Review lecture notes:

1) Inflammation response is a **vary wide and big process** start from regonizing the enemy until repairing is done
2) Inflammatory response happens in (alive/vascularized/viable) tissues
3) The table of the causes of inflammation is **very important** (infections/tissue necrosis/ foreign bodies/ immune reactions)
4) Steps of inflammation (recognize - recruitment - remove - restore - repair)
5) PAPMs VS. DAMPs
6) Exudate vs. trasduatd
7) The table that shows the main differences between neutrophils and macrophages is **very important**
8) The curve that shows the phases of inflammatory response (**important**)
9) Leukocytes activation steps (migration - rolling - adhering - transmigration)
10) NET (it is mainly composed of the DNA of a died neutrophils (apoptosis))
11) Memorize the steps of phagocytosis (**sequentially**)
12) Neutrophils have more granules that are filled of enzymes than macrophages
13) Termination 7 mechanisms (**very important**)
14) The mediators tables **very very important**
15) Arachidonic acid two pathways (very important) with the function of each one
16) Local inflammation / systemic protective effects/ systemic pathological effects
17) The mediator that it is receptors are **G-protein coupled receptors**: chemokines
18) Chemokines are very important in inflammation and maintain the tissue architecture
19) C3b is for phagocytosis (work as in opsonization)
20) Regulation mechanisms of the complement system
21) Serous morphology: transduate
22) Fibrous morphology; exudate
23) M1 (classical pathway) vs M2 (alternative pathway)
24) How CD4+ T cells activate the M1 or M2 (**extremely important**)
25) Eosinophilic inflammation : it is a chronic iflammation
26) Granulomatous (specific type of chronic inflammation) **important** / **remember its cause is unknown**
27) Sacroidosis : unknown etiology
28) Cat scratch disease (**important**)
29) Add ferritin to the list of acute phase proteins **slide 102 (a student ask about it)
30) Angiogenesis play a very important role in Healing (No Angiogenesis —> No Healing)

Tables that are very important

Table 3.5 Principal Mediators of Inflammation

Mediator	Source	Action
Histamine	Mast cells, basophils, platelets	Vasodilation, increased vascular permeability, endothelial activation
Prostaglandins	Mast cells, leukocytes	Vasodilation, pain, fever
Leukotrienes	Mast cells, leukocytes	Increased vascular permeability, chemotaxis, leukocyte adhesion, and activation
Cytokines (TNF, IL-1, IL-6)	Macrophages, endothelial cells, mast cells	Local: endothelial activation (expression of adhesion molecules). Systemic: fever, metabolic abnormalities, hypotension (shock)
Chemokines	Leukocytes, activated macrophages	Chemotaxis, leukocyte activation
Platelet-activating factor	Leukocytes, mast cells	Vasodilation, increased vascular permeability, leukocyte adhesion, chemotaxis, degranulation, oxidative burst
Complement	Plasma (produced in liver)	Leukocyte chemotaxis and activation, direct target killing (membrane attack complex), vasodilation (mast cell stimulation)
Kinins	Plasma (produced in liver)	Increased vascular permeability, smooth muscle contraction, vasodilation, pain

Table 3.7 Cytokines in Inflammation

Cytokine	Principal Sources	Principal Actions in Inflammation
In Acute Inflammation		
TNF	Macrophages, mast cells, T lymphocytes	Stimulates expression of endothelial adhesion molecules and secretion of other cytokines; systemic effects
IL-1	Macrophages, endothelial cells, some epithelial cells	Similar to TNF; greater role in fever
IL-6	Macrophages, other cells	Systemic effects (acute phase response)
Chemokines	Macrophages, endothelial cells, T lymphocytes, mast cells, other cell types	Recruitment of leukocytes to sites of inflammation; migration of cells in normal tissues
IL-17	T lymphocytes	Recruitment of neutrophils and monocytes
In Chronic Inflammation		
IL-12	Dendritic cells, macrophages	Increased production of IFN-γ
IFN-γ	T lymphocytes, NK cells	Activation of macrophages (increased ability to kill microbes and tumor cells)
IL-17	T lymphocytes	Recruitment of neutrophils and monocytes

The most important cytokines involved in inflammatory reactions are listed. Many other cytokines may play lesser roles in inflammation. There is also considerable overlap between the cytokines involved in acute and chronic inflammation.

Table 3.9 Examples of Diseases With Granulomatous Inflammation

Disease	Cause	Tissue Reaction
Tuberculosis	*Mycobacterium tuberculosis*	Caseating granuloma (tubercle): focus of activated macrophages (epithelioid cells), rimmed by fibroblasts, lymphocytes, histiocytes, occasional Langhans giant cells; central necrosis with amorphous granular debris; acid-fast bacilli
Leprosy	*Mycobacterium leprae*	Acid-fast bacilli in macrophages; noncaseating granulomas
Syphilis	*Treponema pallidum*	Gumma: microscopic to grossly visible lesion, enclosing wall of macrophages; plasma cell infiltrate; central cells are necrotic without loss of cellular outline; organisms difficult to identify in tissue
Cat-scratch disease	Gram-negative bacillus	Rounded or stellate granuloma containing central granular debris and recognizable neutrophils; giant cells uncommon
Sarcoidosis	Unknown etiology	Noncaseating granulomas with abundant activated macrophages
Crohn disease (inflammatory bowel disease)	Immune reaction against undefined gut microbes and, possibly, self antigens	Occasional noncaseating granulomas in the wall of the intestine, with dense chronic inflammatory infiltrate

INFECTIONS	**Bacteria, fungi, viruses, parasites And their toxins**
NECROSIS	**Ischemia, trauma, physical and chemical injuries, burns, frostbite, irradiation**
FOREIGN BODIES	**Splinters, dirt, urate crystals (gout), Cholesterol crystals (atherosclerosis)**
IMMUNE REACTIONS	**Allergies and autoimmune diseases**

Transudate	Exudate
Low protein	**High protein**
Low cell content	**Many cells & debris**
Low specific gravity	**Higher specific gravity**
Caused by osmotic/hydrostatic pressure imbalance	**Caused by increased vascular permeability and denotes inflammatory reaction**

Table 3.3 Properties of Neutrophils and Macrophages

	Neutrophils	Macrophages
Origin	HSCs in bone marrow	• HSCs in bone marrow (in inflammatory reactions) • Many tissue-resident macrophages: stem cells in yolk sac or fetal liver (early in development)
Life span in tissues	1–2 days	Inflammatory macrophages: days or weeks Tissue-resident macrophages: years
Responses to activating stimuli	Rapid, short-lived, mostly degranulation and enzymatic activity	More prolonged, slower, often dependent on new gene transcription
• Reactive oxygen species	Rapidly induced by assembly of phagocyte oxidase (respiratory burst)	Less prominent
• Nitric oxide	Low levels or none	Induced following transcriptional activation of iNOS
• Degranulation	Major response; induced by cytoskeletal rearrangement	Not prominent
• Cytokine production	Low levels or none	Major functional activity, requires transcriptional activation of cytokine genes
• NET formation	Rapidly induced, by extrusion of nuclear contents	No
• Secretion of lysosomal enzymes	Prominent	Less

HSC, Hematopoietic stem cells; *iNOS,* inducible nitric oxide synthase; *NET,* neutrophil extracellular traps.
This table lists the major differences between neutrophils and macrophages. The reactions summarized above are described in the text. Note that the two cell types share many features, such as phagocytosis, ability to migrate through blood vessels into tissues, and chemotaxis.

Table 3.8 Role of Mediators in Different Reactions of Inflammation

Reaction of Inflammation	Principal Mediators
Vasodilation	Histamine Prostaglandins
Increased vascular permeability	Histamine C3a and C5a (by liberating vasoactive amines from mast cells, other cells) Leukotrienes C_4, D_4, E_4
Chemotaxis, leukocyte recruitment and activation	TNF, IL-1 Chemokines C3a, C5a Leukotriene B_4
Fever	IL-1, TNF Prostaglandins
Pain	Prostaglandins Bradykinin
Tissue damage	Lysosomal enzymes of leukocytes Reactive oxygen species

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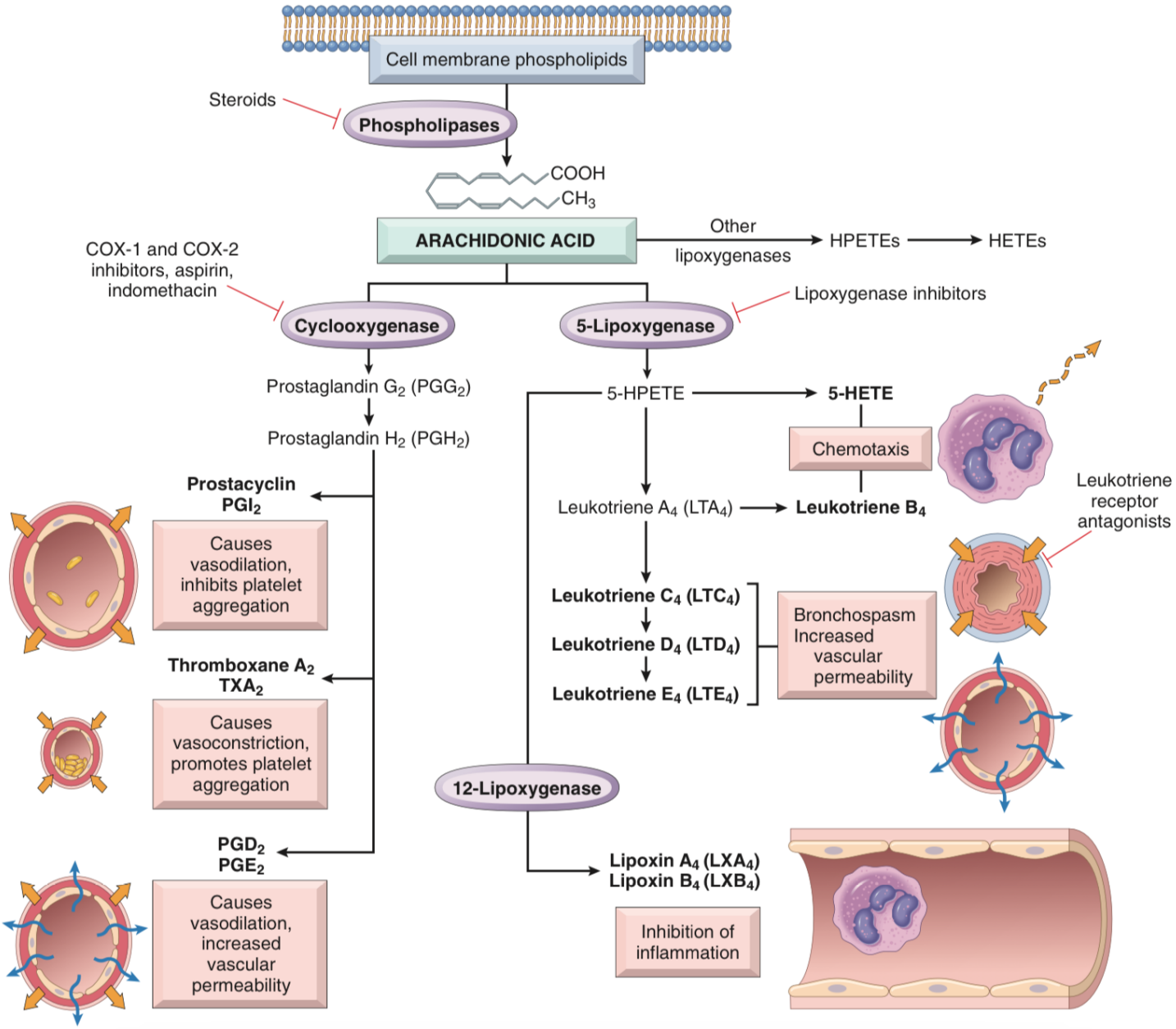
Table 3.6 Principal Actions of Arachidonic Acid Metabolites in Inflammation

Action	Eicosanoid
Vasodilation	Prostaglandins PGI_2 (prostacyclin), PGE_1, PGE_2, PGD_2
Vasoconstriction	Thromboxane A_2, leukotrienes C_4, D_4, E_4
Increased vascular permeability	Leukotrienes C_4, D_4, E_4
Chemotaxis, leukocyte adhesion	Leukotriene B_4
Smooth muscle contraction	Prostaglandins PGC4, PGD4, PGE4



Mediators are produced in rapid bursts
Release is stimulus dependent
Short half-lives
Degradation after release
PMNs short life (apoptosis)
Stop signals production (TGF-ß, IL-10)
Neural inhibitors (cholinergic): inhibits TNF

TH1	INF-ß, activates Macs in classic pathway
TH2	IL-4, IL-5 & IL-13; activates eosinophils and Macs alternative pathway
TH17	IL-17 , induce chemokines secretion and recruits PMNs