Pathology : inflammation pt.3

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DOPAMINE
SCIENTIFIC TEAM

وَتَوَكَّلْ عَلَى الْحَيِّ الَّذِي لَا يَمُوتُ وَسَبِّحْ بِحَمْدِهِ ۚ
وَكَفَىٰ بِهِ بِذُنُوبِ عِبَادِهِ خَبِيرًا

Chemotaxis : movement of WBCs to injury tissue site

- active process
- Induced by CHEMOATTRACTANTS → exogenous / endogenous

Type of Chemoattractant	Bacterial products	Cytokines	Complement system	Lipoxygenase pathway AA metabolites
Simplified explanation	-	They are mediators released by (lymphocytes/macrophages)	-	-
Example	N-terminal peptides	Chemokine family	1)C5a(strongest) 2)plasma proteins	LTB4
Exogenous or endogenous	exogenous	endogenous	endogenous	endogenous

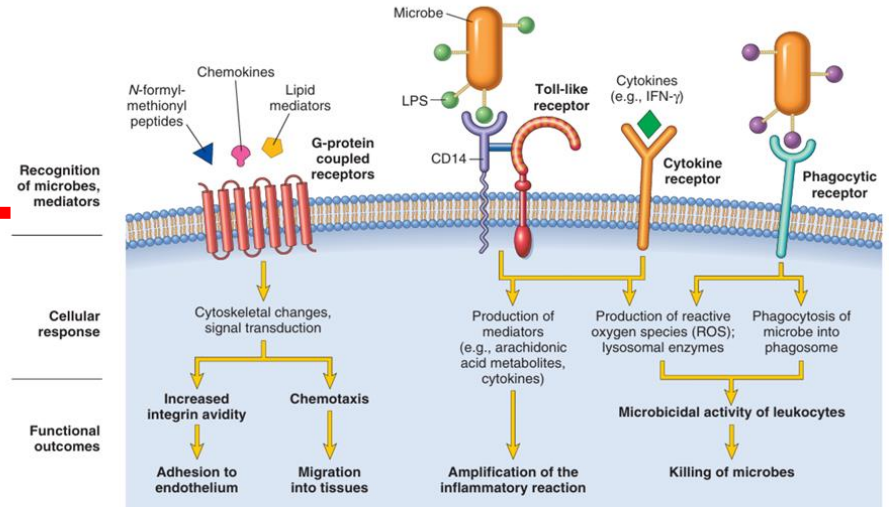
Deciding the type of inflammation :

depend on the **age** + **type** of stimulus

- Neutrophils (PMN) → for 6-24 hrs → recent acute inflammation
- Macrophages , lymphocytes & plasma cells → 24-48 hrs (maybe weeks) → chronic inflammation
- Eosinophils→ allergic inflammation

Ex: inflammation in skeletal cells :
edema → neutrophilic infiltrations → the second day chronic inflammatory cells appear(macrophages & lymphocytes)

Summary :
recognition of microbes and mediators create a cascade changes . (at early phase of recognition , the signal can be amplified)



Leukocyte activation :

(circulating in blood)

Neutrophils + monocytes = function together in phagocytosis and intracellular killing.

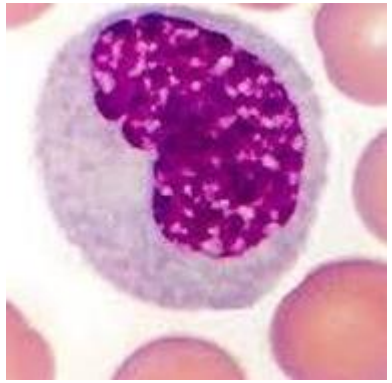
Macrophages*(found at tissue)*

Other functions of activated WBCs:

3. Amplify or limit reaction (cytokines) : **amplify** the inflammatory reaction at the **beginning** , **limit** it at the **end**.

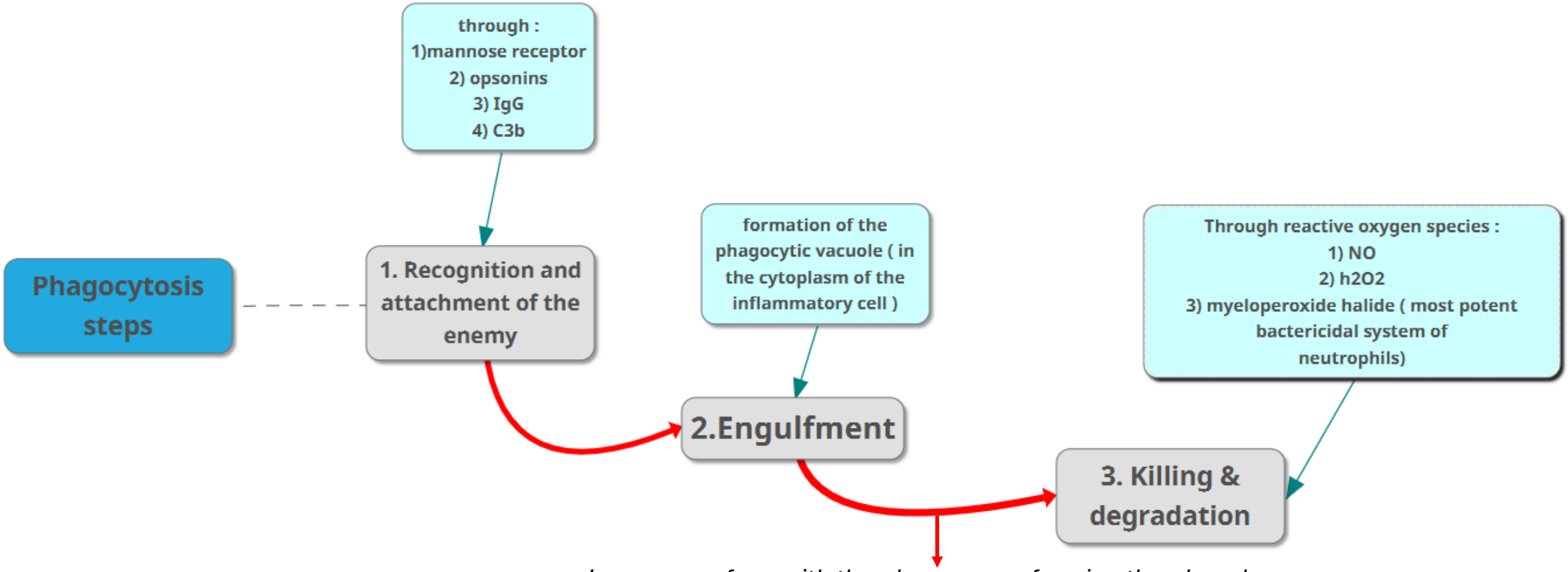
4. Growth factors secretion (repair) : helps in repair

5. T-lymphocytes has also a role in acute inflammation : (T-HELPER-17) produce cytokine IL-17



Monocyte
(kidney shaped nucleus & less granules)

Neutrophil
(multiple nuclei & a lot of granules)


Phagocytosis steps
1. Recognition and attachment of the enemy
through :
1)mannose receptor
2) opsonins
3) IgG
4) C3b
2.Engulfment
formation of the phagocytic vacuole (in the cytoplasm of the inflammatory cell)
3. Killing & degradation
Through reactive oxygen species :
1) NO
2) h2O2
3) myeloperoxide halide (most potent bactericidal system of neutrophils)
Lysosomes fuse with the phagosome, forming the phagolysosome

Nitric Oxide (NO)

Produced from : arginine (by NO synthase)

Types:
eNOS, nNOS, (iNOS) → intracellular killing stimulated by IFN-γ (cytokine)

Function : reaction +superoxide (O2-*) → form ONOO* radical peroxynitrite

Granule Enzymes

Present in :PMNs and monocytes

Types:
Large azurophil (primary)→ produce MPO+ other enzymes
Smaller (secondary) granules→produce lysozyme : they are usually neutralized by **antiproteases** (to be controlled properly in order not to cause harmful effect)

Ex: ά-1 antitrypsin: inhibits elastase

Neutrophile extracellular traps (NETs)

Definition :Thick meshwork of nuclear chromatin binds to peptides and anti-microbial agents after PMN death

Function : traps the invaders allowing other active neutrophiles to target them

Sepsis : NETs play a major role in the pathogenesis of sepsis

Maybe involved in **SLE** which is an autoimmune disease called Systemic Lupus Erythematosus (SLE)

Leukocyte-mediated tissue injury

1. Prolonged inflammation (TB and Hepatitis) → causes tissue damage and injury

2. Inappropriate inflammatory response (auto-immune diseases) → damage of the body's own tissues.
Ex: SLE, Rheumatoid Arthritis, and Mixed Connective Tissue Disease

3. Exaggerated response (asthma and allergic reactions) → causes symptoms and disease . This is the basic mechanism in acute allergic reactions and bronchial asthma