Inflammation

(Concept) Understand the chain, progression, or sequence of vascular and cellular events in the histologic evolution of acute inflammation

SEQUENCE OF EVENTS

• NORMAL HISTOLOGY ➔
• VASODILATATION ➔
• INCREASED VASCULAR PERMEABILITY ➔
• LEAKAGE OF EXUDATE ➔
• MARGINATION, ROLLING, ADHESION ➔
• TRANSMIGRATION (DIAPEDESES) ➔
• CHEMOTAXIS ➔
• PMN ACTIVATION ➔
• PHAGOCYTOSIS: Recognition, Attachment, Engulfment, Killing (degradation or digestion) ➔
• TERMINATION ➔
• 100% RESOLUTION, SCAR, or CHRONIC INFLAMMATION are the three possible outcomes

ACUTE INFLAMMATION

● “PROTECTIVE” RESPONSE
NON-specific ACUTE INFLAMMATION

VASCULAR EVENTS

CELLULAR EVENTS (PMN or PolyMorphonuclear Neutrophil, Leukocyte?, “POLY”, Neutrophil, Granulocyte, Neutrophilic Granulocyte

“MEDIATORS”

ACUTE INFLAMMATION STIMULI for acute inflammation

INFECTIOUS

PHYSICAL

CHEMICAL

Tissue Necrosis
• Foreign Bodies (FBs)
• Immune “responses”, or “complexes”
  Vascular Changes
• Changes in Vascular Flow and Caliber
• Increased Vascular Permeability
  INCREASED PERMEABILITY
• DILATATION
• Endothelial “gaps”
• Direct Injury
• Leukocyte Injury
• Transcytosis (endo/exo)
• New Vessels
LEAKAGE OF PROTEINACEOUS FLUID (EXUDATE, NOT TRANSUDATE)
EXTRAVASATION of PMNs
• **MARGINATION** (PMN’s go toward wall)
• **ROLLING** (tumbling and HEAPING)
• **ADHESION**
• **TRANSMIGRATION** (DIAPEDEESIS)
  ADHESION MOLECULES (glycoproteins) affecting ADHESION and TRANSMIGRATION
• **SECRETINS** (from endothelial cells)
• **INTEGRINS** (from many cells)

**CHEMOTAXIS**

PMNs going to the site of “injury”
AFTER transmigration

**LEUKOCYTE**
“ACTIVATION”

• “triggered” by the offending stimuli for PMNs to:
  — 1) Produce eicosanoids (arachidonic acid derivatives)
     • Prostaglandin (and thromboxanes)
     • Leukotrienes
     • Lipoxins
  — 2) Undergo DEGRANULATION
3) Secrete CYTOKINES
PHAGOCYTOSIS

• RECOGNITION

• ENGULFMENT

• KILLING (DEGRADATION/DIGESTION)
CHEMICAL MEDIATORS

• From plasma or cells

• Have “triggering” stimuli

• Usually have specific targets

• Can cause a “cascade”

• Are short lived
CLASSIC MEDIATORS

• HISTAMINE

• SEROTONIN

• COMPLEMENT
• KININS
• CLOTTING FACTORS
• EICOSANOIDs
• NITRIC OXIDE
• PLATELET ACTIVATING FACTOR (PAF)
• CYTOKINES
• /CHEMOKINES
• LYSOSOME CONSTITUENTS
• FREE RADICALS
• NEUROPEPTIDES
  HISTAMINE
• Mast Cells, basophils
• POWERFUL Vasodilator
• Vasoactive “amine”
• IgE on mast cell
  SEROTONIN
• (5HT, 5-Hydroxy-Tryptamine)
• Platelets and EnteroChromaffin Cells
• Also vasodilatation, but more indirect
• Evokes N.O. synthetase (a ligase)

COMPLEMENT SYSTEM
• >20 components, in circulating plasma
• Multiple sites of action, but LYSIS is the underlying theme

KININ SYSTEM
• BRADYKININ is KEY component, 9 aa’s
• ALSO from circulating plasma
• ACTIONS
  — Increased permeability
  — Smooth muscle contraction, NON vascular
  — PAIN

CLOTTING FACTORS
• Also from circulating plasma
• Coagulation, i.e., production of fibrin
• Fibrinolysis
EICOSANOIDS
(ARACHIDONIC ACID DERIVATIVES)

- Part of cell membranes

1) Prostaglandins (incl. Thromboxanes)

2) Leukotrienes

3) Lipoxins (new)

Prostaglandins
(thromboxanes included)

- Pain

- Fever

- Clotting

Leukotrienes

- Chemotaxis
• Vasoconstriction

• Increased Permeability
  Lipoxins

• INHIBIT chemotaxis

• Vasodilatation

• Counteract actions of leukotrienes
  Platelet-Activating Factor
  (PAF)

• Phospholipid

• From MANY cells, like eicosanoids

• ACTIVATE PLATELETS, powerfully
  CYTOKINES/CHEMOKINES

• CYTOKINES are PROTEINS produced by MANY
  cells, but usually LYMPHOCYTES and
  MACROPHAGES, numerous roles in acute and
  chronic inflammation
TNFα, IL-1, by macrophages

- CHEMOKINES are small proteins which are attractants for PMNs (>40)
- NITRIC OXIDE
  - Potent vasodilator
  - Produced from the action of nitric oxide synthetase from arginine
- LYSOSOMAL CONSTITUENTS
  - PRIMARY
    - Also called AZUROPHILIC, or NON-specific
    - Myeloperoxidase
    - Lysozyme (Bact.)
    - Acid Hydrolases
  - SECONDARY
    - Also called SPECIFIC
    - Lactoferrin
• Lysozyme
• Alkaline Phosphatase
• Collagenase

FREE RADICALS

• O2 – (SUPEROXIDE)

• H2O2 (PEROXIDE)

• OH⁻ (HYDROXYL RADICAL)

VERY VERY DESTRUCTIVE

NEUROPEPTIDES

• Produced in CNS (neurons)

• SUBSTANCE P

• NEUROKININ A

OUTCOMES OF ACUTE INFLAMMATION

• 1) 100% complete RESOLUTION
2) SCAR

3) CHRONIC inflammation
   Morphologic PATTERNs
   of Acute INFLAMMATION
   (EXUDATE)

• Serous (watery)
• Fibrinous (hemorrhagic, rich in FIBRIN)
• Suppurative (PUS)
• Ulcerative

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• TERMINATION →
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CHRONIC INFLAMMATION (MONOS)
CAUSES of
CHRONIC INFLAMMATION

• 1) PERSISTENCE of Infection

• 2) PROLONGED EXPOSURE to insult

• 3) AUTO-IMMUNITY
  Cellular Players
• LYMPHOCYTES
• MACROPHAGES (aka, HISTIOCYTES)
• PLASMA CELLS
• EOSINOPHILS
• MAST CELLS

MORPHOLOGY

• INFILTRATION

• TISSUE DESTRUCTION

• HEALING

GRANULOMAS
GRANULOMATOUS INFLAMMATION
GRANULOMAS
GRANULOMATOUS INFLAMMATION
LYMPHATIC
DRAINAGE

• SITE → REGIONAL LYMPH NODES
SYSTEMIC MANIFESTATIONS
(NON-SPECIFIC)
• FEVER, CHILLS
• C-Reactive Protein (CRP)
• “Acute Phase” Reactants
• Erythrocyte Sedimentation Rate (ESR) increases
• Leukocytosis
• Pulse, Blood Pressure
• Cytokine Effects, e.g., TNF(α), IL-1