**Allergy and Immunology Review Corner:** Chapter 53 of *Middleton’s Allergy Principles and Practice*, Seventh Edition, edited by N. Franklin Adkinson, et al.

**Chapter 53:** Occupational Asthma

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1. High molecular weight compounds are mostly protein or polysaccharides and they behave as complete antigens that can provoke an IgE mediated response directly. Which of the following agents is not a HMW agent?
   A. Latex
   B. Metals
   C. Cereals
   D. Gums

2. What is the risk of asthma attributable to the workplace?
   A. 3%
   B. 6%
   C. 9%
   D. 12%

3. Studies in diisocyanate-induced asthma have shown that alleles within the HLA class II region appear to be associated with an increased or decreased risk of the development of OA. Which allele or allele combination conferred significant protection to exposed healthy controls?
   A. DQB1*0503
   B. DQB1*0201/0301
   C. DQB1*0302
   D. DQB1*501

4. Which agent is the most frequent and most often reported cause of occupational asthma?
   A. Diisocyanates
   B. Acrylates
   C. Wood dust
   D. Latex

5. Which agent that causes OA is atopy is an associated factor for the development of sensitization and that allergic reactions to banana, kiwi, avocado, and chestnut are more frequent in subjects sensitized to this agent?
   A. Baking products
   B. Latex
   C. Cereals
   D. Seafood

6. Which of the following workers would be most likely to develop an IgE mediated asthma?
   A. Janitors
B. Bakers  
C. Hairdressers  
D. Adhesive Handlers

7. What is the single most important risk factor for Occupational Asthma?  
A. Exposure  
B. Atopy  
C. Smoking  
D. Rhinoconjunctivitis

8. Which of the following is most likely to cause occupational asthma through both immunological and non-immunological mechanisms?  
A. Acetic acid  
B. Chlorine  
C. Ethylene oxide  
D. Toluene diisocyanate

9. What agent should you suspect in an automobile worker with occupational asthma who works in finish coating?  
A. TDI  
B. HDI  
C. MDI  
D. LDI

10. Patients with OA and exposure to which of the following agents would have the best prognosis?  
A. TDI  
B. HDI  
C. MDI  
D. LDI

Answers
1. B, page 940  
High-Molecular weight agents are cereals, animal derived allergens, enzymes, gums, latex, and seafoods. Low molecular weight agents are isocyanates, wood dusts, anhydrides, amines, fluxes, chloramines-T, dyes, persulfate, formaldehyde, gluteraldehyde, acrylate, drugs, and metals.

2. C, page 943  
Several large population-based studies of asthma, some including information on occupation, have been carried out. In Europe, the risk of asthma attributable to workplace exposure was found to be 9.9% (2.8-16.5%) of the general population.

3. D, page 947  
DQB1*0503 and the allele combination DQB1*0201/0301 were associated with increased susceptibility to the disease, while the presence of DQB1*501 and the DQA*0101-DQB*0501-DR1 haplotype conferred significant protection to exposed healthy controls.
4. A, pages 951-953
Polyisocyanates are the most common causes of OA in many parts of the world. Diisocyanates are the most important ones used commercially.

5. B, pages 951-952
There are at least 7 latex allergens that have been identified. Allergic reactions to banana, kiwi, avocado, and chestnut are more frequent in subjects sensitized to latex. Prevalence studies of sensitization to latex in health professionals have shown figures of 2.8-16.9%. Atopy is an associated factor for development of sensitization.

6. B, page 940
Bakers are exposed to high molecular weight proteins in cereals, while janitors, hairdressers, and adhesive handlers would more likely be exposed to low molecular weight chemicals. High molecular weight proteins are more likely to cause an IgE-mediated reaction. Low molecular weight proteins can cause an IgE mediated response by acting as a hapten.

7. A, page 944
While atopy, smoking, rhinoconjunctivits, and genetic predisposition are all risk factors for occupational asthma, exposure to the offending agent is the most important risk factor.

8. D, page 942
Toluene diisocyanate-induced asthma occurs not infrequently in individuals who have been previously exposed to the chemical in a spill. Epithelial damage arising from the spill may lead to increased penetration by the diisocyanates into the subepithelial tissue, thus causing sensitization.

9. A, page 952
Toluene diisocyanate (TDI) is found in foam-rubber cushions and finish coating. Methylene diphenyl diisocyanate (MDI) is used in foundries in the making of all mold and core processes for insulation, and hexamethylene diisocyanate (HDI) is used exclusively in spray paints.

10. B, page 952
While most patients with diisocyanate-induced asthma fail to recover years after removal from exposure, those with OA due to HDI seem to show a better prognosis.

Allergy and Immunology Review Corner: Chapter 54 of Middleton’s Allergy Principles and Practice, Seventh Edition, edited by N. Franklin Adkinson, et al.

Chapter 54: Immunologic Non-Asthmatic Diseases of the Lung – Pages 957-971

Prepared by John Tole, MD, University of Mississippi Medical Center & Christopher Martin, MD, Walter Reed Army Medical Center

1. Which is true regarding Wegener's?
A. A strong association between the disease and heavy metal exposure
B. A strong association between the disease and farming
C. Female gender affected more commonly
D. Mean age at onset of approximately 40 years

2. Which is true regarding Wegener's?
   A. Distinctive triad of granulomatous inflammation, neuropathy, and vasculitis
   B. Increased production of IL-12 in monocytes from patients with WG
   C. Renal lesions demonstrate classic immune complex deposition
   D. Antibodies against proteinase-3 is present in <10% of patients with WG

3. Subglottic tracheal stenosis leads to which finding on spirometry?
   A. Flattening of the expiratory phase
   B. Flattening of the inspiratory phase
   C. Flattening of both expiratory and inspiratory phases
   D. Evidence of variable intrathoracic obstruction

4. Which is an example of pathologic findings in Microscopic Polyangiitis?
   A. Non-necrotizing inflammation of capillaries, venules and small to medium-sized arteries
   B. Staining reveals abundant immunoglobulin deposition in the vascular lesions
   C. Pulmonary lesions are associated with alveolar hemorrhage
   D. Renal lesions differ from WG by the presence of diffuse rather than focal changes

5. Immunologic abnormalities in sarcoidosis include?
   A. Accumulation of CD4+ cells that release IL-2
   B. Expansion of the lung α/β TCR pool
   C. Reduced activity of B cells
   D. Decreased release of monocyte-derived cytokines

6. Which of the following is characteristic of Wegener’s granulomatosis?
   A. The segmental necrotizing glomerulonephritis is due to immune complex deposition
   B. A high titer ANCA level offers the best diagnostic yield
   C. 10% are associated with antiproteinase-3 antibodies
   D. 90% of the antineutrophil antibodies are associated with a cytoplasmic pattern of fluorescence

7. Which of the following distinguishes microscopic polyangiitis (MPA) from Wegener’s?
   A. MPA is not associated with the presence of ANCA
   B. MPA does not have granulomatous inflammation
   C. MPA involves necrotizing vasculitis of the small vessels
   D. MPA is more likely to involve the upper airways

8. Which of the following is characteristic of sarcoidosis?
   A. Annual incidence is greatest in African American males
   B. HLA-DR4 is associated with sarcoidosis restricted to the lungs
   C. CD4+ T cells predominate in the granulomas
   D. On BAL fluid, a CD4/CD8 ratio less than one is specific for sarcoidosis
9. Which of the following lung diseases is associated with a necrotizing granuloma surrounded by an eosinophilic infiltrate?
A. Wegener’s granulomatosis
B. Churg-Strauss syndrome
C. Sarcoidosis
D. Goodpasture’s disease

10. Which of the following is characteristic of Goodpasture’s disease?
A. The lung pathology is due to anti-glomerular basement membrane antibodies
B. Anti-GBM antibodies are directed against type I collagen
C. Linear staining of IgA is found along the basement membrane on immunoflourescent studies
D. PFTs reveal an obstructive pattern as well as a decreased DLCO

Answers
1. D, page 957
WG is a disease mostly of Caucasians entering their 5th decade of life. Women and men are affected equally and there are only weak associations between environmental effects and the disease, with research ongoing.

2. B, pages 957-959
The triad is granulomatous inflammation, necrosis, and vasculitis. Renal lesions have no immune complex deposition, and anti-proteinase-3 is detected in >90% of patients.

3. C, page 960
Stenosis is an example of fixed extrathoracic obstruction flattening both phases of respiration.

4. C, page 963
The inflammation is necrotizing. Staining reveals paucity of immunoglobulin deposition, and the renal lesions are identical to WG.

5. A, page 965
There is expansion of the γ/β TCR pool in the lung. B cells become hyperactive and in-situ spontaneously release immunoglobulins. There is an increase in monocyte derived cytokine release.

6. D, page 959
90% of WG is C-ANCA positive (anti-PR3, cytoplasmic pattern). 10% of ANCA+ Wegener’s is associated with anti-MPO antibodies which give the perinuclear, or pANCA, pattern on immunoflourescence. The glomerulonephritis in WG is pauci-immune. The ANCA titer does not correlate well with disease activity—lung tissue via open lung biopsy offers the highest diagnostic yield.

7. B, page 962
The lack of granulomatous inflammation is what differentiates MPA from Wegener’s. ANCA is often present though is more likely pANCA than cANCA. Both MPA and WG affect small vessels. MPA is not known to affect the upper airways, while 95% of Wegener’s patients have upper airway disease.

8. C, page 964
CD4+ T cells predominate in the lesions. The incidence is greatest in African American females followed by African American males, Caucasian females, and then Caucasian males. HLA-B27 is associated with sarcoidosis limited to the lungs, while B13 and B35 are associated with early-onset and A30, B8, DR3 and DR4 with late-onset disease. A CD4/CD8 ration of at least 4 has a 100% PPV in separating sarcoidosis from other forms of ILD.

9. B, page 963
The “allergic granuloma” is the characteristic lesion of CSS. The granulomas of Wegener’s and sarcoidosis lack this trait (sarcoidosis granulomas with CD4+ T cell infiltrate) and Goodpasture’s disease is not associated with granulomas.

10. A, page 698
Anti-GBM antibodies are involved in both renal and pulmonary pathophysiology of Goodpasture’s. The anti-GBM is directed against type IV collagen and immunofluorescence shows linear staining of IgG. Goodpasture’s has a restrictive pattern on PFTs and an increased DLCO.