Pathology of Burns

In the name of God

Dr.Maryam Ghasemi
Professor of pathology
Mazandaran university of medical sciences

Introduction

- A burn is an injury to the skin or other organic tissue primarily caused by exposure to heat or other causative agents (radiation, electricity, chemicals).
- According to WHO, it is a global public health problem, accounting for an estimated 180,000 deaths annually. It is among the leading causes of disability in low and middle-income countries and almost two-thirds occur in the WHO African and South-East Asia regions. Burns do not only affect the skin, they can have other effects on the tissue, organ and system networks such as smoke inhalation, as well as psychological effects. Burns affect all genders although females have slightly higher rates of death from burns compared to males. They also affect all age groups and are the fifth most common cause of non-fatal childhood injuries.

Types of Burns

- **Electrical Burn-**Electrical burn injury is caused by heat that is generated when the electrical energy passes through the body causing deep tissue injury. The magnitude of the injury depends on the pathway of the current, the resistance of the current flow through the tissues, the strength, and the duration of the current flow. it is often associated with cardiac arrest, ventricular fibrillation, and tetanic muscle contractions
- **Scald-**
  often occur in elderly people and children. The common mechanisms are spilling hot drinks or liquids or being exposed to hot bathing water. Scalds tend to cause superficial to superficial partial burns.
- **Flame -** Flame burns are often associated with inhalation injury and trauma. They comprise 50% of adult burns and tend to be mostly deep dermal or full-thickness burns[.
- **Contact Burns -** occur after a loss of consciousness. Contact burns tend to be deep dermal or full-thickness burns.(Ab igne Rash)

Types of Burns

- **Frost bite -** Occurs when the skin is exposed to cold for a long time, causing the freezing of the skin or other underlying tissue. It is due to direct cellular injury from the crystallisation of water in tissue and indirect injury from ischemia.

- **Chemical Burn**
  Chemical agents depending on the duration of exposure and the nature of the agent have different effects on the skin. For example, contact with acid causes coagulation necrosis of the whereby the architecture of the dead tissue can be preserved), while alkaline burns generate liquefy tissue (action necrosis (whereby the tissue is transformed into a liquid.

- **Radiation Burn**
  It is the least common burn injury and the most common type of radiation burn is the sunburn caused by prolonged exposure to Ultraviolet rays (UV). with the use of ionising radiation in industry, high exposure to radiotherapy e.g. X-ray, and nuclear energy. Radiation burns are often associated with cancer due to the ability of ionising radiation to interact with and damage DNA.

Pathophysiology of Burns

- A burns injury depending on the severity of the injury can result in both local and debilitating systemic effects on all other organs and systems distant to the burn area.

Systemic Response

- **In severe burn injury, >30% TBSA,a complex reaction occurs** both from the burn area and in the area distant to the burn. Cytokines, chemokines and other inflammatory mediators are released in excess resulting in extensive inflammatory reactions within a few hours.
- **Different factors contribute to the magnitude of the host response**, **they include**: burn severity (percentage TBSA and burn depth), burn cause, inhalation injury, exposure to toxins, other traumatic injuries, and patient-related factors such as age, pre-existing chronic medical conditions, drug or alcohol intoxication, and timing of presentation to medical aid.
- **This inflammatory response leads to rapid oedema formation** which is caused by increased microvascular permeability, increased hydrostatic microvascular pressure, vasodilation, and increased extravascular osmotic activity. These reactions are due to the direct heat effect on the microvasculature and to the chemical mediators of inflammation. Vasodilation and increased venous permeability at the early stage of the injury are caused by the release of histamine. Also, prostaglandin is released by damage to the cell membranes which causes the release of oxygen-free radicals released from polymorphonuclear leucocytes which activate the enzymes catalyzing the hydrolysis of prostaglandin precursor. These hemodynamic changes lead to continuous loss of fluid from the blood circulation causing increased haematocrit levels and a rapid fall in plasma volume, leading to a decrease in cardiac output and hypoperfusion on the cellular level.

- **burn shock :**occurs if fluid loss is not adequately restored

Inhalation injury:
can be divided into three types: systemic toxicity due to products of combustion (carbon monoxide (CO) and cyanide poisoning); upper airway thermal injury; and lower (bronchi and distal) airway chemical injury.

Effect on the Cardiovascular System
The initial response to a severe burn injury is characterised by hypovolemia and reduced venous return. This concomitantly leads to a decrease in cardiac output, increased heart rate, and peripheral resistance.

Effect on the Respiratory System
Following inhalation, inflammatory mediators are released in the lungs leading to bronchoconstriction and adult respiratory distress syndrome

Effect on the Renal System:
Renal blood flow and glomerular filtration rate are reduced secondary to hypovolemia, diminished cardiac output, and the effects of angiotensin, vasopressin and aldosterone. oliguria as an early sign of renal compromise. Failure to promptly and adequately manage these cases may lead to acute tubular necrosis, renal failure, and mortality.

- **Effect on the Liver**
  There is substantial depletion of the hepatic proteins, alterations in serum levels of triglycerides and free fatty acids are highlighted, both of which are significantly increased secondary to a decrease in fat transporter proteins rendering the liver susceptible for fatty infiltration and hepatomegaly with resultant increased risk of sepsis and burn mortality.

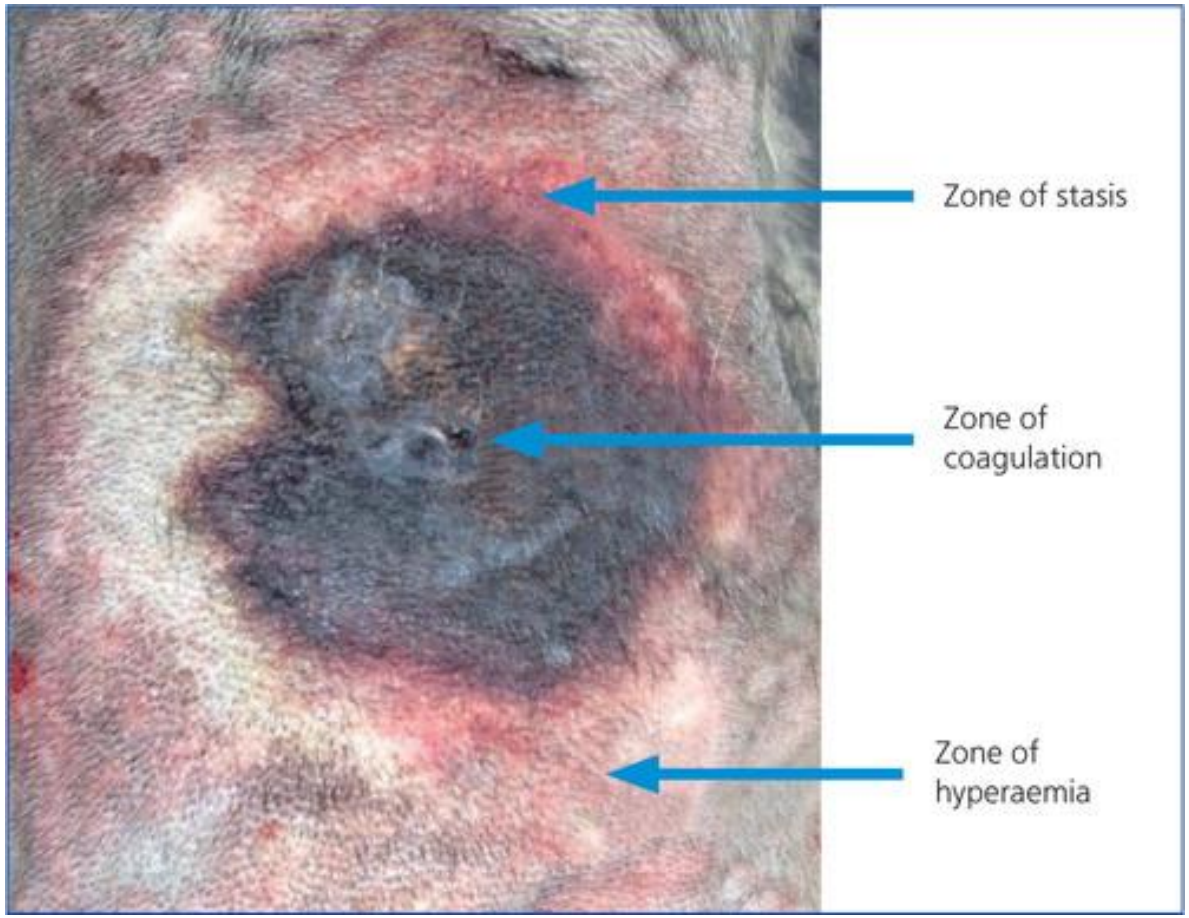
- **Effects on Gastrointestinal System/Metabolism**
  The basal metabolic rate increases up to three times its original rate. This coupled with splanchnic hypoperfusion, necessitates early and aggressive enteral feeding to decrease catabolism and maintain gut integrity. It causes mucosal atrophy, reduced absorptive capacity, and increased surface permeability

- **Effect on the Endocrine System**
  The stress hormones i.e. catecholamine, glucagon and cortisol among other hormones are actively involved at the onset of burns injuries. the stress hormones are thereby considered as the initiators of the hypermetabolic-catabolic and proteolytic-response.

Local Effect

- **This occurs immediately after the injury and the burn wound can be divided into three zones.**
- Zone of coagulation: This occurs at the point of maximum damage and this zone is characterised by irreversible tissue damage due to coagulation of the constituent proteins that occurs as a result of the insult.

- Zone of stasis or zone of ischemia: This zone lies adjacent to the zone of coagulation and it is subject to a moderate degree of damage associated with vascular leakage, elevated concentration of vasoconstrictors, and local inflammatory reactions resulting in compromised tissue perfusion. But the integrity of the tissue in this zone can be saved with proper wound care
- Zone of hyperemia: the outermost zone. characterised by the eased supply and inflammatory vasodilation. The tissue here will recover unless there is severe sepsis or prolong hypoperfusion.


Zone of stasis
Zone of coagulation
Zone of hyperaemia

Classifications of SKIN Burns

- **Burns can be classified according to their severity, depth and size of the burn.**

- **Classification by Depth**

- **Superficial-thickness or first-degree burns** - Superficial thickness burns are burns that affect the epidermis only and are characterised by redness, pain, dryness, and with no blisters. Mild sunburn is an example of a superficial thickness burn.

- **Partial-thickness or second-degree burns** - These burns involve the epidermis and a portion of the dermis. Partial-thickness burns are often broken down into two types, superficial partial-thickness burns and deep partial-thickness burns.

- **Superficial partial-thickness burns** - Partial-thickness burns involve the epidermis and part for the dermis layer of the skin. Superficial partial-thickness burns extend through the epidermis down into the papillary, or superficial, a layer of the dermis. The injured site become erythematous because the dermal tissue has become inflamed. When pressure is applied to the reddened area, The area will blanch, but demonstrate rapid capillary refill upon release of the pressure.

- **Deep partial-thickness burns-** These burns extend deeper into the dermis and cause damage to the hair follicle and glandular tissue. They are painful to pressure, form blisters, are wet, waxy, or dry, and may appear ivory or pearly white.

- **Full-thickness or third-degree burns -** These burns extend through the full dermis and often affect the underlying subcutaneous tissue. Skin appearance can vary from waxy white to leathery grey to charred and black. The skin is dry and inelastic and does not blanch to pressure, it is not typically painful due to the damage to the nerve endings. The dead skin are removed to aid healing and scarring is usually severe. Full-thickness burns cannot heal without surgery.

- **Subdermal or fourth-degree burns -** These involve injury to the deeper tissues, such as muscle or bone. They are often blackened and it frequently leads to loss of the burned part.

Reliable and valid assessment of burn wound depth or healing potential is essential to treatment decision-making, to provide a prognosis, and to compare studies evaluating different treatment modalities.

Burn depth

- There are a number of techniques used to assess burn depth but clinical evaluation of the burn is the method most frequently used.
  It is usually possible to assess the depth of a burn by inspection.

  - **Clinical assessment** depth of a burn wound; however, is accurate in only 60 to 75 percent of the cases, even when carried out by an experienced burn surgeon

Key indicators of depth include

- The appearance of the burn
- The patency of the blood vessels within it
- The level of pain/sensation the patient may experience at the burn site.

Burn depth can be difficult to assess:

- as burns are often a combination of different depths.
- because there are both spatial and temporal changes in perfusion in actual burn patients as most of them have burns of various depths
- It should be reassessed at 48-hours after burn

Assessment of indeterminate burn depth

A variety of methods that aim to improve burn depth assessment are in development or in early clinical use. optical methods can predict burn depth with over 90 percent accuracy.

- **Laser Doppler analysis assays** the velocity of blood cells in the superficial dermis. This is reported as an index and correlated with blood perfusion.
- **indocyanine green** a dye that be injected intravenously and can be imaged byf ultraviolet light showing both an arterial and venous phase. Cameras are available in most large hospitals, and these systems are commonly used to monitor skin perfusion in skin flaps.
- **Thermography** also provides an index of perfusion based on the temperature of the tissue, two-dimensional images of perfusion in large areas.
- **Dermoscopy techniques** correlate nicely with burn depth.
- **Hyperspectral imaging** uses multiple light frequencies to image deoxy and oxyhemoglobin in tissues accurately correlate with burn depth.

Additional tools; include a single-sided planar magnetic resonance (MR) imaging probe, a unilateral MR imaging sensor equipped with a 2D gradient coil system, novel uses of lasers (eg, optimal coherence tomography), spatial frequency domain imaging alone and in combination with laser speckle imaging and video microscopy.

Biopsy and histology of burn wound

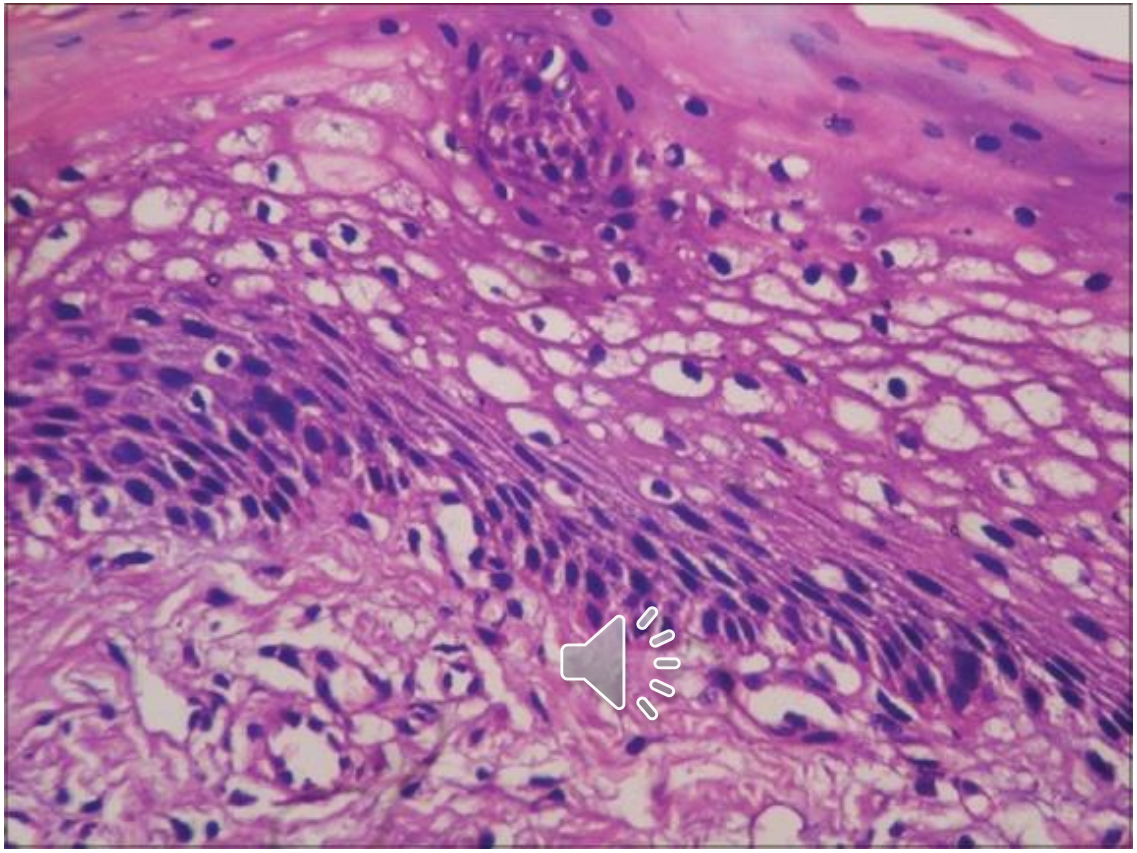
Punch biopsy of burnt tissue and then histological analysis is often regarded as the 'gold standard' of burn depth assessment, providing reference for other diagnostic modalities stated ,to find changes at a cellular and vascular level that would indicate a change in the nature of the tissues, performed by a pathologist on thin ,4μm, tissue section stained with Haematoxylin and Eosin (H&E), Periodic Acid Schiff (PAS) and Masson's trichrome , so as to provide the basis for accurate debridement in the future.

Characteristics should be analyzed by microscopy:

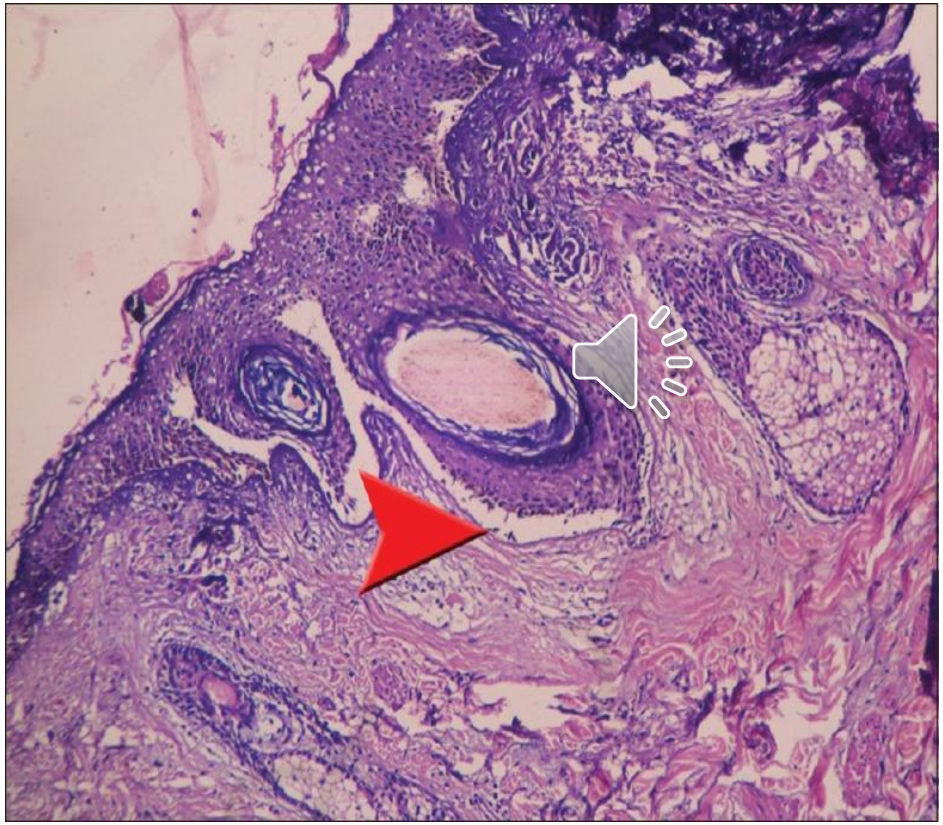
1- the level of viable versus thrombosed blood vessels (micro vascular injury, microthrombi, neutrophil
and inflammatory cell infiltration, blood vessel
occlusion

2- the presence of collagen changes or level of collagen damage, Collagen appears thin, flattened, or absent, with inconsistent sized gaps between fibers.
By Masson's trichrome (Denatured collagen stains red, contrasts with normal blue stain).

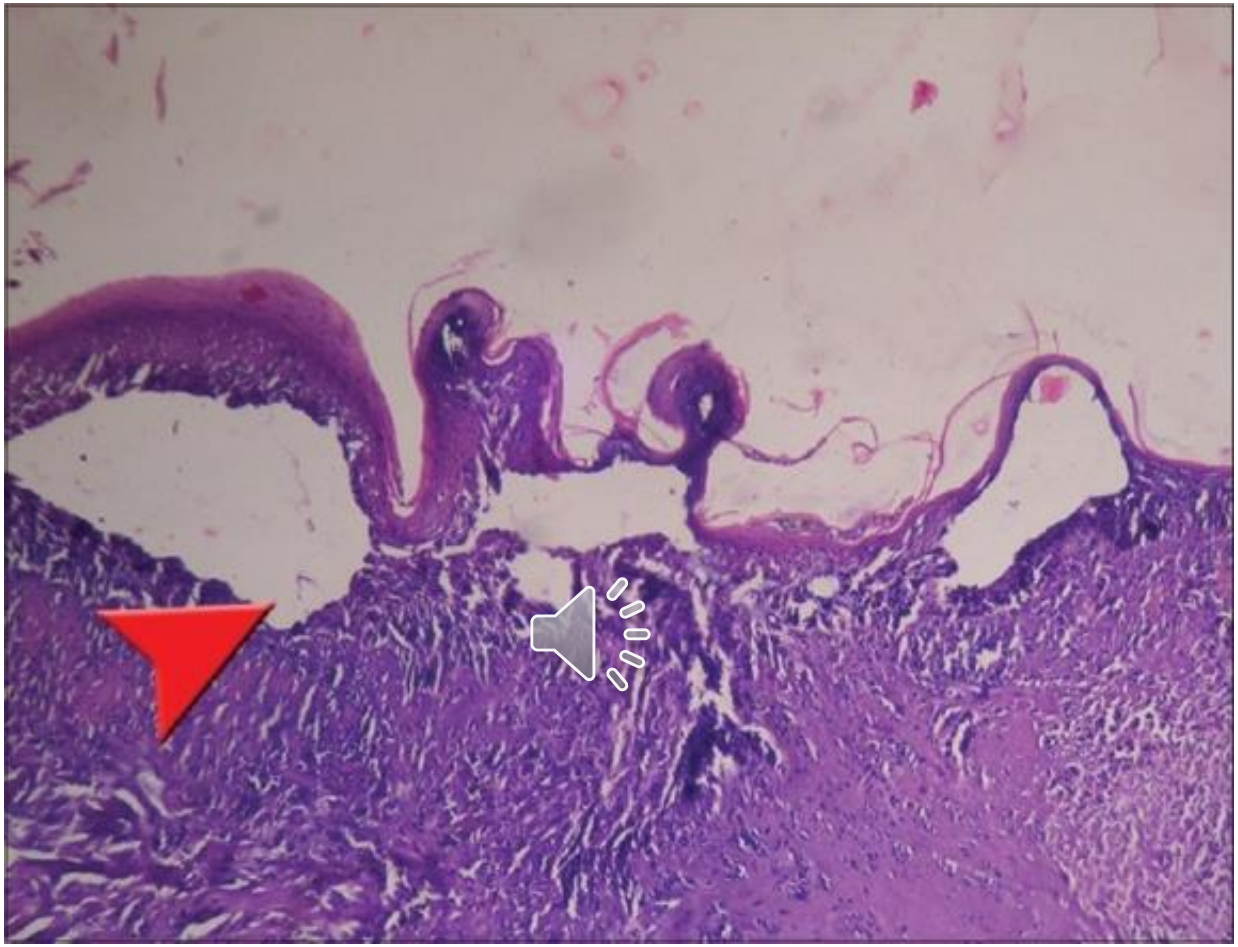
3-the extent of tissue damage (i.e. percentage of dermis thickness destroyed and skin adnexa).



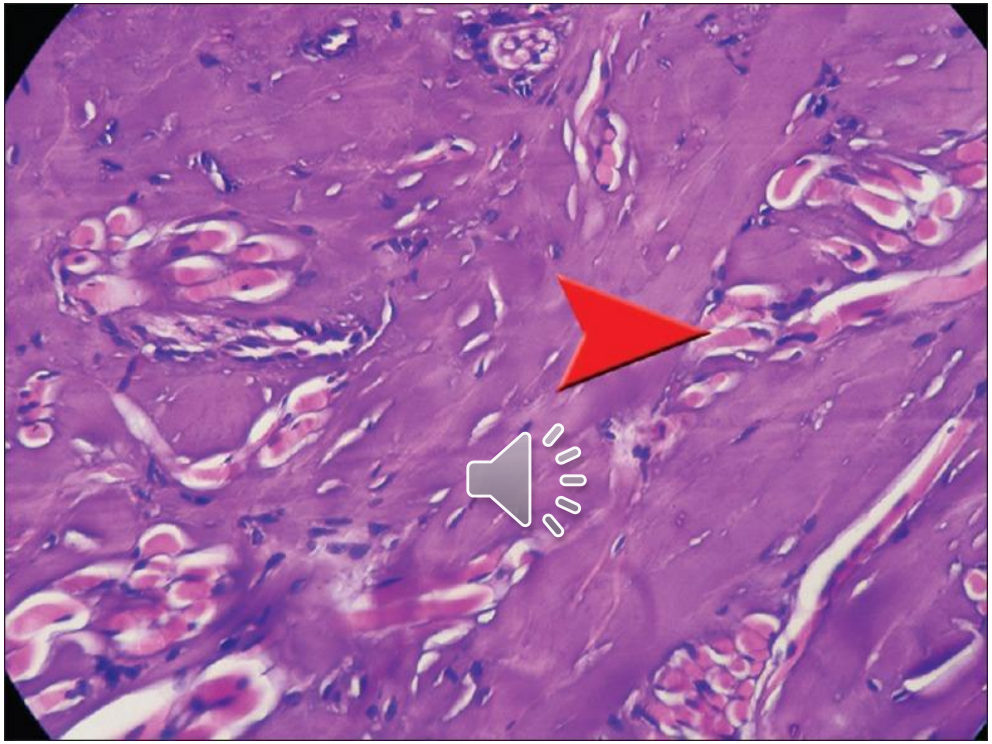
Normal H and E staining pattern with slight PALOR



Cleft formation at junction of epithelium and connective tissue (arrowhead)



Epithelial separation from connective tissue (arrowhead)



Homogenization of connective tissue and smudging of collagen fibres (arrowhead)

Burn healing

- similar to cutaneous wound healing after other types of injuries: first inflammation, then proliferation and remodeling
- One key characteristic of cutaneous burn injuries, is that the skin is a labile tissue with stem cells in the basal layer of the epidermis. This allows the skin to regenerate in response to damage or cell death as long as the basal layer remains intact. However, deep injuries that destroy the regenerative stem cell layer must heal through scar formation.
- These healing processes are mediated by the expression of various growth factors that, upon binding to their receptors, initiate intracellular signaling cascades. transforming growth factor alpha (TGF-α), transforming growth factor beta (TGF-β), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and vascular endothelial growth factor (VEGF).
- These molecules trigger complex cellular responses via changes in gene expression
- Vascular endothelial growth factor and FGF are mediators of angiogenesis. Transforming growth factor alpha is an important mediator of epithelial development, including keratinocyte and fibroblast proliferation and function. Transforming growth factor beta is an FGF and, importantly, inhibits the inflammatory response.

Burn healing

- For superficial and superficial partial-thickness burns, healing occurs most often by primary intention, in which the edges of the wound come together. stem cells from the basal layer of the epidermis divide and produce keratinocytes that migrate to the surface of the wound. This is typically initiated within hours of the injury, and the surface is usually covered within days to weeks depending on injury severity. Next, the basement membrane forms between the epidermis and the dermis, and deep connective tissues are reformed. these burns injuries do not typically form significant scars.
- Deep partial-thickness and full thickness burns typically heal by secondary intention and scar formation, which can take months to years. Wound healing by secondary intention occurs when the edges of the wound do not approximate. Fibroblasts direct granulation tissue formation, which consists of the fibroblasts themselves, myofibroblasts, and capillaries at the site of injury. Initial production of type III collagen by fibroblasts serves as a placeholder and is slowly broken down by collagenases and replaced with stronger type I collagen as the healing process progresses. Myofibroblasts mediate the contraction and closure of the wound via a dynamic process involving actin microfilaments and attachment to components of the extracellular matrix. Although the area of scar tissue will never regain full strength, after about 3 months, the strength of the skin in the area of damage can approach 80%

Excessive Wound Remodeling

- Errors in the remodeling phase of wound healing can result in functional and cosmetic defects.
- Hypertrophic scarring and keloid formation can occur in response to overproduction of connective tissue by fibroblasts during wound healing.
- a wound that takes longer than 2–3 weeks to heal is characterized by an increased risk of hypertrophic scar formation. The incidence of HTS occurrence following burn injuries has been reported to range from 32 to 94%.

- The main differences between hypertrophic scarring and keloids include the extent of the excessive scar formation and the orientation of collagen fibers in the scar. If the scar extends beyond the boundaries of the initial wound it is referred to as a keloid. Keloids also tend to have an increased ratio of type I to type III collagen relative to hypertrophic scars (leading to excessively thick and abnormal collagen bands on histology)

- **Heterotrophic Ossification** also referred to as ectopic ossification and myositis ossificans, is the formation of pathological bone in muscle or soft tissue, which if severe can lead to ankylosis and impaired function

  - Excessive scar contracture, is caused by overactivity of myofibroblasts. This can lead to excessive wound contracture in which the closure of the wound leads to cosmetic and functional limitations. This is particularly true if the injury is near or involves soft tissue around a joint, whereby excessive scar contracture can limit mobility via joint contracture

  - PSEUDOEPITHELIOMATOUS HYPERPLASIA

Development of malignant tumours in chronic burn wounds or scars is extremely rare, but a frequently reported complication. Most of these tumours are squamous cell carcinoma and, more occasionally, basal cell carcinoma and malignant melanoma are reported. The interval between the initial burn and the diagnosis of the tumour is usually long; 20–30 years or moreThe tendency to malignant degeneration of burn scars, described in previous reports of case series, did not result in an excess of squamous cell carcinoma of the skin or of any other type of skin cancer during up to 25 years' follow up of a large unselected cohort of patients hospitalized for burn injuries.

Marjolin's ulcer (MU) is an umbrella term covering squamous cell carcinoma (SCC), basal cell carcinoma and malignant melanoma that develop in chronic wounds, sinuses or scars.

THANKS FOR YOURS ATTENTION