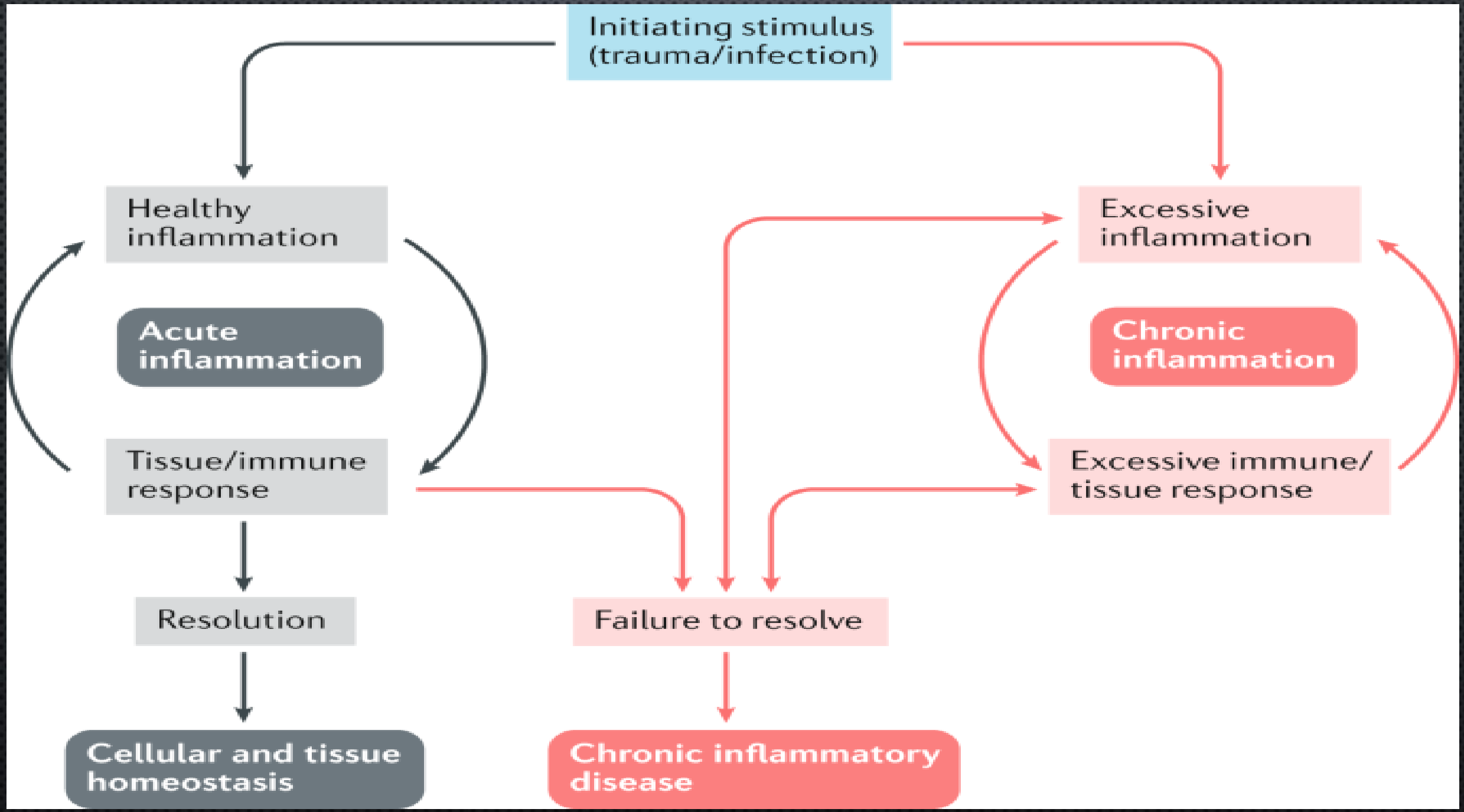
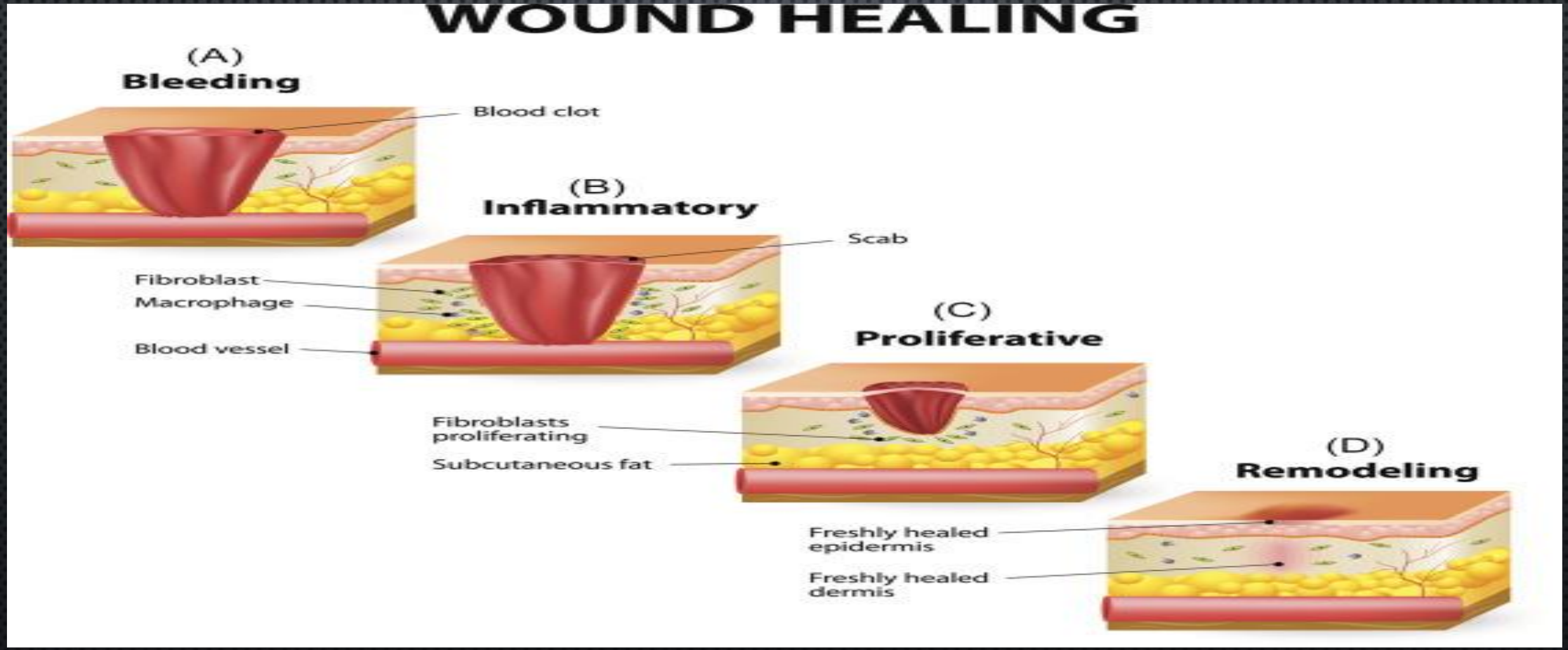

Healing and Repair


Initiating stimulus (trauma/infection)
Healthy inflammation
Acute inflammation
Tissue/immune response
Resolution
Cellular and tissue homeostasis
Excessive inflammation
Chronic inflammation
Excessive immune/ tissue response
Failure to resolve
Chronic inflammatory disease

the term repair →is used for parenchymal and connective tissues

the term healing →is for surface epithelia



Tissue Repair/Healing

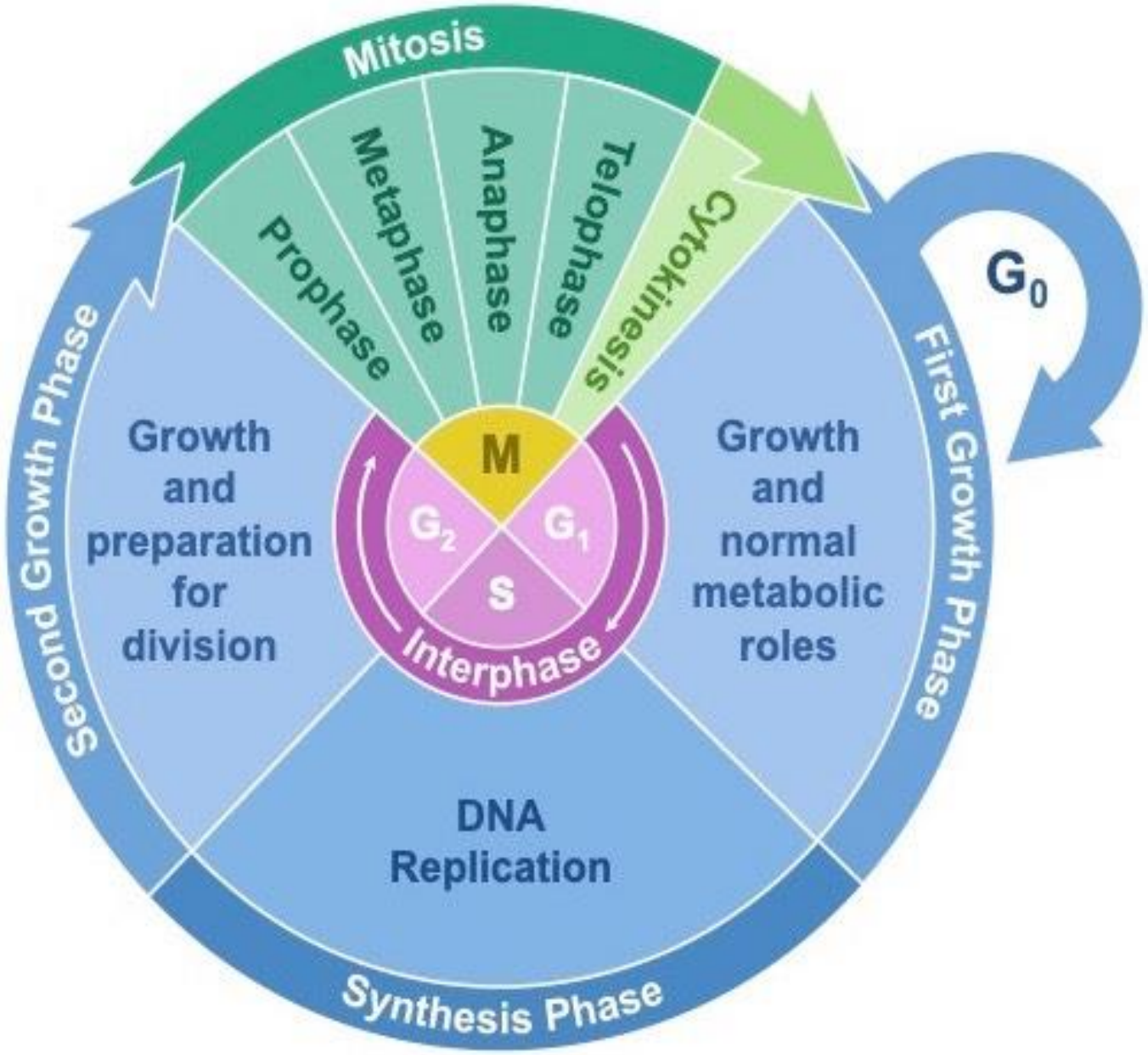
- Repair, sometimes called healing refers to the restoration of tissue architecture and function after an injury.

- Repair of damaged tissues occurs by two types of reactions:
    1. Regeneration.
    2. Connective tissue deposition (scar formation).

Tissue Repair/Healing

- **Regeneration: is complete restitution of lost tissue components identical to those removed or killed by proliferation of residual (uninjured) cells and maturation of tissue stem cells.**

- **Connective tissue deposition (scar formation): If the injured tissues are incapable of regeneration, or if the the tissue is severely damaged, repair occurs by the deposition of connective tissue.**



STAGES OF THE CELL CYCLE

INTERPHASE:

G_1 – Growth and metabolic roles
S – Replication of DNA occurs
G_2 – Growth and more preparation

MITOSIS:

P – Chromosomes are condensed
M – Chromosomes align at cell centre
A – The duplicated DNA segregates
T – Chromosomes are decondensed

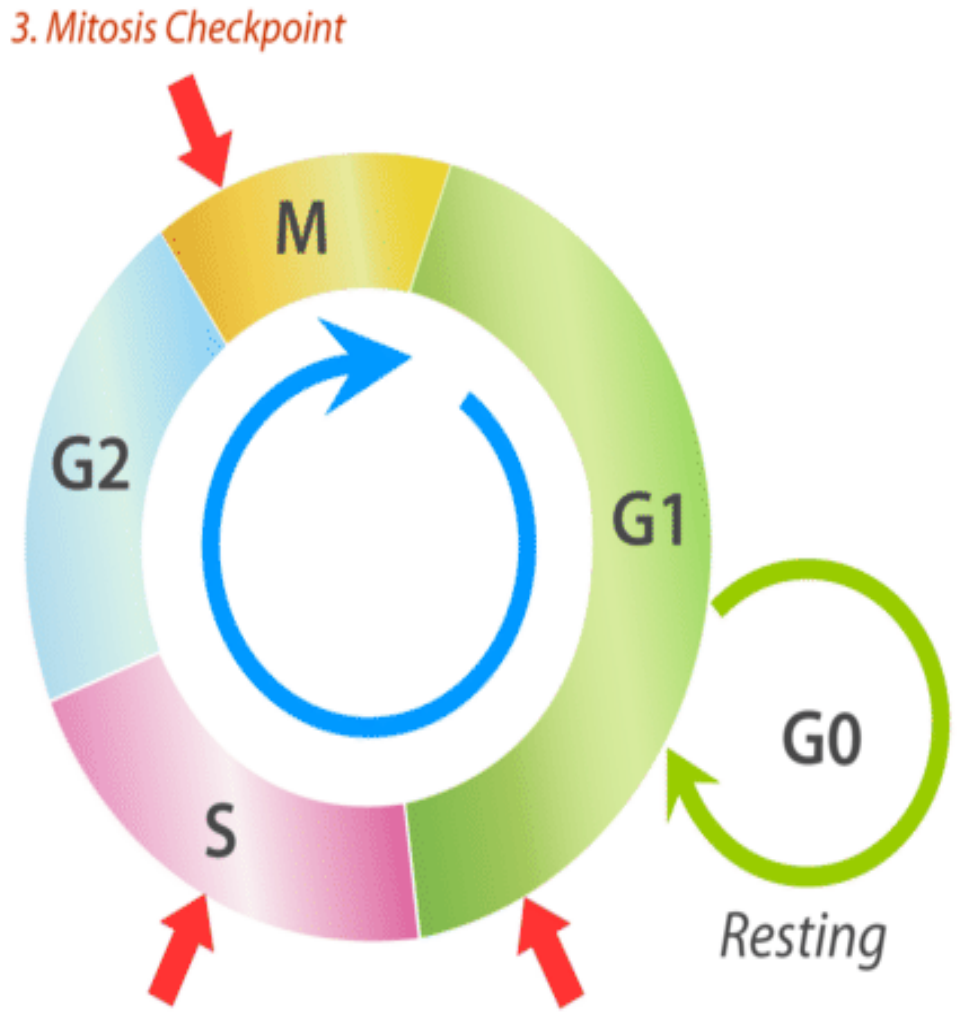
CYTOKINESIS

Cell splits into two daughter cells

RESTING PHASE (G_0)

Cells may leave interphase and enter
Into a non-dividing quiescent phase

The Cell Cycle and the Checkpoints



1. Cell Growth Checkpoint

- Occurs toward the end of growth phase 1 (G1).
- Checks whether the cell is big enough and has made the proper proteins for the synthesis phase.
- If not, the cell goes through a resting period (G0) until it is ready to divide.

2. DNA Synthesis Checkpoint

- Occurs during the synthesis phase (S).
- Checks whether DNA has been replicated correctly.
- If so, the cell continues on to mitosis (M).

3. Mitosis Checkpoint

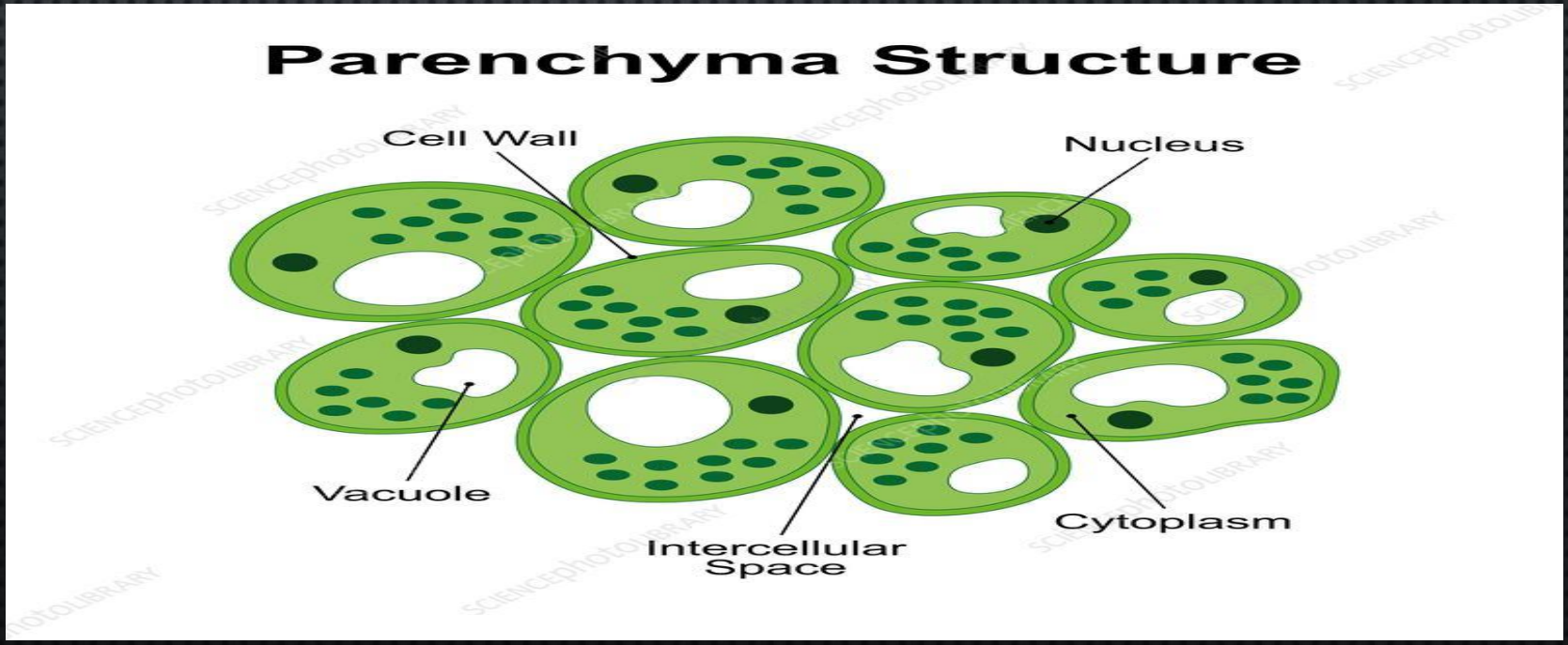
- Occurs during the mitosis phase (M).
- Checks whether mitosis is complete.
- If so, the cell divides, and the cycle repeats.

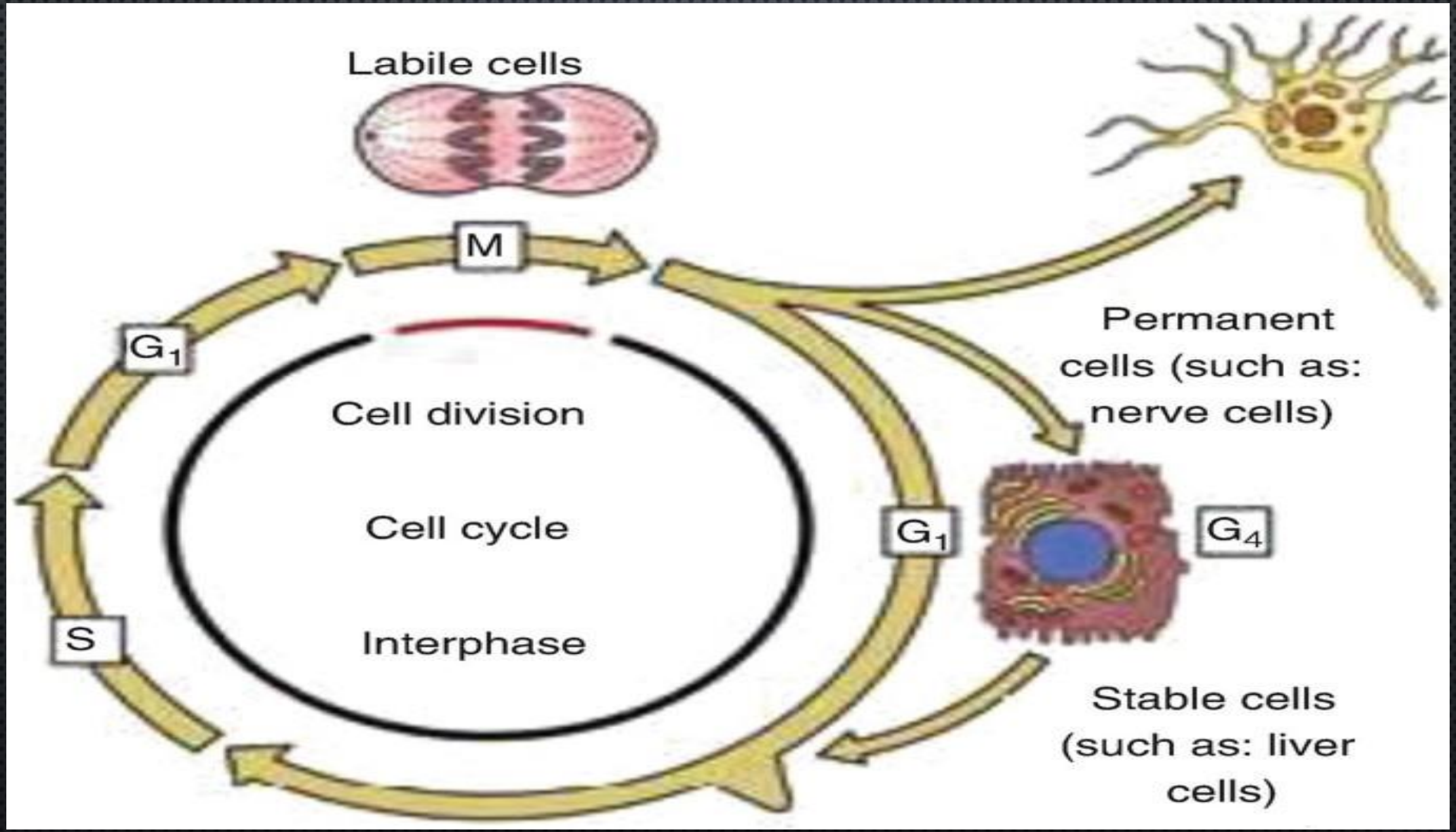
Factors That Influence Tissue Repair

1. Infection
2. Diabetes
3. Nutritional status
4. Glucocorticoids (steroids)
5. Mechanical factors such as increased local pressure.
6. Poor perfusion, due to peripheral vascular disease, arteriosclerosis, and diabetes or due to obstructed venous drainage (e.g., in varicose veins).
7. Foreign bodies such as fragments of steel, glass etc.
8. The type and extent of tissue injury

What is parenchyma in the body?

The functional tissue of an organ as distinguished from the connective and supporting tissue. The main function of parenchyma is to store food and provide turgidity to organ where it is found.




Labile cells
M
G1
Cell division
Cell cycle
Interphase
S
G1
Permanent
cells (such as:
nerve cells)
G4
Stable cells
(such as: liver
cells)

TISSUE REGENERATION

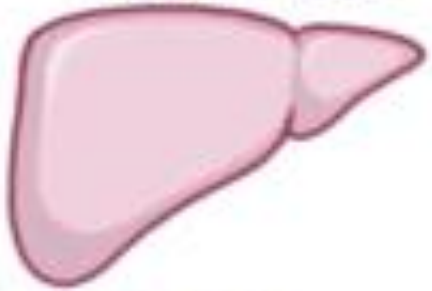
LABILE

* SKIN
* CONNECTIVE TISSUE
* SMALL & LARGE INTESTINE

HEAL WELL
(CONTAIN STEM CELLS)

~ UNDIFFERENTIATED CELLS

STABLE



*LIVER
└USE MATURE DIFFERENTIATED CELLS

~DIVIDE OR REGENERATE
(HYPERPLASIA)

PERMANENT

*SKELETAL MUSCLE
*CARTILAGE
*NEURONS
*CARDIAC TISSUE

WEAK REGENERATIVE CAPACITY
(NO STEM CELLS & CANNOT REPLICATE)

- According to the potential of cell renewal 3 types of cells are present

1)Labile cells

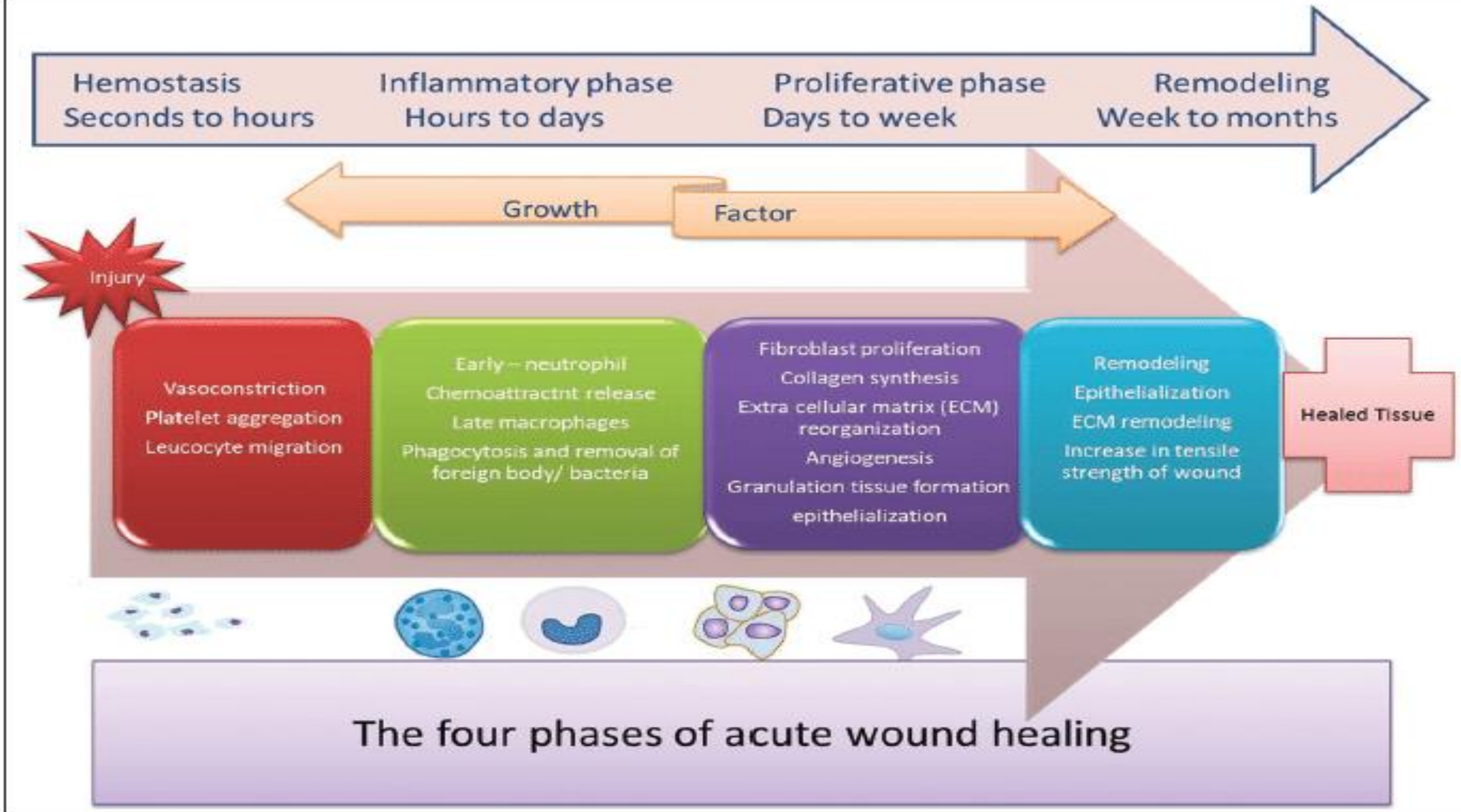
- Regenerate regularly
- Surface epithelial cells
- Surface epithelium of the GIT , Skin

2)Stable cells

- Normally slowly regenerate
- Divide when necessary
- eg. Hepatocytes

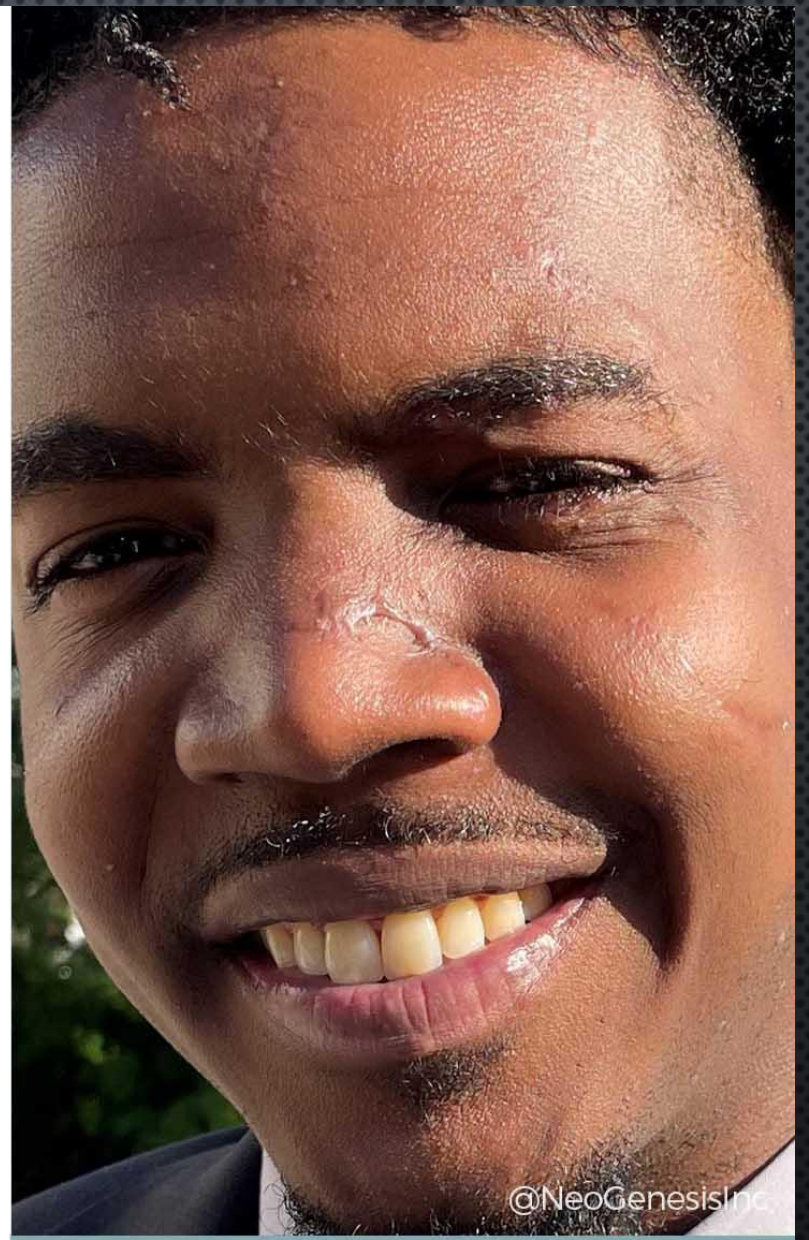
3)Permanent cells

- No effective regeneration
- eg. Neural cells of CNS, cardiac muscle



The four phases of acute wound healing

DAY 0



2 MONTHS


2019.05.07.
2019.05.14
2019.05.20
2019.05.27
2019.06.03
2019.06.11
2019.06.18
2019.06.22
2019.07.22

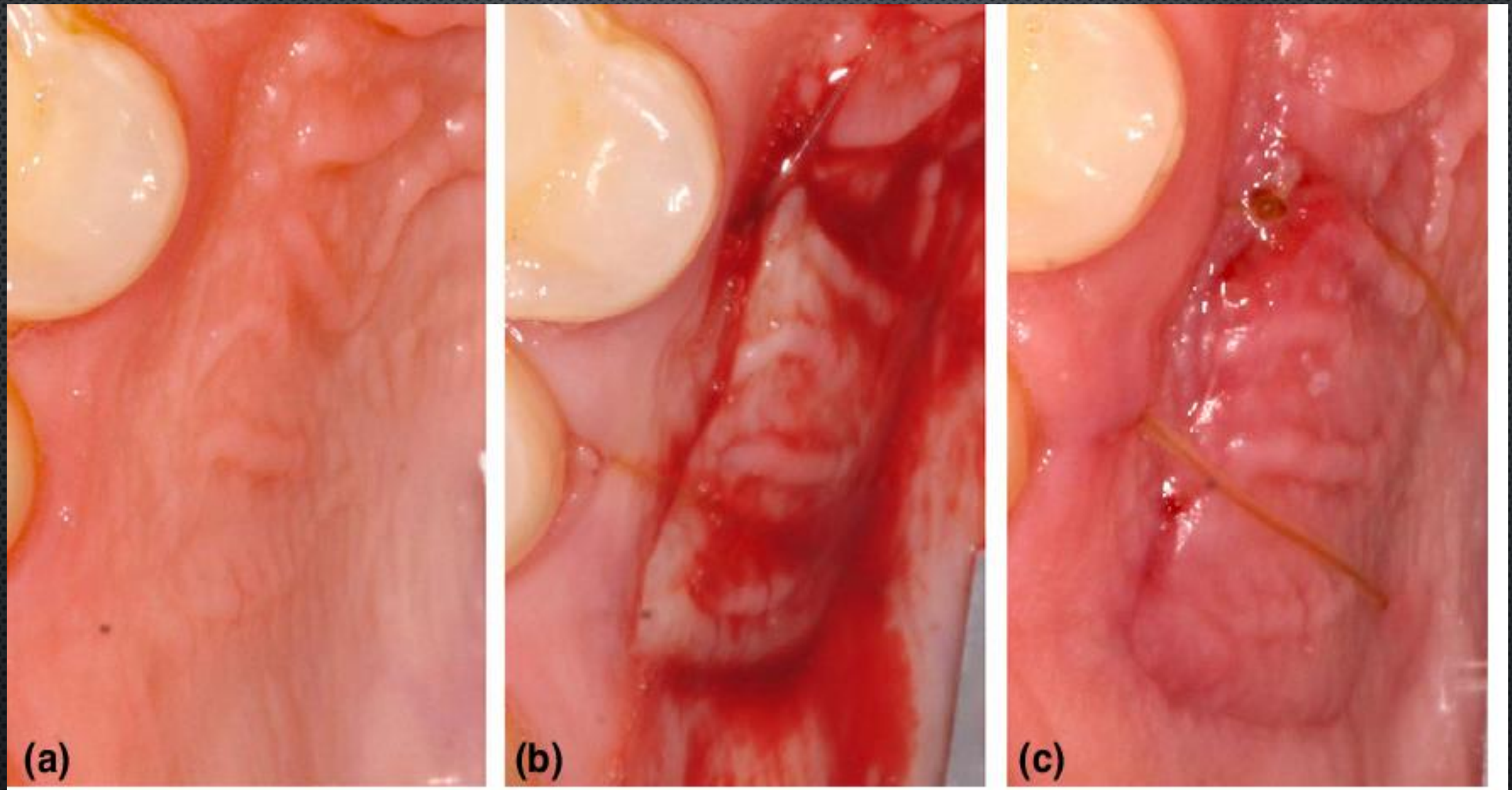


Fig. 1 Clinical images of representative case. (a) Palatal gingiva prior to any interven-

There are five major classes of steroid (LIPID) hormones: testosterone (androgen), estradiol (estrogen), progesterone (progestin), cortisol/corticosterone (glucocorticoid), and aldosterone (mineralocorticoids).

Why do doctors prescribe steroids?

Steroids reduce redness and swelling (inflammation). This can help with inflammatory conditions such as asthma and eczema. Steroids also reduce the activity of the immune system, which is the body's natural defense against illness and infection.

Who needs steroids?

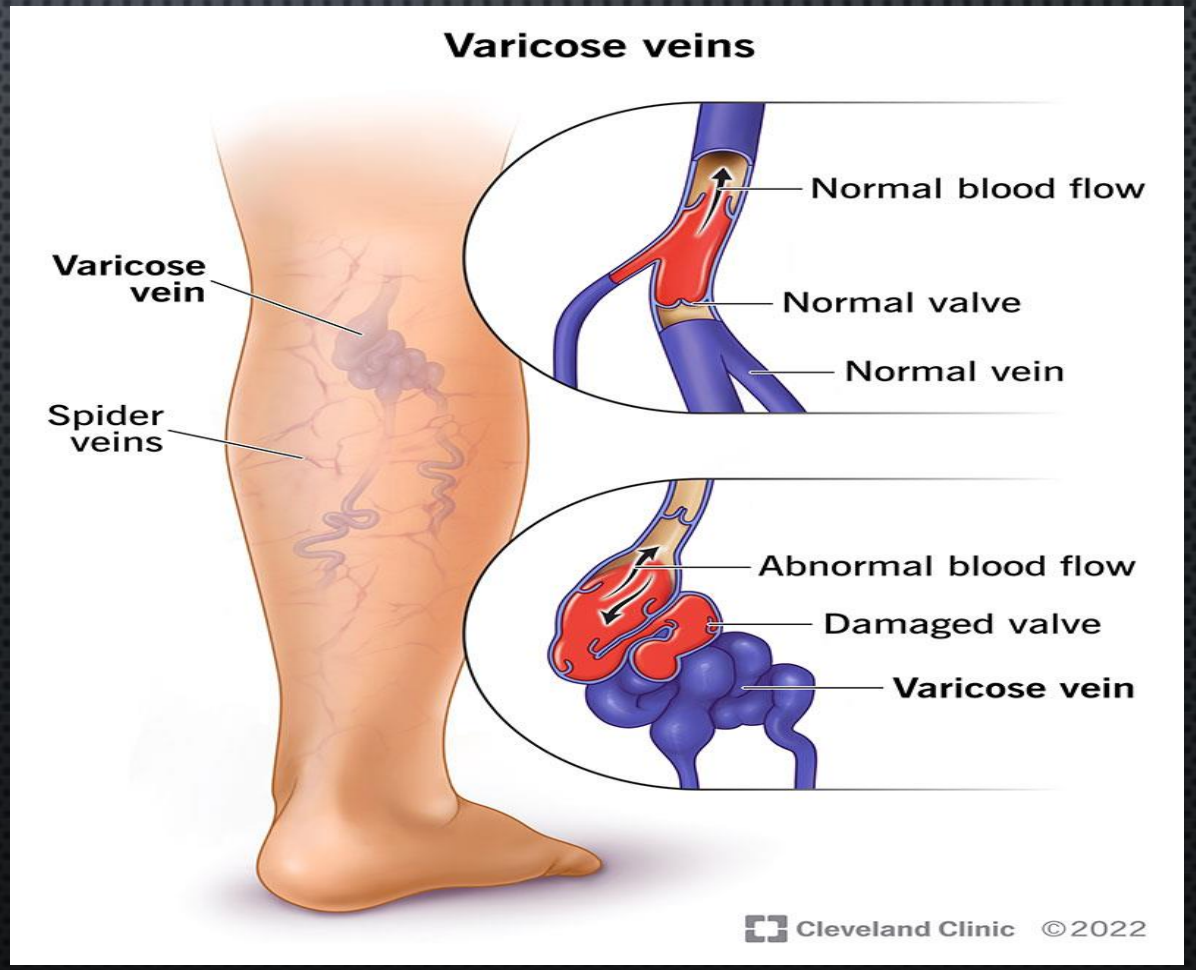
Healthcare providers mainly prescribe anabolic steroids to treat low testosterone (male hypogonadism). But they use it for other conditions as well, such as to stimulate muscle growth for people with certain cancers or acquired immunodeficiency syndrome (AIDS).

Why are steroids important?

Steroids have two principal biological functions: as important components of cell membranes that alter membrane fluidity; and as signaling molecules. Examples include the lipid cholesterol, sex hormones, anabolic steroids, and the anti-inflammatory corticosteroid drug dexamethasone.

You might not be able to start steroids if you have an infection, or if you have any wounds on your body, as steroids might delay these getting better or cover up some of your symptoms. Steroids might affect some medical conditions, such as diabetes, heart or blood pressure problems, or mental health issues.

Varicose veins are swollen, engorged blood vessels that bulge just under your skin's surface. These blue or purple bulges usually appear in your legs, feet and ankles. They can be painful or itchy.



Oral varicose veins

Definitions

- Regeneration

Growth of cells to replace the lost structure

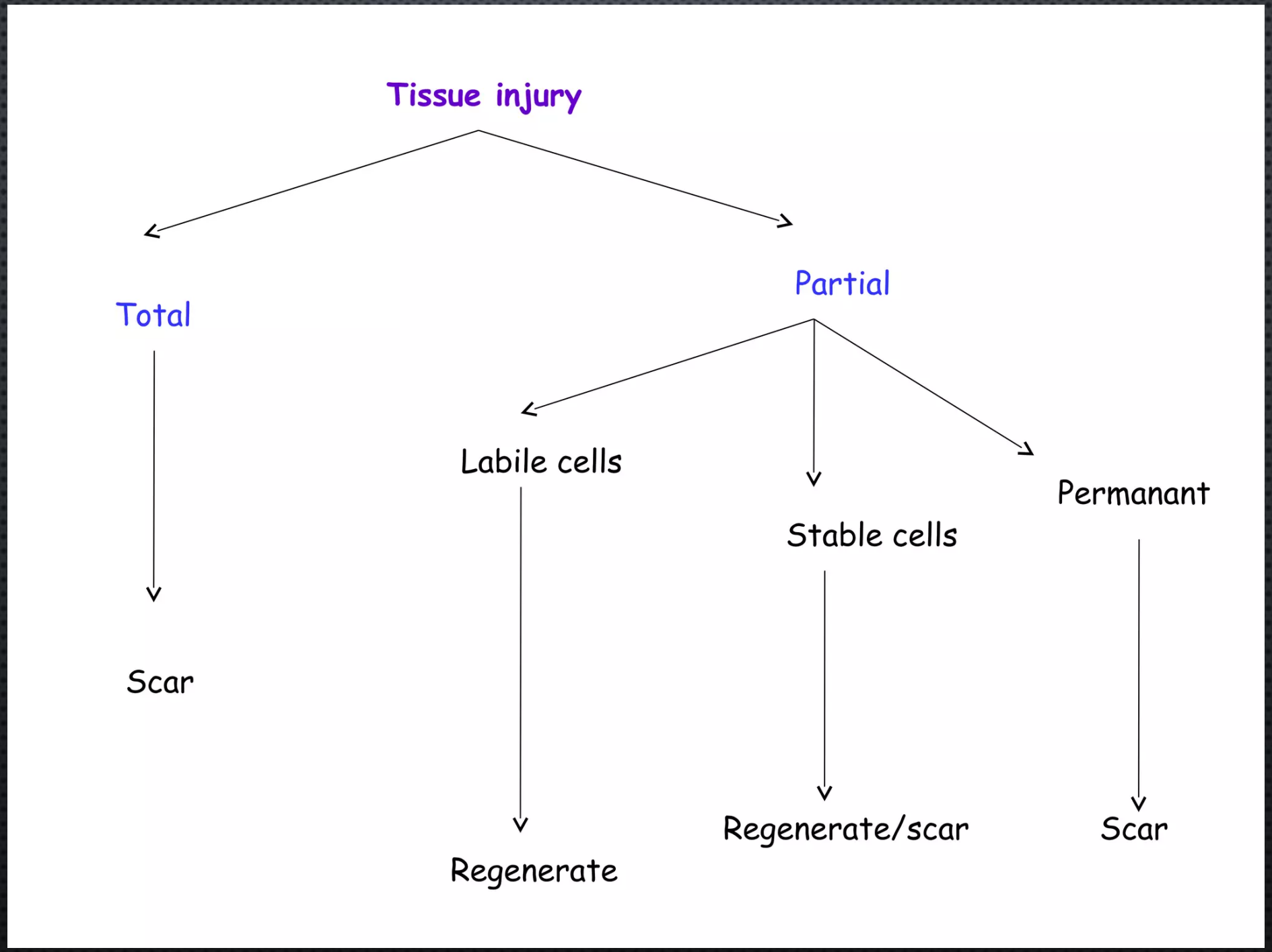
ex: skin,haemopoietic system,GIT

- Healing

Tissue response → 1.wound
→ 2.Inflammatory process
→ 3.cell necrosis

Two processes-Regeneration

Scar formation-laying down of fibrous tissue


Tissue injury
Total
Scar
Partial
Labile cells
Regenerate
Stable cells
Regenerate/scar
Permanant
Scar

Functions of Growth factors and receptors:

Growth factors bind to specific receptors and, ultimately, influence expression of genes that:

1. Promote entry into the cell cycle.
2. Relieve blocks on cell cycle progression (thus promoting replication).
3. Prevent apoptosis.
4. Enhance synthesis of components (nucleic acids, proteins, lipids, carbohydrates) required for cell division.
5. They can also regulate a host of nongrowth activities including migration, differentiation, and synthetic capacity.

Scar formation occurs when

1)Damage to permanent cells

2)Severe destruction of connective tissue frame work

3)With extensive cell injury

4)In chronic inflammation

Steps in repair by scar tissue formation

1)Inflammatory response

- Polymorphs and macrophages
- Remove damaged and dead tissue

2)Proliferation and migration of parenchymal and connective tissue cells

3)Formation of new blood vessels (angiogenesis) and granulation tissue

Steps in repair by scar tissue formation cont.

4) Synthesis of ECM proteins and collagen deposition

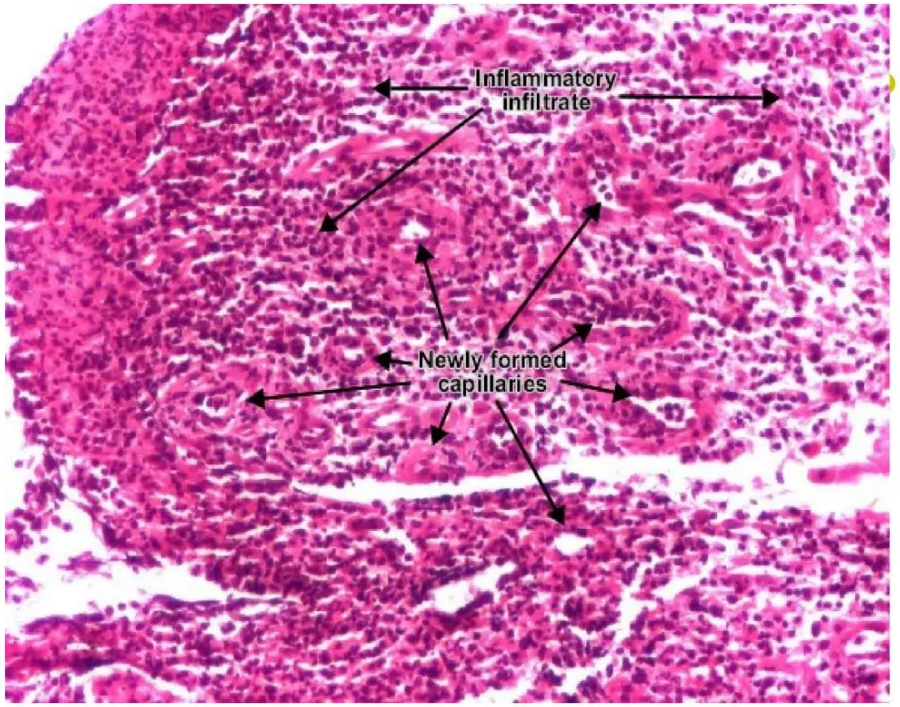
5) Tissue remodeling

6) Wound contraction

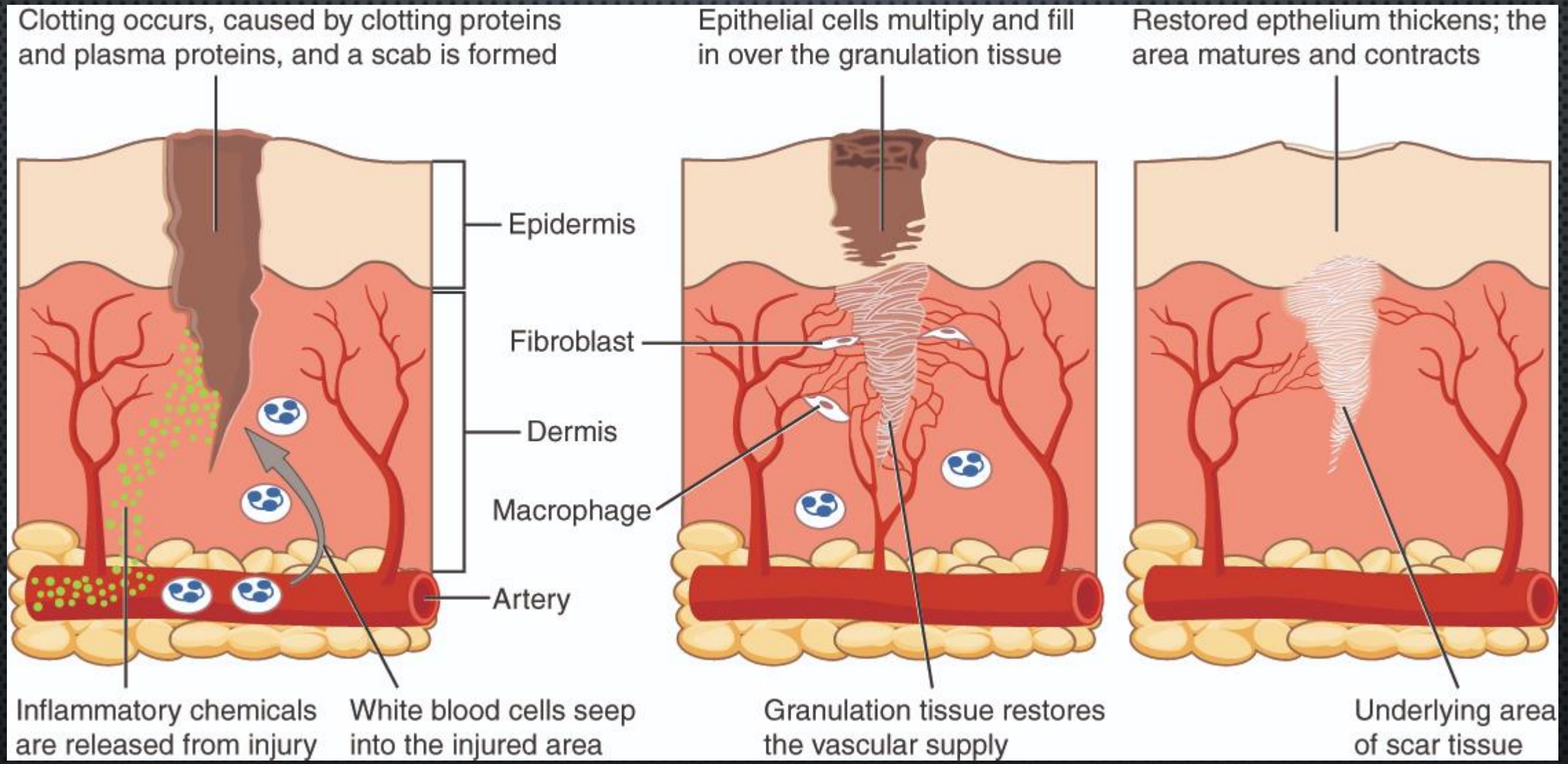
7) Wound strength

What is granulation tissue?

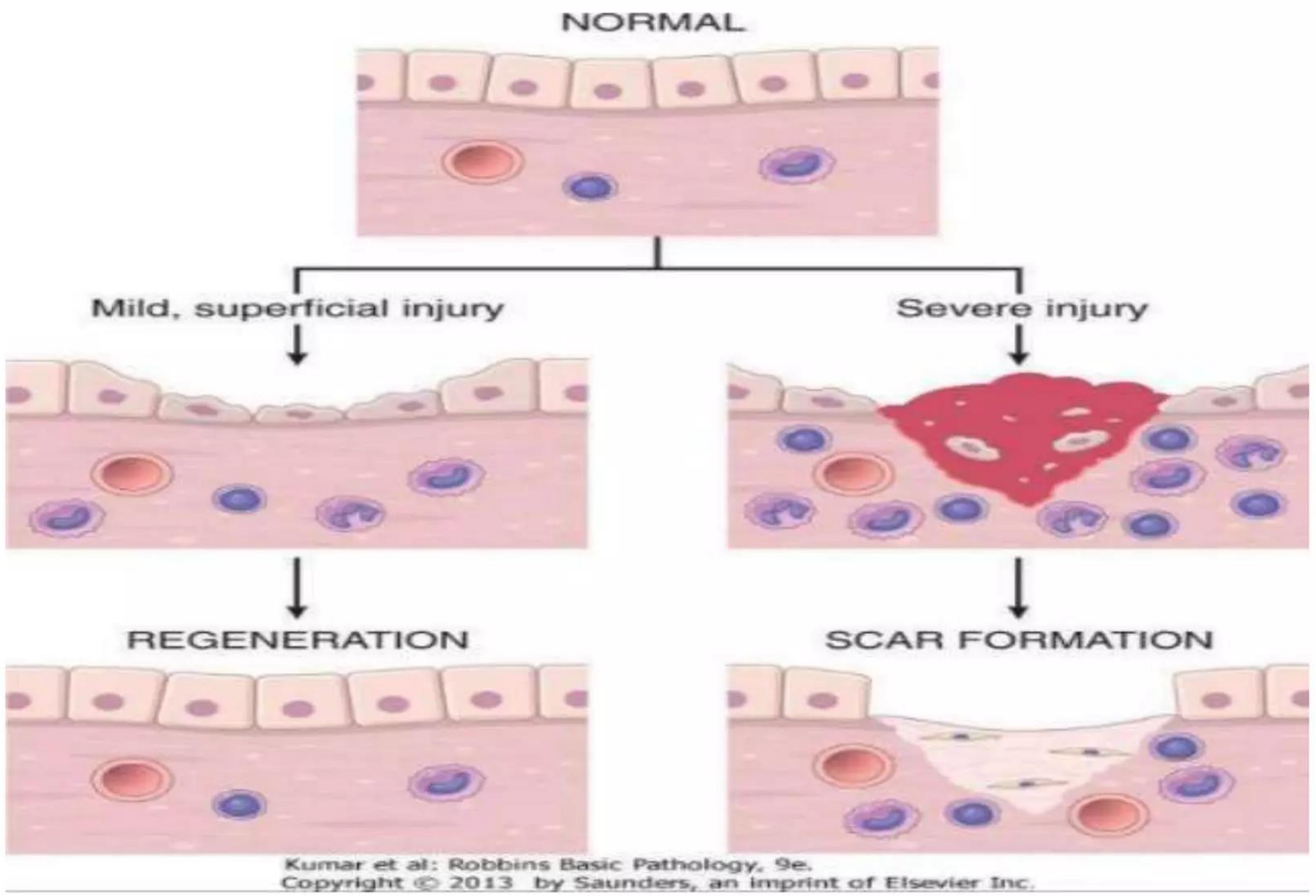
- Highly vascularized connective tissue
- **Composed of –**
  - Newly formed capillaries
  - Proliferating fibroblasts
  - Inflammatory cells in oedematous stroma
- **Macro –**
  - Pink granular
  - Soft and fleshy



new capillaries (result of proliferation of endothelial cells - angiogenesis or neovascularization) in an edematous atmosphere of fibroblasts (spindle shaped), myofibroblasts, mononuclear inflammatory cells, macrophages, neutrophils,


Clotting occurs, caused by clotting proteins and plasma proteins, and a scab is formed
Epithelial cells multiply and fill in over the granulation tissue
Restored epthelium thickens; the area matures and contracts
Epidermis
Fibroblast
Dermis
Macrophage
Artery
Inflammatory chemicals are released from injury
White blood cells seep into the injured area
Granulation tissue restores the vascular supply
Underlying area of scar tissue

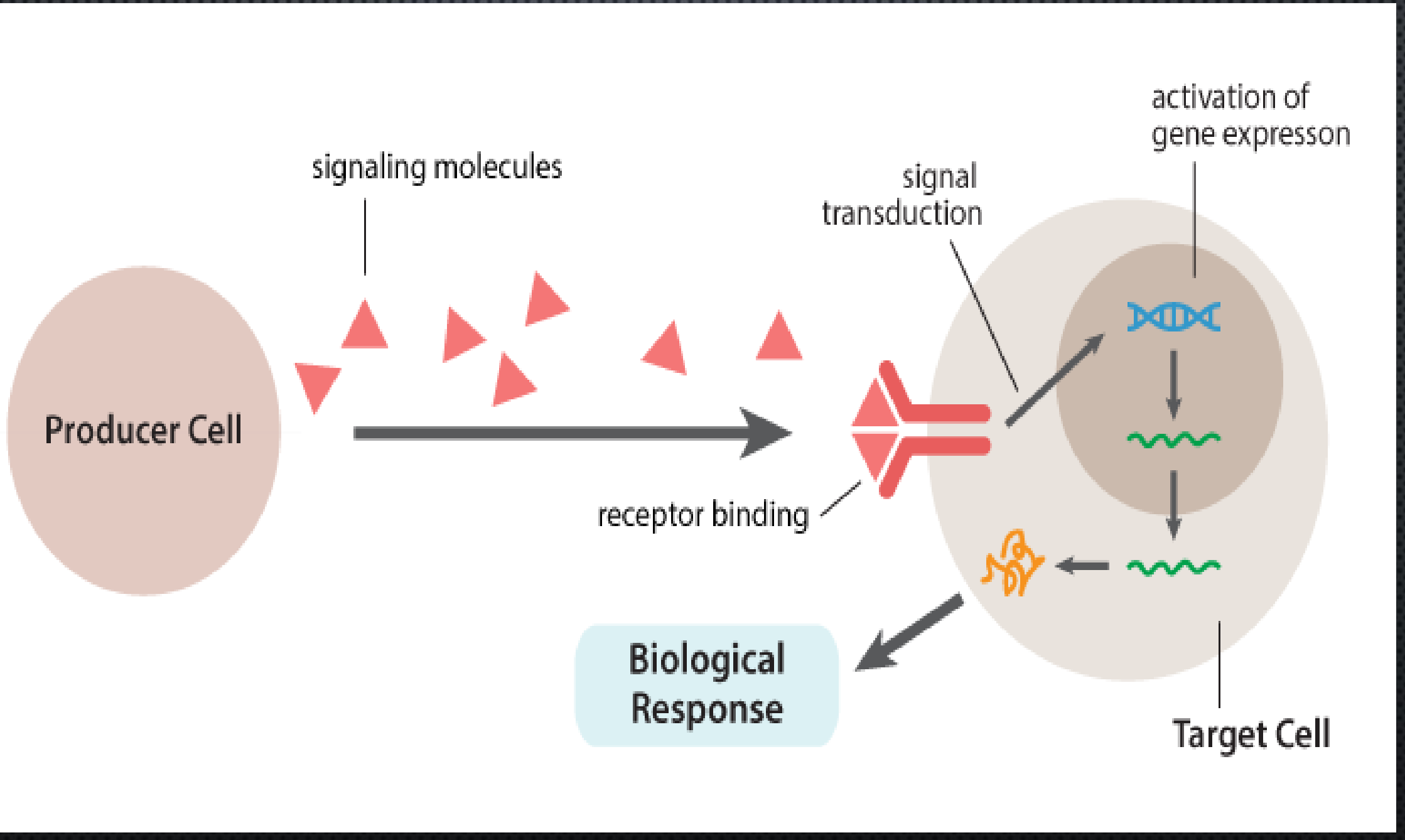
Tissue Repair/Healing



Kumar et al: Robbins Basic Pathology, 9e.

A growth factor, as initially defined, is a secreted biologically active molecule that can affect the growth of cells. This definition has become expanded to include secreted molecules that promote or inhibit mitosis or affect cellular differentiation

Some of the most studied growth factors include the brain-derived neurotrophic factor (BDNF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF-1), erythropoietin (EPO), vascular growth factor (VEGF), transforming growth factor beta (TGF-β), nerve growth factor (NGF)


activation of
gene expresson
signaling molecules
signal
transduction
Producer Cell
receptor binding
Biological
Response
Target Cell

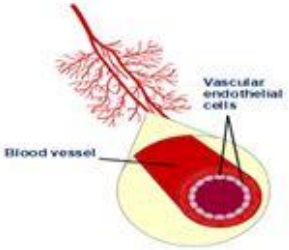
What is angiogenesis?

Formation of blood vessels from existing blood vessels

From

- A) Endothelial precursor cells in BM
- B) From pre-existing vessels

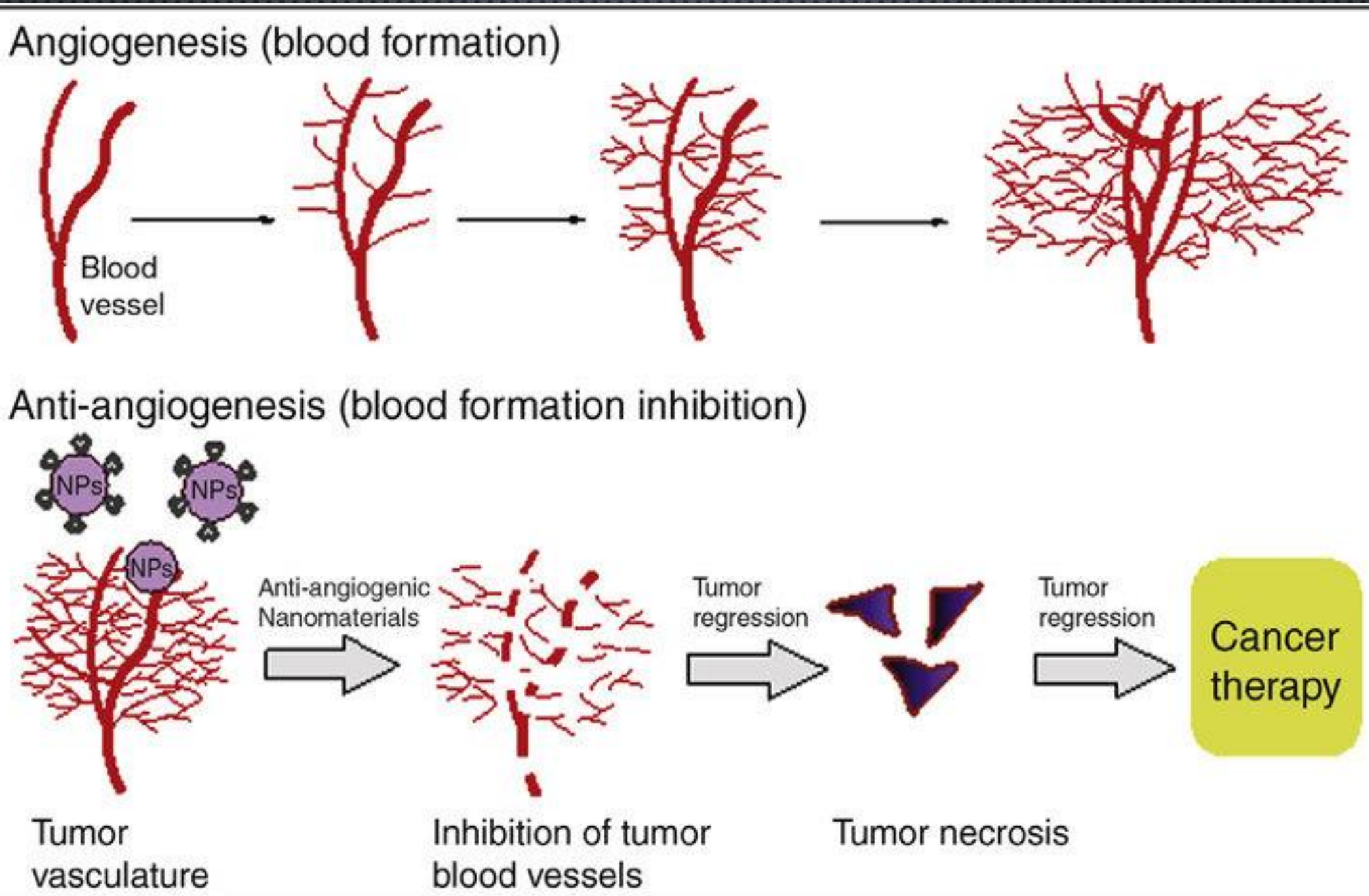
What is angiogenesis



Angiogenesis is the formation of new blood vessels from pre-existing vessels.

Angiogenesis is a normal process in growth and development, as well as in wound healing.

However, this is also a fundamental step in the transition of tumors from a dormant state to a malignant state.


Angiogenesis (blood formation)
Blood vessel
Anti-angiogenesis (blood formation inhibition)
NPs
NPs
NPs
Anti-angiogenic Nanomaterials
Tumor regression
Tumor regression
Cancer therapy
Tumor vasculature
Inhibition of tumor blood vessels
Tumor necrosis