INFLAMMATION & REPAIR

Lecture 4
Acute Inflammation: Vascular events
Winter 2013

Chelsea Martin

Special thanks to Drs. Hanna and Forzan
Course Outline

i. Inflammation: Introduction and generalities *(lecture 1, pp.1-2)*

ii. Classification of inflammation *(lectures 2 and 3, pp. 2-8)*

iii. Acute Inflammation
   i. Vascular events / permeability *(lecture 4, pp. 9-11)*
   ii. Inflammatory cell types *(lecture 5, pp. 12-14)*
   iii. Sequence of events *(lecture 6, pp. 15-20)*
   iv. Chemical mediators *(lecture 7, pp. 20-26)*

iv. Chronic Inflammation *(lecture 8, pp. 27-30)*
   i. Granulomatous inflammation

v. Repair and wound healing *(lecture 9, pp. 31-35)*

vi. Healing in specific tissues *(lecture 9, cont., pp. 35-37)*
Acute Inflammation

Rapid response to an injurious agent that delivers mediators of host defense to the site of injury

- 1. Increased blood flow due to alteration of vessel caliber
- 2. Structural changes in vessels that allow plasma proteins and leukocytes to leave circulation
- 3. Leukocytes emigrate from vessels, accumulate at site of injury, and are activated in order to eliminate offending agent
Cardinal Signs of Inflammation

Celsius, 1st century

- Redness
- Heat \(\rightarrow\) Increased blood flow & edema
- Swelling

Rudolf Virchow, 19th century

- Pain \(\rightarrow\) Leukocytes release tissue damaging proteases along with other inflammatory mediators

- Loss of function
Cat Lung; 8-10 week old male DSH
History of sneezing and nasal discharge progressing to dyspnea

- Congestion
- Neutrophils & Fibrin
- Edema
Cat Lung; Feline Herpesvirus-1
Bronchopneumonia, Fibrinosuppurative, multifocal, acute, marked
Sheep Pleura; *Pasteurella multocida*
Pleuritis, Fibrinosuppurative, locally extensive, acute, marked.
Cow, mitral valve; *Arcanobacterium pyogenes*

Valvular endocarditis, fibrinosuppurative (vegetative), locally extensive, subacute, marked
Cow, kidney; *Arcanobacterium pyogenes*

Nephritis, suppurative, widespread multifocal (embolic), acute, marked.
Cow, kidney; *Arcanobacterium pyogenes*

Nephritis, suppurative, widespread multifocal (embolic), acute, marked with focal liquifactive necrosis.
Inflammatory Stimuli

- Infections
- Trauma
- Physical and Chemical Agents
- Tissue Necrosis
- Foreign Material
- Immune Reactions

Parasites (protozoa)
- Cryptosporidium

Viruses
- Rotavirus

Bacteria
- E. coli

Fungi
- Aspergillus spp.
Acute Inflammation

Primary function
- move defense mechanisms out of vasculature to tissues
- initiate repair
### SEQUENCE of EVENTS:

1. **Vasodilation (increased blood flow)** ➤ **CALOR & RUBOR**
   - arteriolar dilation / opening of capillaries (hyperemia / redness)
   - histamine and Nitric Oxide (primarily)

2. **Increased microvascular permeability: fluids into tissues** ➤ **TUMOR**

3. **Blood flow slows (stasis) and rbc concentration** ➤ **RUBOR**

4. **Cellular events** –
   - a) margination, rolling and adhesion
   - b) emigration of WBC into tissue (exudation)
   - c) accumulation of WBC at sites of injury **TUMOR**
   - d) activation of cells, production of mediators **DOLOR**
   - e) removal of stimulus

5. **Tissue damage / Repair** ➤ **LOSS OF FUNCTION**
1. **Vasodilation** (esp Histamine / NO / PG)

(first arterioles, then capillaries and post capillary venules)
Sequence of Vascular Events

2. Increased Vascular Permeability
   (esp postcapillary venules)
Increase Vascular Permeability

- hallmark of acute inflammation
- normal fluid exchange depends on intact endothelium
Increased Vascular Permeability - Mechanisms

1. Retraction of endothelial cells (gaps) in venules

a) Endothelial cell contraction
   - immediate and transient (15-30 min)
   - mediator binds to receptor → contraction
   - affects only venules

Histamine, Bradykinin, Leukotrienes, etc
Increased Vascular Permeability - Mechanisms

1. Retraction of endothelial cells (gaps) in venules

b) Delayed prolonged leakage

- some mild injuries cause vascular leakage
- begins after a delay of 2 to 12 hrs, but lasts for several hours to days
- see endothelial cell contraction &/or mild degeneration

mild burns, UV irradiation
Increased Vascular Permeability - Mechanisms

2. Direct endothelial injury

- arterioles, venules and capillaries affected
- direct damage due to severe injurious stimuli
- immediate sustained response, lasts hrs to days until damaged repaired

severe burns, bacterial toxins, viruses, etc
Increased Vascular Permeability - Mechanisms

3. Leukocyte Dependent Endothelial Injury

- neutrophils that adhere to the endothelium during inflammation may also injure the endothelial cells and thus amplify the reaction.
- associated with the later stages of inflammation.
- long-lived, lasts hrs to days until damaged repaired.

Reactive $O_2 +$ proteolytic enzymes released from adhered neutrophils.
4. Increased Transcytosis

- normally some transport by channels of vesicles & vacuoles (vesiculovacuolar organelles).
- certain factors can increase the number and size of these channels.

VEGF, histamine(?)
Increased Vascular Permeability - Mechanisms

5. Leakage from New Capillaries

- during the repair process, proliferating endothelial cells are leaky
- mediated by VEGF (vascular endothelial growth factor)
Which mechanism?

- White tailed deer farm.
- Multiple animals affected, some die acutely, some anorexic, reddened eyes / mucosas

Morphologic diagnoses:
- Hydropericardium, severe
- Rumenitis, hemorrhagic & necrotizing, multifocal to coalescing, acute, severe

Etiology:
- Epizootic hemorrhagic disease virus Orbivirus similar to …..

Pathogenesis:
- direct endothelial damage, mainly microvasculature of mucosa and lung
- edema / hemorrhage, thrombosis
Mechanisms are independent, but may all participate at the same time

eg: Thermal Burn

Direct injury to endothelium
- heat (burn)

Endothelial retraction
- histamine, cytokines

Leukocyte mediated endothelial injury
- $O_2$, enzymes
Increased Vascular Permeability - Results

What comes out? - Fluids OR Fluids+Cells

**Transudate**
- fluid
- low protein, few cells
- non-infectious

**Exudate**
- fluid + cells
- high protein, many cells
- infectious

**Modified Transudate**
- in between
## Transudate vs Exudate

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<thead>
<tr>
<th></th>
<th>Exudate</th>
<th>Modified Transudate</th>
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<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Inflammatory</td>
<td></td>
<td>Non-inflammatory</td>
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<td><strong>Etiology</strong></td>
<td>Inflammation / Infection</td>
<td>Long-standing transudates or ↑ Vasc. perm.</td>
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<tr>
<td><strong>Specific Gravity</strong></td>
<td>&gt;1.025</td>
<td>1.017-1.025</td>
<td>&lt;1.017</td>
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<tr>
<td><strong>Protein Content</strong></td>
<td>&gt; 30 g/L</td>
<td>25-75 g/L</td>
<td>&lt; 25 g/L</td>
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<td><strong>Clots?</strong></td>
<td>Often</td>
<td>Varies</td>
<td>Rarely</td>
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<tr>
<td><strong>Inflam. Cells</strong></td>
<td>Many (&gt;5,000-7,000 cell/μL)</td>
<td>Few (1,000-7,000 cell/μL)</td>
<td>Occasional (&lt;1,500/μL)</td>
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<td>Often</td>
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<td>Rare</td>
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- **Vascular damage & leakage**
- ↑ Hydrostatic pressure in capillaries: more dependant on venous pressure than arterial pressure
- ↓ Oncotic pressure in capillaries: Hypoalbuminemia
- Lymphatic obstruction
TRANSUDATES

SUBCUTANEOUS EDEMA

HYDROPERICARDIUM

ASCITES FLUID
EXUDATES

FIBRINOUS

SUPPURATIVE

FIBRINOSUPPURATIVE
What is this fluid?

- 2-year-old MC cat
- long history of upper respiratory tract infection, responsive to antibiotics.
- off feed for 3 days, T-39.6, green mucoid nasal discharge, abdomen feels full of fluid.
- FeLV/FIV negative.
- euthanized at owners request after blood and **abdominal fluid** were analyzed.
What is this fluid?
What is this fluid?

**Abdominal fluid:** Yellow-red, cloudy, viscid, cells consist of non-degenerated neutrophils, macrophages in low numbers

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<td><strong>Sp. Gravity</strong></td>
<td>1.019</td>
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<tr>
<td><strong>Protein</strong></td>
<td>60 g/L</td>
</tr>
<tr>
<td><strong>Cells</strong></td>
<td>5,008 cell/μL</td>
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**Modified Transudate**

**Etiology:** Feline Coronavirus

**Name of disease:** Feline Infectious Peritonitis (FIP)
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5. Tissue damage / Repair ➤ LOSS OF FUNCTION