Chapter 89: Glucocorticoids: Clinical Pharmacology

1. Which of the following treatments of moderate to severe acute asthma in adults is consistent with NHLBI guidelines?
   A. Hydrocortisone or its equivalent, 60 to 80 mg/day until the FEV1 is greater than 70% predicted or personal best.
   B. Prednisone, prednisolone, or methylprednisolone, 60 to 80 mg per day until the PEF is 70% of predicted or personal best.
   B. Hydrocortisone or its equivalent, 120 to 180 mg/day until the PEF is greater than 70% predicted or personal best.
   D. Prednisone, prednisolone, or methylprednisolone, 120 to 180 mg per day until the FEV1 is 70% of predicted or personal best.
   E. Doubling the dose of inhaled corticosteroid, for patients on daily inhaled corticosteroids.

2. Inhaled corticosteroids are indicated for which group of asthmatic patients:
   A. Patients with moderate or severe persistent asthma only.
   B. All patients with persistent asthma.
   C. Children with persistent asthma who have failed leukotriene antagonist therapy.
   D. Patients with intermittent asthma and exercise-induced bronchospasm shortly before exercise.
   E. Infants with two episodes of wheezing and a parental history of atopy.

3. One advantage of “step-down” therapy (in which patients are started on a relatively high dose in order to achieve more rapid and complete suppression of airway inflammation) versus fixed-dose therapy with inhaled corticosteroids is:
   A. Greater increase in FEV1.
   B. Greater decrease in sputum eosinophilia.
   C. More sustained improvement in bronchial hyperresponsiveness.
   D. Fewer side effects.
   E. None of the above.

4. Which of the following is FDA approved for use in children under age 4?
   A. Fluticasone propionate metered dose inhaler
   B. Budesonide Turbuhaler
   C. Budesonide suspension for nebulization.
   D. Ciclesonide powder for inhalation.
   E. None of the above.

5. Which of the following tests is the most sensitive measure of proximal muscle
weakness due to steroid-induced atrophy?
A. Isokinetic muscle testing of hip flexor strength.
B. CPK
C. Aldolase
D. Lactate dehydrogenase
E. Muscle biopsy

6. In treating acute asthma in children, what is the NHLBI guideline recommendation regarding the appropriate clinical situation to safely discontinue glucocorticoid therapy?
A. The patient has a PEF of 70% of predicted / personal best
B. The patient has a PEF of 80% of predicted / personal best
C. Absence of wheezing on auscultation
D. After 2 weeks of therapy
E. None of the above

7. What has been shown regarding the benefit of inhaled glucocorticoids in asthmatic patients?
A. Increased risk of hospitalization
B. Increased risk of severe and life-threatening asthma exacerbations
C. Decreased risk of asthma-related mortality
D. Increased use of short acting beta agonists
E. None of the above

8. Which of the following inhaled glucocorticoids has been shown to exhibit oral glucocorticoid-sparing effects in adults with asthma?
A. Beclomethasone HFA
B. Fluticasone propionate
C. Triamcinolone
D. Flunisolide
E. None of the above

9. Adverse effects associated with systemic glucocorticoids include
A. Hypokalemia
B. Weight gain
C. Diminished IgG levels
D. Pseudotumor cerebri
E. All of the above

10. What is true regarding local adverse effects of inhaled glucocorticoids?
A. Thrush is the most common
B. Oral candidiasis and dysphonia are the least common
C. Dysphonia is likely due to vocal cord myopathy
D. The use of a holding chamber does not alter the incidence of local adverse effects
E. Mouth rinsing using a "swish and spit" technique is not recommended

Answers
1. B, page 1576
http://www.ncbi.nlm.nih.gov/books/NBK7228/#A2569

2. B, page 1579
Section titled:’’ Inhaled glucocorticoids as first-line therapy for all levels of persistent asthma and all ages.’’ See also page 1580 regarding ICS in infants with two episodes of wheezing: ‘’The investigators found no difference in the proportion of children with active wheeze, physician diagnosed asthma, use of asthma medications, lung function, and airway reactivity at age 5 years in those treated with fluticasone propionate compared to those treated with placebo.’’

3. E, page 1582
...clear dose–response relationships are difficult to demonstrate in most patients with asthma. As a result, most studies have failed to demonstrate any advantage with ‘step-down’ over fixed-dose therapy.’’

4. C, page 1582
“Budesonide suspension for nebulization is the only inhaled glucocorticoid preparation currently approved for use in children less than 4 years old, and the only glucocorticoid available in a nebulizable form.”

5. A, page 1586
“Isokinetic muscle testing of hip flexor strength is the most sensitive and objective measure of proximal muscle weakness.70 Muscle enzymes such as CPK, aldolase, and lactate dehydrogenase (LDH) are usually not elevated, and muscle biopsy reveals atrophy, rather than necrosis, of the muscle fibers.”

6. A, page 1576-7
“The NHLBI guidelines recommend administering prednisone, prednisolone, or MPn, 1 mg/kg/dose every 6 hours for 48 hours, then 1–2 mg/kg/day (maximum dose 60 mg/day) in two divided doses until PEF is 70% of predicted or personal best.

7. C, page 1579
See ‘’Effect on asthma morbidity/mortality:’’ A nested case–control analysis of over 12 000 asthmatic patients from Canada, found subjects on chronic BDP therapy to be one-tenth as likely to die or have a near-fatal asthma exacerbation as patients not on inhaled glucocorticoids. In another study, adjusted mortality rate fell from 0.72 to 0.38, while prescriptions for inhaled glucocorticoids rose 479%. These investigators found a highly significant inverse correlation between inhaled glucocorticoid use and asthma mortality.

8. B, page 1583
See "Oral glucocorticoid-sparing effect of the second-generation inhaled
glucocorticoids:” Fluticasone propionate, budesonide, mometasone furoate and ciclesonide have shown greater topical than systemic potencies and were associated with a decreased need for oral glucocorticoids.

9. E, Table 89.3, page 1584. Adverse effects include metabolic, endocrinologic, immunologic, dermatologic, musculoskeletal, ophthalmologic, cardiovascular, hematologic and neurologic effects.

10. C, page 1586. See "Local adverse effects;" Oral candidasis and dysphonia are the most common. The use of a holding chamber decreases the incidence of local adverse effects. "Swish and spit" is recommended.

**Allergy and Immunology Review Corner:** Chapter 90 of *Middleton’s Allergy Principles and Practice, 7th* Edition, edited by N. Franklin Adkinson, et al.

**Chapter 90:** The Chromones: Cromoly Sodium and Nedocromil Sodium

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1. Cromolyn sodium showed significant reduction of which cell in the sputum:
   A: Neutrophil
   B: Eosinophils
   C: Mast cell
   D: Basophill

2. Cromolyn sodium prevents:
   A. Early asthmatic reaction to bronchial challenge
   B. Early and late asthmatic reaction to bronchial challenge
   C. Late asthmatic reaction to bronchial challenge
   D. Did not show effect

3. For children less than 5 years the preferred choice of cromolyn sodium is:
   A. 1% aqueous solution with the addition of a small dose of beta agonist
   B. Inhaled powder from capsule
   C. MDI
   D. Not proven for children less than 5 years

4. Studies of cromolyn sodium in patient with seasonal AR and in allergic and non-allergic perennial rhinitis shown:
   A. Better than placebo
   B. Equal to placebo
   C. No difference
   D. No such studies was conducted
5. Cromolyn sodium in mice has shown to inhibit in vitro and in vivo the effect of:
   A. Parainfluenza
   B. Adenovirus
   C. Influenza
   D. Rhinovirus

6. Intranasal nedocromil sodium had a significant effect on the symptoms of nasal secretions in:
   A. Coronavirus
   B. Rhinovirus
   C. Influenza
   D. Parainfluenza

7. Main adverse effect of cromolyn sodium
   A. Hypersensitivity
   B. Local irritation
   C. Nausea and vomiting
   D. Electrolyte imbalance

8. The metabolism of cromolyn and nedocromil occur in:
   A. Liver
   B. Kidney
   C. Both liver and kidney
   D. Not metabolized and are excreted unchanged in bile and urine.

9. One mode of action of chromones is local reduction of:
   A. IgE
   B. IgM
   C. IgG4
   D. No effect on immunoglobulin

10. The starting dose frequency of MDI cromolyn is:
    A. 4 times daily
    B. 3 times daily
    C. Twice daily
    D. Once daily

Answers
1. B, page 1595
   Kennedy first provided evidence for an anti-inflammatory effect of cromolyn sodium, showing a significant reduction in sputum eosinophils with cromolyn sodium treatment compared to placebo.

2. B, page 1596
   Cromolyn sodium prevents both the early and late reaction to bronchial challenge.
3. A, page 1598
For children under 5 years, the preferred choice is 1% aqueous solution with the addition of a small dose of beta agonist

4. A, page 1598
Two percent and 4% concentrations of cromolyn sodium are available as nasal solutions and have been shown to be better than placebo.

5. C, page 1598
Cromolyn sodium has been shown to inhibit in vitro and in vivo the effect of influenza.

6. B, page 1599
In humans, intranasal nedocromil sodium had a significant effect on the symptoms and nasal secretions in rhinovirus but not on coronavirus infections.

7. B, page 1599
Hypersensitivity has been reported in individual rare cases, but the main adverse effects are local irritation at the site of application that can result in bronchoconstriction, or burning of the eye, nose, and skin.

8. D, page 1593
Studies in animals and humans show that cromolyn and nedocromil are not metabolized and are excreted unchanged in the bile and urine.

9. A, page 1594
Both chromones inhibit IgE production from B cells and tonsillar tissue.

10. A, page 1598
The starting dose frequency for MDI cromolyn is 4 times daily which can be reduced to twice daily when asthma has been controlled.