More on Mast Cells, etc.

Mast Cell Degranulates

1/30/2017
Molecules Released

- cytokines
  - Eosinophil chemotactic factor
- (newly formed) lipid mediators (eicosanoids):
  - prostaglandins
  - Leukotrienes
  - platelet-activating factor
- preformed mediators (from granules):
  - serine proteases (like tryptase, elevated in anaphylaxis)
  - histamine
  - Serotonin (pain, vasoconstriction)
  - proteoglycans, mainly heparin (anticoagulant)

What is a Cytokine?

- large and diverse family of regulators
- small intercellular communication cell-signaling protein molecules
- classified as proteins, peptides, or glycoproteins
- Includes: interleukins, interferons, chemokines

Prostaglandin D2?

- Vasodilation
- Recruits T helper cells, basophils, eosinophils
- Bronchial airway constriction (Asthma)
- Body temp changes
Leucotrienes?

- Sustain inflammation
- Enhance immune cell migration
- Increase bronchoconstriction
- Increase vascular permeability

Platelet-Activating Factor?

- Potent phospholipid activator and mediator of many leukocyte functions (platelet aggregation, inflammation, anaphylaxis)
- Produced in response to specific stimuli by neutrophils, basophils, platelets, endothelial cells.
- Effects:
  - Bronchoconstriction mediator
  - Aggregation of platelets (clot)
  - Blood vessel dilation — airway inflammation, BP drop, reduced blood volume to heart — remember contractility? → shock and in extreme, death.

Histamine?

- Dilates post capillary venules
- Activates the endothelium
- Increases blood vessel permeability → local edema (swelling), warmth, redness, attracts inflammatory cells
- Irritates nerve endings → itching or pain
- Cutaneous signs of histamine release → wheal & flare reaction.
Histamine Types

<table>
<thead>
<tr>
<th>Histamine Receptor</th>
<th>Location</th>
<th>Function</th>
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</thead>
<tbody>
<tr>
<td>H₁</td>
<td>smooth muscle</td>
<td>vasoconstriction</td>
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<tr>
<td></td>
<td>smooth muscle</td>
<td>Smooth muscle constriction</td>
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<td>Separation of nasal epithelial cells (responsible for sneezing)</td>
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<tr>
<td></td>
<td>vasodilation</td>
<td>Bronchial smooth muscle contraction</td>
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<tr>
<td></td>
<td>pain &amp; itching</td>
<td>Separation of nasal nasal epithelial cells (responsible for hives)</td>
</tr>
<tr>
<td></td>
<td>allergic rhinitis symptoms</td>
<td>Vascular engorgement from vasodilation &amp; increased capillary permeability</td>
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<tr>
<td>H₂</td>
<td>H3</td>
<td>Gastric acid secretion</td>
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<tr>
<td>H₃</td>
<td>H4</td>
<td>Decreased neurotransmitter release: histamine, acetylcholine, norepinephrine, serotonin</td>
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<tr>
<td>H₄</td>
<td>Basophils &amp; bone marrow</td>
<td>Chemotaxis</td>
</tr>
</tbody>
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Histamine & The Nose

- Increased vascular permeability → fluid leaves capillaries into tissues → classic allergic reaction symptoms → watery eyes & runny nose

- Allergens bind to mast cells coated w/ IgE in the nasal mucosa → 3 clinical responses:
  1. sneezing (histamine-associated sensory neural stimulation)
  2. hypersecretion from glandular tissue
  3. nasal mucosal congestion (vascular engorgement from vasodilation & increased capillary permeability)

Anaphylaxis?

- Local vs. Systemic
- Type 1
- Systemic effects of histamine release
- Common areas affected:
  - Skin (hives, swelling, itching)
  - GI (pain, diarrhea, vomiting)
  - Respiratory (wheeze, stridor, hypoxia)
  - Cardio (coronary art spasm → infarct, dysrhythmia)
  - CNS (BP drop → control, dizziness, anxiety)