Benha University **Faculty of Science** **Zoology Department** ***Biotechnology***	**1st semester Jan. Exam. 20/ 1 /2020** **Model answers**	**Premaster Exam.** **Histopathological Invest. (Z)** **Total degree: 120 marks** **Time allowed: THREE hours**

Answer ALL the following questions:

Q1: Discuss briefly each of the followings: (20 marks)

a- **Inflammation**: It is an extravascular process in which the active components of the reaction (cells and fluid) are derived from the blood vessels supplying the tissue area involved. It occurs in the connective tissue components, with a characteristic sequence of events.

b- **Granulomata** (definition & classification): It is a focal chronic inflammatory reaction, with macrophages and epithelioid cells in compact masses surrounded by lymphocytes.

Classification of Granulomata according to morphology and immunological status:

1. Morphology:

a. None caseating (e.g. foreign body)

b. Caseating (e.g. tuberculosis)

c. Suppurative (e.g. cat scratch disease)

2. Immunological status

a. Immune – stimulate epithelioid cell formation, healing is by fibrosis. T cytotoxic cells may kill cells and produce areas of necrosis

b. Non-immune – foreign body may attract macrophages without epithelioid cells or cell-mediated immune response. Fibrosis is less marked.

c- **Cellulitis**: It is inflammatory reaction spreading through connective tissue planes.

d- **Abscess**: It is necrotic, suppurative lesion localized by a fibroblastic boundary.

e- **Lymphoma**: It is common tumors that may also involve extra nodal sites. Treatment is by chemotherapy and radiotherapy, with resection for localized extra nodal lymphomas.

Q2: Write a detailed account on these items: - (30 marks)

a) Anti-tumor effector mechanisms:

1) **Cytotoxic T lymphocytes** – may be related to cells with antigens bound to class 1 MHC molecules, especially those that are virus-induced
2) **Natural killer cells** – stimulated by IL-2 to lyse tumor cells not detected by T cells (mechanism for specificity is unknown). Can lyse antibody-coated cells)
3) **Macrophages** – activated by a range of stimuli (endotoxin, interferon gamma)

4) **Antibodies –** potentially kill tumors cells by fixing complement and facilitating killing by macrophages and NK cells (type II hypersensitivity reaction).

b) Immunotherapy of cancer**:**

1. **Adoptive cellular therapy –** lymphocytes from the patient's blood or from the resected tumor are cultured with IL-2 in vitro and re-injected with more IL-2
2. **Cytokine therapy –** injected to stimulate immune cells, and to increase the expression of MHC molecules (e.g. interferon-α for hairy cell leukaemia)
3. **Antibody therapy –** investigated as agents for delivering cytotoxins or enzymes which induce local cytotoxin synthesis.

c) Types of necrosis:

1. **Coagulative** necrosis: the cytoplasm of the necosed cells become eoinophilic and persist for many days (myocardial infarcts).
2. **Colliquative** necrosis: the cells undergo lysis rapidly (brain infarcts).
3. **Caseous** necrosis: Mycobacterium tuberculosis interacts with macrophages.
4. **Gangrenous** necrosis: primary (bacterial toxins) or secondary (ischemia, infection).
5. **Fibroid** necrosis: smooth muscle necrosis, fibrin release (malignant hypertension).
6. **Fat** necrosis: inflammatory response to liberated fat.

Q3: Define APOPTOSIS and indicate the factors causing it, then discuss the changes occurring in the cell? (20 marks)

Answer: **Apoptosis** is a programmed cell death.

-It may be physiological deletion of selected cells (morphogenesis, cyclic hyperplasia of reproductive processes) or it may occur in response to a pathological stimuli.

Apoptosis requires:

1- Activation of specialist machinery for apoptosis (e.g. transglutamase, calcium/magnesium endonucleases).

2- Rise in cytosolic calcium, and induction of new mRNA species for c-fos, c-myc and heat-shock proteins

Changes occurring in the cell:

1. Cytosol and nucleus lost half their volume.
2. Fragmentation of nucleus and cytosol.
3. Condensation of chromatin (pyknosis).
4. Phagocytosis.

Q4: a- Mention the techniques that could be used for tumor detection? (10 marks)

Answer:

Tumors can be detected by the following techniques:

1. Activation of the same X chromosome throughout the cancer (in females).
2. Light chain restriction in a lymphoma.
3. Specific T cell or B cell gene rearrangement.
4. Mutation of a specific cancer gene throughout the tumor.

b- What is the normal function of p53? (10 marks)

Answer: Normal functions of P53 are:

1. DNA damage – p53 is induced and causes the self-elimination of cells that have potentially hazardous genetic damage
2. Inappropriate proliferation.
3. Wild-type p53 binds to DNA and activates a genetic program.
4. Intermittent hypoxia (like that seen in tumor development) induces p53.

c- Write on The role of leukocytes in inflammation response. (10 marks)

Answer:

1- **Neutrophils:** - Produced in large numbers in bone marrow. - First cells to arrive and can function in poor oxygenated conditions. - Involved in the inflammatory response and normal non-specific defenses.

2- **Eosinophil's and basophils:** - Limited phagocytic activity. - Recruited in inflammatory reactions derived from some specific immune responses.

3- **Macrophages:** - Derived from monocytes (bone marrow). - The majority of macrophages in inflammatory processes migrate directly from blood vessels.

Leukocyte migration (margination, adhesion, emigration, chemotaxis)

1- Slowing of blood flow and clumping of erythrocytes forces leukocytes to the periphery (margination).

2- Expression of adhesion molecules between leukocytes and the endothelium occurs (pavementing).

3- Cell adhesion molecules facilitate leukocyte adhesion by binding to a single cell surface glycoprotein found on activated monocytes, fibroblasts and vascular endothelial cells.

4- Chemotaxis – directional movement of phagocytic cells, mediated by a series of chemical messengers

- Motile neutrophils and monocytes are actively phagocytic.

- The PMNs are the first line of defense, migrating 30-40 minutes after injury occurs and reaching a maximum 6-8 hours later. They have a short life span and limited killing potential.
- Monocytes and macrophages appear after 4 hours and peak 16-24 hours after injury occurs. They have greater killing potential and have a role in preparing the tissue for healing and repair. They also produce interleukin, stimulating fibroblast proliferation.

Q5: a) Compare between benign and malignant tumors. (10 marks)

	Benign	Malignant
Mode of growth	Expansile, encapsulated	Expansile, infiltrative
Rate of growth	Slow, may cease	Rapid, progressive
Distant spread	Absent	Frequent
End result	Rarely fatal	Always fatal if untreated

b) "Mononuclear cells are the characteristic features of chronic inflammation", Discuss briefly? (10 marks)

ANSWER: **Chronic inflammation** is a prolonged process in which destruction and inflammation are proceeding at the same time as attempts at healing.

1. Activated *macrophages*, which are motile, capable of phagocytosis, stimulate fibroblasts to divide and are hardy and long, lived.
2. B and T lymphocytes may be involved also, along with plasma cells, eosinophils and fibroblasts.
3. Tissue destruction (e.g. peptic ulcer perforation, rheumatoid arthritis) and Fibrosis (e.g. cardiac valves).

With my best wishes,,,,,,

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