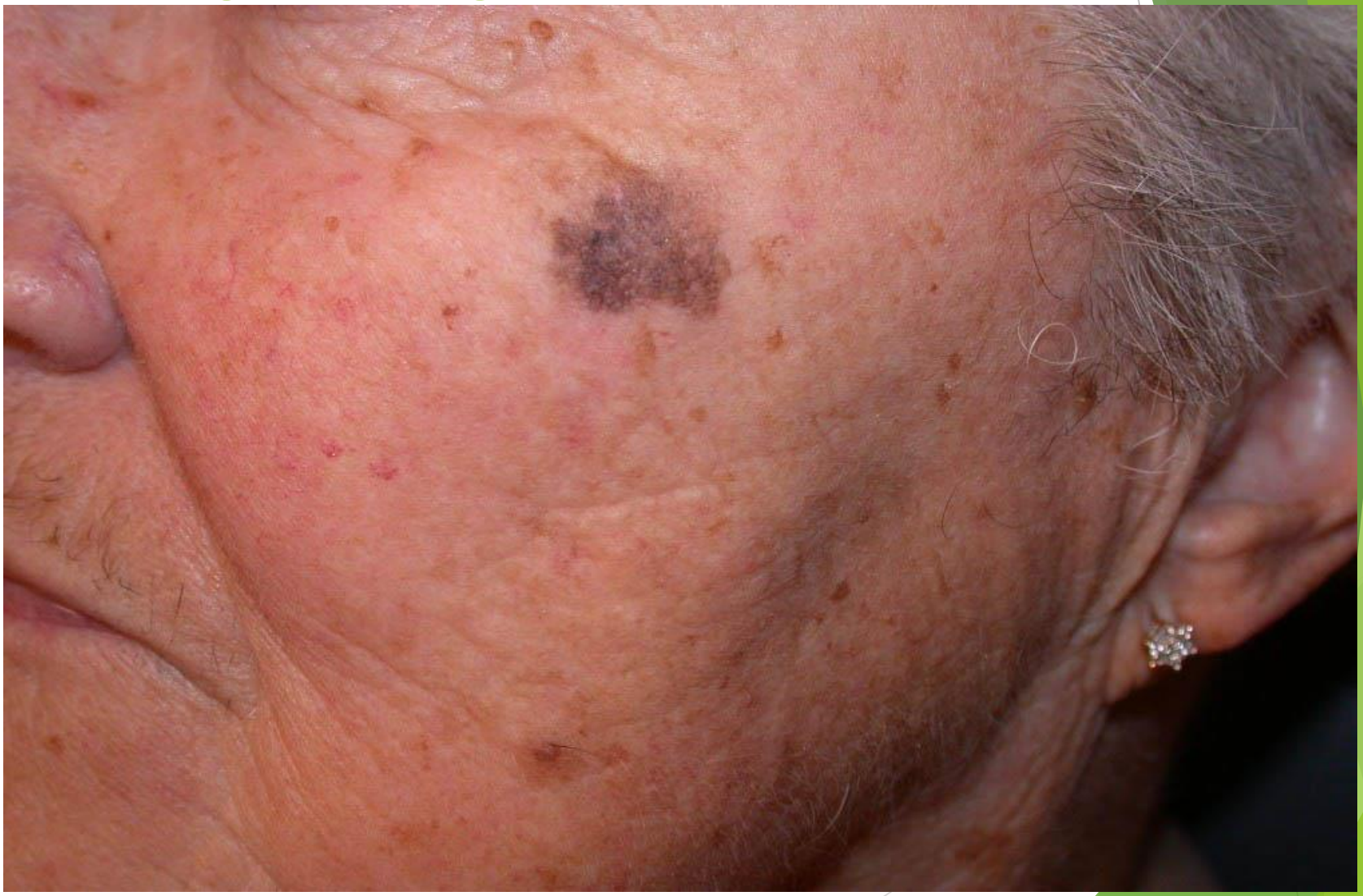
Superficial spreading melanoma



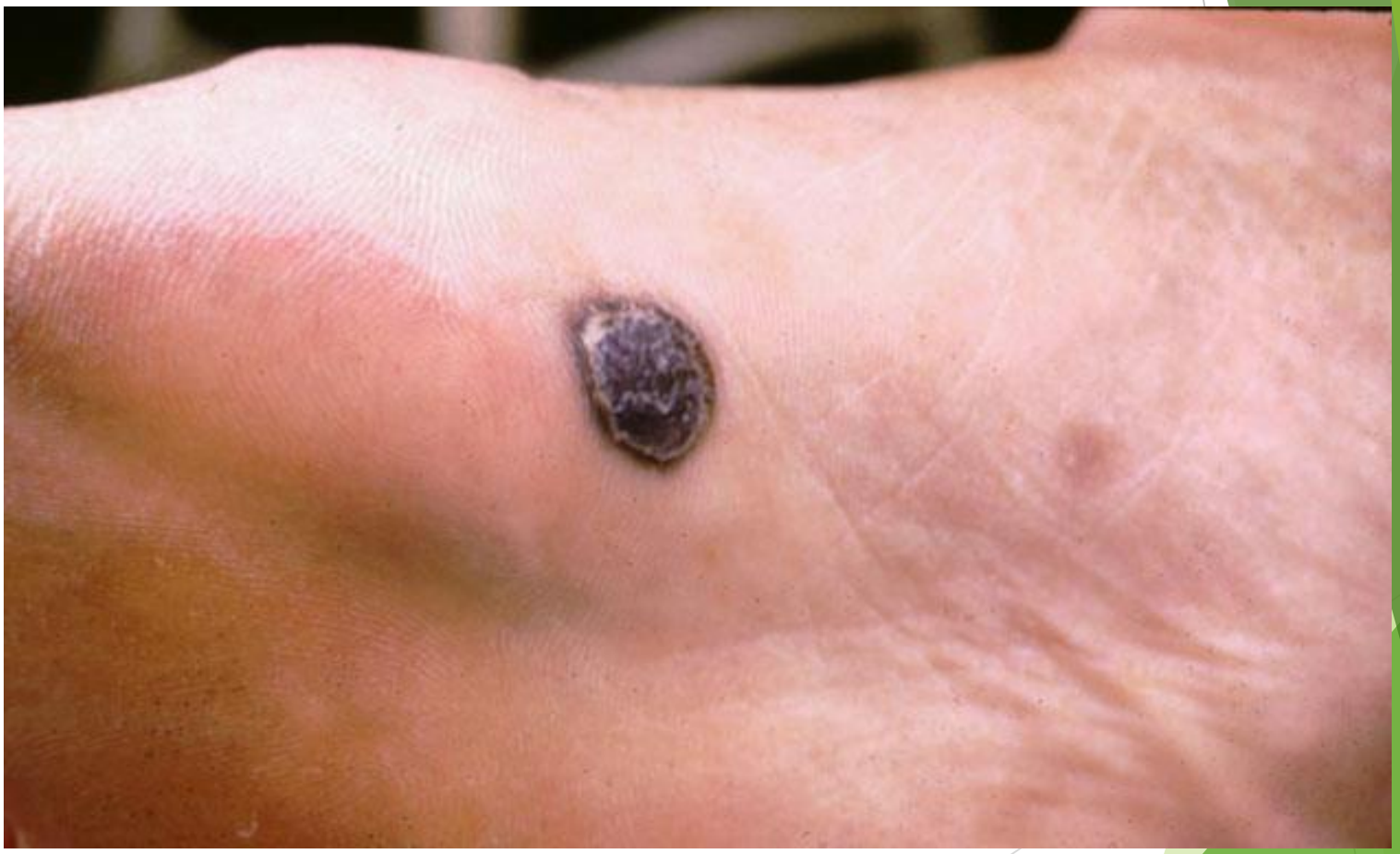
Lentigo maligna melanoma



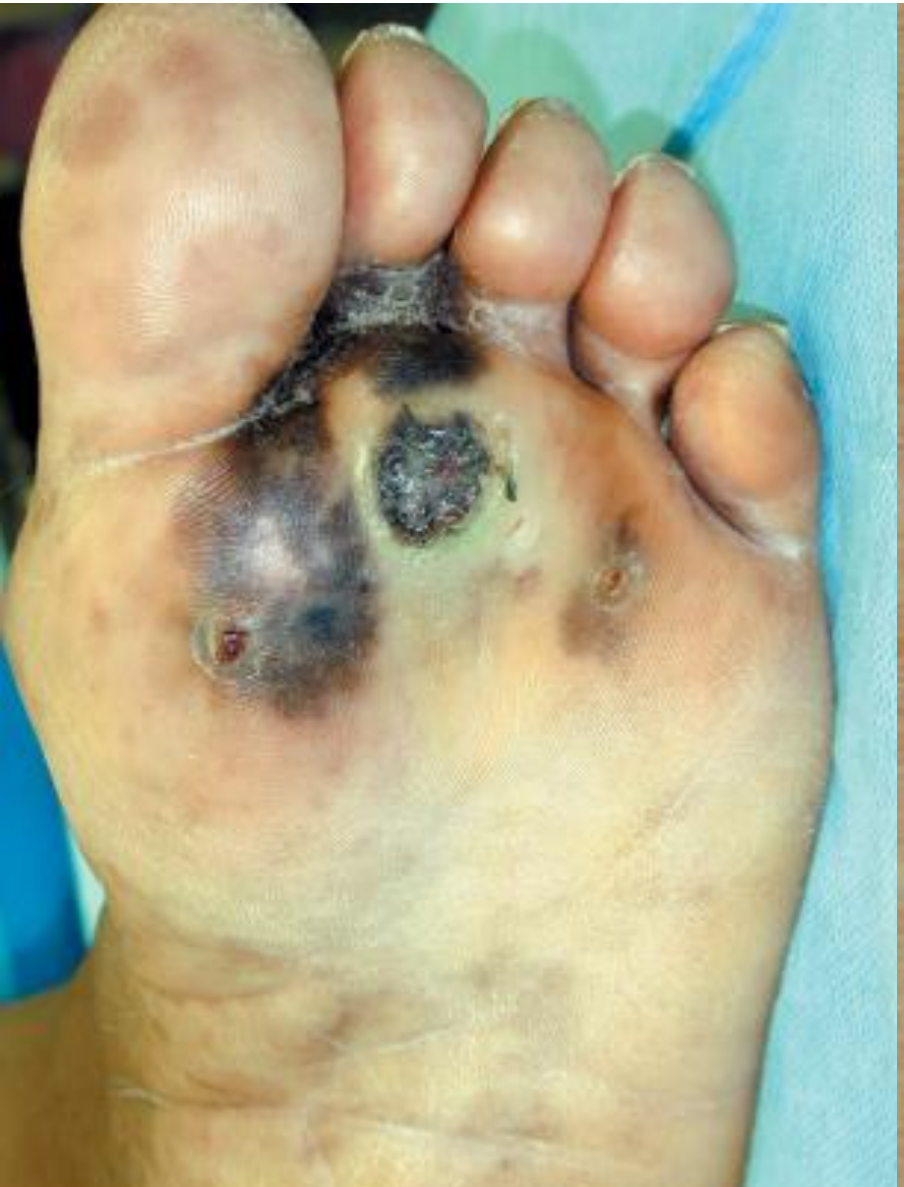
Lentigo Maligna



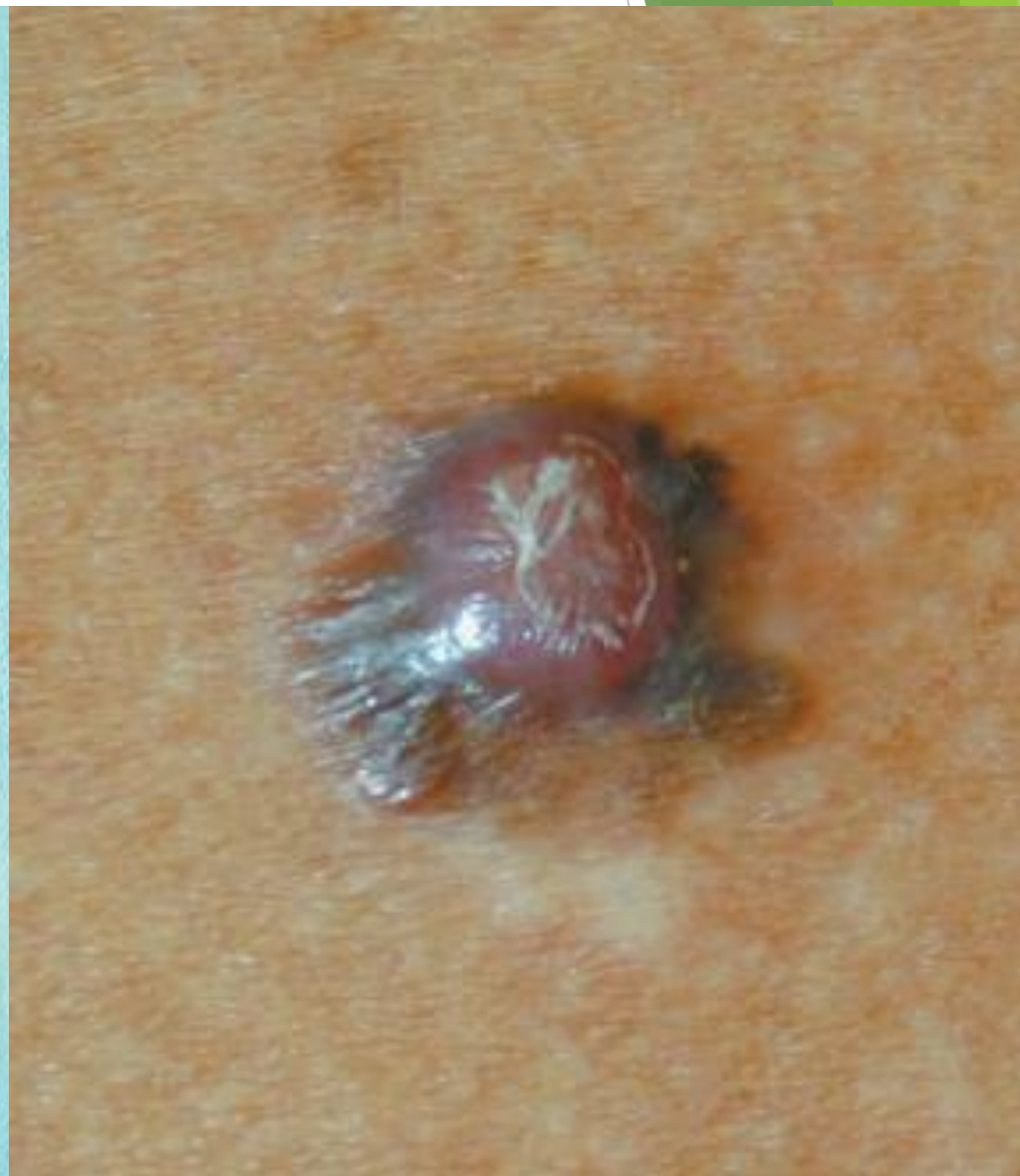
Acral Lentiginous



Acral lentiginous melanoma



Nodular melanoma



Breslow's Depth (old)

Thickness (mm)	Recurrence or metastasis at 5 years
<0.75	0%
0.76-1.5	33%
1.51-2.25	32%
2.26-3	69%
>3	84%

AJCC Classification

Primary Tumor (T)

TX	Can not be assessed
T0	No evidence of Tumor
Tis	Melanoma in situ
T1	Melanoma < 1mm with or without ulceration
T1a	Melanoma < 1mm, level II or level III, No ulceration
T1b	Melanoma <1 mm, level IV or level V with ulceration
T2	Melanoma 1.02-2.0mm, with or without ulceration
T2a	Melanoma 1.01-2.0mm, No ulceration
T2b	Melanoma 1.02-2.0 mm with ulceration
T3	Melanoma 2.01-4.0mm
T4	Melanoma > 4.0mm

Regional LN (N)

NX	can not be assessed
N0	No regional LN Mets
N1	Mets into 1 LN
N1a	Microscopic Mets
N1b	Macroscopic Mets
N2	Mets in 2 or 3 regional LN
N2a	Microscopic Mets
N2b	Macroscopic Mets
N2c	Satellite or in-transit Mets
N3	Metastasis in 4 or more LN

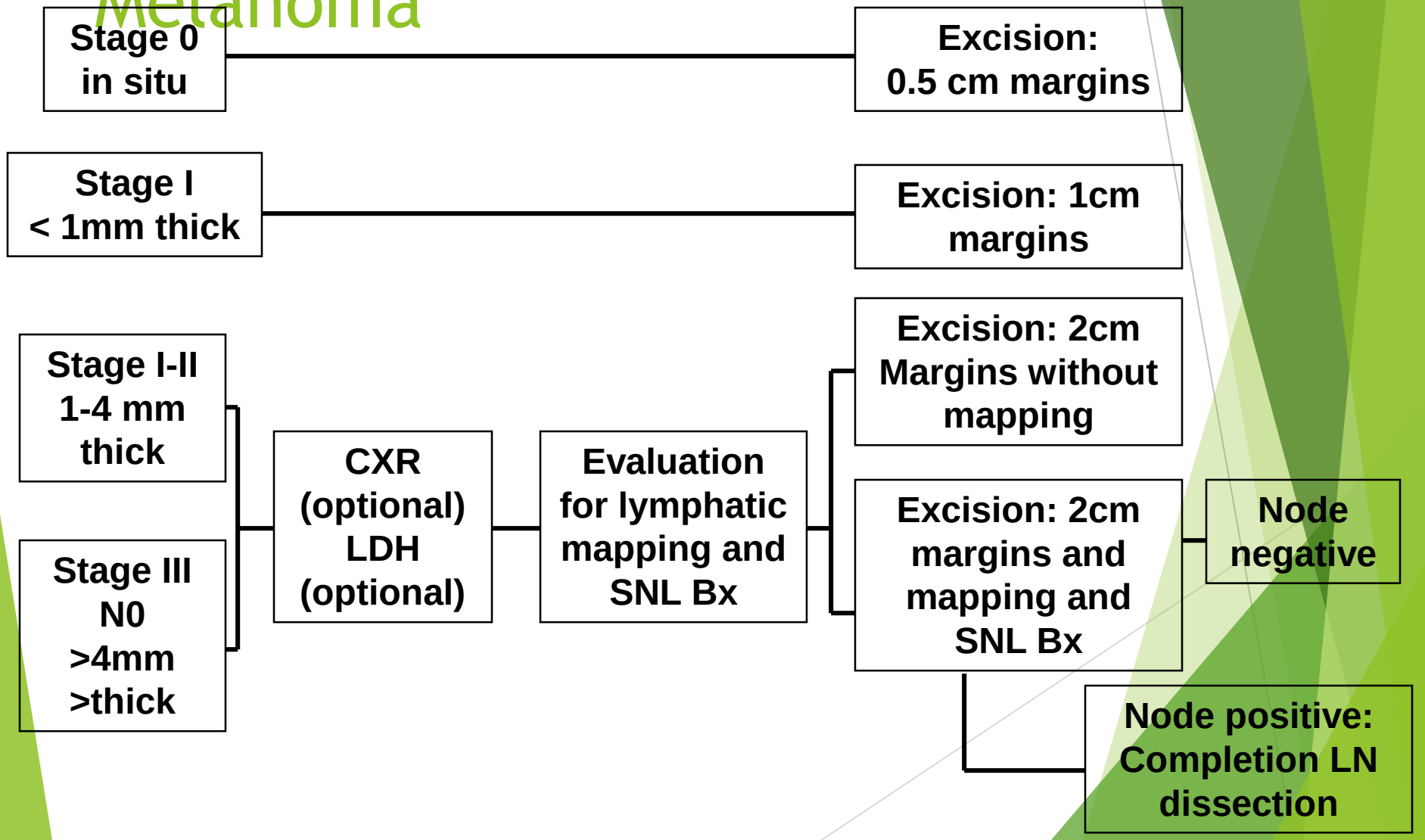
Distant Metastasis (M)

Mx	cannot be assessed
M0	No distant Mets
M1a-c	Distant Mets

Recommended Margins for Surgical Resection

Tumor Thickness (mm)	**Margin Radius (cm)**
In Situ	0.5
<1.0	1.0
1-2	2.0
>2.0	>2.0

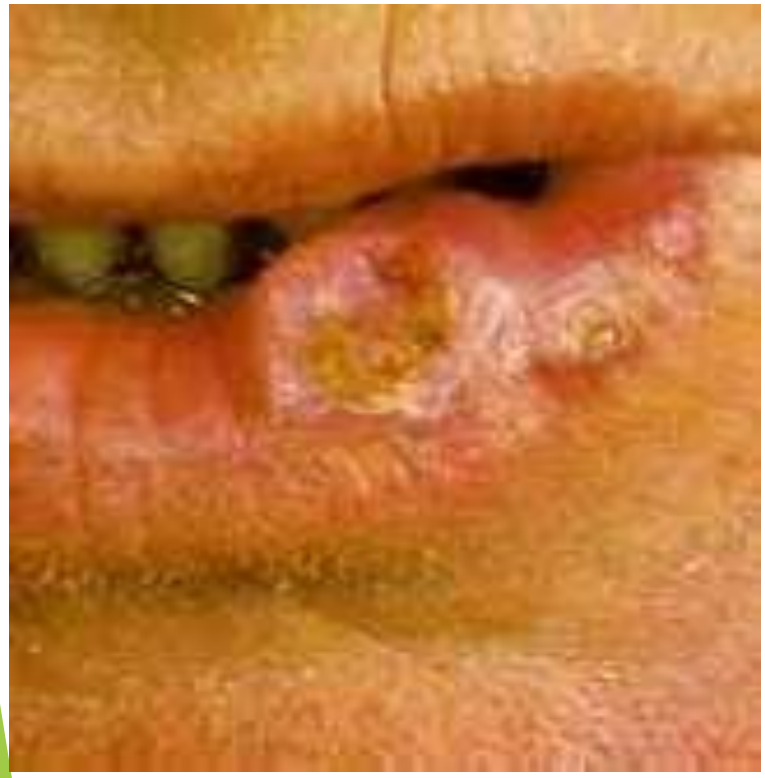
Surgical Management of Melanoma

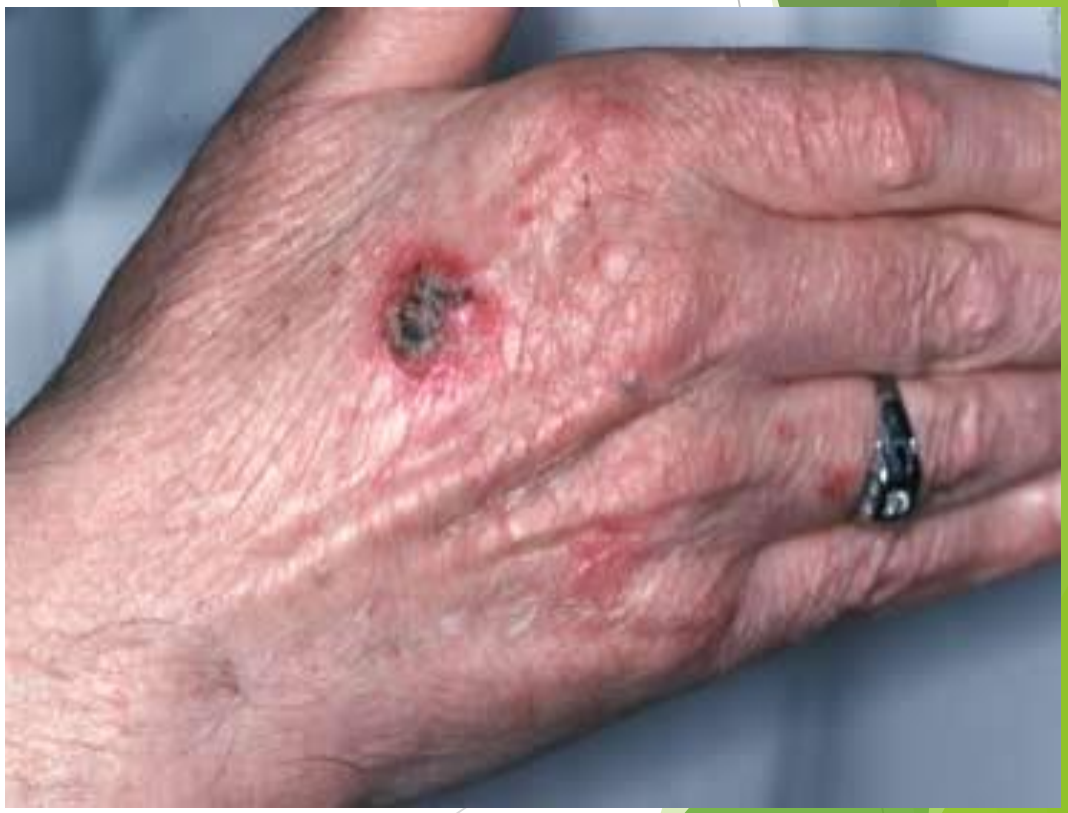


Squamous Cell Carcinoma

- Second most common cancer of the skin, and the most common skin cancer in darkly pigmented racial groups
- Most common etiological factor is ultraviolet light. Most common sites are ears, cheeks, lower lip, areas of burns (Marjolin ulcer) and scars, chronic ulcers, and areas exposed to radiation. Human papillomaviruses, especially types 5, 8, and 14 are also indicated.

Squamous Cell Carcinoma





Squamous Cell Carcinoma

- Most of these lesions arise from actinic keratoses.
- Natural history ranges from slow growth lesions (typical of lesions arising from actinic keratoses) or rapid, early metastatic lesions.

Squamous Cell Carcinoma

- Histiologically the lesions are seen to extend down into the dermis as broad rounded masses or slender strands with keratinization and layers of intercellular bridges.
- **Treatment:** total surgical excision versus irradiation.
- Lymph node dissection is not necessary except in aggressive cancers of the anal and genitalia areas.

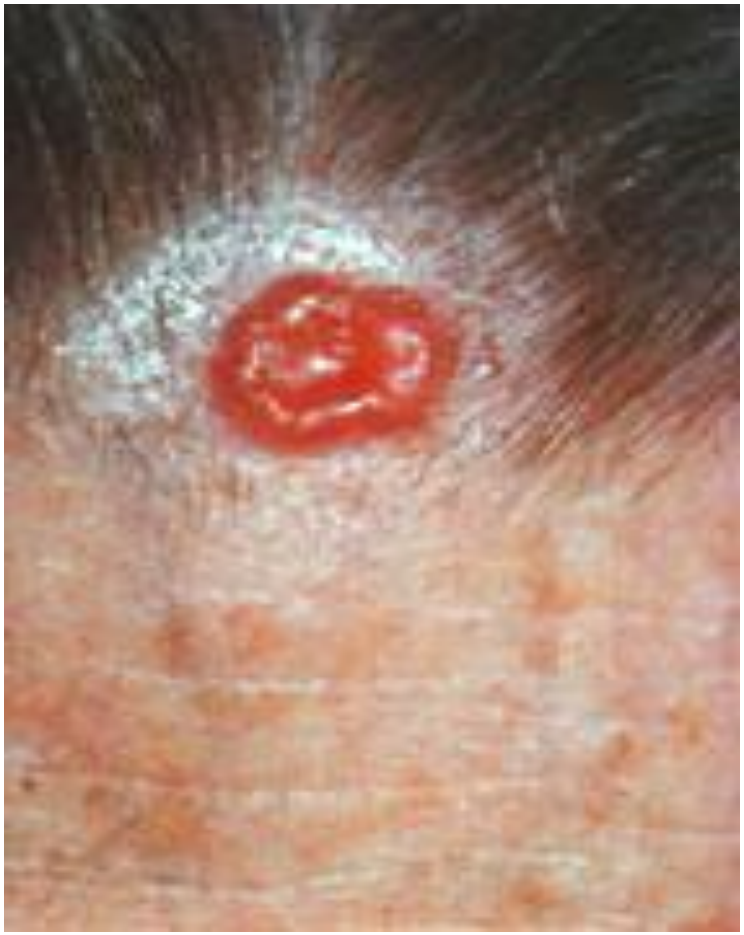
Basal Cell Carcinoma

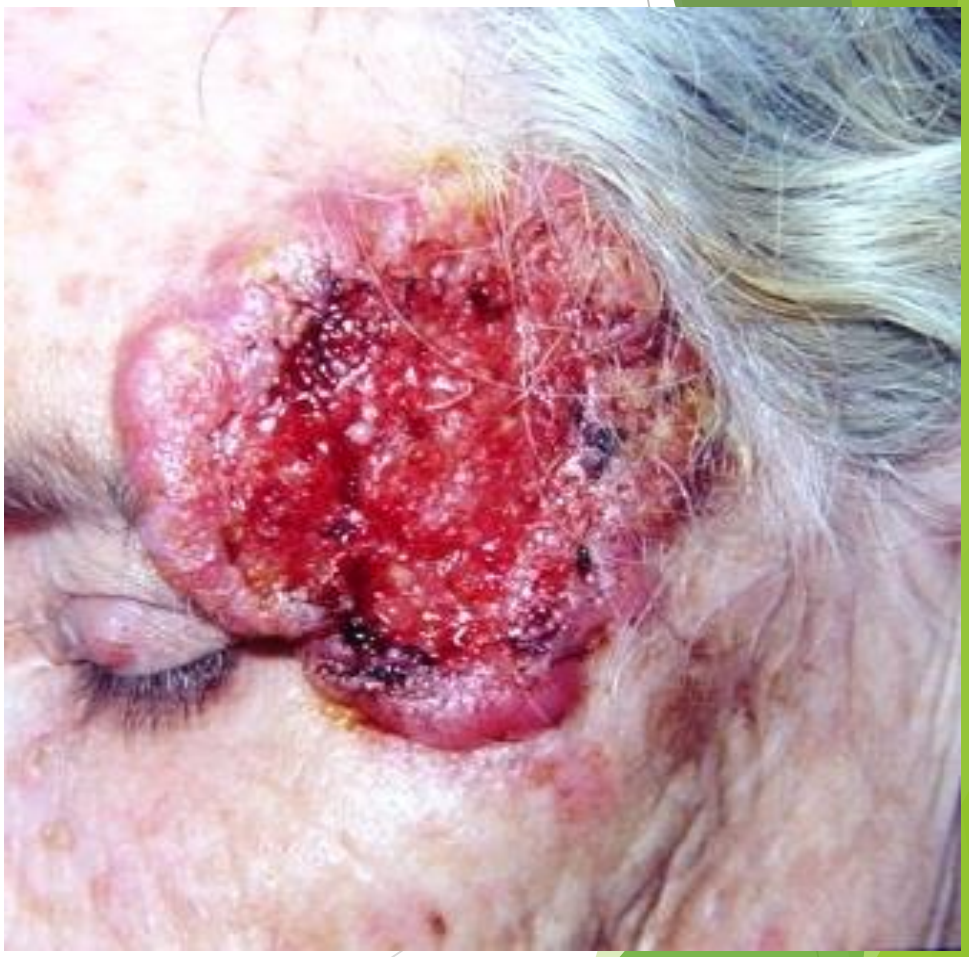
- Most common skin cancer.
- Lesions usually appear on face. More common in men versus women.
- Etiology is exposure to ultraviolet rays; geographic areas where sun is plentiful and increased incidence in fair-skinned individuals.
- Growth rate is very slow, locally invasive and may spread to local tissues or penetrate to the bones of the face and the skull. Metastasis is rare.

Basal Cell Carcinoma

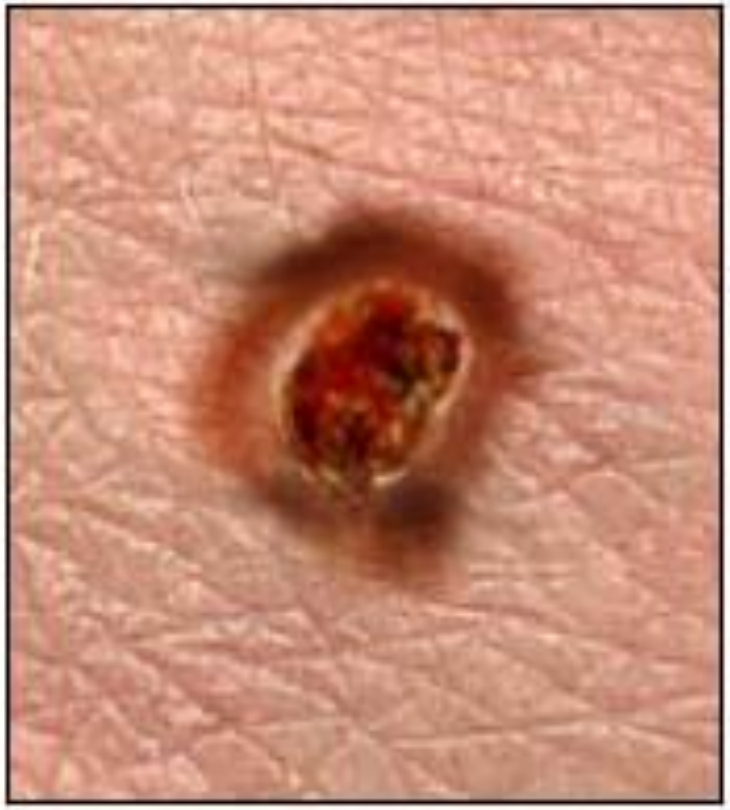
- Typical appearance is small, translucent or shiny “pearly” elevated nodules with telangiectatic vessels present.
- Superficial ulceration may also be present.
- Treatment includes:
  - Curettage and electrodessication with ~ 3 mm free margin
  - Surgical excision with 3-5 mm free margin
  - X-ray therapy for difficult to reconstruct areas (eyelids, tear ducts, nasal tip)

Basal Cell Carcinoma

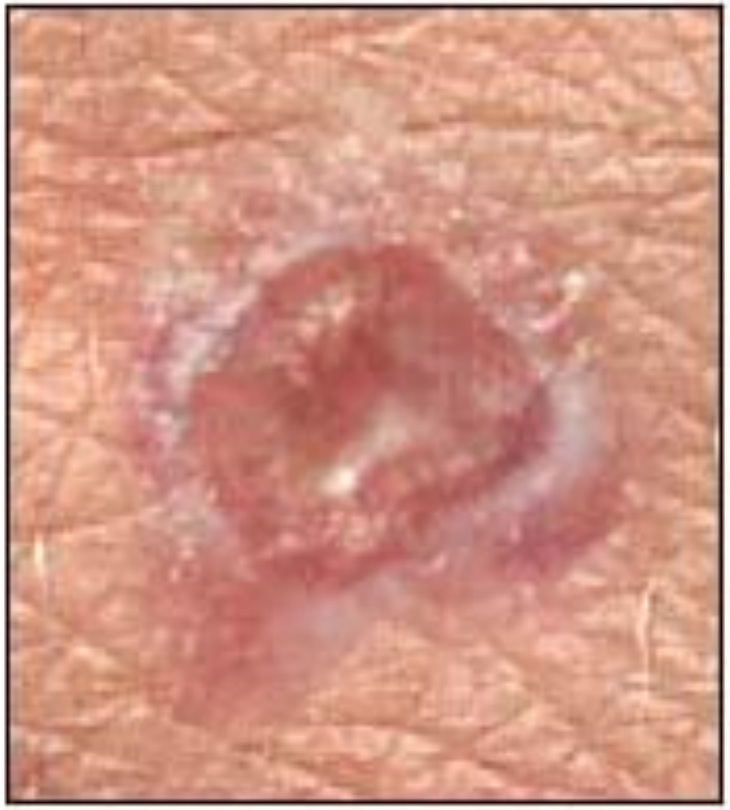




Squamous cell carcinoma



Basal cell carcinoma



Hippocratic Oath

"Primum Non Nocere"

(First Do Not Harm)

Questions?

What is a Keloid?

- Non-cancerous fibrous proliferations that occur in the dermis after trauma or injury to the skin
- Keloids grow beyond the boundaries of the original wound site (vs. hypertrophic scar)
- Etiological factors that determine how a scar becomes a keloid remain unknown

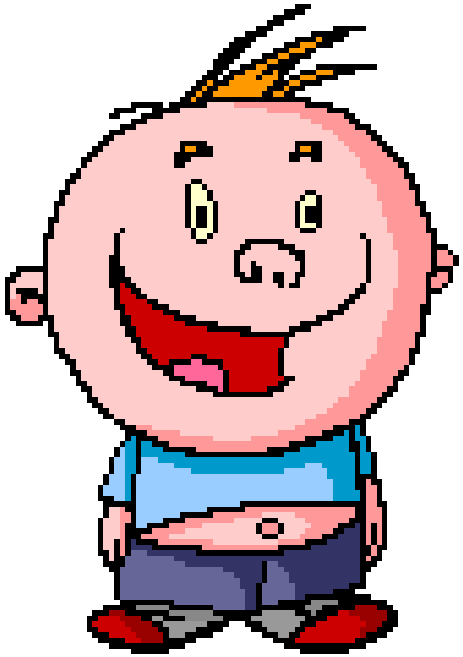
Who and Why?

- Individuals with darker-pigmented skin or who freckle are more predisposed
- Seen largely in Africans, African-Americans, Hispanics, and Asians
- Can be a familial/genetic predisposition
- Can be due to immunological causes
- Bottom line… No one knows!

How? (Pathophysiology)

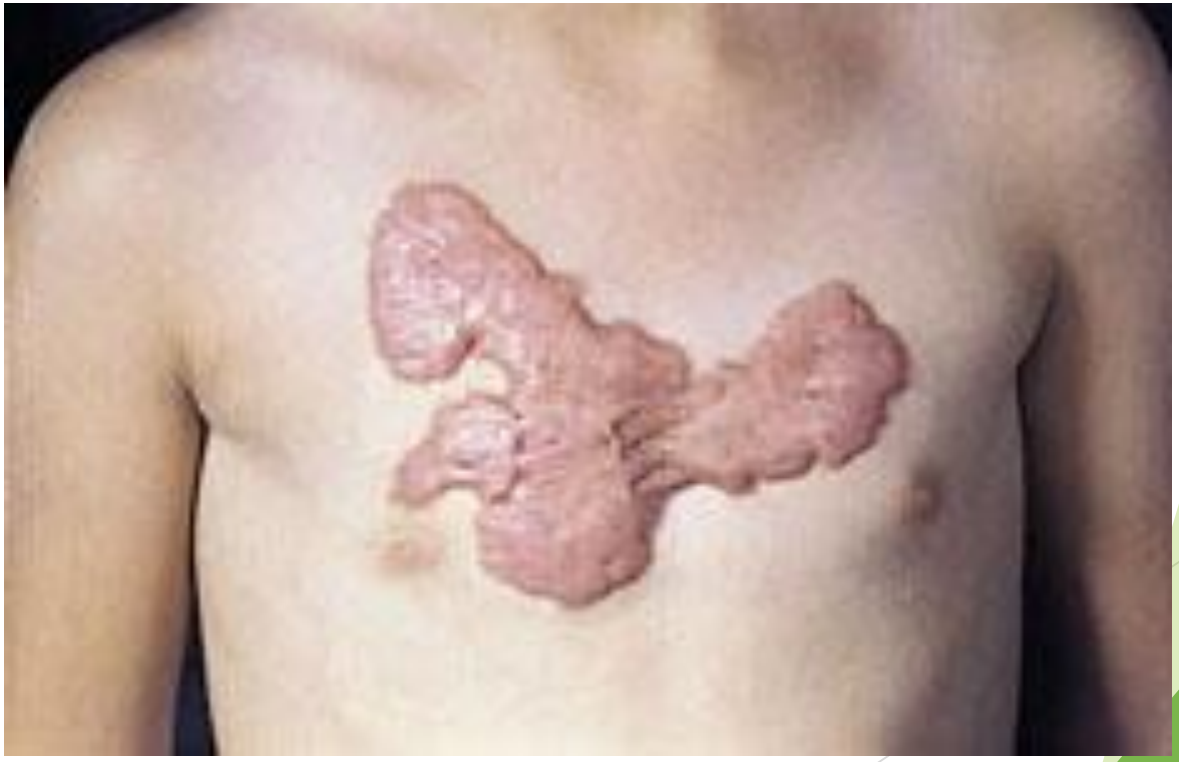
- A result of an overactive inflammatory response and fibroblast proliferation
- A result of an abnormal collagen deposition in healing skin wounds
- Skin wound tension is a contributing factor in keloid formation
- Individuals with an inflammatory or infectious element are at a predisposition for keloids

Ready for the Pictures?



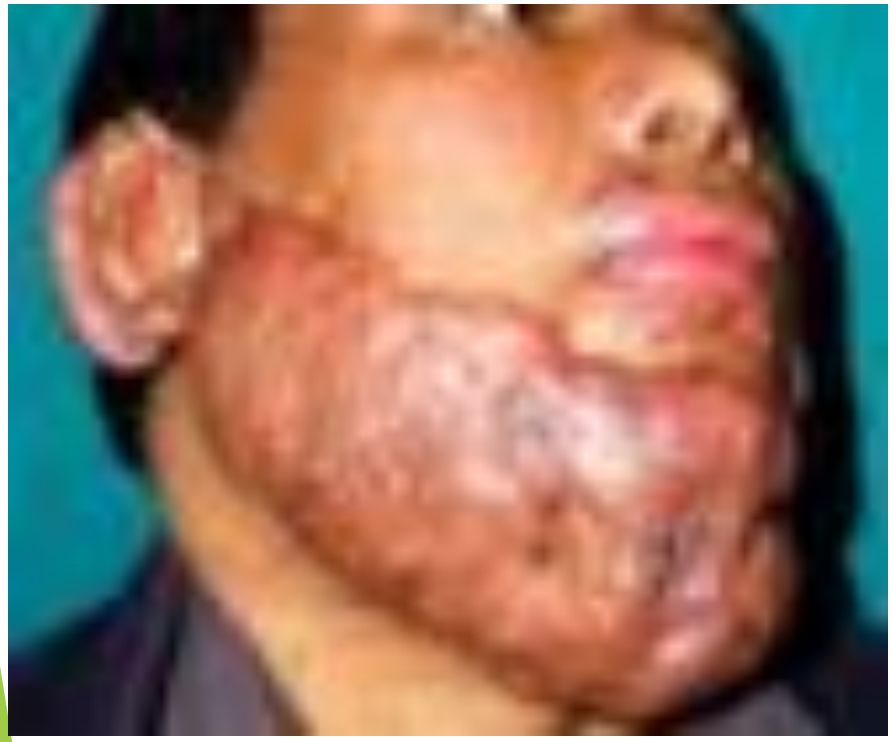
Where?

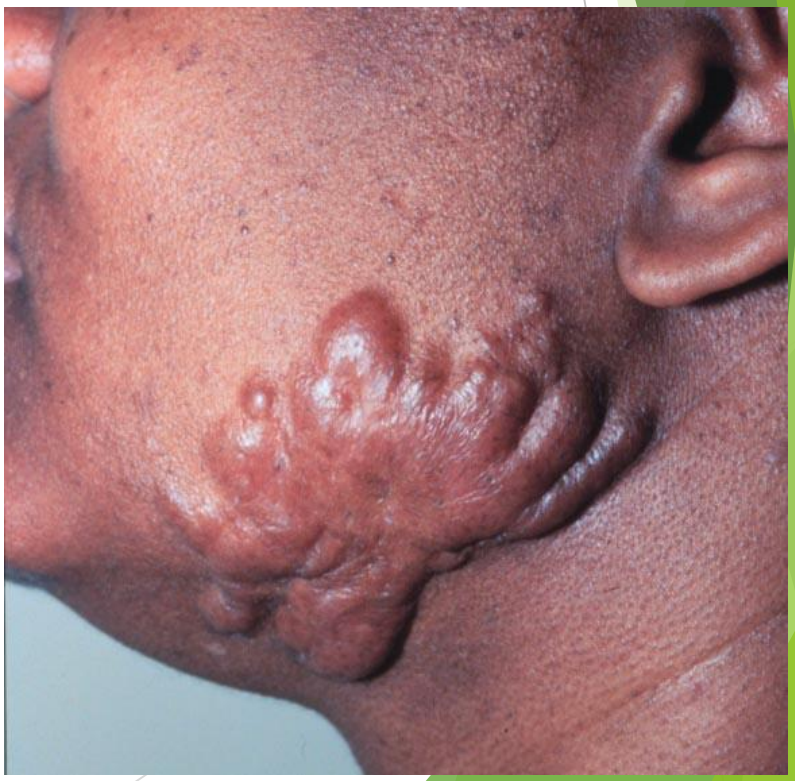
- Anterior Chest



Where?

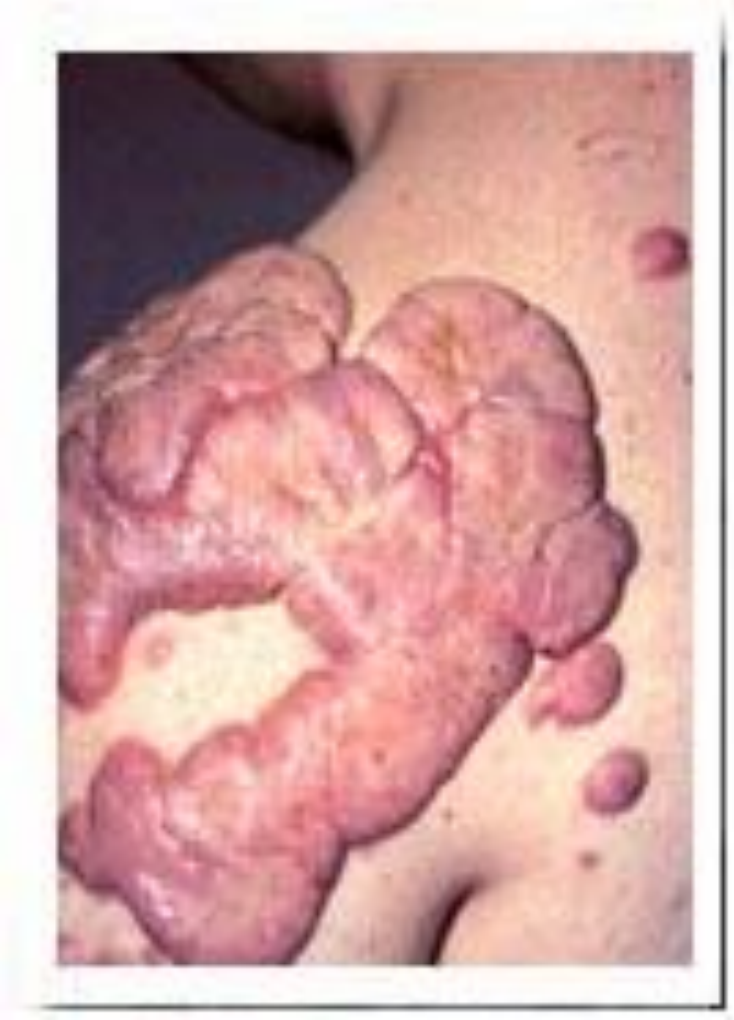
- Mandibular angle



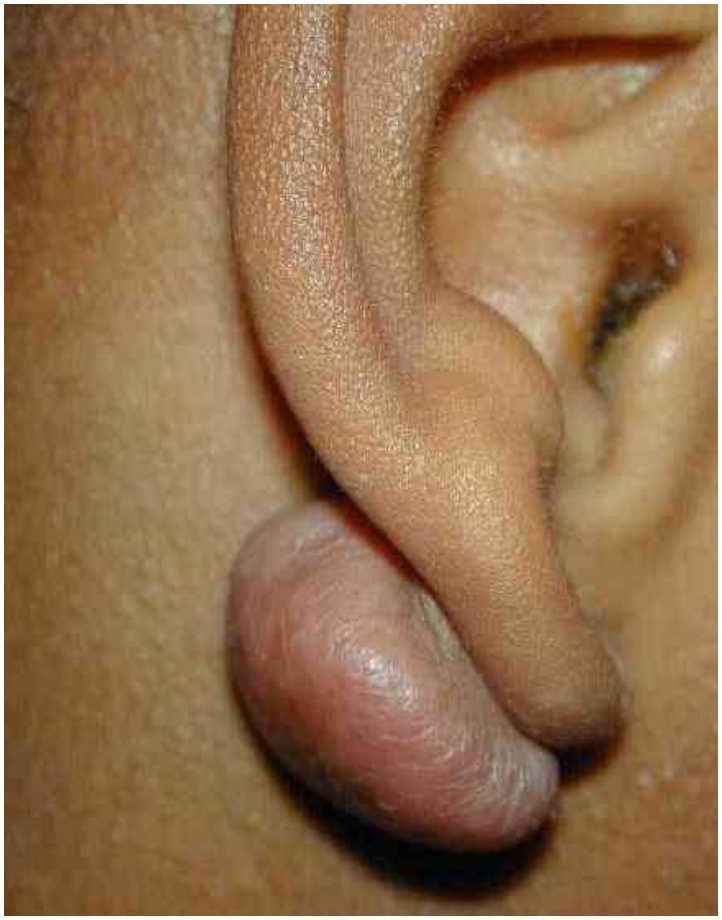


Where?

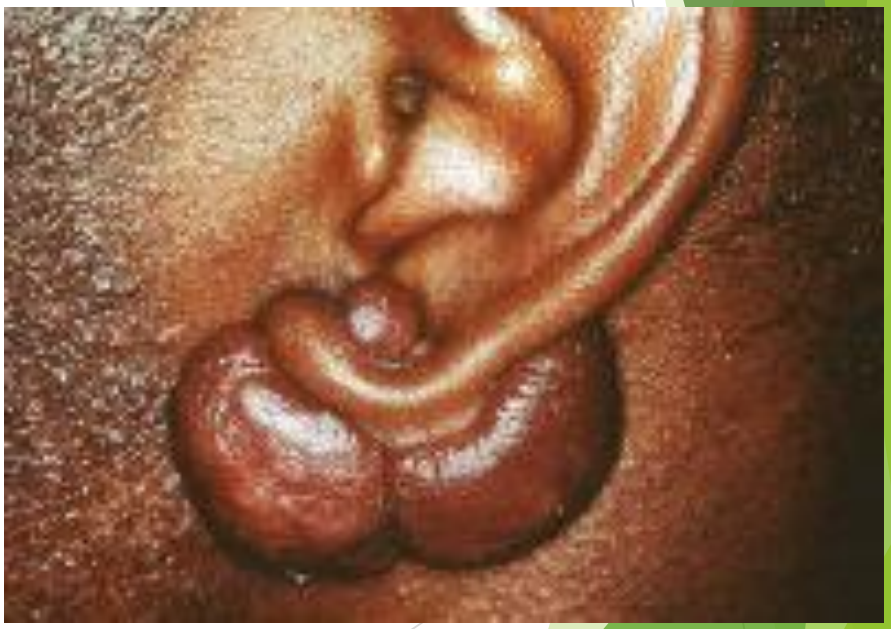
- Shoulder



Where?

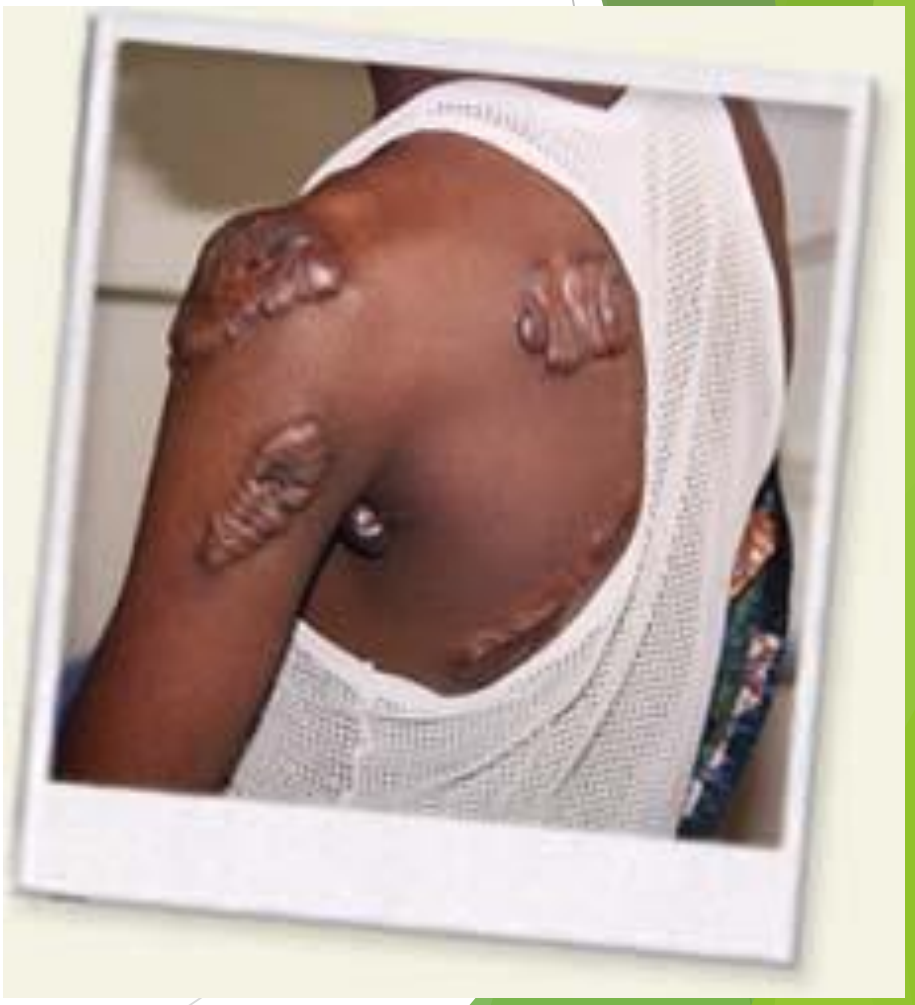


- Earlobes



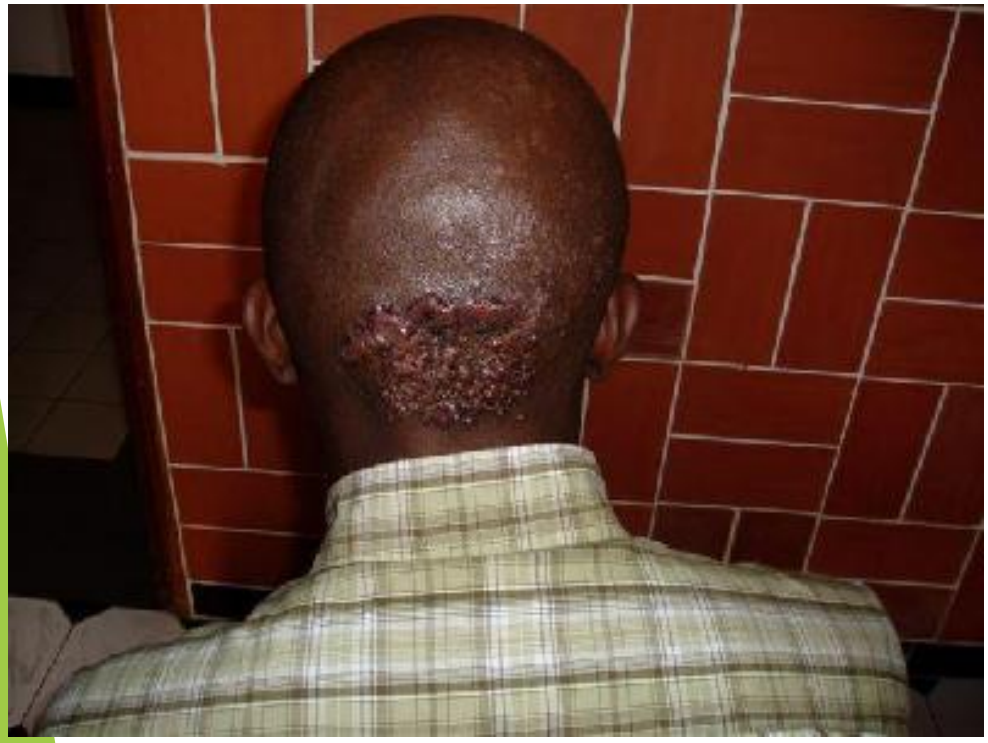
Where?

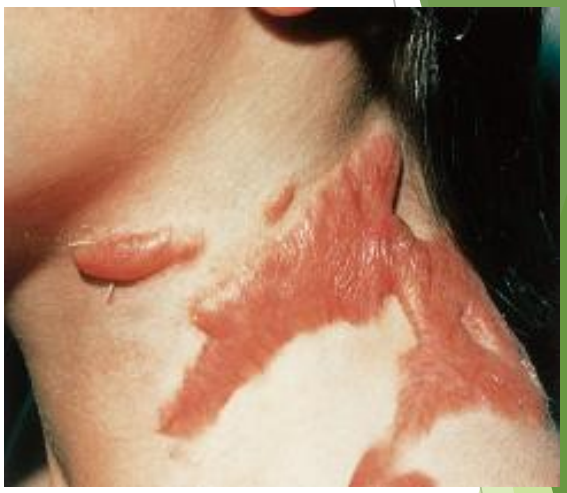
- Upper Arms & Upper Back



Where?

- Posterior Neck





- Lateral Neck

So…What's the Problem?

The Problem

- PROBLEM is with the TREATMENT OPTIONS
- The pathophysiology of these scars is so poorly understood that it is basically unknown
- Surgery is the only approved treatment
- A successful surgical protocol for removal of these types of scars is greatly lacking
- Surgical treatments available today only provide temporary relief
- Often grow back and do so in an aggressive manner

Possible Solutions

- Surgical excision alone
- Post-surgical treatment agents:
  - Mitomycin C solution
  - The dietary compound quercetin
  - Imiquimod 5% topical cream
  - Intralesional corticosteroid injection
  - Topical silicone gel sheets

How they work…

- Mitomycin C solution (MC)
  - An anti-neoplastic agent
  - Has anti-proliferative effects on fibroblasts, stopping keloid formation
  - MC effectively blocks angiogenesis during the healing process of the wound, thus inhibiting keloid development
  - MC is widely available and relatively cheap

How they work…

- The dietary compound quercetin
  - most common sources: apples, onions, red wine, and ginkgo biloba.
  - has strong anticancer, antioxidant, antiviral, anti-inflammatory, and antimicrobial characteristics
  - Inhibit keloid fibroblast proliferation, collagen production, and contraction of keloid derived fibroblasts

How they work…

- Imiquimod 5% topical cream
  - Induces apoptosis in keloidal tissue
- Intralesional corticosteroid injection
  - Inhibit fibroblast growth and break down collagen deposition
  - postoperative steroid injection is the most common form of keloid treatment
  - corticosteroids commonly used include hydrocortisone and dexamethasone.

How they work…

- Topical silicone gel sheets
  - Impermeable to water, reduces hemostasis and therefore, decreases the hyperemia and fibrosis often associated with keloids
  - have been used for more than twenty years to help reduce the size of scarring
  - efficacy and safety of the silicone gel sheets is well established.

And the Winner is…

- Imiquimod 5% topical cream

Aldara™
(IMIQUIMOD)

Analysis

- 13 keloids from 12 patients were surgically removed
- All keloids were present for at least 1 year and free of any treatment for the past 2 months
- A thin layer of imiquimod 5% cream was applied topically each night for 8 weeks
- 4 week asessments
- At 24 weeks, no keloids had recurred

Pilot study of the effect of postoperative imiquimod 5% cream on the recurrence rate of excised keloids (Berman and Kaufman, 2002)

Analysis

- 2 cases of irritation and superficial erosion were reported; resolved with cessation of the cream
- At the 24 week assessment, RECURRENCE RATES of keloids treated with imiquimod 5% cream were LOWER than any previously reported in the literature

Pilot study of the effect of postoperative imiquimod 5% cream on the recurrence rate of excised keloids (Berman and Kaufman, 2002)

Analysis

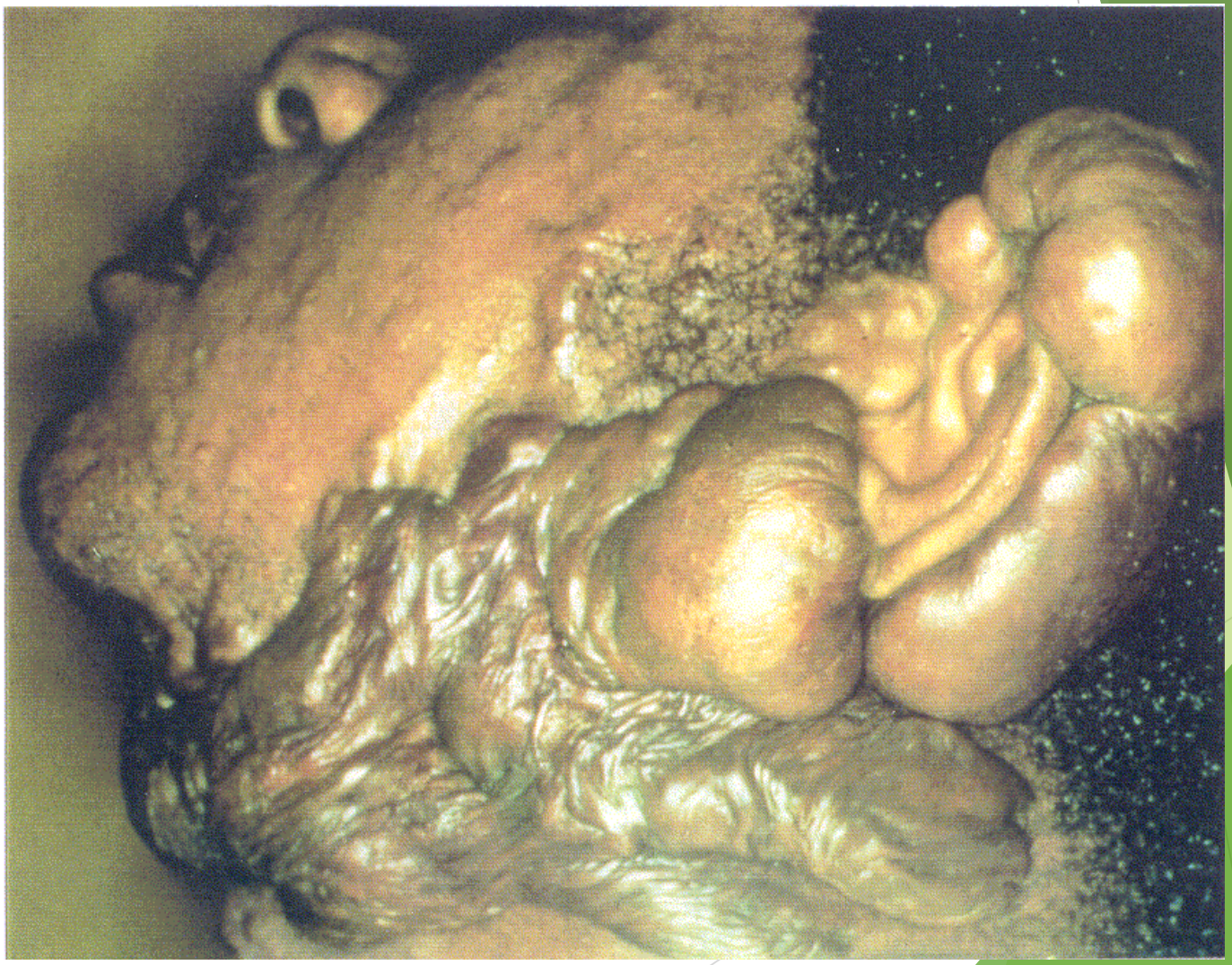
- Study did not control for the effects of vehicle application or other potential variables
- Further comparative studies with longer follow-up periods are needed
- Additional studies needed to determine dosing frequency and duration

Pilot study of the effect of postoperative imiquimod 5% cream on the recurrence rate of excised keloids (Berman and Kaufman, 2002)

Conclusion

- To develop a successful treatment plan for the keloid, two things have to be done:
  - 1. Further research to better understand the causes behind keloid formation
  - 2. Establish a standard surgical protocol
- In short, the topic of keloids is greatly under-exposed.

One More



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