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Solved Past Paper of Special Pathology By Med-Com

For Quick Review Only

4th Year MBBS

Made By MBBS Students of Various Medical Colleges of Pakistan

Managed , Edited & Compiled By:
Muhammad Kamran Mehwar

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Acknowledgement

Alhamdulillah Med-Com has earned its reputation as the only medical organization which is always willing to help other students, making everything easier for them as much as possible. We do believe that goodness and badness never disappear completely; rather it's the dominance of one of them that makes an era good or bad. And we are determined to make this era as good as possible by doing good to others, willingly and selflessly.

Treating human beings properly is a great responsibility for a doctor. We do recommend you to study from recommended syllabus books and use these papers only for quick revision just before exams, as a patient may present with a disease that is not written in past papers.

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CEO Med-Com &
Manager Papers Solving Project

Muhammad Kamran Mehwar
Allama Iqbal Medical College, Lahore
http://www.facebook.com/Doc.M.Kamran
http://www.facebook.com/MedCom.2011

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Annual 2003

Q1: a) Give the outline pathogenesis of RHEMUATIC HEART DISEASE. 4

b) Enumerate the complications of RHEMUATIC HEART DISEASE. Also give an account of laboratory diagnosis of the same. 4

c) What are the HEART FAILURE CELLS? 2

Ans:

(a) Pathogenesis:

Acute rheumatic fever results from host immune responses to group A streptococcal antigens that cross-react with host proteins. In particular, antibodies & CD4+ T cells directed against streptococcal M proteins and can also in some cases recognize cardiac self antigens. Antibody binding can activate complement, as well as recruit Fc-receptor bearing cells (neutrophils & macrophages); cytokine production by the stimulated T cells leads to macrophage activation (e.g., within aschoff bodies). Damage to heart tissue may thus be caused by a combination of antibody- and T cell mediated reactions.

(Reference: Big Robbins 9th edition Page No.558)

b) Complications:

(i) Arrhythmias (particularly atrial fibrillation in the setting of mitral stenosis)
(ii) Thromboembolic complications due to atrial atrial mural thrombi
(iii) Infective endocarditis
(iv) Fibrosis
(v) Cardiac hypertrophy

Lab diagnosis:

The diagnosis of acute rheumatic fever is based on serologic evidence of previous streptococcal infection in conjunction with two or more of so called **Jones criteria**:

(i) Carditis
(ii) Migratory polyarthritis of large joints
(iii) Subcutaneous nodules
(iv) Erythema marginatum skin rashes
(v) Sydenham chorea

(Reference: Medium Robbins 9th edition page no 392)

c) Heart failure cells:

The subsequent breakdown of red cells and hemoglobin leads to the appearance of hemosiderin-laden alveolar macrophages- so called heart failure cell-that reflect previous episodes of pulmonary edema)

(Reference: Medium Robbins 9th edition page no 367)

Supply 2003

Q1: a) Define ATHEROSCLEROSIS. 2

b) Define briefly Role of HDL-Cholesterol and LDL-Cholesterol in ATHEROGENESIS. 4

c) Discuss briefly the Complications of ATHEROSCLEROSIS. 4

Ans: a) Atherosclerosis is defined as hardening of vessels due to the presence of lesion called atheromas (or atheromatous or atherosclerotic plaque) which causes thickening of blood vessels

b) Component of cholesterol that is associated with increased risk is LDL. It delivers the cholesterol to the peripheral tissues while HDL mobilizes cholesterol from developing and existing atheromas and transports it to liver for excretion in the bile. So higher level of HDL correlates with reduced risk.

c) Complications:

- Myocardial infarction (heart attack)
- Cerebral infarction (stroke)
- Aortic aneurysm
- Peripheral vascular disease (gangrene of extremities)

(Reference: Big Robbins 9th edition Page No.492)

Annual 2004

Q1: a) Define ATHEROSCLEROSIS. 2
b) Enlist risk factors leading to ATHEROSCLEROSIS. 2
c) Enlist complications of ATHEROSCLEROSIS along with pathogenesis of each. 6
Ans:

(a) Atherosclerosis is defined as hardening of vessels due to the presence of lesion called atheromas (or atheromatous or atherosclerotic plaque) which causes thickening of blood vessels

(b) Risk factors leading to atherosclerosis :

No modifiable (Constitutional)
✓ Genetic abnormalities
✓ Family history
✓ Increasing age
✓ Male gender

Modifiable
✓ Hyperlipidemia
✓ Hypertension
✓ Cigarette smoking
✓ Diabetes
✓ Inflammation
✓ Hyperhomocysteinemia
✓ Metabolic syndrome
✓ Elevated levels of procoagulants

c) Complications of Atherosclerosis:

- ✓ **Aneurysm and rupture** it is due to the thickening of blood vessels , mural thrombosis or Embolization
- ✓ **Heart attack** is due to the occlusion of coronary artery by a thrombus which is formed by plaque rupture, plaque erosion, plaque hemorrhage, mural thrombosis or embolization
- ✓ **Stroke** is due to the occlusion of internal carotid and middle cerebral artery by a thrombus which is formed by plaque rupture, plaque erosion, plaque hemorrhage, mural thrombosis or embolization
- ✓ **Small bowl infarction** is due to the occlusion of superior mesenteric artery by a thrombus which is formed by plaque rupture, plaque erosion, plaque hemorrhage, mural thrombosis or embolization
- ✓ **Gangrene of extremities and claudication** is result of peripheral vascular diseases due to atherosclerosis
- ✓ **Cerebral atrophy** is due to involvement of circle of willis or internal carotid artery

(Reference: Medium Robbins 9th edition Page No.335, 336 & 342)

Supply 2004

Q1: a) Define and classify ANEURYSM.

b) Describe aetiology and morphology of dissecting aneurysm.

c) Give its clinical course.

Ans:

a) Aneurysm: An aneurysm is a localized abnormal dilation of a blood vessel or the heart that may be congenital or acquired.

Classification of aneurysm:

Aneurysms can be classified on the basis of

1) Macroscopic shape & size
2) Type
3) Location

1. **On the basis of macroscopic shape & size**

Saccular aneurysms	Fusiform aneurysms
These are spherical outpouchings involving only a portion of vessel wall; they vary from 5 to 20 cm in diameter and often contain thrombus.	These are diffuse, circumferential dilations of a long vascular segment; they vary in diameter (up to 20 cm) and in length and can involve extensive portions of the aortic arch, abdominal aorta, or even the iliacs.
Both saccular and fusiform aneurysms come under TRUE aneurysms.	

2. **On the basis of type**

True Aneurysms	False Aneurysms
Aneurysm which involves all 3 layers of an artery includes atherosclerotic, syphilitic & congenital aneurysms. (Both saccular and fusiform aneurysms come under TRUE aneurysms).	Also called pseudoaneurysms, is a collection of blood leaking completely out of vessels but confined to vessel by surrounding tissue.

3. **On the basis of location**
   - Arterial & venous
   - Heart e.g.; coronary artery aneurysms
   - Aorta e.g.; thoracic & abdominal aneurysms
   - Brain e.g.; berry aneurysms
   - Legs including popliteal arteries
   - Kidneys e.g.; renal artery aneurysm
   - Capillary aneurysms

(Reference: Big Robbins 9th edition Page No.501)

b) Aetiology of Dissecting aneurysm:

1. Hypertension
2. Localized or systemic abnormalities of connective tissue affecting aorta (e.g. Marfan syndrome)
3. Iatrogenic causes e.g.; following arterial cannulations during coronary catheterization procedures or cardiopulmonary bypass.
4. Rarely pregnancy can be associated with dissecting aneurysms which may be related to hormone induces vascular remodeling & the hemodynamic stresses of perinatal period.

Morphology of Dissecting aneurysm:

1. **Cystic medial degeneration** is present most frequently.
2. The intimal tear marking the point of origin of the dissection is found in the ascending aorta, usually within 10cm of aortic wall. Such tears are usually transverse or oblique & 1-5cm in length with sharp, jagged edge.

3. Dissection can extend along the aorta retrograde toward the heart as well as distally sometimes all the way into iliac & femoral arteries.
4. Dissecting hematoma spreads along the adventitia causing massive hemorrhage.
5. Sometimes hematoma re-enters the lumen of the aorta, producing second distal intimal tear & new vascular channel within the media of aortic wall forming **"double barreled aorta".**
6. Inflammation is **ABSENT**.

(Reference: Big Robbins 9th edition Page No.504)

c) Clinical course:

- The classic clinical symptoms are sudden onset of excruciating pain, usually beginning in the anterior chest, radiating to the back between the scapulae, and moving downward as the dissection progresses. The pain can be confused with MI.
- Common clinical manifestations include cardiac temponade & aortic insufficiency.
- Dissections can cause vascular obstruction & ischemic consequences such as MI, involvement of spinal arteries can cause transverse myelitis.
- Note: Dissections are of 2 types, Type A & Type B) In type A dissections, rapid diagnosis and institution of intensive antihypertensive therapy coupled with surgical placation of the aortic intimal tear can save 65% to 85% of patients. However, mortality approaches 70% in those who present with hemorrhage or symptoms related to distal ischemia & the overall 10-year survival is only 40% to 60%. Most type B dissections can be managed conservatively; patients have a 75% survival rate whether they are treated with surgery or antihypertensive medication only.

(Reference: Big Robbins 9th edition Page No.505)

Annual 2006

Q1: Write down the role of HYPERLIPIDEMIA ATHEROSCLEROSIS. 6

Ans:

- Hyperlipidemia more specifically, Hypercholesterolemia is a major risk factor for atherosclerosis.
- Even in the absence of other risk factors, hypercholesterolemia is sufficient to stimulate lesion development.
- The major component of serum cholesterol associated with increase risk is LDL cholesterol ("Bad cholesterol").
- LDL is a complex that delivers cholesterol to peripheral tissues.
- While HDL is a complex that mobilizes cholesterol from the periphery and transports it to liver for excretion in the bile.
- Consequently, higher levels of LDL cholesterol correlate with increase risk and higher levels of HDL cholesterol correlates with reduce risk.
- Chronic Hyperlipidemia particularly Hypercholesterolemia, can directly impair Endothelial Cell function by increasing local production of ROS and cause membrane and mitochondrial damage.
- With chronic hyperlipidemia, lipoproteins accumulate within the intima)
- Oxidized LDL is ingested by macrophages through a scavenger receptor resulting in foam cell formation.
- In addition oxidized LDL stimulates the release of Growth factors, cytokines and chemokines that create a vicious cycle of monocyte recruitment and activation.

SUMMERY: Hyperlipidemia ---->increase ROS production---->increase Transcription of endothelial and smooth muscle redox sensitive genes---->increase VcAM-1 ,mCSF,MCP-1 expression by endothelium---->increase Mononuclear leukocyte recruitment---->Enhanced atherosclerotic response.

(Reference: Big Robbins 9th edition Page No.492 & 496)

Supply 2006

Q1: Describe briefly the pathogenesis of RHEMUATIC HEART DISEASE. Also make histological appearance of its specific lesion. 4, 2

Ans:

Pathogenesis:

Acute rheumatic fever results from host immune responses to group A streptococcal antigens that cross-react with host proteins. In particular, antibodies & CD4+ T cells directed against streptococcal M proteins and can also in some cases recognize cardiac self antigens. Antibody binding can activate complement, as well as recruit Fc-receptor bearing cells (neutrophils & macrophages); cytokine production by the stimulated T cells leads to macrophage activation (e.g., within aschoff bodies). Damage to heart tissue may thus be caused by a combination of antibody- and T cell mediated reactions.

Histologic appearance:

1. **Aschoff bodies**, consisting of T lymphocytes,plasma cells and plump of activated macrophages called **Anitschkow cells** are found in any of 3 layers of heart resulting in pericarditis, myocarditis, or endocarditis(**pancarditis**).
2. **MacCallum plaques** are formed, these are plaques formed usually in the left atrium due to stenosis of valves by vegetations, called **verrucae**.

(Reference: Big Robbins 9th edition Page No.558)

Annual 2007

Q1: A 58-year old principal of a medical college is diagnosed with ACUTE MYOCARDIAL INFARCTION after he collapsed on his desk office. He is known hypertensive and smokes 10 to 12 cigarettes per day and drinks socially. Serum cholesterol level is elevated and he confesses being fond of desserts and mithai. His father died of myocardial infarction and his mother has stable angina)

a) Identify the major risk factors for atherosclerosis in this patient and categorize them as constitutive (non-modifiable) and potentially controllable. 3

b) Also list the minor risk factors for atherosclerosis in this patient. 2

Ans:

a)

Nonmodifiable (constitutional)
1. Genetic abnormalities 2. Family history 3. Increasing age 4. Male gender
Modifiable (controllable)
In this patient controllable risk factors are 1. Cigarette smoking 2. Hypertension 3. Hyperlipidemia Other modifiable risk factors also include Diabetes and inflammation

(Reference Big Robbins 9th edition page No.492)

b) Minor risk factors for atherosclerosis:

1. Lack of exercise (Physical inactivity)
2. Competitive, stressful life style(type A personality)
3. Obesity

(Reference Big Robbins 9th edition page No.494)

Annual 2008

Q1: A 65-year-old dictator of a banana republic, who was alcoholic and fond of red meat. Suffered short episodes of unexplained chest pain after he was force to resign and died before he could reach the hospital. At autopsy the pathologist found thickened walls of many arteries including the coronary

arteries with luminal narrowing. The lesions consisted of raised plaques having a soft center with a fibrous cap:

a) What is the process known as and what other arteries it most commonly involves? 3

b) What are the principal components of these plaques? 2

Ans:

(a) Atherosclerosis

It most commonly involves (in descending order) as follows

1. Lower abdominal aorta (abdominal aorta is typically involved too much greater degree than thoracic aorta).
2. The coronary arteries
3. The internal carotid artery
4. The vessels of circle of Willis.

(b) **Components of atherosclerotic plaque:**

Atherosclerotic plaques have 3 principal components:

1. Smooth muscle cells, macrophages & T-cells.
2. Extra-cellular matrix including collagen, elastic fibers & proteoglycans
3. Intracellular and extracellular lipid.

(Reference: Big Robbins 9th edition Page No.498)

Supply 2008

Q1: While performing an autopsy on a prison inmate, the pathologist notices a gray-white scar in the left ventricular wall. Microscopic section from the lesion shows collagen deposition without granulation tissue.

a) If the lesions represent myocardial infarcts, what is the minimum length of the time for which the patient must have survived after the infarction? 1

b) Give the gross and microscopic features of irreversible myocardial injury at 8 hours and 10 days of age. 2, 2

Ans:

(a) 2-8 weeks

(b) At 8 hours

4-12 hr	**Gross:** Dark mottling (occasional)	**Microscopic:** Early coagulation necrosis; edema; hemorrhage

At 10 days

7-10 days	**Gross:** Maximally yellow-tan and soft, with depressed red-tan margins	**Microscopic:** Well developed phagocytosis of dead cells; granulation tissue at margins

(Reference: Big Robbins 9th edition Page No.544)

Annual 2009

Q1: A 70 year old male, chronic smoker was brought to the emergency department with a history of acute chest pain with sweating and developing into a state of shock. He expired on arrival in the hospital. Medical autopsy was carried out were pathologist observed dark mottling of anterior wall of left ventricle, anterior part of septum and apex. The cause of death was declared as Myocardial Infarction.

a) Which coronary artery was critically stenosed in this patient? 0.5

b) What must have been the duration survival after the myocardial infarction and what would be the microscopic picture of this infected area? 2
c) Enumerate complications of myocardial infarction. 2.5
Ans:
a) Left coronary artery
b) 12-24 hours

Patient has survived for **12-24 hr**	**Gross feature as given in question:** Dark mottling	**Microscopic picture of infected area in this case:** Ongoing coagulation necrosis, pyknosis of nuclei, myocyte hypereosinophilia; marginal contraction band necrosis; early neutrophilic infiltrate

(Reference: Big Robbins 9th edition Page No.544)

c) <u>Complications of myocardial infarction: (Mnemonic MAC-VIP):</u>

1. Myocardial rupture
2. Mural thrombus
3. Arrhythmias
4. Contractile Dysfunction
5. Ventricular aneurysm
6. Infarct expansion
7. Pancarditis
8. Papillary muscle dysfunction
9. Progressive late Heart failure

(Reference: Big Robbins 9th edition Page No.547-549)

<u>Supply 2009</u>

Q1: Briefly discuss the role of monocytes in the generation of atheroma)
Ans: Atherosclerosis is a chronic inflammatory response of the arterial wall to endothelial injury. Lesion progression involves interaction of modified lipoproteins, **monocyte-derived macrophages**, T lymphocytes, and the cellular constituents of the arterial wall. According to this model, atherosclerosis results from the following pathogenic events.

Endothelial injury
↓
Accumulation of lipoproteins
↓
Platelet adhesion
↓
Monocyte adhesion to the endothelium
↓
Lipid accumulation
↓
Smooth cell recruitment due to factors released
↓

Smooth cell proliferation & ECM production

Role of Monocytes:

Monocytes differentiate into macrophages & avidly engulf lipoproteins, including oxidized LDL & small cholesterol crystals. Cholesterol crystals appear to be particularly important instigators of inflammation through activation of inflammasome & subsequent release of IL1. Activated macrophages also produce toxic oxygen species that drive LDL oxidation & elaborate growth factors that stimulate smooth muscle cell proliferation.

(Reference: Medium Robbins 9th edition Page No.338 & 340)

Annual 2010

Q1: A 55-year old man presents with left sided facial pain, with palpable left temporal artery. Biopsy of the artery reveals fragmentation of internal elastic lamina, with granulomas containing Langerhan and foreign body giant cells.

a) What is the diagnosis? 1

b) Which other condition should be considered in the differential diagnosis if a granulomatous vasculitis involves the aorta? 1

c) List 3 pathogenic mechanisms involved in non infectious vasculitides? 3

Ans:

a) Giant cell arteritis

b) Takayasu arteritis

c) 1. Immune complex associated vasculitis

2. Antineutrophil cytoplasmic antibodies

3. Antiendothelial cell antibodies

4. Auto reactive T cell

(Reference: Big Robbins 9th edition Page No. 506-508)

Annual 2011

Q1: A 50 year old male presented in emergency room with severe, crushing substernel chest pain radiating to the neck and jaw with discomfort in epigastrium. The pain not resolved with nitroglycerin or rest. On investigation, he was found to be a heavy smoker for the last twenty years with strong family history of hypercholesterolemia) Electrocardiographic abnormalities such as Q-waves, and ST segments abnormalities and T-waves inversion are noted. His blood chemistry is ordered. The patient went into the cardiogenic shock and could not come out of it.

a) What are the morphological changes seen in Myocardial Infarction? 3

b) Give the laboratory evaluation of a patient with Myocardial Infarction. 2

Ans: a)

time	Gross features	Light microscope	Electron microscope
Reversible Injury			
0-0.5 hr	none	None	Relaxation of myofibrils, glycogen loss, mitochondrial swelling
Irreversible injury			
0.5-4 hr	None	Usually none; variable waviness of fibers at border	Sarcolemmal disruption; mitochondrial amorphous densities
4-12 hr	Dark mottling (occasional)	Early coagulation necrosis; edema; hemorrhage	

12-24 hr	Dark mottling	Ongoing coagulation necrosis, pyknosis of nuclei, myocyte hypereosinophilia; marginal contraction band necrosis; early neutrophilic infiltrate	
1-3 days	Mottling with yellow tan infarct center	Coagulation necrosis, with loss of nuclei and striations; brisk interstitial infiltrate of neutrophils	
3-7 days	Hyperemic border; central yellow tan softening	Beginning disintegration of dead myofibers, with dying neutrophils; early phagocytosis of dead cells by macrophages at infarct border.	
7-10 days	Maximally yellow-tan and soft, with depressed red-tan margins	Well developed phagocytosis of dead cells; granulation tissue at margins	
10-14 days	Red-gray depressed infarct borders	Well established granulation tissue with new blood vessels & collagen deposition	
2-8 wk	Gray-white scar, progressive from border toward core of infarct	Increased collagen deposition, with decreased cellularity	
>2 mo	Scarring complete	Dense collagen scar	

(Reference: Big Robbins 9th edition Page No.544)

b) Lab evaluation:

The lab evaluation of MI is based on measuring the blood levels of proteins that leak out of irreversibly damaged myocytes; the most useful of these molecules are cardiac specific troponins T and I (cTnT and cTnI), and the MB fraction of creatine kinase (CK-MB).The diagnosis of MI is established when blood levels of these cardiac biomarkers are elevated.

Time of elevation, peak and back to normal level of these biomarkers are as follows:

Time to elevation of CK-MB, cTnT and cTnI is 3 to 12 hrs
CK-MB and cTnI peak at 24 hours
CK-MB returns to normal in 48-72 hrs, cTnI in 5-10 days, and cTnT in 5 to 14 days.

(Reference: Big Robbins 9th edition Page No.547)

Annual 2012

Q1: A 40 year old female presents with a long H/O joint pains,facial rash,shortness of breath & leg edema) Her ANA (antinuclear-antibody) and double stranded DNA test is positive

a)Describe the lesions that can develop in her mitral valve. 2.5

b)What complications can develop in a patient of bacterial endocarditis? 2.5

Ans: a) Endocarditis of SLE (Libman-Sacks Disease)

- Lesions are small (1-4mm in diameter), single or multiple, sterile, pink vegetations with a warty (verrucous) appearance.
- Histologically the vegetations consist of a finely granular, fibrinous eosinophilic material containing cellular debris including nuclear remnants. Vagitations are often associated with an intense valvulitis, characterized by fibrinoid necrosis of the valve substance and reflecting the activation of complement and recruitment of Fc-receptor-bearing cells.

(Reference: Big Robbins 9th edition Page No.562)

b) Complications:

1. Glomerulonephritis due to antigen-antibody complex deposition in glomerulus

2. Murmurs are present in 90% of patients with left sided IE and may stem from a new valvular defect or represent a pre-existing abnormality.

3. Vegetations sometimes may erode into the underlying myocardium & produce an abscess (**Ring Abscess**).

4. With time fibrosis, calcification and chronic inflammatory infiltrate can develop.

5.Earlier diagnosis and effective treatment has nearly eliminated some previously common clinical manifestations of long standing IE – for example, microthromboemboli (manifest as splinter or subunual hemorrhages),erythematous or hemorrhagic nontender lesions on the palms or soles (Janeway lesions), subcutaneous nodules in the pulp of the digits (Osler nodes), and retinal hemorrhages in the eyes (Roth spots).

(Reference: Big Robbins 9th edition Page No.561)

Supply 2012

Q1: A 56 year old male presents with raised voilaceous plaques over his legs and is formed to be a HIV positive. A biopsy of the lesions revealed a vascular neoplasm. Further investigations revealed lesions with similar histology involving multiple abdominal Viscera)

a) Name the likely tumor. 2

b) List three other forms of the same disease. 2

c) Which viral DNA do you expect to isolate from this tumor? 1

Ans: a) Kaposi sarcoma (AIDS associated / Epidemic KS)

b) 1.Classic KS
2.Endemic African KS
3.Transplant-associated KS
4.AIDS-associated

c) Human Herpes Virus (HHV8)

(Reference: Big Robbins 9th edition Page No.518)

Supply 2013

Q1: Postmortem examination was performed on a 24 year old male who died in a hit and run an accident. Autopsy findings showed raised yellowish plaques in the abdominal aorta) Family member of the deceased also revealed his history of smoking and Hyperlipidemia)

a) Name the lesion in this aorta and give its microscopic features. 1, 2

b) Write FOUR complications that may be associated with such a lesion. 2

Ans:

a) Atherosclerotic plaques.

Microscopic Features:

Atherosclerotic plaques have 3 principal components:

1.Smooth muscle cells, macrophages & T-cells.

2. Extra-cellular matrix including collagen, elastic fibers & proteoglycans:

3.Intracellular and extracellular lipid.

b) Complications:

1) Rupture, ulceration or erosion of the surface of atherosclerotic plaques exposes highly thrombogenic substances and leads to **thrombosis**, which may partially or completely occlude the vessel lumen.

2) Hemorrhage into plaques

3) Atheroembolism

4) Aneurysm formation

(Reference: Big Robbins 9th edition Page No.498, 499)

Supply 2014

Q1: A 40 year old male has a sudden chest pain radiating to left arm. ECG allows Q waves and ST segment elevation. He has a sudden arrhythmic event and despite intervention dies. Autopsy findings shows occlusions of left anterior left descending coronary artery.

a) Which area of the heart is most likely to show the lesion? 1

b) Give the sequence of morphological changes seen in the myocardium between one to three days after the event. 3

c) Write FOUR complications of lesion. 1

Ans:

a) 1.Anterior wall of left ventricle near the apex

2. Anterior portion of ventricular septum

3. The apex circumferentially.

b) Morphologic Changes:

Gross (1-3 Days):

Mottling with yellow tan infarct centre.

Microscopic:

-Coagulation necrosis.

-With loss of nuclei and striations.

-Brisk interstitial infiltrate of neutrophils

c) Complications:

- Contractile dysfunction
- Arrhythmias
- Myocardial rupture
- Ventricular aneurysm
-Pericarditis
-Infarct expansion
-Mural thrombus
-Papillary muscle dysfunction.
-Progressive late heart failure (Chronic IHD)

(Reference: Big Robbins 9th edition Page No.544, 547-549)

Supply 2015

Q1: A 40 year old male is complaining of gradually increasing respiratory discomfort, chronic cough, palpitation and ankle edema for last 2 years .He has history of fever and migratory Polyarthritis attacks as a child.

a) What is most likely diagnosis? 2

b) what are the causes of Myocarditis? 3

Ans:

(a) Diagnosis: Rheumatic Fever

(b) Causes of Myocarditis:

Major causes of myocarditis are classified into 3 categories

1.Infections:
-Viruses (e.g., coxackievirus, ECHO, influenza, HIV, cytomegalovirus) -Chlamydia (e.g., Chlamydophyla psittaci) -Rickettsiae (e.g., Rickettsia typhi , typhus fever) -Bacteria (e.g., Corynobacterium diphtheria, Neisseria meningococcus, Borrelia (Lyme disease)) -Fungi (e.g., Candida) -Protozoa (e.g., Trypanosoma cruzi [Chagas disease], toxoplasmosis) -Helminths (e.g.,trichinosis)
2.Immune-Mediated Reactions
-Postviral -Poststreptococcal (Rheumatic fever) -SLE -Drug hypersensitivity -Transplant rejection
3.Unknown
-Sarcoidosis -Giant cell myocarditis

Reference: Big Robbins 9th edition page No.571

Solved By:

Mohsin Nasir Co-ordinator @ Med-Com From Akhtar Saeed Medical & Dental College, Lahore	Inam Ur Rehman Co-ordinator @ Med-Com From Multan Medical & Dental College, Multan	Hafsa Ilyas Co-ordinator @ Med-Com From University Medical & Dental College, Faisalabad

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Section 2: Haematopoietic & Lymphoid System

Annual 2003

Q1: classify Hodgkin's lymphoma

Ans: Hodgkin lymphoma is of following types

- nodular sclerosis Hodgkin lymphoma
- mixed cellularity Hodgkin lymphoma
- lymphocyte predominance Hodgkin lymphoma
- lymphocyte rich Hodgkin lymphoma
- lymphocyte depletion Hodgkin lymphoma

Q2:

a) Classify Anemia

b) Discuss laboratory diagnosis of MEGALOBLASTIC ANEMIA

c) Tabulate the difference between childhood and adult types of Chronic Myeloid Leukemia?????

Ans:

a) Classification of Anemias (aetiological):

1. Anemia due to blood loss
   - Acute: trauma
   - Chronic: GIT and gynaecological disturbances
2. Anemia due to increased red cell destruction (Hemolytic anemias)
   - Intrinsic abnormalities like hereditary problems, membrane abnormalities, enzyme deficiencies, disorders in hemoglobin synthesis etc
   - Extrinsic abnormalities like infection (malaria), mechanical trauma to red cells, antibody mediated causes etc
3. Anemia due to impaired red cell production
   - Deficiency of substances essential for erythropoiesis like iron deficiency, deficiency of vitamin B12 and folic acid, anemia associated with malnutrition
   - Disturbances of marrow function without deficiency of substances essential for erythropoiesis like aplastic anemia, anemia associated with renal failure, liver diseases, disseminated malignancies etc

b) Laboratory Diagnosis of Megaloblastic Anemia:

- Complete history
- Physical examination
- Complete blood count
  - Hb count decreased, leucopenia, thrombocytopenia
  - Blood smear: oval macrocytes, anisocytosis, poikilocytosis
  - Neutrophils with nucleus having 5 or more lobes (hypersegmentation of nucleus)
- Bone marrow aspiration
  - Erythroid hyperplasia
  - Erythropoiesis – megaloblastic
  - Giant metamyelocytes
- Iron stores INCREASED

BIOCHEMISTRY

- Serum Vitamin B12 assay

- Decreased in pernicious anemia
- Normal range 280 - 1590 ng/l

- Serum folate assay
  - Decreased in folic acid deficiency
- Radioactive Vitamin B12 absorption test (SCHILLING TEST)
- Specialized investigations
  - Serum folate assay
  - Red cell folate assay
  - FIGLU excretion in urine (increased)

Supply 2003

Q1: a) classify non Hodgkin lymphoma
b) Discuss briefly about burkitts lymphoma
c) What are Reed Sternberg cells and lacunars cells?

Ans: non Hodgkin lymphoma has further two subtypes:

1. B cell lymphoma:

- precursor B cell lymphoblastic lymphoma
- small lymphocytic lymphoma
- burkitts lymphoma
- mantle cell lymphoma
- follicular lymphoma
- diffuse large B cell lymphoma
- extra nodal marginal zone lymphoma

2. T cell lymphoma:

- precursor T cell lymphoblastic lymphoma
- mycoses fungoides sezary syndrome

b) Accounts for 30% of non Hodgkin lymphoma) fastest growing human neoplasm. Express surface IgM, pan b call markers (CD19 CD20), germinal center B cell markers (CD10, BCL6)

- PATHOGENESIS: translocations involving fusion of MYC gene on ch.18 with IGH gene on ch.14 results in dysregulation and over expression of MYC gene. Also results from infection with EBV(Epstein barr virus)
- Morphology: Tumor cells are
  - Intermediate in size with round oval nucleus having 2-5 prominent nucleoli in basophilic amorphous cytoplasm (cytoplasm has small lipid filled vacuoles)
  - Increased proliferation and apoptosis of cells
  - This debris is engulfed by macrophages
  - Macrophages surrounded by clear space giving STARRY SKY PATTERN
- Clinical features:
  - affects children and young adults
  - starts at extra nodal sites
  - endemic tumors presents as maxillary and mandibular masses
  - abdominal tumors involve bowel ,ovaries and retroperitoneum
  - Rx: aggressive chemotherapy

C) REED Sternberg cells are

- characteristic neoplastic cells of Hodgkin lymphoma
- with 15-45um diameter
- have enormous multilobate nucleus with prominent nucleoli
- classic RS cell have 2 mirror image nucleus containing inclusion like acidophilic nucleolus surrounded by clear zone(owls eye appearance)

- distinct nuclear membrane

Lacunar cells are a type of reedsternberg cells present in nodular sclerosis hodgkin lymphoma

- have multilobate nucleus
- prominent nucleoli
- Pale staining cytoplasm which during smear preparation torn away leaving nucleus behind in a clear empty giving appearance of lacune. That's why they are called lacunar cells.

Supply 2004

Q1: a) Enlist causes of generalized lymphadenopathy
b) Differences BW tuberculous lymphadenopathy and lymphoma?????

Ans: a) following are some causes of generalized lymphadenopathy

- Viruses CMV,EBV
- Sexually transmitted diseases
- Toxoplasma
- hepatitis b
- rheumatic arthritis
- SLE
- Breast cancer
- AIDS
- TB

Annual 2004

Q1

a) Classify anemia on the basis of RBC morphology and aetiology
b) Enlist causes of aplastic anemia) Give salient features of bone marrow smear of aplastic anemia

Ans:

a) Classification of Anemia:

Morphological Classification:

- Normocytic, Normochromic Anemia (MCV & MCHC within normal rates)
  - Blood loss anemia
  - Aplastic anemia
  - Anemia due to Intrinsic RBC defects
  - Anemia due to Extrinsic RBC defects
- Microcytic, Hypochromic Anemia
  (MCV less than 80fl & MCHC less than 32g/dl)
  - Iron deficiency anemia
  - Anemia of chronic disease
  - Thalassemia
- Macrocytic Anemia
  (MCV more than 100fl)
  - Folate deficiency anemia
  - Vitamin B12 deficiency anemia

Aetiological Classification:

1. Anemia due to blood loss
   - Acute: trauma
   - Chronic: GIT and gynaecological disturbances
2. Anemia due to increased red cell destruction (Hemolytic anemias)
   - Intrinsic abnormalities like hereditary problems, membrane abnormalities, enzyme deficiencies, disorders in hemoglobin synthesis etc

- Extrinsic abnormalities like infection (malaria), mechanical trauma to red cells, antibody mediated causes etc

3. Anemia due to impaired red cell production
   - Deficiency of substances essential for erythropoiesis like iron deficiency, deficiency of vitamin B12 and folic acid, anemia associated with malnutrition
   - Disturbances of marrow function without deficiency of substances essential for erythropoiesis like aplastic anemia, anemia associated with renal failure, liver diseases, disseminated malignancies etc

b) Causes of Aplastic Anemia:

- Idiopathic
- Due to drugs: alkylating agents and antimetabolites
- Idiosyncratic or hypersensitivity reaction to myelotoxic drugs (sulfonamide, chloramphenicol)
- Viral infections
- Ionizing radiation (diagnostic radiography, radiotherapy, radioactive substances

Bone marrow findings:

- Hypocellular bone marrow
- Intertrabecular space occupied by fat
- Lymphocytes and plasma cells are present
- Reticulocytopenia
- Pancytopenia
- Erythropoiesis is decreased

Annual 2006

Q1: Classify Hodgkin lymphoma. Write morphology of mixed cellularity type of Hodgkin lymphoma) Tabulate the clinical differences b/w Hodgkin and non- Hodgkin lymphomas.

Ans: Hodgkin lymphoma is of following types

- nodular sclerosis Hodgkin lymphoma
- mixed cellularity Hodgkin lymphoma
- lymphocyte predominance Hodgkin lymphoma
- lymphocyte rich Hodgkin lymphoma
- lymphocyte depletion Hodgkin lymphoma

Morphology of mixed cellularity type Hodgkin's lymphoma:

- most common form of Hodgkin lymphoma in patient older than 50
- comprises 25%
- there is male predominance
- classic RS cells are plentiful with in a distinctive heterogeneous cellular infiltrate which includes lymphocytes, eosinophils, plasma cells and benign histiocytes
- compared with other subtype it have disseminated disease & systemic manifestation

Differences b/w Hodgkin and non Hodgkin lymphoma

HODGKIN LYMPHOMA	Non HODGKIN LYMPHOMA
• Often localized to single axial group of nodes (cervical, mediastinal structures,paraaortic) • Orderly spread by contiguity • Mesenteric nodes and waldeyer ring rarely involved • Extranodal involvement uncommon	• More frequent involvement of multiple peripheral nodes • Non contiguous spread • Mesenteric nodes and waldeyer ring commonly involved • Extranodal involvement common

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Supply 2006

Q1: a) classify non Hodgkin lymphoma

b) Give microscopic picture of burkitts lymphoma

Ans: non Hodgkin lymphoma has further two subtypes:

1 .B cell lymphoma:

- precursor B cell lymphoblastic lymphoma
- small lymphocytic lymphoma
- burkitts lymphoma
- mantle cell lymphoma
- follicular lymphoma
- diffuse large B cell lymphoma
- extranodal marginal zone lymphoma

2. T cell lymphoma:

- precursor T cell lymphoblastic lymphoma
- mycoses fungoides sezary syndrome

b) It accounts for 30% of children non Hodgkin lymphoma) Mostly infection with EPV results into this lymphoma in genetically predisposed individuals.

Morphology: Tumor cells are

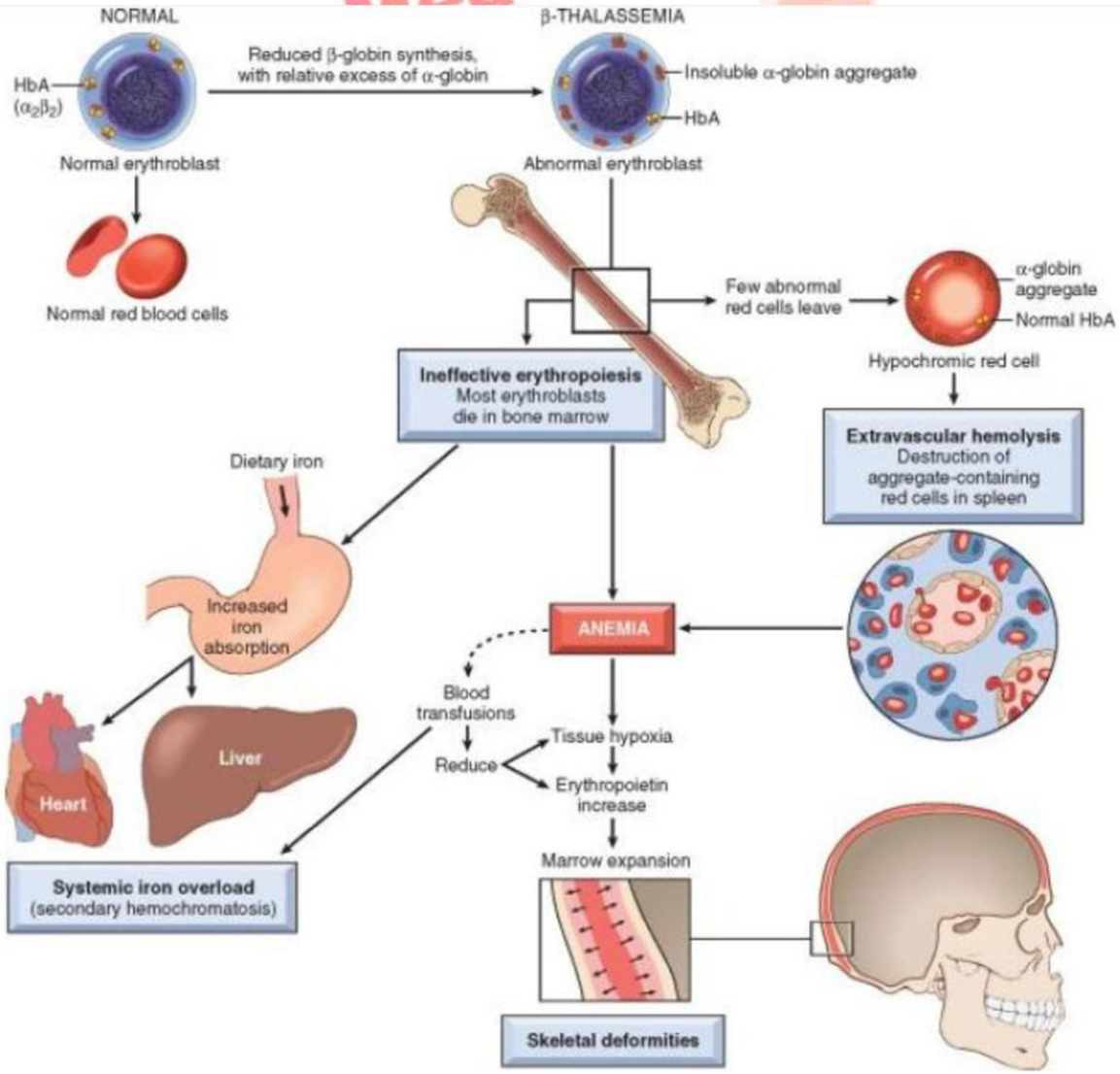
- Intermediate in size with round oval nucleus having 2-5 prominent nucleoli in basophilic amorphous cytoplasm (cytoplasm has small lipid filled vacuoles)
- Increased proliferation and apoptosis of cells
- This debris is engulfed by macrophages
- Macrophages surrounded by clear space giving STARRY SKY PATTERN

P.T.O

Annual 2007

Q1: Illustrate the pathogenesis of anemia, skeletal deformities and hemochromatosis in BETA THALASSEMIA MAJOR with the help of flowchart

Ans:



Supply 2007

Q1: A 50 years old male patient developed generalized lymphadenopathy with low grade evening pyrexia) Biopsy of lymph node shows effacement of architecture with classic REED STERBERG cells in polymorphous background?

a) What is your diagnosis?

b) List five subtypes of the disease with the type of RS cells characteristic of each.

Ans:

a) Mixed cellularity Hodgkin lymphoma

b) There are 5 subtypes of Hodgkin lymphoma:

- nodular sclerosis: lacunar type RS cell
- lymphocyte rich :no subtype
- lymphocyte depletion: no sub type

- lymphocyte predominance : lymphohistiocytic variant RS cell(pop corn)
- mixed cellularity :classic RS cell

Annual 2008

Q1: Peripheral blood film of a 23 year old female with history of jaundice and severe anemia shows numerous sickle-shaped red cells

a) **What type of hemoglobin would Hb electrophoresis show and how is it formed?**
b) **Outline the mechanism of sickling of red cells in this patient**

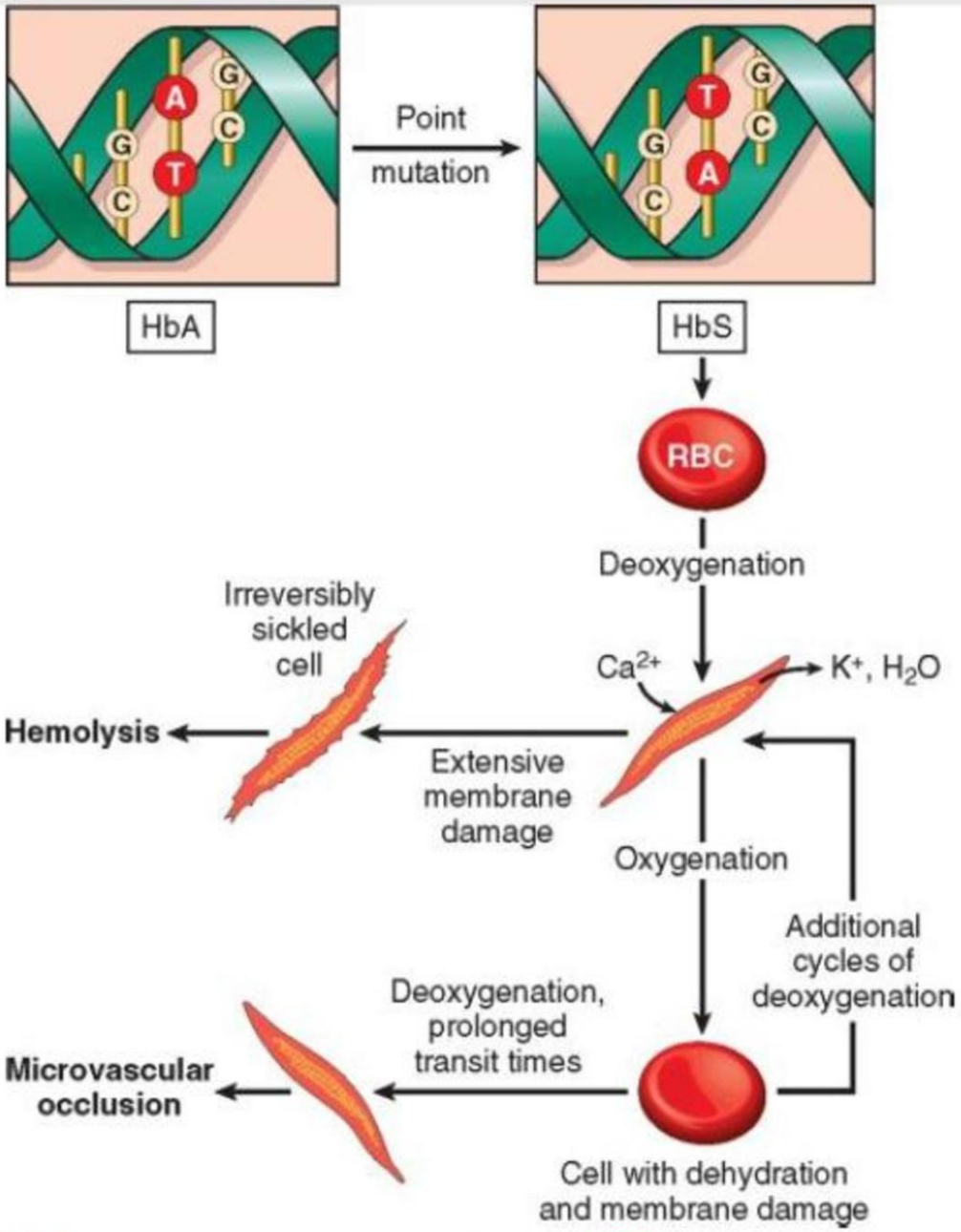
Ans:

a) HbS is the type of hemoglobin that would be present on electrophoresis
It is formed by the substitution of valine for glutamic acid at the 6th amino acid residue of B-globin.

b) Mechanism:

Sickle cell anemia is one of the hemoglobinopathies; it arises from the mutation in the beta-globin chain that creates sickle hemoglobin (HbS)
On deoxygenation, HbS molecules form long polymers, distorting the red cells, which assumes an elongated cresenteric or sickle shape
The sickling of red cells is initially reversible upon reoxygenation
But, every time when red cell membrane gets distorted, it leads to an influx of calcium which causes the loss of potassium and water and also damages the membrane skeleton
Overtime, this cumulative damage creates irreversibly sickled cells, which are rapidly hemolyzed

P.T.O.



Annual 2009

Q1: A 5 years old African child presented with a swelling at angle of jaw which is rapidly increasing in size.it is associated with weight loss and anemia)biopsy of mass reveals microscopic appearance described as starry sky picture

a) what is possible diagnosis?

b) Describe detailed morphology of lesion

c) What is prognosis?

Ans: a) Burkitt lymphoma

b) Tumor cells are

- Intermediate in size with round oval nucleus having 2-5 prominent nucleoli in basophilic amorphous cytoplasm (cytoplasm has small lipid filled vacuoles)
- Increased proliferation and apoptosis of cell
- This debris is engulfed by macrophages
- Macrophages surrounded by clear space giving STARRY SKY PATTERN

c) It is the fastest growing human neoplasm but with aggressive chemotherapy regimens majority of patients can be cured.

Annual 2010

Q1: A 30 year old woman has a long standing history of menorrhagia

a) **What etiological type of anemia would you expect in this woman?**
b) **What would her peripheral smear and bone marrow aspirate show?**
c) **List three serological tests that you would recommend in this patient?**

Ans:

a) Iron Deficiency Anemia

b) Peripheral smear:

- Microcytosis
- Hypochromia
- Increased central pallor of red cells
- Pencil cells

Bone marrow aspirate:

- Erythroid hyperplasia _ mainly mature normoblasts
- Erythropoiesis _ micronormoblastic
- Granulopoiesis _ normal
- Megakaryopoiesis _ normal
- Marrow cellularity _ slightly increased

c) Serological tests:

- CBC _ Hb, hematocrit, platelet count
- Blood smear
- RBC indices _ MCV, MCH, MCHC
- Iron levels _ serum ferritin, TIBC, transferrin, saturation of iron

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Annual 2011

Q1: with acute blood loss, the immediate threat to the patient is hypovolemia (shock) rather than anemia) If the patient survives, hemodilution begins at once and achieves its full effect within 2 to 3 days, unmasking the extent of red cell loss. The anemia is normocytic and normochromic) Recovery from blood loss anemia is enhanced by a rise in erythropoietin level, which stimulates increased red cell production within several days. The onset of marrow response is marked by reticulocytosis. Keeping in view this information. Give:

a) **Adult reference ranges of red blood cells**
b) **Morphological and diagnostic criteria for iron deficiency anemia**

Ans:

a) **Red cell ranges:**

TABLE 14-2 -- Adult Reference Ranges for Red Cells [*]

Measurement (units)	Men	Women
Hemoglobin (gm/dL)	13.6–17.2	12.0–15.0
Hematocrit (%)	39–49	33–43
Red cell count (× 10 6 /µL)	4.3–5.9	3.5–5.0
Reticulocyte count (%)	0.5–1.5	
Mean cell volume (fL)	82–96	
Mean cell hemoglobin (pg)	27–33	
Mean cell hemoglobin concentration (gm/dL)	33–37	
Red cell distribution width	11.5–14.5	

b) Morphological and diagnostic criteria for Iron Deficiency Anemia:

It includes

- Anemia with hypochromic and microcytic red cell indices (decreased Hb, MCV, MCH, MCHC)
- Decreased or absent iron stores
- Serum ferritin _ decreased
- TIBC _ increased
- % saturation of iron binding protein _ decreased
- Red cell protoporphyrin _ increased
- Response to Iron therapy

Supply 2013

Q1: A 55 year old female presents with long standing history of menorrhagia) on examination, she looks pale and complains of palpitation and dyspnoea) her lab shows Hb 8.0mg/dl, MCV: 55fl, MCH: 18pg, MCHC: 20

a) What is the most likely diagnosis?
b) Give the differential diagnosis of the disease.
c) Write three biochemical tests to confirm the diagnosis

Ans:

a) The most probable diagnosis is Iron Deficiency Anemia

b) Differential Diagnosis:

- Iron deficiency anemia
- Anemia of chronic disease
- Blood loss anemia
- Beta Thalassemia
- Sideroblastic anemia

c) Biochemical tests:

- Complete blood count (Hb, RBC count, platelet count etc)
- RBC Indices (MCV, MCH, MCHC)
- Blood smear
- SERUM IRON
- TIBC (Total iron binding capacity)
- TRANSFERRIN levels
- % SATURATION OF IRON BINDING CAPACITY
- RED CELL PROTOPORPHYRIN

Annual 2014

Q1: A 43 year old female presents with weakness, lassitude and anorexia for last 6 months. She has pallor and glossitis with low hemoglobin. Her peripheral smear shows macro-ovalocytes and hypersegmented neutrophils

a) What is the probable type of anemia?
b) What are the causes of this type of anemia?

Ans:

a) The most probable type of anemia in this case is Folic Acid Deficiency Anemia (Megaloblastic Anemia)

b) Causes:

- Inadequate diet
- Impaired absorption
- Malabsorption
- Intrinsic intestinal disorder
- Use of anticonvulsants

- Use of oral contraceptives
- Hemodialysis
- Intrinsic factor deficiency & vitamin B12 deficiency
- Gastrectomy
- Pregnancy
- Disseminated coagulation
- Folic acid antagonists

SOLVED BY

AMNA TARIQ
NAWAZ SHARIF MEDICAL COLLEGE, GUJRAT
&
FAJAR SHABBIR
LAHORE MEDICAL AND DENTAL COLLEGE, LAHORE

Section 3 : Respiratory System

Annual 2003

Q1:

a) Classify Lung tumors (5)
b) Define Atelactasis. (2)
c) Discuss pathogenesis of Bronchiectasis. (3)

Ans: a) Histological classification of malignant epithelial Lung tumors:

1. Adenocarcinoma
2. Squamous cell carcinoma
3. Large cell carcinoma
4. Small cell carcinoma
5. Adenosquamous carcinoma
6. Carcinoma with pleomorphic, sarcomatoid elements
7. Carcinoid tumor
8. Carcinoma of salivary gland types
9. Unclassified carcinoma

{pg no 505 Robbins}

b) It is loss of lung volume caused by inadequate expansion of air spaces.

1. Resorption atelactasis
2. Compression atelactasis
3. Contraction atelactasis

{pg no 460 robbins}

c) Pathogenesis:

Two main processes occur: Obstruction & chronic persistent infection. Normal clearance mechanism is hampered by obstruction, so secondary infection follows which cause damage to walls leading to weakening & dilation. Conversely a persistent necrotizing inflammation in the bronchi may cause obstructive secretions, inflammation throughout the wall.

{pg no 470 Robbins}

Supply 2003

Q1: Define & classify emphysema. (4) **{pg no 463 Robbins}**

Ans: Emphysema: It is characterized by abnormal permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by the destruction of their walls without significant fibrosis.

Types:

1. Centriacinar emphysema
2. Panacinar emphysema
3. Irregular emphysema
4. Distal acinar emphysema

Annual 2004

Q1: Define Emphysema. And list its types. Give pathogenesis of emphysema. (2, 3, 5) {pg no 463 Robbins}

Ans: Emphysema: It is characterized by abnormal permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by the destruction of their walls without significant fibrosis.

Types:

1. Centriacinar emphysema
2. Panacinar emphysema

3. Irregular emphysema
4. Distal acinar emphysema

Pathogenesis: Exposure to toxic substances such as tobacco smoke induces inflammation with accumulation of neutrophils, macrophages & lymphocytes in the lung. Elastases, cytokines & oxidants released causing injury. Elastin degradation products further increase inflammation, unless checked by antielastases & anti oxidants. In emphysema there is loss of not only epithelial & endothelial cells but also mesenchymal cells.

Supply 2004

Q1: a) Define & classify pneumonia. (pg no 488 Robbins)
b) Give aetiology, gross, microscopic features & fate of Lobar

Ans:

a) Pneumonia: It can be very broadly defined as any infection in the lung.

Classification: It is best to classify pneumonias by the specific etiological agents.

1. Community Acquired acute pneumonia:
- Streptococcus pneumoniae
- Haemophilus influenzae
- Moraxella catarrhalis
- Staphylococcus aureus

2. Community Acquired Atypical pneumonia
- Mycoplasma pneumonia
- Chlamydia spp.
- Viruses: RSV, influenza A & B etc

3. Nosocomial pneumonia
- Gram negative rods
- S.aureus

4. Aspiration pneumonia
- Anaerobic oral flora
- Aerobic bacteria

5. Chronic pneumonia
- Nocardia
- Actinomyces
- Granulomatous: M.Tuberculosis, Histoplasma capsulatum

6. Necrotizing pneumonia
- Anaerobic bacteria
- S.aureus, K.pneumoniae, Streptococcus pyogenes Pneumonia.

b) Aetiology: pneumococcal lung infections usually are acquired by aspiration of pharyngeal flora (pneumoniae)

Gross & microscopic feature: lobes pass through 4 stages:

1. Congestion: Lobes are heavy, red & boggy. Sinks in water, abundant red frothy fluid when squeezed. Histologically vascular congestion with proteinaceous fluid, neutrophils & many bacteria in the alveoli.

2. Red Hepatization: Lobe has a liver like consistency. Histologically alveolar spaces are packed with neutrophils, red cells & fibrin.

3. Gray Hepatization: Lung is dry, gray & firm. Histologically alveolar spaces dense network of fibrin, neutrophils, lysed RBCs

4. Resolution: Exudates within alveoli produce granular, semifluid debris that is resorbed ingested by macrophages.

Fate: Abscess, Empyema, Meningitis, Arthritis, Infective endocarditis, pleural effusion, suppurative pericarditis

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Annual 2006

Q1: Enumerate the condition associated with the development of Acute Respiratory Distress Syndrome. (6) {pg no 461 Robbins}

Ans:

1. Direct lung injury:

Common causes: Pneumonia, Aspiration of gastric contents. Uncommon causes: Pulmonary contusion, Fat embolism, near drowning, Inhalation injury, and Reperfusion injury.

2. Indirect lung injury:

Common causes: Sepsis, Severe trauma with shock

Uncommon causes: Cardiopulmonary bypass, acute pancreatitis,

Drug overdose, Transfusion of blood products, Uremia.

Supply 2006

Q1: a) What are the types of Pneumonia? (2) {pg no 488 Robbins}

Ans: Classification: It is best to classify pneumonias by the specific etiological agents.

1. Community Acquired acute pneumonia:

Streptococcus pneumoniae
Haemophilus influenzae
Moraxella catarrhalis
Staphylococcus aureus

2. Community Acquired Atypical pneumonia

Mycoplasma pneumonia
Chlamydia spp.
Viruses: RSV, influenza A & B etc

3. Nosocomial pneumonia

Gram negative rods
S.aureus

4. Aspiration pneumonia

Anaerobic oral flora
Aerobic bacteria

5. Chronic pneumonia

Nocardia
Actinomyces
Granulomatous: M.Tuberculosis, Histoplasma capsulatum

6. Necrotizing pneumonia

Anaerobic bacteria
S.aureus, K.pneumoniae, Streptococcus pyogenes Pneumonia.

b) Aetiology: pneumococcal lung infections usually are acquired by aspiration of pharyngeal flora (pneumoniae)

Gross & microscopic feature: lobes pass through 4 stages:

1. Congestion: Lobes are heavy, red & boggy. Sinks in water, abundant red frothy fluid when squeezed. Histologically vascular congestion with proteinaceous fluid, neutrophils & many bacteria in the alveoli.

2. Red Hepatization: Lobe has a liver like consistency. Histologically alveolar spaces are packed with neutrophils, red cells & fibrin.

3. Gray Hepatization: Lung is dry, gray & firm. Histologically alveolar spaces dense network of fibrin, neutrophils, lysed RBCs

4. Resolution: Exudates within alveoli produce granular, semifluid debris that is resorbed ingested by macrophages.

Complication: Abscess, empyema, solid fibrous tissue, meningitis, arthritis, infective endocarditis, pleural effusion.

Annual 2007

Q1: Following bone marrow transplantation, a patient develops high grade fever with chills, chest X ray shows pulmonary infiltrates. (1.5, 2, 1.5) {pg no 500+504 Robbins}

a) List three major causes of pulmonary infiltrates in such patients with two examples for each.

b) What pulmonary infections are likely to occur in an AIDS?

Ans:

a) 1. Bacterial agents: P. aeruginosa, Mycobacterium spp.
2. Viral agents: Cytomegalovirus & herpes virus
3. Fungal agents: P. jiroveci, Candida spp.
4. Patient at CD 4+ count> 200 cells/mm3

b) Bacterial & tubercular infections are more likely to occur.

Annual 2008

Q1: A 22 years old medical student from Islamabad suffers from seasonal attacks of episodes of respiratory difficulty with cough productive of copious watery secretions. The episodes last for a few hours at a time. A skin test for paper mulberry pollen is positive. (pg no 468 Robbins)

a) What is the diagnosis? Give the basic pathological mechanism underlying this condition. (2)

b) List the 3 major groups of chemical mediators which are implicated in this response. (3)

Ans: Atopic Asthma

Pathogenesis: Atopic form of asthma is associated with an excessive TH2 reaction against environmental antigens. Cytokines produced by TH2 cells account for most of the feature of asthma. IL-4 stimulates IgE production, IL-5 activates eosinophils, and IL-13 stimulates mucus production & also promotes IgE production by B cells. IgE coats submucosal mast cells, which on exposure to allergens, release granular contents. This induces two waves of reaction. Early phase dominated by bronchoconstriction, inc mucus production. Late phase reaction consists of inflammation with activation of eosinophils, neutrophils & T cells.

b) 1. I group: IL C4, D4, E4 & acetylcholine
2. II group: Histamines, PGD2, PAF
3. III group: IL-1, IL-6 & TNF

Supply 2008

Q1: A 6 year old boy living in Islamabad suffer from attacks of severe dysponea, wheezing & cough each year during the spring season. He remains asymptotic between episodes. (pg no 468 Robbins)

a) What is the diagnosis? (1)

b) What is the pathological basis for this condition? What are acute reaction & late response in its pathogenesis? (1, 3)

Ans: a) Atopic Asthma

b) Pathogenesis: Atopic form of asthma is associated with an excessive TH2 reaction against environmental antigens. Cytokines produced by TH2 cells account for most of the feature of asthma. IL-4 stimulate IgE production, IL-5 activates eosinophils, IL-13 stimulates mucus production & also promote IgE production by B cells. IgE coats submucosal mast cells, which on exposure to allergens, release granular contents. This induces two waves of reaction. Early phase dominated by bronchoconstriction, inc mucus production. Late phase reaction consist of inflammation with activation of eosinophils, neutrophils & T cells.

Annual 2009

Q1: Respiratory function tests were performed in a 60 years old chronic smoker his FEV-I was reduced. He complained of progressively worsening dyspnoea. Wheezing was present. His chest X-ray at

admission revealed evidence of pneumothorax and lung collapse. (pg no 466+465 Robbins)

a) What further complications can develop in this patient? (2)

b) How did smoking play its role in his lung pathology? (3)

Ans: a) Secondary pulmonary hypertension, pulmonary failure, respiratory acidosis, hypoxia, coma & cor pulmonale.

b) Tobacco smoke induces ongoing inflammation with accumulation of neutrophils, macrophages & lymphocytes in the lung. Elastases, cytokines & oxidants are released causing epithelial injury & proteolysis of the extracellular matrix. Elastin degradation further increase inflammation. Unless checked by a1-antitrypsin & anti oxidants, the cycle of inflammation & ECM proteolysis continues.

Supply 2010

Q1: A 30 years old male diagnosed as a case of community acquired pneumonia was admitted in pulmonology ward. Upper lobe consolidation was seen on chest X-ray. He developed Empyema.

a) Describe the pathogenesis of development of this complication. (2) (pg no 488 Robbins)

b) If he continue non responsive to antibiotics what other complications can arise? (3)

Ans: a) In lobar pneumonia , infection leads to the recruitment of neutrophils macrophages which helps to combat the infection but on long standing or when becomes chronic and entire lobe is involved the toxic debris ,suppurative material may start accumulating and spreading which leads to pus formation especially in pleural cavity thus empyema and abcess formation arise as complication. .

b) Meningitis, Arthritis, Infective endocarditis, pleural effusion, suppurative pericarditis

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Annual 2010

Q1: A 65 years old smoker with history of 30 pack years presents with severe dyspnoea, on examination he is found to have a barrel chest & prolonged expiration. Spirometery shows expiratory airflow limitation. (pg no 464 Robbins)

a) What are the two major clinically important types of this disease (1)

b) What are the two major pathogenic mechanisms involved? Give salient features of each (4)

Ans: a) **1.** Centriacinar emphysema **2.** Panacinar emphysema

b) Tobacco smoke induces ongoing inflammation with accumulation of neutrophils, macrophages & lymphocytes in the lung. Elastases, cytokines & oxidants are released causing epithelial injury & proteolysis of the extracellular matrix. Elastin degradation further increase inflammation. Unless checked by a1-antitrypsin & anti oxidants, the cycle of inflammation & ECM proteolysis continues.

2. TGF-b1 polymorphism a1 antitrypsin deficiency result in inadequate repair of elastin injury caused by inhaled toxins. MMPs also show pathogenic role in emphysema.

Annual 2011

Q1: A 32 years old male comes to the ER with rapid onset of respiratory insufficiency, cyanosis and severe arterial hypoxemia that is refractory to oxygen therapy and progressive multisystem organ failure. He is diagnosed to have ARDS (pg no 461 Robbins)

a) What clinical disorders are associated with development of Acute Respiratory Distress Syndrome? 3

b) Give pathogenesis of Acute Respiratory Distress Syndrome. (2)

Ans: a)

1. Direct lung injury:

Common causes: Pneumonia, Aspiration of gastric contents. Uncommon causes: Pulmonary contusion, Fat embolism, near drowning, Inhalation injury, and Reperfusion injury.

2. Indirect lung injury:

Common causes: Sepsis, Severe trauma with shock

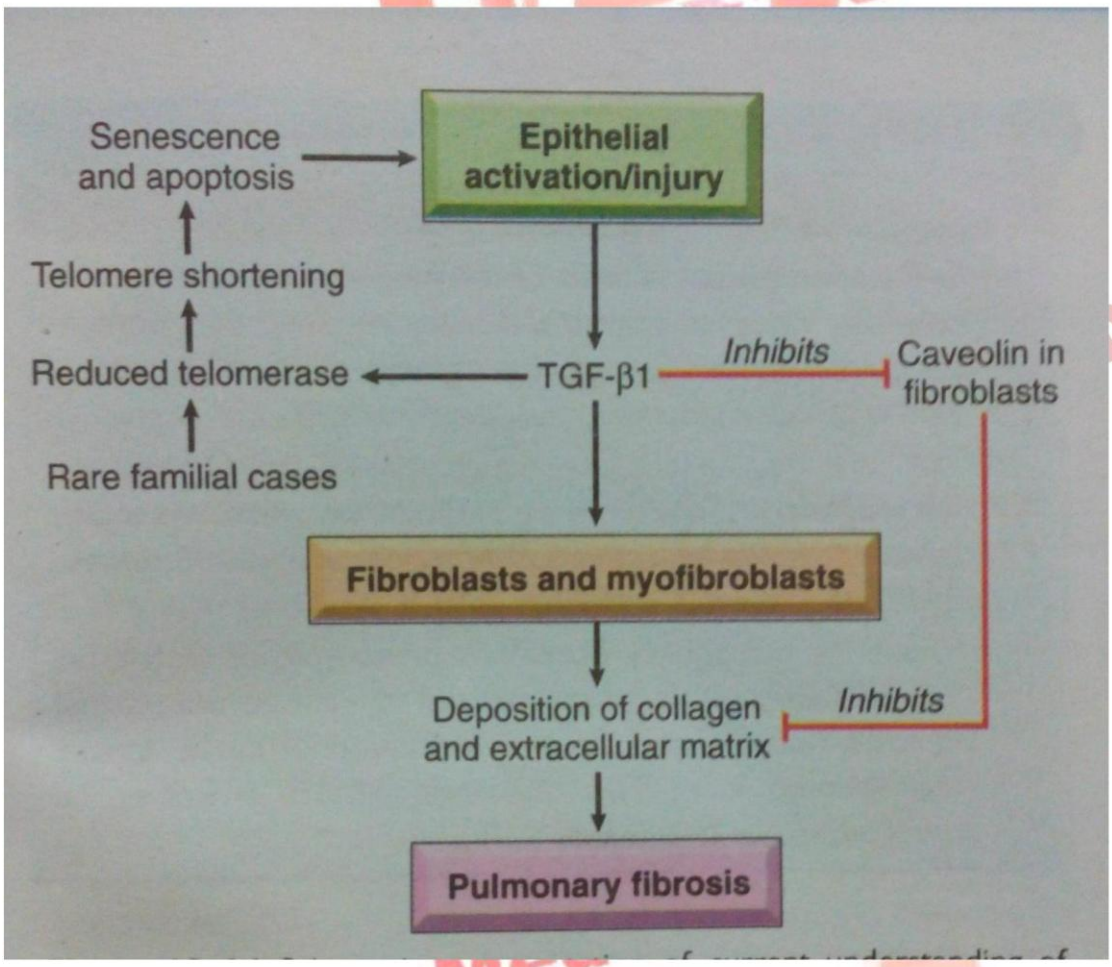
Uncommon causes: Cardiopulmonary bypass, acute pancreatitis,

Drug overdose, Transfusion of blood products, Uremia.

b) In ARDS the integrity of alveolar capillary is compromised by either endothelial or epithelial injury or both. Damage result in increased vascular permeability & alveolar flooding, loss of diffusion capacity & surfactant abnormalities. Lung injury is caused by an imbalance of pro-inflammatory & anti-inflammatory mediators. There is increased synthesis of IL-8, release of IL-1, TNF leads to endothelial activation. Neutrophils have an important role in the pathogenesis of ARDS. Activated neutrophils release a variety of products that cause damage to the alveolar epithelium & endothelium.

Supply 2011

Q1: Give a flow chart outlining the pathogenesis of idiopathic pulmonary fibrosis. (5) {pg no 473 Robbins}



Annual 2012

Q1: Give an account of etiological factors for bronchogenic carcinoma. (5) {pg no 505 Robbins}

Ans:

1. Genetic factors
2. Cigarette smoking
3. Increased incidence in miner of radioactive ores
4. Activating mutations of the epidermal growth factor receptor
5. Asbestos workers
6. Worker exposed to dust containing arsenic, chromium, nickel, vinyl chloride
7. Exposure to mustard gas

Supply 2012

Q1: Give a flow chart outlining the pathogenesis of idiopathic pulmonary fibrosis. (5) {pg no 473 Robbins}

Ans: See Annual 2011 Above.

Supply 2013

Q1: A 25 years old male presented with abrupt onset of high grade fever and chills. He had productive cough with mucopurulent sputum. X-ray chest revel consolidation of right lower lobe

a) What is the most likely diagnosis? (1) (pg no 488 Robbins)

b) Write gross and microscopic picture of this lesion. (4)

Ans: a) Lobar pneumonia

b)

1. Congestion: Lobes are heavy, red & boggy. Sinks in water, abundant red frothy fluid when squeezed. Histologically vascular congestion with proteinaceous fluid, neutrophils & many bacteria in the alveoli.

2. Red Hepatization: Lobe has a liver like consistency. Histologically alveolar spaces are packed with neutrophils, red cells & fibrin.

3. Gray Hepatization: Lung is dry, gray & firm. Histologically alveolar spaces dense network of fibrin, neutrophils, lysed RBCs

4. Resolution: Exudates within alveoli produce granular, semifluid debris that is resorbed ingested by macrophages.

Fate: Abscess, Empyema, Meningitis, Arthritis, Infective endocarditis, pleural effusion, suppurative pericarditis

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Annual 2013

Q1: A 55 years old male who is heavy smoker had chronic cough for the last three years. He expectorates large quantity of foul smelling sputum in the morning. Now he has developed fever and sputum has greenish specks of mucus. Cardiac shadow is also enlarged. Sputum show many gram negative bacilli and neutrophils along with mucus plugs. (pg no 479 Robbins)

a) What type of respiratory disease he is suffering from and name the bacteria which have resulted in this disease? (1)

b) Name four etiological causes of this respiratory disease. (4)

Ans: a) Bronchiectasis.

Bacteria: Staphylococcus aureus or Klebsiella spp.

b) 1. Bronchial obstruction
2. Congenital or hereditary conditions eg. Cystic fibrosis, Immunodeficiency states, kartagener syndrome
3. Necrotizing & suppurative pneumonia
4. Rheumatoid arthritis
5. Systemic Lupus erythmatosis (SLE)
6. IBD

Annual 2014

Q1: A chronic smoker develops progressive dyspnea. He is barrel hested and on breathing, his expiration is prolonged. (pg no 63 robbins)

a) What is the disease he is suffering from? (1)

b) Name types of this disease. (2)

c). Write two complications that can occur in this patient. (2)

Ans: a) Emphysema

b) 1.Centriacinar emphysema
2. Panacinar emphysema

3. Distal acinar emphysema
4. Irregular emphysema

c) Secondary pulmonary hypertension, pulmonary failure, respiratory acidosis, hypoxia, coma & cor pulmonale.

Supply 2014

Q1: A 20 years old girl with history of chest tightness, wheezing & dyspnea cough up copious mucous containing Charcot-Leyden crystals & Curschmann spirals. Her peripheral blood picture how marked eosinophilia. Her mother also gives history of eczema in family. (pg no 468 Robbins)

a) Give the most likely diagnosis. (1)

b) Write the mediators involved in pathogenesis of this disease (4)

Ans: a) Asthma

b) Many inflammatory mediators are involved in pathogenesis of this disease like...

- IL-4...stimulate IgE production
- IL-5...activates eosinophils
- IL-13...stimulate mucus production
- Histamine
- IL-6
- TNF
- PGD2
- PAF

Supply 2015

Q1: A 65 years old smokers present in the medical OPD with complain of cough, occasionally hemoptysis, chest pain, anorexia, weight loss & clubbing for 5 months. A tumor is suspected.

a) What is the provisional diagnosis? (pg no 506 Robbins)

b) Write note on Mesothelioma. (Pg no 512 Robbins)

Ans: a) Squamous cell carcinoma

b) Malignant mesothelioma arising in parietal or visceral pleura, related to occupational exposure to asbestos like shipyard workers, miners, insulators. It is preceded by pleural fibrosis & plaque formation, seen in CT scan. At autopsy the affected lung typically is ensheathed by a yellow-white, firm, sometimes gelatinous layer of tumor. Normal mesothlial cells are biphasic, giving rise to pleural lining cells. Therefore, histologically, mesotheliomas conform three patterns.

1. Epithelial, in this cuboidal cells line tubular & microcystic spaces
2. Sarcomatous, in this spindled & sometimes fibroblastic appearing cells grow
3. Bipolar having sarcomatous & epithelial areas.

SOLVED BY
IRAM MAHMOOD,
SHALAMAR MEDICAL AND DENTAL COLLEGE, LAHORE

Section 4: Kidney

Supply 2003

Q1: Classify renal tumors?

Ans: Classification:

- Oncocytoma
- Renal cell carcinoma
- Clear cell carcinoma
- Papillary renal cell carcinoma
- Chromophobe renal carcinomas. (pg no 547 med rob)

Q2: Define nephrotic syndrome?

Ans: Clinical complex that include Massive proteinuria, hypoalbuminemia, generalized edema, Hyperlipidemia & lipiduria (pg no 524 med rob)

Annual 2004

Q1: Enlist causes of Hematuria?

Ans:

- Kidney stones
- internal bleeding
- bladder infection
- prostatitis
- urinary tract infection
- Kidney cancer.

Supply 2004

Q1: Give aetiology, pathogenesis, gross and microscopic picture of Poststreptococcal glomerulonephritis?

Ans: Pathogenesis: This cluster of disease is characterized histologically by diffuse proliferation of glomerular cells associated with influx (exudation) of leukocytes. These lesions are typically caused by immune complexes. Typical features such as hypocomplementemia and granular deposits of igG and complements on the GBM are seen. The relevant antigens probably are streptococcal proteins. Specific antigens implicated in pathogenesis include streptococcal exotoxin B (Sep B) and streptococcal GAPDH. Both activate the alternative complement pathway and have affinity for glomerular proteins and plasmin. It is not clear if immune complexes are formed mainly in circulation or in situ (the latter by binding of antibodies to bacterial antigens "planted" in the GBM).

Morphology: Light microscopic picture:

1) the most characteristic change is a fairly uniform increase cellularity of the glomerular tuft that effects nearly all glomeruli hence term "diffuse".

2) The increased cellularity caused by both proliferation and swelling of endothelial and mesangial cells and by infiltrating neutrophils and monocytes.

3) Sometimes there is necrosis of capillary walls.

4) In a few cases "crescents" may be observed within the urinary space, formed in response to the severe inflammatory injury.

Electron microscopy:

1) Shows deposited immune complexes arrayed as subendothelial, intramembranous or most often, subepithelial humps nestled against the GBM.

2) Mesangial deposits are also occasionally present.

Immunofluorescence findings:

Scattered granular deposits of igG and complement within capillary walls. (Page no 529 medium robins)

Annual 2006

Q1: Give the pathogenesis and morphology of acute proliferative post streptococcal glomerulonephritis?
Ans: Same as Q1 of Supply 2004 above.

Q2:
a) Name causes of painless hematuria?
b) Describe briefly morphology of Transition cell carcinoma?
Ans: a)

- benign papilloma
- Squamous cell carcinoma
- transitional cell carcinoma
- Invasive papillary carcinoma
- Flat non invasive carcinoma
- Renal cell carcinoma

b) Morphology:

- low grade cancer(usually papillary and are not invasive)
- high grade cancer (papillary or flat and are usually invasive)
- Most common sites: lateral or posterior walls at base of the bladder.

Annual 2007

Q1: Clinical pyelonephritis is most commonly caused by ascending infection. Give the five major steps in its pathogenesis?
Ans: Adhesion of bacteria to mucosal surfaces is followed by colonization of the distal urethra (and introitus in females)
1) Hematogenous infection
2)intrarenal reflux
3)urinary bladder obstruction : congenital or acquired
4)uretral instrumentation: catheterization and cystoscopy
5)vesicoureteral reflux (page no 534 medium robins)

Annual 2008

Q1: A 62 years old female from a remote town in south Punjab presents with generalized body edema. Labs show hypoalbuminemia and macroalbuminuria .Fasting blood sugar levels are more than 200mg/dl on 2 consecutive days. The patient gives history of fainting episodes for which she has been consulting the local 'pir'. What spectrum of changes would you expect to find on a renal biopsy from this patient?
Ans: Diabetic nephropathy
Three lesions are encountered :
1) glomerular lesions
2)renal vascular lesions principally arteriosclerosis
3)pyelonephritis, including necrotizing papillitis
The most important lesions are capillary basement membrane thickening ,diffuse mesangial sclerosis and nodular glomerulosclerosis.

Supply 2008

Q1: Sections from transurethral resection of bladder tumor reveal lamina propria invasion by a papillary urothelial carcinoma
a) what is pathologic stage T for this tumor
b)Give American joint commission on cancer staging for bladder carcinoma

c) Illustrate the four gross morphologic types of bladder cancer.

Ans: a) T1

b)

Ta…….. Non invasive, papillary
Tis…….carcinoma in situ (non invasive, flat)
T1…..lamina propria invasion
T2…..muscularis propria invasion
T3a…..microscopic extra-vesicle invasion
T3b…..grossly apparent extra-vesicle invasion
T4….invade adjacent structures (page no 967 big robins)

c)

1) papillomas
2)papillary urothelial neoplasms of low malignant potential
3)low grade papillary urothelial carcinomas
4)high grade papillary urothelial cancers
5)invasive urothelial cancer (page no 966 big robins)

Annual 2009

Q1: A school going 7 year old boy complains of few weeks onset of gradual lethargy, fatigue and passage of small volume of dark colored urine following an episode of upper respiratory tract infection. On examination mild hypertension is present.

a) What will be the characteristic findings of urine examination in this patient?

b) Describe the renal biopsy findings?

Ans a)

- Black color
- gross hematuria
- Proteinuria.

b) Light microscopy diffused mesangial proliferation, segmental inflammation
Electron microscopy: electron dense deposit in the mesangium
Immunofluorescence: mesangial deposition of igA

Supply 2009

Q1: A young male presents with nephritic syndrome. He is HCV +ve on serology. Renal biopsy was carried out which revealed on light microscopy an accentuation of lobular arrangement of glomerular tuft and a double contour of GBM.

a) What will be the electron microscopic and detailed light microscopic picture of this biopsy?

b) Describe the role of APC gene in colorectal carcinoma.

Ans: a) Light microscopy: Enlarged hypercellular glomeruli due to
1) infiltration by leukocytes both neutrophils and monocytes
2) proliferation of endothelial and mesangial cells
3) in severe cases by crescent formation

Electron microscopy:

Discrete, amorphous, electron-dense deposits on the epithelial side of membrane, often having the appearance of 'humps' presumably representing there antigen-antibody complexes at the subepithelial cell surface.

Immunofluorescence microscopy:

Granular deposits of IgG & C3 & IgM in the mesangium and along the GBM. Immune complexes are often focal and sparse.

(Page no 911 big robins)

Annual 2010

Q1: A 4 year old girl presents with generalized edema and laboratory results show proteinuria in excess of 3.5 gm per day with hypoalbuminemia. The patient improved dramatically on corticosteroid administration

a) what is the most likely diagnosis?

b) What are the light microscopic and ultra-structural and Immunofluorescence finding for this disease?

Ans: a) minimal change disease

b) Light microscopy:

Glomeruli appear normal. Cells of proximal convoluted tubules often are heavily laden with protein droplets and lipids but this feature is secondary to tubular reabsorption of lipoproteins passing through the diseased glomeruli.

Electron microscopy:

GMB appears normal. The only obvious glomerular abnormality is the uniform and diffuse effacement of the foot processes of the podocytes. Cytoplasm of podocytes appears flattened over the external aspect of GBM. Epithelial cell vacuolization, microvillus formation and occasional focal detachments are also present.

(Page no 524 med rob)

Annual 2011

Q1: Write short note on nephrotic syndrome.

Ans: nephrotic syndrome refers to clinical complex that includes

1)massive proteinuria with daily protein loss in the urine of 3.5 g or more in adults
2)Hypoalbuminemia with plasma albumin levels less than 3g/dl
3)Generalize edema the most obvious clinical manifestation
4)Hyperlipidemia and lipiduria.

Causes:

- Primary Glomerular Disease:
- membranous nephropathy
- minimal change disease
- focal segmental glomerulosclerosis
- membranoproliferative glomerulonephritis
- IgA nephropathy and others
- Systemic Disease and Renal manifestation:
- diabetes mellitus
- Amyloidosis
- systemic lupus erythematosis
- ingestion of drugs
- infections(malaria, syphilis, hepatitis B, HIV infection)
- malignancy(carcinoma, melanoma)
- miscellaneous(bee sting allergy, hereditary nephritis)

(Page no 524 med rob)

Supply 2011

Q1: A 35 year old female who has been treated unsuccessfully for a resistant lower urinary tract infection (E.coli now presents with fever ,malaise, pain at costovertebral angle and leukocyte casts in urine .

a) Diagnosis?

b) Illustrate with diagram the steps in the pathogenesis of this condition

Ans: a) acute pyelonephritis

b) See Q1 in Annual 2007 above.

Annual 2012

Q1: A 22 years old male is brought to emergency dept after a road side accident, where he is found to be hypotensive with severe internal bleeding .He is given several units of blood by transfusion & is shifted to ICU for monitoring .Within 36 hours, a slight decrease in urine output and increase in blood urea nitrogen is noted and by 72 hours there is marked decrease is urine output. Laboratory studies at 72 hours were:
serum potassium: 5.1 mEq/L, BUN: 25mg/dL, creatinine: 2.5mg/dL, urinalysis: mild hematuria, Mild proteinuria, granular casts, renal tubular epithelial cells in sediment
a) Diagnosis?
b) Enumerate any three causes of this condition.
Ans: a) Acute tubular necrosis
b) Causes:

1) Severe glomerular diseases manifesting clinically as RPGN
2) acute tubular injury caused by diffuse renal vascular diseases, such as microscopic polyangitis & thrombotic microangiopathies and
3) acute drug induced allergic interstitial nephritis which often is not associated with tubular injury

(pg no 537 med rob)

Q2: A retroperitoneal tumor was detected in a 2 year old boy .CT scan revealed the location to be in the lower pole of kidney, 10 cm in diameter, the child was losing weight rapidly. CT guided FNA was done which showed a triphasic morphology of the tumor with embryonic tissue as well
a) name the commonest childhood tumor of kidney?
b) Give the microscopic picture?
c) On what factors does its prognosis depend upon?
Ans: a) Wilms tumor
b) Microscopy:

* contain aborative glomeruli and tubules, primitive blastemal cells& rhabdomyoblasts
* Shows nests and sheets of primitive blastema with intervening mesenchyme
* Foci of muscles, bones, cartilage containing cholesterol crystals and lipid macrophages may be seen

c) Degree of anaplasia in the stromal component correlate with prognosis.

Supply 2013

Q1: Approximately 10 days after an episode of pharyngitis an 8 year old girl suddenly becomes lethargic, febrile and nauseous. Her urine output is reduced and coca colored. Urine analysis shows mild proteinuria hematuria and RBC casts.ASO titer is raised
a) Diagnosis?
b) Give light microscopic findings of renal biopsy performed in such a case?
c) Give clinical course of this disease?
Ans: a) acute proliferative (post streptococcal) glomerulonephritis.
b) See Q1 in Supply 2004 above.
c) Clinical course:

- Malaise , slight fever, nausea and nephritic syndrome
- In the usual case oliguria, azotemia and hypertension are only mild to moderate.
- There is gross hematuria, the urine appearing smoky brown rather than bright red.
- serum antistreptolysin O antibody elevated
- end stage renal disease.(pg no 529 me rob)

Annual 2013

Q1: A 30 year old male who is infertile and has been taking indigenous drugs from Hakims has developed edema on the legs .On examination blood pressure is 180/110mmHg.the routine blood picture is normal .The serum cholesterol is 330mg/dl. Serum albumin is 2.3gm/dL and globulin is 4.1 gm/dL. The BUN is 46mg/dL and serum creatinine is 2.8 gm/dL. The urine examination revealed 3+ proteins on dip stick .The 24 hour urinary protein is 3.0gm/dL. The renal biopsy revealed thickened glomerular walls and capillary lumen is narrow .The silver methamine stain show spikes on GBM .The tubular lumen contains eosinophilic cast .There is low inflammatory infiltrate in interstitium .

A) What kind of kidney disease he has developed?

b) Name four causes of nephrotic syndrome?

c) Name two pathognomic mechanisms of glomerulonephritis?

Ans: a) membranous nephropathy

b)

- minimal change disease
- focal segmental glomerulosclerosis
- membranoproliferative GN
- igA nephropathy

c)

1) antibody mediated injury

2)cell mediated immune injury.

Annual 2014

Q1: A 40 years old female presented with insidious onset of nephrotic syndrome. Her Renal biopsy was performed. Light microscopy showed uniform diffuse thickening of glomerular capillary wall. E/M showed electron dense Ig containing immune complexes in sub-epithelial region. Immunoflourescene microscopy showed immunoglobulins and complement in the granular deposits

a) Diagnosis?

b) Enumerate four causes of secondary form of this glomerular disease?

Ans: a) membranous nephropathy

b)

1) Infections

2)malignant tumors particularly carcinoma of lung and colon and melanoma

3)systemic lupus erythematosis and other autoimmune conditions

4)exposure to inorganic salts

5)Drugs (penicillamine, captopril, NSAIDs)

(pg no 526 med rob)

Supply 2014

Q1: A 55 years old chronic smoker with severe emphysema and a four months history of urinary frequency and urgency is seen in the urology clinic. He has red tinged urine with numerous RBCs and few WBCs. Cytoscopy shows large ulcerating mass on the right bladder wall .Biopsy is obtained and there is strong suspicion of invasion in the muscular layer.

a) What is the most likely diagnosis?

b) Write the histological picture and grade of this lesion

c) Give four risk factors of this disease.

Ans: a) Urothelial or transitional cell carcinoma of bladder

b) Four morphological pattern:

1) Urothelial papilloma

2) invasive papillary carcinoma

3) flat non invasive carcinoma

4) flat invasive carcinoma

Grading:

1) urothelial papilloma
2)Urothelial neoplasm of low malignant potential
3)papillary urothelial carcinoma grade 1
4)papillary urothelial carcinoma grade 2
5)papillary urothelial carcinoma grade 3

c) Risk factors:

1. Cigarette smoking
2. Industrial exposure to arylamines.

SOLVED BY
ZARLISH SARWAR,
SHARIF MEDICAL AND DENTAL COLLEGE, LAHORE

Section 5: GIT

Supply 2003

Q1: Describe etiology, Pathogenesis and Morphology of peptic ulcer?

Ans: Etiology: Peptic ulcer disease (PUD) most often is associated with H.pylori infection or NSAID use. PUD also may occur in the esophagus as a result of GERD or acid secretion by ectopic gastric mucosa, and in the small intestine secondary to gastric heteropia within a Meckel diverticulum.

Pathogenesis: H. pylori infection and NSAID use are the primary underlying Causes of PUD. The imbalances of mucosal defenses and damaging forces that cause chronic gastritis are also responsible for PUD. Thus, PUD generally develops on a background of chronic gastritis.

Gastric hyperacidity is fundamental to the pathogenesis of PUD. The acidity may be caused by H. pylori infection, parietal cell hyperplasia, excessive secretory responses, or impaired inhibition of stimulatory mechanisms such as gastrin release (e.g. Zollinger-Ellison syndrome).

Cofactors in peptic ulcerogenesis include chronic NSAID use; cigarette smoking, which impairs mucosal blood flow and healing; and high-dose corticosteroids, which suppress prostaglandin synthesis and impair healing. Peptic ulcers are more frequent in persons with alcoholic cirrhosis, COPD. Hypercalcemia (caused by chronic renal failure and hyperparathyroidism) stimulates gastrin production and therefore increases acid secretion. Finally, psychological stress may increase gastric acid production and exacerbate PUD. Bile reflux (particularly deoxycholic acid and lysolecithin) and pancreatic Secretions may contribute to the development of gastric ulcers.

Morphology:

Location: Peptic ulcers are four times more common in the proximal duodenum than in the stomach. Duodenal ulcers usually occur within a few centimeters of the pyloric valve and involve the anterior duodenal wall.

Gross: The classic peptic ulcer is a round to oval, sharply punched-out defect. The base of peptic ulcers is smooth and clean as a result of peptic digestion of exudates.

Microscopy: Inflammation with neutrophilic infiltrate. Abundance of necrotic debris with granulation tissue and fibrosis.

Annual 2005

Q1: a) Enumerate ulcero-inflammatory conditions of small and large intestine.

b) Describe morphology of crohn disease.

Ans: a) Ulcero-inflammatory conditions of small intestine and large intestine are called inflammatory bowel disease.

Inflammatory bowel disease consists of two entities

1-Ulcerative Colitis

2-Crohn's disease

b) Morphology of Crohn's disease:

Location: The most common sites involved by Crohn disease at presentation are the terminal ileum, ileocecal valve, and cecum.

Gross: The presence of multiple, separate, sharply delineated areas of disease, resulting in skip lesions, is characteristic of Crohn disease and may help in differentiation from ulcerative colitis. Strictures are common. Initially single or multiple Aphthous ulcers form which may coalesce to form linear serpentine like ulcer along axis of the bowel. Normal mucosal folds are lost and edema is present. Sparing of interspersed mucosa results in a coarsely textured, cobblestone appearance in which diseased tissue is depressed below the level of normal mucosa.

The intestinal wall is thickened as a consequence of transmural edema, inflammation, submucosal fibrosis, and hypertrophy of the muscularis propria, all of which contribute to stricture formation. In cases

with extensive transmural disease, mesenteric fat frequently extends around the serosal surface (creeping fat).

Microscopy: The microscopic features of active Crohn disease include abundant neutrophils that infiltrate and damage crypt epithelium. Clusters of neutrophils within a crypt are referred to as a crypt abscess and often are associated with crypt destruction. Ulceration is common in Crohn disease, and there may be an abrupt transition between ulcerated and normal mucosa. Repeated cycles of crypt destruction and regeneration lead to distortion of mucosal architecture; the normally straight and parallel crypts take on bizarre branching shapes and unusual orientations to one another.

Annual 2006

Q1: Define peptic ulcer. Breifly explain the mechanism of gastric ulcer

Ans: Definition of Peptic ulcer:

""Peptic ulcer disease" is focal destruction of the mucosa of the stomach and small intestine, mainly the proximal duodenum. It is caused by gastric secretions"

Mechanism of Gastric ulcer: H. pylori infection and NSAID use are the primary underlying causes of Gastric ulcers. The imbalances of mucosal defenses and damaging forces that cause chronic gastritis are also responsible for Gastric ulcers. Thus, Gastric ulcers generally develop on a background of chronic gastritis.

Gastric hyperacidity is fundamental to the pathogenesis Of Gastric ulcers. The acidity may be caused by H. pylori infection, parietal cell hyperplasia, excessive secretory responses, or impaired inhibition of stimulatory mechanisms such as gastrin release (e.g. Zollinger-Ellison syndrome). Cofactors in peptic ulcerogenesis include chronic NSAID use; cigarette smoking, which impairs mucosal blood flow and healing; and high-dose corticosteroids, which suppress prostaglandin synthesis and impair healing.

Gastric ulcers are more frequent in persons with alcoholic cirrhosis, COPD. Hypercalcemia (caused by chronic renal failure and hyperparathyroidism) stimulates gastrin production and therefore increases acid secretion. Finally, psychological stress may increase gastric acid production and exacerbate Gastric ulcers.

Bile reflux (particularly deoxycholic acid and lysolecithin) and pancreatic secretions may contribute to the development of gastric ulcers.

Q2: a) Name Salivary gland tumors.

b) Briefly describe Adenoid cystic Carcinoma.

Ans: a) Benign:

1. Pleomorphic Adenoma
2. Warthin tumor
3. Oncocytoma
4. Basal cell Adenoma
5. Canalicular adenoma
6. Ductal Papillomas

Malignant:

1. Mucoepidermoid Carcinoma
2. Adenocarcinoma
3. Acinic Cell carcinoma
4. Adenoid cystic carcinoma
5. Malignant mixed tumor
6. Squamous cell carcinoma

b) Adenoid cystic carcinoma is a relatively uncommon tumor, which in approximately 50% of cases is found in the minor salivary glands (in particular the palatine glands). Among the major salivary glands, the parotid and submandibular glands are the most common locations.

Morphology:

Gross: They are generally small, poorly encapsulated, infiltrative, gray-pink lesions.

Microscopy: They are composed of small cells having dark, compact nuclei and scant cytoplasm. These cells tend to be disposed in tubular, solid, or cribriform patterns reminiscent of cylindromas arising in the adnexa of the skin .The spaces between the tumor cells are often filled with a hyaline material thought to represent excess basement membrane.

Q3: Name ulcerative lesions of GIT and tabulate Differences between Ulcerative colitis and Crohn disease.

Ans: <u>Ulcerative lesions of GIT:</u>

1. Esophageal ulcers
2. Buccal ulcers
3. Herpetic ulcers of viral esophagitis
4. Stress ulcer
5. Curling ulcer
6. Cushing ulcer
7. Peptic ulcer
8. Duodenal ulcers
9. Ischemic Bowel Disease.
10. Infectious ulcers of colon (Typhoid, Shigellosis e.t.c.)
11. Ulcerative colitis
12. Crohn Disease
13. Solitary rectal ulcer syndrome

Q4: Tabulated Differences between Crohn Disease and Ulcerative colitis.

Ans:

P.T.O

Feature	Crohn Disease	Ulcerative Colitis
Macroscopic		
Bowel region	Ileum ± colon	Colon only
Distribution	Skip lesions	Diffuse
Stricture	Yes	Rare
Wall appearance	Thick	Thin
Microscopic		
Inflammation	Transmural	Limited to mucosa
Pseudopolyps	Moderate	Marked
Ulcers	Deep, knife-like	Superficial, broad-based
Lymphoid reaction	Marked	Moderate
Fibrosis	Marked	Mild to none
Serositis	Marked	Mild to none
Granulomas	Yes (~35%)	No
Fistulae/sinuses	Yes	No
Clinical		
Perianal fistula	Yes (in colonic disease)	No
Fat/vitamin malabsorption	Yes	No
Malignant potential	With colonic involvement	Yes
Recurrence after surgery	Common	No
Toxic megacolon	No	Yes

Annual 2007

Q1: A 28 year old Female has recurrent attacks of bloody mucoid Diarrhea with abdominal cramps, which are relieved by defecation. Each episode lasts for 4-5 days followed by symptom free period of 3-4 months. Colonoscopy shows pancolitis extending from rectum to the splenic flexure.

a)What is your diagnosis?

b) What features will a colonoscopy show?

c) What is the role of intestinal flora in pathogenesis?

Ans: a) Ulcerative colitis

b) On colonoscopy, Ulcerative colitis is seen to involve the rectum and extends proximally in a continuous fashion to involve part or all of the colon. Skip lesions are not seen. Disease of the entire colon is termed pancolitis. Involved colonic mucosa may be slightly red and granular-appearing or exhibit extensive broad-based ulcers.

The transition between diseased and uninvolved colon can be abrupt .Ulcers are aligned along the long axis of the colon but typically do not replicate the serpentine ulcers of Crohn disease. Isolated islands of regenerating mucosa bulging into the lumen to create small elevations, termed pseudopolyps may be seen. Chronic disease may lead to mucosal atrophy and a flat, smooth mucosal surface lacking normal folds. Strictures do not occur.

c) Leading theories suggest that genetically predisposed individuals develop dysregulated mucosal immune responses to gut flora, leading to bowel inflammation. The T-cell response in ulcerative colitis is TH2 dominant and mediated by natural killer T cells. This combination of factors leads to mucosal hyper responsiveness to commensal bacteria and an exaggerated immune response causing chronic inflammation and damage.

Ongoing studies suggest that ill-defined mixtures containing probiotic, or beneficial, bacteria also may combat disease in experimental models, as well as in some patients with Inflammatory bowel Disease, although the mechanisms responsible are not well understood.

Supply 2007

Q1: a) How will you differentiate "Diffuse" type of gastric carcinoma from "Intestinal" type on histology?
b) Define early gastric carcinoma and advanced gastric carcinoma. List four host factors associated with increased incidence of gastric carcinoma?
Ans: a)

Diffuse type gastric carcinoma	Intestinal type gastric carcinoma
Non Bulky	Bulky
Infiltrative growth Pattern	Glandular growth Pattern
Arises de novo from gastric mucous cells	Arises by metaplasia of gastric mucous cells
Are composed of discohesive cells with large mucin vacuoles that expand the cytoplasm and push the nucleus to the periphery, creating a signet ring cell morphology	Typically grow along broad cohesive fronts to form either an exophytic mass or an ulcerated tumor
A mass may be difficult to appreciate in diffuse gastric cancer	Mass can easily be seen and observed
Desmoplastic reaction occurs which results in Linitis plastica	No desmoplastic reaction and thus no linitis plastic is seen
Neoplastic cells have large mucin vacuole that pushes the nucleus into periphery.	The neoplastic cells often contain apical mucin vacuoles, and abundant mucin may be present in gland lumina

b) Early gastric carcinoma: It is a Gastric carcinoma which is confined to the mucosa and submucosa regardless of presence and absence of perigastric lymph nodes metastasis.
Advanced gastric carcinoma: It is gastric carcinoma which has invaded beyond submucosa into the muscularis layer and beyond and has more extensive metastatic spread.
Four host factors associated with increased incidence of gastric carcinoma:

1. Mutations (e.g. CDH1(diffuse type) and APC genes(FAP and Intestinal type))
2. High salt diet
3. Smoking
4. Alcohol abuse
5. Diabetes
6. Proton pump Inhibitor use
7. Overweight and obesity

Q2: A 55 year old male patient is found to have a 3cm polyp in the right colon while he is being evaluated for anemia.

a) **List three non neoplastic and three neoplastic types of colorectal polyps**
b) **Give major histological features of three types of colorectal adenomas.**

Ans: a) Non neoplastic polyps:

1. Hyperplastic polyp
2. Hamartamatous polyp

3. Juvenile polyp
4. Lymphoid polyp

Neoplastic polyp:

1. Sessile serrated adenomas
2. Polyps with invasive adenocarcinomas
3. Polyps with Intramucosal carcinomas.

b) Histological features of three types of colorectal Adenomas:

Adenomas can be classified as tubular, tubulovillous, or villous on the basis of their architecture.

Tubular adenomas: Tubular adenomas tend to be small, pedunculated polyps composed of small, rounded or tubular glands.

Villous adenomas: Villous adenomas, which often are larger and sessile, are covered by slender villi.

Tubulovillous adenomas: Tubulovillous adenomas have a mixture of tubular and villous elements.

Annual 2008

Q1: Endoscopic gastric biopsy from a 65yrs old man presenting with epigastric pain reveals a moderately differentiated glandular tumor not invading beyond submucosa. Adjacent mucosa shows ulceration and presence of H.pylori. Subsequent gastrectomy shows a 1cm flat lesion with perigastric lymph node metastasis.

a) What morphological feature has the greatest effect on clinical outcome?

b) List important, host, environmental and genetic risk factors for gastric carcinoma?

Ans:

a) Extent of Invasion (not beyond submucosa) and nodal metastasis as it Shows whether the cancer is early or advanced. (It is early in this case).

b) Environmental risk factors:

1. Helicobacter pylori infection
2. EBV infection
3. Smoking
4. Opium
5. Salt
6. Alcohol
7. Meat
8. Foundary working
9. Uranium mining

Host risk factors:

1. Obesity
2. Lack of physical work
3. Male gender
4. above 50yrs of age
5. Family history
6. Previous stomach surgery

Genetic risk factors:

1. Type A blood
2. Mutation in CDH1, which encodes the cell adhesion protein E-cadherin.
3. Mutation of TP53
4. Loss of function mutation in APC gene
5. Gain-of-function mutations in the gene encoding β-catenin
6. Loss-of-function mutations in TGFβRII, BAX, CDKN2A.

Supply 2008

Q1: A colectomy specimen of 35 yrs old woman with history of intermittent attacks of mild diarrhea with fever and abdominal pain, shows skip lesions in form of sharply demarcated areas of ulceration and fissuring, also involving the distal ileum. What features would you expect to find on microscopic examination of diseased segment?

Ans: The microscopic features of active Crohn disease include abundant neutrophils that infiltrate and damage crypt epithelium.

Clusters of neutrophils within a crypt are referred to as a crypt abscess and often are associated with crypt destruction. Ulceration is common in Crohn disease, and there may be an abrupt transition between ulcerated and normal mucosa. Epithelial metaplasia, another consequence of chronic relapsing injury, often takes the form of gastric antral appearing glands (pseudopyloric metaplasia). Paneth cell metaplasia also may occur in the left colon, where Paneth cells normally are absent Noncaseating , a hallmark of Crohn disease, are found in approximately 35% of cases and may arise in areas of active disease or uninvolved regions in any layer of the intestinal. Granulomas also may be found in mesenteric lymph nodes.

Annual 2009

Q1: A 60 Years old male present with a history of frequent attacks of cutaneous flushes, cyanosis, diarrhea, cough, wheezing and enlarged nodular liver. On CT scan a tumor was detected in the terminal ileum with hepatic metastasis.

a) What is this tumor?
b) Give its morphology?
c) Explain generation of symptomatology by this tumor?

Ans. a) carcinoid tumor. A neuroendocrine tumor often producing serotonin.

b) Morphology:

1. Gross: Small round yellow mass mucosa but mucosa is intact

2. Microscopy: Neoplastic cells are arranged in discrete island, trabeculae, strands, gland or sheets of uniform cell with scant, pink granular cytoplasm and a round oval stippled nucleus. Cells are monotonously similar to each other. Less mitotic activity cytological atypia and polymorphism. Cells contain secretory granules.

c) The symptoms are caused by the bioactive compound produce by this tumor and that is serotonin and histamine.

Q2: A 25Y Old male gave few months history of dyspepsia .on gastroscopy gastric ulcer was seen. The gastric biopsy revealed heavy colonization by small curved spiral organism on the surface of mucosa.

a) Name the causative organism?
b) What is the role of this micro organism in producing this gastric pathology?

Ans: a) H. pyloric

b) Pathogenesis:

After initial exposure to H.pylori gastritis may develop in two patterns

1. An antral type may lead to high acid production and ulceration or may cause intestinal metaplasia leading to adenocarcinoma
2. Pan gastritis causing lymph proliferative disorder leading to MALT Lymphoma

H.pylori causes these patterns due to its virulence which is due to following factors.

1. Flagella. It allows the bacteria to move in viscous mucus.
2. Urease. It converts urea into ammonia chloride and monchloramine which increase the gastric PH.
3. Adhesion. Adherence enhances bacterial attachment to surface foveolar cells.
4. Toxins. cagA encode VacA toxin which cause epithelial injury.

These factors create an imbalance between mucosal protective and damaging forces.

Supply 2009

Q1: A 70Y old male gave history of bleeding per rectum and tenesmus for the past three months followed by sudden development of features of intestinal obstruction .Emergency laparotomy revealed an obstructing tumor in the rectum which histologically turned out to be an adenocarcinoma

a) What prognostic factors will determine the survival of this patient?

b) Describe the role of APC gene in colorectal carcinoma?

Ans: a) Prognostic factors:

Following factors determine the survival of patient.

1. The depth of invasion of carcinoma. If depth of invasion is more then prognosis will be poor and it will be a poorly differentiating tumor
2. Presence or absence of lymph node involvement and if lymph node are involved then how many lymph nodes are involved.
3. Status of metastases if yes then very poor prognosis.
4. Increase telomerase expression show genetic instability and cell cycle disturbances.

b) Apc gene role:

APC gene have two copies for a normal function these two copies must be normal. If both copies become mutated due to hereditary and sporadic reasons then adenocarcinoma develop. APC is negative regulator of b-catenin .APC normally bind to b-catenin and promotes its degradation. With the loss of this function b-catenin accumulated and it translocates to nucleus where it activates the transcription of MYC-K and cyclin D1 which promotes proliferation. This pathway leads to emergence of carcinoma.

Q2: In a village of a Gujranwala an outbreak occurred with school children getting fever, abdominal pain and diarrhea. The labs results were

TLC: 3500

DLC lymphocytes 75%

Smear negative for malarial parasites. Widal test positive during 2nd week of illness. Cases started presenting with intestinal perforation as well as acute abdominal emergency

A) What will be the gross appearance of intestine illness? Compare these features with that of tuberculosis intestine?

B) What is the intestinal pathology in these children?

Ans: Ans: Grossly intestine show areas of ulceration necrosis and perforation.

In both cases

1. Intestinal hemorrhage due to bleeding in congested payer's patches this is a serious complication
2. Intestinal perforation in the distal ileum is common and serious complication.

And difference in both is that

1. In TB ulcers are transverse whereas in typhoid ulcers are longitudinal.
2. In TB caeseous necrosis with chronic inflammation of tissues occur where it is absent I n typhoid.

B) Pathology in children:

The children are suffering from typhoid fever. It spread through contaminated food and water. S. typhoid is taken by M. cell and then engulf by mononuclear cell present in the lymphoid tissues.

This causes hypertrophic of payer patches in the terminal ileum. They also cause sloughing off musical cell and form longitudinal ulcers.

Annual 2010

Q1. A 30Y Old female has recurrent episodes of bloody diarrhea long symptoms free interval. Sigmoidoscopy shows proctocolitis with continuous involvement of mucosa and extending to the splenic flexure

A) What is your diagnosis?

B) List the gross and microscopy features u would expect to find a colonic resection from this patient?

Ans:

A) Ulcerative colitis

B) Gross Examination findings:

1. It always involves the rectum or may involve the colon.
2. Colonic mucosa may show broad – base ulcers
3. Isolated island of regenerating mucosa bulge into the lumen to create small elevations called pseudopolyps.
4. There are thin bowel walls.
5. Mucosal atrophy may be seen.
6. Toxic megacolon due to destruction of submucosal ganglia so there is dilation of colon

Microscopy findings:

1. Continuous lesions.
2. Inflammatory infiltrate, crypt abscesses may be seen.
3. Inflammation limited to mucosa and submucosa.
4. Non presence of granulomas.

Q2: A 65Y old man presents with anemia and stool for occult blood is positive. A 3.5 cm sessile cauliflower like mass is noted in the rectum on sigmoidoscopy. The remaining mucosa appears normal.

A) List the three types of adenomas you will consider in the differential diagnosis?

B) What factors determine the risk of malignancy in similar cases?

Ans:

A) Adenomas are of three types.

1. Tubular adenomas
2. Villous adenomas
3. Tubulovillous adenomas

B) Risk factors of malignancy:

1. Degree of dysplasia determines risk factors for cancer. More dysplasia more malignant is the cancer.
2. Size of tumor correlates with malignancy .Adenomas less than 1cm in diameter and large than 4cm may develop into cancer.

Annual 2011

Q1: A 60Y old female comes for consultation in your clinic with history of local pain at the base of the tongue and difficulty in chewing. Previously she has been asymptomatic but recently she noticed ulceration at the mentioned site.

A) What are risk factors that make her a candidate for oral cancer?

B) Give the morphological details of Squamous cell carcinoma?

Ans:

A) Risk factors.

1. Tobacco use for a long time
2. Alcohol intake.
3. Mutation in tumor suppressor genes like P53
4. Leukoplakia and erythroplakia
5. Immunosuppression and genetic susceptibility.

B) Morphology:

1. Mostly lesion involve ventral surface of tongue, floor of mouth, lower lip, gingiva.

2. Early lesion appear as pearly white to gray, circumscribed thickening of mucosa closely resembling leukoplakic patches.
3. They may show exophytic fashion to produce visible and palpable nodular masses or may assume endophytic invasive pattern with central necrosis to form cancerous ulcer.
4. The squamous cell may show keratinization.
5. Epithelial dysplasia may be high or low grade.
6. Lymph nodes metastasis is present at the time of diagnosis.

Q2: A 50Y old male give history of epigastric discomfort and weight loss for the past 2 months. He has had no symptoms before this endoscopy biopsy was planned and sent for histopathology. The findings are given in the diagram.

A) What is the diagnosis?
B) Give the microscopic growth patterns of this neoplasm.
C) Give the risk factors for gastric carcinoma?

Ans:

A) Gastric carcinoma

B) Followings are growth patterns of carcinoma

1. Exophytic masses
2. Ulcerative masses.
3. Infiltrative masses.
4. Flat or depressed.
5. Excavated.

C) **Risk factors:**

1. H. pylori induced chronic gastritis.
2. Loss of E.cadherin due to mutation in CDH1.
3. Pernicious anemia
4. Partial gastrectomy.
5. Nitrites derived from nitrates found in food and drinking water.

Supply 2011

Q1: A 65Y old writer with a history of 45 packs develops progressive dysphagia to solids and liquids. An endoscopy reveals a 5cm ulcerated mass in the middle esophagus .The gastroesophageal junction is normal.

A) What type of esophagus cancer do you expect to find on histology?
B) List the four major categories of risk factors predisposing to this type of cancer with one example of each.

Ans:

A) Esophageal squamous cell carcinoma involving upper one third.

B) **Risk factors:**

1. Long standing esophagitis.
2. Achalasia
3. plummer- Vinson syndrome
4. Alcohol consumption.
5. Tobacco use.
6. Mutation in p53.
7. HPV.
8. Deficiency of vitamins like b1, b3& b5.

Q2: Endoscopy in a 55Y old man a known case of gastro esophageal reflux disease reveal tongue of velvety red mucosa extending into lower esophagus from stomach.

A) What is your diagnosis?
B) What feature would you look for in biopsy to confirm u diagnosis?
C) What is the major complication in this lesion and what biopsy feature will predict its risk?

Ans:

A) Barrett esophagus.

B) **Biopsy findings:**

1) Barrett esophagus appear as a salmon pink velvety mucosa between the smooth, pale pink esophageal squamous mucosa and the more lush light brown gastric mucosa.
2) It show tongues like projection extending up from the gastro-esophageal junction.
3) Esophagus of metaplastic mucosa contains goblets cells.
4) Low grade dysplastic changes.

C) Major complication of Barrett esophagus are stricture, intestinal metaplasia, ulceration, bleeding. Epithelial dysplastic changes may increase the risk of adenocarcinoma.

Annual 2012

Q1: A 12Y old boy complained of episodes of bleeding per rectum for the past few years, now increasing in frequency. Colonoscopy was carried out which revealed multiple polyps covering the mucosa. Out of the polyps was biopsied which show tubular glands with hyper-chromatic columnar lining.

A) What local complications can develop in this patient explain?
B) Enlist multiple polyposis syndromes and give their clinical significance.

Ans:

A) Patient is suffering from colonic adenomas. Complication will depend on the size and degree of dysplasia and if both factors are increase than risk of malignancy will increases.

B) Multiple polyposis syndrome are as follow

Syndrome	GIT lesions	Clinical significance
Juvenile polyposis	Mainly in rectum. Non malignant potential may be sporadic or genetic. May cause rectal bleeding or infraction	Pulmonary arteriovenous malformation clubbing and increase risk of adenocarcinoma
Peutz-Jegher's syndrome	Multiple GIT hamartomatous + mucocutanoeos pigmentations	Increase risk of cancer of colon lungs uterus. usually involve small intestine then large intestine and stomach rarely
Cronkhite Canada syndrome	Non hereditary. Hamartomatous colonic polyps' crypt dilation.	NAIL atrophy hair loss ,Nail splitting cutaneous hypo/hyper pigmentation
Cowden syndrome	Macrocephaly lipoma, hemangioma, ganglioneuroma benign skin lesions	Increase risk of thyroid breast, uterus, and skin.

FAP	Greater than 100 polyps show colonic adenoma. Have different types colonic polyps, attenuated polyps, Gardeners syndrome, Turcot syndrome	Increase risk of adenocarcinoma

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Q2: A 35Y old male working at a bank cash counter gives history of pain abdomen, diarrhea with mucus and blood for the past few years. He started losing weight and became anemic. He noticed periods of remission as well for few months but symptoms relapsed again. His stool was negative repeatedly for parasites.

A) What will be the microscopy appearance of his rectal biopsy?

B) Enlist ulcero-inflammatory conditions of Intestine?

Ans:

A) Patient is suffering from ulcerative colitis.

Microscopic features.

1. Neutrophilic infiltration of the epithelial layer may produce collection of neutrophils in crypt lumina forming crypt abscesses.
2. Isolated island of regenerating mucosa bulge upward to create pseudopolyps.
3. Adjacent ulcers interconnect to create tunnels covered tenuous mucosal bridges.
4. Extensive broad base ulcerations.

B)
1. Crohn's disease
2. Ulcerative colitis

Supply 2012

Q1: A 65y old writer with a history of 45 packs develops progressive dysphagia to solids and liquids. An endoscopy reveals a 5cm ulcerated mass in the middle esophagus. The gastroesophageal junction is normal.

A) What type of esophagus cancer do u expect to find on histology?

B) List four major categories of risk factors predisposing to this type of cancer with one example of each.

Ans:

A) Squamous cell carcinoma.

B) **Risk factors:**

Esophageal disorder
1. Achalasia
2. Plummer Vinson syndrome.
3. Esophagitis.

Life style
1. Alcohol consumption.
2. Tobacco abuse.

Dietary
1. Deficiency of vit A, C, B1.
2. Deficiency of trace metals zinc, molybdenum.

Genetic predisposition.
1. Tylosis.

Q2: Endoscopy in a 55Y old man, a known case of GERD reveals tongues of velvety red mucosa extending into lower esophagus from stomach.

A) What is your provisional diagnosis?

B) What features would u look for in a biopsy to confirm u diagnosis?
C) What is the major complication of this lesion and what biopsy feature will help u to predict its risk?
Ans:
A) Barrett esophagus.
B) 1. The esophageal squamous epithelium is replaced by metaplastic columnar epithelium containing goblet cells.
2. Irregular circumferential bands displacing squamous columnar junction cephalad.
3. Velvety red mucosa with tongues extending up from gastroesophageal junctions.
4. The dysplastic changes may be seen in mucosa raising the risk of cancer.
C) The major complication that arises from Barrett esophagus is adenocarcinoma.
The following biopsy finding funding helps us to predict adenocarcinoma
1. If we see dysplastic changes in the mucosa it may indicate the risk of cancer.
2. Metaplasia may increase its risk.

Annual 2013

Q1. A) Enumerate four types of Malabsorption syndromes?
B) Briefly describe morphology of celiac disease?
Ans:
A) 1. Defective intraluminal syndrome.
Pancreatic insufficiency due to pancreatitis
Zollinger Ellison syndrome with inactivation of pancreatic enzyme by excess gastric acid secretion
2. Primary Mucosal Cell Abnormality.
Defective terminal digestion.
Disaccharides deficiency
Abetalipoprotenima
3. Reduced Small intestinal surface Area.
Gluten sensitive enteropathy
Short gut syndrome.
4. Infection.
Tropical sprue
Whipple disease
5. Lymphatic Obstruction
Lymphoma
Tuberculosis
B) **Morphology of celiac disease:**
1. Loss of villi in proximal intestine.
2. Increased intraepithelial lymphocytes.
3. Increased plasma cell in the lamina propria.

Supply 2013

Q1: A 62Y old female has a five month history of nausea vomiting and 7 kg weight loss. Abdominal CT scan show diffusely thickened wall of stomach. Endoscopy shows the loss of antral rugal folds and a rigid thickened wall with 5cm irregular areas of ulceration. Biopsy is taken from the edge of ulceration.
A) What is u likely diagnosis?
B) What would be the microscopic picture of the biopsy specimen?
C) What are the four risk factors associated with it?
Ans: A) Diffuse type gastric cancer.
B) Microscopic features:
1. Display infiltrative growth pattern and are composed of discohesive cell with large vacuoles.

2. Signet ring cell because of large mucin nucleus is pushed to one site.
3. The stomach become rigid and thickened because of desmoplastic reaction due to which the gastric wall become stiffen and diffuse rugal flattening and impart a leather bottle appearance termed as linitis plastica.

C) Risk factors:

1. Chronic gastritis with intestinal metaplasia
2. Infection with H.plyori
3. Loss of E- cadherin due to mutation
4. EBV infection.

Q2: A 22Y old male presented in OPD with history of diarrhea. He had recently started smoking due to job stress. His GIT symptoms worsened with smoking .on physical examination he had clubbing of fingers and uveitis. Colonoscopy shows lesion consisting of area of edema and mucosal ulceration separated by normal mucosa.

A) What is u diagnosis?

B) What are microscopic features typically present in the lesion?

C) Is there any risk of malignancy?

Ans:

A) Crohn disease

B) Microscopic Features:

1. Non caseating granulomas.
2. Creeping fats.
3. Cobblestone appearance.
4. Paneth cell metaplasia occurs in left colon.
5. Inflammation with neutrophilic infiltration into the epithelial layer and accumulation in crypts is called crypt abscesses.
6. Ulcerations.
7. Chronic mucosal damage.

C) Risk of colonic adenocarcinoma in patient with crohn disease is slight 1 to 3% where as in ulcerative colitis risk is high 5 to 25 %.

Annual 2014

Q1: A 70Y old women present in medical OPD with a history of weight loss, decrease appetite and epigastric discomfort. On examination, she is thin not cachectic. Stool is positive for occult blood. An upper GI series reveal gastric ulcer with an irregular border. Biopsy is positive for adenocarcinoma.

A) What condition predispose to the development of gastric carcinoma

B) What are microscopic features of gastric carcinoma?

Ans:

A) Predisposing condition:

1. Mutation of E- cadherin function.
2. H. Pylori infection.
3. EPV
4. Chronic gastritis
5. Diet containing food that may generate nitrites

B) Microscopic Features:

1. Intestinal carcinoma tends to be bulky and composed of glandular structures.
2. Intestinal type adenocarcinoma grows as exophytic mass or ulcerative mass.
3. Diffuse type adenocarcinoma has a signet ring cell.
4. Stomach become stiff rigid due to desmoplastic reaction and show appearance of leather bottle known as linitis plastica.

Supply 2014

Q1: A 58Y old male present with weakness fatigue weight loss and alteration of bowl habit for more than 6 months. On investigation there is pallor and stool for occult blood is positive.

A) What are possible causes?

B) What further investigation would you perform to reach diagnosis?

Ans: A) colonic adenocarcinoma

B) Following investigation we will perform.

1. PR Examination.
2. Proctoscopy.
3. Colonoscopy
4. CT Scan
5. Tumor marker CEA(carcino Embryogenic Antigen)
6. Endoscopy (Colonoscopy or proctoscopy) with biopsy.

SOLVED BY
SABEEH CHUGHTAI
RASHID LATIF MEDICAL COLLEGE LAHORE
&
SHAMSA SHAFIQUE
PAK RED CRESCENT MEDICAL COLLEGE LAHORE

Section 6: Liver, Gall bladder, Pancreas

Annual 2003

Q1: Give laboratory diagnosis of obstructive jaundice.

Ans:

1- Serum Total Bilirubin, raised
2- Serum direct biliribin, raised
3-Urine Bilirubin, positive
4-Serum Alkaline Phosphatase, raised
5-Serum GG, raised
6-Ultrasound
7-CT Scan
8-MRCP
9-ERCP
10-Angiogram
11-Biopsy

Annual 2004

Q1: a) Enumerate the causes of Jaundice.

b) How will you use the laboratory tests make diagnosis in a patient with jaundice?

Ans:

a)

Unconjugated Hyperbilirubinemia:

1. Excess Production of Bilirubin:

- Hemolytic anemias
- Resorption of blood from internal hemorrhage
- Ineffective erythropoiesis syndromes

2. Reduced Hepatic Uptake:

- Drug interference
- Diffuse hepatocellular disease

3. Impaired Bilirubin Conjugation:

- Physiological jaundice of new born

Conjugated Hyperbilirubinemia:

1. Decreased hepatocellular excretion:

- Deficiency in canalicular membrane transporters
- Drug induced canalicular membrane dysfunction
- Hepatocellular damage or toxicity

2. Impaired intra or extra hepatic bile flow:

- Inflammatory destruction of intra hepatic bile ducts, gall stones, carcinoma pancreas

b)

1- Total Serum Bilirubin
2- Direct Bilirubin
3- Urine bilirubin
4- Urine Urobilinogen

Supply 2004

Q1: a) Define cholelithiasis.

b) Classify gall stones.

c) Discuss aetiology and complications of gall stones.

Ans:

a)

Presence of stones in gall bladder

b)

Gall stones are classified as:

1- Cholesterol stones

2- Pigment stones:

a- Black stones

b- Brown stones

c)

Cholesterol is rendered water-soluble by aggregation with bile-salts and lecithins. When cholesterol concentrations exceed the solubilizing capacity of bile, gall stones are formed. Cholesterol gall stones formation is enhanced by hypomobility of the gall bladder (stasis) and by mucus hypersecretion.

Pigment stones are formed in the presence of unconjugated bilirubin in the biliary tree which occurs in hemolytic anemias and infection of biliary tree.

Complications:

Empyema, perforation, fistulas, inflammation of the biliary tree, obstructive cholestasis or pancreatitis.

Annual 2006

Q1: write down the sequence of development of serological markers of hepatitis B viral infection, both acute and chronic. Strengthen your answer by labeled graphic presentation.

Ans:

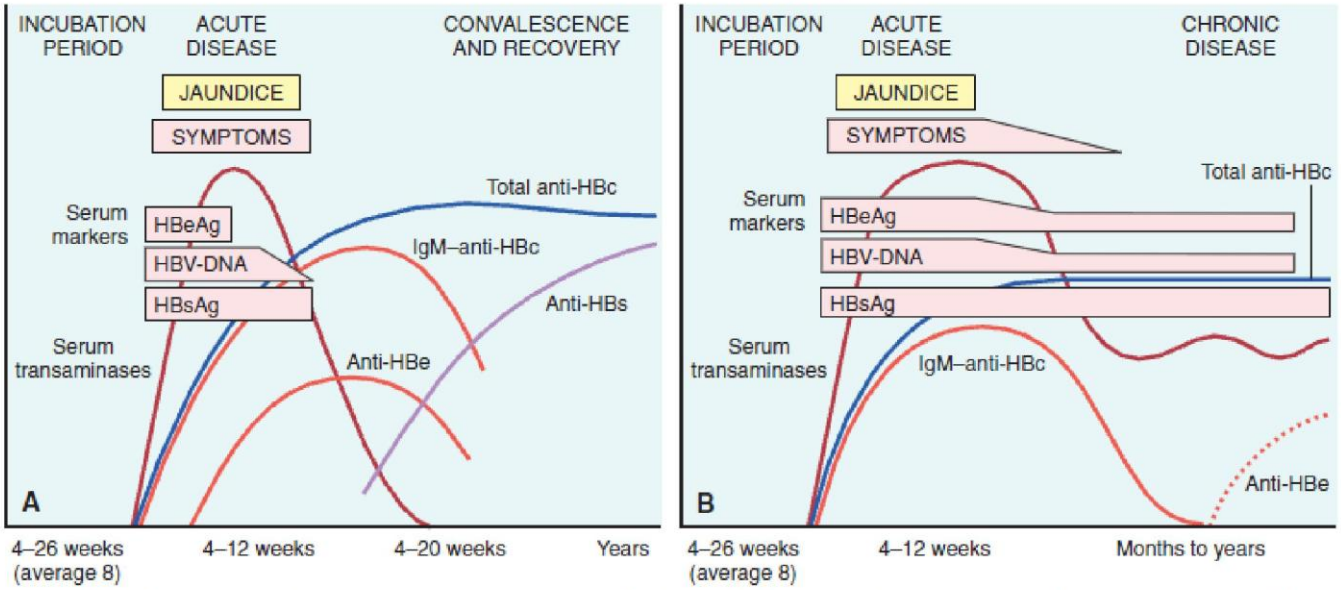

Figure 15–11 The sequence of serologic markers in acute hepatitis B infection. **A,** Resolution of active infection. **B,** Progression to chronic infection. See text for abbreviations.

Supply 2006

Q1: a) Tabulate important causes of acute pancreatitis.

b) Morphological changes of pancreas in this condition.

Ans:

a)

Metabolic:

- Alcoholism
- Hyperlipoprotienemia

- Hypercalcemia
- Drugs

Genetic:

- Mutation in cationic trypsinogen and trypsin inhibitors genes

Mechanical

- Gall stones
- Trauma
- Iatrogenic injury

Vascular:

- Shock
- Atheroembolism
- Polyarteritis Nodosa

Infectious:

- Mumps
- Coxsackie virus

b)

Basic alterations in acute pancreatitis:

1-Microvascular leakage edema
2-Necrosis of fat by lipases
3-an acute inflammatory reaction
4-preoteolytic destruction of pancreatic parenchyma
5-Destruction of blood vessels leading to interstitial Hemorrhage.

Q2: a) Classify Cirrhosis.
b) Describe briefly the mechanism of hepatic encephalopathy.
Ans:
a)

There is no satisfactory classification of cirrhosis save for specification of presumed underlying etiology. The only classification is:

- 90% cases of cirrhosis are caused by all the known causes.(Chronic viral hep, auto immune etc)
- 10% are referred as cryptogenic cirrhosis, which in recent years are recognized as probable, burned out NASH.

b)

Liver is the organ where metabolism of many subs. Including amino acids and DNA bases, takes place. By-product of this metabolism i.e. Ammonia is converted into lesser toxic substances like urea and uric acid. But in diseased or decompensated liver, this metabolism along with other detoxifying mechanisms and is disturbed. This results in accumulation of toxic substances in the bloodstream that are normally removed by the liver resulting in its increased levels in the blood. Hyper ammonemia and inc. Levels of other toxic metabolites may gain entry into the brain in the setting of liver failure. These neurotoxic substances may then contribute to morphologic changes in astrocytes leading to Brain damage which manifests as neuropsychiatric abnormalities (personality changes, intellectual impairment, dec. Level of consciousness). This is called **Hepatic encephalopathy.**

Annual 2007

Q1: A 1-month old infant presenting with jaundice is diagnosed with extrahepatic biliary atresia.
a) What are the major histological features on liver biopsy?
b) What two enzymes are likely to be raised in this condition?
Ans:
a)

Ductular reaction

Portal tract edema
Fibrosis
Parenchymal cholestasis

b)

Aminotransferase
Alkaline Phosphatase

Supply 2007

Q1: A 60 years old male patient having chronic viral hepatitis B is discovered to have an 8 cm mass lesion in right lobe of the liver. Serum AFP is markedly elevated. Give 5 important factors, which contribute to development of this tumor in patients of chronic hepatitis B.

Ans:

1- Cell death/necrosis
2- Regeneration
3- Poor regulation of hepatocytes replication with increased cell turn over.
4- Inflammation
5- Fibrosis/cirrhosis

HbV does not contain oncogenes. The HBV-X gene may have some oncogenic potential (causing mutations in oncogenes or tumor suppressor genes leading to genomic instability). Acquired defects in DNA repair may also be a contributing factor. The tumorigenic capacity of this virus probably relates primarily to their capacity to cause chronic inflammation and increased cell turn over.

Annual 2008

Q1: a) what are three main types of liver disease associated with chronic consumption of alcohol?
b) Give the salient histological features of each.

Ans:

a)

Hepatic steatosis, alcoholic hepatitis, cirrhosis

b)

Hepatic steatosis:

Fat accumulation begins in centrilobular hepatocytes. Lipid droplets range from small (microvesicular) to large, the largest filling &expanding the cell and displacing the nucleus. As steatosis becomes more extensive, the lipid accumulation spreads outwards from the central vein to hepatocytes in the midlobule and then the periportal regions. Macroscopically, fatty liver is large, soft, yellow and greasy.

Alcoholic Hepatitis:

Hepatocytes ballooning, Mallory-denk bodies, Neutrophils infiltration, Liver cell necrosis.

Cirrhosis:

Bridging fibrous septa in the form of delicate bands linking portal tract with one another (central portal-fibrous septa), fibrosis, Parenchymal nodules containing hepatocytes encircled by fibrosis (Laennec cirrhosis), Disruption of architecture of entire liver with a brown, shrunken organ, liver.

Q2: List two laboratory tests each for the evaluation of hepatocytes integrity, biliary excretory function and hepatocytes function.

Ans:

Hepatocytes Integrity: Serum levels of AST, ALT
Biliary Excretory Function: Serum Bilirubin total, direct, delta Urine bilirubin
Hepatocytes function: Serum albumin, serum ammonia

Annual 2009

Q1: A 50 year old lady presents with H/O dull right upper quadrant pain and flatulence of the past one year. Plain X-ray revealed no stone in the gall bladder. Ultrasound was advised. Following the cholectectomy was performed, lumen of the bladder was found to be full of stones.
a) Enlist various types of gall stones.
b) What are the expected microscopic features of removed gall bladder?
c) What complications can develop in this gall bladder (if surgery was not performed)
Ans:
a) See Q1 in Supply 2004 above
b)

Gall bladder may be contracted, of normal size, or enlarged. Mucosal ulcerations are infrequent; submucosa and subserosa are often thickened from fibrosis. In the absence of superimposed signs of acute inflammation, mural lymphocytes are the only signs of inflammation.

c)
If surgery is not performed, following complications can arise:

- Acute Cholecystitis
- Bacterial superinfection with cholangitis or sepsis
- Gall bladder perforation and local abcess formation
- Gall bladder rupture with diffuse peritonitis
- Biliary enteric (cholyecystenteric) fistula, with drainage of bile into adjacent organs, entry of air and bacteria into the biliary tree, and potentially gall-stone induced intestinal obstruction (ileus)
- Aggravation of pre-existing medical illness, with cardiac, pulmonary and renal or liver decompensation.

Supply 2009

Q1: A 40 years old Taiwanese is admitted in medical ward with ascites. On examination two well defined solid nodules were detected in liver. Alpha fetoprotiens level was 1000ng/ml
a) what could be the possible diagnosis
b) in your opinion, which etiological factor is operative in this patient for producing this tumor.
c) What is the mechanism of development of Ascites in this patient?
Ans:
a)

Hepatocellular carcinoma

b)

Viral Hepatitis B.

In Taiwan and many other Asian countries, High incidence of HCC is due to vertical transmission of HBV (the carrier state starts in infancy)

c)
Ascites may develop by one of the following mechanism:

- Increased movement of intravascular fluid into the extravascular space of Disse, caused by sinusoidal hypertension and hypoalbuminemia.
- Leakage of fluid from hepatic interstitium into the peritoneal cavity. Normal lymph flow is 800-1000 ml/day. With cirrhosis, hepatic lymphatic flow approaches 20 L/day.

Q2: A 20 years old medical student presents with symptoms of fever, nausea, vomiting and pain in right hypochondrium. There is history of passage of dark colored urine. History reveals that he had a meal at a road side restaurant three weeks ago. Lab. Investigation shows:
Serum Bilirubin: 8.5mg/dl (normal 0.2-1.2)
AST: 800U/L (Normal upto 40 U/L)
ALP: 150 U/L (normal 50-120 U/L)

Total Protein: 7.2 mg/dl (normal=6.2-8.5mg/dl)
Albumin=3.8g/dl
Urine Bilirubin and Urobilinogen= +ve
a) what is the likely diagnosis? What does the raised transaminase indicate?
b) Why does bilirubin & Urobilinogen appear in urine in this condition? What form of bilirubin is present in plasma & urine?
Ans:
a)
Hepatitis A. Raised Transaminase indicate Hepatocytes Injury
b)
Bilirubin appears in urine due to decrease conjugation by the diseased liver. And since urobilinogen is a product of bilirubin, so with increased levels of bilirubin in the body, urobilinogen appears in the urine too.
In Plasma, both conjugated and un-conjugated Bilirubin is present while In Urine only conjugated bilirubin.

Annual 2010

Q1: A biopsy from a 60-years old patient of chronic liver disease (hep. C positive) shows a nodular architecture.
a) What histological features are necessary for diagnosis of cirrhosis?
b) What type of collagen is deposited in cirrhosis of liver and what cell type produce it?
Ans:
a)
1- Fibrous septa in the form of delicate bands or broad scars around multiple adjacent lobules. Log-standing fibrosis is generally irreversible as long as the disease persists. Regression is possible if the underlying cause is reversed.
2- Parenchymal nodules, ranging in size from very small to large, encircled by these fibrous bands. Ductular reactions at the periphery of most cirrhotic nodules.
b)
Collagen type 3 & 1 are deposited in the space of Disse. Produced by Perisinusoidal stellate cells which also lie in the space of disse.

Annual 2011

Q1: A 40 years old obese female complaints of excruciating colicky (spasmodic) pain in right hypochondrium and dyspepsia. Her gall bladder reveals gall stones by ultrasonography.
a) What are the different types of gall stones?
b) Give the risk factors involved in the aetiology of gall stones?
Ans:
a)
See Above Q1 of Supply 2004
b)

Table 15–8 Risk Factors for Gallstones

Cholesterol Stones
Demography: Northern Europeans, North and South Americans, Native Americans, Mexican Americans
Advancing age
Female sex hormones
Female gender
Oral contraceptives
Pregnancy
Obesity and insulin resistance
Rapid weight reduction
Gallbladder stasis
Inborn disorders of bile acid metabolism
Dyslipidemia syndromes
Pigment Stones
Demography: Asian more than Western, rural more than urban
Chronic hemolysis (e.g., sickle cell anemia, hereditary spherocytosis)
Biliary infection
Gastrointestinal disorders: ileal disease (e.g., Crohn disease), ileal resection or bypass, cystic fibrosis with pancreatic insufficiency

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Supply 2011

Q1: List two laboratories test each for the evaluation of hepatocytes integrity, biliary excretory function & hepatocytes synthetic function.

Ans:

Hepatocytes Integrity: Serum levels of AST, ALT

Biliary Excretory Function: Serum Bilirubin total, direct, delta Urine bilirubin

Hepatocytes function: Serum albumin, serum ammonia

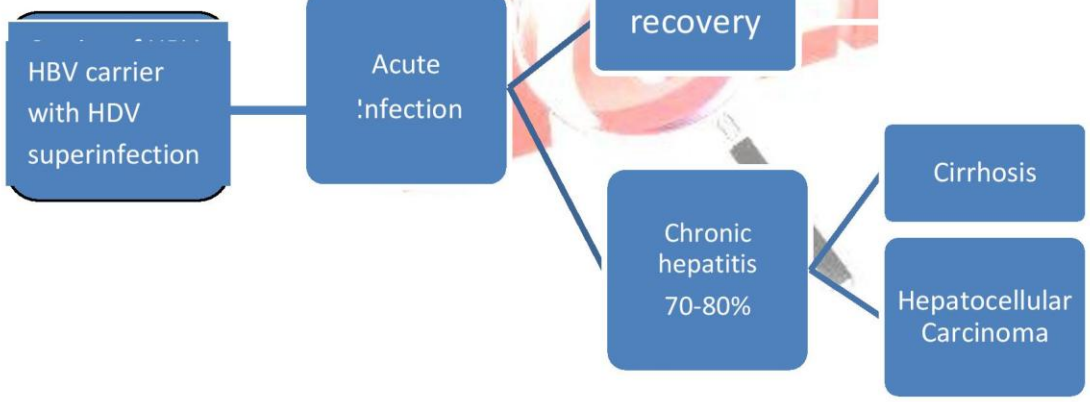
Q2: With the help of flow diagram illustrate the possible outcomes in the following case scenarios.

a) A carrier of HBV with HDV super infection.

b) Draw a chart showing serological marker for hepatitis B virus in acute infection with resolution.

Ans:

a)



b)

Figure 15.11 A, Intermediate Robbins.

Annual 2012

Q1: A 25 years old health care worker got a job in Middle East. As a visa obtaining policy, he was required to undergo detailed medical check-up. His ALT was 250 IU/L & serology results showed positive anti-HCV. He was warned about the possible complications of his state.

a) What is the natural course of this disease?

b) What test would you do before starting the management? How does the virus play its role in hepatic neoplasia development?

Ans:

a)

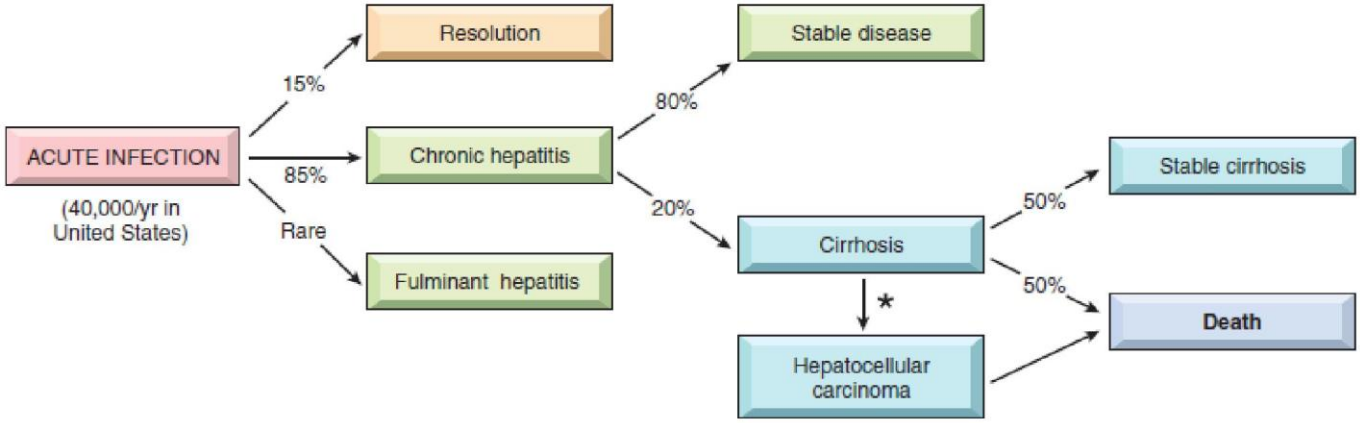


Figure 15–13 The potential outcomes of hepatitis C infection in adults, with their approximate annual frequencies in the United States. The population estimates are for newly detected infection; because of the decades-long lag time for progression from acute infection to cirrhosis, the actual annual death rate from hepatitis C is about 10,000 per year and exceeded 22,000 deaths per year by 2008. *The risk of hepatocellular carcinoma is 1% to 4% per year.

Incubation period for Hep. C ranges from 2-26 weeks.

b)

PCR assay for HCV RNA, 3rd generation ELISA for antibody detection. The universal feature of **hepatocellular carcinoma** is the presence of structural and numerical chromosomal abnormalities indicative of genomic instability. Several factors contribute in creating this instability. In HCV, the tumirogenic capacity relates primarily to its capacity to cause chronic inflammation, regeneration, increased cell turn over and cirrhosis. Acquired defects in DNA repair may also be a contributing factor.

Annual 2013

Q1: A 56 years old man c/o fatigue, loss of appetite and weight loss of 10 kg over the last 6 months. The lab tests revealed HBS antigen positive and anti-HCV and anti-HAV negative. The alpha-fetoprotein is 50 times higher than normal. The CT scan shows 10.6cm solid mass in the left lobe of liver. The spleen looks normal.

a) Name 4 causative factors of this tumor.

b) Briefly mention 3 mechanisms of induction of this tumor by viruses.

Ans:

a)

Causative Factors: HBV, HCV, alcoholic cirrhosis, Aflatoxin exposure, NAFLD.

b)

Mechanisms of Induction:

1- Inflammation and regeneration, seen in all forms of chronic hepatitis, are believed to be the main contributors to acquired mutations in genomic DNA.

2- Acquired mutations in specific oncogenes and tumor suppressor genes contribute to dysregulated growth and further increase in genomic instability.

3- Acquired defects in DNA repair, particularly those in repair systems for double-stranded DNA breaks, also perpetuate DNA damage and may cause chromosomal defects.

Supply 2013

Q1: Define Cirrhosis. Give its causes and complications.

Ans:

Cirrhosis is defined as a diffused process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules.

Causes: Chronic viral infections, alcoholic or non-alcoholic steatohepatitis (NASH), autoimmune diseases affecting hepatocytes and/or bile ducts, and iron over load.

Complications: Decreased liver function, Portal hypertension, Progressive Liver Failure, Increased risk for development of hepatocellular carcinoma.

Annual 2014

Q1: A 55-year old African male presented in medical OPD with history of abdominal pain, fatigue and weight loss. His liver function tests (LFTs) were marginally disturbed. Abdominal ultrasound reveals a mass in liver. His serum alpha-fetoprotein levels were raised.

a) What is the diagnosis?

b) What is the microscopic picture of this lesion?

c) Write 4 etiological factors of this disease.

Ans:

a)

Hepatocellular Carcinoma

b)

On histological examination, HCCs range from well differentiated lesions that reproduce hepatocytes arranged in cords, trabeculae or glandular patterns, to poorly differentiated lesions, often composed of large, multinucleate, anaplastic giant cells.

In the better differentiated variants, globules of bile may be found within the cytoplasm of the cells and in pseudocanaliculi b/w cells. Acidophilic Hyaline Inclusions within the cytoplasm may be present, resembling Mallory bodies. There is little stroma in most hepatocellular carcinomas, explaining their soft consistency.

A distinctive clinicopathological variant of HCC is the fibrolamellar carcinoma. It usually consists of single tumor with fibrous bands coursing through it, superficially resembling focal nodular hyperplasia. The fibrolamellar variant has a better prognosis than that of the other, more common variants.

c) HBV, HCV, Alcoholic cirrhosis, Aflatoxin exposure.

SOLVED BY:
RABIA ANAM
PUNJAB MEDICAL COLLEGE, FAISALABAD.

Section 7 : MALE REPRODUCTIVE SYSTEM

Annual 2006

Q1: Classify testicular tumor, give briefly morphology of teratoma? 4, 2

Ans:

1- **Germ cell tumors**
   - Seminoma
   - Spermatocytic seminoma
   - Embryonal carcinoma
   - Yolk sac tumor
   - Polyembryoma
   - Choriocarcinoma
   - Teratoma (mature, immature, white malignant transformation)
   - Mixed germ cell tumors

2- **Sex cord stromal tumors**
   - Leydig cell tumor
   - Sertoli cell tumor (Androblastoma)
   - Granulosa cell tumor
   - Mixed forms

3- **Combined germ cell-sex cord stromal tumors**
   - Gonadoblastoma

4- **Other tumors**
   - Malignant lymphoma (5%)
   - Rare tumors

Supply 2006

Q1: a) Name the diseases involving prostate?

B) Give briefly morphology, grading and staging of carcinoma of prostate?

Ans: a)

1- Acute prostatitis
2- Chronic prostatitis
3- Benign prostatic hyperplasia
4- Prostate cancer

b) Morphology:

Gross: The prostate may be enlarged normal in size or smaller than normal. Prostatic carcinoma is located in the peripheral zone especially in the posterior zone.

Microscopic: Four histological types are described;

1- Adenocarcinoma
2- Transitional cell carcinoma
3- Squamous cell carcinoma
4- Undifferentiated carcinoma

Adenocarcinoma is the more common type found in 96% of cases.

Staging:

- The tumor found incidentally or a clinically unsuspected cancer in prostate removed for benign disorders (stage A)
- The tumor palpable by DRE (digital rectal examination) but confined to the prostate (stage B)
- Tumor has extended locally beyond the prostate into the surrounding tissues (stage C)
- The tumor is associated with distant metastasis (stage D)

Grading:

1- Mostofi's (WHO) histological grading criteria of prostate
   GRADE 1: Well differentiated
   GRADE 2: Moderately differentiated
   GRADE 3: poorly differentiated
2- GLEASON's microscopic grading system based on:
   i- Degree of glandular differentiation
   ii- Growth pattern of the tumor in relation to stroma

For clinical staging of prostate cancer TNM system is considered international standard.

Annual 2007

Q1: a) what three serum marker would you order in a pt with testicular mass?
b) What is the value of serum markers in context of testicular tumors?

Ans:

- Alpha feto proteins AFP
- Human chorionic gonadotropin HCG
- Lactate dehydrogenase LDH

b)

a. Seminoma ------ 10% pt. have elevated HCG.
b. Embryonal carcinoma------ Negative
c. Yolk sac tumor---------- 90% Pt. have elevated AFP
d. Choriocarcinoma-------- 100% PT. have elevated HCG.
e. Teratoma---------- Negative
f. Mixed tumors-------- 90% pt. elevated HCG or AFP.

Annual 2008

Q1: A 54 year old male develops frequency of micturition urgency overflow incontinence and nocturia. DRE reveals nodular prostate enlargement and serum PSA is less than 4ng/dl. Sextant prostate biopsy is negative for malignancies?

a) What is diagnosis?
b) If a prostactomy was done in this pt. what gross and morphological features would you expect to see?

Ans: a) BPH Benign prostatic hyperplasia.

b) Morphology:

Gross: The enlarge prostate is nodular smooth and firm and weighs 2 to 4 times its normal weight that is 40-80grams the appearance on cut section varies depending upon whether the hyperplasia is predominantly of glandular or fibromuscular tissues.

- In primarily glandular benign enlargement of prostate the tissue is yellowish pink, soft, honey combed and milky fluid exudates
- Fibromuscular BEP the cut surface is firm homogenous and does not exudates milky fluids.

Histological features:

- Glandular hyperplasia predominates in most cases and is identified by exaggerated intra acinar papillary infoldings with delicate fibrovascular cores.
- Fibromuscular hyperplasia is when present as dominant component and appears as aggregates of spindle cells forming and appearance akin to fibromyoma of the uterus.
- The glandular lumina often contain inspissated, protienaceous secretory material known as corpora amylacea.

Annual 2009

Q1: Name any four germ cell tumors of testis? Enumerate biological markers secreted by such tumors that can be detected in the blood?

b) Enumerate the predisposing influences that can contribute to the pathogenesis of germ cell tumors of the testis?

Ans:

Germ cell tumors:

- Seminoma
- Spermatocytic seminoma
- Embryonal carcinoma
- Yolk sac tumor
- Polyembryoma
- Choriocarcinoma
- Teratoma (mature, immature, white malignant transformation)
- Mixed germ cell tumors

Biological markers:

- AFP
- HCG
- LDH
- Carcinoembroynic antigen CEA
- Human placental lactogen
- Placental alkaline phosphatase
- Testosterone
- Estrogen
- Luteinizing hormone

b)

- Cryptorchid testis
- Androgen insensitivity syndrome
- Klienfielter syndrome
- Peutz-Jegher's syndrome (sertoli leydig cell tumors)
- Inguinal hernia, mumps orchitis

Supply 2009

Q1: A 70 year old man has increasingly difficulty with urination he has a feeling of urgency but each time the volume of urine is small he has difficulty in starting and stopping the urination. His problem has progressed over last few years his PSA are slightly increased but has been stable over this time?

a) Diagnosis?

b) Microscopic appearance of prostate?

c) Enumerate secondary changes that can occur in the low urinary tract and kidney in this condition?

Ans: a) benign prostatic hyperplasia BPH.

b)

i) Glandular hyperplasia predominates in most cases and is identified by exaggerated intra acinar papillary infoldings with delicate fibrovascular cores.

ii) Fibromuscular hyperplasia is when present as dominant component and appears as aggregates of spindle cells forming and appearance akin to fibromyoma of the uterus.

- The glandular lumina often contain inspissated, protienaceous secretory material known as corpora amylacea.

c)

- Obstructive uropathy (post renal azotemia, bilateral hydronephrosis. Bladder diverticula, bladder wall smooth muscle hypertrophy/ hyperplasia
- Bladder infections
- Prostatic infarcts

Annual 2010

Q1: pt. presents with the palpable mass in the abdomen and found to have unilateral cryptorchidism?

a) **List three testicular tumors that could be found in this patient**?
b) **Give histological features of teratoma?**

Ans:

a)

- Seminoma
- Embryonal carcinoma
- Choriocarcinoma

b)

Three types of teratoma

i) Mature teratoma
ii) Immature teratoma
iii) Teratoma with malignant transformation.

Mature Teratoma: Is composed of disorderly mixture of a variety well differentiated structures such as cartilage smooth muscles, intestinal and respiratory epithelium.

Immature Teratoma: is a composed incompletely differentiated and primitive or embryonic tissue along with some mature elements. Primitive or embryonic tissue commonly present is poorly formed cartilage, mesenchymal, neural tissues, abortive eye, intestinal and respiratory tissues etc. Mitosis is usually frequent.

Teratoma with Malignant Transformation: this is rare form in which one or more tissue elements show malignant transformation, such malignant changes resemble morphologically with typical malignancy in other organ and tissues and commonly includes rhabdomyosarcoma, squamous cell carcinoma and adenocarcinoma.

Supply 2011

Q1: In a 70 year old man presented with testicular mass, would you favor?

a) **Diagnosis of classical or spermatocytic seminoma?**
b) **What morphological features would confirm your provisional diagnosis?**

Ans: a) The spermatocytic seminoma most commonly occurs in the 6th decade of life or in patients above 65 years of age. Whereas the classic seminoma occurs commonly in 4th decade of life. So in this case spermatocytic seminoma is diagnosed.

b)

Gross: Spermatocytic seminoma is the homogenous, larger, softer, more yellowish and gelatinous then the classic seminoma.

Histological: The tumor cells varies considerably in size from lymphocyte like to huge mono nucleate or multi nucleated giant cells, majority of the tumor cells are of intermediate cells. The cell has eosinophilic cytoplast devoid of glycogen the nuclei of intermediate and large cells have filaments pattern, mitosis are often frequent.

Stroma lacks lymphocytic and granulumatous reactions that are seen in classic seminoma.

Annual 2012

Q1: a) Give the pathogenic classification of testicular tumors.

b) **What is mode of spread of testicular tumors?**

Ans: a)

1- Germ cell tumors

- Seminoma
- Spermatocytic seminoma
- Embryonal carcinoma
- Yolk sac tumor
- Polyembryoma
- Choriocarcinoma
- Teratoma (mature, immature, white malignant transformation)
- Mixed germ cell tumors

2- Sex cord stromal tumors

- Leydig cell tumor
- Sertoli cell tumor (Androblastoma)
- Granulosa cell tumor
- Mixed forms

3- Combined germ cell-sex cord stromal tumors

- Gonadoblastoma

4- Other tumors

- Malignant lymphoma (5%)
- Rare tumors

b)

Seminomas: these often confined to the testis for long intervals. Metastasis most commonly occurs in the iliac and paraaortic lymph nodes particularly in the upper lumber region. Hematogenous metastasis occurs late in the course of disease.

Non Seminomas: these tend to metastasize earlier by lymphatic as well as by hematogenous route, hematogenous metastasis are most common in the liver and lungs.

Malignant testicular tumor most of germ cell origin which can be seminoma or non seminoma. Sex cord tumors are mostly benign that don't metastasize.

Annual 2013

Q1: A 10 year old boy was enlarged testis for last four years now the swelling has increase in size the ultrasound shows the cystic and echodense areas the resection of mass has been done in the section there are closely packed pleomorphic large cells with hyperchromatic nuclei and prominent nucleoli there are papillary structures, there were 6 atypical mitotic figures/10 HPF and Schiller Dural bodies are seen, there muci carmine stain was negative the blood levels shows high AFP.

a) What type of tumor boy has developed?

b) Name other four germinal cell tumor?

Ans: a) Yolk sac testicular tumor.

b)

- Seminoma
- Spermatocytic seminoma
- Embryonal carcinoma
- Polyembryoma
- Choriocarcinoma
- Teratoma (mature, immature, white malignant transformation)
- Mixed germ cell tumors

Supply 2013

Q1: A 34 year old man within 5 months history of dragging scrotal sensation is found to have enlarged left testis ultrasound reveals a solid mass orchidectomy is performed which reveals a grey white mass

with lobulated appearance immunohistological stain of specimen is positive for placental alkaline phosphatase. (RALP)?

a) **Diagnosis and microscopic pic of lesion?**
b) **Four risk factors for this neoplasm?**

Ans:

It is a seminoma.

Microscopic: Seminoma are soft well demarcated grey white tumor that bulge from the cut surface of the affected testis, microscopically seminoma are composed of large uniform cells with distant cell borders , clear , glycogen rich cytoplasm and round nuclei with conspicuous nucleoli the cells are often arrayed in small lobules with intervening fibrous septa. In 15% cases syncytiotrophoblast are present that are the source of minimally elevated serum HCG.

b)

- Cryptorchid testis
- Androgen sensitivity syndrome
- Klienfielter syndrome
- Peutz-Jegher's syndrome
- Inguinal hernia
- Mumps orchitis

Annual 2014

Q1: A 26 year old man presented with testicular mass. On microscopy of resected mass there were lobules of tumor cells separated by fibrous septa the neoplastic cell is large and round has distant cell membrane clear cytoplasm central nucleus and prominent nucleoli?

a) **Diagnosis?**
b) **Name 2 markers of this tumor?**
c) **Enumerate 3 types of tumor?**

Ans: a) Germ cell tumor that is seminoma

b)

- HCG
- Placental alkaline phosphatase

c)

- Spermatocytic seminoma
- Embryonal carcinoma
- Teratoma
- Choriocarcinoma
- Yolk sac tumor

Supply 2014

Q1: A 67 year old man has three year history of increasing difficulty of micturition including frequency hesitancy and dribbling. DRE reveals enveloped prostate the consistency is rubbery and nodular and not tender to palpation one year ago his serum PSA was 5ng/ml and still that level when resected?

a) **Diagnosis?**
b) **Hormonal mechanism in pathogenesis?**
c) **Complications of the disease if left untreated?**

Ans: a) Benign prostatic hyperplasia BPH.

b)

Increase sensitivity of prostate tissues to dihydroxytestosterone DHT causes the hyperplasia of

glandular and stromal cells DHT binds to nuclear androgen receptors which regulate the expression of genes that support the growth and survival of prostatic epithelium and stromal cells, the stromal cell contains 5 alpha reductase and are the sites of DHT synthesis.

Glandular hyperplasia develops nodules in the transitional zone.

Stromal hyperplasia develops nodules in the peri urethral zone

c)

- Obstructive uropathy (post renal azotemia, bilateral hydronephrosis, bladder diverticula , bladder wall smooth muscle hyperplasia)
- Bladder infection
- Prostatic infarcts

Q: A 35 year male presents to OPD with rapidly enlarging left lingual mass for three months history reveals presence of small swelling since birth at same site on examine left scrotal sac is empty?

a) Diagnosis?

b) Describe morphology of teratoma?

Ans: a)

Cryptorchidism of the left testis

b) Three types of teratoma

i) Mature teratoma

ii) Immature teratoma

iii) Teratoma with malignant transformation.

Mature Teratoma: Is composed of disorderly mixture of a variety well differentiated structures such as cartilage smooth muscles, intestinal and respiratory epithelium.

Immature Teratoma: Are composed incompletely differentiated and primitive or embryonic tissues along with some mature elements. Primitive or embryonic tissue commonly present is poorly formed cartilage, mesenchymal, neural tissues, abortive eye, intestinal and respiratory tissues etc. Mitosis is usually frequent.

Teratoma With Malignant Transformation: this is rare form in which one or more tissue elements show malignant transformation, such malignant changes resemble morphologically with typical malignancy in other organ and tissues and commonly includes rhabdomyosarcoma , squamous cell carcinoma and adenocarcinoma.

SOLVED BY:
AQEEL ZARAIT &
M ZEESHAN CHAUDHARY
MOHTARIMA BENAZIR BHUTTO SHAHEED MEDICAL COLLEGE,
MIRPUR, AZAD JAMMU & KASHMIR.

Section 8: Breast

Annual 2003

Q1: a) Classify tumors of breast.
b) Give morphological features of fibro adenoma of breast.
c) Give an outline of pathogenesis of breast cancer in association with different receptors pertaining to breast in female.
Ans:
a)
Benign tumors:

- Fibro adenoma
- Phyllodes tumor
- Intraductal papilloma

Malignant tumors:

Non invasive:

- DCIS
- LCIS(lobular carcinoma insitu)

Invasive:

- Invasive ductal carcinoma
- Invasive lobular carcinoma
- Medullary carcinoma
- Tubular carcinoma

b)
Gross:
Size varies from 1-10 cm in diameter.
Well circumscribed rubbery grayish white nodules that bulges above the surrounding tissue and often contain slit like spaces
Microscopy:
Fibroblastic stroma containing glandular and cystic spaces.
Glandular spaces may be open round to oval and irregular (pericanalicular fibro adenoma) or compressed irregular clefts due to extensive proliferation (intracanalicular fibro adenoma).
c)
1) Germ line BRCA2 mutation →flat epithelial atypia → atypical ductal hyperplasia →DCIS→ER positive HER2 negative
2) Germ line TP53 Mutation → atypical apocrine adenosis→DCIS→HER2 positive
3) Germ line BRCA1 mutation →DCIS→ER negative HER2 positive.

Supply 2003

Q1: A 45 years old lady complains of a lump in her right breast which is hard in consistency.
a) Which relatively noninvasive investigation will you advice in order to evaluate benign or malignant nature of the lesion?
b) What are prognostic markers of carcinoma of breast?
Ans:
a)

- mammography
- ultrasonography
- MRI

b)

Major prognostic markers:

1) Invasive carcinoma vs. carcinoma insitu
2) Distant metastasis
3) Lymph nodes metastasis
4) Tumor size
5) Local advanced
6) Inflammatory carcinoma
7) Lymph vascular invasion

Minor prognostic factors

1) Molecular subtype
2) Special histological type
3) Histological grade
4) Proliferative rate
5) Estrogen and progesterone
6) HER2 over expression

Supply 2004

Q1: a) Name benign and malignant neoplasm of the breast.
b) Give gross and microscopic appearance of fibro adenoma of breast
Ans: See Q1 in Annual 2003 above.

Annual 2005

Q1: Write a short note on fat necrosis breast?
Ans:

Painless, palpable mass, skin thickening or retraction or mammographic densities or calcifications. About half of affected women have a history of breast trauma or prior surgery.

Acute lesions may be hemorrhagic and contain central areas of liquefactive necrosis with and macrophages.

Giant cells calcifications and hemosiderin make their appearance and eventually the focus is replaced by scar tissue.

Ill defined, firm ,grey- white foci are seen grossly.

Annual 2006

Q1: a) Classify breast tumors
b) Give the morphology of lobular carcinoma
Ans:
a)

Benign tumors:

- Fibro adenoma
- Phyllodes tumor
- Intraductal papilloma

Malignant tumors:

Non invasive:

- DCIS
- LCIS(lobular carcinoma insitu)

Invasive:

- Invasive ductal carcinoma
- Invasive lobular carcinoma

- Medullary carcinoma
- Tubular carcinoma

b)

- LCIS consists of uniform population of cells with oval or round nuclei and small nuclei including ducts and lobules.
- Mucin positive signet ring cells
- Cribriform spaces or papillae
- No calcification
- No necrosis
- Indian file like pattern
- Cells discohesively arrange
- ER and PR expressed while HER2 not observed

Supply 2006

Q1: a) Name benign tumors of breast.
b) Give morphological features of fibro adenoma of breast.
Ans: See Q1 in Annual 2003 above.

Annual 2007

Q1: a) A pathologist is grading a breast tumor according to scarf-bloom-Richardson system. What 3 morphological features will he access?
b) What is the significance of ER/PR and Her2-neu status in breast carcinoma?
Ans:
a)

- 1: nuclear grade
  - 2 : tubules formation
  - 3 : mitotic rate
  - Well differentiated
  - Moderately differentiated
  - Poorly differentiated

b)

Over expression of this membrane bound protein is almost always caused by amplification of the gene. Over expression can be determined by immunohistochemically or by fluorescence in situ hybridization. Over expression is associated with poor prognosis.

Supply 2007

Q1: a) List 4 major and 2 minor risk factors of breast cancer.
b) List the evolving morphological spectrum of lesions that eventually results in invasive carcinoma of breast.
Ans:
a) Major:

- Geographic factor
- Age
- Family history
- Pregnancy
- Benign breast disease

Minor:

- Oral contraceptives
- Diet

- Cigarette smoking

Annual 2008

Q1: A mastectomy specimen from a 42 year old female shows a 2 cm tumor which is well differentiated ductal carcinoma of no special type with a minor in situ component. 2 of 14 axillary lymph nodes are positive for metastatic tumor. The tumor is estrogen receptor and progesterone receptor negative and Her2-neu positive. There is no distal metastasis.

a) Which of these tumor characteristics have a greater effect on clinical outcome of this patient?

b) Identify all the prognostic and predictive factors listed here and give relative importance of each.

Ans: a)

b)

1) Tumor size: if tumor size is 1cm then prognosis is excellent in this case tumor is of 2cm so poor prognosis.

2) Lymph nodes involvement: if no node is involved more survival rate 70-80%
One to three nodes involve: survival rate 35-40%
If more than 10 positive: 10-15% survival rate

3) Distant metastasis: no distant metastasis so more curable

4) HER2 over expression →poor survival

Annual 2009

Q1: A 45 years old lady complains of a lump in her right breast which is hard in consistency.

a) Which relatively noninvasive investigation will you advice in order to evaluate benign or malignant nature of the lesion?

b) What are prognostic markers of carcinoma of breast?

Ans:

a)

- CBC (to rule our infection)
- MAMMOGRAPHY (for soft breast tissue i.e. old age)
- Ultrasound (young patient with firm breast tissue)
- Bone scan, MRI, chest x-ray, abdominal ultrasound (for malignancy)

b)

- Estrogen receptor (ER) and progesterone receptor (PR). Breast cancer cells with ER and/or PR depend on estrogen and/or progesterone to grow. Testing for ER and PR is done to find out if a cancer is likely to be successfully treated with hormone therapy, such as tamoxifen
- Human epidermal growth factor receptor 2 (HER2). This protein is present in large amounts in 20% to 25% of breast cancers. Anti-HER2 treatments block HER2 to stop the growth of cancer cells. Testing for HER2 helps doctors know if a cancer can be treated with anti-HER2 treatments, such as trastuzumab (Herceptin), and in some cases, may suggest whether additional treatment with chemotherapy may be helpful.
- Cancer antigen 15-3 (CA 15-3), cancer antigen 27.29 (CA 27.29), and carcinoembryonic antigen (CEA)
- Urokinase plasminogen activator (uPA) and plasminogen activator inhibitor (PAI-1). Higher-than-normal levels of these tumor markers in the cancer tissue may mean that the cancer is more aggressive (faster growing).

Supply 2009

Q1: A 60 yrs old female presents with a hard lump in the breast. It was excised and diagnosed as invasive ductal carcinoma of the breast. No special type

a) Describe morphology

b) What further investigation will u suggest on the biopsy tissue before u start a treatment?

Ans:

a)

Gross appearance:

Most common tumors: firm to hard, radio dense mass with irregular boarders

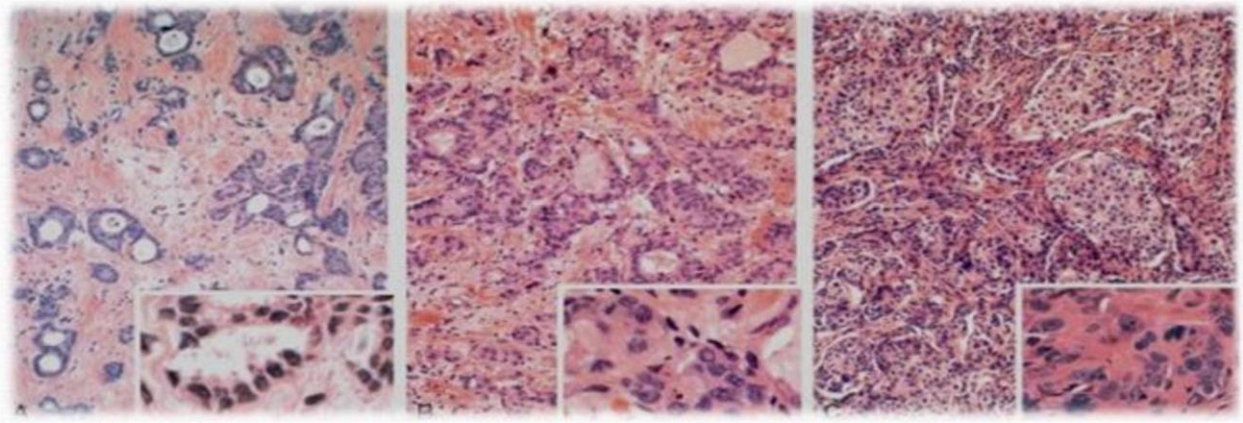
Less frequently: well circumscribed boarders, soft consistency

- When cut/scrapped, characteristic grafting sound d/t small, pin point foci or streaks of chalky white elastic stroma and occasionally small foci of calcification.

Histologic

Invasive Carcinoma – NST- HPE

Features	Well diff. Ca	Mod. diff.Ca	Poorly diff. Ca.
Tubule formation	Prominent	Less,solid clusters/ single infiltrating cells	Ragged nests/solid sheets of cells
Nuclei	Small,round,mono morphic	Greater nuclear pleomorphism	Nuclei – enlarged,irregular.
Mitotic figures	Rare	Present	Numerous
Proliferation rate	-	-	High
Tumour necrosis	-	-	Present



b)

After studying the morphology of the biopsy material, following studies are done to find out the causing mutation, thus defining prognosis and designing a proper treatment regimen.

- MOLECULAR SUBTYPE:
- SPECIAL HISTOLOGIC TYPE
- HISTOLOGIC GRADE
- PROLIFERATIVE RATE
- ESTROGEN AND PROGESTERON RECEPTORS
- HER2

Annual 2010

Q1: A top tennis player was diagnosed with fibrocystic disease of the breast with atypical ductal hyperplasia. Routine mammography showed an area of increased density.

a) How does this diagnosis affect the patient's risk of developing breast cancer?

b) What other factors will modify the risk/ (inc. or Dec.)

c) Define atypical hyperplasia

Ans:

a)

The relative risk of developing carcinoma in fibrocystic disease is 3% but due to atypia it is increased to 4 to 5 (13%-17%)

b)

Risk increased by

- Nulliparous women
- Early menarche
- Late menopause
- Radiation exposure
- Tobacco
- Environmental toxins

Risk decreased by

- Bilateral prophylactic mastectomy
- Estrogen antagonist (tamoxifen)

c)

Atypical Ductal Hyperplasia is a precancerous condition in which cells become monochromic with complex architectural pattern.

Supply 2010

Q1: A 60 years old female presents with a hard lump in the breast. It was incised and diagnosed an invasive ductal carcinoma breast. No special type

(a) Describe morphology

(b) What further investigations will you suggest on biopsy tissue before starting treatment in this patient?

Ans: See Q1 in Supply 2009 above.

Annual 2011

Q1: An 18 years old female presents with solitary, discrete, movable mass in the right breast which enlarges late in the menstrual cycle. FNAC is performed. Which shows a benign breast lesion?

(A) What is the most likely diagnosis

(B) Give morphological features of the lesion

Ans:

a) Fibro adenoma

b)

Gross morphology

Spherical, sharply circumscribed, rubbery, grayish white, freely movable nodules -bulge above the surrounding tissue and contain slit like spaces.

Size, less than 1 cm to large tumors that replace most of the breast

Occur mostly in upper quadrant of breast

Microscopic

- Delicate and myxoid stroma resembling normal intralobular stroma, composed of loose fibroblastic stroma containing glandular and cystic spaces lined by single or multiple layers of cells
- Glandular spaces may be open, round to oval and regular (pericanalicular fibro adenoma) or compressed, irregular clefts due to extensive stromal proliferation (intra canalicular fibro adenoma)

Supply 2011

Q1: 55 years old female presented with an eczema like lesion on her left nipple shows large malignant polygonal cells with pale cytoplasm interspread with an otherwise normal epidermis of nipple

(A) What is diagnosis?
(B) What type of malignant breast lesion you expect to find underneath the nipple?
(C) What are various types of underlying breast lesion?

Ans:

a) Paget disease of nipple

b)

Ductal carcinoma in situ will leads to invasive ductal carcinomas, Apocrine carcinoma, and Micro papillary carcinoma

c)

- Ductal carcinoma in situ (DCIS)
- Comedo DCIS
- Non comedo DCIS

Annual 2012

Q1: Give an account of ductal carcinoma in situ of breast

Ans:

Ductal carcinoma in situ is malignant proliferation of epithelial cells limited to ducts and lobules by basement membrane.

Features:

- Architecture of the tissue is not preserved
- Calcification
- Always detected via mammography
- No nipple discharge

Types:

- Comedo dics
- Non comedo DICS
- Paget disease

Risk factors for recurrence:

- High nuclear grade and necrosis
- Extent of disease
- **Positive surgical margins**

Supply 2012

Q1: A 60 yrs old female presents with a firm lump in the right breast. On mammography examination areas of calcification are seen. Biopsy of the lump shows pleomorphic cells with hyperchromatic nuclei without invasion of the basement membrane

(A) What is most likely diagnosis
(B) Name architectural subtypes of this pathology
(C) Give morphological picture of comedo carcinoma

Ans:

a) Ductal carcinoma in situ

b)

- Comedo DCIS
- NON COMEDO DCIS
- Solid DCIS
- Papillary DCIS

c)

Characterized by solid sheet of pleomorphic cells with high grade hyperchromatic nuclei and area of central necrosis, Periductal connective tissue, Chronic inflammation

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Annual 2013

Q1: A 50 years old women presents with 2cm firm mass in upper outer quadrant of her RT breast. Biopsy material shows atypical cells within the ducts with extensive necrosis. No invasion into surrounding fibrous tissue is seen

(A) What is most likely diagnosis?

(B) Give role of ER, PR HER-2/Neu in breast cancer prognosis and treatment.

Ans:

a) Ductal carcinoma in situ

b)

- ER/PR +ve tumors gives best response of hormonal therapy so best prognosis
- HER-2/Neu positive patients give better response to monoclonal antibodies (transtuzumab) thus better prognosis.

Supply 2013

Q1: A 28 years old female presents with lump in the rt. Breast for past 1 year. She gave a history of child birth 4 months back. The lump has inc. in size since then. On examination the lump is freely mobile and sharply circumscribed.

(A) What is most likely diagnosis

(B) Write morphology of fibro adenoma.

Ans:

a) Fibro adenoma

b)

Morphology

Gross:

- Tumor varies in size from <1cm to large tumors
- Well circumscribed, rubbery, grayish white nodule bulging above the surrounding tissue with often slit like spaces

Microscopic

- Delicate and often myxoid stroma resembling intralobular stroma
- Epithelium may be surrounded by stroma (pericanicular pattern)
- Epithelium may be compressed and distorted by it (intra canalicular pattern)

Annual 2014

Q1: A 55 year old women presented with a 3 cm mass in upper outer quadrant of rt. Breast since last 3 month. She had needle aspiration cytology positive for malignant cells.

(A) What different types of breast cancers she can suffer from

(B) Enlist the risk factors of carcinoma breast

Ans:

a)

Noninvasive/ in situ carcinoma

- Intraductal carcinoma
- Lobular carcinoma in situ

Invasive carcinoma

- Infiltrating (invasive) ductal carcinoma
- Infiltrating (invasive) lobular carcinoma
- Medullary carcinoma
- Colloid (mucinous) carcinoma
- Papillary carcinoma
- Tubular carcinoma

- Adenoid cystic carcinoma
- Secretory carcinoma
- Inflammatory carcinoma
- Carcinoma with metaplasia
- Paget's disease of nipple

b)

- AGE → incidences inc. with age- peaks at 75-80 yrs
- GENDER → only 1% in men
- AGE AT MENARCHE & MENOPAUSE → early menarche and late menopause increases the risk
- AGE AT FIRST LIVE BIRTH → nulliparous women/late pregnancy →proliferation of cells with pre neoplastic charges
- FIRST- DEGREE RELATIVES WITH BREAST CANCER → mother, sister → inc. risk increased
- GENETIC MUTATION
- RACE/ETHINICITY
- BENIGN BREAST DISEASE
- ESTROGEN EXPOSURE
- BREAST DENSITY
- RADIATION EXPOSURE
- CARCINOMA OF CONTRALATERAL BREAST
- DIET
- OBESITY
- EXERCISE
- BREAST FEEDING
- ENVIRONMENTAL TOXINS

Annual 2015

Q1: A 55 yr. old women presented with a 3 cm mass in the upper outer quadrant of right breast since last 3 months. She had a needle aspiration cytology positive for malignant cells?

A) What different types of cancer she can suffer from?

B) Enlist the risk factors of carcinoma of breast

Ans: See Q1 in Annual 2014 above.

Supply 2015

Q1: A 25 yr. female presents with a vague nodularity of breast. There is a family history of breast cancer. Ultrasound examination reveals multiple simple cysts likely to be benign

A) What is likely diagnosis

B) What is Paget disease of the nipple?

Ans:

a) Non proliferative Breast change (fibrocystic disease of breast)

b)

Paget's disease is a rare manifestation of breast cancer (1%-4%) that presents as a unilateral erythematous eruption with a scale crust.

- Pruritis is common
- Malignant cells extend from DCIS into the nipple skin without crossing the basement membrane, through the ductal system via lactiferous sinuses.
- The tumor cells will disrupt the normal epithelial barrier, allowing the extracellular fluid to seep out onto the nipple surface.

Diagnosis:

Paget's disease of nipple is detected by

- Nipple biopsy
- Cryptologic preparation of the exudate

Solved By
Laraib Amjad
Allama Iqbal Medical College, Lahore
&
Faiza Rafique
Rashid Latif Medical College, Lahore

Section 9: Female Reproductive System

Annual 2003

Q1: Enumerate Hormone secreting tumors of ovary. (3)

Ans: Most of the sex cord cell tumors secrete hormones.

- Granulosa cell tumors
- Pure thecomas
- Sertoli- Leydig cell tumors
- Hilus cell tumors (Pure leydig cell tumor)

(Big Robbins, 9th edition. Page 1032-1034)

Annual 2004

Q1: a) Enlist Ovarian Neoplasms (5)

b) Give gross and microscopic features of mature teratoma (5)

Ans:

Table 22-5 WHO Classification of Ovarian Neoplasms

1-Surface Epithelial-Stromal Tumors:

A- Serous tumors

a) Benign (cystadenoma, cystadenofibroma)
b) Borderline (serous borderline tumor)
c) Malignant (low- and high-grade serous adenocarcinoma)

B- Mucinous tumors

a) Benign (cystadenoma, cystadenofibroma)
b) Borderline (mucinous borderline tumor)
c) Malignant (mucinous adenocarcinoma)

C- Endometrioid tumors

a) Benign (cystadenoma, cystadenofibroma)
b) Borderline (endometrioid borderline tumor)
c) Malignant (endometrioid adenocarcinoma)

D- Clear cell tumors

a) Benign
b) Borderline
c) Malignant (clear cell adenocarcinoma)

E- Transitional cell tumors

a) Benign Brenner tumor
b) Brenner tumor of borderline malignancy
c) Malignant Brenner tumor

F- Epithelial-stromal

G- Adenosarcoma

H- Malignant müllerian tumor

2-Sex Cord-Stromal Tumors:

a) Granulosa tumors
b) Fibromas
c) Fibrothecomas
d) Thecomas
e) Sertoli-Leydig cell tumors
f) Steroid (lipid) cell tumors

3-Germ Cell Tumors:

a) Teratoma
   i. Immature
   ii. Mature
       Solid
       Cystic (dermoid cyst)

b) Monodermal (e.g., struma ovarii, carcinoid)
c) Dysgerminoma
d) Yolk sac tumor
e) Mixed germ cell tumors

4-Metastatic Cancer From Non-ovarian Primary:

a) Colonic, appendiceal
b) Gastric
c) Pancreaticobiliary
d) Breast

b)

Gross:

- Benign teratomas are bilateral in 10% to 15% of cases.
- Characteristically they are unilocular cysts containing hair and sebaceous material.
- Sectioning reveals a thin wall lined by an opaque, gray-white, wrinkled epidermis, frequently with protruding hair shafts.
- Within the wall, it is common to find grossly evident tooth structures and areas of calcification.

Microscopically:

- the cyst wall is composed of stratified squamous epithelium with underlying sebaceous glands, hair shafts, and other skin adnexal structures. In most cases tissues from other germ layers can be identified, such as cartilage, bone, thyroid, and neural tissue.
- Dermoid cysts are sometimes incorporated within the wall of a mucinous cystadenoma.
- About 1% of the dermoids undergo malignant transformation, most commonly to squamous cell carcinoma, but also to other cancers as well (e.g., thyroid carcinoma, melanoma).

Annual 2006

Q1: a) Name the various risk factors of carcinoma cervix. (3)
b) Give the clinical staging of Carcinoma Cervix. (3)

Ans:

These are related to both host and viral characteristics. These are

- Exposure to HPV
- Viral oncogenicity
- Inefficiency of immune response
- Presence of Co-carcinogens

These Include:

1. Multiple sexual partners
2. A male partner with multiple previous or current sexual partners
3. Young age at first intercourse
4. High parity
5. Persistent infection with a high oncogenic risk HPV, e.g., HPV 16 or HPV18
6. Immunosuppression
7. Certain HLA subtypes
8. Use of oral contraceptives
9. Use of nicotine

b)

Cervical cancer is staged as follows:

Stage 0—Carcinoma in situ (CIN III, HSIL)
Stage I—Carcinoma confined to the cervix
Ia — Preclinical carcinoma, that is, diagnosed only by Microscopy
Ia1 — Stromal invasion no deeper than 3 mm and no wider than 7 mm (so-called microinvasive carcinoma)
Ia2 — Maximum depth of invasion of stroma deeper than 3 mm and no deeper than 5 mm taken from base of epithelium; horizontal invasion not more than 7 mm
Ib — Histologically invasive carcinoma confined to the cervix and greater than stage Ia2
Stage II—Carcinoma extends beyond the cervix but not to the pelvic wall. Carcinoma involves the vagina but not the lower third.
Stage III—Carcinoma has extended to the pelvic wall. On rectal examination there is no cancer-free space between the tumor and the pelvic wall. The tumor involves the lower third of the vagina.
Stage IV—Carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum. This stage also includes cancers with metastatic dissemination.

Supply 2006

Q1: Name trophoblastic tumors. Their site of origin. Describe briefly morphology of Choriocarcinoma. (1, 1, 4)
Ans:

- Choriocarcinoma

Site of Origin:
More commonly placental origin. Less likely in ovaries.
Morphology:

- More commonly of placental origin, choriocarcinoma, like the yolk sac tumor, is an example of extraembryonic differentiation of malignant germ cells.
- It is generally held that a germ cell origin can be confirmed only in prepubertal females, because after this age an origin from an ovarian ectopic pregnancy cannot be excluded.
- Most ovarian choriocarcinomas exist in combination with other germ cell tumors, and pure choriocarcinoma is extremely rare.
- They are histologically identical to the more common placental lesions.
- The ovarian tumors are aggressive and have usually metastasized hematogenously to the lungs, liver, bone, and other sites by the time of diagnosis.
- Like all choriocarcinomas they elaborate high levels of chorionic gonadotropins, which may be helpful in establishing the diagnosis or detecting recurrences.
- In contrast to choriocarcinomas arising in placental tissue, those arising in the ovary are generally unresponsive to chemotherapy and are often fatal.

Annual 2007

Q1: A 45 year old female patient developed a peanut sized nodule in an old midline laparotomy scar, which becomes painful during menstrual period. The excised nodule consists of normal looking endometrial tissue gland and stroma.
a) Give three theories of pathogenesis of such lesions. (3)
b) List four sites of this process other than the abdominal wall. (2)
Ans:
a) Pathogenesis: The pathogenesis of endometriosis remains elusive. Proposed origins of endometriotic lesions fall into two main categories:
1) those that propose an origin from the uterine endometrium and
(2) those that propose an origin from cells outside the uterus that have the capacity to give rise to endometrial tissue. The leading theories are as follows:

• **The regurgitation theory** proposes that endometrial tissue implants at ectopic sites via retrograde flow of menstrual endometrium. Retrograde menstruation through the fallopian tubes occurs regularly even in normal women and can explain the distribution of endometriosis within the peritoneal cavity.
• **The benign metastases** theory holds that endometrial tissue from the uterus can "spread" to distant sites (e.g., bone, lung, and brain) via blood vessels and lymphatic channels.
• **The metaplastic theory** suggests that endometrium arises directly from coelomic epithelium (mesothelium of pelvis or abdomen), from which the müllerian ducts and ultimately the endometrium itself originate during embryonic development. In addition, mesonephric remnants may undergo endometrial differentiation and give rise to ectopic endometrial tissue.
• **The extrauterine stem/progenitor cell** theory is a recent idea that proposes that stem/progenitor cells from the bone marrow differentiate into endometrial tissue.

b) Sites:

It occurs in the following sites, in descending order of frequency:
(1) ovaries;
(2) uterine ligaments;
(3) rectovaginal septum;
(4) cul de sac;
(5) pelvic peritoneum;
(6) large and small bowel and appendix;
(7) mucosa of the cervix, vagina, and fallopian tubes; and
(8) laparotomy scars.

Supply 2007

Q1: A 55-years-old female has a benign cystic ovarian epithelial neoplasm:
a) What are the two major types of these tumors? How do they differ in their epithelial lining?
b) List three major categories of primary ovarian neoplasms according to their cell/tissue origin. Give an example of each.

Ans: a)

1- Serous Tumors
2- Mucinous Tumors

Serous tumors	**Mucinous Tumors**
Serous tumors may present as either a multicystic lesion in Which **papillary epithelium** is contained within a few fibrous walled cysts **(intracystic)** or as a mass projecting from the ovarian surface? Benign tumors typically have a smooth glistening cyst wall with no epithelial thickening or with small papillary projections.	Benign mucinous tumors are characterized by a lining of **tall, columnar epithelial cells with apical mucin that lack cilia.** The vast majority demonstrates gastric or intestinal type differentiation, with uncommon tumors showing endocervical type mucinous differentiation instead

b)

Neoplasm	**Cell/tissue origin**	**Example**
Surface Epithelial stromal tumors	Mullerian Epithelium	Serous tumors Mucinous tumors
Germ cell tumors	Germ cells	Teratoma dysgerminomas
Sex cord stromal tumors	Ovarian Stroma; derivative of Sex cord of embryonic gonads.	Granulosa cell tumors Leydig cell tumors

Annual 2008

Q1: A 45-year-old female with multiple sex partners has a cervical PAP smear done as a part of routine screening for cervical cancer. The smear is reported as CIN 2 with advice for further workup;

(a) Screening for DNA of which virus is most pertinent to the current scenario?

(b) What role does the said virus play in pathogenesis of cervical cancer?

Ans: a) HPV

b)

Pathogenesis:

- High-risk HPVs are by far the most important factor in the development of cervical cancer. **HPVs** are DNA viruses that are typed based on their DNA sequence and grouped into those of high and low oncogenic risk.
- There are **15** high risk HPVs that are currently identified, but **HPV-16** alone accounts for almost 60% of cervical cancer cases, and
- **HPV-18** accounts for another 10% of cases;
- other HPV types contribute to less than 5% of cases, individually.
- Most HPV infections are transient and are eliminated by the immune response in the course of months.
- On average, 50% of HPV infections are cleared within 8 months, and 90% of infections are cleared within 2 years.
- The duration of the infection is related to HPV type; on average, infections with high-risk HPVs last longer than infections with low oncogenic risk HPVs (13 months versus 8 months, respectively).
- Persistent infection increases the risk of the development of cervical precursor lesions and subsequent carcinoma.
- The ability of HPV to act as a carcinogen depends on the viral proteins E6 and E7, which interfere with the activity of tumor suppressor proteins that regulate cell growth and survival.
- Although HPV infects immature squamous cells, viral replication occurs in maturing squamous cells.
- Normally, these more mature cells are arrested in the G1 phase of the cell cycle, but they continue to actively progress through the cell cycle when infected with HPV, which uses the host cell DNA synthesis machinery to replicate its own genome.
- viral E7 protein binds the hypo phosphorylated (active) form of RB and promotes its degradation via the proteasome pathway, and also binds and inhibits p21 and p27, two important cyclin-dependent kinase inhibitors.
- Removal of these controls not only enhances cell cycle progression, but also impairs the ability of cells to repair DNA damage.
- This defect in DNA repair is exacerbated by the viral E6 proteins of high-risk HPV subtypes, which bind to the tumor suppressor protein p53 and promote its degradation by the proteasome.
- In addition, E6 up-regulates the expression of telomerase, which leads to cellular immortalization.
- The net effect is increased proliferation of cells that are prone to acquire additional mutations that may lead to cancer development.
- By contrast to high-risk HPVs, the E7 proteins of low risk HPVs bind RB with lower affinity, while the E6 proteins of low-risk HPVs fail to bind p53 altogether and instead appear to dysregulate growth and survival by interfering with the Notch signaling pathway.
- Another factor that contributes to malignant transformation by HPV is the physical state of the virus.
- The viral DNA is integrated into the host cell genome in most cancers.
- This configuration increases the expression of E6 and E7 genes, and may also dysregulate oncogenes near the sites of viral insertion, such as MYC.

- By contrast, viral DNA is extrachromosomal (episomal) in precursor lesions associated with high risk HPVs and in condylomata associated with low risk HPVs.
- Even though HPV has been firmly established as a common cause of cervical cancer, it is not sufficient to cause cancer.
- This conclusion is supported by the fact that a high percentage of young women are infected with one or more HPV types during their reproductive years, but only a few develop cancer.
- Thus, other factors, such as exposure to co-carcinogens and host immune status, influence whether an HPV infection regresses or persists and eventually progresses to cancer.

Annual 2009

Q1: A 28- year old female goes to her physician for routine examination. Pelvic examination reveals no abnormalities. A PAP smear report indicates severely dysplastic cells. A cervical biopsy shows CIN III.

(a) Give the important risk factors for CIN and invasive carcinoma of cervix. (2)

(b) Give the spectrum of precancerous lesions of the cervix based on histology, progressing to Carcinoma (2)

Ans: a)

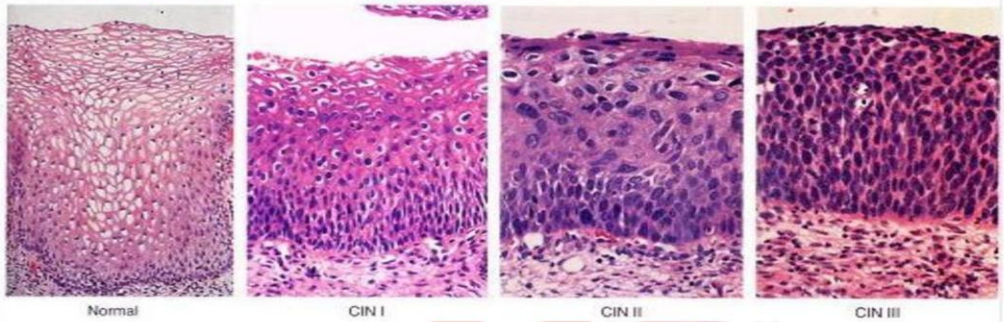
These are related to both host and viral characteristics. These are

- Exposure to HPV
- Viral oncogenicity
- Inefficiency of immune response
- Presence of Co-carcinogens

These Include:

i. Multiple sexual partners
ii. A male partner with multiple previous or current sexual partners
iii. Young age at first intercourse
iv. High parity
v. Persistent infection with a high oncogenic risk HPV, e.g., HPV 16 or HPV18
vi. Immunosuppression
vii. Certain HLA subtypes
viii. Use of oral contraceptives
ix. Use of nicotine

b)



Spectrum of cervical intraepithelial neoplasia: normal squamous epithelium for comparison; LSIL (CIN I) with koilocytic atypia; HSIL (CIN II) with
progressive atypia and expansion of the immature basal cells above the lower third of the epithelial thickness; HSIL (CIN III) with diffuse atypia, loss of maturation,
and expansion of the immature basal cells to the epithelial surface.

Based on the cells of origin, enumerate the most common carcinomas of cervix. (1)

- Squamous cell carcinoma
- Adenocarcinoma

Supply 2009

Q1: A 45-years old female feels pressure sensations but no pain in her pelvic region for the past 6 months. On examination, there is right adnexal mass. An ultrasound scan shows a 10cm fluid filled cystic mass in her right ovary. A FNAC is performed and cytological examination of clear fluid aspirated from the mass reveals clusters of malignant cells surrounding psammoma bodies.

(a) What is likely diagnosis? (1)

(b) Give the gross and microscopic appearance of this tumor. (4)

Ans: a)

Serous cystadenocarcinoma

b)

Gross:

- Serous tumors may present as either a multicystic lesion in which papillary epithelium is contained within a few fibrous walled cysts (intracystic) or as a mass projecting from the ovarian surface.
- Benign tumors typically have a smooth glistening cyst wall with no epithelial thickening or with small papillary projections.
- Borderline tumors contain an increased number of papillary projections Larger areas of solid or papillary tumor mass, tumor irregularity, and fixation or nodularity of the capsule are features associated with malignancy.
- Bilaterality is common, occurring in 20% of benign serous cystadenomas, 30% of serous borderline tumors, and approximately 66% of serous carcinomas.
- A significant proportion of both serous borderline tumors and malignant serous tumors involve the surface of the ovary

Microscopy:

- the cysts are lined by columnar epithelium, which has abundant cilia in benign tumors.
- Microscopic papillae may be found.
- **Serous borderline tumors** exhibit increased complexity of the stromal papillae, stratification of the epithelium and mild nuclear atypia, but invasion of the stroma is not seen.
- This epithelial proliferation often grows in a delicate, papillary pattern referred to as "micropapillary carcinoma," which is thought to be the precursor to **low-grade serous carcinoma.**
- **High-grade serous carcinomas** are distinguished from low-grade tumors by having more complex growth patterns and widespread infiltration or frank effacement of the underlying stroma.
- The individual tumor cells display marked nuclear atypia, including pleomorphism, atypical mitotic figures, and multinucleation.
- The serous tubal intraepithelial carcinomas consist of cells morphologically identical to high-grade serous carcinomas but are distinguished by the lack of invasion.
- The cells of invasive high-grade serous carcinoma can even become so undifferentiated that serous features are no longer recognizable.
- Concentric calcifications (psammoma bodies) characterize serous tumors, but are not specific for neoplasia.
- Ovarian serous tumors, both low- and high-grade, have a propensity to spread to the peritoneal surfaces and omentum and are commonly associated with the presence of ascites.
- As with other tumors, the extent of the spread outside the ovary determines the stage of the disease.

Annual 2010

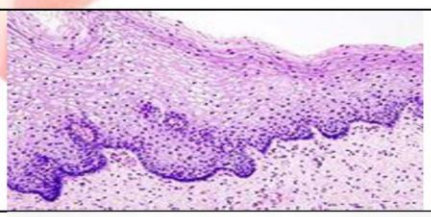
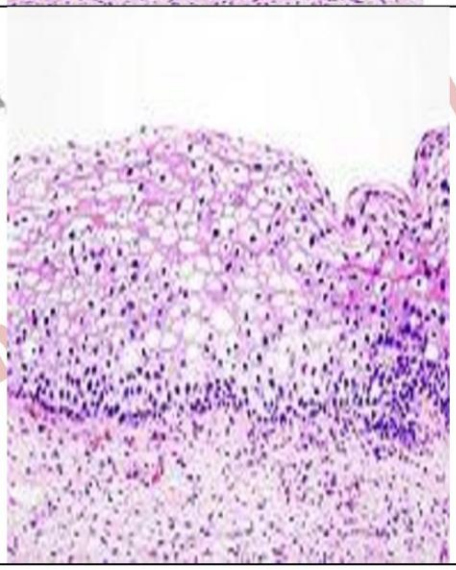
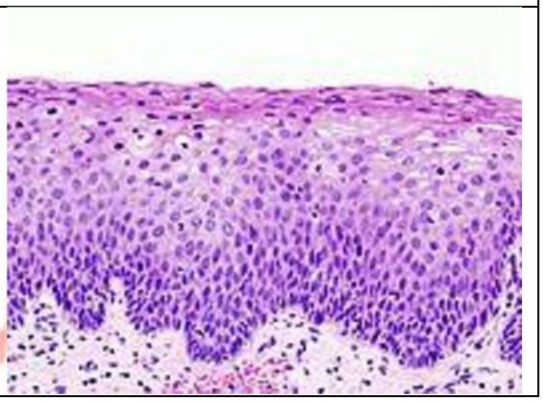
Q1: A cervical biopsy from 35 year old sexually active female is submitted to you for reporting;

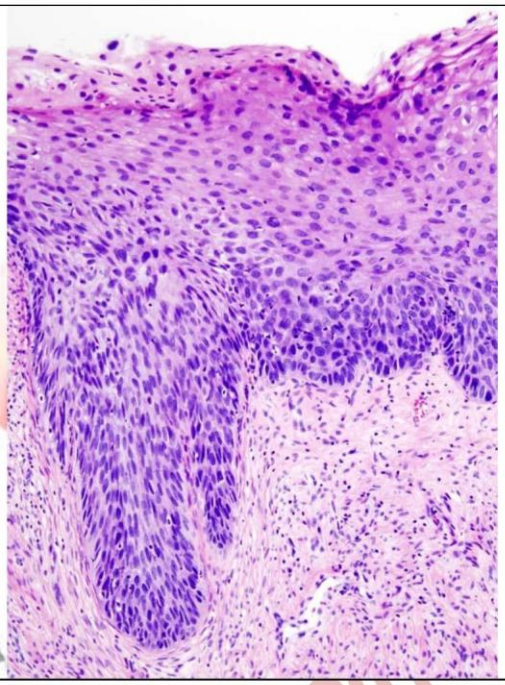
Previous PAP smear exam has shown low grade intraepithelial neoplasia on two occasions and a high grade intraepithelial lesion subsequently.

(a) Outline the grading system you would use to histologically classify the cervical epithelial lesions in this patient. (4)

(b) What are the two commonest HPV genotypes associated with high grade cervical intraepithelial lesions? (01)

Ans:

Histology/Grade	Corresponding Cytology	Description	Image
-------	----------	Normal Cervical epithelium	
CIN (Grade 1)	LSIL	The least risky type represents only mild dysplasia, or abnormal cell growth.[3] It is confined to the basal 1/3 of the epithelium. This usually corresponds to infection with HPV, and may be cleared by immune response, though it can take several years to clear.	
CIN 2/3	HSIL	Formerly subdivided into CIN2 and CIN3.	
CIN 2 (Grade 2)		Moderate dysplasia confined to the basal 2/3 of the epithelium	

CIN 3 (Grade 3)		Severe dysplasia that spans more than 2/3 of the epithelium, and may involve the full thickness. This lesion may sometimes also be referred to as cervical carcinoma in situ.	

b) HPV 16 and 18. Sometimes 31 n 33 as well

Supply 2011

Q1: List the four major groups of ovarian tumors. Which ovarian tumors are associated with BRCA1 and BRCA 2 mutations? (4, 1)

Ans:

Four groups;

1- Surface Epithelial stromal tumors
2- Sex cord-stromal tumors
3- Germ cell tumors
4- Metastatic tumors from non ovarian primary

BRCA 1 & 2:

Serous tumors

Annual 2012

Q1: A 42-years old female complains of heavy a menstrual period that lasts for several days. This has been occurring for last 3 months and has been associated with pain and fatigue. Physical examination shows large uterus with multiple palpable masses. Lab investigations show her Hb 13.3g/dl and hematocrit 33%.

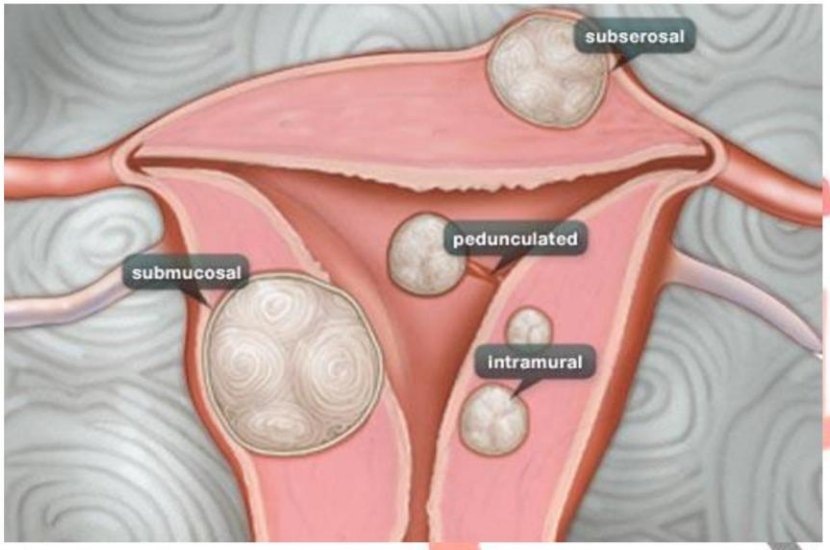
(a) What is the most likely diagnosis? Enumerate the sites of involvement of this tumor. (2)
(b) How does the size of this neoplasm change under the hormonal influence? (1)
(c) Give the microscopic appearance of this tumor. (2)

Ans:

Fibroid (Leiomyomas)

Sites of involvement:

1- Intramural
2- Subserosal
3- Submucosal
4- Pedunculated



b)

Tumor is directly affected by hormones like oestrogen and progesterone. The size increases under the influence of oestrogen. But progesterone is antagonist. It may not regress the size of the tumor but it doesn't allow it to increase in size rapidly.

c)

Leiomyomas are typically composed of bundles of smooth muscle cells that resemble the uninvolved myometrium. Usually, the individual muscle cells are uniform in size and shape and have the characteristic oval nucleus and long, slender bipolar cytoplasmic processes. Mitotic figures are scarce. Benign variants of leiomyoma include atypical or bizarre (symplastic) tumors with nuclear atypia and giant cells, and cellular leiomyomas. Both have a low mitotic index, helping to distinguish these benign tumors from leiomyosarcomas

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Annual 2013

Q1: Routine PAP smear of a 40-years old lady is found to have dysplastic cells. Cervical biopsy revealed full thickness epithelial neoplasm without invasion.

(a) What is the category of CIN? (01)

(b) Give the name of virus with its strains which can be responsible for this lesion? (1)

(c) List the six groups of epithelial tumors of ovary. (3)

Ans: a) CIN 3

b) HPV 16 n 18

c)

1- Serous
2- Mucinous
3- Endometrioid
4- Clear cell
5- Transitional cell
6- Epithelial stromal

Supply 2013

Q1: A 44-years old woman with blood tinged vaginal discharge for one month has biopsy followed by hysterectomy. The gross appearance of uterus shows exophytic irregular lesion around the cervical os.

(a) What is the most likely diagnosis? (1)

(b) Give the staging system of the neoplasm. (3)

(c) Name the risk factors associated with neoplasm. (1)

Ans: a) Ca. Cervix

b)

Cervical cancer is staged as follows:

Stage 0—Carcinoma in situ (CIN III, HSIL)

Stage I—Carcinoma confined to the cervix

Ia—Preclinical carcinoma, that is, diagnosed only by Microscopy.

Ia1—Stromal invasion no deeper than 3 mm and no wider than 7 mm (so-called microinvasive carcinoma)

Ia2—Maximum depth of invasion of stroma deeper than 3 mm and no deeper than 5 mm taken from base of epithelium; horizontal invasion not more than 7 mm

Ib—Histologically invasive carcinoma confined to the cervix and greater than stage Ia2

Stage II—Carcinoma extends beyond the cervix but not to the pelvic wall. Carcinoma involves the vagina but not the lower third.

Stage III—Carcinoma has extended to the pelvic wall. On rectal examination there is no cancer-free space between the tumor and the pelvic wall. The tumor involves the lower third of the vagina.

Stage IV—Carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum. This stage also includes cancers with metastatic dissemination.

c)

These are related to both host and viral characteristics. These are

- Exposure to HPV
- Viral oncogenicity
- Inefficiency of immune response
- Presence of Co-carcinogens

These Include:

i. Multiple sexual partners
ii. A male partner with multiple previous or current sexual partners
iii. Young age at first intercourse
iv. High parity
v. Persistent infection with a high oncogenic risk HPV, e.g., HPV 16 or HPV18
vi. Immunosuppression
vii. Certain HLA subtypes
viii. Use of oral contraceptives
ix. Use of nicotine

Annual 2014

Q1: A 27-year old female sex worker presented with a complaint of white colored vaginal discharge. The cytological examination of her PAP smear revealed numerous atypical cells indicating malignancy.

(a) What is the risk factor associated with this cancer? (2)

(b) Cancer of which part of genital tract is present? (1)

(c) Write down the staging of this cancer. (2)

Ans: a)

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- Exposure to HPV
- Viral oncogenicity
- Inefficiency of immune response
- Presence of Co-carcinogens

These Include:

i. Multiple sexual partners
ii. A male partner with multiple previous or current sexual partners
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iv. High parity
v. Persistent infection with a high oncogenic risk HPV, e.g., HPV 16 or HPV18

vi. Immunosuppression
vii. Certain HLA subtypes
viii. Use of oral contraceptives
ix. Use of nicotine

b) cervix

c) Cervical cancer is staged as follows

Stage 0—Carcinoma in situ (CIN III, HSIL)

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Ia—Preclinical carcinoma, that is, diagnosed only by Microscopy.

Ia1—Stromal invasion no deeper than 3 mm and no wider than 7 mm (so-called microinvasive carcinoma)

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Ib—Histologically invasive carcinoma confined to the cervix and greater than stage Ia2

Stage II—Carcinoma extends beyond the cervix but not to the pelvic wall. Carcinoma involves the vagina but not the lower third.

Stage III—Carcinoma has extended to the pelvic wall. On rectal examination there is no cancer-free space between the tumor and the pelvic wall. The tumor involves the lower third of the vagina.

Stage IV—Carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum. This stage also includes cancers with metastatic dissemination.

Supply 2014

Q1: A 48-year old female presented with the 4 months history of abdominal pain and enlargement is found to have right ovarian mass on CT. Paracentesis yields cloudy fluid contains psammoma bodies and cuboidal cells. Serum CA-125 is markedly raised. Surgery is performed and ovarian mass shows areas of papillary growth on the surface.

(a) What is diagnosis? (1)

(b) Write three microscopic features of the lesion. (3)

(c) Give the importance of CA-125 in this lesion. (1)

Ans: a) Serous Cyst Adenocarcinoma

b)

1- Papillary projection
2- Psammoma bodies
3- Fixation or nodularity of capsule

c)

1- Early detection by raised levels
2- Important in monitoring of tumor treatment
3- Persistent raised levels with chemotherapy indicates poor prognosis.

Supply 2015

Q1: A 63-years old female comes to OPD with post-menopausal bleeding.

(a) What are the possible causes? (2)

(b) Write a note on uterine leiomyoma. (3)

Ans: At this age, the most common cause is Endometrial Cancer Or it may be Ovarian or fallopian tube carcinoma Other causes may include

1- Endometrial Hyperplasia
2- Cervical cancer
3- Atrophic vaginitis
4- Endometrial polyps
5- Endometritis

b)

Gross:

- Leiomyomas are sharply circumscribed, discrete, round, firm, gray-white tumors varying in size from small, barely visible nodules to massive tumors that fill the pelvis.
- Except in rare instances, they are found within the myometrium of the corpus.
- Only infrequently do they involve the uterine ligaments, lower uterine segment, or cervix.

Sites:

They can occur

i. within the myometrium **(intramural)**,
ii. just beneath the endometrium **(submucosal)** or
iii. beneath the serosa **(subserosal).**

Cut section:

- Whatever their size, the characteristic whorled pattern of smooth muscle bundles on cut section usually makes these lesions readily identifiable.
- Large tumors may develop areas of yellow-brown to red softening.
- Leiomyomas are typically composed of bundles of smooth muscle cells that resemble the uninvolved myometrium.

Microscopy:

- Usually, the individual muscle cells are uniform in size and shape and have the characteristic oval nucleus and long, slender bipolar cytoplasmic processes.
- Mitotic figures are scarce.
- Benign variants of leiomyoma include atypical or bizarre (symplastic) tumors with nuclear atypia and giant cells, and cellular leiomyomas.
- Both have a low mitotic index, helping the distinguish these benign tumors from leiomyosarcomas.

SOLVED BY
JAVERIA REHMAN
UNIVERSITY MEDICAL AND DENTAL COLLEGE, FAISALABAD

Section 10: ENDOCRINOLOGY

Annual 2006

Q1. Name salivary gland tumors.
Ans:

Benign	Malignant
Pleomorphic adenoma	Mucoepidermoid carcinoma
Warthin tumor	Adenocarcinoma
Oncocytoma	Acinic cell carcinoma
Basal cell adenoma	Adenoid cystic carcinoma Squamous cell carcinoma
Ductal papilloma	Malignant mixed tumor

Annual 2007

Q1: While examining H & E sections from a thyriodectomy specimen, a pathologist notices a lesion having a follicular pattern of growth.
a. What is the differential diagnosis of such lesions?
b. List the three nuclear features diagnostic for papillary carcinoma of thyroid.
Ans: a)

1. follicular adenoma
2. follicular carcinoma
3. papillary carcinoma (follicular variant)

b)

1. nuclei of papillary carcinoma cells contain very finely dispersed chromatin
2. this chromatin imparts an optically clear appearance, giving rise to designation "ground glass" or "orphan Annie eye" nuclei
3. invaginations of cytoplasm (pseudo-inclusions)
4. psammoma bodies

Q2. Give laboratory findings of serum T3, T4 and TSH levels in typical case of Grave's disease, Hashimotos thyroiditis; diffuse non-toxic goiter and multinodular goiter.
Ans: See Q2 Annual 2010

Annual2008

Q1: A biopsy from soft tissue mass in the iliac fossa revealed metastatic carcinoma most consistent with a diagnosis of metastatic follicular carcinoma of thyroid gland. A search into previous record of the patient showed history of nodulectomy for a 2cm cold thyroid nodule 8 years back. The lesion was reported as follicular adenoma
a. if you were to re-examine the slides from the thyroid nodules which part of the lesion. would you examine most carefully and why?
b. what is most common mode of metastasis for follicular thyroid cancer and what are the commonest site for metastasis?
Ans: a) Capsule, to distinguish it from the follicular adenoma …..to exclude capsular or vascular lesion.
b) Hematogenous spread: lungs, liver, bones

Supply 2008

Q1: A 32 years old female patient presents with visual disturbance, hirsutism and moon facies. 24 hours urinary free cortisol levels are elevated. CT scan shows a space occupying lesion in the pituitary gland impinging on the optic chiasm

a. what is the diagnosis?

b. list two other aetiological types of this disease.

c. How will you determined the etiological cause of this disease in the lab if no radiological data is available?

Ans: a) Cushing disease

b) Cushing syndrome, Ectopic ACTH production from tumor of any organ. E.g. small cell carcinoma of lungs.

c) Administration of dexamethasone normally will suppress pituitary ACTH production, resulting in suppression of adrenal cortisol production & decrease in urinary free cortisol. But in case of ectopic & adrenal Cushing ACTH will not suppress.

Q2: Write down the pathogenesis of the graves disease.

Ans: Graves's disease is autoimmune disorder in which a verity of antibodies may be present in the serum, Including antibodies to the TSH receptor, thyroid peroxisomes & thyroglobulin:

1. Thyroid stimulating immunoglobulin (TSI):
2. thyroid growth stimulating immunoglobulins (TGIs):
3. TSH binding inhibitor immunoglobulins (TBBII):

Annual 2009

Q1: An 18 years old known diabetic girl, suddenly felt ill, developed vomiting and became drowsy. She was taken to the emergency, where on examination she had B.P of 95/60mm of Hg with pulse rate 112/min and cold extremities. She had deep, sighing respiration (kussuaul‟s respiration) and her breath smelt of acetone.

a. what is the likely diagnosis?

b. give any four clinical and four metabolic features of this condition.

Ans: a) Diabetic ketoacidotic coma

b) Severe insulin deficiency→ inc lipolysis→ increase free fatty acid level→ inc FFA oxidation in liver → ketone bodies formation → ketonemia and ketonuria → acidosis→ diabetic coma

1. acetone breath
2. osmotic diuresis
3. dehydration
4. ketonemia, ketonuria
5. metabolic acidosis

Q2: Write a short note on insulin resistance.

Ans: The resistance to the effects of insulin on glucose uptake, metabolism and storage is called insulin resistance. It is characteristic feature of type 2 diabetes. The evidence that insulin resistance has a major role in the pathogenesis of type 2 D.M can be gauged from the findings that:

1. Insulin is often detected 10 to 20 years before the onset of diabetes in predisposed Individuals (offspring of type 2 diabetic).
2. in prospective studies the insulin resistance is the best predictor for subsequent progression to diabetes.

■ genetic defect of insulin receptor and insulin signaling pathway

■ obesity and insulin resistance

Annual2010

Q1: A 45 years old woman presents with painless enlargement of thyroid. On examination her physical and mental responses appear sluggish. Histological examination of thyroidectomy specimen shows

lymphocytic infiltrate with germinal centre formation along with thyroid follicles, few showing Hurthle cell change.

a. give diagnosis and immunological mechanism of cell injury.

b. name two endocrine diseases associated with this condition

Ans: Hashimoto thyroiditis

Pathogenesis:

● the possible reaction of CD4+ T cells to thyroid antigens, thus producing cytokines – Interferon γ (IFN-γ). Which promote inflammation & activate macrophages, as in Delayed type hypersensitivity reactions.

● CD8+ cytotoxic T cell mediated cell death:

● binding of antithyroid antibodies followed by antibody dependent cell mediated cytotoxicity mediated by natural killer cells

b)

1. subacute granulomatous thyroiditis
2. subacute lymphocytic thyroiditis

Q2: Give laboratory findings of serum T3, T4 & TSH level in typical cases of Grave's disease, Hashimotos thyroiditis; diffuse non-toxic goiter and multinodular goiter.

Ans:

Graves's disease:

■ TSH: ↓
■ T3: ↑
■ T4: ↑

Hishimoto thyroiditis: initial phase

■ TSH ↓
■ T3 ↑
■ T4 ↑

Delayed phase

■ TSH: ↓
■ T3: ↑
■ T4: ↑

Diffuse & multinodular Goiter

■ TSH ↓ or normal compensatory increased
■ T3 ↓ or normal
■ T4 ↓ or normal

Supply 2010

Q1: A 40 years female presents with enlarge nodular thyroid. Her thyroid function tests were:

TSH: 8.0 mUI/L (normal: 0.20-4.0 mUI/L)

T3: normal

T4: 30 nmol/l (normal 55-160 nmol/l)

a. What other relevant investigation can you demand in this patient and what is the expected result?

b. what will be the microscopic morphology of thyroidectomy specimen? How do they correlate with the underlying thyroid pathology?

Ans: a) radioactive iodine uptake - ↓

Annual 2011

Q1: A 30 years old female presents with soft, warm and flushed skin. Heat intolerance and excessive sweating. She gives history of weight loss despite increase appetite & frequent attacks of diarrhea, palpitation and experiences nervousness, tremor and irritability. On examination she has a wide, staring

gaze and lid lag are present. She is provisionally diagnosed to have thyrotoxicosis.
a. what is triad of manifestations in grave disease?
b. what are the morphological features of a thyrotoxic thyroid?
Ans: a)

1. thyrotoxicosis
2. ophthalmopathy
3. dermopathy

b)
Gross:
1. diffused hypertrophy & symmetrical enlarge
2. On cut section
-Soft meaty appearance resembling normal muscles
Microscopic:
epithelium tall & more corroded, small papillae projecting into the follicular. lumen, pale colloid, lymphoid infiltrate with germinal centre.

Q2: A 35 years old female presents with generalized apathy, mental sluggishness, restlessness, cold intolerance and obesity. She is suspected to have myxedema.
a. what lab tests will you order to confirm the diagnosis?
b. What lab findings are going to be present if she is diagnosed to have hashimoto? thyroiditis?
c. why some patients with graves' disease spontaneously developed episodes of hypothyroidism?
Ans: a)

- TSH level. increased in primary hypothyroidism
- T4 Level ↓
- T3 level ↓

b) Antimicrosomal & antithyroglobulin antibodies
c) TSH-binding inhibitor immunoglobulins (TBII): These anti-TSH receptor antibodies prevent TSH from binding normally to its receptors on thyroid epithelial cell. Some forms of TBBIIs mimic the action of TSH and resulting in the stimulation of thyroid epithelial cell activity. Whereas other forms may actually inhibit the thyroid cell function.

It is not usual to find the coexistence of stimulating and inhibiting immunoglobulins in the serum of the same patient, this finding explain why some patient with grave disease spontaneously develop episodes of hypothyroidism.

Annual 2012

Q1: A 20 yr old male presents with an enlarged lymph node in the neck. Thyroid gland was not visible on examination.FNA of lymph node shows metastasis from the tumor. The nuclei of tumor cell showed longitudinal grooving & intra nuclear inclusion.
a. What can be the possible primary site of this tumor?
b. Describe morphology of this tumor n mode of spread.
Ans: a) Papillary Carcinoma of Thyroid
b)
Gross:
Solitary or multi focal lesion
May be circumscribed or encapsulated
On cut surface may appear granular n sometimes may contain papillary fibrosis n calcification
Microscopy:
1. nuclei of papillary carcinoma cells contain very finely dispersed chromatin

2. this chromatin imparts an optically clear appearance, giving rise to designation "ground glass" or "orphan Annie eye" nuclei
3. invaginations of cytoplasm (pseudo-inclusions)
4. psammoma bodies

Mode of spread: Hematogenous

Annual 2013

Q1: A 32 yr old male develops firm swelling at the angle of Mandible below the ear. The FNA is taken. The smears revealed uniform looking large cells with Central nuclei & granular Acidophilic Cytoplasm. There was no nodular mass in the parotid region. The man recovered well after surgical removal.
a. What is the type of Tumor that he has developed n name 4 other tumors of this origin
b.What are the microscopic features of Warthin Tumor?
Ans: Warthin Tumor

Benign	**Malignant**
Pleomorphic adenoma	Mucoepidermoid carcinoma
Warthin tumor	Adenocarcinoma
Oncocytoma	Acinic cell carcinoma
Basal cell adenoma	Adenoid cystic carcinoma Squamous cell carcinoma
Ductal papilloma	Malignant mixed tumor

b)
Gross:
Pale grey surface punctated by narrow cystic or cleft like spaces filled with mucinous or serous secretion on resection
Microscopy:
1. Cystic spaces are lined by a double layer of Neoplastic Epithelial Cells Resting on dense lymphoid stroma n bearing germinal centers
2. This layer is distinctive... Having surface palisade of Columnar cells having abundant finely granular eosinophilic cytoplasm (Oncocytic appearance)
3. Oncocytes are epithelial cells stuffed with mitochondria
4. Foci of metaplasia are also present

Q2: A biopsy from lymph node in the neck revealed metastatic carcinoma, most consistent with diagnosis of metastatic papillary carcinoma of thyroid.
a. If u re-examine the slides, which 3 most imp microscopic findings in papillary carcinoma of thyroid will u expect?
b. Name 4 carcinomas of thyroid.
Ans: a)
1. nuclei of papillary carcinoma cells contain very finely dispersed chromatin
2. this chromatin imparts an optically clear appearance, giving rise to designation "ground glass" or "orphan Annie eye" nuclei
3. invaginations of cytoplasm (pseudo-inclusions)
4. psammoma bodies

b)
1. Paplillary Carcinoma 75-85%
2. Follicular Carcinoma 5-15%
3. Medullary Carcinoma 5%

4. Anaplastic Carcinoma <5%
5. Lymphoma

Supply 2013

Q1: An elderly lady was brought to the emergency room in a drowsy state with sign of severe dehydration. Lab results showed
Plasma Na+= 158mmol/L (135-145)
K+=5.0mmol/L (3.5-5.0)
HCO3=22mmol/L (24-32)
Urea=80mg/dl (10-45)
Creatinine=1.4mg/dl (0.3-1.2)
Glucose=700mg/dl
Osmolality 320mOsm/kg (285-295)
Urine was Positive for Ketones
a. Give ur diagnosis.
b. List the causes of coma in a diabetic pt.
Ans: a) Hyperosmolar non-ketotic coma
b)

1. Hyperglycemia
2. Diabetic Ketoacidosis
3. Hyperosmolar non-ketotic coma

Q2: A 45 yr old female is seen in surgical OPD with left thyroid lobe enlargement & a large non tender left cervical lymph node, thyroid nodule in left lobe. Her neck CT scan shows a cystic mass with associated enlarged lymph node.
a. What is the most likely diagnosis?
b. Give the characteristic microscopic features of this lesion.
c. Name the risk factor for this disease
Ans: a) Papillary carcinoma of thyroid
b)

1. nuclei of papillary carcinoma cells contain very finely dispersed chromatin
2. this chromatin imparts an optically clear appearance, giving rise to designation "ground glass" or "orphan Annie eye" nuclei
3. invaginations of cytoplasm (pseudo-inclusions)
4. psammoma bodies

c) Exposure to ionizing radiation during the 1st 2 decades of life

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Annual 2014

Q1: A middle aged woman presents with Diffuse n Symmetrical enlargement of Thyroid with gradually developing Hypothyroidism. She was diagnosed as a case of Hashimoto Thyroiditis
a. What is the pathogenic Mechanism of the disease?
b. What are the diseases to which she is at the risk of Developing?
Ans: a)
Pathogenesis:

- the possible reaction of CD4+ T cells to thyroid antigens, thus producing cytokines – Interferon γ (IFN-γ). Which promote inflammation & activate macrophages, as in Delayed type hypersensitivity reactions.
- CD8+ cytotoxic T cell mediated cell death:
- binding of antithyroid antibodies followed by antibody dependent cell mediated cytotoxicity mediated by natural killer cells

b)

1. subacute granulomatous thyroiditis
2. subacute lymphocytic thyroiditis

Supply 2014

Q1: A 47 year old woman has Tachycardia & heat intolerance with a 6 kg weight loss over 4 months. On examination there is a diffuse Thyroid Enlargement. Her Thyroid scans shows uniformly increased uptake in Entire Gland. Results of TFTs are awaited.

a. What is ur likely diagnosis?

b. Give the Autoimmune mechanism in the pathogenesis of this disease.

c. What changes are expected in the TFTs in this case?

Ans: a) Grave's Disease

b)

Graves's disease is autoimmune disorder in which a verity of antibodies may be present in the serum, Including antibodies to the TSH receptor, thyroid peroxisomes & thyroglobulin:

1. Thyroid stimulating immunoglobulin (TSI):
2. thyroid growth stimulating immunoglobulins (TGIs):
3. TSH binding inhibitor immunoglobulins (TBBII):

c) Graves disease: ■ TSH: ↓
■ T3: ↑
■ T4: ↑

SOLVED BY
FAYZAAN FAROOQ
SARGODHA MEDICAL COLLEGE , SARGODHA

Section 11 : Musculoskeletal System

Annual 2003

Q10: a) Classify tumours of bone.
b. Define sequestrum and involucrum associated with inflammatory bone disease.
Ans:

Histologic type	Benign	Malignant
Hematopoietic 40%		Meyloma Malignant lymphoma
Chondrogenic 22%	Osteochondroma Chondroma Chondroblastoma Chondromyxoid fibroma	chondrosarcoma Differentiated chondrosarcoma Mesenchymal chondrosarcoma
Osteogenic 19%	Osteod osteoma Osteoblastoma	Osteosarcoma
Fibrogenic	Fibroma Non-ossifying fibroma Fibrous histocytoma	Fibrosarcoms
Unknown origin 10%		Giant cell tumor Unicameral cyst Aneurismal bone cyst
Neuroectodermal		Ewing sarcoma
Notochordal	Benign notochordal cell tumor	Chordoma

b)
Sequestrum:

In osteomyelitis , the lifted periosteum impairs the blood supply to the effected region, and both the suppurative & ischemic injury may cause segmental bone necrosis; the dead piece of bone is called sequestrum.

Involucrum:

After the first week chronic inflammatory cells become numerous & their release of cytokines stimulate osteoclastic bone resorption, ingrowth of fibrous tissue & deposition of reactive bone in the periphery. When the newly deposited bone forms a sleeve of living tissue around the segment of devitalized infected bone, known as involucrum.

Annual 2005

Q1: Write a note on: Giant cell tumour of bone
Ans:

♦ common in 20s-40s of age
♦ GCTs are dominated by multinucleated osteoclast type giant cell hence the synonym Osteoclastoma
♦ it is benign and locally aggressive
♦ current opinion suggests that the giant cell component is likely a reactive macrophage Population & the mononuclear cells neoplastic.

Morphology:

● tumors are large or red brown with frequent cystic degeneration

● they are composed of uniform oval mononuclear cells with frequent mitosis
● they are composed of uniform oval mononuclear cells with frequent
Mitosis with scattered osteoclast type joint cells containing 100 or more nuclei
● necrosis, hemorrhage and reactive bone formation are also commonly present.

Clinical course:

- majority of GCTs arise in the epiphysis of the long bones around the knee.
- frequently cause arthritis like symptoms.
- occasionally GCTs presents as pathologic fractures
- radiographically, GCTs are large, purely lytic & eccentric, the overlying cortex is frequently destroyed, producing a bulging soft tissue mass with a thin shell of reactive bone.
- although GCTs are histologically benign, roughly half recur after simple curettage & as many as 4 % metastasize to the lungs.

Annual 2006

Q1: Name bone forming tumours. Briefly write morphological features of osteogenic sarcoma

Histologic type	Benign	Malignant
Hematopoietic 40%		Meyloma Malignant lymphoma
Chondrogenic 22%	Osteochondroma Chondroma Chondroblastoma Chondromyxoid fibroma	chondrosarcoma Differentiated chondrosarcoma Mesenchymal chondrosarcoma
Osteogenic 19%	Osteod osteoma Osteoblastoma	Osteosarcoma
Fibrogenic	Fibroma Non-ossifying fibroma Fibrous histocytoma	Fibrosarcoms
Unknown origin 10%		Giant cell tumor Unicameral cyst Aneurismal bone cyst
Neuroectodermal		Ewing sarcoma
Notochordal	Benign notochordal cell tumor	Chordoma

Morphology of Osteogenic Sarcoma

Gross:

- ♦ gritty, gray-white tumors, often exhibiting hemorrhage and cystic degeneration.
- ♦ frequently destroy the surrounding cortices and produce soft tissue mass.
- ♦ production of mineralized or unmeneralized bone (osteoid) by malignant cell.
- ♦ when malignant cartilage is abundant,tumor is called chondroblatic osteosarcoma

Microscopy:

- ♦ hyperchromatic nuclei
- ♦ bizarre tumor giant cells
- ♦ more mitosis

Annual 2007

Q7: a. Describe pathogenesis of gouty arthritis.

b. Give salient features of tuberculous osteomyelitis.

Ans:

Primary causes:

1. overproduction of uric acid by de novo synthesis and salvage pathway.
2. reduced excretion of uric acid

Secondary causes:

1. increased nucleated cell turnover e.g leukemia
2. decreased renal excretion e.g lead poisoning & alcoholism

b)

- bone infection complicates an estimated 1 to 3 % of cases of pulmonary tuberculosis.
- the organism usually reach the bone through the blood stream & by direct spread
- with hematogenous spread long bones & vertebrae are favored site
- lesions are often solitary but can be multicentric in immunocompromised patients.
- because the tubercle bacillus is microaerophilic, the synovium is common site due to high oxygen pressure.
- the infection then spreads to the adjacent epiphysis, where it cause typical Granulomatous inflammation with caseous necrosis and extensive bone destruction.
- tuberculosis of vertebral bodies causes vertebral deformity and collapse with Secondary neurologic deficit.

Annual 2008

Q1: A 30 years old develops excruciating pain in the first metatarsophalangeal joint following a weekend of binge drinking. The pain was associated with localized hyperemia, warmth and tenderness.

a. what is the likeliest diagnosis and what laboratory tests will you order to confirm the diagnosis?

b. Describe the morphology of tophus.

Ans: a) Gout

Lab Tests: 1. X-ray , serum & urine: uric acid levels, joint aspiration is confirmatory

b)

- Tophi are the pathognomonic hallmarks of the gout
- formed by large aggregations of urate crystals surrounded by an intense inflammatory reactions of lymphocytes, macrophages and foreign body giant cells, attempting to engulf the mass of crystals.
- tophi can appear in articular cartilage of joints & peri articular ligaments.
- superfacial tophi can lead to large ulcerations of the overlying skin

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Supply 2008

Q1: What is osteoarthritis, and what are the predisposing factors for its development.

Ans: The degenerative disease of joint in which degeneration of articular cartilage occur.

Primary osteoarthritis: without apparent initiating cause

Secondary osteoarthritis: predisposing conditions:

- previous traumatic injury
- developmental deformity
- underlying systemic diseases:
  a) diabetes
  b) ochronosis
  c) hemochromatosis
  d) obesity

Annual 2009

Q1: A 14 years old boy presents with a one month H/O pain in the knee joint. There is H/O weight loss

and pallor but no fever. X-rays of knee joint reveals densely sclerotic lesion in the distal femur extending from the growth plate into the diaphysis. The periosteum is lifted, forming an angle with the cortex. The surrounding soft tissue resembles a "sun burst" on the radiograph.

a. what is the likely diagnosis?

b. Enumerate the common sites involved by this tumor.

c. Give different subtypes of this tumor.

Ans: Osteosarcoma

b)

- ◄ metaphyseal region of the long bones
- ◄ 60% occurring about the knee
- ◄ 15% around the hip
- ◄ 10% at the shoulder
- ◄ 8% in the jaw

c)

1. primary osteosarcoma
2. solitary osteosarcoma
3. intramedulllary osteosarcoma
4. poorly differentiated osteosarcoma

- ➢ On the basis of site of involvement: (medullary vs cortical)
- ➢ on the basis of degree of differentiation: (solitary vs multicentric)

Annual 2010

Q1: A 45 years old child presents with morning stiffness which started from small joints of hand, and now involves wrist, elbow and knees bilaterally. On examination the joints are found swollen. The x-ray studies show peri-articular osteopenia.

a. What is most likely diagnosis?

b. Give the histological features of this disease.

Ans: a) Rheumatoid arthritis

b)

1. Inflammation of Synovial stroma by aggregation of Lymphoid cells , B cells , Plasma cells & Dendritic cells & Macrophages

2.Inc. in vascularity due to vasodilation & angiogenesis with hemosiderin deposits

3.Aggregations of organizing fibrin covering portion of synovium & floating in the joint space as **Rice Bodies**

4.Neutrophilic accumulation within Synovial Fluid

5.Pannus formation & fibrous ankylosis

Annual 2011

Q1: a. Classify the tumors of the bones.

b. Give morphology of osteosarcoma.

Ans:

a) See answer in **Annual 2014 Q1 (b)** part below

b)

Gross:

♦ gritty, gray-white tumors, often exhibiting hemorrhage and cystic degeneration.

♦ frequently destroy the surrounding cortices and produce soft tissue mass.

♦ production of mineralized or unmeneralized bone (osteoid) by malignant cell.

♦ when malignant cartilage is abundant,tumor is called chondroblatic osteosarcoma

Microscopy:

♦ hyperchromatic nuclei
♦ bizarre tumor giant cells
♦ more mitosis

Supply 2011

Q1: A 14 yr old boy presents with a mass around knee joint. X-ray shows a large destructive, mixed lytic & blastic mass lifting the periosteum with reactive periosteal bone formaation.
a.What is most likely the diagnosis?
b.What is the defining feature of this tumor on Histological Examination?
c.What are the most common sites for this tumor?
Ans: a) Osteosarcoma
b) Bizzare tumor giant cells, Formation of bone by this tumor
c)

- 15% around the Hip
- 10% around the shoulder
- 8% in the Jaw

Annual 2012

Q1: a. What is Gout?
b. Enumerate major morphological manifestations of Gout. Give features of any two.
Ans: a) It is a disease marked by transient attacks of acute arthiritis initiated by crystallization of urates within & about joints leading eventually to chronic gouty arthiritis & appearance of Trophi.
b)
Mnemonic GCAT
1.Gouty Neuropathy
2.Chronic trophaceous Arthritis
3.Acute Arthritis
4.Trophi
Acute Arthritis:

- Dense Neutrophilic Infiltration
- MSU crystals in cytoplasm of Neutrophils
- Crystals arranged in clusters in Synovium which are needle shaped
- Synovium is edematous containing Lymphocytes & Plasma Cells

Trophi:

- Pathognomic hallmarks of Gout
- Large aggregations of urate crystals surrounded by macrophages,lymphocytes & large foreign body giant cells
- Trophi may appear in articular cartilage of Joints,Ligaments & Tendons

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Supply 2012

Q1: An 8 yr old child presents with painful enlarging mass over lateral aspect of thigh. On X-ray destructive lytic tumor was seen extending on soft tissues with an onion skin appearance
a. What is ur diagnosis?
b.Give Gross & Microscopic picture of this lesion.
c.Name any 2 childhood tumors.
Ans: a) Ewing Sarcoma
b)
Gross:
Soft , tan white & frequently contains areas of hemorrhage & Necrosis

Microscopic:

- Composed of sheets of uniform small,round cells that are slightly larger than lymphocytes
- Cells have scant cytoplasm appearing clear as it is rich in glycogen
- Presence of **Homer Wright Rosettes**
- Few mitotic figures

c)

1.Ewing Sarcoma
2. Giant cell carcinoma

Annual 2013

Q1: A 20 yr old boy had a progressively enlarging painful mass in the metaphyseal region of left tibia. Radiograph showed that tumor had broken through the cortex & has lifted the periosteum due to mixed lytic & blastic lesion.

a. What is ur diagnosis?

b.Name any 4 histological subtypes of this tumor.

Ans: Osteosarcoma

b)

1.Primary osteosarcoma
2.Solitary Osteosarcoma
3. Intra medullary Osteosarcoma
4. Poorly differentiated Osteosarcoma
5.Osteoblastic/Chondroblastic
6.Fibroblastic
7.Telengiectatic
8.Small cell
9.Giant cell

Supply 2013

Q1: Define Rheumatoid Arthiritis & give the characteristic Histological Features in the Joint

Ans: Definition:

A chronic systemic inflammatory disorder that may affect many tissues & organs (heart,skin,blood vessels & muscles) but principally affects the joints, producing a non suppurative proliferative & inflammatory synovitis that often progresses to destruction of articular cartilage & ankylosis of joints.

Histological Features:

1. Inflammation of Synovial stroma by aggregation of Lymphoid cells , B cells , Plasma cells & Dendritic cells & Macrophages

2.Inc. in vascularity due to vasodilation & angiogenesis with hemosiderin deposits

3.Aggregations of organizing fibrin covering portion of synovium & floating in the joint space as **Rice Bodies**

4.Neutrophilic accumulation within Synovial Fluid

5.Pannus formation & fibrous ankylosis

Annual 2014

Q1: A 15 yr old boy developed a painful progressively enlarging mass at upper end of tibia.Radiographically, there was triangular shadow b/w cortex & raised ends of periosteum (Codman's Triangle)

a. What is ur Diagnosis?

b. Classify primary bone tumors.

Ans: a) Osteosarcoma

Supply 2014

Q1: A 20 yr old girl comes to surgical OPD with a painful discharging sinus just below the knee joint. On examination , the site shows features of Inflammation.She is also running fever from last 3 weeks.

a. What is ur diagnosis?

b. How can u confirm the diagnosis?

Ans: a) Chronic Osteomyelitis

b)

1. X-ray.... characteristic findings of a lytic focus of bone destruction surrounded by a zone of sclerosis
2. Blood culture
3. Biopsy
4. Bone culture

SOLVED BY
FAYZAAN FAROOQ
SARGODHA MEDICAL COLLEGE , SARGODHA

Section 12: Nervous System

Annual 2003

Q1: Discuss briefly the laboratory diagnosis of child with meningitis?

Ans:

CSF ANALYSIS

Features	Normal	Acute pyogenic (Bacterial)	Acute lymphocytic (Viral)	Chronic meningitis (tuberculosis)
Naked eye appearance	Clear and colorless	cloudy	Clear or slightly turbid	Clear or slightly turbid forms fibrin coagulum on standing
CSF pressure	60-150mm H2O	Elevated above 180mm H2O	Elevated above 250mm H2O	Elevated above 300mm H2O
Cells	0-4 lymphocytes/microliter	10-10,000 neutrophils/ul	10-100 lymphocytes/ul	100-1000 lymphocytes/ul
Proteins	40-45 mg/dl	Markedly raised	raised	raised
Glucose	50-80mg/dl	Marked reduced	normal	reduced
Bacteriology	Sterile	Causative organisms present	sterile	Tubercle bacilli present

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Annual 2006

Q1: Classify brain tumors? Give morphological features of meningioma?

Ans:

1. **Tumors Of Neuroglia (Gliomas)**
   - Astrocytoma
   - Oligodendroglioma
   - Ependymoma
   - Choroid plexus papilloma
2. **Tumors Of Neurons**
   - Neuroblastoma
   - Ganglioneuroblastoma
   - Ganglioneuroma
3. **Tumors Of Neurons And Neuroglia**
   - Ganglioglioma
4. **Poorly-Differentiated And Embryonal Tumors**
   - Medulloblastoma
   - Neuroblastoma
   - PNET
5. **Tumors Of Meninges**
   - Meaningioma
   - Meningeal sarcoma
6. **Nerve Sheath Tumors**
   - Schwannoma (neurilemmoma)
   - Neurofibroma

- Malignant nerve sheath tumors

7. **Other Primary Intraparenchymal Tumors**
   - Heamangioblastoma
   - Primary CNS lymphoma
   - Germ cell tumors
8. **Miscellanous Tumors**
   - Malignant melanoma
   - Craniopharyngioma
   - Pineal cell tumors
   - Pituitary tumors
9. **Tumor Like Lesions**
   - Epidermal cyst, Dermoid cyst, Colloid cyst
10. **Metastatic Tumors**

Morphology of Meningioma:

Gross: Meaningioma is well circumscribed solid spherical or hemispherical mass of varying size, the tumors is firmly attached to dura, cut surface is firm and fibrous sometimes with foci of calcification.

Microscopically: Divided into 5 types.

- Meaningiotheliomatous (Syncytal): it is solid mass of polygonal cells with poorly defined cell membrane, cells have round to oval center nuclei and finely granular cytoplasm.
- Fibrous (Fibroblastic Meaningioma): Tumor cell form parallel or interlacing bundles.
- Transitional (Mixed Tumors): Combination of cells with syncytial and fibroblastic features. Some of the whorls contain psammomma bodies due to calcification of the central core of whorls.
- Angioblastic Meaningioma: It has 2 patterns heamangioblastic pattern resembles heamangioblastoma of the cerebellum and heamangioparicytic pattern which is indistinguishable from heamangiopericytoma elsewhere in the body.
- Anaplastic Malignant Meningioma: Invades the underline brain and spinal cord and it is associated with extraneural metastasis to lungs brain and spinal cord. Tumor consists of origin with sharp line of demarcation from adjoining brain tissues usually surrounded by zone of edema.

Annual 2007

Q1: a) Differentiate btw contusion and concussion injures to the brain?

b) Describe certain features of cerebrovascular diseases?

Ans: a)

Contusions and laceration:

these are the result of direct damage to the brain parenchymal particularly cerebral hemispheres most often they are results of blunt trauma overlying skull may or may not be fractured. Traumatic sub arachnoid hemorrhage invariably accompanies cerebral contusions. Microscopically brain parenchymal at the affected site is hemorrhagic necrotic and fragmented on healing lesion appears as shrunken areas with golden brown hemosidren pigment on the surface.

Concussion:

it is caused by closed head injury and its characterized by transient neurological dysfunction and loss of consciousness. Invariably, there is completely neurological recovery after some hour to days. Morphologically severe concussion may cause diffuse axonal injury. the changes are minimal to small multiple hemorrhages.

b)

Basic principle:

- Neurological defeicet due to cerebrovascular compromise major cause of morbidity and mortality .

- Due to ischemia (85%) or hemorrhage (15%). This is becuz neurons are depend on glucose as essential energy source and undergo necrosis within 3-5 minutes.

Global Cerebral Ischemia: Causes

- Cardiac arrest
- Hypovolemic shock
- Septic shock
- C0 poisoning
- Repeated episodes of hypoglycemia

COMPLICATIONS:

- Cerebral atrophy producing laminal necrosis neuron undergo apoptosis and appear as red neurons.
- water shed infarcts occur at the junction at arterial territories.
- Stroke

Ischemic stroke:

Sudden loss of blood circulation to an area of brain resulting in loss of neurological functions.

SUBTYPES:

- Thrombotic stroke: is due to ruptures of an atherosclerotic plaque. Atherosclerosis usually develops at branch points results in pale infarct at the periphery of the cortex.
- Embolic stroke: mostly due to emboli in the left side of the heart. Usually involves the middle cerebral artery. It results in hemorrhagic infarct at the periphery of the cortex.
- Lacunar stroke: Cystic area of micro infarction less than 1mm. these are caused by hyaline arteriosclerosis due to hypertension or pregnancy.

Intracerebral hemorrhage:

Bleeding in the brain parenchyma these are classically due to rupture charcot bouchard micro aneurysms of the lenticulo striate vessels. Basal ganglia is the most common site.

Sub arachenoid hemorrhage:

Bleeding into the sub arachenoid space patient presents as a sudden headache with nuchal rigidity. Lumber punctures shows xanthochromia (yellow hue due to bilirubin breakdown), most frequently located in the anterior circle of willis at branch points of the Anterior cerebral artery and it is associated with Marfan syndrome and autosomal dominant polycyctic kidney disease.

Annual 2008

Q1: a) List three types of glial tumors?

b) List three most common tumors metastatic to brain?

Ans: a)

- Astrocytoma
- Oligodendroglioma
- Ependymoma

b)

In order of decreasing frequency:

Lung < Breast < skin (melanoma) < kidney < GIT.

Supply 2008

Q1: Define meningioma? And mention morphological characters of its different types?

Ans: Meaningioma arise from meningiothelial cells of arachinoid. Most meaningiomas are benign and can be removed successfully. Most common sites are major venous sinuses parasagittal. Other common sites are within the cerebral ventricles foraman magnum cerbellopontine angle and spinal cord.it is associated with neurofibromatosis type 2.

Morphology:

Gross: Meaningioma is well circumscribed solid spherical or hemispherical mass of varying size, the tumors is firmly attached to dura, cut surface is firm and fibrous sometimes with foci of calcification.

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Annual 2009

Q1: A 6 year old girl develops acute vomiting and neck rigidity. MRI reveals a tumor in the posterior fossa consisting large cyst with nodular mass attached to its wall (cyst with mural nodule). Histological examination shows large elongated astrocytes with long bipolar processes and Rosenthal fibers?

a) what is most likely diagnosis? Describe the tumors derived from glial cells?

b) Name the common poorly differentiated neoplasm of the brain? Give two general characteristic of this neoplasm?

Ans: a) Pilocytic astrocytoma.

Tumors Of Neuroglia (Gliomas)

- Astrocytoma
- Oligodendroglioma
- Ependymoma
- Choroid plexus papilloma.

b)

Glioblastoma multiform (WHO grade 4 astrocytoma)

Characteristics:

- Most aggressive of astrocytomas
- Usually arises in the cerebral hemispheres, crosses the corpus callosum (butterfly lesion).
- Region of necrosis surrounded by normal brain tissue which is distorted and endothelial cell proliferation.
- These are GFAP(Glial fibrillary acid protein) positive.

Supply 2009

Q1: A 50 year old female had right sided headache for 5 year but recently noted mild weakness in her right hand. CT scan shows well circumscribed lateral mass compressing the right hemisphere at the frontal parietal junction.

a) What is diagnosis? Give morphological features of this neoplasm?

b) Enumerate factors that overall affects the prognosis of this tumor?

Ans: a) Meningioma

Features:

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Most meningiomas are easily separable from the underline brain, some tumors infiltrate the brain, a features that is associated with increased risk of recurrence of neoplasm. The overall prognosis is determined by the

- Lesion size
- Location of the lesion
- Surgical accessibility
- Histological grade.

Annual 2010

Q1: A 4 year child presents with space occupying lesion in cerebellum histological exams shows poorly differentiated tumor with marked cellularity and sheets of plastic cells?

a) Diagnosis?

b) How does the tumor spread and what is the most ominous complications?

Ans: a) Medulloblastoma

b) Tumor spread locally as well as to distant sites

- Neural Invasion: It invades by the CSF to:
  - Meninges
  - Ventricles
  - Sub arachnoid space
- Distant metastasis:
  - Lungs
  - Liver
  - Vertebra
  - pelvis

Annual 2011

Q1: A 34 year old man presented with headache vomiting and giddiness, the CT scan shows a 3X4cm lesion in the parietal the histological exam reveals atypical astrocytes with scattered bizzare mitotic pictures the provisional diagnosis is grade II astrocytoma?

a) Enumerate 3 non glial tumors of brain?

b) Name two genes associated with astrocytoma?

Ans: a)

- Meningioma
- Schwannoma
- Meningioblastoma

b)

- P53
- Retinoblastoma tumor suppressor
- Gain of functions in the oncogene PI3K.

Supply 2011

Q1: List and give brief account of three microscopic abnormalities of alzehmier's disease?

Ans:

a) Senile neuritic plaque
b) Neurofibrillary tangles
c) Amyloid angiopathy
d) Granulo vacuolar degeneration.

- **Senile Neuritic Plaques:** is most obvious lesion and consists of focal area which has central core of a-beta amyloid surrounded by neuronal cell processes containing tau proteins, micro glial cells and astrocytes. These are located in grey matter. A-beta stains with congo-red and best visualize with silver stain.
- **Neurofibrillary Tangle:** Is filamentous collection of neurofilaments and neuro tubules in the cytoplasm of the neurons. These are due to hyper phosphorylated tau proteins in neurons.
- **Amyloid Angiopathy:** A-beta is present in the cerebral vessels increases the risk of hemorrhage.
- **Granulo Vacuolar Degeneration:** Is the presence of multiple small intra neuronal cytoplasmic vacuoles, some of which contain one or more dark granules called Hirano bodies.

Annual 2012

Q1: What are the two principle types of ischemic injury of brain? Give underline cause of each type?

b) Enumerate 2 broad groups of brain infarcts on the basis of their microscopic appearance?

Ans:

Types:

- Global cerebral ischemia
- Ischemic stroke

Global Cerebral Ischemia: Causes

- Cardiac arrest
- Hypovolemic shock
- Septic shock
- C0 poisoning
- Repeated episodes of hypoglycemia

COMPLICATIONS:

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- Lacunar stroke: Cystic area of micro infarction less than 1mm. these are caused by hyaline arteriosclerosis due to hypertension or pregnancy.

b)

- Anemic infarct
- Hemorrhagic infarct.

Supply 2012

Q1: List and give brief account of three major microscopic abnormalities of Alzehmier disease?

Ans: Same as supply 2011.

Supply 2013

Q1: a) Classify glioma?

b) Give morphological pictures of infiltrating astrocytoma?

Ans: a)

- Astrocytoma
- Oligodendroglioma
- Ependymoma
- Choroid plexus papilloma

b)

It shows variegated appearance with some areas showing grey white appearance while others are yellow and soft with foci of hemorrhages and necrosis. The surrounding normal brain tissues is distorted and infiltrated by yellow tumor tissue.

Annual 2014

Q1: A 1 year old neonate develops fever and signs of meningeal irritation his LP was done. CSF lab results shows cloudy, CSF neutrophils were 3500/mm3 Glucose was undetectable protein was 120mg/dl. On gram stain few gram negative bacilli were seen.

a) Diagnosis?

b) Most likely microorganism?

c) Name three childhood brain tumors?

Ans: a) Bacterial meningitis

b) N. Meningitis

c)

In order of decreasing frequency

- Cystic cerebellar astrocytoma
- Medulloblastoma
- Brain stem gliomas

Supply 2014

Q1: a) Enlist gliomas?

b) Give morphology of psammamatous meningioma?

Ans: a)

- Astrocytoma
- Oligodendroglioma
- Ependymoma
- Choroid plexus papilloma

b) It contains combination of cells with syncytial and fibroblastic features. Some of the whorls contain psammomma bodies due to calcification of the central core of whorls often around central capillary size blood vessels. Other form of degenerative changes like xanthomatous and myxomatous degeneration may also be encountered in psamamatous (transistional/mixed) variety.

Q: A 12 year old girl presents to the emergency room with high grade fever headache neck stiffness photophobia and irritability. LP is done

a) what is provisional diagnosis?

b) What are different test done on LP specimen?

Ans: a) Meningitis

b)

- Physical characters of the sample like Color, turbidity etc.
- CSF proteins
- CSF glucose
- CSF IgG Index
- Routine CSF electrophoresis
- High resolution CSF electrophoresis for detecting oligoclonal bands and myelin basic proteins in demyelinating diseases.
- CSF white blood cell count
- Gram stain.

SOLVED BY:
AQEEL ZARAIT &
M ZEESHAN CHAUDHARY
MOHTARIMA BENAZIR BHUTTO SHAHEED MEDICAL COLLEGE,
MIRPUR, AZAD JAMMU & KASHMIR.

THE END