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Wound Healing & Management

Objectives

- Define the wounds.
- Discuss the phases of wound healing .
- List the types of wound healing .
- Recognize the factors affecting wound healing:
  - Local
  - Systemic
- Identify the abnormal wound healing which include:
  - Keloid
  - Hypertrophic scar

Colour Index

- Main Text
- Males slides
- Females slides
- Doctor notes
- Textbook
- Important
- Golden notes
- Extra

Editing File

Collagen:

- Left handed helix involving 3 polypeptides.
- Most abundant family of proteins in the human body (30%).
- > 19 types of collagen have been identified.

Types of Collagen:

Type I:
is the major structural component of **bones, skin, tendons &** muscles.

Type II:
is found predominantly in **cartilage**.

Type III:
is found in association with type I collagen in varying ratios depending on the type and maturity of tissue (predominant type in **granulation tissue**). [1]

Type IV:
collagen is found in the **basement membrane** of arteries, nerves, & tendons.

Type V:
is found in the **cornea**.

- Wound Strength is 80% of original after remodelling (healing).
- Lysine and proline hydroxylation required for cross linkage (the main step in collagen synthesis)[2].
- Differs in relative composition of hydroxylysine and hydroxyproline and cross-linking
  - **Type I ≅ 90% of all collagen in body**
  - ★ Normal skin ratio - **Type I:Type III = 4:1**
  - Hypertrophic / immature scar 2:1 ratio

★ **Formation inhibited by:**
Colchicine, penicillamine, steroid, Vit.C deficiency and Fe deficiency.

★ They activate collagenase which degrades collagen synthesis and inhibits cross linkage hydroxylation of lysine and proline.

1. E.g. in traumatic wounded skin (associated with healing). Can also be found in newborns.
2. Biochemistry: collagen synthesis events: procollagen gets converted to collagen by proline and lysine hydroxylation (essential component to have complete collagen synthesis).

Wound:

Definition:

The skin is the largest organ in the body, and when there is a wound it will lead to the disruption of normal anatomical structure and function. Wound is classified[1] as acute vs. chronic.

Wound healing: is restoration of integrity and continuity of injured tissue to reestablish homeostasis of that tissue and to stabilize the entire organism's physiology.

Wound healing requires the coordinated completion of a variety of cellular activities, including **phagocytosis**, **chemotaxis**, **mitogenesis**, **synthesis of collagen** and **extracellular matrix** components[2].

Classification of Healing:

By type:

01

1. **Primary:** proximation of the edges and migrations of cells from edge to edge (horizontal).
2. **Delayed primary:** we wait for 2-4 days then we proximate by primary healing.
3. **Secondary:** Horizontal contraction by myofibroblast and epithelization.
4. **partial-thickness wound healing:** No contraction, only vertical epithelization.

By timing:

02

1. **Acute** (First week)
2. **Subacute** (Lasts for 1-6 weeks.)
3. **Chronic** (Lasts for > 6 weeks)

By abnormal healing:

03

1. **Overgrowth**[3]: (Hypertrophic vs. Keloid).
2. **Undergrowth:** (chronic unstable wound[4]).
3. **Abnormal pigmentation.**
4. **Contour abnormality.**

1. Wounds can be classified according to the mechanism of injury:
   Incised wounds: A sharp instrument causes these; if there is associated tearing of tissues, the wound is said to be lacerated •
   Abrasions: These result from friction damage and are characterized by superficial bruising and loss of a varying thickness of skin and underlying tissue.
   Degloving injuries: These result from shearing forces that cause parallel tissue planes to move against each other: for example, when a hand is caught between rollers or in moving machinery. And others, **Crush injuries**, **burns** and **gunshot wounds**
2. During a wound healing process there are different cellular activities that happen, the end result of the process is synthesis of collagen.
3. Due to increased collagen production.
4. E.g. pressure sore, and diabetic wounds.

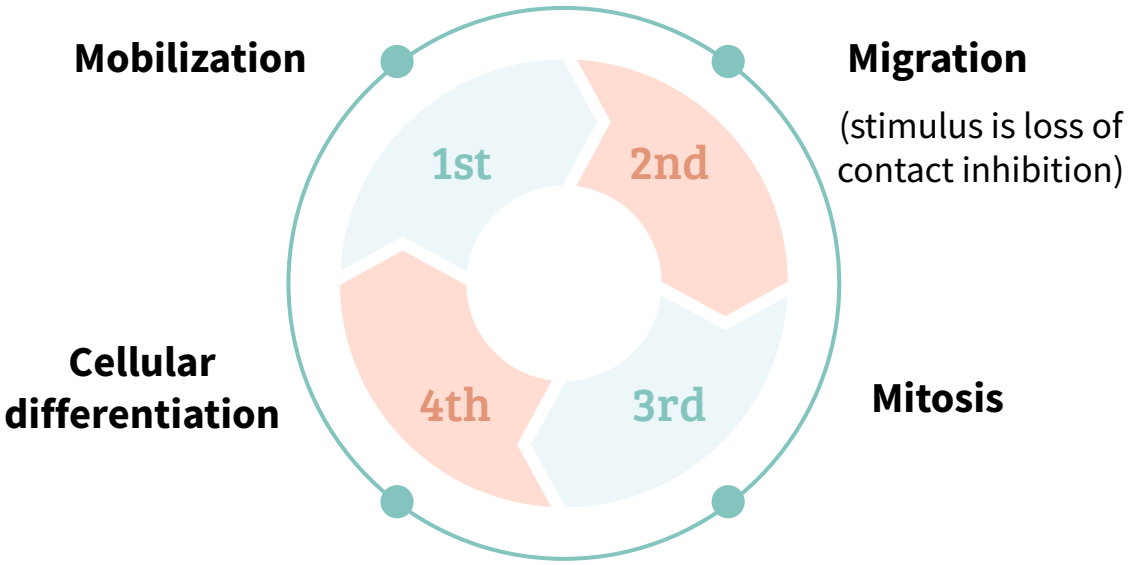
Wound:

Classification of Wound Closure:

Primary healing (1st intention)	Secondary healing (2° intention)	Tertiary healing (3° intention)
• Primary closure by suturing the edges together. • Within hours of repairing full-thickness surgical incision. • Results in mortality of minimal number of cellular constituents. • Considered the most efficient method and results when a clean incised surgical wound is meticulously apposed.	• Wound left open to heal[1] by processes of **granulation**, **contraction**[2], and **epithelialization**[3]. • Results in more intense inflammatory response. • Larger quantity of granulation tissue with pronounced contraction of wounds.	• Delayed primary closure • Desired for contaminated wounds (infected wounds)[4]. • Phagocytosis of contaminated tissues well underway by 4th day. • Foreign materials walled off by macrophages. • 3° intention healing describes the situation where a wound healing by 2nd intention (neglected traumatic wound/burn) is treated by excising its margins and then apposing them or covering the area with a skin graft. • The final cosmetic result may be better than if the wound had been left to heal by 2° intention.

Epithelial Repair:

- Epithelial continuity is reestablished across a wound: Multiple events happen during the healing process. The cells (from the two edges of the wound) mobilize & migrate to the middle and get in proximity then duplicate by mitosis and differentiate to different cells.



1. You keep the wound open (you do dressing and wound care but no suturing) and it heals by itself by contraction of myosin and actin, as well as epithelialization of dermis and epidermis, and it usually takes longer than primary healing.
2. **Contraction** results in edge to edge (**horizontal**) repair.
3. **Epithelialization** results in **vertical** repair.
4. Tertiary healing is a combination of primary healing and secondary healing. Clean the contaminated wound, wait for about 3 days and then re-approximate it by suturing.

Phases of Wound Healing:

01 Heamostasis[1] (5-10min)

★ **Main cells in this phase: platelets**

- **Initial** response to injury = **constriction** followed by dilation.
- Platelet plug forms after adherence to exposed subendothelial collagen via vWF
- Platelets degranulate releasing: ADP, thromboxane-A2, bradykinin, and 5-HT → further vasoconstriction and platelet aggregation.
- Platelets stimulated to release :

platelet derived growth factor (PDGF)

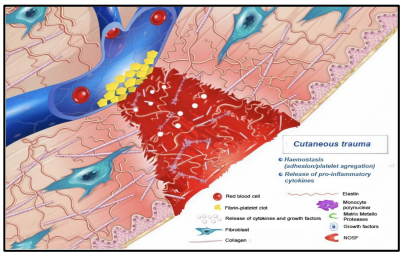
a. made by macrophages, endothelial cells, fibroblasts
b. chemotaxis, fibroblast stimulation

transforming growth factor β (TGFβ)[2] ★

a. made by macrophages, platelets, fibroblasts
b. fibrinogenesis, angiogenesis, chemotaxis, immune suppression

fibroblast growth factor

a. made by macrophages and endothelial cells
b. angiogenesis and chemotaxis



- Form the platelet plug
- Degranulation of platelets (release of cytokines and growth factors)
- Activation and recruitment of neutrophils

1. Considered as phase zero or part of the inflammatory phase. This phase is delayed by bleeding disorders.
2. ★ It has a **major role** in wound healing. The main source for the production of TGFβ is the Alpha granules of platelets. Excess production of TGF-β isoforms causes abnormal scars (Hypertrophic and Keloid scars).

Phases of Wound Healing cont.:

02 Inflammatory/Migratory "lag" phase[1] (1-4 Days)

Typically starts immediately after hemostasis.

Main cells in the inflammatory phase: in the first 24 hours → **PMNs (neutrophils)**

After 24 hours → Macrophages.

Classically represented by:

01 **Rubor (redness) caused by:**

- vasodilation
- primarily result of prostacyclin (PGI_2) and histamine, also caused by prostaglandin A, D, E (PGA, PGD, PGE)

02 **Tumour (swelling):**

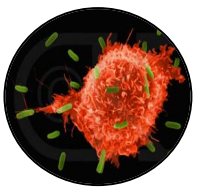
- caused by leakage of plasma proteins through gaps in vascular endothelium
- edema potentiated by PGE_2, prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$)

03 **Calour (heat)**

Increased local temperature secondary to both:

- Increased blood flow
- Elevated metabolic rates

04 **Dolour (pain)**



Macrophages :

- Phagocytosis
- Wound debridement
- activation of fibroblast
- Angiogenesis
- Matrix synthesis (granulation tissue formation) regulation

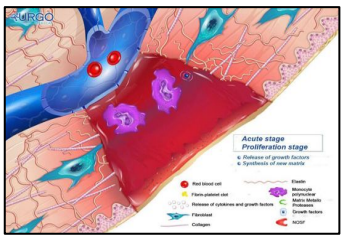
1. Characterized by an inflammatory response to injury, through an increased capillary permeability, proliferation of capillaries at wound edges and accumulation of protein-rich exudate preceding collagen synthesis

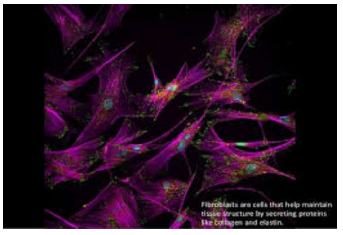
Phases of Wound Healing cont.:

03

Proliferative/Fibroplasia "incremental" [1] (3 days - 3 weeks)

- Begins 2-3 days after wounding.
- ★ **Signalled by arrival of fibroblasts** (**Main cells in the proliferative phase**, they play a role in collagen synthesis).
  - Driven by macrophage-derived **bFGF**, **TGFβ**, **PDGF** to proliferate and synthesize glycosaminoglycans (**GAGs**) and **proteoglycans** (building blocks of new extracellular matrix of granulation tissue and collagen).
  - Also produce **bFGF**, **TGFβ**, **PDGF**, **keratinocyte growth factor**, **insulin-like growth factors-1**.
  - Dominant cell type peaking at 7-14 days.
- Collagen synthesis[2] (net production for next 3-6 weeks).
- ↑ Keratinocyte mitosis, ↑Endothelial cells and ↑Angiogenesis (from vessels at wound margins).
- Lasts 2-4 weeks depending on site and size of wound with slowing of fibroblast migration and proliferation.
- Different cells differentiate into different types and new blood vessels are formed (angiogenesis).





Collagen and elastin synthesis

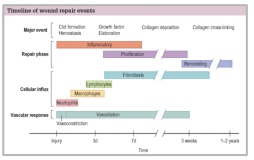
1. In this phase there is progressive collagen synthesis by fibroblasts and a corresponding increase in tensile strength with Increased collagen turnover. This phase is delayed by: Microvascular diseases (Diabetes), Macrovascular (Atherosclerosis).
2. Arterial oxygen tension (PaO2) is a key determinant of the rate of collagen synthesis.

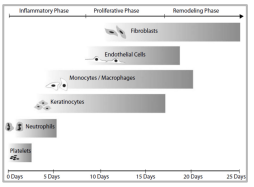
04

Remodeling /Maturation (3 weeks - one year)

- Begins approx. 3 weeks after injury
- Collagen synthesis and degradation are accelerated but in equilibrium with collagen breakdown (no net increase in collagen content)[1]
- Collagen deposition peaks by 3rd week
- Large capillaries growing into wound regress/disappear
- Indurated, raised, pruritic scar becomes mature scar
- Collagen fibers become organized
- **Type III collagen replaced by type I collagen**
- **re-establishing normal 4:1 ration (I:III)**:

  Duration depends on age, genetics, type of wound, location (1-2 years)[2].
- Tensile strength increases to 80% of pre-injured skin[3]





Factors Affecting Wound Healing:

General (patient):

1. Nutrition[4]
2. Drugs/Toxins[5]
3. Age[6]
4. DM
5. Smoking[7]
6. Vascular disease
7. Obesity
8. Systemic diseases
9. Idiopathic
10. Inherited diseases
11. Surgical technique[8]

Local (wound):

1. Oxygen
2. Infection
3. Acidity
4. Radiation
5. Loss of growth factors
6. Denervation (in diabetics)
7. Iatrogenic
8. Edema
9. Cancer[9]
10. Foreign body

1. The major event in the remodeling phase.
2. Type three collagen is the main collagen present in the wound healing process. In abnormal wound healing (such as in hypertrophic scars and keloids) we have a higher ratio that could reach up to 1:30 so you'll have high collagen type 3 compared to the normal ratio, and you'll have abnormal scarring.
3. Especially in healing tendons, muscles, and blood vessels. For example for tendons it reaches up to 60-80%, but for normal wounds it usually reaches 100%.
4. Patients with pressure sore are usually malnourished therefore the healing process is usually delayed in such patients, Malnutrition has to be severe before healing is affected. Protein availability is most important, and wound dehiscence and infection are common when the serum albumin is low. Healing problems should be anticipated if recent weight loss exceeds 20%. Vitamin C is essential for proline hydroxylation and collagen synthesis.
5. E.g. penicillin, steroids and chemotherapy.
6. Elderly patients are more prone to have chronic wounds, they heal poorly because of impaired blood supply, poor nutritional status or intercurrent disease.however, they still form 'good' scars.
7. Vasoconstriction →reduced oxygen delivery.
8. Dead spaces must be avoided, as the accumulation of blood and exudate encourage infection. Correct suturing of the deeper layers avoids dead space and often allows the skin edges to fall together without tension. 5/0 or 6/0 sutures are appropriate for the face, stronger ones (3/0 or 4/0) are needed for incisions near joints and still stronger ones for the abdominal wall
9. Chemo and radiotherapy lead to fibrosis of the skin as well as stenosis of the arteries.

Classification of contamination in Surgical wounds

(WHO classification of wound)[1]:

1 Clean:

- nontraumatic, non infected wounds & no breach of Resp, GI, or GU tract.
- No spillage of the content of the tract itself.
- ★ E.g. thyroid and breast surgeries.
- No need for antibiotics.
- Infection rate should be less than 1%.
- Use of Ab prophylaxis isn't recommended.

2 Contaminated[2] "Dirty":

- Fresh traumatic wounds; major break in sterile technique, **nonpurulent inflammation**; in or near contaminated skin.
- Major spillage.
- ★ E.g. hemicolectomy or resection of the intestine with spillage, emergency surgery for perforated diverticular disease, or drainage of a subphrenic abscess.

3 Clean-contaminated:

- Small breach in protocol; Resp/GI/GU tract are entered with minimal contamination.
- Very minor spillage of the content.
- ★ E.g. cholecystectomy, uncomplicated appendicitis, intestinal resection ONLY if there was no spillage.
- Infection rates in excess of 5% may suggest a breakdown in wards.

4 Infected:

- **Purulent infection**.
- Traumatic & severe wounds.
- They have positive culture and require broad spectrum antibiotics.
- ★ E.g. traumatic open bone fracture, and purulent pyogenic perforated appendicitis.

★ Acute wound[3]:

- Cleansing
- Exploration and diagnosis[4]

- Debridement if needed
- Tetanus immunization status[5]

- Replacement of lost tissues where indicated
- Skin cover if required

- Dressing
- Skin closure without tension

1. To determine whether the administration of antibiotics is needed or not.
2. When wound contamination is anticipated, topical or systemic antibiotics can be used for prophylaxis .For example, systemic antibiotic is normally used to reduce the risk of infection during gastrointestinal surgery and when prosthetic material (hip joint, cardiac valves, arterial bypass) is inserted.
3. If it's a major trauma start with ATLS, if not start with vital signs. Don't jump to the wound directly, the patient should be stable, history needs to be taken, examination needs to be done, and then manage the wound.
4. To identify any risk factors that may interfere with wound healing.
5. In acute traumatic wounds, tetanus prophylaxis is routine.

Ideal Scar:

01
- Flat
- Narrow
- Pliable

02
good colour and contour match to surrounding skin

03
parallel to or within resting skin tension lines (RSTL)[1]

04
does not restrict function or distort normal anatomy[2]

05
- matures within 6-18 months
- Asymptomatic and painless

Abnormal Scars (IMPORTANT):

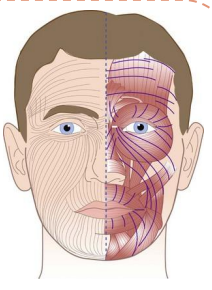
Keloid scar
excision can be done as an alternative.

Hypertrophic scars
These scars should not be excised.

Wide scar
Caused by traumatic wounds that are not closed properly.

Features	Hypertrophic scar	Keloid scar[3]
Genetic	Not familial	May be familial
Race	Not race related	Black > White
Sex	Female = Male	Female > Male
Age	Children	10-30 years
Borders	Remains within wound	Outgrows wound area
Natural history	Subsides with time	Rarely subsides
Site	Flexor surfaces	Sternum, shoulder, face
Aetiology	Related to tension	Unknown

1. For example when you operate on the forehead (frontalis muscle), RSTL are perpendicular to the muscle fibers, therefore you should do the scar horizontally rather than vertically to decrease the tension, create less visible scars & decrease the risk of hypertrophic scar.
2. Wounds that cross a joint (hands, fingers, etc) are at high risk for causing functional defects due to contracture (myofibroblasts).
3. Classical presentation: 20 year old African American female, with a scar in the earlobe.
   - Keloid scars have high recurrence rate.



Vancouver Scale:

Scar characteristic	Description
Pigmentation	
0	Normal color that closely resembles the color over the rest of one's body
1	Hypopigmentation
2	Hyperpigmentation
Vascularity	
0	Normal color that closely resembles the color over the rest of one's body
1	Pink
2	Red
3	Purple
Pliability	
0	Normal
1	Supple: flexible with minimal resistance
2	Yielding: giving way to pressure
3	Firm: inflexible, not easily moved, resistant to manual pressure
4	Banding: rope-like tissue that blanches with extension of the scar
5	Contracture: permanent shortening of scar producing deformity or distortion
Height	
0	Normal: flat
1	<2 mm
2	<5 mm
3	>5 mm

Treatment of hypertrophic scar and keloid[1]:

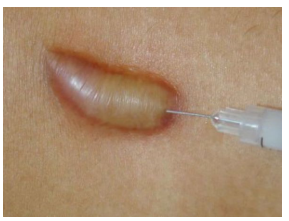
- Prevention

Non surgical:

- Pressure: compression garment.
- Silicone sheets or gels.

Medical [2]:

- 5-FU (Fluorouracil is a chemotherapy).
- Intralesional Steroids (first-line therapy).
- Radiation

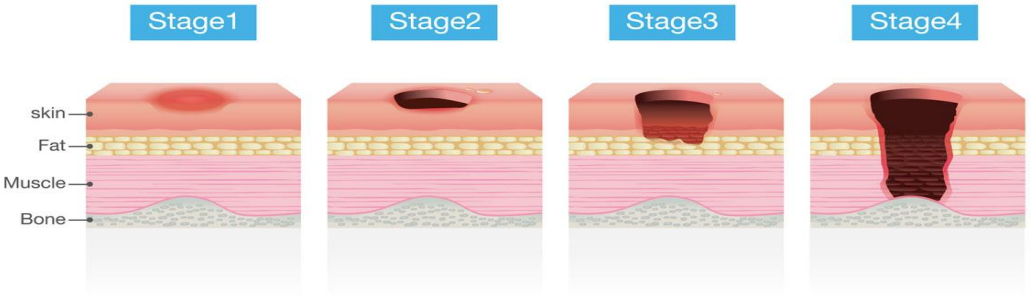


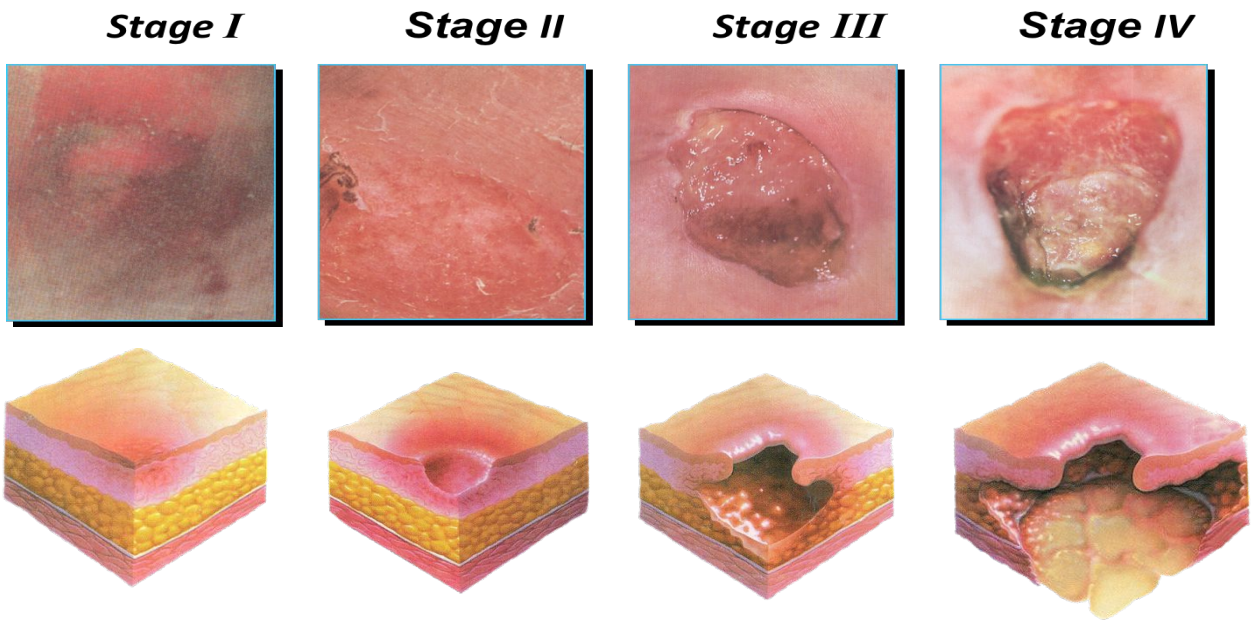
- Laser
- Surgery
- In keloids, if the measures described above fail, the best treatment approach is a combination of intralesional excision followed immediately by low-dose radiotherapy.

1. We should take measures to prevent it from occurring in the first place. You prevent HTS, by avoiding tension in creating a scar parallel to the RSTL, minimal undermining (raising the skin and going underneath it), minimal electrocauter (leads to seroma formation → high tension) closing layer, no strangulation (put spaces between each suture).
2. How does radiation and chemotherapy heal HTS if it leads to reduced wound healing? the unit of given radiation therapy is the guide. Patients that receive radiation therapy for cancer receive high amounts of radiation compared to HTS. The second thing is that HTS has abnormal collagen synthesis (high turnover of collagen) and radiation stops this by causing fibrosis and less formation of collagen.

- There's still a 10% chance of recurrence after treatment.

Pressure Sores A.K.A Bed Ulcers:





- develops if the patient doesn't move while sleeping for 2 hours (bed sore).
- mainly involves the epidermis.
- produces erythema, avoided by changing the position every 30 min.

- Involves the epidermis and the upper dermis.

- Involves the epidermis, dermis and upper fascia.

- Involves the fascia and can reach to the muscle, tendons and bones and they usually develop osteomyelitis.

- Stage 1 and 2 require non-medical intervention.

Summary

Recall

Q1: What inhibits wound healing?
Answer: Infection, ischemia, DM, malnutrition, anemia, steroids, cancer, radiation, and smoking.

Q2: How long a sutured wound epitheliazes?
Answer: 24 to 48 hours.

Q3: Define the following terms:

- Primary Wound Closure:

Answer: Suture wound closed immediately (a.k.a "first intention").

- Secondary Wound Closure:

Answer: Wound is left open and heals over time **without sutures** (a.k.a "secondary intention"); it heals by granulation, contraction, and epithelialization over weeks (leaves a large scar).

- Delayed Primary Closure

Answer: Suture wound closed 3-5 days **AFTER** incision (classically 5 days).

Q4: Define the following terms:

- Clean Wound:

Answer: Elective, nontraumatic wound without acute inflammation; usually closed primarily.
Infection rate: <1.5%

- Clean-contaminated Wound:

Answer: Operation on the GI or respiratory tract without unusual contamination or entry into the biliary or urinary tract.
Infection rate: <3%

- Contaminated Wound:

Answer: Acute inflammation, traumatic wound, GI tract spillage, or a major break in sterile technique.
Infection rate: ≈5%

- Dirty Wound:

Answer: Presence of pus, perforated viscus, or dirty traumatic wound.
Infection rate: ≈33%

Wound healing:

Classification		
By type	**By timing**	**By abnormal healing**
1. Primary 2. Delayed primary 3. Secondary 4. Partial-thickness wound healing	1. Acute 2. Chronic	1. Overgrowth -hypertrophic - keloid 2. Undergrowth (chronic unstable wound) Contour abnormality)

Summary

Classification of Wound closure:

Primary 1st intention
Suture

- Primary closure
- Within hours
- Mortality of minimal number of cellular constituent

Secondary 2nd intention
No suture

- wound left open to heal by processes (granulation, contraction, epithelization)

Tertiary 3rd intention
Suture after 3 days

- delayed primary closure
- Contaminated wounds

Phases of wound healing:

Haemostasis 5-20 mins
aim to stop bleeding

-Vascular constriction
-Platelet aggregation
-Degranulation
-Thrombus formation

-platelet stimulus to release: PDGF, TGF B, FGF

Inflammatory 1-4 d

-Neutrophil infiltration
-Monocyte infiltration and differentiation to macrophage
-Lymphocyte infiltration

- Clinically represented by :Rubor, Tumour, Calour, Dolour

Proliferative 3d-3wks

1- Re-Epithelization
2- Angiogenesis
3- Collagen Synthesis
4- ECM formation

Epithelial repair: mobilization, migration, mitosis, cellular differentiation

Remodeling 3wks-1y

1- Collagen Remodeling (collagen type lll replaced by type l until ratio of 1:4)

2- vascular maturation and regression

Scars:

01

Ideal scars:

- flat narrow
- Good color
- Parallel to RSTL
- Doesn't restrict function
- Asymptomatic
- Mature 6-18m

Abnormal scars:

02

- **Hypertrophic:** Common in children, remain with in wound, subside, flexor surface, related to TENSION.
- **Keloid:** Common in black, 10-30 yrs females, outgrow wound area; sternum, shoulder, face.
- **Wide:** Traumatic wounds that are not closed properly

Doctor's Quiz

MCQ

Q1: The following are the sequence of events and phases taking place in wound healing?
- A) Remodelling, epithelization & contracture
- B) Inflammatory, proliferative & remodeling
- C) Vasoconstriction, epithelization & contracture
- D) Proliferative, remodelling and wound synthesis

Q2: The major cell/s involved in the proliferative phase is/are:
- A) PMN
- B) Fibronectin
- C) Fibroblast
- D) Collagen

Q3: The difference between secondary & partial thickness healing is:
- A) Contracture only in secondary healing
- B) Contracture only in partial thickness healing
- C) Epithelization only in secondary
- D) Epithelization only in partial thickness healing

Q4: Perforated gastric ulcer or Perforated appendicitis is/are:
- A) Clean
- B) Clean-contaminated
- C) Contaminated
- D) infected

Q5: All of the following is/are characteristics of ideal scar except:
- A) Painful
- B) Flat
- C) No restriction of movement
- D) Adequate color

Q6: All of the following is characteristic of keloid:
- A) Crosses border
- B) Genetic predisposition
- C) Common in earlobes/ chest in African
- D) All of the above

Q7: Preventive measures of HTS is/are:
- A) Adequate suture bite closure
- B) Free tension closure
- C) Non-strangulated sutures
- D) Minimal undermining/ electrocautery
- E) All of the above

Answers

Q1	B	Q4	C	Q7	E
Q2	C	Q5	A		
Q3	A	Q6	D		

Quiz

MCQ

Q1: which one of the following will have most normal progression of wound healing after surgery?

A) A 35 obese female with hyper tention
B) A 73 years old male looking healthy
C) A 47 years old male with Diabetes
D) A 40 years old female with peptic ulcer

Q2:a 25 years old african female had an otoplasty a week ago(cosmetic ear surgery), what is the complication of wound healing that is most probably she would get ?

A) hypertrophic wound
B) Hypertrophic wound
C) Keloid wound
D) Prolonged healing process

Q3:A 35-year-old woman undergoes an elective laparoscopic cholecystectomy for symptomatic cholelithiasis. Which of the following wound classes best describes her procedure?

A) Class I, Clean
B) Class II, Clean/contaminated
C) Class III, Contaminated
D) Class IV, Dirty

Q4: A 60-year-old diabetic man undergoes incision and drainage of an infected boil on his back. The wound is left open and packed daily. Week by week, the wound grows smaller and eventually heals. Which of the following terms describes the method of wound closure by the patient?

A) Primary intention
B) Secondary intention
C) Tertiary intention
D) Delayed primary closure e. Delayed secondary closure

Q5: Which of the following statements about the process of wound healing are true?

A) The inflammatory phase begins 2–3 days after the injury.
B) The proliferative phase lasts from 3 days to 3 weeks following the injury.
C) The remodelling phase involves fibroblast activity and production of collagen and ground substance.

Q6: Which of the following statements are true?

A) Healing by primary intention results in minimum inflammation and the best scar.
B) Tertiary intention involves immediate closure of the wound.
C) A crushed and contaminated wound is best suited for healing by primary intention.
D) Primary repair of all structures should be attempted in an untidy wound

Answers

Q1	D	Q4	B
Q2	C	Q5	B
Q3	B	Q6	A

Extra Questions

Good Luck!

Team leaders:

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Feedback