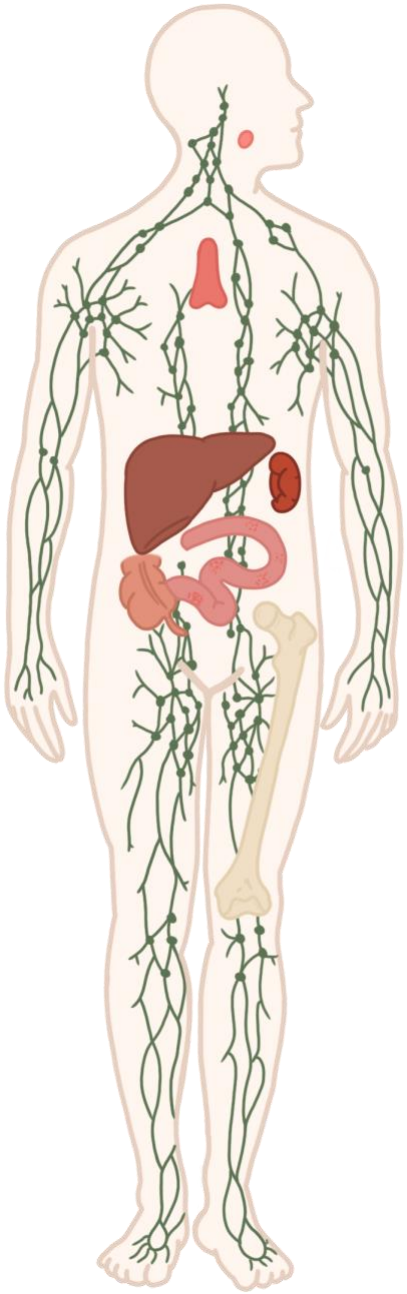

Immunology Answer Key

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Booklet Disclaimer

About StudyAid

StudyAid is a student organization at the Jagiellonian University in Krakow. Throughout the academic year we host seminars in the major theoretical subjects: anatomy, physiology, biochemistry, immunology, pathophysiology, supplementing the lectures provided by the university. We are a group of 25 tutors, who are students at JU, each with their own field of specialty. To make our seminars as useful and relevant as possible, we teach in an interactive manner often using drawings and diagrams to help students remember the concepts. In addition to most seminars we create booklets, on which the seminars are based to aid the students in following the presentations. If you have any questions, do not hesitate to contact StudyAid at www.studyaid.no, we are always happy to answer any questions you may have academically related or not.

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Section 1

1. Fill in the missing words

a) The immune system can be organized into 4 different categories, Innate vs. adaptive and humoral vs. cell mediated. The innate immunity starts immediately after invasion of microbe, and is always on standby. The adaptive immune system is slower, but is also more specific, which means their actions are more effective.

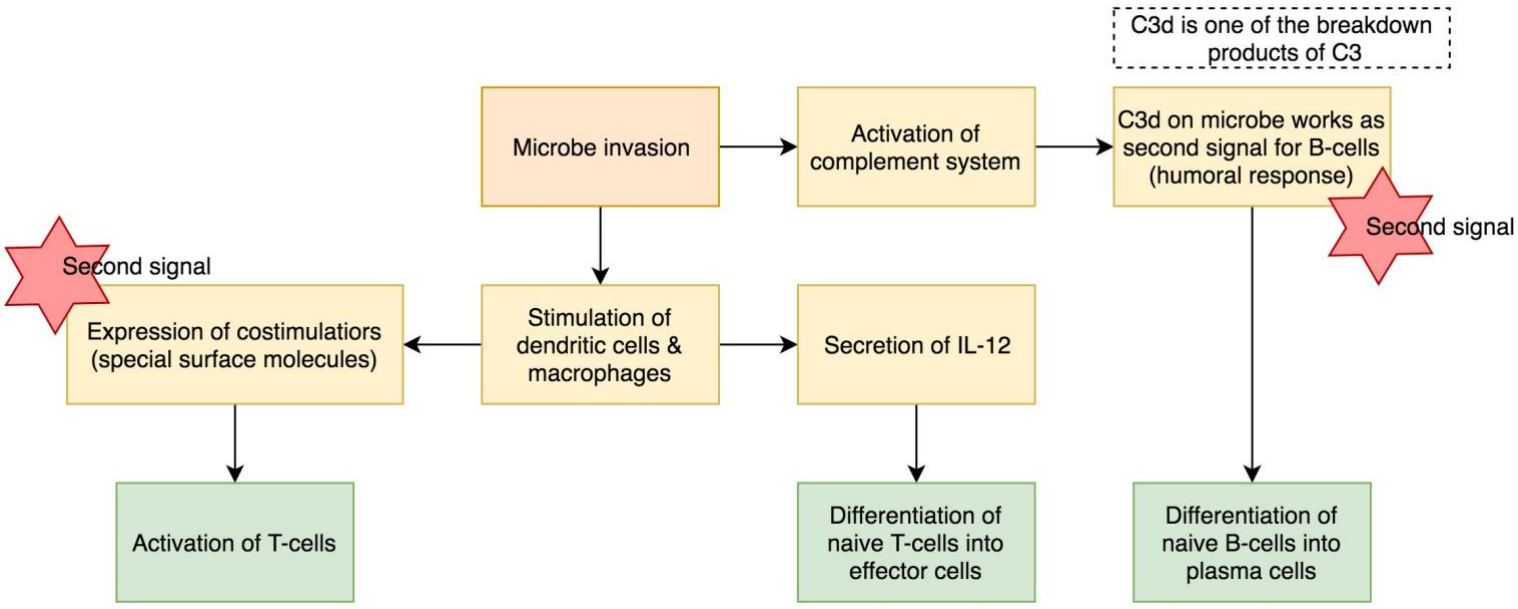
The organs of the immune system can be divided into primary and secondary organs. The primary organs, or central organs, is where the B- and T-cells learn how to respond to foreign antigens, and not our own. The secondary organs, also called the peripheral organs, is where the adaptive immune response is initiated. The secondary immune organs are important, because they ensure that APCs, lymphocytes and antigens are at a high enough concentration in the same place, so an immune response can occur.

In the lymph nodes, the B-cells are located in the follicles, and when they are activated by antigens, they form a germinal center in the follicle. The T-cells are located in the paracortex of the lymph node. The B-cells are located in follicles in the spleen as well, but T-cells are located in the periarteriolar lymphoid sheath of the spleen. The lymph nodes and the spleen serves the same purpose, filtering out unwanted material, but the lymph nodes filter lymph and the spleen filters blood.

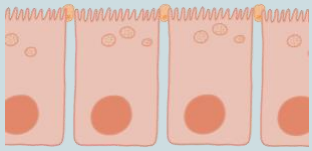
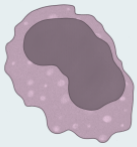
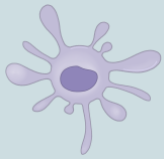
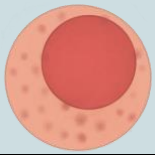
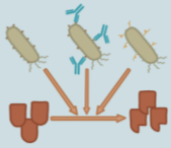
There's three main types of immune cells, lymphocytes, antigen presenting cells and effector cells.

The innate immune system consists of 5 main components: epithelial barriers, phagocytes, dendritic cells, natural killer cells and the complement system.

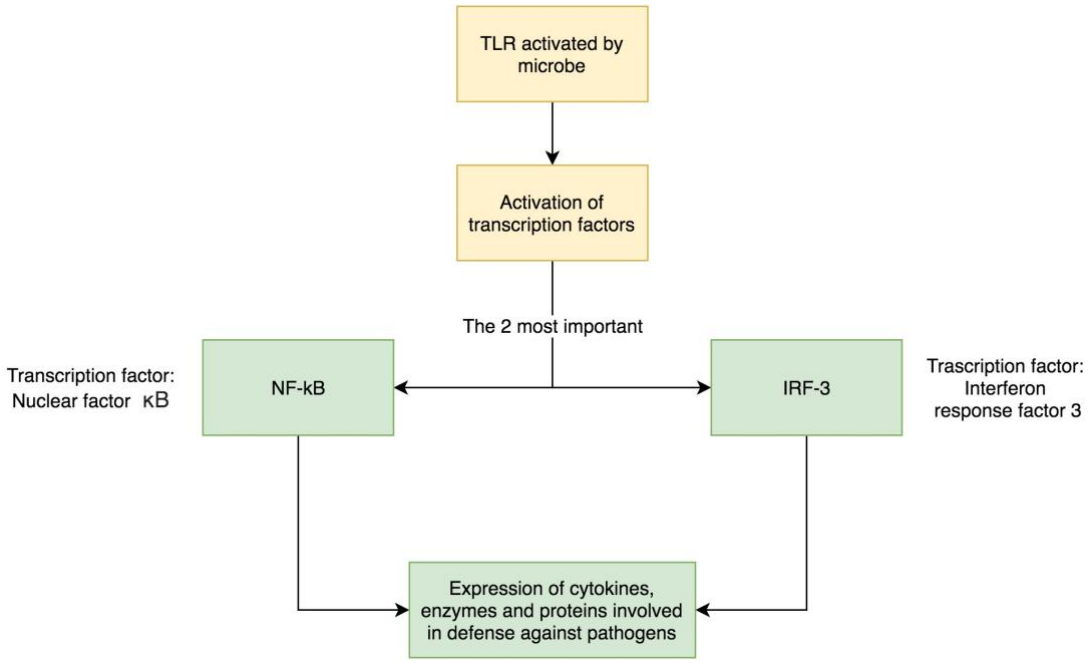
b)



c)

Component	Function		Location
Epithelial barriers 	Physical barrier Production of peptide antibiotics Killing of bacteria by intraepithelial lymphocytes[1]		GI tract, respiratory tract, skin
Phagocytes Ingest and kill microbes	Neutrophils 	First responder to inflammation site	Blood and infected extravascular tissues
	Monocytes 	Recruited to inflammation site after neutrophils	As monocytes: In blood As macrophages: In extravascular tissues
Dendritic cells 	Secretes inflammatory cytokines		Tissues and follicles of lymph nodes (follicular dendritic cells)
Natural killer cells 	Recognize damaged cells, kills them by activating apoptosis and secretes IFN-γ which activates macrophages		Blood
Complement system 	Kill and opsonize microbes, recruit neutrophils		Blood

d)



2. Choose the correct answer. Which response is <u>not</u> a part of the innate immune response?

a) Secretion of inflammatory cytokines like IFN-y and IL-12
b) Killing of damaged host cells by apoptosis
c) Antibody production
d) Opsonization of bacteria

3. What does the C5 convertase consist of, and what does it do?

C5 convertase is the result of covalent bonds between different C3b molecules and the antigens they bind to on microbes. It cleaves C5 into its metabolites.

4. Fill in the missing information.

Activation of the complement system		
Alternative pathway	Classical pathway	Lectin pathway
Triggered when complement proteins come in contact with microbial surface. Host cells have regulatory proteins to prevent this, but microbes do not.	Triggered by activation of the C1-complex, which occurs when the C1 protein binds to IgM or IgG antibodies on antigens.	Triggered when mannose-binding lectin (free in plasma) binds mannose on microbes. Activates the classical pathway, but without presence of an antibody.

Section 2

1. How do the antigen receptors on B-cells and T-cells recognize such a diverse set of antigens, while still managing to produce similar activating signals in the cells?

The part of the lymphocyte receptors that is variable (and is the cause of the variability) is a very small part of the receptor, while the larger part is constant, and does not change. This causes the receptor to overall be mostly the same, which allows all the receptors to produce the same kind of signals despite binding to different antigens.

2. Place the sentences in the appropriate boxes.

1. Clonally distributed
2. Recognize peptide antigens on MHC molecule
3. Form a cell receptor complex when binding antigens
4. Consists of a variable region and a constant region
5. Recognize basic shapes of molecules
6. Produce signal to cell from external stimuli

B-cell receptors	T-cell receptors	Both
5	2	1, 3, 4, 6

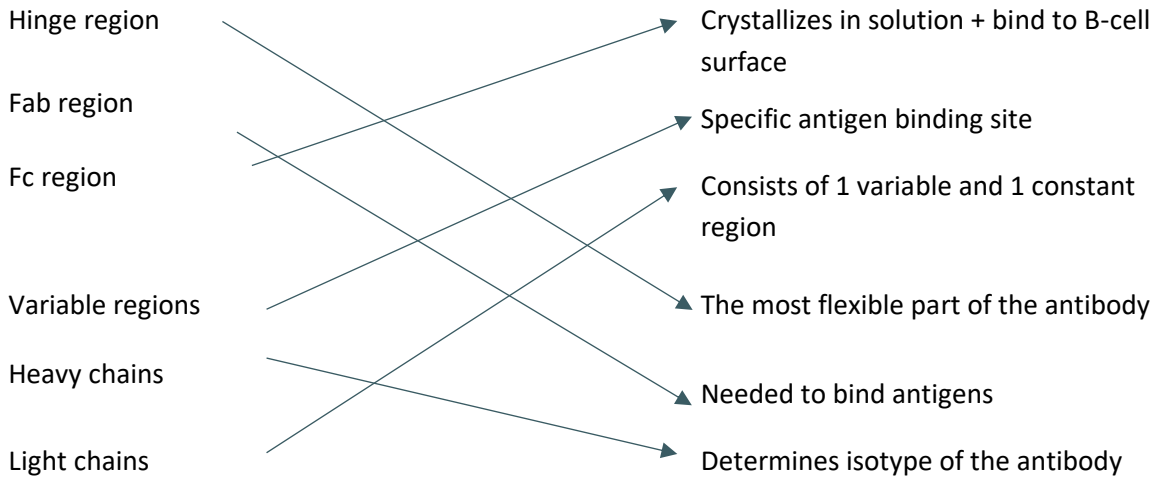
3. How are the light and heavy chains bound together?

With disulfide bonds.

4. What is the difference between affinity and avidity?

Affinity is the strength of the bond between a monovalent antibody and an epitope.
Avidity is the strength of the bonds between a multivalent antibody and an antigen with many epitopes (many antigenic determinants). Avidity = affinity x number of epitopes

5. Draw a line between the term and the correct information.



6. What is a cross-reaction in the setting of antibodies and antigens?

a) When two antibodies bind to each other
b) When an antibody produced against one specific antigen loses its ability to bind to that antigen
c) When an antibody produced against one antigen binds to an antigen of similar structure
d) When to antigens binds to each other to form a super-antigen

7. Fill in the missing words

a)

High K_d	**Low K_d**
Low affinity	**High affinity**

b) fill in the appropriate number of antigen binding sites

IgG	**IgD**	**IgE**	**Secretory IgA: Dimer**	**Secretory IgM: Pentamer**
2 antigen binding sites			4 antigen binding sites	10 antigen binding sites

c)

	IgG	IgD	IgE	IgA	IgM
Serum concentration (mg/mL)	13.5	Only trace amounts	0.05	3.5	1.5
Secreted as	Monomer	Not secreted, only found on cell membrane!	Monomer	Monomer, *dimer*, trimer	Pentamer

8. Which immunoglobulin protein is the first to be produced in a developing B-cell?

a) IgD
b) IgA
c) IgM
d) IgE
e) IgG

9. What is the main function of IgG, IgE and IgA?

IgG: Opsonization
IgE: Helminthic defense and allergies
IgA: Mucosal protection, for example in the oral cavity

Section 3

1. Which of these cells are <u>not</u> able to present MHC associated antigens?

a) Erythrocytes
b) Platelets
c) Epithelial cells
d) Neurons
e) a and b

They are not nucleated or APCs, so they do not have MHC molecules on their cells surface.

2. Which MHC domain does the CD4 and CD8 co-receptors bind to?

CD8 binds to the α3 domain of the MHC 1 molecule
CD4 binds to the β2 domain on the MHC 2 molecule

3. Recall that both MHC 1 and 2 are produced in the endoplasmic reticulum (ER). Why are the cytosolic antigens that are pumped into the ER by the TAP only captured by MHC 1, not by MHC 2?

a) MHC 2 has an occupied peptide cleft, so it can't bind peptides in the endoplasmic reticulum.
b) MHC 1 and MHC 2 are produced in separate compartments of the endoplasmic reticulum
c) MHC 2 can't bind the type of peptides that are transported by the TAP molecule
d) MHC 1 has much stronger affinity to the peptides from cytosol

Remember that the MHC 2 binds their peptides in vesicles after the DM protein has removed the invariant chain with the CLIP sequence that occupies the peptide cleft on MHC 2

4. Why is the processing of microbes by the two classes of MHC so crucial?

The T-cells aren't able to distinguish between intra- and extracellular microbes. The MHC molecules allow for our immune system to react optimally to different types of microbes by "telling" the T-cells which type of microbe (intracellular or extracellular) is infecting our body. Only then, the T-cells can "decide" which methods to use.

5. Place the correct B-cell in the spot it belongs to.

Type of B-cell	Location	Main task
Follicular B-cells	Germinal center of spleen and lymph nodes	T-cell dependent response to protein antigen
Marginal zone B-cells	Marginal zone of spleen and lymph nodes	T-cell independent antibody responses
B-1 cells	Mucosal tissues and peritoneal cavity	

6. Place the different antigens in the category they belong in.

T-cell independent	T-cell dependent
Polysaccharides **Lipids**	**Peptides**

7. Which of these steps are not a part of B-cell priming in the follicles of lymph nodes?

a) Endocytosis of antigens
b) Antigen presentation by dendritic cell to B-cell
c) C3d on microbe binds to CD21 on B-cell
d) Expression of B7 proteins on B-cell

8. When the B-cell migrates out of the follicle, it decreases expression of CXCR5 which responds to cytokines in the follicle, and increases expression of CCR7, which responds to cytokines in the T-cell zone.

9. How does the CD40-CD40L interaction improve B-cell (APC) ability to present antigens to T-cells?

By stimulating more B7 expression on B-cells.

10. Fill in the empty boxes

Molecule on B-cell	Matching molecule on helper T-cell	Function of the coupling
Antigen in MHC 2	**T-cell receptor**	Initiation of t-cell mediated B-cell activation
MHC 2	CD4 co-receptor	**Amplification of signal within T-cell**
B7 proteins: CD80 and CD86	CD28	Induce IL-4 receptor expression on B-cell and expression of CD40L on T-cell
CD40	CD40L	**Cytokine secretion by T-cell + Increased B7 expression on B-cell**

11. Why is isotype switching and affinity maturation important in the humoral immune response?

Isotype switching ensures that the right type of response is produced for different microbes. For example, IgE will stimulate helminthic defense, while IgG will opsonize bacteria. Affinity maturation is important to be able to fight off prolonged of chronic infections.

Section 4

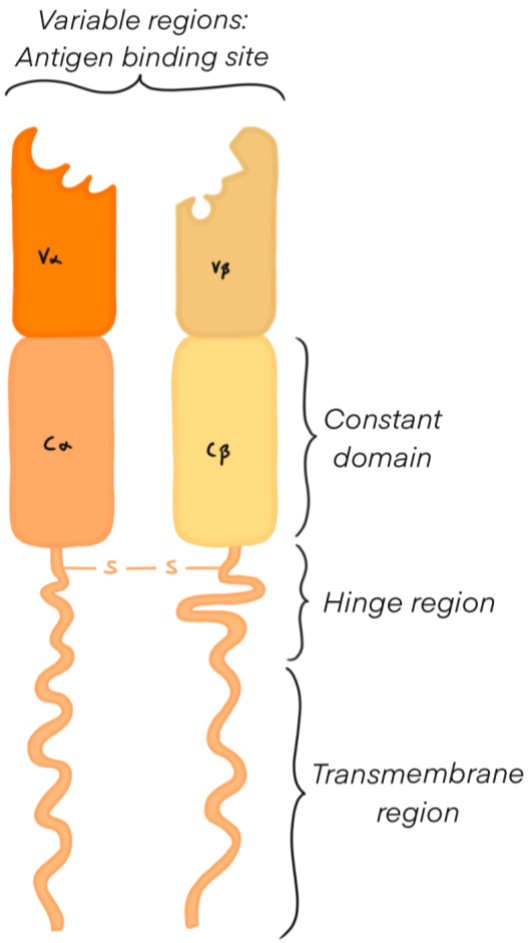
1. Which cells are considered "professional" antigen presenting cells?

1. Dendritic cells
2. Macrophages
3. B-cells

2. What kind of antigens does T-cells respond to?

a) Soluble antigens
b) Protein antigens only
c) Antigens in association with MHC
d) Antigens on antibody
e) a and c

3. Fill in the words on the T-cell receptor. Which part is the antigen binding site?



4. When an APC meets a T-cell, which factors determine if the T-cell reaches the activation threshold needed for signals to occur in the T-cell?

a) At least 5 TCRs must bind antigens at the same time
b) 2 TCRs must bind to antigens at the same time, and it must last a certain amount of time
c) A TCR must be in contact with an antigen for at least 10 minutes to elicit a response
d) There's no specific factors play a role
e) b and c

5. What does the TCR complex consist of?

TCR + CD3 + ζ protein = TCR complex

6. What is the role of LFA-1?

a) A molecule that suppresses T-cell action when it binds to B7
b) Binds to ICAM-2 on host cells
c) Initiate the T-cell response
d) Adhesion molecules on T-cells

7. Explain how CTLA4 suppress the immune response.

CTLA4 is similar to the CD28 receptor on T-cells, but when CTLA4 binds to B7, it initiates inhibitory signals.

8. What is cross-presentation? What is the result?

Cross-presentation is when a dendritic cell presents antigens both via MHC 1 and MHC 2 after ingesting infected host cell this allows the dendritic cells to activate helper T-cells and cytotoxic T-cells at the same time. This is beneficial because $CD8^+$ T-cells need helper T-cells to become fully activated, and by cross-presentation by dendritic cells, both cell types are activated close to each other.

9. What happens as the response to T-cell activation?

1. Secretion of cytokines and expression of cytokine receptors, especially IL-2 and IL-2R
2. Clonal expansion
3. Differentiation

10. Which cytokines stimulate the differentiation of a T_H0-cell to T_H1-cells, T_H2-cells, T_H17-cells and CTLs?

IL-12 ⟶ T_H1-cells
IL-4 ⟶ T_H2-cells
IL-1 ⟶ T_H17-cells

11. What are memory cells, what is their function?

Memory cells are long lived T-cells that survive even when the infection is over. Located in lymphoid organs, mucosal tissues and the circulation. Allows for rapid expansion of antigen specific clones if the lymphocytes are re-exposed.

12. Expression of which molecules decide where T-cells will migrate?

a) CD28
b) Adhesion molecules
c) CXCR5, CCR7
d) b and c

13. What are effector functions of T_H1- cells?

a) Killing infected host cells and activating macrophages
b) Hypersensitivity type 2 and activating dendritic cells
c) Delayed type hypersensitivity and macrophage mediated killing
d) Hypersensitivity type 1

14. What are the 3 steps of the delayed hypersensitivity reaction?

1. Sensitization
2. Repeat exposure
3. Inflammation (hypersensitivity)

15. Fill in the empty boxes

<table>
<tr><th>Cytokine</th><th>Cytokine function</th><th>Final effect stimulated by T_H2-cells</th></tr>
<tr><td>IL-5</td><td>Stimulates eosinophil activation and B-cell secretion of IgA</td><td rowspan="2">Helminths are killed by the secretion of granule proteins from eosinophils and IgE-mediated mast cell granulation. When T_H2-cells secrete IL-4 and IL-5, they mediate helminth defense.</td></tr>
<tr><td rowspan="2">IL-4</td><td>Stimulates B-cells to secrete IgE and IgG4 (non-complement fixing) antibodies</td></tr>
<tr><td rowspan="2">IL- 10</td><td rowspan="2">Inhibits microbicidal activity of macrophages and suppress T_H1-cells</td><td rowspan="3">By mediating these processes, the T_H2-cells mediate anti-inflammatory signals and tissue repair.</td></tr>
<tr><td rowspan="2">IL-13</td><td>Activate macrophage expression of mannose receptors</td></tr>
<tr><td>Increases fibroblast collagen synthesis and fibrosis</td></tr>
</table>

	Classical pathway	Alternative pathway
T-cells involved	T_H1-cells	T_H2-cells
Stimulatory cytokines	IFN-γ	IL-4, IL-10, IL-13
Main effect	Inflammatory Tissue damage	Anti-inflammatory Tissue repair

16. How does CTLs kill their target cells?

Granzymes: Activate caspases and induce apoptosis
Perforins: Mediates the entry of granzymes into the cytosol

Section 5

1. What is the role of immune tolerance?

- Activate and deactivate the number of lymphocytes based on demand
- Differentiate between foreign-antigens and self-antigens
- Differentiate between foreign-antigens and allergens

2. Place the correct phrases in the appropriate boxes

Central tolerance	Peripheral tolerance
Bone marrow Immature lymphocytes Positive selection Thymus	Clonal anergy Fas-FasL CTLA-4 upregulation Mature lymphocytes Veto cell

3. What is the role of peripheral tolerance and why do we need it?

- Recognize autoreactive lymphocytes that have "escaped" the thymus/bone marrow
- Protects the body from autoimmune reactions

4. What is not a mechanism of the veto cell?

a. Apoptosis of autoreactive T cell
b. Mimics self-antigen recognition
c. Fas-FasL mediated apoptosis
d. Upregulation of CLTA.4 on cell surface – *occurs during clonal anergy*

5. Fill in the missing words

a)

1. Autoreactive T_C cell binds to MHC-1 on veto cell provoking self-antigen reaction and cytotoxic stimulation
2. Veto cell redirects T_C cell toxicity via parallel signaling of self-CD8 and MHC-$1\alpha 3$ on T_C cell
3. Via the binding of death receptor Fas-FasL cytotoxic stimuli is sent back to the T_C cell
4. Resulting in apoptosis

b)

1. APC presents self-antigen to T cell
2. T cell upregulates CTLA-4 on cell surface
3. CTLA-4 binds B7 (CD 80/86)
4. Inactivation of T cell and no immune response

c) What are the names of the regulatory processes mentioned in task a and b?

a) The veto cell, b) Clonal anergy
Peripheral tolerance

6. Receptor editing – place the boxes in the correct order

1	2	3	4
Recognition of self-antigen by immature B cell	Reactivation of immunoglobulin gene recombinant reaction creating new immunoglobulin light chains	New immunoglobulin light chains are attached to previously expressed immunoglobulin heavy chains	New antigen receptor is produced

7. What mechanism does not induce apoptosis?

a. Mitochondrial pathway
b. Negative selection
c. Clonal anergy
d. Fas-FasL binding

8. Fill in the blanks

Organ	Barrier
Gonads in the testis	Blood-barrier made up by sertoli cells
Central nervous system	Blood-brain barrier
Thyroid	Blood-barrier made up by thyroid epithelial cells
Anterior chamber of the eye	Blood-retinal barrier
Placenta	Mother-fetus blood barrier

Section 6

1. List the four types of hypersensitivity

Type I – Anaphylactic, immediate hypersensitivity, or allergy
Type II – Cytotoxic, or antibody-mediated hypersensitivity
Type III – Immune complex
Type IV – Delayed, or T-cell mediated

2. Fill in the effector mechanisms

	Effector mechanism	Clinical manifestation
Type I	IgE	Allergic reaction Asthma
Type II	IgM, IgG Complement 3b	Autoimmune disorders
Type III	IgM, IgG Complement 3a, 4a, 5a	Serum sickness Vasculitis Systemic lupus erythematosus
Type IV	T-cells	Contact dermatitis

3. Fill in the blanks

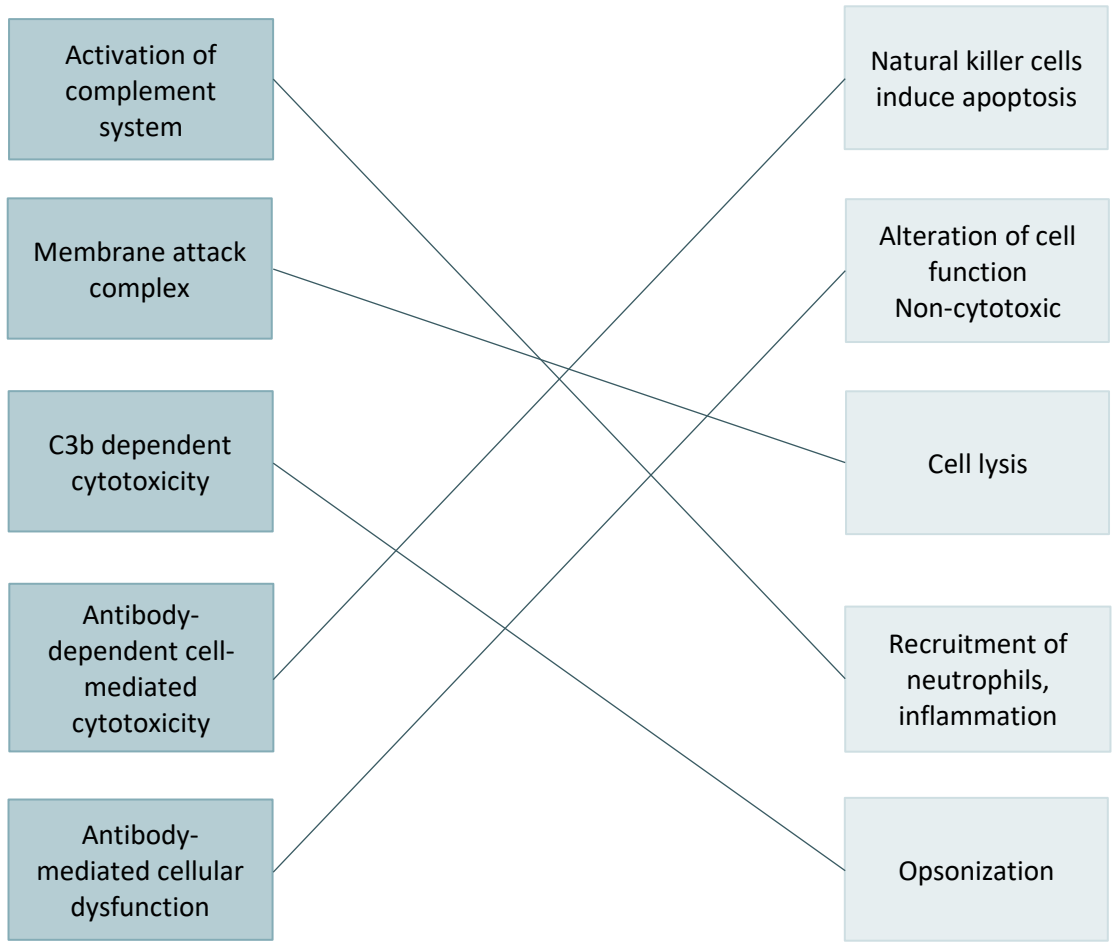
1. Allergen exposure
2. APC transports allergen to _lymph node_ and presents it to T_H cell
3. IL-_4_, IL-_5_, IL-_10_ convert T_H0 → T_H2 cell
4. T_H2 cell releases IL-_4_ and stimulates B cell to undergo antibody switching from IgM → _IgE_
5. _IgE_, specific to the allergen, attach to the _ Fcε _ receptors on _mast cells_

4. Second exposure to an allergen results in all of the following except

a. Cross-link of allergen to IgE antibodies on mast cell
b. Inflammation
c. Vasoconstriction
d. Histamine release

- There is vasoDILATION and increased vascular permeability

5. Connect the correct mechanism with its corresponding description



6. What is disorder is associated with immune complex hypersensitivity?

a. Vasculitis
b. Diabetes mellitus type I
c. Systemic lupus erythematosus
d. Graves disease
e. a and c are correct

- Diabetes mellitus type I is a $CD8^+$ T cell hypersensitivity (type IV)
- Graves disease is an antibody-mediated cellular dysfunction (type II)

7. What type of hypersensitivity does a tuberculin skin test elicit?

a. Type I – Anaphylactic
b. Type II - Cytotoxic
c. Type III – Immune complex
d. Type IV - Delayed

8. Place the correct phrases in the appropriate boxes

Acute phase	Proliferative phase
Minutes Innate immune system Mast cells Macrophages Histamine TNF, IL-1 Neutrophils Adhesion Complement	Days Adaptive immune system Macrophages Growth factor Angiogenesis Fibroblasts Collagen Scar tissue

9. What cells are recruited by the complement system in type III hypersensitivity reactions?

a. Plasma cells
b. Mast cells
c. Neutrophils
d. T_H cells

10. Match the number with the corresponding letter

1 – c
2 – g
3 – e
4 – a
5 – f
6 – b
7 – d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