1. Adverse reactions to IVIG infusion include flushing, nausea, headache, and myalgia. These effects are most often dependent on what variable?
   A. Infusion rate
   B. Total dose of IVIG
   C. IgA content of IVIG preparation
   D. Renal function

2. Lymphocytopenia due to the effects of glucocorticoids are selective and have the greatest effect this type of lymphocyte in the peripheral circulation.
   A. T cells
   B. B cells
   C. NK cells
   D. Plasma cells

3. This agent prevents the dephosphorylation of NFAT by binding FK506 binding protein (FKBP)-12 which inhibits calcineurin thus inhibiting both T-lymphocyte signal transduction and IL-2 transcription.
   A. Sirolimus
   B. Tacrolimus
   C. Cyclosporine
   D. Mycophenolate mofetil

4. This agent is an IL-1 receptor antagonist approved for treatment of rheumatoid arthritis and has been shown to be an effective treatment in Familial Mediterranean Fever.
   A. Etanercept
   B. Abetacept
   C. Anakinra
   D. Adalimumab

5. By which of the following mechanisms does sirolimus act?
   A. Inhibition of calcineurin
   B. Inhibition of inosine monophosphate dehydrogenase
   C. Inhibition of dihydrofolate reductase
   D. Inhibition of mTOR

6. Which of the following immunoglobulins is found in the highest concentration in IVIG?
A. IgG
B. IgA
C. IgM
D. IgE

7. In nomenclature of monoclonal antibodies, which of the following letters, when inserted as an infix preceding the –mab stem, denotes primate?
   A. u
   B. o
   C. i
   D. a

8. Which of the following suffixes denotes a chimeric monoclonal antibody (contains >5% mouse protein)?
   A. -umab
   B. -omab
   C. -zumab
   D. –ximab

9. Approximately what percentage of lymphocytes undergo intermitotic death following total body irradiation?
   A. 20%
   B. 40%
   C. 80%
   D. 100%

10. Which of the following is an alkylating agent that forms covalent bonds with DNA, leading to mutations, DNA fragmentation, and cell death?
    A. Azathioprine
    B. Cyclophosphamide
    C. Cyclosporin
    D. Mycophenolate mofetil

**Answers**

1. A, page 397
   “The most common side effects include flushing, HA, nausea/vomiting, and myalgias that are often infusion rate dependent.”

2. A, page 400
   “It is noteworthy that lymphocytopenia is selective; i.e., T lymphocytes are depleted from the circulation to a greater extent than are B lymphocytes [in regard to glucocorticoid administration].”

3. B, page 404
   “…tacrolimus (binds) to the FK506 binding protein. The resulting complex subsequently bind to calcineurin…involves the inhibition of phosphatase activity of calcineurin and
prevention of NFAT dephosphorylation.”

4. C, page 415
“Anakinra is an IL-1 receptor antagonist that blocks IL-1, a protein involved in the inflammation and joint destruction associated with RA.”

5. D, page 405
“Unlike the similarly named tacrolimus, sirolimus is not a calcineurin inhibitor. The mechanism of action of sirolimus is distinct from that of cyclosporine and tacrolimus. …Sirolimus initially binds intracellularly to the same immunophilin FKBP-12 as tacrolimus, after producing the immunosuppressive sirolimus-FKBP-12 complex, it subsequently binds to and inhibits the activation of a regulatory kinase, known as the mammalian target of rapamycin (mTOR).”

6. A, page 396
“Ninety-five to 99 percent of the IVIG is IgG (with trace amounts of IgA and IgM), and IgG subclass distribution of approved products is similar to that of normal human serum.”

7. C, page 396, Box 11-2
”The following letters identify the animal source of the product and are inserted as infixes (i.e., letters inserted into a word) preceding the –mab stem: u – human, o – mouse, a – rat, e – hamster, i – primate, xi – chimera.”

8. D, page 396, Box 11-2
“The suffix of the product name denotes its class and is based on purity and the degree of residual foreign protein in the preparation: -umab = human monoclonal antibody (100% human and contains no mouse protein), -omab = mouse protein (100% mouse protein), -zumab = humanized monoclonal antibody (contains <5% mouse protein), -ximab = chimeric monoclonal antibody (contains >5% mouse protein), and –cept = receptor-antibody fusion protein (receptor attached to Fc of IgG1).”

9. C, page 399
“Following TBI [total body irradiation], 80% of lymphocytes undergo prompt intermitotic death (i.e., killing of the cells between two successive mitoses during the cell cycle).”

10. B, page 399
“Cyclophosphamide is an alkylating agent that forms covalent bonds with DNA, leading to mutations, DNA fragmentation, and cell death.”

Allergy and Immunology Review Corner: Chapter 12 of Immunology IV: Clinical Applications in Health and Disease, by Joseph A. Bellanti, MD.

Chapter 12: Immunity to Bacteria
1. Which of the following is recognized by TLR-2 and unique to the cell wall of Gram-Positive bacteria?
   A. Lipopolysaccharide (LPS)
   B. Peptidoglycan
   C. Lipoarabinomannan
   D. Lipoteichoic acid

2. Phosphatidylinositol 3-phosphate (PI3P), a host-membrane component essential in the synthesis of phagolysomes is blocked by which of the following virulence factors?
   A. Lipopolysaccharide (LPS) of Gram-negative bacteria
   B. Lysins produced by Shigella and Listeria
   C. S. aureus protein A
   D. Adhesins including fimbriae and pili
   E. Glycolipids in M. tuberculosis

3. Which of the following Toll-Like-Receptors and its corresponding Pathogen-Associated Molecular Patterns (PAMP) is incorrectly matched?
   A. TLR4 recognizes LPS
   B. TLR6 recognizes Diacyl lipoproteins
   C. TLR9 recognizes Unmethylated CpG DNA of bacteria
   D. TLR5 recognizes Lipoarabinomannan
   E. TLR2 recognizes Lipoteichoic acids

4. Which of the following is not involved in improving opsonization?
   A. Complement C3b
   B. IgM
   C. IgG
   D. Mannose-binding Lectin
   E. Complement C3a

5. Which of the following is not an aspect of the IL-23/IL-17 pathway of T-cell-Macrophage interaction during bacterial infection?
   A. Enhanced killing of Intracellular pathogens
   B. Induction of epithelial cells to secrete antimicrobial peptides such as beta-defensins and S-100 proteins
   C. Production of granulopoietic and chemotactic factors such as G-CSF and IL-8
   D. Production of IL-22

6. Which of the following pathogens produce proteases that cleave sIgA, disrupting mucosal immunity?
   A. Haemophilus influenzae
   B. Neisseria gonorrhoeae
   C. Mycobacteria tuberculosis
D. Both H. influenzae and N. gonorrhoeae

7. Which of the following types of pathogen-recognition receptors (PRRs) recognize intracellular bacterial or viral components and leads to direct activation of the inflammasome?
   A. Toll-like receptors (TLRs)
   B. NOD-like receptors (NLRs)
   C. C-type lectin receptors (CLRs)
   D. All of the above

8. In acute bacterial infections, there are two main mechanisms of bacterial clearance by phagocytes. Which of the following statements is true regarding these two mechanisms?
   A. Encapsulated organisms are readily phagocytosed by neutrophils.
   B. Encapsulated organisms undergo an enhanced process of phagocytosis through antibody and complement production.
   C. Unencapsulated organisms undergo enhanced phagocytosis by macrophages medicated by T cells.
   D. Unencapsulated organisms undergo unenhanced phagocytosis by macrophages only.

9. Which of the following pro-inflammatory cytokines is critical for the continuous recruitment of mononuclear cells into granulomas in order to maintain effective containment of mycobacterial foci of infection?
   A. INF-gamma
   B. Macrophage-derived TNF-alpha
   C. T cell-derived TNF-alpha
   D. Both macrophage-derived and T cell-derived TNF-alpha

10. Which of the following organisms is INCORRECTLY matched with its produced exotoxin?
    A. Escherichia coli and heat-labile enterotoxins
    B. Staphylococcus aureus and heat-stable enterotoxins
    C. Bacillus anthracis and anthrax toxin
    D. Clostridium botulinum and botulinum toxin

Answers
1. D, page 432
   Lipoteichoic acid is only found on gram-positive bacteria, and is recognized by TLR-2. Peptidoglycan is found on gram-positive, gram-negative and mycobacteria (it comprises a larger portion of the cell wall of gram positives though). Lipoarabinomannan is only found on the cell wall of mycobacteria. LPS is associated with gram-negative organisms and is recognized by TLR-4.

2. E, page 437
   Glycolipids inhibit PI3P preventing the formation of phagolysosomes to elude intracellular destruction of the mycobacterium. Lysins help the organism to escape the phagosome, but does not interfere with PI3P. S. aureus protein A leads to activation of
TNFR1. Adhesins help bacterial invade the host and prevent cell wall exposure to TLRs and other PRRs. The long chain of LPS prevents complement deposition and membrane attack complex insertion into the membrane, and the O antigen of LPS allows different strains of the same species to re-infect the host.

3. D, page 443
TLR5 recognizes the flagellin of bacteria. Lipoarabinomannan is part of mycobacteria and is recognized by TLR2. All the other pairs are correct.

4. E, pages 437-438
Complement component C3a is an anaphylatoxin and is responsible for recruitment and migration of PMNs. All the other choices are agents that enhance opsonization.

5. A, pages 448-449
The enhanced clearance of intracellular pathogens is mediated by the IL-12/IFN-gamma pathway. IL-12 release following macrophage phagocytosis of intracellular organism causes activation of the IL-12R leading to synthesis of IL-2 and subsequent synthesis of IFN-gamma. The binding of IFN-gamma to its receptor leads to the activation of STAT1 and NF-kB pathways to kill the intracellular organism. All the other choices are elements part of the IL-23/IL-17 pathway that is important in normal bacterial clearance especially at mucosal surfaces.

6. D, page 437
sIgA protects the mucosal surface against inhaled and ingested bacterial pathogens, many pathogenic bacteria, such as H. influenzae and N. gonorrhoeae, produce proteases that cleave IgA, making the molecule ineffective.

7. B, page 442
NLRS are nonmembrane associated PRRs unlike TLRs and CLRs. They recognize intracellular bacterial or viral components. They discriminate between pathogenic and commensal bacteria and directly activates the inflammasome. TLRs and CLRs recognize membrane-bound PRRs only and TLRs activates the inflammasome INDIRECTLY.

8. B, page 445
Nonencapsulated organisms are readily phagocytosed by neutrophils in an opsonin-unenhanced fashion and are readily killed. In contrast, encapsulated organisms are often poorly ingested by neutrophils alone; however, with the production of antibody and complement opsonization, phagocytosis by neutrophils is greatly enhanced and subsequent killing is permitted. Although Tcell-mediated immune mechanisms can enhance phagocytosis by macrophages, since such organisms are not regularly phagocytosed by macrophages, this scheme normally appears to be of relatively lesser importance.

TNF-alpha derived from infected alveolar macrophages initially induces recruitment of a mixed cellular alveolar and interstitial infiltrate. Under the influence of TNF-alpha and T
cell-derived IFN-gamma, mononuclear cells accumulate to form a highly structured granuloma. Macrophage and T-cell-derived TNF-alpha is necessary to continuously orchestrate the recruitment of mononuclear cells into granulomas to contain the mycobacteria.

10. B, page 433
Exotoxins are proteins released extracellularly into the medium or at local sites in which it grows. Endotoxins consist of lipid and polysaccharide moieties that form part of the bacterial cell wall. Certain strains of bacteria produce many exotoxins that are associated with specific clinical entities. Staphylococcus produces a variety of exotoxins (A, B, C, D, E and F) that are responsible for staphylococcal food poisoning, enterocolitis, exfoliative skin disorders, and toxic shock syndrome.