# Describe the Pathophysiology of Burns

Burns & Plastic Surgery

## Introduction

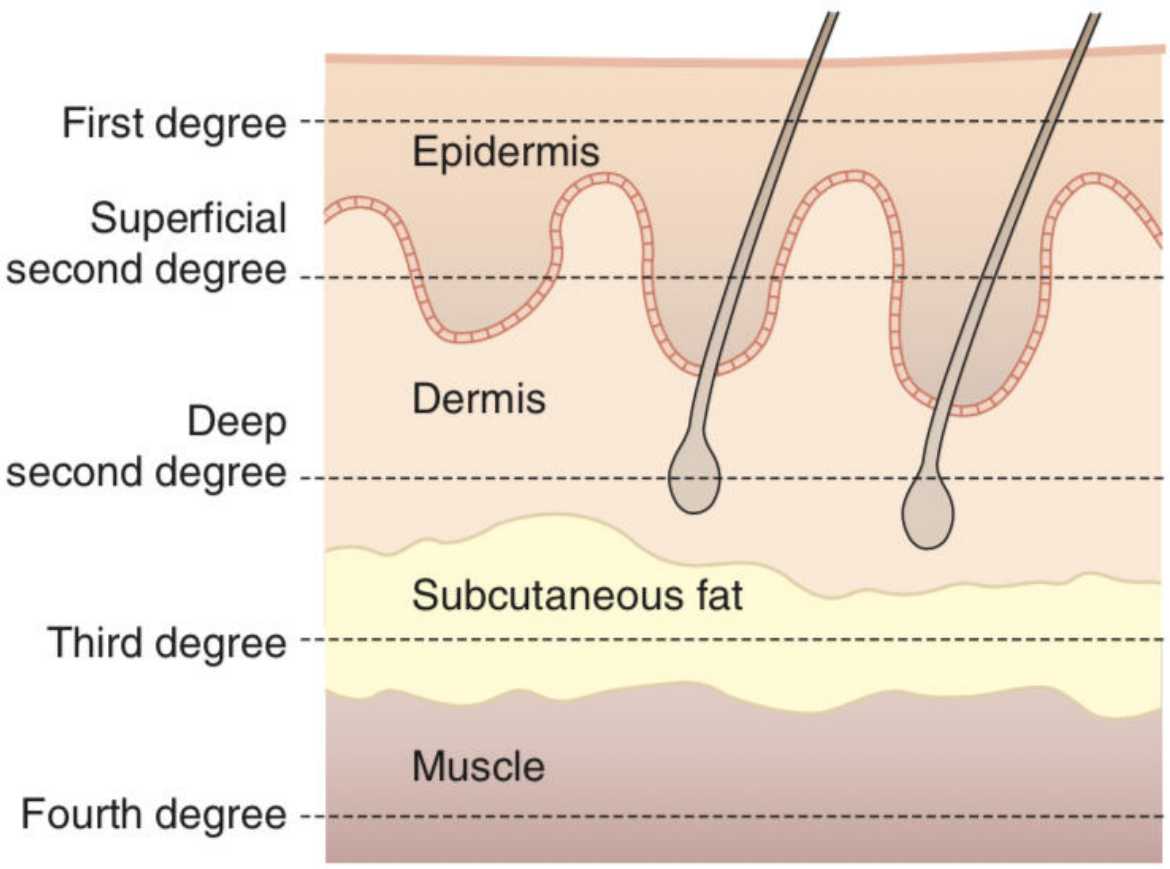
- 66% of burn injuries occur at home
- Fatalities at extremes of age
- Flame and Scald most common cause
- Scald burn victims commonly< 5years
- Survival rate for all burns 94.6%

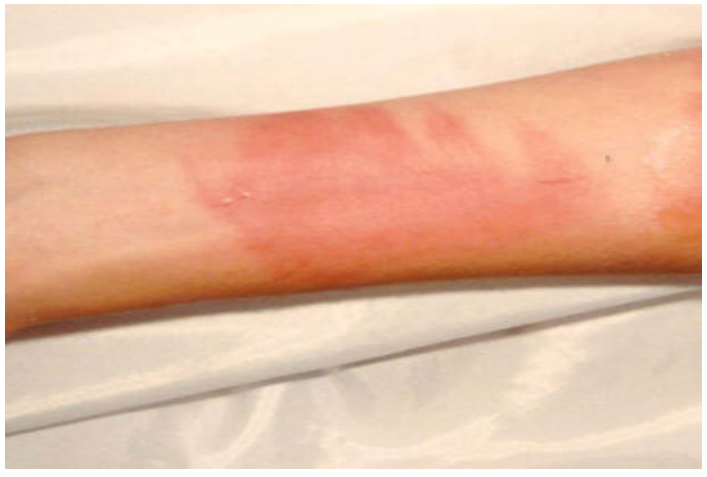
# Burn Classification

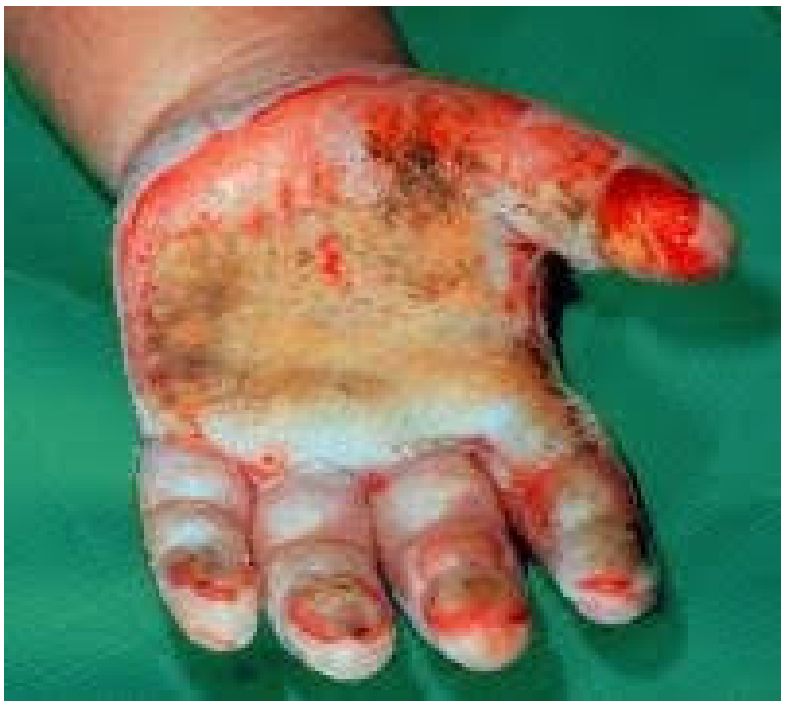
Causes

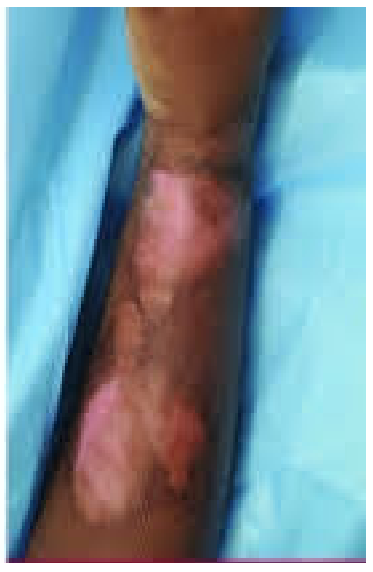
- Flame
- Scald
- Contact
- Chemical
- Electricity

# Classification ..





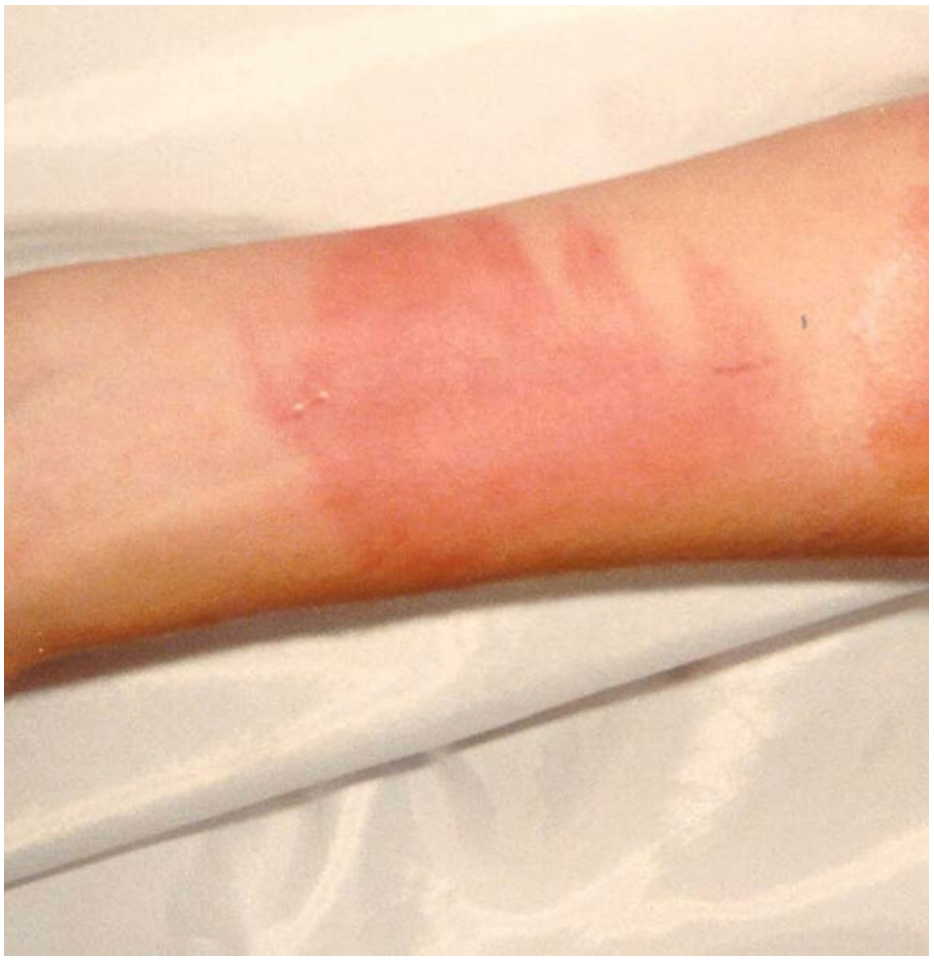




# Depth of Burn

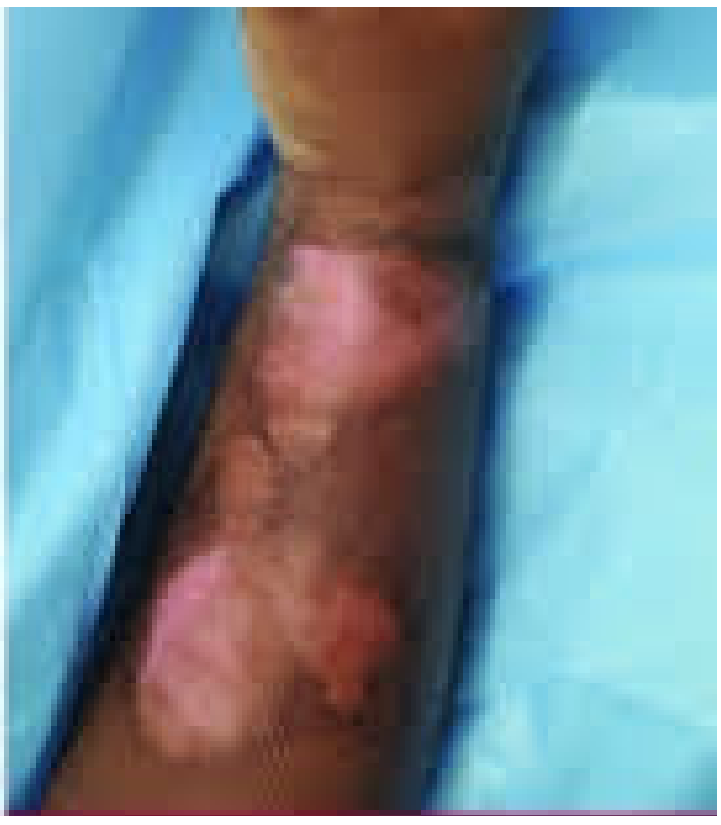
1st Degree

- Burns involving only the epidermis.
- Erythematous and very painful but do not form blisters.
- Sunburns fit this category of superficial, epidermal injury.
- Within 3–4 days, the dead epidermis sloughs and is replaced by regenerating keratinocytes.



2nd degree (Superficial dermal burns)

- Extend into the papillary dermis and characteristically form blisters.
- Appearance is pink, wet and hypersensitive to touch.
- Painful as uncovering the wound allows currents of air to pass over it.
- These wounds blanch with pressure as the blood flow to the dermis is increased due to vasodilation.
- Superficial dermal burns usually heal within 2–3 weeks without risk of scarring and therefore do not require operation.

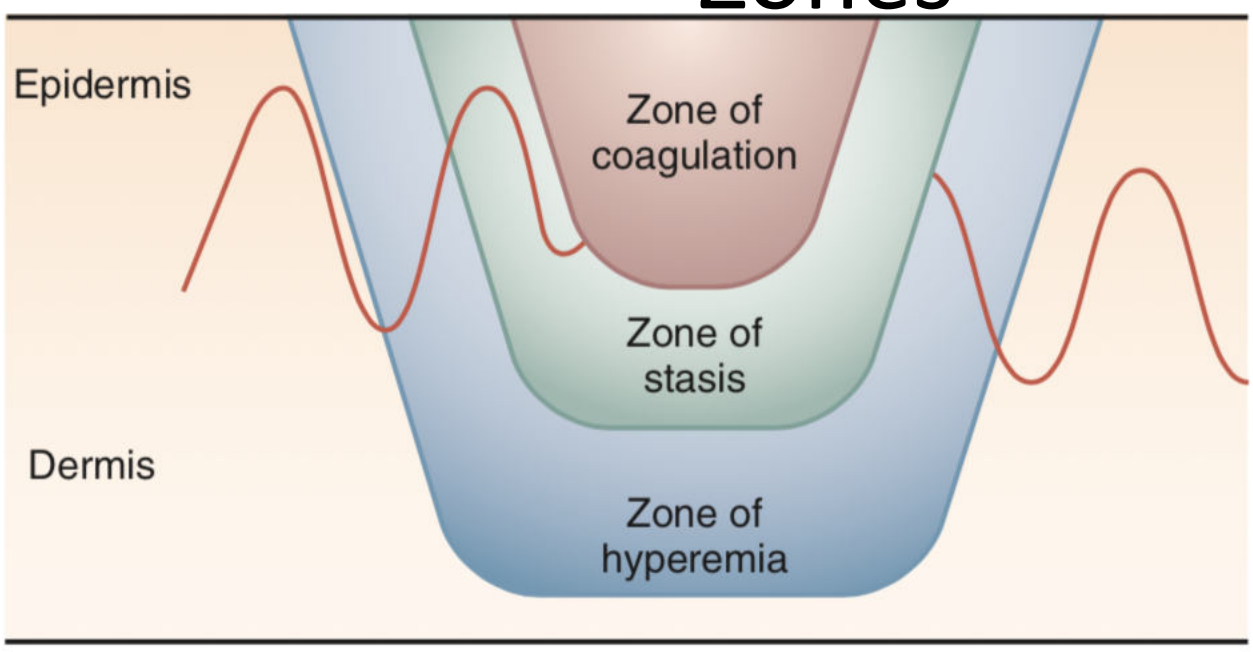
3rd degree (Deep Dermal Burns)

- Extend into the reticular dermis and generally will take 3 or more weeks to heal.
- They also blister, but the wound surface appears mottled pink and white
- The patient complains of discomfort and pressure rather than pain.
- When pressure is applied to the burn, capillaries refill slowly
- **Partial-thickness burns that are predicted not to heal by 3 weeks should be excised and grafted.**

4th Degree (Full Thickness)

- Full-thickness burns involve the entire dermis and extend into subcutaneous tissue.
- Their appearance may be charred, leathery, firm, and depressed when compared to adjoining normal skin.
- These wounds are insensitive to light touch and pinprick.
- Non-charred full-thickness burns can be deceptive as they may have a mottled appearance
- Must be excised and grafted early

# Local Changes in Burn Injury- Jacksons Zones



Zone of Stasis

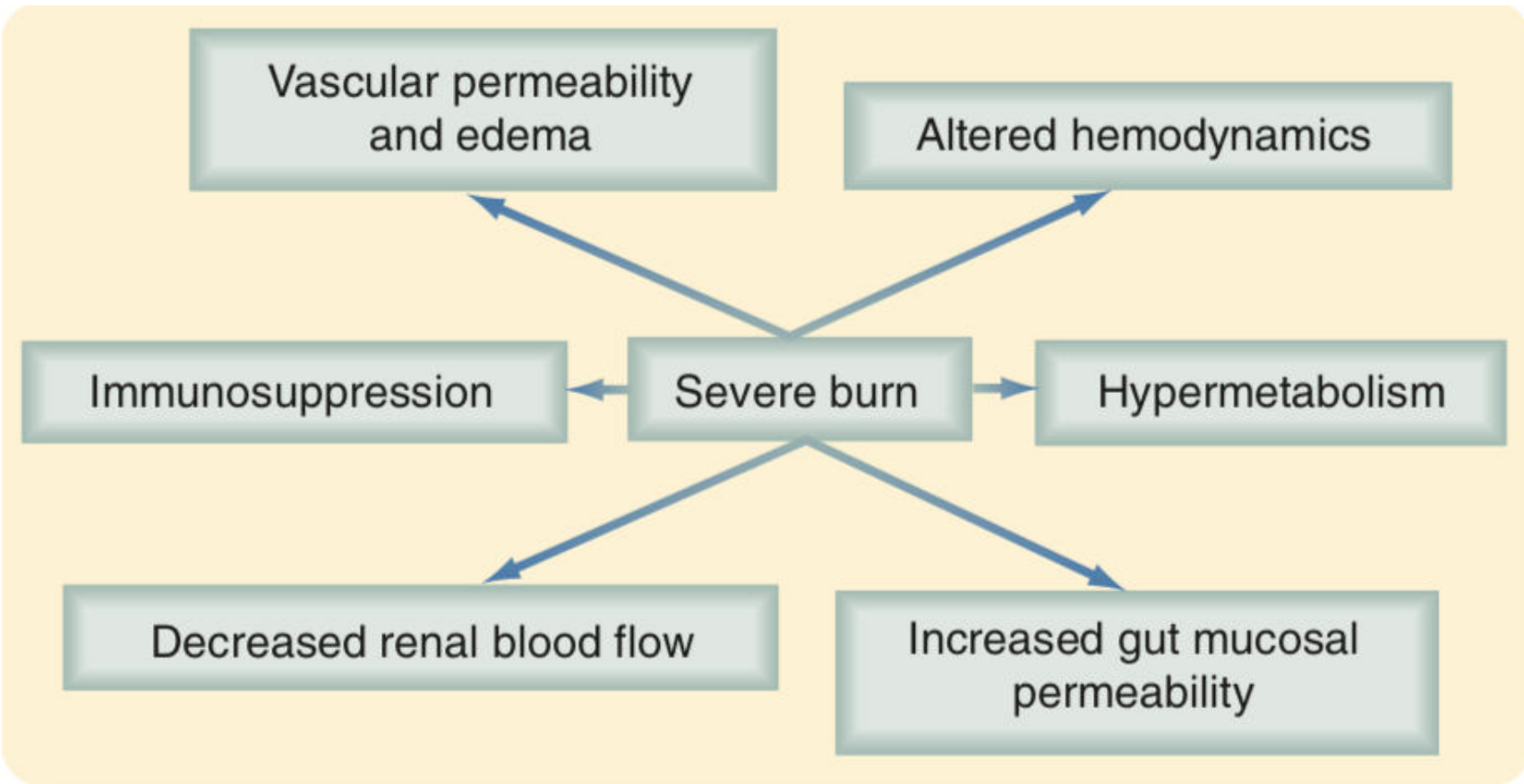
- Can survive or go on to coagulative necrosis. The zone of stasis is
- associated with vascular damage and vessel leakage.
- Thromboxane A2, and Bradykinin a potent vasoconstrictor, is present in high
- Local endothelial interactions with neutrophils mediate some of the local inflammatory responses associated with the zone of stasis.

- studies demonstrate that blockage of leukocyte adherence with anti-CD18 or anti-intercellular adhesion molecules & monoclonal antibodies improve tissue perfusion and tissue survival in animal models.

Zone of Hyperemia

- Contains viable tissue
- No risk of necrosis
- Characterized by vasodilation due to effect from zone of stasis

# Systemic Changes in Severe burns(>40%)



# Hypermetabolic Response

Phase 1 of Post Burn Metabolic phenomenon(Ebb Phase)

- Lasts 48 hours
- Decrease in Cardiac Output/$O_2$ Consumption
- Causes hyperglycemia

Phase 2 ( Flow phase)

- Begins after 48 hours
- Increase in metabolic rate and cardiac output
- Hyperglycemia in spite of raised insulin
- Reaches a plateau in about 5-7 days
- Persists upto 1-3 years

- 10-50 fold increase in corticosteroid and catacholamine levels
- Results in Protein breakdown in muscles
- Amino Acids ( Alanine ) from protein breakdown recruited for gluconeogenesis
- Fat breakdown in liver leads to glycerol formation which is used for gluconeogenesis
- End product of anaerobic respiration in the burn wound (lactate) sent for gluconeogenesis

- Glucose is delivered to peripheral tissue but glucose oxidation does not occur
- This in turn raises insulin levels
- Overall effect is loss of lean body mass

10% loss- decreased immune function

20% loss- chronic infections

30% loss- pneumonia & pressure ulcers

40% loss- Can lead to death

- Severe burns cause upto 25% loss

- Increased cotisol also causes transport of calcium and magnesium from long bones
- Decreased bone mineral density and content leading to susceptibility to fractures

# Immune Dysfunction

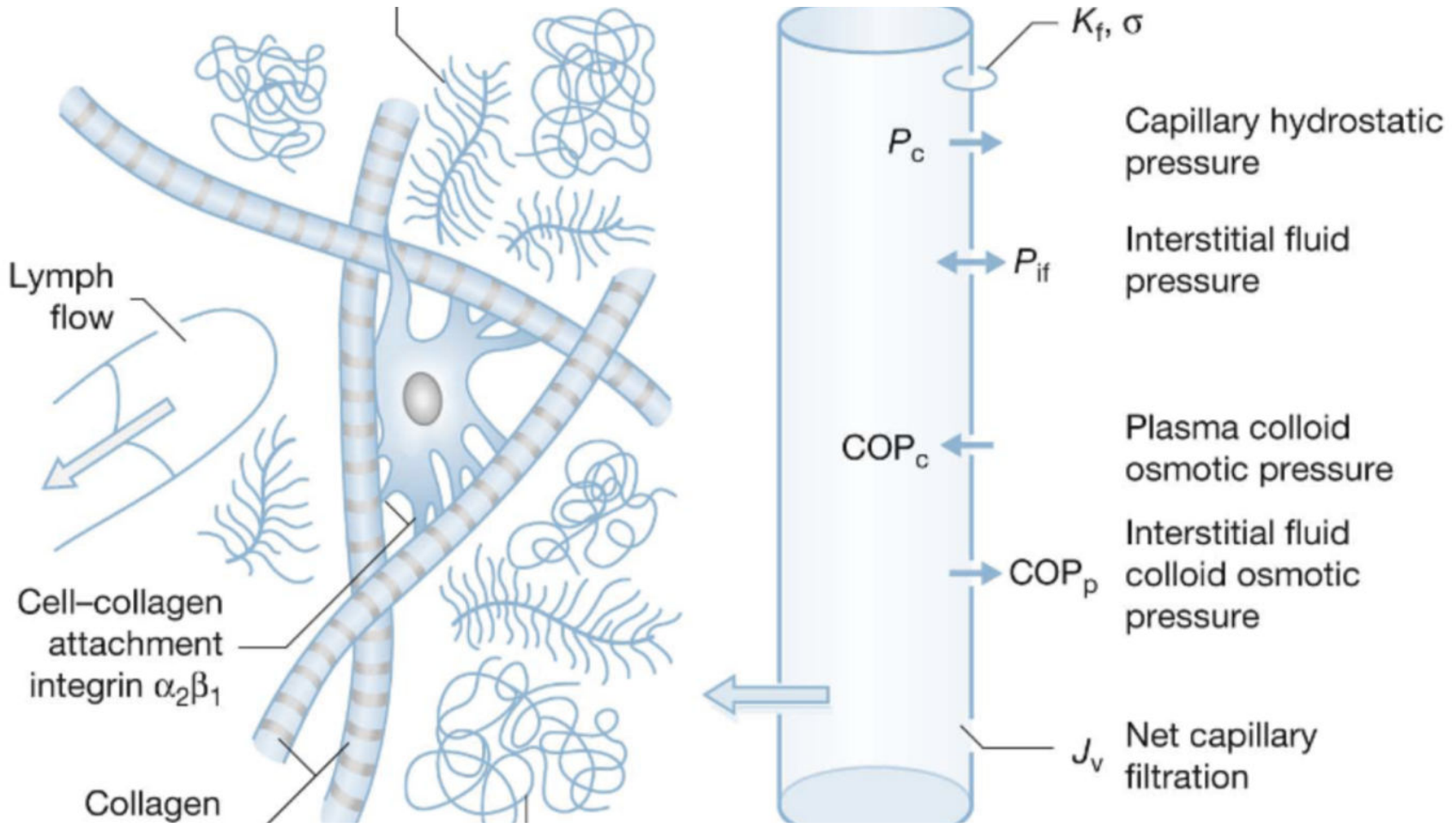
- Depressed function of Macrophages, Neutrophils, T cells and B cells
- Even though G-CSF levels actually increase after severe burn but bone marrow G-CSF receptor expression is decreased, which may in part account for the immunodeficiency seen in burns
- Release of negative regulators of myeloid growth decrease Macrophage production

- Neutrophil counts increase after severe burn but they are dysfunctional
- Altered diapedesis, chemotaxis and phagocytosis due to loss of CD11b/CD18
- Decreased Respiratory burst due to deficiency of p47-phox activity
- Poor motility sue to impaired actin mechanics
- Counts begin to fall after 72 hours

- Depressed T helper function
- Polarization from $Th^1$ to $Th^2$ immune response
- IL2 and IFN-γ responsible for initiation of phagocytosis and intracellular killing is decreased
- Increase in IL4 and IL 10 which is mostly antibody based immunity
- Cytotoxic T lymphocyte activity also decreased

- Administration of IL 10 antibodies and growth factors decreases the effect of the polarization of immune response

# Inflamation and Odema-Landis Starling Equation




$$J_v = K_f \left[ (P_c - P_{if}) - \sigma (\pi_p - \pi_{if}) \right]$$

| Variable | Normal or baseline | Post-burn | Δ |
|---|---|---|---|
| $P_c$ | ~25 mmHg | ~50 mmHg | ↑ ~25 mmHg |
| $\Pi_P$ | 20–28 mmHg | 15 to 18 mmHg | ↓ ~10 mmHg |
| $P_i$ | −2 to 0 mmHg | ~100 mmHg non-resuscitated non-perfused skin and −5 mmHg perfused skin | ↓ ~100 mmHg ↓ 3–5 mmHg |
| $\Pi_{if}$ | 10–15 mmHg | 13–18 mmHg in burn wound ↓ and with resuscitation hypoproteinemia in non-burned skin | ↑ ~3 mmHg |
| σ | ~0.9 | ~0.5 | ↓ ~0.4 |
| $K_f$ | ~0.003 mL/min/mmHg/100 g (leg) | ↑ 2–5× | |

# Mediators involved in edema formation

- Mast cells in the burned skin release histamine in large quantities immediately after injury, which elicits a characteristic response in venules by increasing intercellular junction space formation causing increased permeability
- Serotonin released from aggregated platlets causes pulmonary vasoconstriction

- Mediators causing Increased permeability

Prostaglandin E2 and I2

Free Oxygen Radicles

Thromboxane A2 & B2

- Leukotrines B4 and D4 cause pulmonary hypertension
- Angiotensin & Vasopressin responsible for systemic vasoconstriction and gut ischemia

- In the first 12 hours there is an abrupt increase in the fluid levels in the burn tissue
- After 24 hour there is a more gradual increase in fluid content both in burned and non burned soft tissue
- This gradual 3$^{rd}$ space loss is eventually responsible for burn shock

- Prompt and adequate fluid resuscitation improves outcome of the burn patient
- It is imperative to avoid Over –resuscitation as well
- This trend of providing fluid in excess of the Parkland formula has been termed ‘fluid creep’

- Complications of fluid creep are

Eye injuries due to elevated orbital pressures

Pulmonary edema

Prolonged mechanical ventilation

Graft failure

Need for fasciotomy of uninjured extremities

Abdominal Compartment Syndrome

- Intra-abdominal pressure (IAP) >30 cmH2O is defined as intra-abdominal hypertension (IAH).
- ACS is sustained IAH + clinically tense abdomen combined + ventilation aberrations due to elevated pulmonary inspiratory pressures

OR

oliguria despite aggressive fluid resuscitation

# Myocardial Dysfunction

- Myocardial contractility is depressed along with relaxation capacity leading to a stiff myocardium
- Possible causes for this are

Raised Intracellular calcium levels

Circulating Myocardial depressant factor( not isolated)

Raised TNF alpha levels

- Even though contractility is depressed , the cardiac Output may be increased upto 130-150% for a period of 2 years
- Adrenergic stimulation causes increased heart rate as well as raised Systemic and Pulmonary vascular resistance
- Mortality occurs because of cardiac stress in a setting of myocardial dysfunction

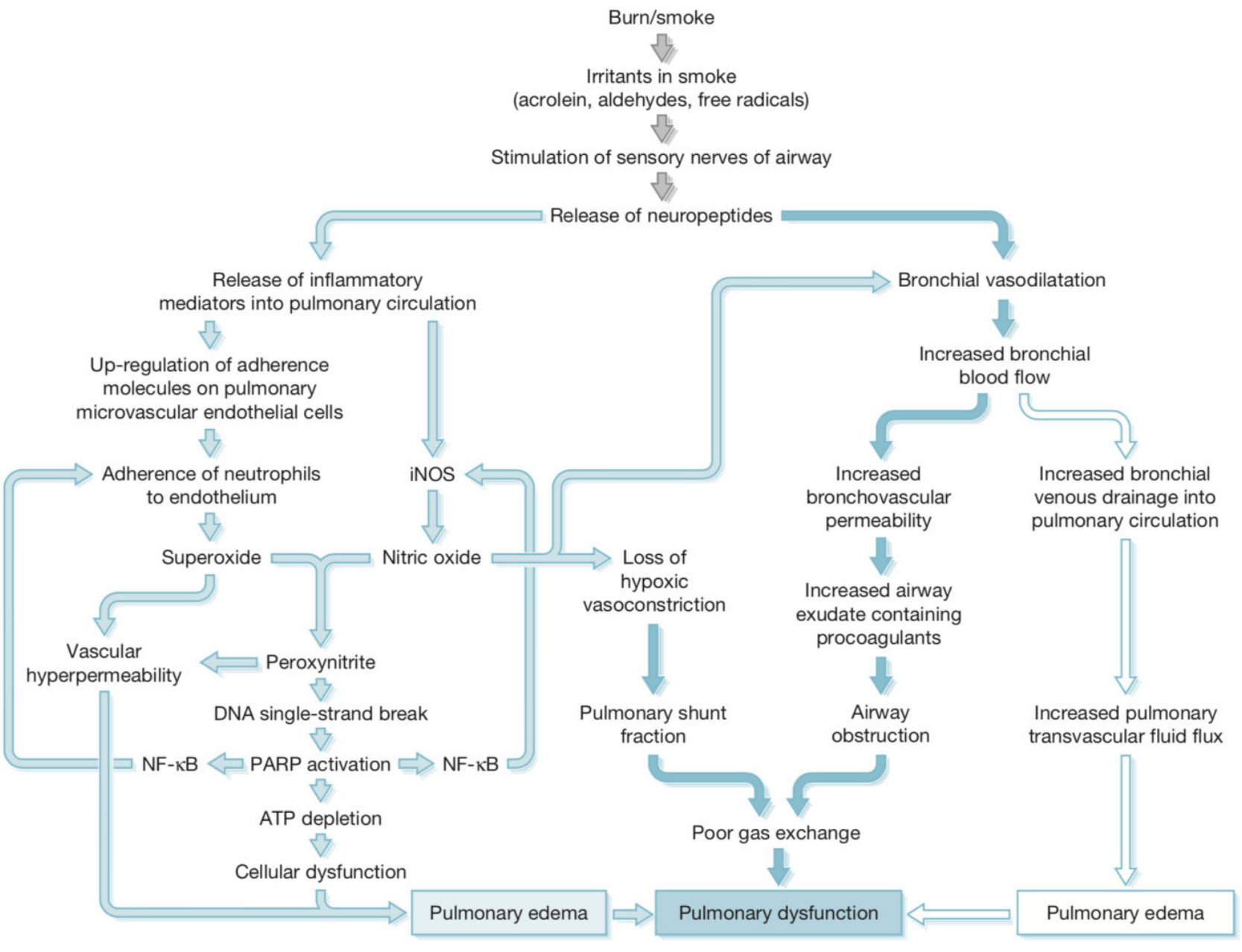
# GI System

- Apoptosis of epithelium of Small intestine mucosa
- Vesiculation of microvilli with breakdown of actin filaments in the microvilli of small intestine
- Loss of brush border lipase activity – loss of fatty acids
- Poor uptake of Glucose and amino acids from the lumen

- Increased gut permeability leading to fluid loss
- Vasoconstriction leading to ischemia which causes bacterial and endotoxin translocation across the mucosa causing septicemia
- Inverse relation between blood flow and gut permeability

# Lungs

- In large burns there is a pronounced increase in pulmonary vascular resistance (PVR)
- Both pre and post capilary vasoconstriction occurs which causes pulmonary odema
- Hypo-protenemia still remains the dominant cause of pulmonary odema
- In case of inhalational injury factors released due to injury to bronchial tree and lung parenchyma occurs




# Renal Dysfunction

- Local and Systemic cytokine release causes decreased renal blood flow which causes Acute Kidney Injury
- Free Oxygen Radicles can cause direct tubular damage
- Other factor maybe myoglobinurea following rhabdomyolysis ( Myoglobin> 1500-3000ng/ml)
- AKI may occur despite adequate fluid resuscitation by Parkland Formula

- Imperative to identify and diagnose Acute Kidney Injury so that patient can be shifteds for renal replacement therapy( Dialysis)
- RIFLE and AKIN criteria developed to aid diagnosis and plan therapy
- AKIN is modification of RIFLE with only change that it should be applied within 48 hours of burn injury

| (A) The Acute Dialysis Quality Initiative (ADQI) criteria for the definition and classification of AKI (i.e. RIFLE criteria) | | |
|---|---|---|
| Risk | Increase in serum creatinine ≥1.5X baseline or decrease in GFR ≥25% | <0.5 mL/kg/h for ≥6 h |
| Injury | Increase in serum creatinine ≥2.0X baseline or decrease in GFR ≥50% | <0.5 mL/kg/h for >12 h |
| Failure | Increase in serum creatinine ≥3.0X baseline or decrease in GFR ≥75% or an absolute serum creatinine ≥354 μmol/L with an acute rise of at least 44 μmol/L | <0.3 mL/kg/h ≥24 h or anuria ≥12 h |

| (B) The proposed Acute Kidney Injury Network (AKIN) criteria for the definition and classification of AKI | | |
|---|---|---|
| Stage 1 | Increase in serum creatinine ≥26.2 μmol/L or increase to ≥150–199% (1.5- to 1.9-fold) from baseline | <0.5 mL/kg/h for ≥6 h |
| Stage 2 | Increase in serum creatinine to 200–299% (>2–2.9 fold) from baseline | <0.5 mL/kg/h for ≥12 h |
| Stage 3 | Increase in serum creatinine to ≥300% (≥3-fold) from baseline or serum creatinine ≥354 μmol/L with an acute rise of at least 44 μmol/L or initiation of RRT | <0.3 mL/kg/h ≥24 h or anuria ≥12 h |

- Even though creatinine is not the ideal biochemical marker of kidney dysfunction it still remains the gold standard
- New markers of AKI, such as cystatin-C, have shown promise as earlier detectors of changes in GFR
- In order to differentiate pre renal from renal failure it is important to analyze the following indices

| Urinary index | Prerenal | Renal |
|---|---|---|
| $U_{osm}$ (mOsmol/L) | >500 | <350 |
| $U_{Na}$ (mEq/L) | <20 | >40 |
| Specific gravity | 1.020 | 1.010 |
| $U_{creat}/P_{creat}$ | >40 | <20 |
| Fractional excretion of sodium | <1 | >2 |
| Fractional excretion of urea | <35 | >50 |

$$\text{FeNa} = [(\text{urine sodium} \times \text{plasma creatinine})/(\text{plasma sodium} \times \text{urinary creatinine})]$$

- Fractional excretion of urea is a more reliable indicator as it negates the effect of diuretic use

# Change in Membrane Potentials

- Membrane potential in non burned distant tissues such as skeletal muscles , nerves, Gi tissues partially depolarize ( from -90 to -70)
- Cell death can occur at resting potentials of -60
- This change causes action potential dampening which may be responsible for tissue dysfunction
- This change is brought about increased sodium conductance
- The factor which leads to this has not yet been identified but it has a complex and probably dynamic structure