The Immune System and its Diseases. Part 3.

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Outline

Infectious disease and host defense interactions:
- Role of co-pathogens in infectious disease
  - Influenza and secondary bacterial infection
- Molecular mimicry and autoimmune disease
  - Myasthenia gravis
- Equine purpura hemorrhagica
  - Acute type III hypersensitivity

Role of co-pathogens in infectious disease
Primary respiratory viral infection with secondary bacterial pneumonia
Anatomic defences in the respiratory tract: The mucociliary escalator

- Ciliated respiratory cells line bronchi, bronchioles, trachea and much of nasal cavity
- Beat in one direction moving mucus to throat for swallowing
- Mucus secreting cells also plentiful – sticks to bacteria

Insults that can damage the mucociliary escalator or impair its function

- Viral replication in epithelial cells
  - Kills cells and induces inflammation
  - Many viruses
    - Pig, dog and human influenza
    - Adenoviruses
    - Paramyxoviruses
- Smoke exposure – e.g. cigarettes
- Cold air -
- Irritant gases – e.g. ammonia

Influenza damages anatomic respiratory defences and significantly increases risk for secondary bacterial infection

- Inflammation
- Loss of epithelial cells
- Regenerating epithelial cells lack cilia
- Loss of activity of mucociliary escalator results in markedly increased susceptibility to bacteria infection i.e. pneumonia
Secondary bacterial lung infection is a major sometimes life-threatening complication of influenza infection

Risk factors:
- Severity of initial viral damage
- Exposure to bacterial pathogens
- Host immunity
  - Very young and old
  - Chronic illness, HIV, transplant patients

Molecular mimicry and acquired myasthenia gravis

Critical role of the neuromuscular junction in signaling to muscle

What is acquired myasthenia gravis?

Symptoms and signs
- Fatigability
- Muscle weakness
  - In severe forms difficulty breathing
- Circulating antibodies to acetylcholine receptor
  - Inhibits normal receptor signaling function
- Most cases respond to immunosuppressive therapy
Possible role of molecular mimicry in acquired myasthenia gravis

- Some cases of myasthenia gravis develop following self-limiting infectious disease
  - Association with herpes simplex 1 (HSV1) infection in some cases [HSV1 causes cold sores in people].
  - Acetylcholine receptor has regions with sequence and antigenic properties similar to a HSV1 protein

Other disease where molecular mimicry mechanisms are thought to be involved

- Encephalitis due to human immunodeficiency virus [HIV]
- Post streptococcal infection in man
  - Post-infectious arthritis
  - Post-infectious glomerulonephritis
  - Rheumatic heart disease in man secondary to Streptococcal pyogenes pharyngitis
    - Myocarditis, valvular degeneration
    - Cross-reactivity of antibodies with heart tissue and M protein of bacterium

Purpura hemorrhagica: Acute post-streptococcal type III hypersensitivity
Typical history in a case of equine purpura hemorrhagica

Infection with certain Streptococcus equi strains

Abscessation of sub-mandibular lymph nodes (=purulent lymph adenitis)

Recovery [most cases]

Small percentage of cases develop life-threatening purpura hemorrhagica typically 1-2 weeks after the Streptococcal infection

Main features of purpura hemorrhagica

- Purpura
- Edema
- Systemic and acute vasculitis (microscopically)
  - Secondary infarcts in some cases
- Thrombocytopenia

Purpura hemorrhagic in horses

Proposed mechanism

Infection with Strep. equi

Immune response with antibody production

Antibodies bind to Strep. equi antigen released into blood stream

Immune complexes – Ab-Ag – deposit in vessel walls

Immune complexes induce inflammatory response in vessel walls
Example questions from pigments lecture

• What is icterus?
• Why is icterus often present with hepatic disease?
• Where are aged red cells normally degraded?
• Provide two basic causes of iron deficiency anemia?
• Why is anemia often present in animals and people with chronic renal disease?
• Explain what is meant by the term ‘autosomal recessive disease’

Example questions from hemostasis lecture

• What does the term consumption coagulopathy mean?
• Where are clotting factor proteins produced?
• What feature of the clotting protein system enables a rapid response to thrombogenic stimuli?
• Why can bone marrow injury be associated with increased tendency to bleed?
• What other signs might you expect in an animal or person with bone marrow disease?

Examples questions from acute inflammation lecture

• State five signs of acute inflammation
  – For three of these state briefly how they occur
• How do neutrophils kill bacteria?
• What is an abscess?
• State three factors that will determine whether a localized infection becomes systemic and cause life threatening disease
**Examples questions from chronic inflammation lecture**

- What cell types are common in chronic inflammation?
- Protein factors produced by macrophages promote what processes? (name two)
- Name one pathogen or disease that is often associated with granulomatous inflammation?
- Why is there inflammation during the healing process – even when infection is absent?
- Name two features of granulation tissue
- Under what circumstances is granulation tissue most likely to form?

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**Example questions from immune system I lecture**

- Describe the structure of an antibody
- Name two mechanisms by which antibodies can promote killing of microorganisms
- How does the complement system destroy bacteria?
- Name an important cell type involved in innate immunity

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**Example questions from immune system II lecture**

- Name a cell-type critical for the immediate response in type I hypersensitivity
- Name one disease caused by a type III hypersensitivity immune response
- What are the immediate life-threatening signs in a person or animal with anaphylaxis?
- How do you think a toxic drug reaction differs from a drug hypersensitivity reaction?