Chapter 18

Practical Applications of Immunology

Vaccines

18-1 Define vaccine.
18-2 Explain why vaccination works.
18-3 Differentiate the following, and provide an example of each: attenuated, inactivated, toxoid, subunit, and conjugated vaccines.
18-4 Contrast subunit vaccines and nucleic acid vaccines.

Vaccines

18-5 Compare and contrast the production of whole-agent vaccines, recombinant vaccines, and DNA vaccines.
18-6 Define adjuvant.
18-7 Explain the value of vaccines, and discuss acceptable risks for vaccines.

History of Vaccines

Variolation: inoculation of smallpox into skin (eighteenth century)
Vaccination:
  - Inoculation of cowpox virus into skin (Jenner)
  - Inoculation with rabies virus (Pasteur)
8 Vaccines Used to Prevent Bacterial Diseases

9 Vaccines Used to Prevent Viral Diseases

10 Vaccines Used to Prevent Viral Diseases

11 Vaccines for Persons Aged 0–6 Years
   - Hepatitis B
   - Rotavirus
   - DTaP
   - Haemophilus influenzae type b
   - Pneumococcal
   - Inactivated poliovirus
   - Influenza

12 Vaccines for Persons Aged 0–6 Years
   - MMR
   - Varicella
   - Hepatitis A
   - Meningococcal

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   - What is the etymology (origin) of the word vaccine? 18-1
   - Vaccination is often the only feasible way to control most viral diseases; why is this? 18-2

14 Types of Vaccines
   - Attenuated whole-agent vaccines
     - MMR vaccine
   - Inactivated whole-agent vaccines
     - Salk polio vaccine
   - Toxoids
     - Tetanus vaccine

15 Types of Vaccines
• Subunit vaccines
  • Acellular pertussis
  • Recombinant hepatitis B
• Nucleic acid (DNA) vaccines
  • West Nile (for horses)

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18 The Development of New Vaccines
• Culture pathogen
• rDNA techniques
  • In plants
• Adjuvants
• Deliver in combination

19 Safety of Vaccines
• Therapeutic index
  • Risk-versus-benefit calculation

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Experience has shown that attenuated vaccines tend to be more effective than inactivated vaccines. Why? 18-3
• Which is more likely to be useful in preventing a disease caused by an encapsulated bacterium such as the pneumococcus: a subunit vaccine or a nucleic acid vaccine? 18-4

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• Which type of vaccine did Louis Pasteur develop, whole-agent, recombinant, or DNA? 18-5
• What is the derivation of the word adjuvant?
  • 18-6
• What is the name of a currently used oral vaccine that occasionally causes the disease it is intended to prevent? 18-7
22 Diagnostic Immunology
- 18-8 Differentiate sensitivity from specificity in a diagnostic test.
- 18-9 Define monoclonal antibodies, and identify their advantage over conventional antibody production.
- 18-10 Explain how precipitation reactions and immunodiffusion tests work.
- 18-11 Differentiate direct from indirect agglutination tests.

23 Diagnostic Immunology
- 18-12 Differentiate agglutination from precipitation tests.
- 18-13 Define hemagglutination.
- 18-14 Explain how a neutralization test works.
- 18-15 Differentiate precipitation from neutralization tests.
- 18-16 Explain the basis for the complement-fixation test.

24 Diagnostic Immunology
- 18-17 Compare and contrast direct and indirect fluorescent-antibody tests.
- 18-18 Explain how direct and indirect ELISA tests work.
- 18-19 Explain how Western blotting works.
- 18-20 Explain the importance of monoclonal antibodies.

25 Diagnostic Immunology
- Sensitivity: probability that the test is reactive if the specimen is a true positive
- Specificity: probability that a positive test will not be reactive if a specimen is a true negative
- Immunologic-based tests
  - Guinea pigs with TB injected with Mycobacterium tuberculosis: site became red and slightly swollen

26 Monoclonal Antibodies (Mabs)
- Hybridoma: “immortal” cancerous B cell fused with an antibody-producing normal B cell
  - Produces monoclonal antibodies
Monoclonal Antibodies (Mabs)
- Muromonab-CD3: for kidney transplant
- Infliximab: for Crohn’s disease
- Comalizumab: for allergic asthma
- Rituximab: rheumatoid arthritis
- Trastuzumab: Herceptin for breast cancer

Monoclonal Antibodies
- Chimeric Mabs: genetically modified mice that produce Ab with a human constant region
- Humanized Mabs: Mabs that are mostly human, except for mouse antigen-binding sites
- Fully human antibodies: Mabs produced from a human gene on a mouse

What property of the immune system suggested its use as an aid for diagnosing disease: specificity or sensitivity? 18-8
- The blood of an infected cow would have a considerable amount of antibodies against the infectious pathogen in its blood. How would an equivalent amount of monoclonal antibodies be more useful? 18-9

Hemagglutination
- Hemagglutination involves agglutination of RBCs
- Some viruses agglutinate RBCs in vitro
• Hemagglutination inhibition: antibodies prevent hemagglutination

Why does the reaction of a precipitation test become visible only in a narrow range? 18-10
Why wouldn’t a direct agglutination test work very well with viruses? 18-11
Which test detects soluble antigens, agglutination or precipitation? 18-12
Certain diagnostic tests require red blood cells that clump visibly. What are these tests called? 18-13

In what way is there a connection between hemagglutination and certain viruses? 18-14
Which of these tests is an antigen–antibody reaction: precipitation or viral hemagglutination inhibition? 18-15

Enzyme-Linked Immunosorbent Assay
• Also called ELISA
• Enzyme linked to Ab is the indicator

Serological Tests
• Direct tests detect antigens (from patient sample)
• Indirect tests detect antibodies (in patient’s serum)
54 Serological Tests
- Precipitation: soluble antigens
- Agglutination: particulate antigens
- Hemagglutination: agglutination of RBCs
- Neutralization: inactivates toxin or virus
- Fluorescent-antibody technique: antibodies linked to fluorescent dye
- Complement fixation: RBCs are indicator
- ELISA: peroxidase enzyme is the indicator

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- Why is complement given its name? 18-16
- Which test is used to detect antibodies against a pathogen: the direct or the indirect fluorescent-antibody test? 18-17
- Which test is used to detect antibodies against a pathogen: the direct or the indirect ELISA test? 18-18
- How are antibodies detected in Western blotting? 18-19
- How has the development of monoclonal antibodies revolutionized diagnostic immunology? 18-20

56 Question 1
- Patient’s serum, influenza virus, sheep RBCs, and anti-sheep RBCs are mixed in a tube
- Influenza virus agglutinates RBCs
- What happens if the patient has antibodies against influenza virus?

57 Question 2
- Patient’s serum, Chlamydia, guinea pig complement, sheep RBCs, and anti-sheep RBCs are mixed in a tube
- What happens if the patient has antibodies against Chlamydia?