Chapter 11

Corticosteroids in Respiratory Care
Clinical Indications for Use of Inhaled Corticosteroids

- **Step 2 asthma**: Symptoms greater than 2 days/week, but <1 time/day and/or >2 nights/month with symptoms, FEV\(_1\) or peak expiratory flow (PEF) 80% predicted or greater, but PEF variability at 20% to 30%

- **COPD**

- **Intranasal aerosol agents**: Management of seasonal and perennial allergic and nonallergic rhinitis
Physiology of Aerosolized Corticosteroids

- Identification and Source
  - Adrenal cortical hormones
    - Glucocorticoids
      - a.k.a. glucocorticosteroids, or steroids
    - Mineralocorticoids
      - Regulate body water
    - Sex hormones
      - Cause secondary sex characteristics
Physiology of Aerosolized Corticosteroids (cont’d)

The hypothalamic-pituitary-adrenal axis

- Pathway for release and control of corticosteroids
- Stimulation of the hypothalamus causes impulses to be sent to median eminence
- Corticotropin-releasing factor (CRF) is released
- Corticotropin, or adrenocorticotropic hormone (ACTH), stimulates the adrenal cortex to secrete glucocorticoids
Physiology of Aerosolized Corticosteroids (cont’d)

- Hypothalamic-pituitary-adrenal suppression with steroid use
  - Body cannot distinguish between *endogenous* and *exogenous*
  - Administration of glucocorticoid drugs raises the body’s level
  - Inhibits the hypothalamus and pituitary glands
  - Referred to as *HPA suppression* or *adrenal suppression*
Physiology of Aerosolized Corticosteroids (cont’d)

- The diurnal steroid cycle
  - Production of the body’s own glucocorticoids follows a rhythmic cycle, termed *diurnal* or *circadian rhythm*
  - *Cortisol levels are highest in the morning around 8 a.m.*
  - Examples of interference with cycle:
    - Jet lag
    - Coming off of a night shift
Alternate-day steroid therapy

- Mimicks natural diurnal rhythm by giving a steroid drug early in the morning, when normal tissue levels are high
- On alternate day, regular diurnal secretion in hypothalamic-pituitary-adrenal (HPA) system can resume
Nature of Inflammatory Response

- Inflammation
  - *Triple response*:
    - **Redness**: Local dilation of blood vessels, occurring in seconds
    - **Flare**: Reddish color several centimeters from the site, occurring 15 to 30 seconds after injury
    - **Wheal**: Local swelling, occurring in minutes
Nature of Inflammatory Response (cont’d)

- *Increased vascular permeability*: An exudate is formed in the surrounding tissues
- *Leukocytic infiltration*: White cells emigrate through capillary walls (diapedesis) in response to attractant chemicals (chemotaxis)
Nature of Inflammatory Response (cont’d)

- **Phagocytosis:** White cells and macrophages (in the lungs) ingest and process foreign material such as bacteria

- **Mediator cascade:** Histamine and chemoattractant factors are released at the site of injury, and various inflammatory mediators such as complement and arachidonic acid products are generated
Nature of Inflammatory Response (cont’d)

- Inflammation in the airway
  - Chronic bronchitis and asthma most common
  - Treatment with antiinflammatory agents such as glucocorticoids is important to reduce the basal level of airway inflammation and thereby reduce airway hyperresponsiveness and the predisposition to acute episodes of obstruction
Aerosolized Corticosteroids

- Aerosolized corticosteroid agents
  - *Beclomethasone dipropionate* (QVAR)
  - *Triamcinolone acetonide* (Azmacort)
  - *Flunisolide* (AeroBid, AeroSpan)
  - *Fluticasone propionate* (Flovent HFA, Flovent Diskus)
Aerosolized Corticosteroids (cont’d)

- *Budesonide* (Pulmicort Respules, Pulmicort Turbuhaler)
- *Mometasone furoate* (Asmanex Twisthaler)
- Ciclesonide (Alvesco)
  - Alvesco is not yet available in the United States
  - Available as intranasal agent, Omnaris

- **Combination Products**
  - *Fluticasone propionate/salmeterol* (Advair)
  - *Budesonide/formoterol* (Symbicort)
Aerosolized Corticosteroids (cont’d)

- Evidence of a beneficial, complementary interaction between glucocorticoids and β-adrenergic agonists
- Steroids increase β<sub>2</sub>-adrenergic receptor transcription
- Inhaled corticosteroid therapy can provide partial protection against development of tolerance
- Salmeterol has been shown to promote binding of the glucocorticoid receptor to the response element of the cell’s nuclear DNA
Aerosolized Corticosteroids (cont’d)

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Aerosolized Corticosteroids (cont’d)

- Intranasal corticosteroids
  - All of the steroids available as orally inhaled agents are also available in an intranasal formulation
  - However, agents will have different trade names
  - Used for treatment of allergic or inflammatory nasal conditions and seasonal or perennial allergic or nonallergic rhinitis and to prevent reoccurrence of nasal polyps
Pharmacology of Corticosteroids

● Mode of action
  ➢ Steroids modify the inflammatory response by inducing gene expression within the cell
Pharmacology of Corticosteroids (cont’d)

- Mode of action (cont’d)
  - Three general actions of suppression
    - Upregulate the transcription of antiinflammatory genes for substances such as lipocortin
    - Suppress factors such as activator protein-1 (AP-1) and nuclear factor-κB (NF-κB), which cause transcription of genes involved in inflammation
    - Upregulate the expression of inhibitors of NF-κB, such as the inhibitor protein IκBa
Pharmacology of Corticosteroids (cont’d)

- Effect on WBC count
  - Demargination: Depletion of neutrophil stores reduces their accumulation at inflammatory sites and in exudates
  - Overall increase in the white cell count can then be seen in patients
  - Constriction of microvasculature to reduce leakage of cells and fluids into inflammatory sites
Pharmacology of Corticosteroids (cont’d)

- **Effect on β receptors**
  - Restore responsiveness to β-adrenergic stimulation
  - Enhance β-receptor stimulation by increasing the number and availability of β receptors on the cell surfaces and by increasing affinity of the receptor for β agonists
Hazards and Side Effects of Steroids

- Systemic administration of steroids
  - Suppression of the HPA axis
  - Immunosuppression
  - Psychiatric reactions
  - Cataract formation
  - Myopathy of striated skeletal muscle
  - Peptic ulcer
Hazards and Side Effects of Steroids (cont’d)

- Systemic administration of steroids (cont’d)
  - Fluid retention
  - Hypertension
  - Increased WBC count
  - Dermatological changes
  - Slowing of growth in children
  - Hyperglycemia
Hazards and Side Effects of Steroids (cont’d)

- Systemic side effects with aerosol administration
  - Of major concern:
    - HPA suppression
    - Loss of bone density
    - Growth restriction in children
Hazards and Side Effects of Steroids (cont’d)

- Systemic side effects with aerosol administration (cont’d)
  - Potential:
    - Adrenal insufficiency
    - Allergic inflammation after cessation
    - Suppression of HPA function
    - Growth reduction in children
Hazards and Side Effects of Steroids (cont’d)

- Topical (local) side effects with aerosol administration
  - Most common:
    - Oropharyngeal candidiasis (oral thrush)
    - Dysphonia
  - What to do:
    - Use minimal dose
    - Use reservoir
    - Rinse mouth after use
Clinical Application of Aerosol Steroids

- Use in asthma
  - Early use in asthma
  - For acute severe asthma
  - Clinical use of inhaled corticosteroids
Clinical Application of Aerosol Steroids (cont’d)

- Use in COPD
  - Relieves symptoms
  - Little or no effect on $\text{FEV}_1$
Respiratory Care Assessment of Inhaled Corticosteroid Therapy

- Instruct patient in correct use of delivery system
  - Controller…not a rescue agent!
- Respiratory rate and pattern
- Breath sounds
- Pulse
- Subjective response
- Use of peak flow meter
- Exacerbations, missed work/school, ER visits
- Assess for side effects