Pathology

Phagocytes

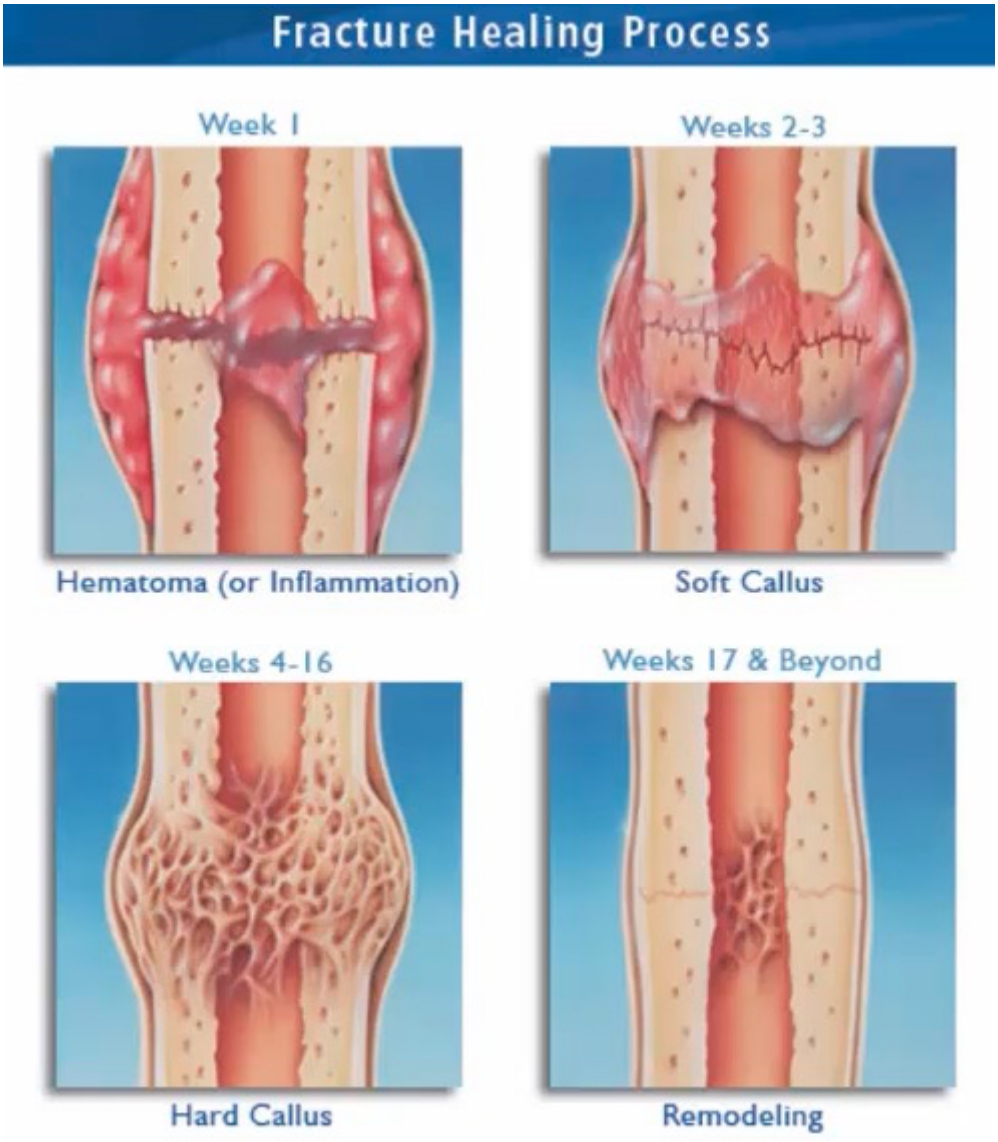
1. Granulocytes - neutrophils, eosinophils, basophils
2. Monocytes, macrophages, dendritic cells

Monocytes in bone marrow 20-40 hrs —> into blood stream and become reticuloendothelial system (liver, spleen, lymph nodes)
Become self-replicating in blood
Activated by cytokines such as IFN-gamma

1. Primary closure
    1. Suture a wound together
2. Delayed primary closure
    1. Delayed surgical closure, 2-3 days
    2. Eg dog bite or other contaminated wound, after washout, leave open for 1-2 days
3. Secondary intension healing
    1. Granulation tissue and epithelialisation
    2. SLOW process of healing

Phases of wound healing

1. Haemostasis
    - Platelet aggregation
    - Clotting cascade
    - Initial release of inflammatory factors: bradykinin, histamine, serotonin, complement proteins
2. Inflammatory
    1. Complement cascade activated
    2. Neutrophils migrate to remove necrotic tissue/bacteria - active for up to 4 days
    3. Monocytes —> migrate to wound site to become macrophages. Cytokines and growth factors released
3. Proliferative
    1. Begins day 2
    2. Fibroblasts start to form extra-cellular matrix
    3. Angiogenesis
    4. Granulation
    5. Epithelialisation - basal epidermal cells divide and migrate across new ECM
4. Remodelling
    1. More organised matrix remodelling
    2. Macrophages, fibroblasts, granulocytes
    3. *SCAR formation* - myofibroblasts promote tissue contraction - scar contraction and shrinkage
    4. Process up to 1 year - *avascular, acellular scar*



1. Reactive phase
    1. 1 week
    2. Platelet migration, haematoma formation, acute inflammation, fibroblast migration
2. Soft callous
    1. 2-3 weeks
    2. Chondroblasts and fibroblasts —> migrate into granulation tissue —> lay down hyaline cartilage
    3. Osteoblasts lay down ‘woven bone’ over hyaline cartilage = soft callous
3. Hard callous
    1. 1-3 months
    2. Osteoblasts lay day woven bone and trabecular bone
    3. Callous visible on XR by about 6 weeks
4. Remodelling
    1. Up to years
    2. Osteoblasts and osteoclasts —> remodelling of bone
    3. Trabecular bone replaced with stronger compact bone

Tendon Healing

Fibroblasts produce type III collagen within first week, large amounts of

Fibroblasts produce type III collagen within first week, large amounts of disorganized collagen produced by three weeks, this is gradually remodeled over up to 18 months to type I collagen.

Nerves
Neuropraxia
Axonotmesis – axon degenerates but surrounding tissues intact. Nerve can regenerate up to 2cm/month
Neurotmesis – neural integrity lost. Recovery is limited, but can improve with surgical repair

Cardiac Muscle
Necrotic muscle is invaded by granulation tissue and fibroblasts and ultimately replaced by scar tissue

Brain
No fibroblasts in the brain. Necrotic area ultimately removed by gliosis and volume of brain lost. Neuroplasicity allows some regain of function.

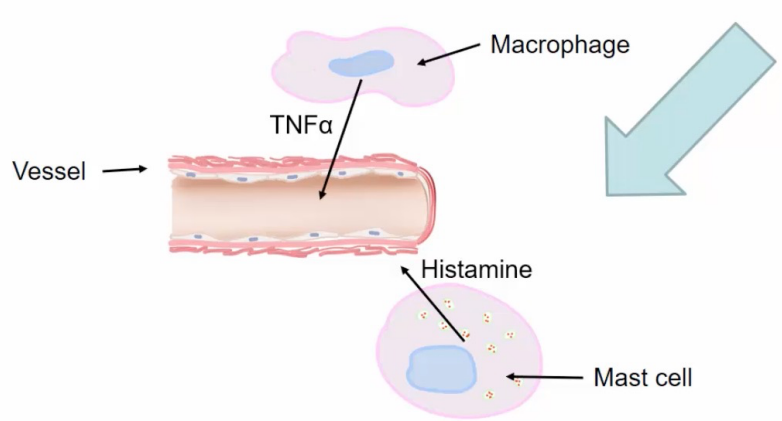
INFLAMMATION

Functions of inflammation

1. Deal with problem - e.g. virus/bacteria
2. Reduce damage
3. Initiate healing

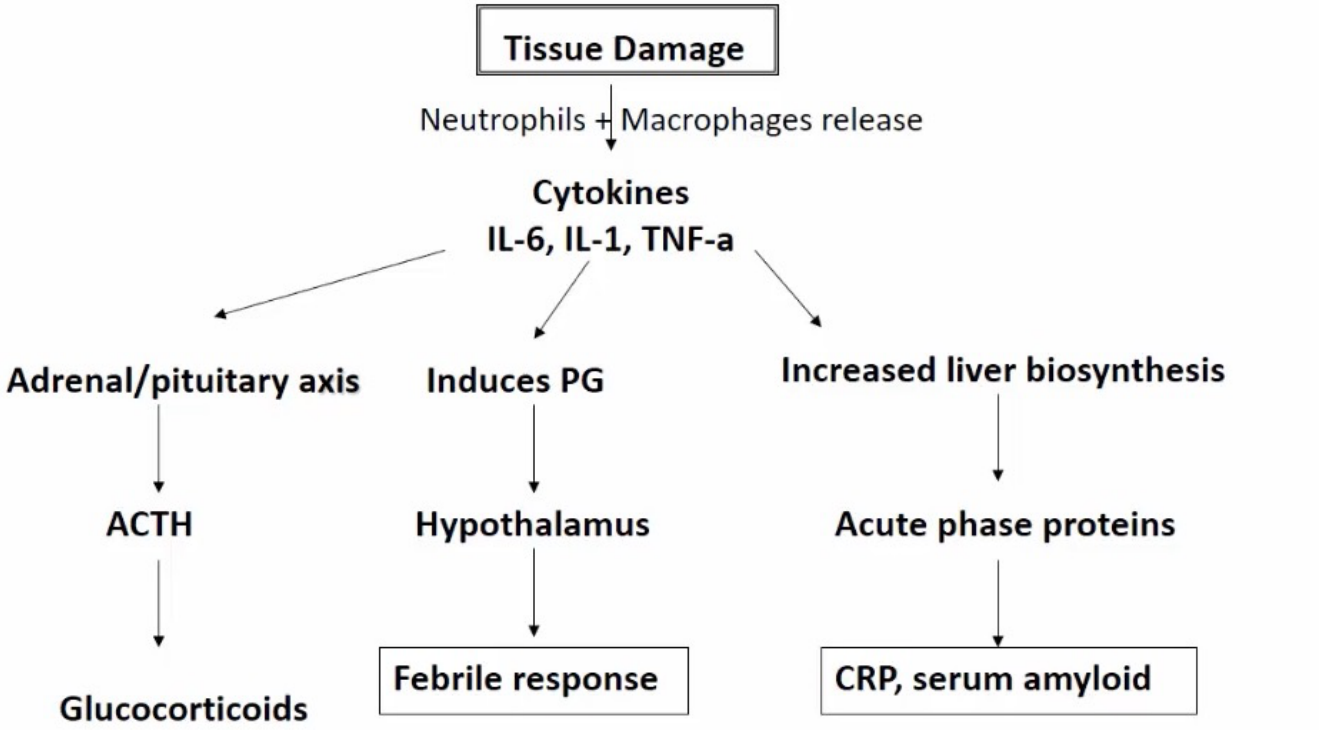
Acute phase reaction

Sentinel cells = dendritic cells, macrophages, mast cells



1. Injury —>
   - Macrophages phagocytose and release TNFa
   - Mast cells release histamine
2. —> these act on the endothelium of vessels, causes release of:
   - NO
   - Prostacyclin

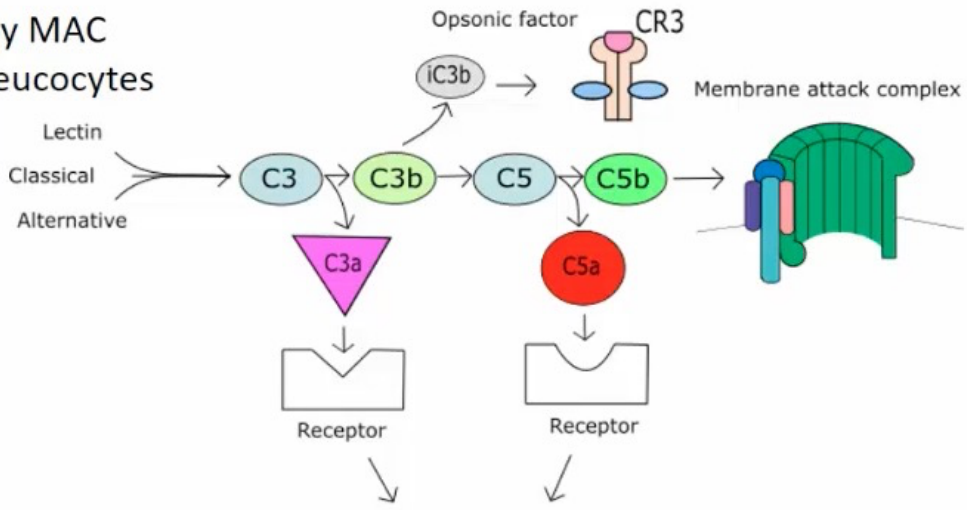
3. —> causes vasodilation
4. —> neutrophils adhere to vessel wall
    - Release of IL, cytokines etc
5. —> ↑ permeability of vessels —> allows neutrophils to migrate into tissues



Complement

Triggers:
1. Classical pathway IgG or IgG-antigen complex
2. Alternate pathway C3b binds to pathogen surface
3. Lectin pathway

Role
1) Lysis of bacteria by MAC
2) Chemotactic for leucocytes
3) Opsonisation
4) Inflammation



Prostaglandin and Eicosanoids

emergency courses

Leukotrienes
Produced in leukocytes from arachidonic acid.
Many actions in inflammation.
LTD4 important in smooth muscle contraction. Overproduced in asthma and allergic rhinitis

Prostaglandins
Many types in many tissues. Produced by COX-1 and COX-2.

Thromboxanes
Produced by activated platelets. Promote platelet aggregation and vasoconstriction.

Prostacyclins
Released by vascular endothelium. Vasodilator. Inhibit platelet aggregation.

2

HYPERSENSITIVITY REACTIONS

Type 1
Allergic / anaphylaxis / anaphylactoid

- Anaphylaxis =
  - Mast cells with *pre-formed* antibodies (IgE) attached —> bind to antigen
  - Mass degranulation —> histamine and other vasoactive substances
  - Tissue oedema, hypotension
- Anaphylactoid =
  - mast cells *without* pre-formed antibodies
  - *DIRECT* release of histamine etc from mast cells, not immune mediated

Type 2
Cytotoxic

- Antibody (IgM / IgG) binding with inappropriate antigen in body
- Circulating Abs bind to things that they shouldn't and cause mayhem
- Eg - RA, SLE, good pastures, transfusion reaction

Type 3

Immune complex (IgG / IgM)

- Circulating Abs and antigen combine and precipitate out as immune complexes to cause damage themselves
- Immune complexes cause small vessel damage

Type 4

Cell mediated

- **No** antibodies involved - *antigen directly stimulates T lymphocytes*
- Release of lymphokines and other inflammatory mediators
- Later stage reaction - graft rejection, contact dermatitis, tuberculin skin reaction (Mantoux test)