Septate Branching / acute angle Branching - aspergillus

Immunofluorescence -

microscopy - Dichroic mirror (allows only 2 light)

Background - Black.

Acanthamoeba - optically greenish white - cell wall

calcofluor white stain.

INFLAMMATION

- Acute Inflammation -

I) Vascular events - - Ist Transient vasoconstriction

↓

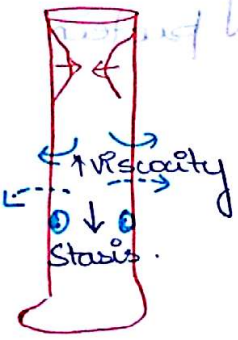
Vasodilatation

↓

↑ Vascular Permeability. - Hallmark of acute inflammat.

↓

Stasis (So that neutrophil can deviate to periphery).



Vascular Permeability

1) Endothelial gap - (m/c - mechanism)

- at the level of venules. except lungs - capillaries.

- Immediate / Transient response.

2) Direct endothelial injury - Immediate + prolonged

mild endothelial injury - Sunburn / radiation,

↓

delayed + prolonged

3) Leucocyte mediated - delayed Prolonged

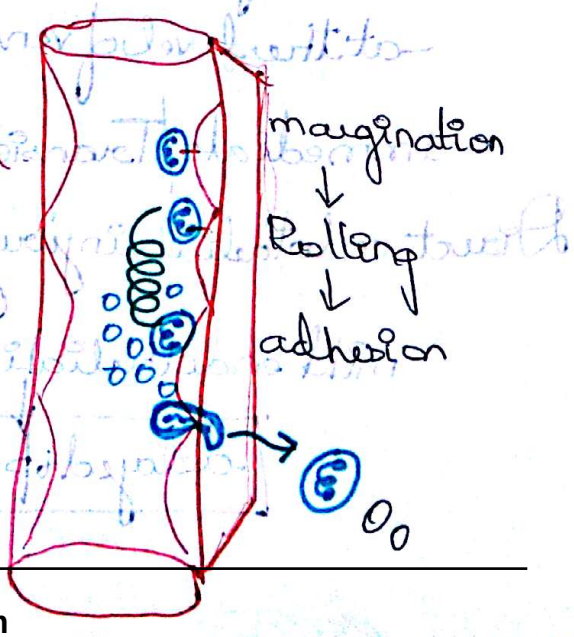
Endothelial gap

Endothelial Contraction (dominant)
- active
- Immediate & Transient
→ Chemical mediators.
Histamine/Serotonin.
Cm + R
↓
oxidative Phosphorylation
↓
↑ ATP production (short time, ↑energy)
↓ (active)
Polymerization of cytoskeletal protein

Endothelial Retraction
- passive
- Delayed & Prolonged.
- cytokine mediated.
↓
Reorganisation of cytoskeletal protein.

II Cellular events - Intravascular

i) Margination - Transient attachment of neutrophils to cell wall require Selectin



Selectin [CD-62]

P Selectin - Rolling only.

E - Selectin - endothelial

L -

2) Rolling - By Pselectin.

3) Adhesion - By Integrin - V-CAM.
I-CAM.

4) Pavementing - Overlayering of neutrophils.

Cytokine - activate both endothelium & Neutrophil → express
PECAM-1

Intravascular: NT - RAP.

5) Diapedesis - Transmigration of leucocytes through endothelial gap ; PECAM-1 - CD-31 (most P-adhesion molecule for diapedesis)

6) Chemotaxis - unidirectional movement, toward chemotactic stimuli. → i) Exogenous - Bacteria Toxin.

ii) Complements - C5a > C3a > C4a.
most potent anaphylatoxin - C5a.

iii) Cox pathway - PGI F2α PGI D2α (for neutrophil

iv) Liporygenase Pathway - LTB4

7) Phagocytosis

Adhesion molecules -

1) Selectin - cell to cell interaction only.
2) Integrin - cell to cell & cell to matrix interaction.
3) Ig Surface molecule - PECAM
4) Mucin like protein - Heparan sulphate

Leucocyte - Adhesion Defect -

→ Autosomal Recessive

→ Recurrent infection.

→ Neutrophilia [Leucocytosis]

LAD - I

m/c & aggressive.

β_2-chain of β_2 integrin

→ delayed cord separation of umbilical cord stump.

LAD - II

Sialyl Lewis ligand

a) Bombay Blood group.

LAD - III

FERMT - 13 gene mutation

immune defi

Bleeding like glanzmann thrombasthenia

i) Phagocytosis

Eosinophils also phagocytic - for parasites

ECM protein (fibronectin) can also be a opsonin

Opsonins
→ Best - IgG > IgM.
→ C3b.

Steps of Phagocytosis

I Recognition
↓ due to opsonization.

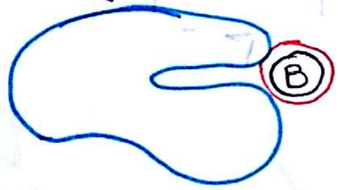
Scavenger Receptor - FcγIII R -
C3b | FcIgG.

Attachment

↑↑ Ca^{2+} → GTP↑
↓
polymerisation of actin.

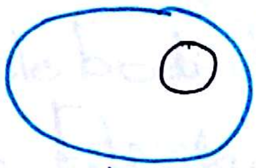
↓

Pseudopod.



↓

II Engulfment.



+
Lysosome - Respiratory Burst (Release of granules)
↓
NADPH oxidase

↓

Phagolysosome.

(Killing)
↓
acid Hydrolyases ← lysosomes
↓
Degradation

Killing & Degradation

Mechanism of Killing

Killing

O_2 dependent

m/c; m-effective

O_2 —(NADPH oxidase)→ O_2^- (superoxide FR.)

—(SOD)→ H_2O_2

H_2O_2 —(MPO, Cl^-)→ $HOCl^-$

H_2O_2-MPO Halide System

$HOCl^-$ most effective bactericidal agent in Phagocytic cells

Eosinophilic peroxide + I^- —(H_2O_2)→ HOI^- (Hypoiodide.)

HOI^- — most effective Parasitical agent.

O_2 Independent killing

→ Lactoferrin.

→ Lysozyme.

→ major Basic protein

Granulomatous disease

→ Phagocytosis - recurrent

defective Respiratory burst - PHOX gene mutation

membranous
- m/c type
- X-linked recessive
- Gp91phox.

cytoplasmic
- Autosomal Recess
- less common.
- p47, p67 } PHOX

Chediak Hegashi Syndrome-

Defect — Chemotaxis << Phagocytosis.

LYST gene mutation (Lysosomal Transferase)

→ Neutrophil → infection.

→ Platelets - Bleeding disorder.

α → Factor V, VIII, Fibrinogen.

β - PAF-4.

→ Schwann cells — Peripheral neuropathy.

→ Melanocytes → Albinism.

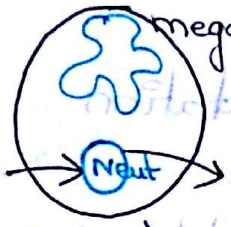
→ Dark-purple granules. (Dohle bodies)
Damaged Rough endoplasmic Reticulam

→ Septicemia m/c Cause

→ MDS

→ Chediak Hegashi Syndrome

Emperipolesis- → No change in morphology / physiology of cell.



Active penetration of one cell to another cell

→ 1) megakaryocte of NTDS.

2) Lymphoproliferative disorders - CTL

3) Rossi - Dorfman Syndrome

4) Autoimmune Hepatitis.

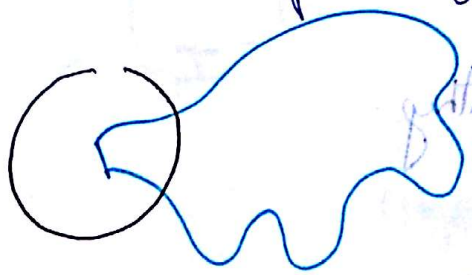
NET - Neutrophilic extracellula Traps.

for Histone polynucleotid complex breakdown

→ Arginine - required.

Traps formed by Thrown out nuclear chromatin

by help of arginine that breaks Histones.



Thrown out nuclear chromatin

↓

Possess antimicrobial Traps.

NETosis → process of throwing out

→ Beneficial Suicide

Inflammatory mediators

Origin - Liver | cells

Plasma mediators

- Bradykinin
- Complement
  - C5a - potent anaphylactin
  - C3b - potent opsonin
  - C5-9 - MAC
    - ↑ Infection ⇒ encapsulated organism.
  - m|I - Cg → Perforin
    - punch Hole
  - C5-8 - lysis
- Clotting factors

Cellular mediators

Preformed

→ Histamine (Histidine)
- Richest in mast cells.

→ Serotonin - Richest Platelet

→ Heparin

Newly synthesized

I] Arginine → NO.

II] EFA → AA metabolites
- Linoleic acid
  - LOX
  - COX

III] PAF

IV] Cytokines: IL, TNF

→ Histamine | PAF | Serotonin | Bradykinin:
- → Vasodilation
- → ↑ Vascular Permeability.
- → Smooth muscle Contraction.

Histamine - both vasoconstrictor & vasodilation
- ↓
- in large arteries.

→ PAF: Transcellular Signal Transduction.
- Vasoconstriction > vasodilatation.

Bradykinin - m/I Inflammation - Pain

m/I Role in acute inflammation - vascular permeability

Pain

m/I Substance - Substance P.

Bradykinin m/I function - Pain

Arachidonic acid Metobolites

AA (Lox pathway)

5 - LOX → LTA_4 - B_4

C_4, D_4, E_4 } SRS - A.

12 LOX

Lipoxin - anti-inflammatory Substance.

→ inhibit neutrophilic chemotaxis

→ activate macrophage & monocyte - apoptosis of neutrophil

→ inhibit natural killer cell

Cox

AA → $PGIG_2$ → PGH_2

PGH_2 → PGI I_2 (Prostacyclin) + Thromboxane A_2 + $PGIE_2\alpha$

endothelial Richest Source

Thromboxane A_2 - Richest Source Platelet

Thromboxane A_2 i) Plateletaggregation ii) Vasoconstaiction.

PGI_2 Endothelial cell
i) Vasodilation
ii) Plate antiaggregation

PGE2α : pain & fever.
PGF2α G2α - chemotaxis.

QQQ

CYTOKINES :

→ Soluble proteins
→ Synthesized by both Hematopoeitic & non Hematopoeitic cell
→ associated with immunological repair & wound Healing
- Cytokines are highly specific.

IL-2 - Hi - growth factor - NK cells
IL-4 - mast cells
IL-5 - Eosinophils.
IL-6 - Plasma cells - & pathogenesis of multiple myeloma
IL-8 : neutrophil chemotaxis.

Most Important Cytokines

IL-1 : Fever, m/I.
other pyrogens - IL-6; TNF α, IFN-γ, ciliary neutrophic factors.

Acute inflammation } m/I - TNF-α.
Septic Shock
SIRS
Cancer Cachexia } TNF-α.

vi] Fibrosis - TGF-β

vii] Angiogenesis - VEGF

Synthesis of acute Phase Reactant → IL-6

Both morphogenic + mitogenic activity (cell proliferation)

↓

Organogenesis → BMP (TGF-β family) Q

→ Granuloma formation - INF-γ > TNF-α (Both)

→ Anti-Inflammatory Cytokine - IL-4, 6, ~~10, TGFβ~~ (Both pro anti I)

IL-10, 13, TGFβ

CHRONIC INFLAMMATION

1) Mononuclear cell infiltration

macrophage >> Lymphocyte

Cytokine

2) Tissue destruction → Hallmark of chronic inflammation.

3) Wound Healing

Granuloma - Pattern of chronic inflammation.

Mechanism - TB Ag → Macrophage → IFN-γ

↓

CD4TH1

↓

IFN-γ

1) Macrophage → epithelioid cells

N foamy

Oval

N elongated.)

Function ER activated → Release of enzymes

II function - Phagocytosis.

2) Lymphocyte proliferation & differentiation.

Fibrinoid necrosis - contain fibrin + immune complexes

Q.

Epithelium

cell

BM

→ Brunner gland cells.

Epithelioid

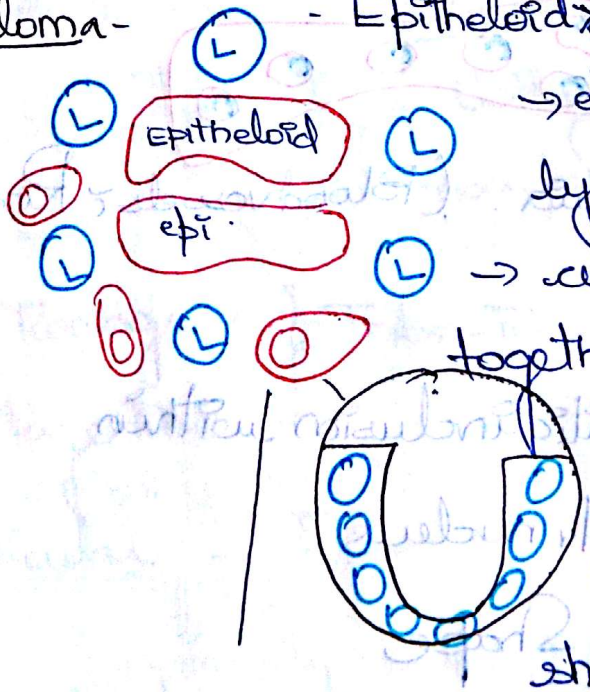
No Basement membrane

→ Islet cells of pancreas

→ Leydig cells

→ Theca lutein cells.

Granuloma - - Epithelioid > macrophage.



→ epithelioid surrounded by lymphocytes + plasma cells.

→ cell wall fragile & fuse together.

Langhans giant cells - peripheral horse shoe shaped nuclei arrangement.

Foreign body giant cells - nucleus Haphazardly arranged.

Non-caseating granuloma - Hodgkin's
Sarcoidosis.
Tuberculoid Leprosy (non-necrotizing)

TB - Both metastasis.
Caseating & non-caseating

Caseating: TB, (plain, cotton-wool like fluffy area)
Histoplasmosis
Syphilis
Coccidiomycosis

Special Types - Granuloma

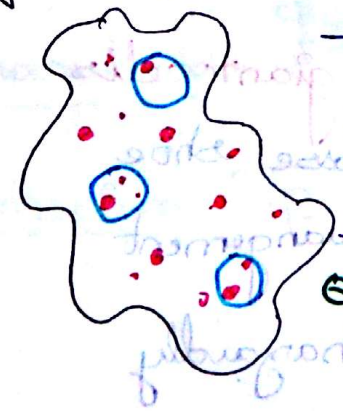
→ Stellate granuloma - neutrophils are present.
Cat Scratch disease, LGV, Syphilis

→ Eosinophilic granuloma - Churgg-Strauss disease

→ Durks Granuloma -

↓
Field stain. In Cerebral malaria. (Blood vessels & Ring forms)

Types of Giant cells -

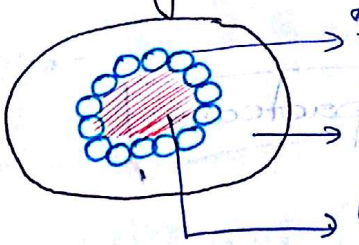


→ eosinophilic inclusion within both cytosol & nucleus
→ amoeboid shape

Wathin Findeley giant cells

Hecht's pneumonia - measles pneumonia

ii) Touton giant cells - Xanthoma



Wound Healing

→ Granulation Tissue - Hallmark of wound Healing:

i) Fibroblasts (proliferating) 

ii) Proliferating Blood vessels  - varying Sizes/ shape.

iii) Non Specific inflammation.

Collagen - Both Type I & III [also in liver cirrhosis]

Collagen - Source of collagen myofibroblasts except in Liver - Stellate cells (ITO cells).

bONE - Type - I → Collagen vulgaris
+ skin - max. tensile strength.

Cart Twolage - } Type - II
Cartilage Fibw

In Reticular - Type - III

Basement membrane - Type - IV
(Floor)

Granulation Tissue → Scar Tissue

www.FirstRanker.com

Tissue Remodelling.

Matrix metallo protease

Imp-Co-factor Zinc

Cutaneous Wound Healing

Primary intension

Surgical incision

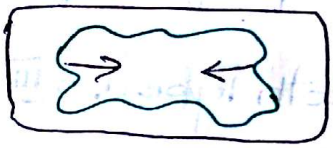
with opposed edges

No wound Contraction

Secondary intesion

Loss of Tissue..

Wound Heading ∵ gap → Wound Contraction.



myofibroblast - Responsible for wound contraction.

↑

origin - mesenchyme.

→ Special Type of fibroblast, smooth muscle like contractio

Chronology -

D_1 - Appear 1st - Platelet > Neutrophils (appears 1st by chemotaxis).

Neutrophil (lifespan) < Peripheral blood - 6hours
Tissue +3days

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Platelet's life span - 7 days

Day 3 - Macrophages, early granulation tissue

Day 5 - Maximum granulation Tissue & epidermal thickness Recovered.

Day 14 - maximum collagen deposition.

Day 28 - Scaring completed.

Myocardial Infarction -

Day 7-10 - early granulation Tissue.

Day 10-14 - maximum granulation Tissue.

2 month - Scaring complete.

Strength gain after cutaneous wound Healing -

Day 7 (1 week) - 10% of original.

100% → never acheive

maximum strength - at the end of 3rd month - 70-80%.

Fetal Cutaneous wound Healing - No Scarring.

Due to lack of expression of Osteopontin gene.

→ No fibrosis → TGF-β X