Autocoids

PHRM 203
Allison Beale
Overview - Autocoid types

• Biogenic amines
  – Histamine and serotonin (5-HT)

• Biogenic peptides
  – Angiotensin and Kinins (Bradykinin, etc.)

• Small proteins
  – Cytokines (Interleukins, Tissue Necrosis Factor [TNF], etc.)

• Endothelium-derived agents
  – Nitric oxide (NO)

• Membrane-derived agents
  – Eicosanoids (Leukotrienes [LTs], prostaglandins [PGs], thromboxane [TXA], platelet activating factor [PAF], etc.)
## Select Autocoid Effects

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Effect</th>
<th>Autocoid(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth muscle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchi</td>
<td>Bronchoconstriction</td>
<td>Histamine, bradykinin, LTs, serotonin, PAF</td>
</tr>
<tr>
<td>Uterus</td>
<td>Contractions</td>
<td>PG-E₂, PG-F₂</td>
</tr>
<tr>
<td>Blood vessels</td>
<td>Vasoconstriction</td>
<td>ANG-II, TXA₂, PG-D₂, PG-F₂</td>
</tr>
<tr>
<td></td>
<td>Vasodilation/”leakiness”</td>
<td>Histamine, NO, bradykinin, PGs</td>
</tr>
<tr>
<td>White blood cells</td>
<td>Chemotaxis</td>
<td>LTs, kinins, PG-D₂</td>
</tr>
<tr>
<td>Glands</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JG – renin release</td>
<td></td>
<td>PGI₂ &amp; PGE₂</td>
</tr>
<tr>
<td>PC - ↑gastric acid</td>
<td></td>
<td>Histamine</td>
</tr>
<tr>
<td>↓ gastric acid &amp; ↑ gastric mucous</td>
<td></td>
<td>PGE₂</td>
</tr>
<tr>
<td>Sensory Neurons</td>
<td>Lower threshold for pain/itch</td>
<td>Histamine, PGs and kinins</td>
</tr>
<tr>
<td>Platelets</td>
<td>Aggregation/coagulation</td>
<td>TXA₂, Serotonin, ADP, PAF, etc.</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>Fever</td>
<td>LTs, TNFα, ILs, PGs</td>
</tr>
</tbody>
</table>

ANG-II = angiotensin-2; IL = interleukins; JG = juxtaglomerular cells of kidney; LT = leukotrienes; NO = nitric oxide; PAF = platelet activating factor; PC = parietal cells of stomach; PG = prostaglandins; TNF = tissue necrosis factor; TX = thromboxane;
Inflammatory response to tissue injury

Calor, dolor, rubor, tumor
Biogenic amines: Histamine

- Histamine released from Mast cells also basophils, eosinophils & platelets
  1. IgE cross-linking
  2. Binding by complement
  3. Direct “injury” (physical or chemical)
     “Injury” by some drugs (opioids, tubocurarine, vancomycin…), & by T⁰, pressure & mechanical injury...

Mast cell stabilizers, e.g., cromolyn, block IgE activated Ca²⁺ channels

Preformed mediators (in granules) include histamine, heparin, serotonin & enzymes.

Newly synthesized = PGD₂, LTC₄, and cytokines including TNFα, IL₄, IL₅ and IL₆

www.healthsystem.virginia.edu/internet/hematology/images/Mast-cell-and-basophil-100x-website-arrow.jpg
Biogenic amines: Histamine

• Receptors are all GPCR
  – $H_1$
    • Smooth muscle, endothelium, CNS
  – $H_2$
    • GI glands, vascular smooth muscle, cardiac muscle, Mast cells
  – $H_3$
    • CNS (basal ganglia, hippocampus and cortex), myenteric plexus
  – $H_4$
    • WBCs - eosinophils and neutrophils, GI & CNS

$H_3 = \text{Predominantly presynaptic auto & hetero-receptors}$
Biogenic amines: Histamine

- $\text{H}_1$ Receptor
  - *Relaxes small blood vessels*
    - *vasodilation of arterioles*
  - *Contracts other smooth muscle*
    - *Vasoconstriction elsewhere*
      - venoconstriction $\rightarrow$ upstream edema
  - *GI*
  - *Bronchi*
  - *Stimulates sensory nerve endings (itch, pain)*
  - *Sleep/arousal functions in CNS (as a neurotransmitter)*
  - Classic antagonist: Chlorpheniramine
Biogenic amines: Histamine

- **H$_2$** Receptor
  - Mediates gastric acid secretion
  - Smooth muscle relaxation (including vasodilation)
  -mast cell & basophil degranulation
  - Antagonist = Ranitidine (Zantac®)
Biogenic amines: Histamine

• $\text{H}_3$ Receptor
  – *Heteroreceptors on noradrenergic, serotoninergic, GABAergic and glutamatergic neurons and sensitive C-fibers*
    • ↓ neuronal firing and histamine release from depolarized terminals
  – *CNS sleep functions*
  – *Activate eosinophils to express adhesion proteins*
Biogenic amines: Histamine

- $H_4$ Receptors
  - Mediates histamine-induced chemotaxis of mast cells, leukotriene $B_4$ production and mast cell-dependent neutrophil recruitment
  - Auto- and heteroreceptors as with $H_3$
  - CNS sleep functions
**Antihistamines**

- \( H_1 \) Antagonists (e.g., diphenhydramine)
  - \( \otimes \) some smooth muscle effects NOT BRONCHOCONSTRICTION in humans
  - \( \otimes \) vasodilation & \( \otimes \) capillary permeability
  - \( \otimes \) to varying degrees histamine-evoked salivary, lacrimal & other exocrine secretions
  - **Block muscarinic receptors** (atropine-like effect)
  - \( \uparrow \) or \( \downarrow \) CNS (sedation likely, but chlorpheniramine \( \rightarrow \uparrow \) CNS)
  - \( \otimes \) motion sickness
  - **Local anesthetic effects for some, not related to** \( H_1 \)
### 1<sup>st</sup> Generation (H<sub>1</sub>) Antihistamines

*Adapted from: Table 26-2, p 291, Brenner*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Duration (hrs)</th>
<th>Sedation</th>
<th>Antiemesis /Motion</th>
<th>Anti-ACh</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpheniramine 🏎️ ⛅-B</td>
<td>6-24</td>
<td>L-M</td>
<td>-0-</td>
<td>M</td>
</tr>
<tr>
<td>Dimenhydrinate Dramamine ® &amp; others</td>
<td>4-6</td>
<td>H</td>
<td>M</td>
<td>H</td>
</tr>
<tr>
<td>Diphenhydramine 🏎️ ⛅-B Benadryl® &amp; others</td>
<td>8-12</td>
<td>H</td>
<td>M</td>
<td>H</td>
</tr>
<tr>
<td>Hydroxyzine Atarax® &amp; others</td>
<td>6-24</td>
<td>H</td>
<td>L-M (good anti-itch)</td>
<td>M</td>
</tr>
<tr>
<td>Meclizine (see GI lecture) Antivert® &amp; others</td>
<td>12-24</td>
<td>M</td>
<td>H</td>
<td>M</td>
</tr>
<tr>
<td>Promethazine 🏎️ ⛅-C Phenergan® &amp; others</td>
<td>4-6</td>
<td>H</td>
<td>H</td>
<td>H</td>
</tr>
</tbody>
</table>
Chlorpheniramine

• Uses
  – Temporary relief of respiratory allergy symptoms.

• Warnings
  – Hypersensitivity
  – Narrow-angle glaucoma
  – Peptic ulcer
  – Symptomatic prostatic hypertrophy
  – Asthma/COPD
  – Urinary retention
  – Not for use in newborn or premature infants and in breast-feeding mothers.
Diphenhydramine (Benadryl)

• **Uses**
  – All **allergic reactions** including anaphylaxis (with epinephrine)
  – **Motion sickness**
  – **Anti-Parkinson’s, drug-induced Extrapyramidal Symptoms**
  – Occasional **sleep aid**

• **CONTRAINDICATIONS**
  – Use in Neonates or Premature Infants or Nursing mothers
  – Use as a Local Anesthetic: Because of the risk of local necrosis
  – Hypersensitivity to diphenhydramine

• **WARNINGS**
  – Narrow-angle **glaucoma**, stenosing **peptic ulcer**, pyloroduodenal obstruction, symptomatic **prostatic hypertrophy**, or **bladder-neck obstruction**.
  – Over dosage in Kids may cause **hallucinations**, convulsions, or death. Kids may experience **excitation**.
  – In the Elderly (≥ 60 years), antihistamines are more likely to cause **dizziness, sedation**, and **hypotension**.
Promethazine (Phenergan)

- Phenothiazine
- Uses
  - Variety of allergic reactions
  - Sedation (pre-, post-op or obstetric) and anxiolytic
  - Anti-emetic for pre-, peri- and post-op (only IM)
  - Anti-motion sickness
  - Adjunctive to meperidine or another analgesic for controlling post-op pain
- Boxed warning:
  - Fatal respiratory depression possible in kids <2 years old
  - Severe chemical tissue injury regardless of route
- Other warnings
  - CNS & respiratory depression, ↓seizure threshold, may photosensitize patient, bone marrow depression, NMS

NMS alert ✍

NMS = neuroleptic malignant syndrome seen in drugs that lower DA levels

Routes: IV/IM, PR (refrigerate), PO, enteral solution (NO SC)

Photo-sensitizer icon

8/19/14 A Beale

PHRM 203 - Autocoids
Focus on Scrombroid Fish Poisoning

- **Histidine** in fish metabolized to histamine
  - Bacteria

- Symptoms post-ingestion
  - Vomiting, nausea, headache, flushing, sweating

- Treatment
  - $H_1$ antagonist
    - Diphenhydramine

*Diphenhydramine is a “go to” drug for ALL types of allergic reactions.*
# 2nd Generation (H₁) Antihistamines

*Adapted from: Table 26-2, p 291, Brenner*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Duration (hrs)</th>
<th>Sedation</th>
<th>Antiemesis/motion</th>
<th>Anti-ACh</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetirizine</td>
<td>12-24</td>
<td>L</td>
<td>-0-</td>
<td>VERY L</td>
</tr>
<tr>
<td>Zyrtec® &amp; others</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fexofenadine</td>
<td>12-24</td>
<td>VERY L</td>
<td>-0-</td>
<td>VERY L</td>
</tr>
<tr>
<td>Allegra® &amp; others</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loratadine</td>
<td>24</td>
<td>VERY L</td>
<td>-0-</td>
<td>VERY L</td>
</tr>
<tr>
<td>Claritin®</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azelastine</td>
<td>12-24</td>
<td>L-M</td>
<td>-0-</td>
<td>L (dry mouth)</td>
</tr>
<tr>
<td>Astelin®</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Routes:** PO, topical, metered nasal spray, ophthalmic drops
**H$_2$ Antagonists**

- Suppress basal gastric acid secretion
  - Most ulcers don’t heal due to overnight acid secretion
  - Few ADRs
    - Elderly patients may experience CNS ADRs
      - Confusion, delirium

- Cimetidine (Tagamet)
- Ranitidine (Zantac)
- Famotidine (Pepcid)

*We’ll cover these in the GI section*
Biogenic amines: 5-HT

- Serotonin (5-HT) Receptors
  - 80% in GIT

- Biosynthesis from tryptophan
  - Constricts GI and CV smooth muscle
  - Enhances platelet aggregation
  - CNS neurotransmitter
    - Mood, appetite, & sleep regulation, memory & learning
  - 14 5-HT receptor subtypes coupled to different trans-membrane signaling systems

Enterochromafin cells in GIT make 5-HT
- To move food along
- XS stored in platelets
- Lots of 5-HT in response to irritants leads to diarrhea... and vomiting (triggers CTZ)
### Serotonergic drugs in clinical use

*Goodman & Gilman’s The Pharm. Basis of Therapeutics 11th Ed., p 306*

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Drugs</th>
<th>Action</th>
<th>Clinical use</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-HT&lt;sub&gt;1A&lt;/sub&gt;</td>
<td>Buspirone ϒ-β (Buspar®)</td>
<td>Partial agonist</td>
<td>Anxiety, depression PO</td>
</tr>
<tr>
<td>5-HT&lt;sub&gt;1D&lt;/sub&gt;</td>
<td>Sumatriptan (Imitrex®) ϒ</td>
<td>Agonist</td>
<td>Migraine PO, SC, nasal spray</td>
</tr>
<tr>
<td>5-HT&lt;sub&gt;2A/2C&lt;/sub&gt;</td>
<td>Trazodone ϒ-γ (Desyrel®), Methysergide (Sansert®)</td>
<td>Antagonist</td>
<td>Migraine, depression, schizophrenia PO</td>
</tr>
<tr>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Ondansetron ϒ-β (Zofran®)</td>
<td>Antagonist</td>
<td>CINV, RINV, PONV PO, IV, IM</td>
</tr>
<tr>
<td>5-HT&lt;sub&gt;4&lt;/sub&gt;</td>
<td>Cisapride (Propulsid®)</td>
<td>Agonist</td>
<td>GI disorders</td>
</tr>
<tr>
<td>5-HT&lt;sub&gt;transporter&lt;/sub&gt;</td>
<td>Fluoxetine (Prozac®), ϒ-γ Sertraline (Zoloft®), SSRI’s</td>
<td>Inhibitor</td>
<td>Depression, OCD, PTSD, panic disorder… PO</td>
</tr>
</tbody>
</table>

5-HT<sub>3</sub> = only LGIC; found in CTZ & GI – will trigger emesis, diarrhea
Biogenic peptides

• **Angiotensin** *(angiotensin II = AngII = A2)*
  – Produced in response to **renin** release by kidneys
    • Very potent hypertensive agent

• **Kinins** *(Bradykinin, kallidin)*
  – Production triggered by tissue damage, allergic reactions, viral infections & other inflammatory events
    • Stimulate the pain response
    • *Arteriolar* dilation (POTENT, 10x histamine)
    • ↑ vascular permeability (leakiness)
    • Stimulate prostaglandin synthesis
    • Stimulate smooth muscle contractions, in GI tract, in lungs of asthmatics (bronchoconstriction!!)

*Ang II produced by ACE*  
*Bradykinin broken down by ACE*  
*Tachykinin receptors are NK₁, NK₂ & NK₃. NK₁ is the receptor for Substance P*
Angiotensin II
Corticosteroids
Estrogen
Thyroid hormones
Lipopolysaccharide (LPS)

Liver

Angiotensinogen
($\alpha_2$ globulin, made in liver, circulating in plasma)

↓Na$^+$ or ↓BP, β1 stimulation

Kidney

Renin

Angiotensin I (A1)

ACE in Lungs, etc

Angiotensinogen

↑Sympathetic tone

Ventricular remodeling

Vasoconstriction

Release of ADH & Aldosterone

Stimulate Ca$^{++}$ Influx

↑Thirst

↑BP

A2

Liver

Renin

Angiotensin I (A1)

Angiotensinogen

($\alpha_2$ globulin, made in liver, circulating in plasma)
Synthesis Triggers

- Angiotensinogen
  - ↑ Plasma levels of:
    - Angiotensin II
    - Corticosteroids
    - Estrogen
    - Thyroid hormone
    - LPS (bacterial endotoxin)
  - Note: angiotensinogen is a plasma protein synthesized in the liver

- Renin
  - ↓ BP (detected by baroreceptors)
  - ↓ Intra renal pressure at the juxtaglomerular apparatus
  - ↓ NaCl to kidney
  - Sympathetic stimulation (β₁)
  - Prostaglandins produced by macula densa cells
  - Note: renin is an enzyme, AKA angiotensinogenase, produced by juxtaglomerular (granular) cells surrounding the afferent renal arterioles

No NSAIDs with any drug affecting RAAS – increased kidney failure risk
## Angiotensin II Effects

Adapted from: p798, 11th Ed, Goodman & Gilman’s

<table>
<thead>
<tr>
<th>Δ Peripheral resistance</th>
<th>Δ Renal function</th>
<th>Δ CV structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. ↑Peripheral noradrenergic NT</td>
<td>2. ↑Aldosterone release from adrenal cortex - ↑Na⁺ reabsorption, ↓K⁺ excretion in distal nephron)</td>
<td></td>
</tr>
<tr>
<td>4. ↑Catecholamine release from adrenal medulla</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**RAPID PRESSOR RESPONSE**

**SLOW PRESSOR RESPONSE**

**CV HYPERTROPHY & REMODELING**
Direct Renin Inhibitor 🕵️‍♂️ -D

• **Aliskiren (Tekturna) 🥤**
  – Indicated for HT
  – Not for diabetics on ACEI or ARBs due to hyperkalemia and risk of kidney failure
  – High fat meal DECREASES absorption
    • Develop a pattern for taking pills
  – ADRs
    • Fetotoxicity, hyperkalemia*, angioedema, hypotension, decreased kidney function*

PO  ■ = *fetotoxic*

* Requires monitoring
### Angiotensin Converting Enzyme Inhibitors (ACEI) 🌞 -D

<table>
<thead>
<tr>
<th>Drug</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril (Capoten)</td>
<td>HT, Left ventricular dysfunction after MI, CHF, diabetic nephropathy, off label uses</td>
</tr>
<tr>
<td>Benazepril (Lotensin)</td>
<td>Prodrug - HT, CHF, chronic renal failure, asymptomatic left ventricular dysfunction</td>
</tr>
<tr>
<td>Enalapril (Vasotec)</td>
<td>Prodrug - HT, CHF</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>HT, CHF, diabetic complications</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>HT, CHF (prodrugs)</td>
</tr>
<tr>
<td>Trandolapril</td>
<td></td>
</tr>
</tbody>
</table>

113M Rx’s of the top 6 ACE inhibitors in 2007 – Dosage must be individualized

■ = fetotoxic

PO, IV
ACE Inhibitor Problems

- Hypotension
- **Cough** - 5-20% of patients
- Hyperkalemia
- *Acute renal failure*
- **Teratogenic fetotoxic**
- Skin rash
- Proteinuria
- *Taking with food* ↓ absorption 30-40%

These effects may be due to ↑ bradykinin

Boxed warning: fetotoxic

Some people have more Bradykinin B2 receptors

ACEI work better in non-blacks

Angioedema (may be life threatening) ~0.1%
- Dysgeusia (loss of taste)
- Neutropenia (1/500)
- *Glycosuria* (no hyperglycemia!)
- Hepatotoxicity
- Drug interactions
  - Antacids
  - NSAIDs
  - K⁺ sparing diuretics

8/19/14 PHRM 203 - Autocoids
Angioedema in a 68 yr. old African American Woman on ACE inhibitor

Photo by David E. Winchester, MD, Resident, Department of Internal Medicine, and Margaret L. Plews-Ogan, MD, MS, Associate Professor and Division Head of General and Geriatric Medicine, University of Virginia Health System, Charlottesville

http://www.residentandstaff.com/issues/articles/2007-02_06.asp
Angiotensin II receptor blocker

ARBs (antagonists) -D

- Candesartan - Atacand
- Eprosartan - Teveten
- Irbesartan - AVAPRO -D
- Losartan — COZAAR (see CV lectures)
- Olmesartan - Benicar
- Telmisartan - Micardis
- Valsartan - DIOVAN -D

Boxed warning: fetotoxic

AT₁ receptor blockers
- Smooth muscle
  - vasoconstriction
- Adrenal gland
  - aldosterone release

Indications
- Irbesartan (Avapro)
  - HT, Type 2 diabetic nephropathy
- Valsartan (Diovan)
  - HT, HF, left ventricular dysfunction after MI
Bradykinin-related

In 2007, Bayer discontinued this drug, but it may still be used through a process set up by the FDA

- **Aprotinin - Trasylol**
  - Potent inhibitor of kallikrein and other serine proteases
    - Natural protease inhibitor harvested from cow lungs
    - Identical to Bovine Pancreatic Trypsin inhibitor
  - Kallikreins are the enzymes that produce kinins
    - Bradykinin
      - Bronchospasm, vasodilation, edema, pain, activate PLA…
  - Indication: ↓ blood loss during coronary artery surgery
    - Boxed warning: May cause fatal 1st dose anaphylaxis

IV through central line
Small proteins

• Cytokines
  – Cell signaling molecules
    • Chemokines (dozens, each attract specific WBCs into specific tissues)
    • Lymphokines (secreted by activated B & T lymphocytes)
    • Interleukins & Interferons (signaling molecules between WBCs)
    • Tumor Necrosis Factors $\alpha$ & $\beta$ (cause apoptosis)
    • Erythropoietin (regulates RBC production) and Thrombopoietin
      (regulates platelet production)
  – Clinically significant drugs to be discussed elsewhere

• Cytokine storm
  – $\oplus$ feedback loop - cytokines $\uparrow$ # of T-cells that $\uparrow$
cytokines that $\uparrow$ # of T-cells…

HIV uses cytokine receptors CXCR4 & CCR5 to enter WBCs

Cytokine storm is what kills in pandemic influenza, SARS, etc.
Endothelium-derived agents

• NO - Nitric oxide
  – Intracellular and cell-to-cell messenger
    • $t_{1/2}$ of seconds
  – Mediator of pain perception, etc, in CNS
  – $\oplus$ Macrophage induced cytotoxicity
  – $\ominus$ platelet aggregation & adhesion
  – Vasodilator
    • XS NO $\rightarrow$ inflammation
    • Sildenafil (Viagra) $\oplus$ a 5PDE inhibitor that $\uparrow$ NO activity

PO

Sounds like Nitrous oxide $N_2O$
Membrane-derived agents

**Eicosanoids**

- **Biosynthesis**
  - Precursor = essential fatty acids
  - 20 carbons
  - 3, 4, or 5 double bonds
    - 8, 11, 14-eicosatrienoic acid
    - 5, 8, 11, 14-eicosatetraenoic acid (*Arachidonic acid, ω-6*)
      » Derived from linoleic acid (9, 12-octadecadienoic acid)
      or directly ingested
    - 5, 8, 11, 14, 17-eicosapentenoic acid (*EPA, ω-3*)
      » Major constituent of fatty fish oil
Membrane-derived agents

• **Eicosanoids** (eikosi = Greek, “twenty”)
  
  – **Leukotrienes**  
    • Produced by all WBC’s - LTA$_4$-LTF$_4$
  
  – **Prostaglandins**  
    • Produced by all nucleated cells, except lymphocytes

  – **Thromboxanes**  
    • Produced by platelets

  – **Platelet Activating Factor (PAF)**  
    • Produced by neutrophils, basophils, platelets, endothelial cells

*Derived from Arachidonic acid, the Eicosanoids, LTs and PGs, TXA and PAF, are all LIPIDS*

Produced in same pathway as PGs & therefore blocked by NSAIDs such as aspirin… which is why aspirin is anticoagulant!
Arachidonic Acid

LOX

PGD₂

Bronchoconstriction,

↑lung mucous,

WBC attraction,

leaky blood vessels

PGE₂

PGE₂ – Vaso/bronchodilation, FEVER, PAIN, ↓ GASTRIC ACID,

↑Gastric mucous, uterine contractions, ↑hormone release, ↓NE release

PGF₂

PGF₂ – Bronchoconstriction, strong uterine contractions

PGI₂

PGI₂ – Vaso/bronchodilation, PAIN, ⊗ ⊗ ⊗ PA

TXA₂

TXA₂ – ⊗ ⊗ ⊗ PA (Platelet Aggregation)

203 - Autocoids

8/19/14 A Beale
## Eicosanoid Related

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
<th>Mechanism</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>LT-inhibitors</td>
<td>Zileuton (Zyflo CR)</td>
<td>5-lipoxygenase (LOX)</td>
<td>Asthma&lt;br&gt;Note 2008 FDA warning - Neuropsychiatric effects of agitation, aggression, anxiousness, insomnia, dream abnormalities, suicidal ideation &amp; behavior possible&lt;br&gt;Zileuton &lt;sup&gt;!&lt;/sup&gt; (Zyflo CR)&lt;br&gt;Montelukast (Singulair)&lt;br&gt;Zafirlukast (Accolate)</td>
</tr>
<tr>
<td></td>
<td>Montelukast (Singulair)&lt;br&gt;Zafirlukast (Accolate)</td>
<td>Blocks LT receptor</td>
<td></td>
</tr>
<tr>
<td>NSAID</td>
<td>Ibuprofen (Advil)</td>
<td>COX</td>
<td>Pain and inflammation</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>Dexamethasone (Dexasone, etc.)</td>
<td>Indirectly phospholipase A₂</td>
<td>Anti-inflammatory, anti-allergic, anti-emetic and anti-neoplastic</td>
</tr>
<tr>
<td>Prostaglandin</td>
<td>Misoprostol (Cytotec)</td>
<td>PGE₁ analog</td>
<td>Heal gastric ulcers, abortifacient&lt;br&gt;(in combo with diclofenac, a NSAID, for arthritis: Arthrotec)</td>
</tr>
</tbody>
</table>

8/19/14

PHRM 203 - Autocoids