

SGD (APOPTOSIS)

Q-1 A patient developed leiomyoma, smooth muscle neoplasm the nuclei are hyperchromatic and bizzare. Some cells are dying and some are being formed.

- 1) What is the mechanism of death in cancer cells?
- 2) How does this differ from other type of cell death?
- 3) In cell injury, why the cytoplasm is glassy?

Q-2 A young man of 22 years admitted in hospital due to jaundice. Laboratory test revealed raised ALT and AST. True cut biopsy of liver reveals presence of pink bodies in hepatocytes with mild inflammation.

- 1) What is most likely pathological process involved in formation of these bodies?
- 2) Describe the pathophysiology of apoptosis?

Q-3

- 1) What is meant by apoptosis?
- 2) Describe the pathological process showing apoptosis?
- 3) Briefly describe morphological and characteristic features of the cells showing apoptosis?

(c) Write down its mechanism.

Key:

a) metaplasia

b) it is a reversible change in which one differentiated cell type (epithelial or mesenchyme) is replaced by another cell type.

c) It is a reversible change in which one adult cell type is replaced by another cell type. In this type of cellular adaptation, a cell type sensitive to a particular stress is replaced by another cell type better able to withstand the adverse environment. Metaplasia is thought to arise by reprogramming of stem cells to differentiate along a new pathway rather than a phenotypic change of already differentiated cells.

SGD # 4 Apoptosis , Intracellular accumulation, calcification.

- 1- A 30 year old man presented with severe headache which occurred off and on for last 3 years. Now its unbearable. CT scan showed a mass attached to meninges. The mass is composed of whirling pattern with round dark purple bodies.
- a- What is the name of these bodies
 - b- What do they represent.
 - c- How does this phenomenon differ from similar kind of phenomenon.
 - d- What are other sites where these can be found or this process can occur.

KEY

- a- Psammoma bodies
- b- Dystrophic calcification
- c- Metastatic calcification. serum ca levels are raised. While in dystrophic calcification the serum calcium levels are normal.
Metastatic calcification living cells like blood vessels.
Dystrophic calcification over dead tissues.
- d- Any area where necrosis can occur, papillary carcinoma thyroid, serous papillary carcinoma of ovary. Enzymatic fat necrosis.

Cell Injury

A 56 years old man recovered from myocardial infarction. He reached hospital in first hour and was given thrombolytic therapy. If it had been possible to see his microscopic sections of his heart during ischemic period.

- a- Which of the change you expect at cellular level.
- b- What other changes can develop.
- c- How does it differ from changes if the patient reached hospital after 4 hours and what changes do you expect. *→ Coagulative*
- d- What biochemical changes do occur if there is prolonged ischemia.

KEY

- a- Swelling of endoplasmic reticulum, mitochondria, and cell itself.
- b- Fatty change, blebs, amorphous densities.
- c- Cell death may occur, coagulative necrosis.
- d- Reversible and irreversible cell injury. Na K pump failure, Ca influx, increased glycolysis, increased lactic acid, reduced PH, activation of enzymes and cell organelle damage.

3- A 50 year old man suddenly experienced severe chest pain radiating to left jaw and arm. His cardiac enzymes were raised. After 4 hours of severe chest pain and agony he died. On autopsy the heart was examined carefully and it was found that death of myocytes occurred.

- a- What is the pathological process that caused death of the myocytes and the patient?
- b- Why this peculiar kind of lesion occurs in heart?
- c- What other organs can be involved by this lesion?
- d- What are the characteristic microscopic features which make this lesion very peculiar?

KEY

a- ~~Ischemic necrosis~~

b- Because heart is supplied by single artery

~~Ischemic necrosis~~ ✓

d- Cell membranes are intact, nuclei are lost. Protein coagulates and there is no enzymatic reaction.

SGD Healing & Repair



A BLACK SKIN PERSON SUUFERED WITH WITH THERMAL INJURY AND WAS TREATED IN UNIT OF TRAUMA CENTER OF HOSPITAL. AFTER 6 MONTHS ABNORMAL SKIN APPREANCE AT PLACE OF WOUND WHICH APPEARED AS ABOVE IN FIGURE.

- A. What is this type of lesion? → Keloid
- B. What is the composition of this lesion? raised to tumours Scar due to accumulations of collagen & individual bed position
- C. What are others complication of wound healing?

Composition → Keloid
 → collagen → 2 dermal layers → Proud flesh
 → Hyaluronan
 → Fibronectin → Dermoids
 → Infection

• Collagen
 • Hyaluronan

2- A 34 years old male with long history of alcoholism. Biopsy revealed clear spaces.

a-What is the most likely substance accumulated in the hepatocytes.

b- what is the causative agent in this scenario.

c-what do you call it.

d-what are different types of intracellular accumulations.

KEY

a- Triglycerides ✓

b- Alcoholism ✓

c- Steatosis ✓

d- Melanin, carbon in lungs(anthracois), lipofuscin, hemosiderin, copper.

.. Melanin

6- A 38 years old female presented with multiple purpuric skin lesions. Biopsy shows vasculitis.

- a- What kind of lesion do you expect in this patient?
- b- What is the morphological feature of this lesion?
- c- What is the pathogenesis?
- d- What are other conditions where this can occur?

KEY.

- a- Fibrinoid necrosis ✓
- b- Fibrin leakage and pink vessel wall ✓
- c- Antigen and antibody complex deposition. Fibrin leakage.
- d- Serum sickness, arthus reaction, post streptococcal glomerulonephritis, polyarteritis nodosa. Wegner's granulomatosis.

Antigen & antibody complex.

Serum sickness
streptococcal (tonleone)

SGD-

Topic. Necrosis

1- A 35 years old asymptomatic man showed a 3 cm nodule in the apical portion of right lung. The nodule was excised and sectioning showed a well circumscribed nodule with soft, white cheesy centre.

Culture of the tissue from the nodule grew mycobacterium tuberculosis.

- a- Which pathological process has occurred in this tissue
- b- Give two characteristic feature of this kind of lesion.
- c- What other sites can be involved by this lesion?
- d- What are the other similar kinds of lesions with one example each?

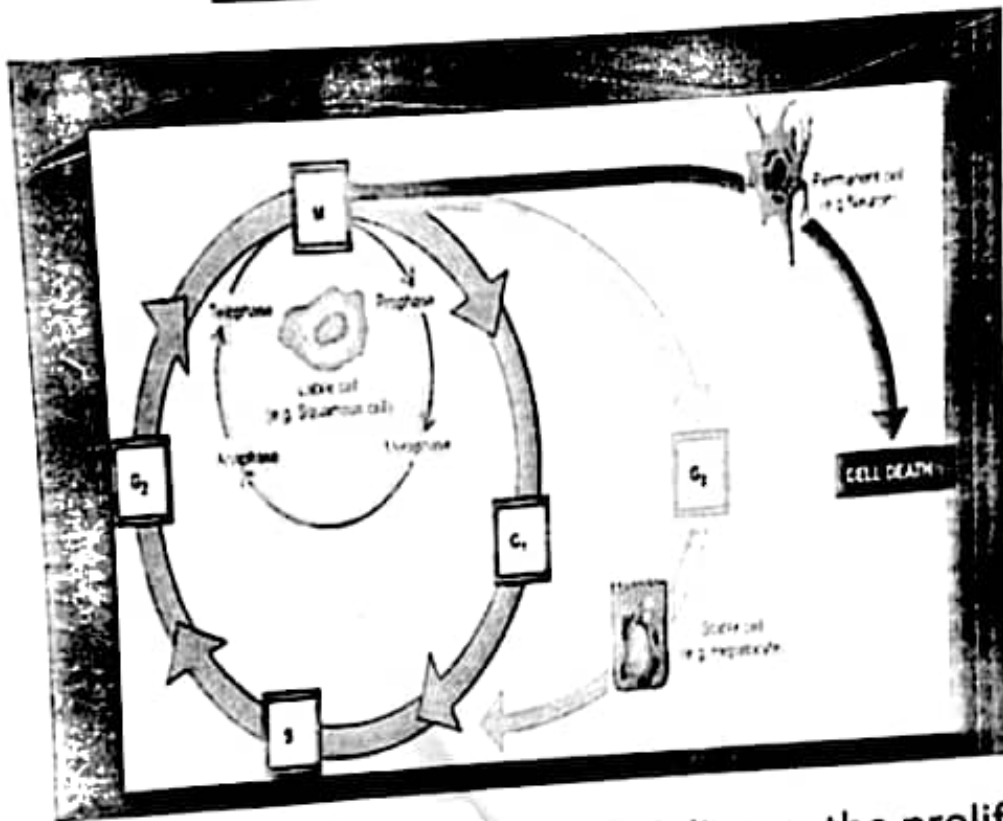
KEY:

- a- Caseous necrosis
- b- Granulation formation and caseous necrosis
- c- Lymph node and skin, brain, liver, kidney, epididymus.

- FC. Fat necrosis — pancreas and breast
- Coagulative necrosis — heart and kidney
- Dry gangrenous — diabetic foot
- Wet Gangrene — superimposed bacterial infection and intestines
- Fibrinoid necrosis — blood vessels with vasculitis.

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SGD Healing & Repair



1. Please see the diagram above and discuss the proliferation of tissue cells:

- a. Labile cells
- b. Stable cells
- c. Permanent cells

2. Discuss the various growth factors influencing the healing and repair. *EGF, PDGF, FGF, TGF- β*

3. What are MMP's and their role in healing?

EGF, PDGF, TGF, cytokines

Healing by First Intention (Primary Union)

This is defined as healing of a wound which has the following

Characteristics:

- i. Clean and uninfected;
- ii. Surgically incised;
- iii. Without much loss of cells and tissue;
- iv. Edges of wound are approximated by surgical sutures

Healing by Second Intention (Secondary Union)

This is defined as healing of a wound having the following characteristics:

- i. Open with a large tissue defect, at times infected;
- ii. Having extensive loss of cells and tissues;
- iii. The wound is not approximated by surgical sutures but is left open

- 5- A 25 year old female is breast feeding her 2 year old boy. She gave history of blow to her breast by head of the baby. After 15 days she developed a mass. Biopsy was done and it showed sheets of fat cells surrounded by macrophages.
- a- What is the most likely lesion?
 - b- What is the other site where this lesion can also occur?
 - c- What are the other morphological changes which can happen if left untreated?
 - d- Can this kind of lesion occur in a patient who receives blow in epigastrium.

KEY

- a- **Fat necrosis**
- b- **Pancreas, omentum**
- c- **Calcium deposition, capsulification.**
- d- Yes, because of pancreas.

- 4- A 60 years old diabetic female is having numbness of toes of her feet. She has a history of diabetes for the last 20 years. One day she woke up and found her toes black colored and there were no sensations. The doctor suggested to amputate her toes.
- a- What is the most likely diagnosis?
 - b- What is the most likely cause for this kind of lesion in this patient?
 - c- What will happen if doesn't care for her toes anymore?
 - d- What is the effect of bacterial infection in this particular case?
 - e- What are other sites of this kind of lesion?

KEY

- a- Dry Gangrene
- b- Ischemia and diabetes
- c- Superimposed bacterial infection
- d- Conversion to wet gangrene
- e- Intestines

2- A child is born with syndactyly (fusion of the finger webs).

a) What went wrong during embryogenesis that lead to this condition?

b) What are the enzymes that initiate apoptosis?

c) How do these caspases function?

d) What are the pathways that activate caspases?

e) Give examples of physiologic and pathologic apoptosis.

Key:

a) apoptosis ✓

b) caspases ✓

c) apoptosis is mediated by caspases by activating proteases and endonucleases. Proteases break down the cytoskeleton and endonucleases break down DNA.

d) caspases are activated by multiple pathways.

1. Intrinsic mitochondrial pathway ✓

2. Extrinsic receptor ligand pathway. ✓

3. Cytotoxic CD8 positive T-cell mediated pathway.

e) Physiologic apoptosis:

Endometrial shedding during menstrual cycle, removal of cells during embryogenesis

Pathologic apoptosis:

CD 8 positive T cell mediated killing of virally infected cells.

Apoptosis

- 1- A patient developed leiomyoma, smooth muscle neoplasm; the nuclei are hyperchromatic and bizzare. Some cells are dying and some are being formed.
 - a- What is the mechanism of death in cancer cells?
 - b- What happens to nuclei, if the process of cell death occurs?
 - c- How does this differ from other type of cell death?
 - d- What is fragmentation of nucleus called? *pyknotic oökenic*
 - e- What is fading away of nucleus.
 - f- In cell injury, why the cytoplasm is glassy.

KEY

- a- Apoptosis
- b- Pyknosis
- c- No inflammation, programmed, physiological and pathological, enzymes are activated.
- d- Karyorrhexis
- e- Karyolysis
- f- As glycogen is depleted.

glycogen

Key:

- a) Hyperplasia
- b) Hyperplasia is defined as the increase in the number of cells in an organ or tissue in response to a stimulus which leads to increase in the size of the organ. It can be physiologic or pathologic.
- c) Breast, endometrium of uterus, prostate, liver
- d) After partial hepatectomy, growth factors are produced in the liver that engage receptors on the surviving cells and activate signaling pathways that stimulate cell proliferation. But if the proliferative capacity of the liver cells is compromised, as in some forms of hepatitis causing cell injury, hepatocytes can instead regenerate from intrahepatic stem cells.

HYPERTROPHY

- 1) A 25 years old, 32 weeks pregnant lady had ultrasound abdomen done on which her uterus was enlarged.
 - (a) What mechanism is responsible for her enlarged uterus?
 - (b) Define the process.
 - (c) Write down its mechanism.

Key:

- a) Hypertrophy
 - b) It refers to an increase in the size of the cells that results in increase in the size of the affected organ.
 - c) it is the result of increased production of cellular proteins. It occurs by mechanical stress through stretch receptors (which are soluble mediators that stimulate cell growth). They trigger RNA synthesis and protein production that cause hypertrophy. Increase in expression of genes for contractile protein as a result of activation of alpha adrenergic receptors on the surface of myocytes.
- 2) A body builder develops his arm muscles by doing exercise.
 - (a) What type of adaptation is this?
 - (b) Define the process.
 - (c) Write down its mechanism.
 - (d) Give 3 pathologic examples of this process.

Key:

- a) Hypertrophy

Cell Injury SGD

Cellular Adaptations

Hyperplasia

1. After the birth of her first child, a 19 year old woman breast fed the infant for about one year. Which of the following processes that occurred in the breast during pregnancy allowed her to breast feed the infant.

- What is the process going on in the above scenario?
- Define the process.
- Name organs where this process can occur.
- Write down mechanism for this process.

Key

- Hyperplasia
- Hyperplasia is defined as the increase in the number of cells in an organ or tissue in response to a stimulus which leads to increase in the size of the organ. It can be physiologic or pathologic.
- Breast, endometrium of uterus, prostate, liver
- There are 2 types of cells. Dividing and non-dividing. Hyperplasia occurs in dividing cells under the influence of growth factors and certain hormones. It occurs as the result of growth factor driven proliferation of mature cells and in some cases by increased out put of new cells from tissue stem cells.

2) A 52 years old man suffering from hepatocellular carcinoma, underwent surgical lobectomy of his liver.

- What will happen to his remaining part of liver after surgery?
- Define the process.
- Name organs where this process can occur.
- Write down mechanism for this process in this scenario.

Key

a) Atrophy

b) It is defined as a reduction in the size of an organ or tissue due to a decrease in cell size and number. It can be physiological or pathological.

c) The mechanism of atrophy consists of a combination of decrease protein synthesis and increased protein degradation in cells. Protein synthesis decreases because of reduced metabolic activity. The degradation of cellular proteins occurs by ubiquitin-proteasome pathway. Atrophy is also accompanied with increased autophagy.

Metaplasia

1) A 32 Year old man experiences heartburn and gastric reflux after eating a large meal. After many months of symptoms he undergoes upper gastrointestinal endoscopy, and a biopsy specimen of the esophageal epithelium is obtained showing intestinal metaplasia and goblet cells.

- What is the process going on in the above scenario?
- Define the process.
- Name organs where this process can occur.
- Write down mechanism for this process.

Key

a) metaplasia

b) it is a reversible change in which one differentiated cell type (epithelial or mesenchyme) is replaced by another cell type.

c) Esophagus, cervix, urinary bladder, lung

d) it is a reversible change in which one adult cell type is replaced by another cell type. In this type of cellular adaptation, a cell type sensitive to a particular stress is replaced by another cell type better able to withstand the adverse environment. Metaplasia is thought to arise by reprogramming of stem cells to differentiate along a new pathway rather than a phenotypic change of already differentiated cells.

2) A chronic cigarette smoker underwent a change in the normal lining epithelium of the respiratory tract from ciliated columnar epithelium to squamous epithelium.

- What is the process going on in this person?
- Define the process.

2- A 65 years old woman suddenly lost consciousness, on awakening 1 hour later, she could not speak or move her right leg and arm. A CT scan was done and it showed a cystic area in the left parietal lobe. The brain tissue has been changed into a viscous mass.

- a- What pathological process has occurred in this patient?
- b- What are the most important causative agents?
- c- Give sites where this kind of lesion can occur.

liquefactive necrosis is

KEY:

a- Liquefactive necrosis ✓

b- Fungal infection and bacterial infection ✓

c- Pus formation, abscess ✓

- b) it refers to an increase in the size of the cells that results in increase in the size of the affected organ.
- c) it is the result of increased production of cellular proteins. It occurs by mechanical stress through stretch receptors (which are soluble mediators that stimulate cell growth). They trigger RNA synthesis and protein production that cause hypertrophy. Increase in expression of genes for contractile protein as a result of activation of alpha adrenergic receptors on the surface of myocytes
- d) Hypertrophy of cardiac muscles and hypertension. Hypertrophy of heart valves.
Hypertrophy of uterine smooth muscles.

ATROPHY

- 1) Gross examination of the brain on autopsy of a 90 years old man with a long history of atherosclerotic disease reveals shrunken brain with loss of brain substance, narrowed gyri & widened sulci.
- (a) Which process of cellular adaptation has occurred?
- (b) Define the process.
- (c) Write down its mechanism.
- (d) Give any two other causes of this cellular adaptation with examples.

Key:

a) Atrophy

b) it is defined as a reduction in the size of an organ or tissue due to a decrease in cell size and number. It can be physiological or pathological.

c) the mechanism of atrophy consist of a combination of decrease protein synthesis and increased protein degradation in cells. Protein synthesis decreases because of reduced metabolic activity. The degradation of cellular proteins occurs by ubiquitin-proteasome pathway.

d) Decreased work load e.g. immobilization of a limb, loss of endocrine stimulation e.g. loss of hormone stimulation in menopause .

- 2) A 45 years old woman was investigated for hypertension and was found to have enlargement of the left kidney. The right kidney was smaller than normal. Contrast studies revealed stenosis of right renal artery.
- (a) The size change in the right kidney is an example of which of the adaptive changes?
- (b) Define the process.
- (c) Write down its mechanism.

M. Rizwan
Roll No: F17-129
21 BBS 3rd Year

SGD Healing & Repair



A YOUNG MAN OF 35 YEARS SUFFERED WITH TRAUMA AND GOT FIRST AID FROM HOSPITAL EMERGENCY ROOM. AFTER FEW MONTHS, HE NOTICED THAT THERE IS SOME SWELLING AND RAISED SKIN AT THE SITE OF TRAUMA WHICH APPEARED AS SHOWN IN ABOVE PICTURE.

in raised
low to

A. What is type of this lesion?

Hypertrophic scar

B. What is Patho-physiology of this lesion?

C. What are factors effecting the wound healing?

They are firm, raised, erythematous plaque or nodules that manifest when matrix fails to properly heal.

They also result from pathologic wound healing.

→ Infections

→ Diabetes

→ Nutritional status

→ Glucocorticoids

→ Foreign bodies