INFLAMMATION

L 27 - CHEMICAL MEDIATORS

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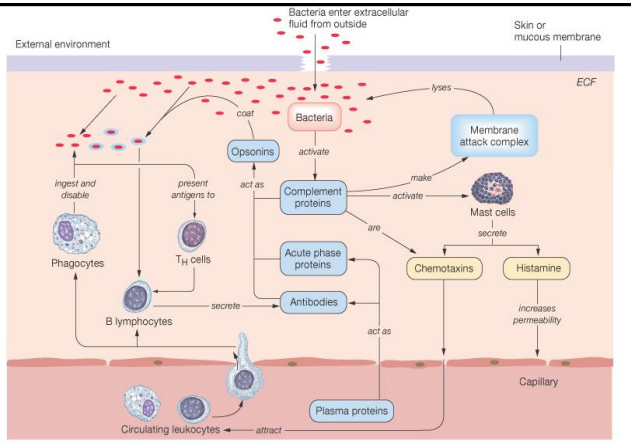
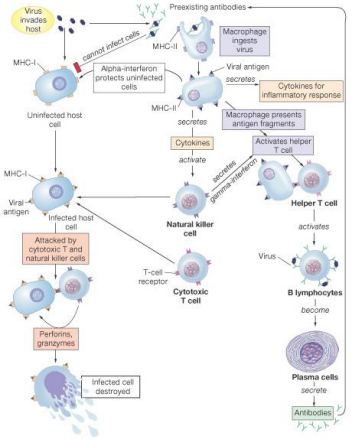
Most Important Inflammatory Mediators

- Vasodilation
  - Prostaglandins
  - NO
- Vascular Permeability
  - Histamine, Serotonin
  - C3a, C5a (through amines)
  - Bradykinin
  - Leukotirenes C4,D4,E4
  - PAF
- Chemotaxis, leukocyte activation
  - C5a
  - LTB4
  - Chemokines
  - LPS
- Fever
  - IL-1, IL-6, TNF
  - Prostaglandins
- Pain
  - Prostaglandins
  - Bradykinin
  - Serotonin
- Tissue damage
  - Neutrophil and macrophage lysosomal contents
  - O_2 metabolites
  - NO

Mediators of Acute Inflammation.

Mediator	Vasodilation	Immediate	Sustained	Chemotaxis	Opsonin	Pain
Histamine	+	+++	–	–	–	–
Serotonin (5–HT)	+	+	–	–	–	–
Bradykinin	+	+	–	–	–	++
Complement 3a	–	+	–	–	–	–
Complement 3b	–	–	–	–	+++	–
Complement 5a	–	+	–	+++	–	–
Prostaglandins	+++	+	+?	–	–	
Leukotrienes	–	+++	+?	+++	–	–
Lysosomal proteases	–	–	++	–	–	–
Oxygen radicals	–	–	++	–	–	–





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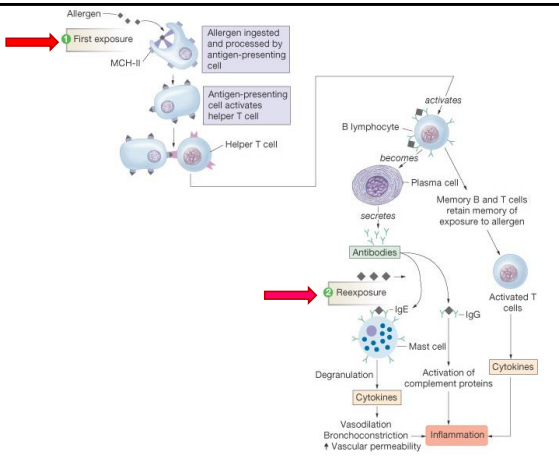

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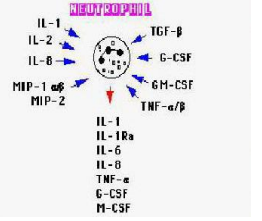
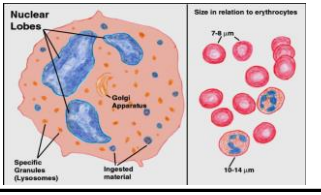
CELLS OF INFLAMMATION

1. NEUTROPHILS

- First Cells
- Short Lived (1-2 Days)
- 10-14 µm
- Fast Mover
- Bactericidal
- Recently, — Abundant — Virally Induced Lesions.





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ANTIMICROBIAL OR CYTOTOXIC SUBSTANCES,

- Neutral Proteinases,
- Acid Hydrolases
- Azurophil Granule -- Myeloperoxidase (Mpo)
  - MPO ---- green color of pus.
- Defensins, — cytotoxic to a broad range of bacteria, fungi and some viruses.
- Bacterial permeability-increasing (BPI) protein — Perforins
- Lactoferrin sequesters free iron

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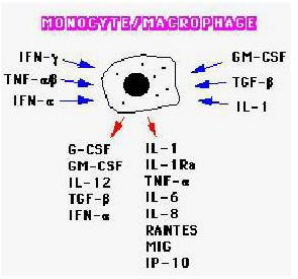
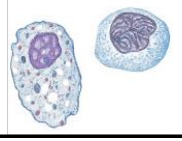
2. MONOCYTE / MACROPHAGE

- Long Lived
- Slow Mover
- In Tissues 15 – 80 µm
- Giant Cells
- Major Function — Phagocytosis Of Bacteria, Tissue Debris and Lipid Residues
- Also Active Against Fungi, Protozoa and Viruses.





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Fixed macrophages

- The hepatic Kupffer cells,
- sinus histeocytes of lymph nodes,
- microglia cells of nervous system
- and pulmonary intravascular macrophages

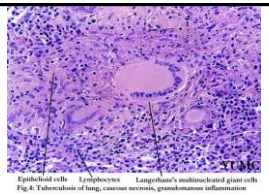

Fig.4: Tuberculosis of lung, caseous necrosis, granulomatous inflammation

FUNCTIONS

- Involved at all stages of the immune response.
- Activated macrophages — intracellular **bacteria**, pathogenic **protozoa**, **fungi** and **helminths** as well as against **tumours**,
- After phagocytosis, — prevent replication:
  - Low pH and lack of nutrients in a phagolysosome.
  - The toxic reaction — ROI, hypochlorite, myeloperoxidase, neutral proteases and lysosomal hydrolases.
  - Produce microbiostatic effector molecules at a steady-state

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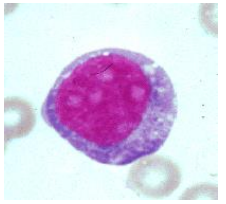
3. LYMPHOCYTES AND PLASMA CELLS

- Participate late in an inflammatory reaction
- Major cell in chronic inflammation
- Involvement of lymphocytes from the beginning – Leptospirosis in dogs
- Lymphocytes are slow-mover than neutrophils and monocytes



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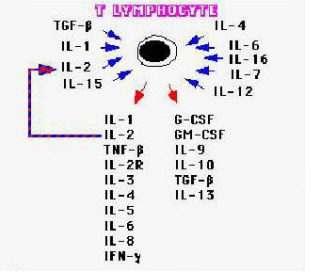
T-LYMPHOCYTES

- Helper T-lymphocytes (Th- Cells) - produce cytokines for B and CTL
- Cytotoxic T-lymphocytes (CTL) - kill target cells.
- Absence of Th cells can occur as in HIV infection



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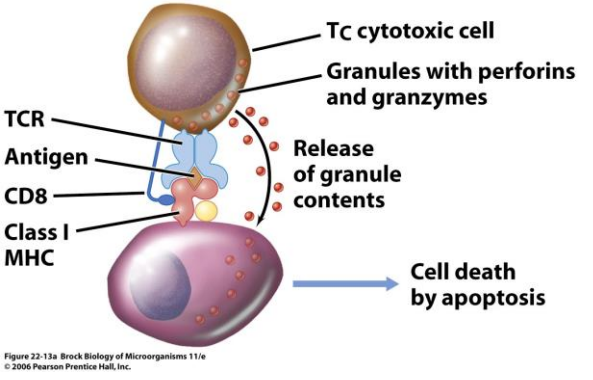

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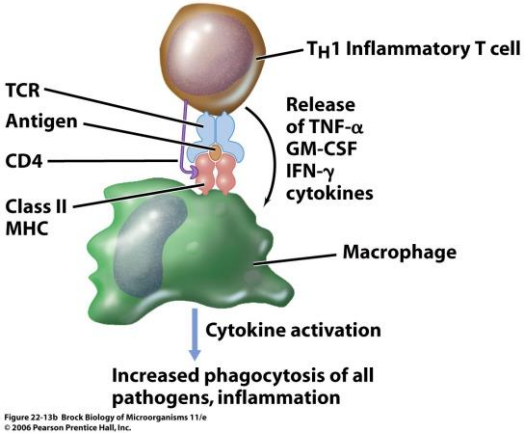

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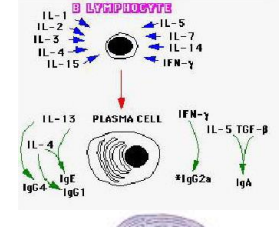
B-LYMPHOCYTES

- B-lymphocytes - express Ig molecules on surface.
- Plasma Cells – Ab secreting B-cells
- In humans, eight isotypes exist:
  - IgM,
  - IgG1, IgG2, IgG3, IgG4,
  - IgA1, IgA2,
  - IgE.
- Different Igs — different functions.
- In the blood, IgG is most prevalent than IgM and IgA.
- Abs – clear bacterial and some fungal infections.
- Bound Abs can activate complement and/or attract killer cells, neutrophils, macrophages



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QUESTIONS
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