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

↓

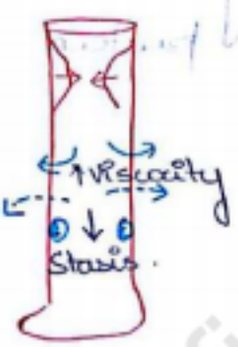
Vasodilatation

↓

↑ Vascular Permeability - Hallmark of acute inflammd.

↓

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 www.FirstRanker.com

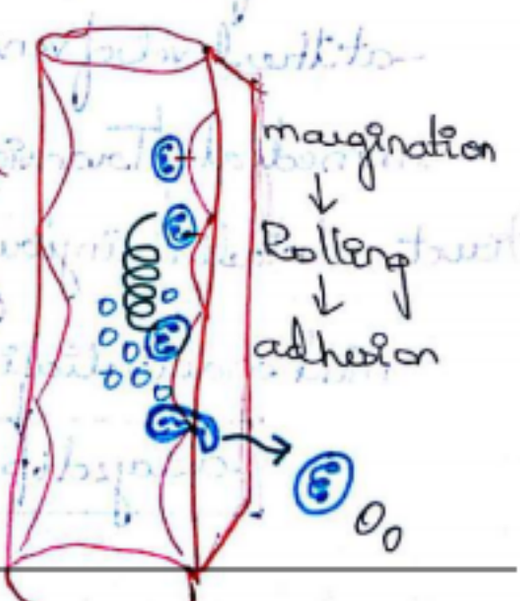
Endothelial gap

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

1) 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 – $C_{5a} > C_{3a} > C_{4a}$.
most potent anaphylatoxin – C_{5a}.

iii) Cox pathway – $PGI_{2\alpha}$ $PGD_{2\alpha}$ (for neutrophil

iv) Lipoxygenase Pathway – LTB_4

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 seperation of umbilical cord stump.

LAD - II

Sialyl Lewis ligand
a/: Bombay Blood group.

LAD - III

FERMT - 1 gene mutation
immune defi
Bleeding like glanzmann thrombasthenia

1) Phagocytosis

Basinophils also phagocytic - for parasites.

Opsonins - ECM protein (fibrinonectin) can also be opsonin

→ Best - IgG1 > Igm.

→ C3b.

Steps of Phagocytosis

I Recognition

due to opsonization.

Scavenger Receptor - TcR III R -

Attachment

C3b / Fc IgG1.

Ca^{2+} → GTP↑

↓

polymerization of actin.

Pseudopod.

II Engulfment.

Phagosome

+

Lysosome - Respiratory Burst (Release of granules)

↓

NADPH oxidase

Phgdysosome.

Killing

↓

lysosomes

acid Hydrolyases

↓

Degradation

Killing + Degradation

Mechanisms of Killing

Killing

O_2 dependent

m/c; m-effective

$O_2 \xrightarrow{\text{NADPH oxidase}} O_2^-$ (superoxide ?R.)

$\xrightarrow{SOD}$

H_2O_2

H_2O_2 - MPO Halide System

$\xrightarrow{MPO,\ Cl^-}$

$HOCl^-$

most effective bactericidal agent in Phagocytic cells

Eosinophilic peroxide + I^-

H_2O_2 → HOI^- (Hypoiodide)

most effective Parasitical agent

O_2 independent killing

→ Lactoferrin.

→ Lysozyme.

→ major Basic protein

Job's Syndrome / Hyperimmunoglobulinemia E syndrome

→ Phagocytosis - recurrent staphylococcal infections

defective Respiratory burst - PHOX gene mutation

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

cytoplasmic
- Autosomal Recessive
- 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 Reticulum

→ 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

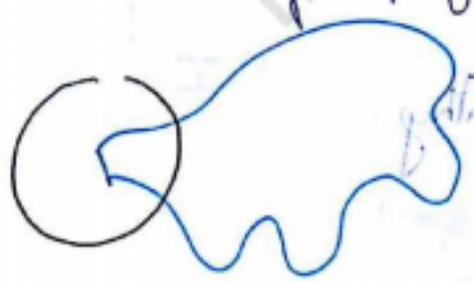
3) Rosai-Dorfman Syndrome

4) Autoimmune Hepatitis.

NET - Neutrophilic extracellular Trap -
for Histone polynucleotid complex breakdown

→ Arginine - required.

Traps formed by Thrown out nuclear chromatin
by help of arginine that breaks Histones.



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.

mII - C9 → Perforin

punch Hole

C5-8 - lysis

Cellular mediators

Preformed

→ Histamine (Histidine)

- Richest in mast cells.

→ Serotonin - Richest Platelet

→ Heparin

Newly synthesized

I] Arginine → NO.

II] EFA → AA metaboli.

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 Pain

m/I Role in acute inflammation – vascular permeability

Pain

m/I Substance – Substance P

Bradykinin m/I function – Pain

Arachidonic acid Metabolites

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

PGI G_2 → PG H_2

PG H_2 → PGI I_2 (Prostacyclin) – endothelial Richest Source

PG H_2 → Thromboxane A_2 – Richest Source Platelet

PG $E_{2\alpha}$

Thromboxane A2 - i) Plateletaggregation
ii) Vasoconstriction.

PGI2 - 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; TNFα, IFN-γ, ciliary neutrophic factors.

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

TNF-α.

vi] Fibrosis - TGF

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

↓

CD4 TH1

↓

IFN-γ

1) Macrophage → epithelioid cell

Foamy

Oval

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.

Epithelioid

epi.

L

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 metastatic
Caseating & non-caseating

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

Special Types - Granuloma

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

→ Eosinophilic granuloma - Churgg-Strauss disease

→ Dusk's Granuloma - 
↓
Field stain. In Cerebral malaria. (Blood vessels & Ring forms)

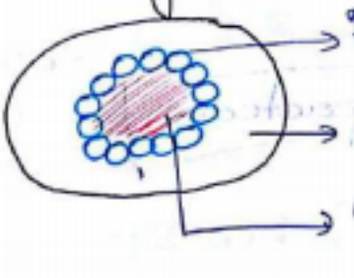
Types of Giant cells -

→ eosinophilic inclusion within both cytosol & nucleus
→ amoeboid shape

Wathin Findeley giant cells

Hecht's pneumonia - measles pneumonia

ii) Foam 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

Tissue Remodelling:

Matrix metallo proteases

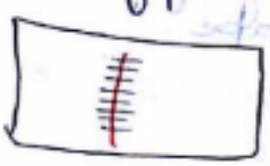
Imp-Co-factor Zinc

Cutaneous Wound Healing

Primary intension

Surgical incision

with opposed edges

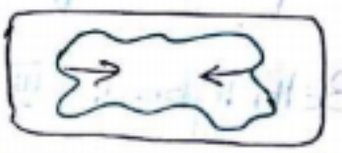


No wound Contraction

Secondary intension

Loss of Tissue..

Wound Healing ∵ 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

Platelet life span - 1 day

Day 3 - Macrophages, early granulation tissue

Day 5 - Maximum granulation Tissue & epidermal thickness Recovered.

Day 14 - maximum collagen deposition.

Day 28 - Scaring completed.

Myocardial Infaction -

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.