Acute Inflammation

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What is acute inflammation?

What is inflammation? A localized, regional or systemic response of the body to foreign material, perceived foreign material, or damaged host tissue. It comprises specific inflammatory cells and soluble inflammatory mediators that are directed at destroying and removing the inciting cause.

What does acute mean? Sudden onset and / or having had a short duration (1-~3-7days)
What is the purpose of acute inflammation?

- Isolates source of infection e.g. abscess
- Destroys disease causing microorganisms [viruses, bacteria and fungi] and parasites [protozoa and metazoa]
- Early degradation of dead tissue e.g. myocardial infarct

  - In the process of destroying microorganisms and parasites acute inflammation has damaging effects on tissues and organs
  - Local tissue damage is often the cost required to prevent life threatening systemic infections

Relationship between acute and chronic inflammation

- Acute inflammation: [1-7 days]
  - Locally life-threatening e.g. brain abscess

- Chronic inflammation
  - Persistent chronic inflammation
  - Life-threatening

- Residual tissue damage [scar]
  - Clean up phase, several days to months
  - Many disease examples
    - Asthma
    - Lupus [systemic lupus erythematosus]
    - Flea allergy in dogs
    - Immune-mediated hemolytic anemia

Acute inflammation can be a pathologic rather than protective process

- Aberrant activation of the acute inflammatory response can damage various tissues and organs without having any benefits
- Many disease examples
  - Asthma
  - Lupus [systemic lupus erythematosus]
  - Flea allergy in dogs
  - Immune-mediated hemolytic anemia
- This will be covered in the lecture on immune-mediated diseases [autoimmunity and hypersensitivity]

These topics will be covered in a later lecture

Many scenarios of disease progression and/or resolution – depends on many factors including pathogen, host and treatment-related variables
What are the symptoms and signs of acute inflammation?

• Rubor
• Tumor
• Dolor
• Calor
• Functio laesa

Celsus (ca 30 BC–38 AD)

What are the symptoms and signs of acute inflammation?

Mechanisms of Acute Inflammation. I

• Overview
• Initiation of acute inflammation
• Vascular response
• Cellular response
• Destruction of micro-organisms
• Involvement of lymphatics and lymph nodes in inflammation
• Systemic effects of inflammation
Overview of Acute Inflammation

Initiation
- Vasodilation – rubor, calor
- Leakage of proteins – tumor
- Emigration of neutrophils
- Destruction of foreign material
- Resolution

Initiation of acute inflammation. I.

- High diversity of stimulants of acute inflammation
  - Infectious [viruses, bacteria, fungi, parasites]
  - Non-infectious tissue damage / death
    - Burn, frost bite, hypoxic damage, foreign bodies, trauma
  - Many factors released from dead tissue promote inflammation
- Many sensing mechanisms for acute inflammatory stimulants
  - Complement system*
  - Toll-like receptors
  - Antibodies*

* Covered in more detail in this and subsequent lectures

Vascular response. I.
Vasodilation and increased vascular permeability

Inflammatory exudates – key points
- Supply factors key to mediating inflammation
- Rich in proteins e.g. immunoglobulins, complement
- Rich in cells e.g. neutrophils
- Exudates on surface or in substance of tissue / organ
Vascular response. II: Mechanisms of increased vascular permeability

- Mast cell release histamine – see later lecture. NO is a gas released by various cell types e.g. endothelial cells and macrophages.
- Also, endotheliotropic infectious agents
- Type III hypersensitivity – see later lecture.

Cellular response. I: Neutrophils

- Derived from bone marrow precursor cells (myeloblasts)
- Same lineage as eosinophils and basophils
- Destruction of bone marrow (many causes) will deplete neutrophils in blood [neutropenia] and predispose towards infectious disease

Cellular response. II: Neutrophil migration

KEY ROLE OF VARIOUS INDUCED CELL-ADHESION MOLECULES ON ENDOTHELIAL CELLS, NEUTROPHILS AND EXTRA-CELLULAR MATRIX WITHIN TISSUE
Cellular response. III. Neutrophil structure and function.

Neutrophil granules contain a large number of proteins required to mediate inflammation and promote pathogen killing:
- Tissue migration: collagenase, elastase, laminin receptors
- Pathogen killing: myeloperoxidase
- Pathogen degradation / digestion: lysosomal hydrolases

Cell Response. IV. Binding to pathogen and phagocytosis

Opsonization and phagocytosis:
- Critical role of IgG and complement proteins
- Critical role of neutrophil receptors for IgG and complement components
- Fc receptor
- CR1
- Critical role of signaling pathways to stimulate phagocytosis once receptor binding occurs


Myeloperoxidase (MPO)

\[ \text{H}_2\text{O}_2 + 2\text{Cl}^- \rightarrow \text{HOCl} + 2\text{e}^- \]

NADPH oxidase

\[ \text{O}_2 + \text{NADPH} \rightarrow \text{O}_2^- + \text{NADP}^+ \]
\[ \text{O}_2^- + 2\text{H}^+ + \text{Fe}^{2+} \rightarrow \text{Fe}^{3+} + \text{OH}^- + \text{OH}^- \]

Myeloperoxidase contains heme group - explains yellow-green pus

Destruction of bacteria etc by oxygen radicals
Cell Response. VI. Destruction of pathogen, tissue and exudation

Draining of pus onto surface of site of inflammation

Focal accumulation of pus in tissue cavities = abscessation

Liver abscessation

Role of lymphatics in inflammation. I.

Tissue exudate drains into lymphatics and enters regional nodes
Activates local immune response in node (humoral and cell-mediated components). Lymphoid hyperplasia and/or inflammation (lymphadenitis)
Provides future immunity for specific agent.

Systemic effects of acute inflammation

- Leukocytosis – increase in white cells in blood
  - Increased bone marrow release
  - Increased bone marrow proliferation
- Acute phase proteins
  - C-reactive protein, serum amyloid A, fibrinogen
  - Levels increase in blood, liver-derived proteins
- Fever
  - Helps inflammatory process, can be harmful
  - Pyrogens – bacterial products, Interleukin -1, Tumor-necrosis factor alpha
  - Role of hypothalamus
Classification of acute inflammation suggests underlying causes in species specific manner

- Necrotizing enteritis may suggest Salmonella in some species e.g. human
- Purulent lymphadenitis may suggest Streptococcal infection in some species e.g. horses
- Serous arthritis may suggest Mycoplasma in some species e.g. pigs

Summary – consequences of acute inflammation

- Efficacy of inflammatory and immune response
- Local acute inflammation
- Systemic inflammation (e.g. septicemia)
- Death
- Complete resolution - no scar
- Resolution - with scar
- Persistent chronic inflammation

Example examination questions

- State five signs of acute inflammation
  – For three of these state briefly how they occur
- How do neutrophils kill bacteria?
- What is an abscess?
- State three factors that will determine whether a localized infection becomes systemic and cause life threatening disease