Characteristics of acute inflammation (cellular events, chemical mediators, systemic effects)
Morphologic patterns of acute inflammation according to the exudate

Chronic inflammation
Granulomatous inflammation
Tissue repair and wound healing

Chronic inflammation

Chronic inflammation **is a response of prolonged duration** (weeks or months) in which *inflammation*, *tissue injury*, and *attempts at repair* coexist, in varying combinations.

Causes of Chronic Inflammation

-Persistent infections
-Hypersensitivity diseases-autoimmun diseases
-Prolonged exposure to potentially toxic agents, either exogenous or endogenous
-The role of inflammation in neurodegenerative diseases,metabolic syndrome and the associated type 2 diabetes, and certain cancers
-Foreign bodies

Cellular players: macrophages, lymphocytes, plasma cells, eosinophyls,mast cells

Morphologic Features

Infiltration with mononuclear cells

Tissue destruction

Attempts at healing

Non- exudative

1. Macrophages

The dominant cells in most chronic inflammatory reactions

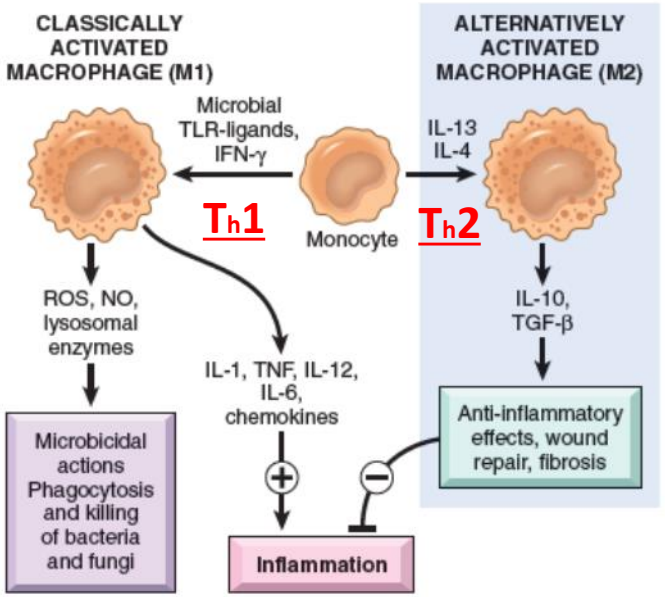
Circulating cells of this lineage are known as monocytes .

-Classical macrophage activation-

To kill ingested organisms, and secrete cytokines that stimulate inflammation.

-Alternative macrophage activation-

Tissue repair: They secrete growth factors that promote angiogenesis, activate fibroblasts, and stimulate collagen synthesis.



2.Lymphocytes

As the mediators of adaptive immunity, provides defense against infectious pathogens

These cells are often present in chronic inflammation and when they are activated, the inflammation tends to be persistent and severe.

3.Eosinophils

In immune reactions mediated by IgE and in parasitic infections

4.Mast cells

In both acute and chronic infl ammatory reactions

5. Leukocytes „acute on chronic”

Macrophages

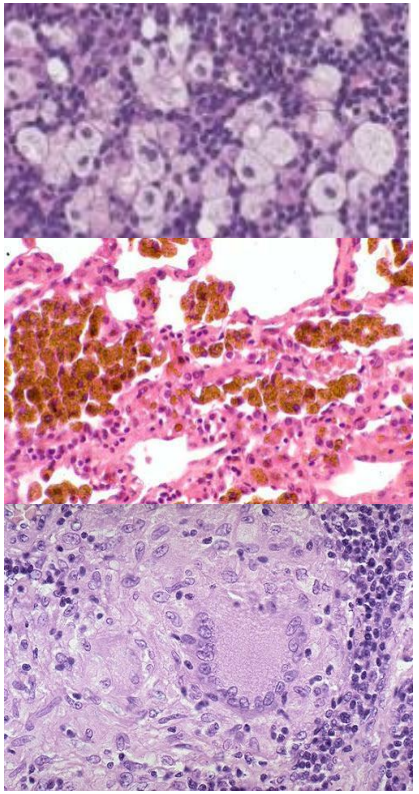
Morfological type

Foamy cytoplasm

Haemosiderin-laden

Epitheloid cells

Giant cells

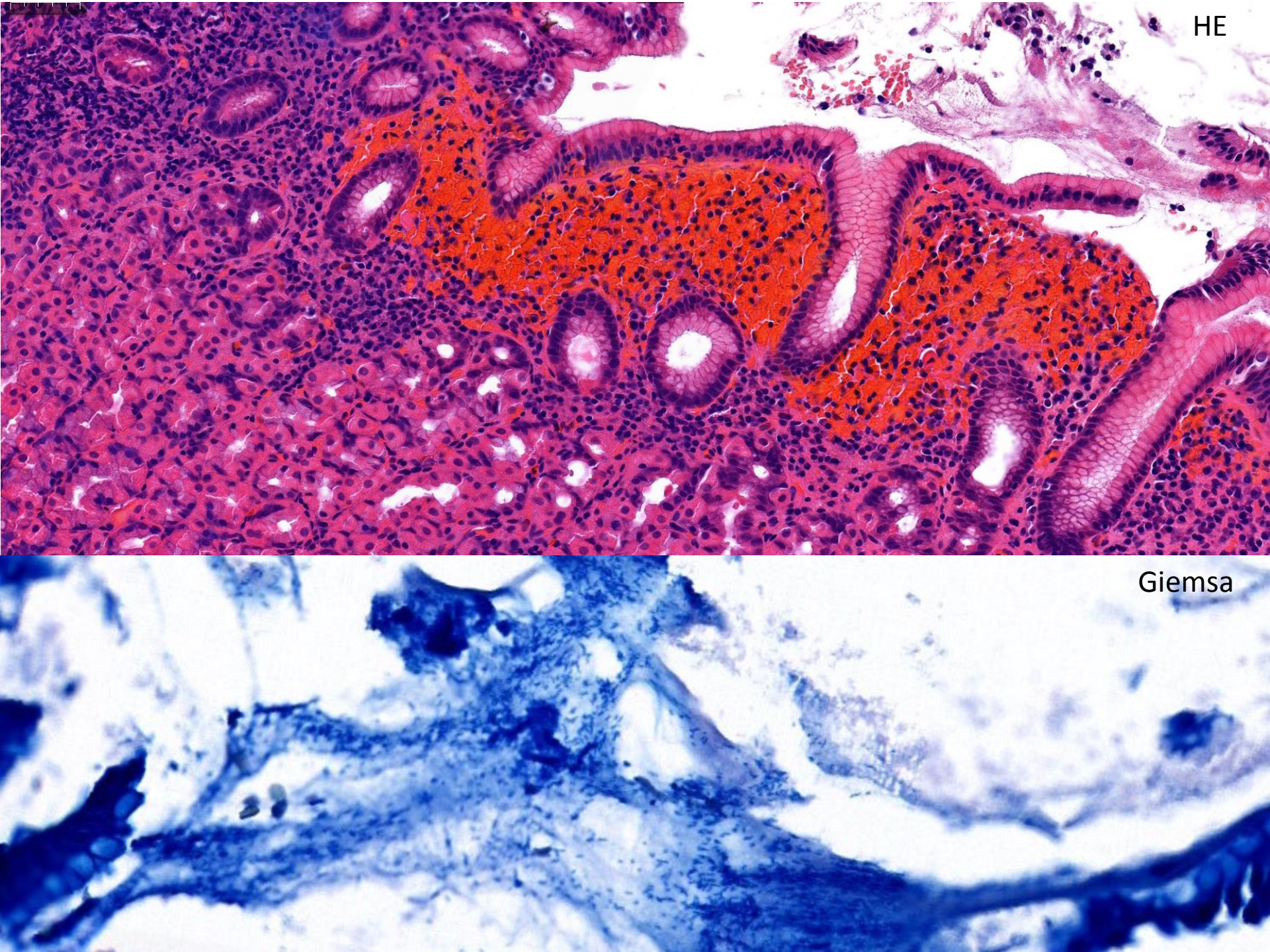


Fibrosis

- Fibroblast activation, collagen production: TGF-ß, PDGF, FGF
- Angiogenesis: VEGF (vascular endothelial growth factor), FGF

Cicatrisatio-cicatrix formation

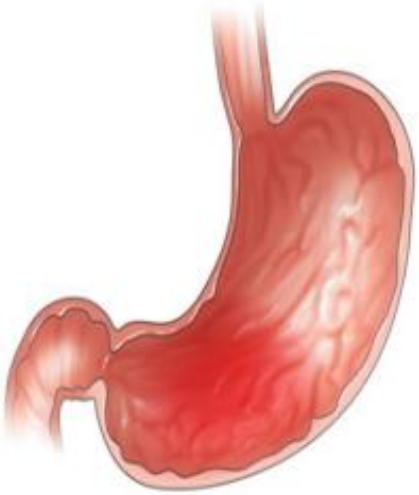
Pleuritis chronica adhaesiva
Pericarditis chronica adhesiva
Cicatrix myocardii
Cirrhosis hepatis


HE
Giemsa

Chronic *H. pylori* infection

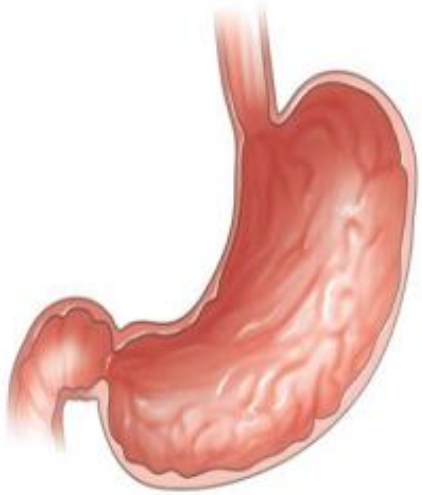
Duodenal ulcer phenotype

- Around 10-15% of infected subjects
- Antral predominant Gastritis
- High gastrin and acid secretion
- Impaired inhibitory control of acid secretion
- Protection from gastric cancer



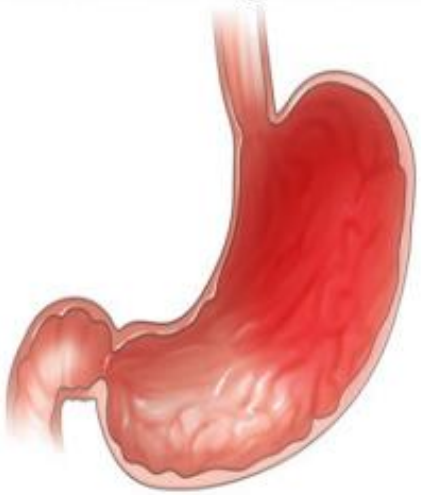
Simple gastritis phenotype

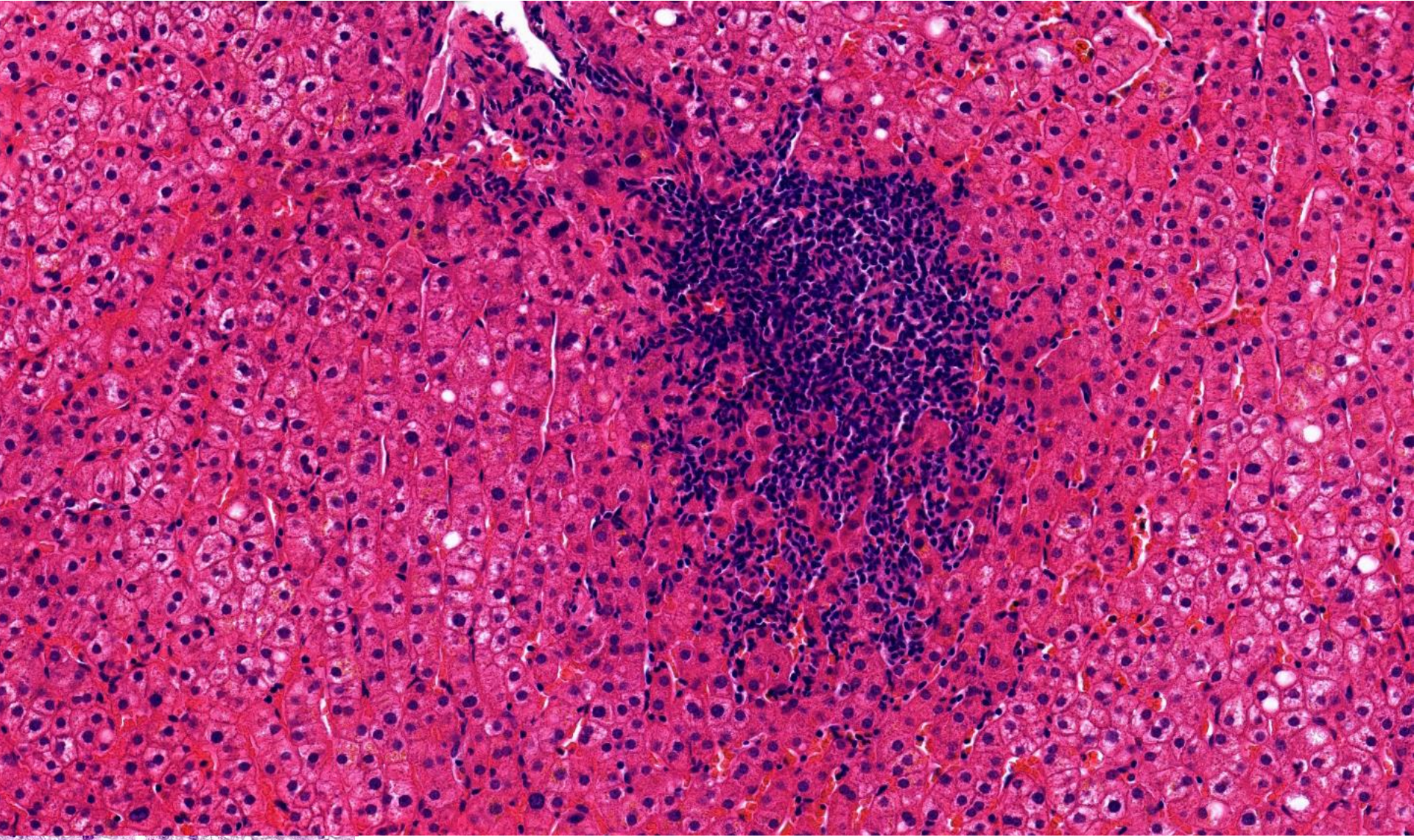
- Majority of infected subjects
- Mild mixed gastritis
- High gastrin but normal acid secretion
- No gastric atrophy
- No significant clinical outcome

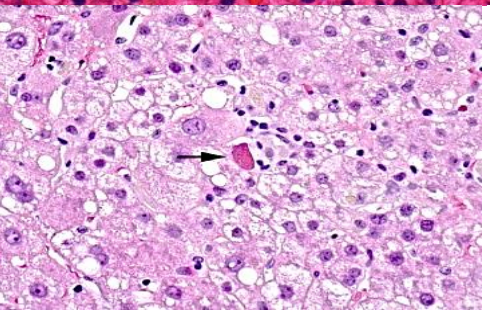


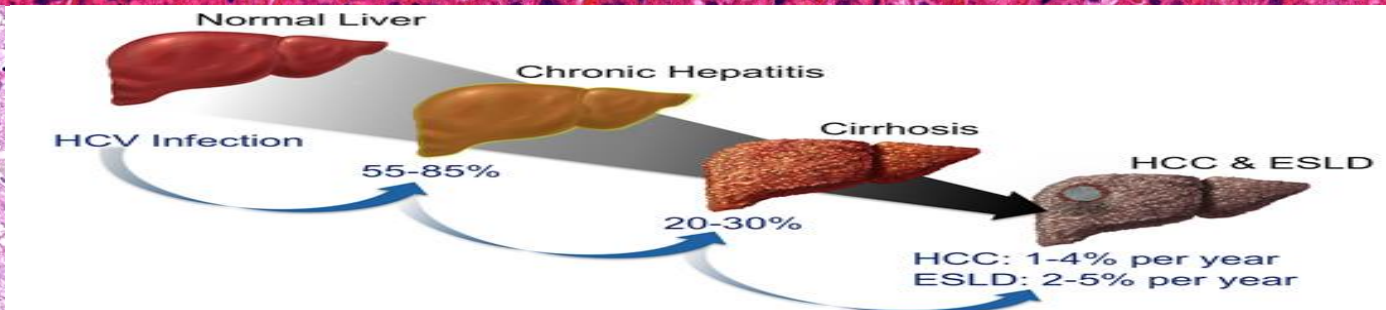
Gastric cancer phenotype

- Around 1% of infected subjects
- Corpus-predominant gastritis
- Multi-focal atrophic gastritis
- High gastrin
- Hypo/achlorhydria
- Low pepsinogen I and pepsinogen I/II ratio
- Increased risk of gastric cancer








Normal Liver
Chronic Hepatitis
HCV Infection
Cirrhosis
HCC & ESLD
55-85%
20-30%
HCC: 1-4% per year
ESLD: 2-5% per year

Granulomatous Inflammation

Granulomatous inflammation is a form of chronic inflammation characterized by the presence of ***granuloma***

epithelioid cells (modified macrophages) compulsary
giant cells (fusion of epithelioid cells) –often
lymphocytes
fibroblasts

CLASSIFICATION
1.Immune-granulomas → INFECTIVE (tuberculosis, lues, leprosy cat-scratch disease)
1.Immune-granulomas → NON-INFECTIVE (sarcoidosis, rheumatic fever,PBC, Wegener)
2.Foreign-bodies granulomas (keratin, lipogranuloma, surgical suture,)

OR

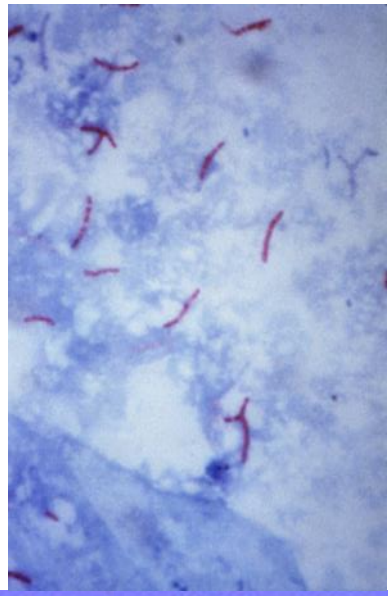
a/ necrotising (tbc, lues, rheumatic nodule)
b/ non necrotising (sarcoidosis, Crohn disease)

Langhans Foreign-body type Touton

giant cells

TBC

most common infectious disease on the world
Cause: Mycobact. Tuberculosis

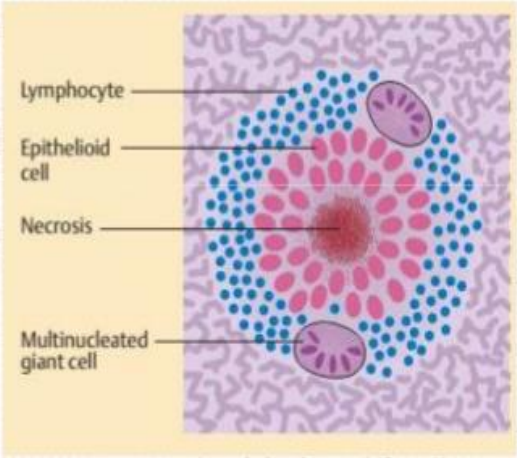


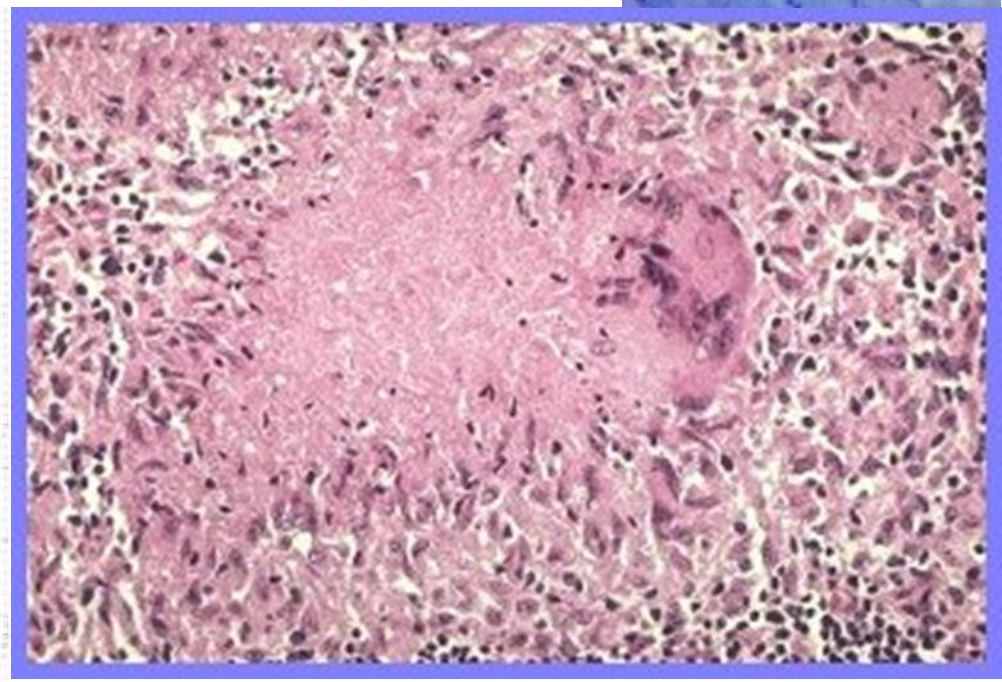
Primery (Ranke-Ghon complex (tuberculoma,lyphangiitis, lymphadenitis)
Postprimery

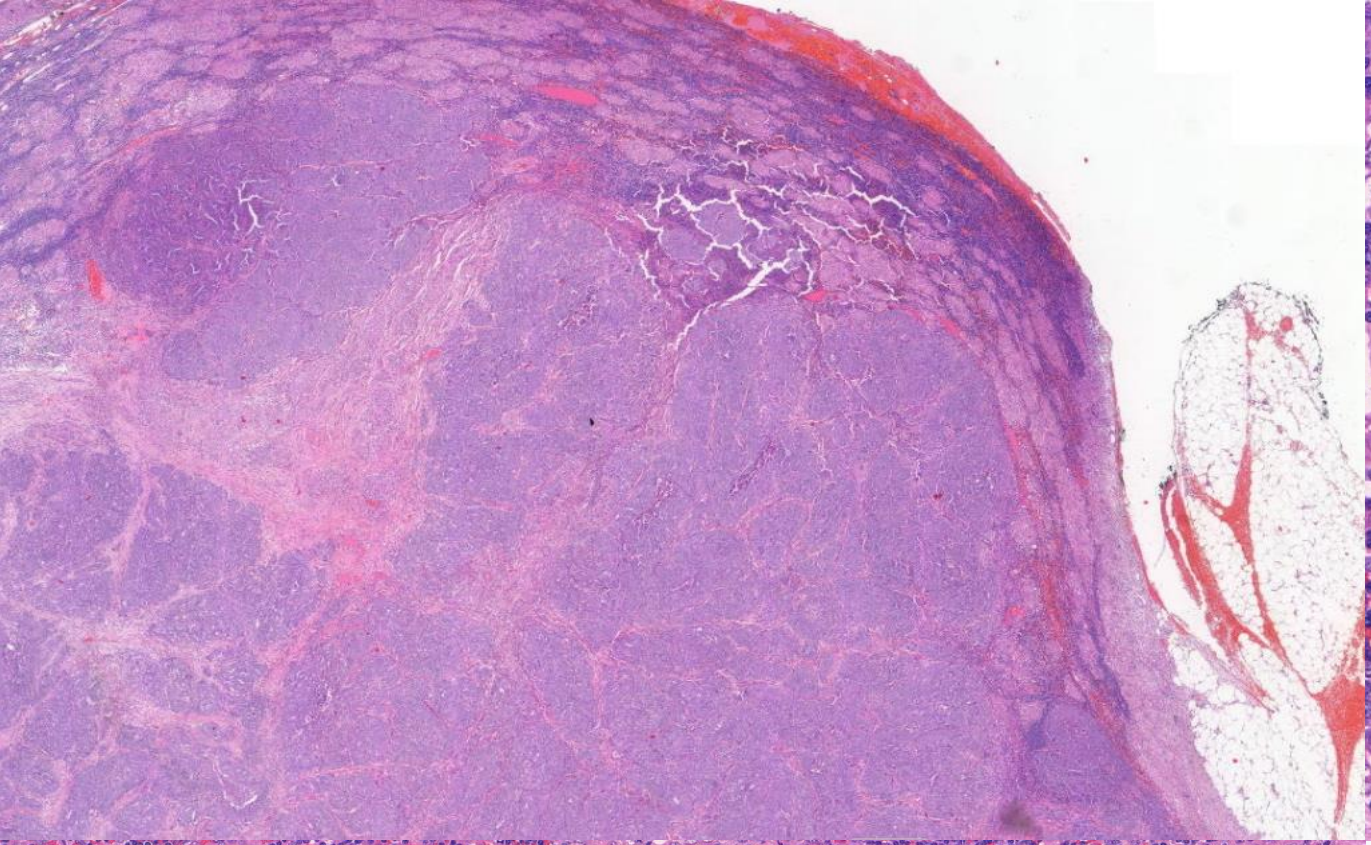
Demonstration of pathogen: Ziehl-Neelsen, auramin, PCR
Spreading:local, lymphogenic, haematogenic, canalicular, serous membranes

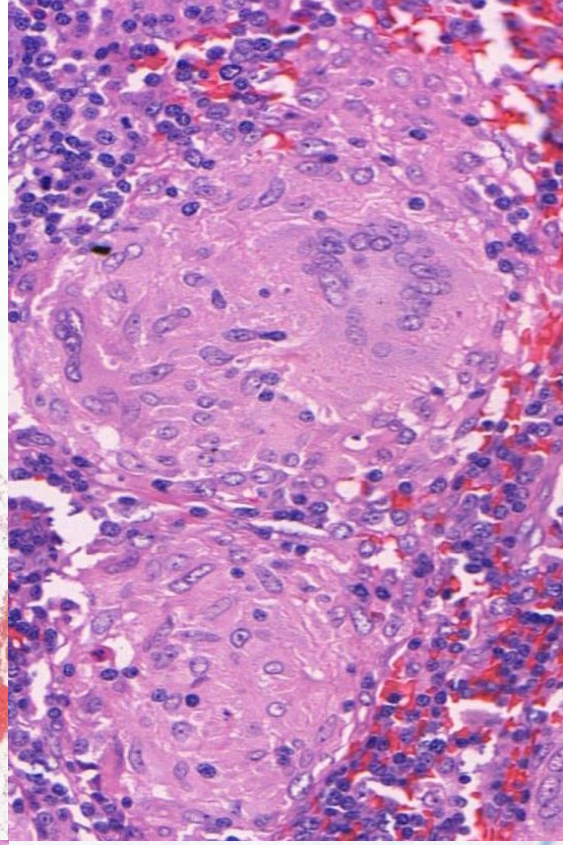
COMPOSITION OF GRANULOMA

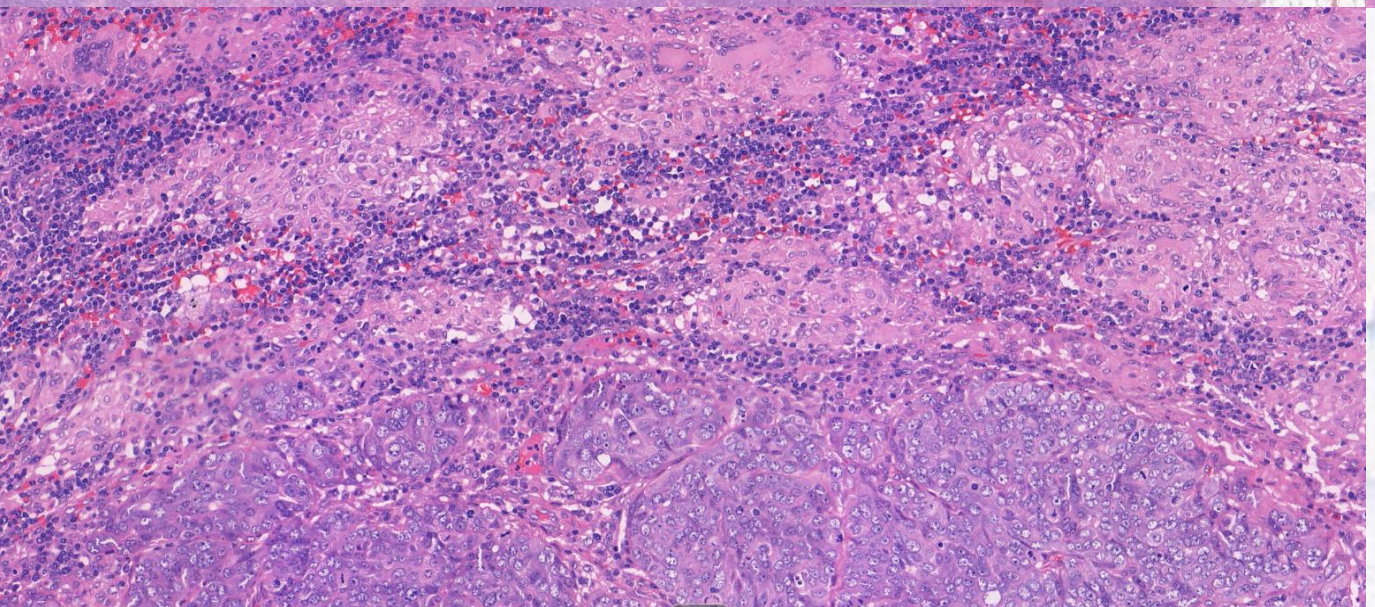
- Following structural components
  - Epitheloid cells
  - Multinucleate giant cells
  - **Lymphoid cells** - cell mediated immune reaction
  - Necrosis & Fibrosis.

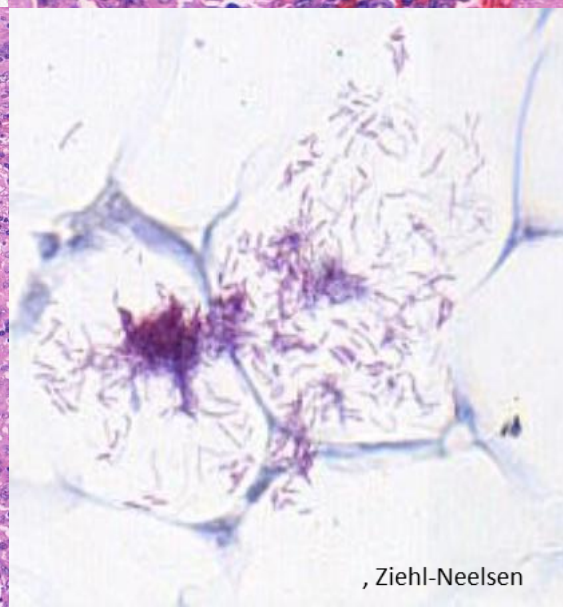












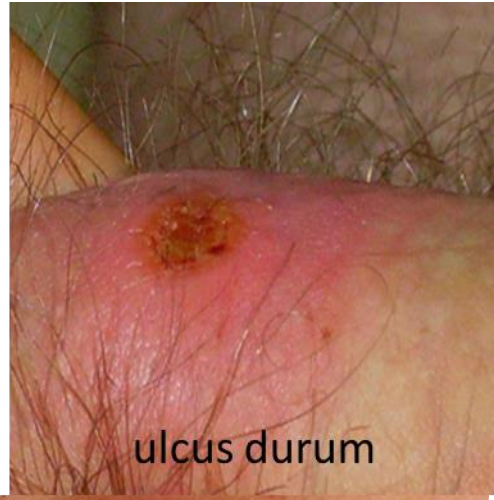
, Ziehl-Neelsen

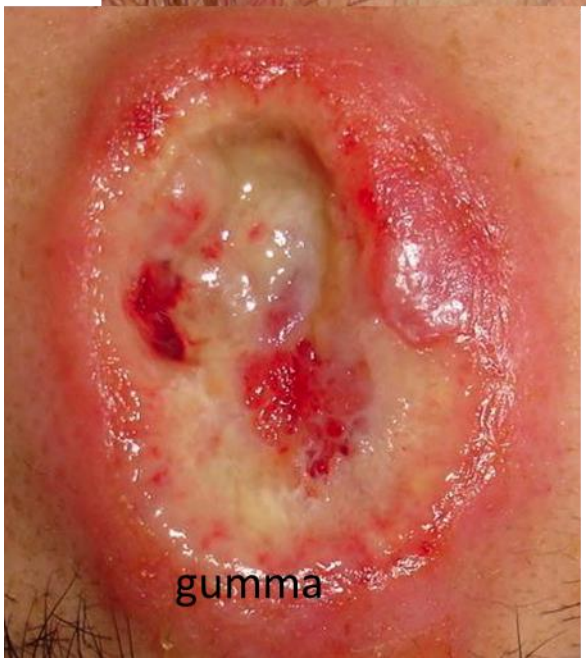
Syphilis, lues

Cause: Treponema pallidum

Acquired form

Primary: ulcus durum, bubo indolens
Secundary: bakteremia, exanthaemas
Tertiary: granulomatous – gumma
Cardiovasc: aneurysma
Neuoro sy: tabes dorsalis, paralysis prgr.


ulcus durum


gumma

Congenital

Severe
Pemphigus syphiliticus
Hepato-splenomegaly
Pneumonia alba
Dubois-abscess

Mild form: Hutchinson's triad
-blunted upper incisor teeth known as Hutchinson's teeth
-inflammation of the cornea known as interstitial keratitis
-deafness from auditory nerve disease

Granulomatous Inflammation

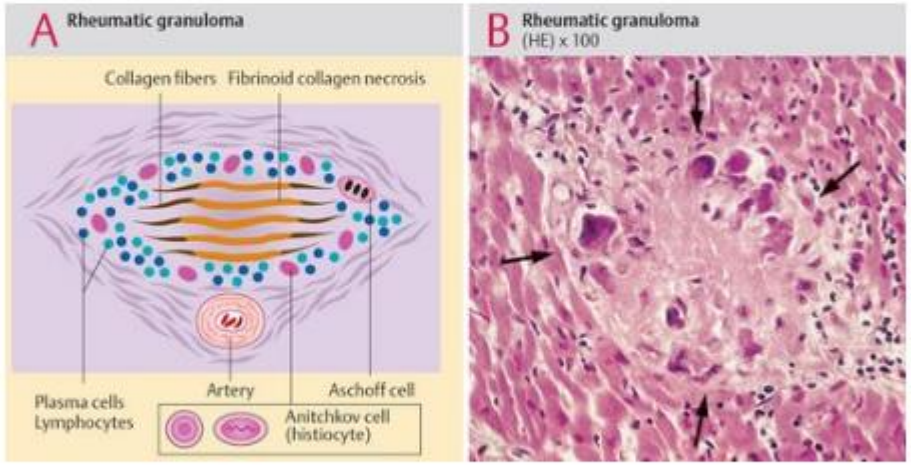
Rheumatic fever

Morphology:

A. Acute Rheumaic Heart Disease:

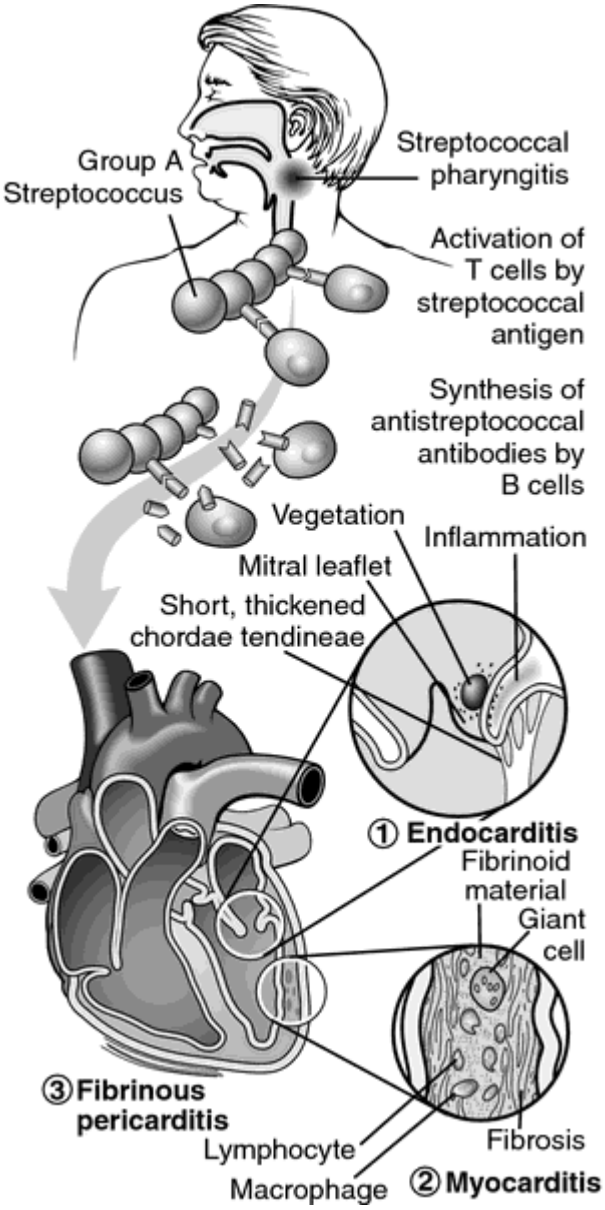
1. **Aschoff bodies or Rheumatic granuloma: Fibrinoid necrosis** demarcated by:

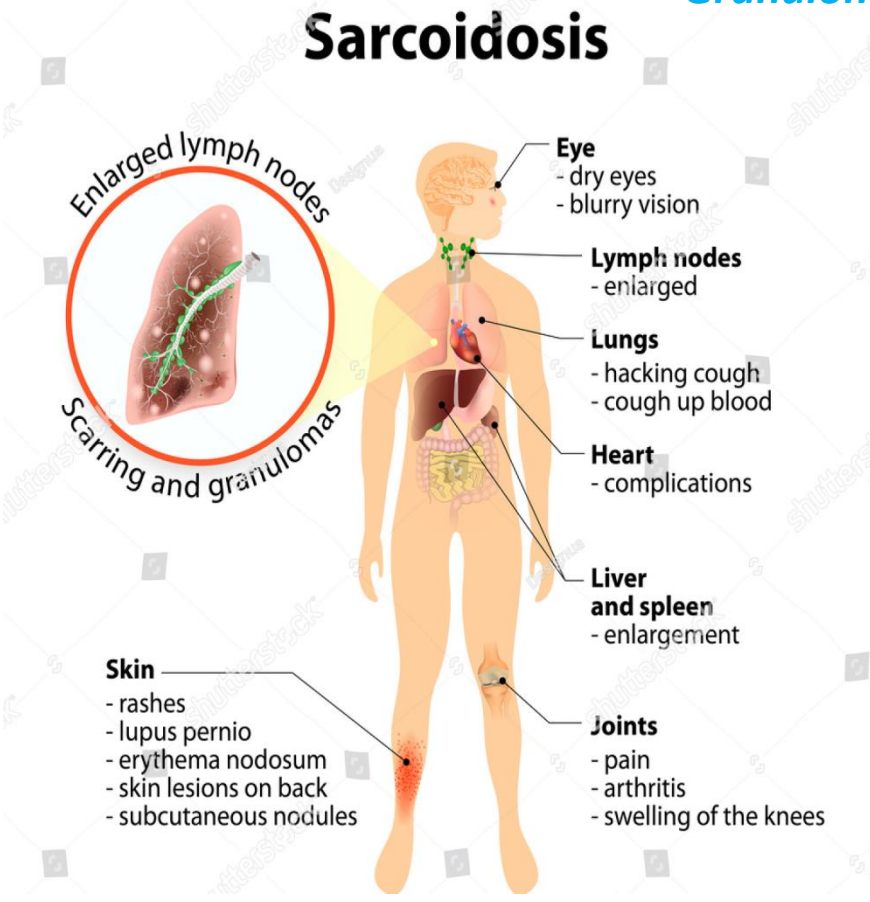
- **Antischkow cells** (Specialized histiocytes resembling Epithelioid cells which appears **catterpillar like** in cross section and owl's eye in longitudinal section)
- **Lymphoplasmacytic** infiltrate (Sparse)
- Rarely **Aschoff cells** (Inflammatory Giant cells)



2. **Pancarditis:** Diffuse inflammation and Aschoff Bodies in any of the 3 layers of heart – pericardium, myocardium, endocardium (including valves)

- Pericardium: **"Bread and Butter" Pericarditis** (Fibrinous or Serofibrinous)
- Myocardium: **Myocarditis** (Scattered Aschoff bodies within interstitial connective tissue)
- Endocardium: Fibrinoid necrosis along the lines of closure of valves forming 1 to 2 mm **+vegetations**

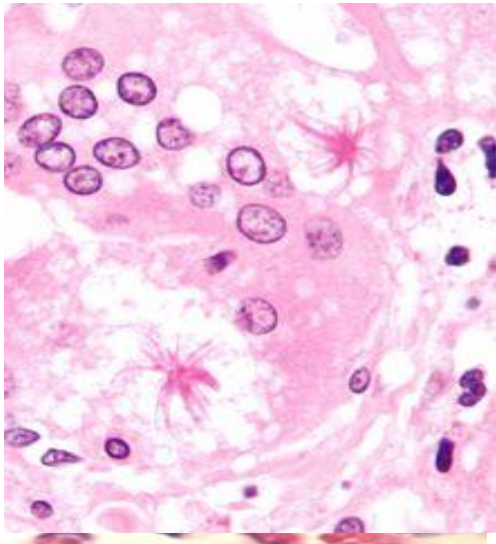




Non-caseating, non-infective granulomas

Giant cells with:

- Asteroid body
- Schaumann ~s body



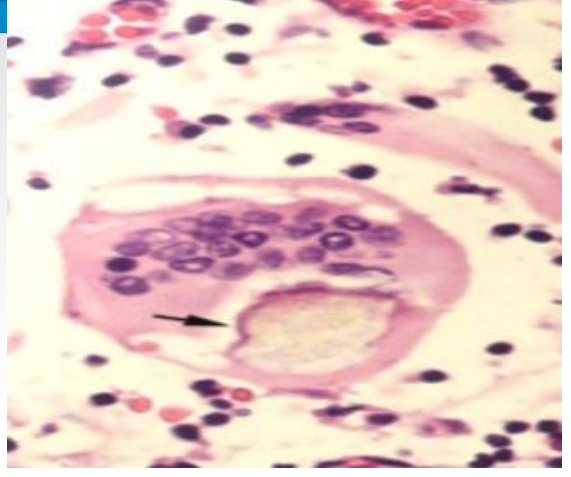
Etiology

- Disease of unknown cause.
- Possible infectious & transmissible cause in genetically susceptible individuals.
- Possible environmental exposure cause.
- Possible genetic-environmental interactions.
- Possible autoimmune cause.

Pathophysiology of Sarcoidosis

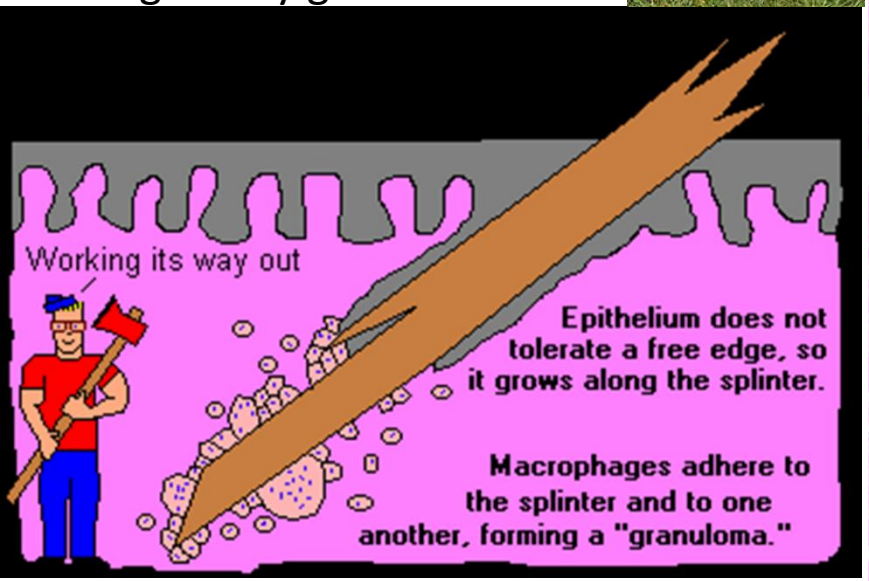
Clip slide

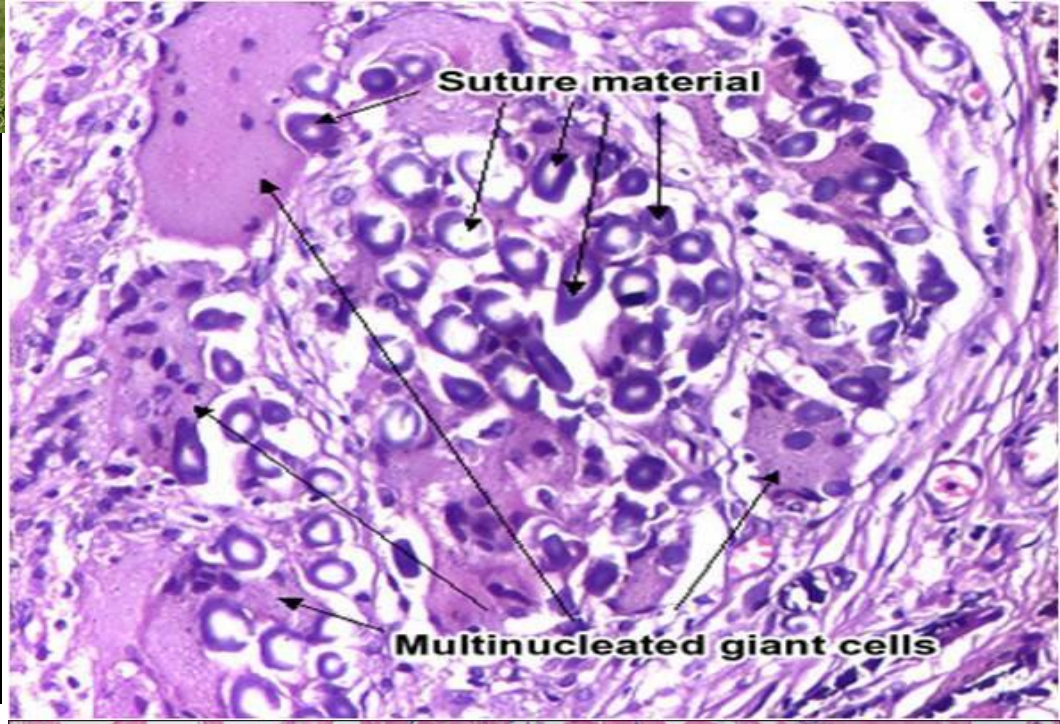
- **Non-caseating epithelioid cell granuloma** is the characteristic lesion of sarcoidosis.
- It occurs along perivascular, peribronchial & septal region areas rich in lymphatic vessels.
- Granuloma consists of a central collection of modified mononuclear phagocytes called **epithelioid cells.**
- Epithelioid cells are mature macrophages that gain secretory & bactericidal capabilities but lose some phagocytic capability.

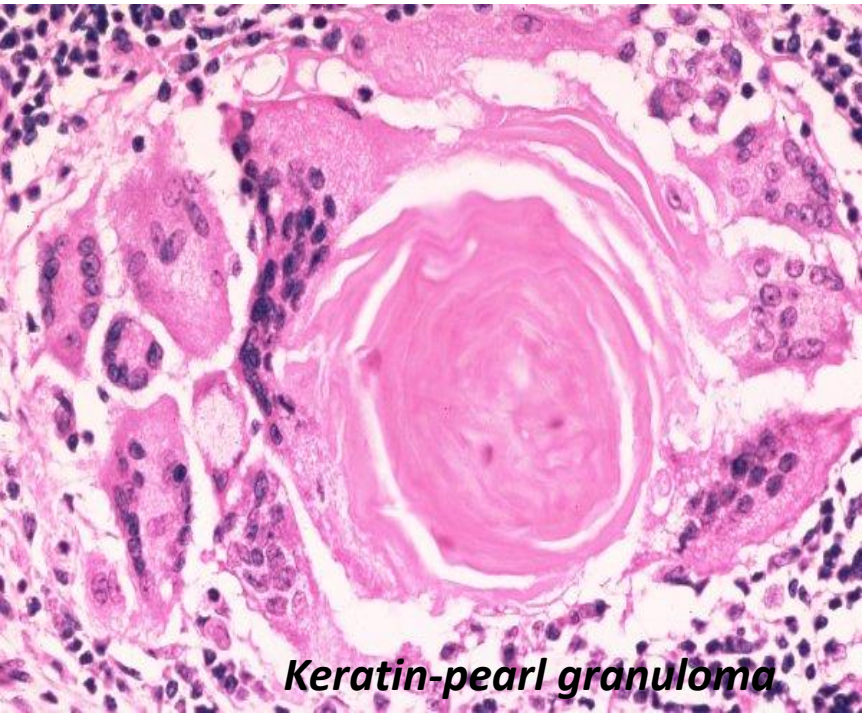


Granulomatous Inflammation

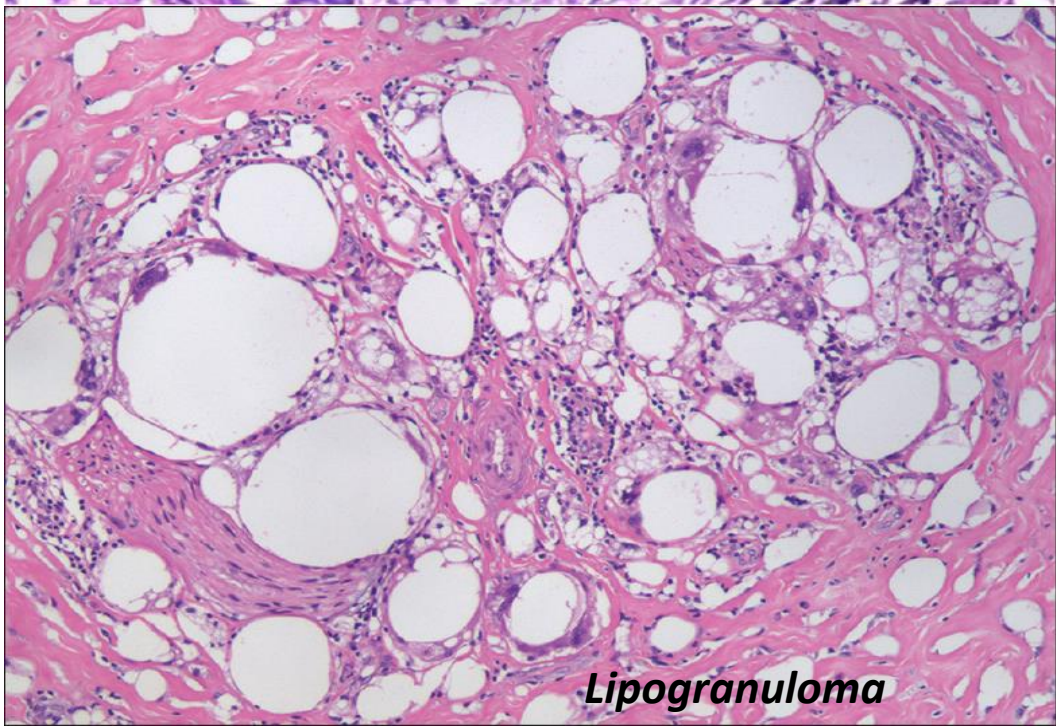
Foreign body granuloma







Keratin-pearl granuloma



Lipogranuloma

Harmfull consequences of inflammation

Overshooting

A/inflammatory reaction again harmless lesions: appendicitis, crystals
B/hypersensitive ,autoimmune diseases
C/Too intense reaction: endotoxin shock, ARDS sepsis (infectios SIRS)
D/ autoinflammatory disorders (rare regulatory diseases, systemic diseases e.g. diabetes, atherosclerosis)

Chronic inflammatory reactions caused fibrosis

Failure of inflammation

a/congenital defects: neutropenia, LAD, chronic. granulomatous disease

b/acquired lesions: neutropenia, splenectomy, saturation of macrophages (hemolysis, immunocomplex diseases) leukocyte malfunction (alcohol, extensive burns), failure of blood supply, diabetes, malignant tumours

Chronic inflammation and malignancies

Reflux-disease, inflammatory bowel diseses, H.pylori, EBV, schistosomiasis, smoking

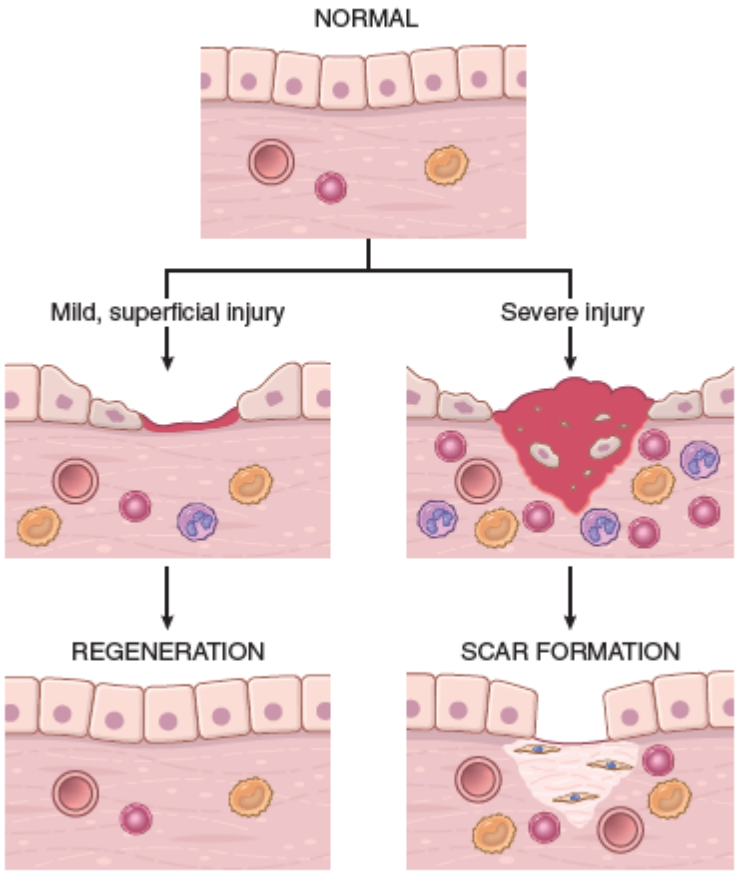

STOP!
71
Comune di CAGLIARI
passo
carrabile

TISSUE REPAIR

Repair of damaged tissues occurs

regeneration : proliferation of residual (uninjured) cells

healing : the deposition of connective tissue to form a scar



We rank cells according to their ability to regenerate:

LABILE CELLS ("continuous replicators") are constantly replenishing their neighbors that have died or been shed. Examples include the epithelium of skin, mucous membranes, oviducts, ducts; urothelium; endometrium; seminiferous tubules; bone marrow; lymphoid tissue.

STABLE CELLS ("discontinuous replicators") can proliferate rapidly in response to need, especially when required to replace lost neighbors. These include all glandular parenchymal cells, as well as fibroblasts, endothelial cells (cuboidal, and called "angioblasts", when they are healing), and osteoblasts.

PERMANENT CELLS ("non-replicators") have very limited ability to undergo mitosis or be replenished after birth. These cells include glia, neurons, and cardiac (non-failing heart).

Mechanisms of Tissue Regeneration

In epithelia of the intestinal tract and skin, injured cells are rapidly replaced by proliferation of residual cells

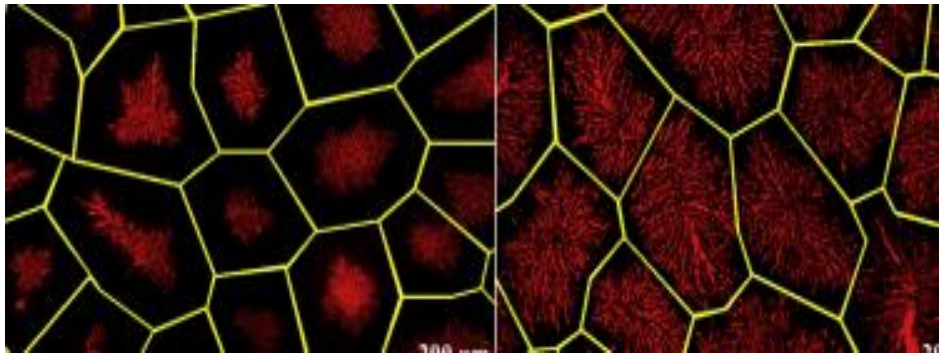
Tissue regeneration can occur in parenchymal organs whose cells are capable of proliferation, but with the exception of the liver, this is usually a limited process.

Liver Regeneration

From hepatocyte- after partial hepatectomy, or pvl

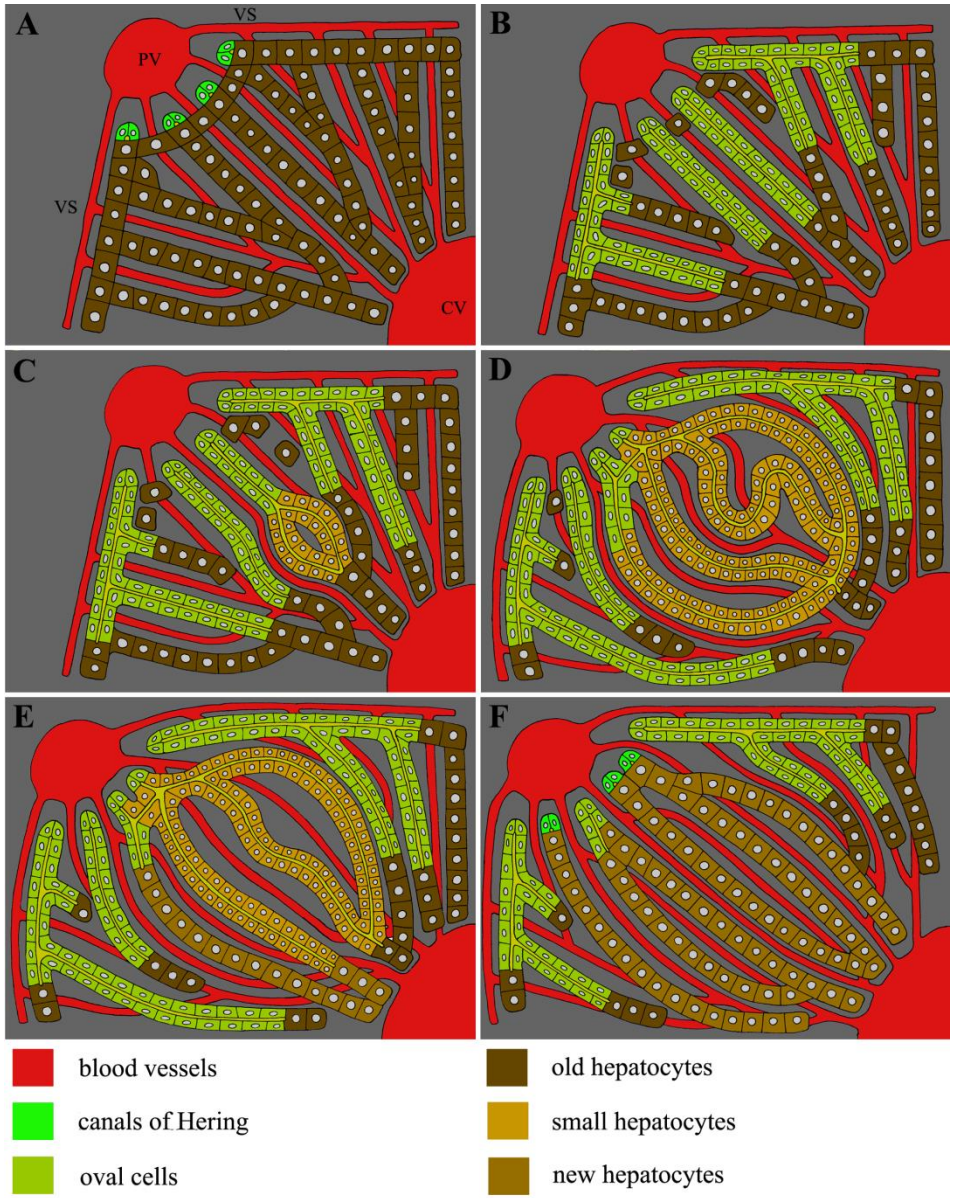
From stem cells- when the hepatocyte are unable to divide

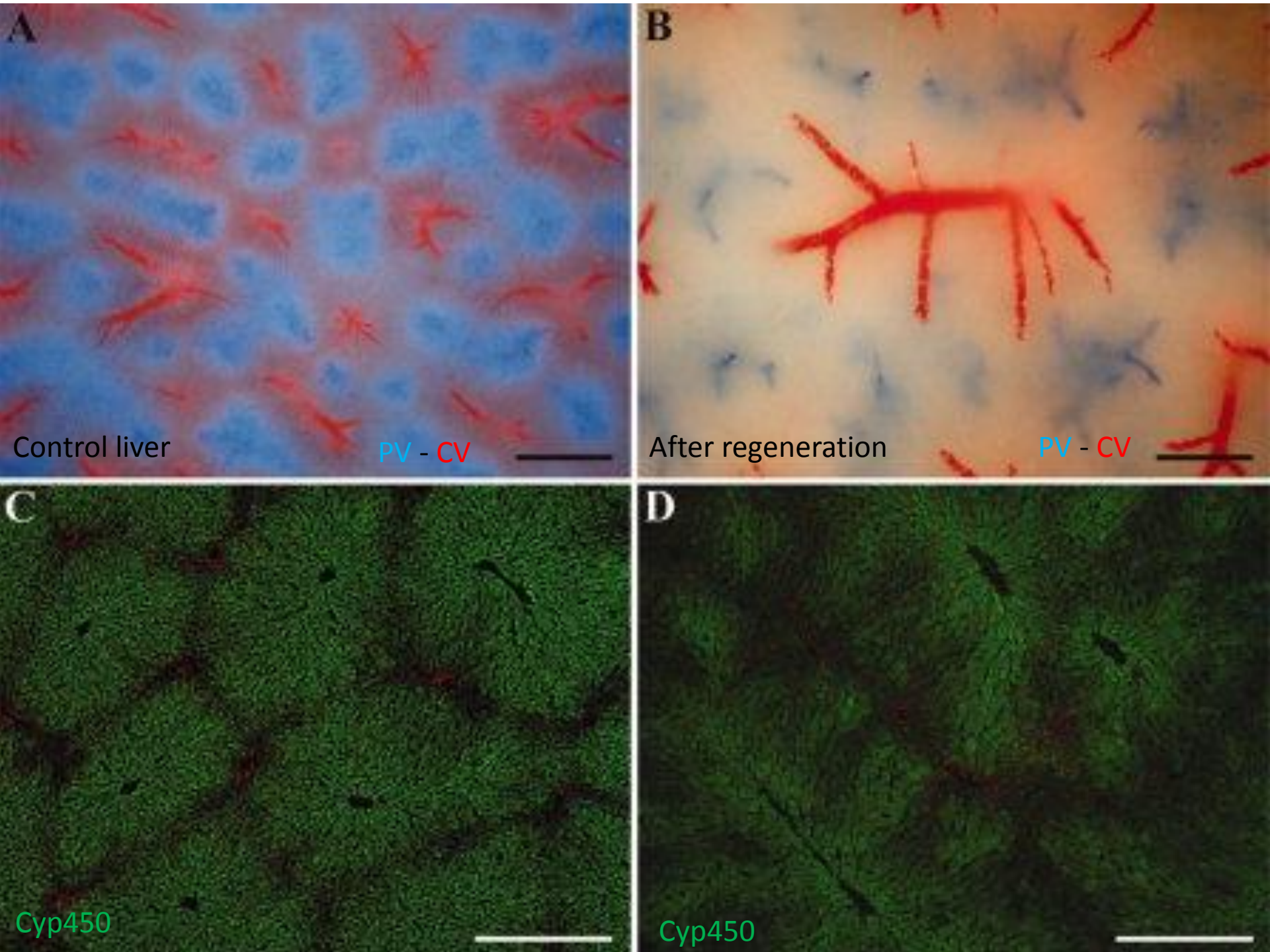
-Oval cells, intermediary hepatobiliary cells



The size of the lobules in control liver and after regeneration

Liver regeneration from stem cells




A
Control liver
PV - CV
B
After regeneration
PV - CV
C
Cyp450
D
Cyp450

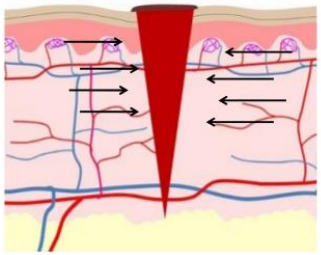
Healing

Definition

- The process by which the body is trying to achieve anatomical integrity of the injured part and to restore full function

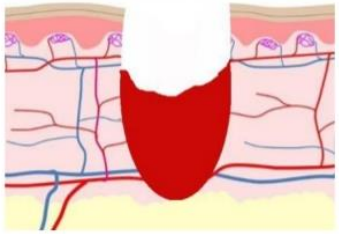
• Primary Intention

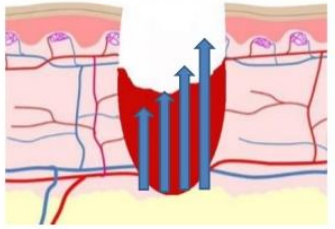
- Occurs when:
  - The edges are clean and held together with ligatures
  - There is little gap to bridge Healing
- Healing properties (When uncomplicated)
  - Occurs quickly
  - Rapid ingrowth of wound healing cells (macrophages, fibroblasts, etc.)
  - Restoration of the gap by a small amount of scar tissue.
- soundly united within 2 weeks
- Dense scar tissue is laid down within 1 month



• Secondary Intention

- Occurs when:
  - The edges are separated
  - The gap can not be directly bridged
  - Extensive epithelial loss
  - Severe contamination
  - Significant subepithelial tissue damage
- Healing properties
  - Occurs slowly
  - Granulation; healing from the bottom towards the surface
  - Restoration of the gap by a small amount of scar tissue.
- Scaring
- Wound contracture



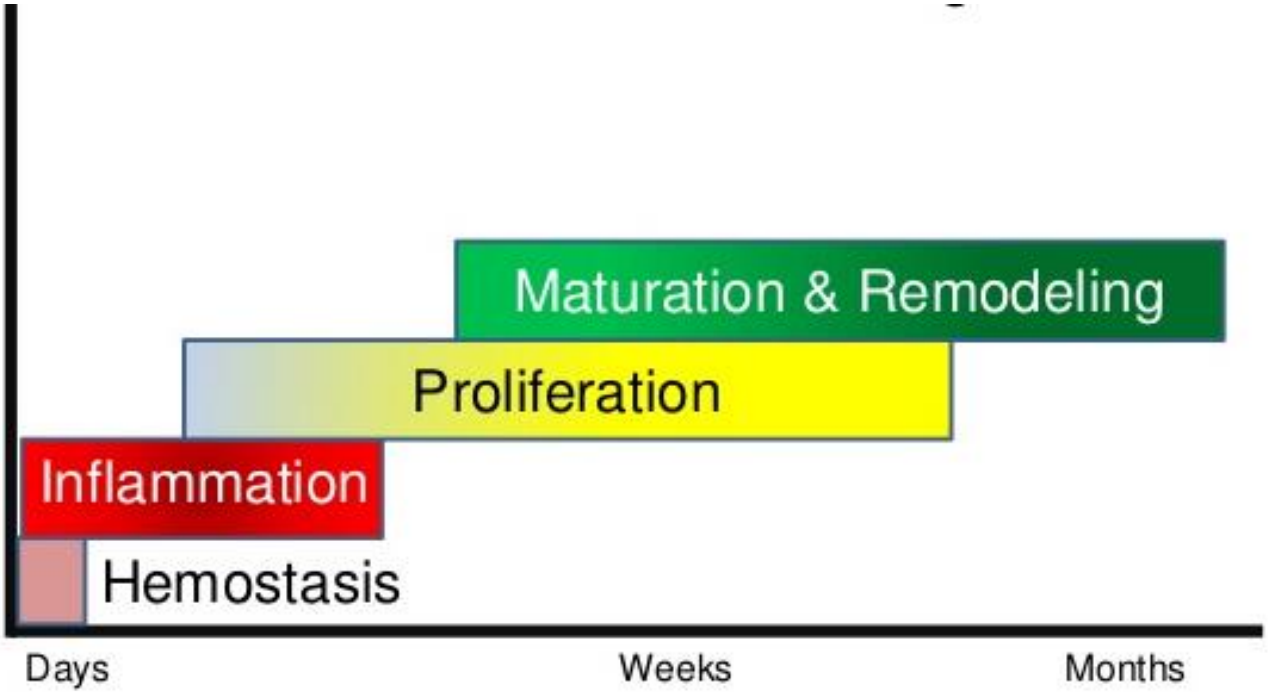


Differences between primary and secondary healing

Feature	Primary healing	Secondary healing
Cleanness	Clean	Unclean
Infection	Generally uninfected	May be infected
Margins	Surgically clean	Irregular
Healing	Scanty granulation tissue	Granulation tissue fill the gap
Healing period	Short	long
Healing direction	Direct healing	From the bottom to the edge
Outcome	Neat linear scar	Contracted irregular wound

Despite the differences in time taken and amount of scar tissue produced, the sequence of events in wound healing by primary and secondary intention is similar

Steps in Scar Formation



Normal sequence of wound healing

- Inflammatory phase
- Proliferative Phase
- Remodeling Phase

Starts 1st day lasts from 3-5 days

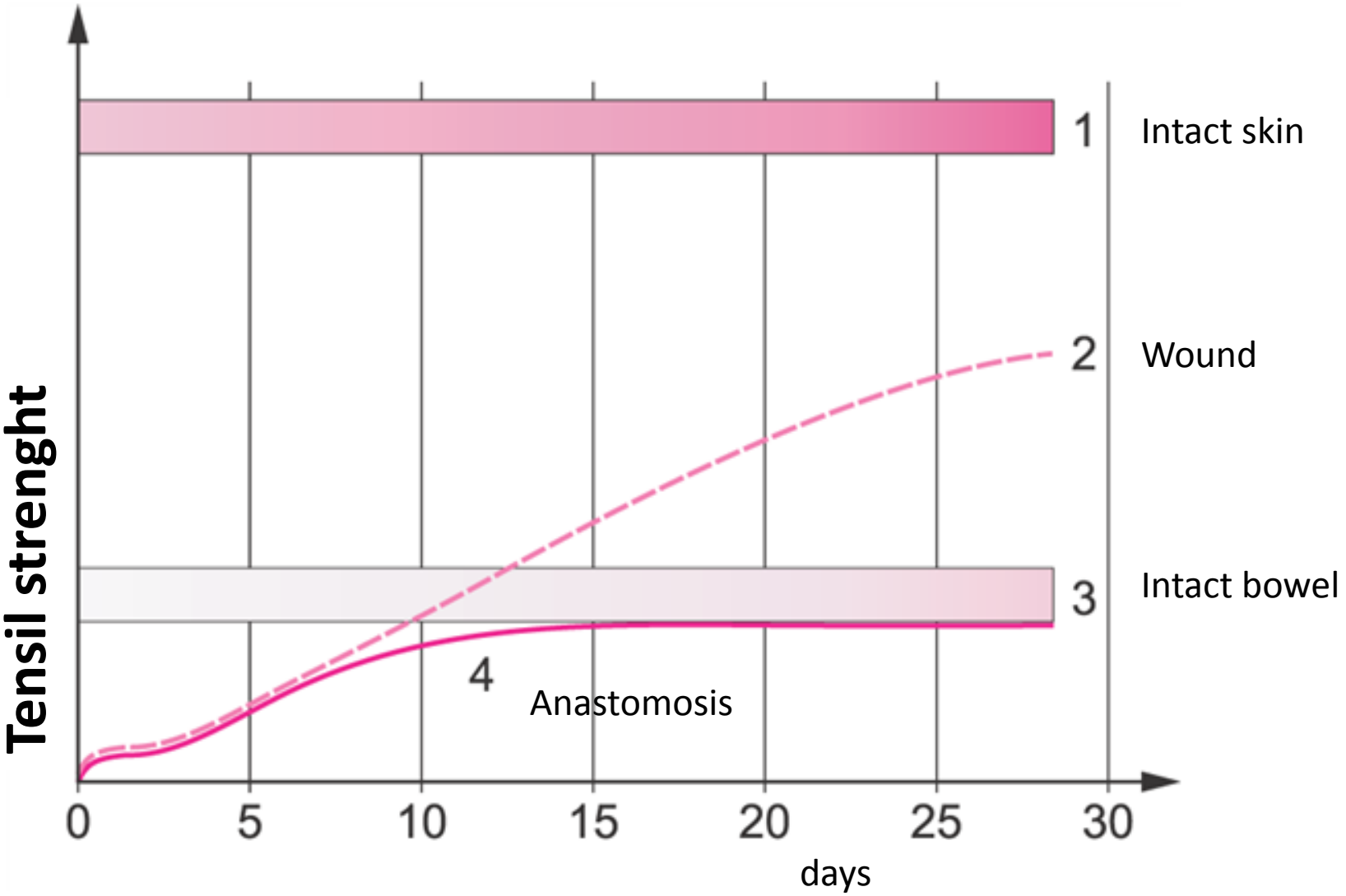
- 1st vasoconstriction
- 2nd blood clot formation
- 3rd platelets aggregation
- 4th platelets degranulation
- 5th vasodilatation
- 6th chemotaxis
  - Leucocytes
  - Neutrophils
  - Macrophages

Starts 3rd day lasts for 3rd week

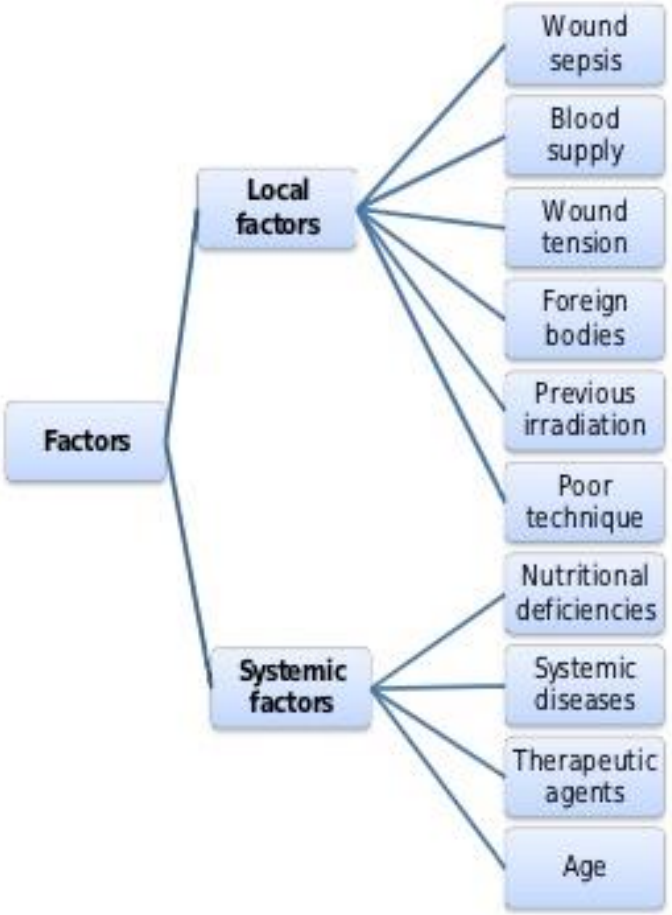
- 1st Angiogenesis
- 2nd fibroblasts migration
- 3rd formation of granulation tissue
- 4th reepithelialization

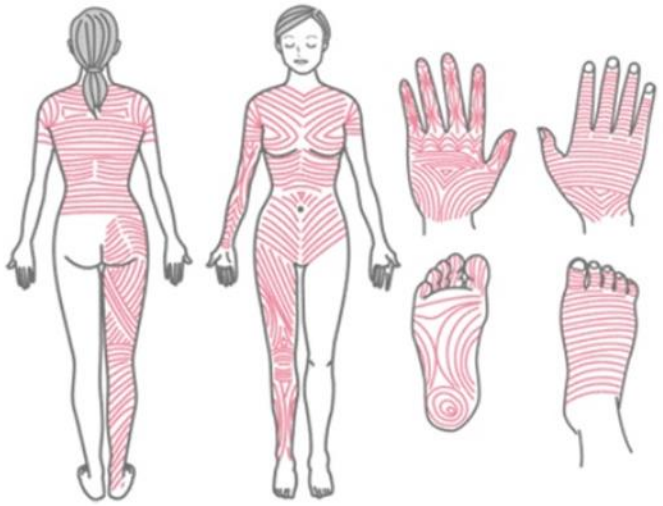
Starts from weeks to years

- The fibroblasts start to disappear
- Collagen type III is gradually replaced by stronger type I collagen
- The tensile strength of the scar tissue gradually increase


Tensil strenght
1
Intact skin
2
Wound
3
Intact bowel
4
Anastomosis
0
5
10
15
20
25
30
days

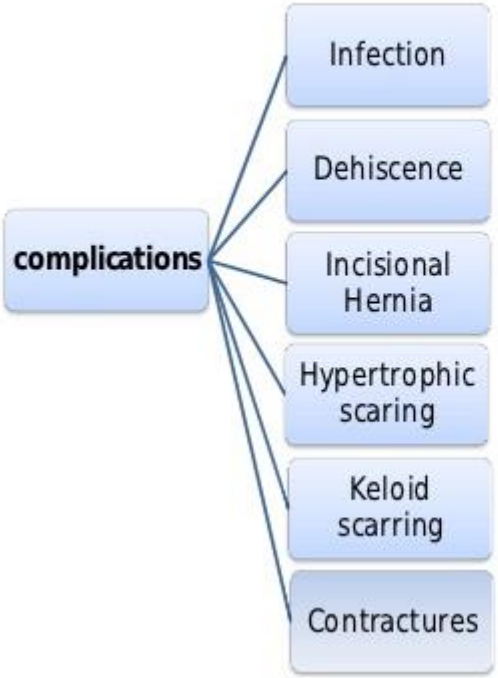
Factors affecting healing

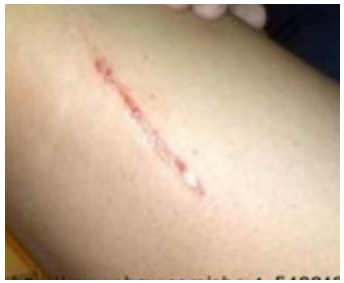


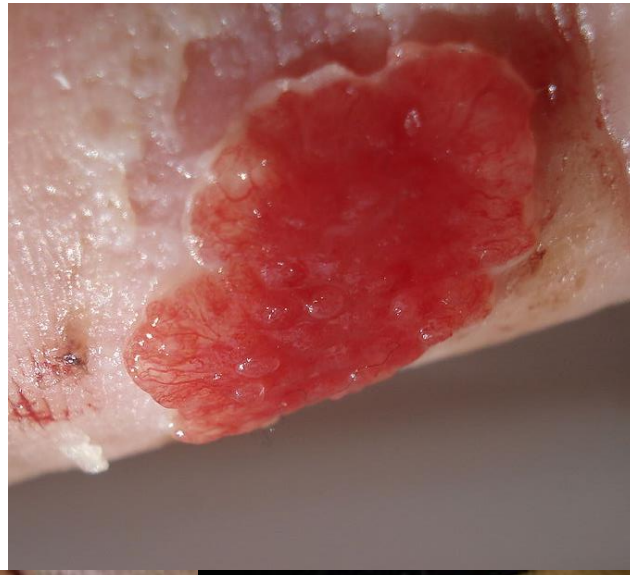


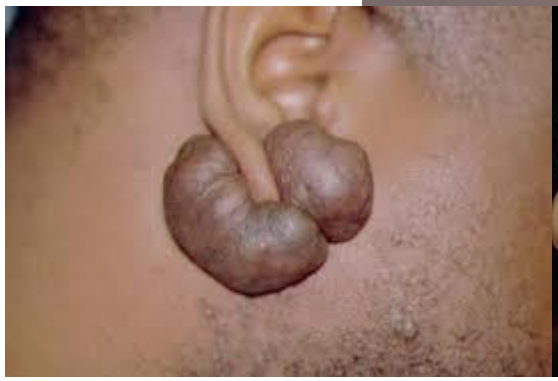
langer lines

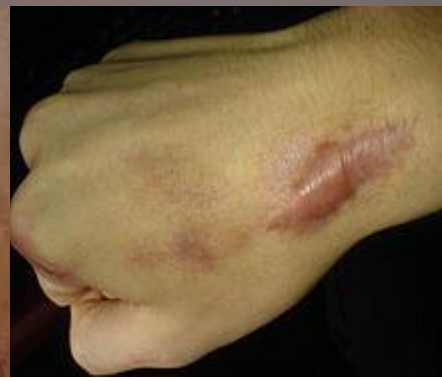
Complications of wound healing











Sometimes the granulation tissue undergoes striking proliferation beyond the wound margins. This is called EXUBERANT GRANULATIONS by physicians and "proud flesh" by the public.

More intractable are KELOIDS, (literally "crab claws") disfiguring scars with excessive collagen production, seen primarily in darkly-pigmented people.