RSPT 2217
Corticosteroids

Chapter 11

The Inflammatory Response

- A general definition of inflammation is the response of vascularized tissue to injury
- First described in the first century A.D. and revised in the 20th century as follows – known as the triple response:
  - redness: the local dilation of blood vessels, occurring in seconds
  - flare: a reddish color several centimeters from the site, occurring 15-30 seconds after injury
  - wheal: local swelling, occurring in minutes

The Inflammatory Response

- The process of inflammation, producing the visible results is caused by the following four major categories of activity:
  - increased vascular permeability: produces and exudates into surrounding tissues
  - leukocytic infiltration: the emigration of white cells through capillary walls (diapedesis) in response to attractant chemicals (chemotaxis)
  - phagocytosis: white cells and macrophages ingest and process foreign material, such as bacteria
  - mediator cascade: histamine and chemoattractant factors are released at the site of the injury and various inflammatory mediators are generated

Inflammation in the Airway

- Airway inflammation can occur in the lungs in response to a variety of causes
  - direct trauma (GSW, stabbing)
  - indirect trauma (blunt chest injury)
  - inhalation of noxious or toxic substances (chlorine gas, smoke)
  - respiratory infections and systemic infections producing sepsis and septic shock with acute respiratory distress syndrome (ARDS)
  - allergic and non-allergic stimulation in asthma

Inflammation in the Airway

- The two most common inflammatory diseases of the airway are chronic bronchitis and asthma
- Asthmatic reactions are distinguished into an early-phase and late-phase reaction
- Following an insult to the asthmatic airway by an allergen, cold air, viral infection or noxious gas, there is evidence that the early-phase response is caused by immunoglobulin E (IgE)-dependent activation of mast cells, which can release inflammatory mediators
- The immediate response is bronchoconstriction, which peaks at around 15 minutes and declines over the next hour

Inflammation in the Airway

- Although this bronchoconstriction may self-limit or respond to β agonists, the progression of cellular events can continue
- Mast cell mediators and the release of cytokines recruit other inflammatory cells (eosinophils, basophils, monocytes/macrophages, lymphocytes) and other cytokines, causing the late-phase response
- During this late-phase response, mast cells and recruited inflammatory cells release a range of inflammatory mediators
- The late-phase response occurs 6-8 hrs. after a challenge and may last up to 24 hrs.
Corticosteroids

- Adrenocorticosteroids are naturally occurring hormones secreted by the adrenal cortex. They are classified into three groups according to chemical structure and major physiological effects
  - glucocorticosteroids (anti-inflammatory and immunosuppressant actions)
  - mineralocorticosteroids (maintenance of fluid and electrolyte balance)
  - sex hormones
- Of these, the glucocorticosteroids are the primary ones used in respiratory care for their anti-inflammatory properties

Corticosteroids

- Mechanism of action
  - Pharmacologic actions are varied. The major actions pertaining to respiratory care are:
    - anti-inflammatory action - inhibits the formation and release of inflammatory mediators by interfering with the degranulation of the mast cell
    - increased sympathomimetic effects - inhibits COMT
    - enhanced ciliary transport - increase mucus secretion by altering mucus composition
    - enhanced sympathomimetic responsiveness - indirectly stimulates cAMP production by restoring responsiveness to β-adrenergic stimulation
    - improved sense of well being

Corticosteroids

- Indications
  - asthma – recommended for maintenance and control therapy of chronic asthma, identified in the NAEPP EPR-II as Step 2 asthma (greater than 2 days/week of symptoms, greater than 2 nights/month with symptoms, FEV1 or PEF 80% ± 20% or greater)
  - COPD – not currently recommended by the American Thoracic Society for other than acute exacerbations; however, many COPD patients report lessened symptoms when taking aerosol corticosteroids
  - active interstitial lung disease
  - neonatal respiratory distress syndrome
  - ARDS
  - aspiration pneumonitis

Corticosteroids

- Contraindications
  - hypersensitivity to any of the formulation's ingredients
  - systemic fungal infections
  - pts. with psychoses
  - PUD
  - acute glomerulonephritis
  - herpes simplex of the eye
  - severe diabetes mellitus

Corticosteroids

- Precautions
  - not indicated for the rapid relief of bronchospasm
  - if recommended aerosol dosages are exceeded (generally ≥ 1000 µg/day), the HPA transport mechanism may be affected
  - during pregnancy, use only if benefits outweigh the potential risks to the fetus
  - prolonged therapy may result in Cushingoid syndrome (moon face, edema, hump back) with adrenal insufficiency
  - when tapering dosages, watch for withdrawal syndrome: anorexia, nausea, vomiting, lethargy, headache, hypotension
  - administer PO forms with food
  - local administration is preferred when indicated
  - long-term therapy requires lowest effective dose

Corticosteroids

- Adverse reactions (systemic administration)
  - suppression of the HPA system and adrenal cortex
  - fluid and electrolyte imbalance - Na+ and fluid retention, edema, hypokalemia, met. Alkalosis
  - cardiovascular - fat embolism, thromboembolism, arrhythmias, syncope, hypertension
  - GI - pancreatitis, abdominal distention, nausea, vomiting, weight gain, PUD, perforation of the small and large bowels
  - CNS - headache, vertigo, insomnia, restlessness, seizures, mood swings, depression, euphoria
  - musculoskeletal - muscle wasting, muscle pain, osteoporosis, delayed healing
  - misc. - growth suppression, obesity, Cushingoid appearance, hyperglycemia, diabetes, immunosuppression, cataract formation, increased WBC
Corticosteroids

- Adverse reactions (aerosol administration)
  - local - throat irritation, hoarseness, dry mouth, coughing, oropharyngeal fungal infection (Candida albicans or Aspergillus niger); rinsing and gargling after administration may prevent this infection
  - systemic - suppression of HPA mechanism
  - other - bronchospasm, rashes

Aerosol Corticosteroids

- Beclomethasone Dipropionate HFA (hydrofluoroalkane)
  - Brand name: QVAR
  - Dosage form
  - MDI: 40 mcg/actuation, 80 mcg/actuation
  - Dosage
    - adults ≥ 12 yr.: 40-80 mcg bid, 40-160 mcg bid**
    - children ≥ 5 yr.: 40-80 mcg bid
      - * recommended starting dose if on bronchodilators alone
      - ** recommended starting dose if on inhaled corticosteroids previously

- Flunisolide
  - Brand names: AeroBid, AeroBid-M
  - Dosage form
  - MDI: 250 mcg/actuation
  - Dosage
    - adults and children ≥ 6 yrs.: 2 inh bid; adults: no more than 4 inh daily; children ≥ 15 yr.: no more than 2 inh daily

- Flunisolide Hemihydrate HFA
  - Brand names: Aerospan
  - Dosage form
  - MDI: 80 mcg/actuation
  - Dosage
    - adults ≥ 12 yr.: 2 inh bid; no more than 4 inh daily
    - children 6-11 yr.: 1 inh daily; no more than 2 inh daily

- Fluticasone Propionate
  - Brand names: Flovent HFA, Flovent Diskus
  - Dosage form
    - MDI: 44, 110 or 220 mcg/actuation
      - Diskus: 50, 100, 250 mcg/actuation
  - Dosage
    - (MDI): adults ≥ 12 yr.: 88 mcg bid, 88-220 mcg bid**, 880 mcg bid***
      - (Diskus): adults 100 mcg bid*, 100-250 mcg bid**, 1000 mcg bid***; children 4-11 yr.: 50 mcg bid
        - * recommended starting dose if on bronchodilators alone
        - ** recommended starting dose if on inhaled corticosteroids previously
        - *** recommended starting dose if on oral corticosteroids previously

- Triamcinolone Acetonide
  - Brand names: Azmacort
  - Dosage form
  - MDI: 100 mcg/actuation
  - Dosage
    - adults ≥ 12 yr.: 2 inh tid or qid
    - Children ≥ 6 yr.: 1-2 inh tid or qid
# Aerosol Corticosteroids

### Budesonide
- **Brand names:** Pulmicort Turbuhaler (DPI), Pulmicort Respules (nebulizer solution)
- **Doseage form**
  - DPI: 200 mcg/actuation
  - SVN: 0.25 mg/2ml; 0.5 mg/2ml unit dose respules
- **Doseage**
  - SVN: adults: 1 respule daily, children 6-12 yrs.: 0.5 mg or 1 mg once daily or twice daily in divided doses
  - * recommended starting dose if on bronchodilators alone
  - ** recommended starting dose if on inhaled corticosteroids previously
  - *** recommended starting dose if on oral corticosteroids previously

### Ciclesonide
- **Brand names:** Alvesco
- **Dosage form**
  - MDI: 80 or 160 mcg/actuation
- **Dosage**
  - For patients ≥ 12 years
  - * recommended starting dose if on bronchodilators previously
  - ** recommended starting dose if on inhaled corticosteroids previously
  - *** recommended starting dose if on oral corticosteroids previously

### Mometasone
- **Brand names:** Asmanex
- **Dosage form**
  - Asmanex Twisthaler DPI: 110 (100) or 220 (200) mcg/actuation
- **Dosage**
  - For patients ≥ 12 years
  - Recommended starting doses
    - 220 mcg daily in the evening*, 220 mcg daily in the evening**, 440 mcg bid***
    - * recommended starting dose if on bronchodilators previously
    - ** recommended starting dose if on inhaled corticosteroids previously
    - *** recommended starting dose if on oral corticosteroids previously
  - Recommended maximum daily doses
    - 440 mcg*, 440 mcg**, 880 mcg***

### Fluticasone Propionate/Salmeterol
- **Brand names:** Advair Diskus (DPI), Advair HFA (MDI)
- **Dosage form**
  - DPI: 100, 250 or 500 mcg fluticasone and 50 mcg salmeterol/inh; MDI: 45, 115 or 230 mcg fluticasone and 21 mcg salmeterol/actuation
- **Dosage**
  - (DPI): adults & children ≥ 12 yr.: 100/50, 1 inh bid (starting dose if not currently taking corticosteroids); maximum recommended dose is 500/50 bid
  - (DPI): children ≤ 4 yr.: 100/50, 1 inh bid for those who are symptomatic while taking corticosteroids
  - (MDI): adults & children ≥ 12 yr.: 2 inh bid
Corticosteroids

Aerosol Corticosteroids

- **Budesonide/Formoterol fumarate HFA**
  - Brand names: Symbicort
  - Dosage form
    - MDI: 80 or 160 mcg budesonide and 4.5 mcg formoterol/actuation
  - Dosage
    - MDI: adults & children ≥ 12 yr.: 160/9 bid; 320/9 bid; daily maximum 640/18
    - SVN: adults: 1 respule daily, children 6-12 yrs.: 0.5 mg or 1 mg once daily or twice daily in divided doses

- **Mometasone/Formoterol**
  - Brand name: Dulera
  - Dosage form:
    - MDI: 100 or 200 mcg mometasone and 5 mcg formoterol/actuation
  - Dosage
    - MDI: adults & children ≥ 12 yr.
      - 100 mcg/5 mcg, 2 inhalations twice daily; daily maximum 400/20
      - 200 mcg/5 mcg, 2 inhalations twice daily, 2 inhalations twice daily; daily maximum 800/20

  - * recommended starting dose if on bronchodilators alone
  - ** recommended starting dose if on inhaled corticosteroids previously
  - *** recommended starting dose if on oral corticosteroids previously

Oral, IV & IM Corticosteroids

- **Dexamethasone**
  - Brand names: Decadron, Hexadrol
  - Mode of action: potent, long-acting anti-inflammatory agent; rapidly absorbed after oral administration
  - Dosage forms: oral, IV

- **Hydrocortisone Sodium Succinate**
  - Brand name: Solu-Cortef
  - Mode of action: relatively short-acting anti-inflammatory agent; normal daily secretion of hydrocortisone in humans is 10-25 mg; normal plasma level is 5-30 mg/100; used in the tx of status asthmaticus and other acute chest diseases
  - Onset of action: app. 60 min.; peak action: app. 5 hrs.; excreted within 12 hrs.
  - Dosage forms: oral, IV, IM

- **Methylprednisone**
  - Brand names: Solu-Medrol (IV, IM), Medrol (oral)
  - Mode of action: potent intermediate-acting anti-inflammatory agent; alternate drug to hydrocortisone for hypersensitivity reactions, status asthmaticus, aspiration pneumonitis, ARDS
  - Onset of action: slow, 12-24 hrs.
  - Duration: long, up to 1 week
  - Dosage form: oral, IV, IM

- **Prednisone**
  - Brand names: Orasone, Deltasone, Meticorten
  - Mode of action: intermediate-acting anti-inflammatory agent; 3-5 times more potent than hydrocortisone; metabolized to its active form prednisolone in the liver
  - Dosage form: oral

- **Prednisolone**
  - Brand names: Delta-Cortef, Sterane, Hydeltrasol
  - Mode of action: essentially the same as prednisone; one of the more commonly used corticosteroids for allergic and inflammatory conditions
  - Dosage form: oral, IV, IM