## Question 1.
### Ischaemic cell injury

1. What are the stages of ischaemic cell injury?
   - Initial Reversible
   - Irreversible (prolonged ischaemia injury and necrosis)

2. Describe the sequence of events that occur in reversible ischaemic cellular injury.
   - Due to loss of oxidative phosphorylation $\rightarrow$ decreased ATP $\rightarrow$ failure of sodium pump $\rightarrow$ loss of K$^+$; influx of Na$^+$ and H$^+$ $\rightarrow$ iso-osmotic cell swelling.
   - **Increase in Ca$^{++}$** initially released from intracellular stores then influx of Ca$^{++}$ across plasma membrane $\rightarrow$ failure of ATP generation, activation of enzymes, induction of apoptosis $\rightarrow$ membrane and nuclear damage.
   - Decreased cellular pH due to increased lactate (increased anaerobic metabolism)
   - Loss of glycogen, decreased protein synthesis
   - Loss of microvilli, formation of cell surface blebs, myelin figures, mitochondria + ER swelling, ribosome detachment clumping of nuclear chromatin fatty change

3. Describe the morphological changes of irreversible ischaemic injury
   - Severe swelling of mitochondria
   - Extensive damage to plasma membrane
   - Swelling of lysosomes
   - Cell death by necrosis/apoptosis

### Notes
- Bold (3 items)

## Question 2.
### Septic Shock

1. How do microbial constituents initiate septic shock?
   - Interact with **cells of the innate immune system** (Neutrophils/Macrophages/Others) to release inflammatory mediators (& immunosuppressants)
   - Interact with **humoral elements of innate immunity** to activate complement and coagulation pathways
   - Act on **endothelium**

2. What is the effect of endothelial cell activation and injury during septic shock?
   - Thrombosis
   - Increased vascular permeability
   - Vasodilation

3. How does endothelial activation result in DIC (disseminated intravascular coagulation)?
   - Sepsis favours coagulation
     - Increased tissue factor production
     - Decreased fibrinolysis
     - Stasis
     - Decreased washout of activated coagulation factors
     - Results in multiple fibrin rich thrombi
   - Increased hypoperfusion

### Notes
- Consumption Coagulopathy = DIC

### Consumption Coagulopathy
- DIC
- **Consumptive** and some detail
| Question 3. Hypertension | 1. What factors are thought to contribute to essential hypertension? | Multiple genetic polymorphisms and interacting environmental factors:  
**Genetic factors**  
- familial, multi-gene foci interactions  
- single gene disorders altering Na reabsorption (rare)  
**Vasoconstrictive influences**  
- vasoconstriction/structural change in vessel wall  
  -> increase in peripheral resistance -> primary hypertension  
**Environmental factors**  
- stress, obesity, smoking, physical inactivity, high salt intake | 2 of 3 bold, with detail |
| --- | --- | --- |
| 2. What are the long term consequences of essential hypertension? | Major risk factor for atherosclerosis  
- Coronary artery disease  
- Cerebrovascular disease  
- Aortic dissection  
- Renal failure  
- Cardiac hypertrophy  
- Cardiac failure  
- Multi infarct dementia  
- Retinal changes | 4 of 7 consequences |
| 3. Describe the clinical features of malignant hypertension? | Clinical syndrome characterised by  
- severe hypertension with SBP > 200, DBP > 120  
- renal failure  
- encephalopathy  
- CVS abnormalities  
- retinal haemorrhages  
  +/- papilloedema  
- often superimposed on previous benign hypertension  
- < 5% of hypertensive patients  
- rapidly rising BP  
- untreated -> death in 1-2 years | Must mention 3 organ systems. |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>PROMPTS:</td>
<td>What <strong>organisms</strong> cause atypical pneumonia?</td>
<td>- Strep pneumoniae</td>
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<tr>
<td>What <strong>organisms</strong> cause atypical pneumonia?</td>
<td>What <strong>viruses</strong> may cause atypical pneumonia?</td>
<td>- Haemophilus influenza</td>
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<tr>
<td></td>
<td></td>
<td>- Moraxella catarrhalis</td>
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<td></td>
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<td>- Staph aureus</td>
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<td></td>
<td></td>
<td>- Legionella pneumophilia</td>
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<td></td>
<td></td>
<td>- Others eg klebsiella pneumonia, pseudomonas</td>
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<tr>
<td>Atypical pneumonia</td>
<td>Viral</td>
<td></td>
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<tr>
<td></td>
<td>- Mycoplasma pneumonia</td>
<td></td>
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<tr>
<td></td>
<td>- Chlamydiae spp</td>
<td></td>
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<tr>
<td></td>
<td>- Coxielle burnetti (Q fever)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>- RSV, parainfluenza, influenza A+B, adeno virus, SARS virus</td>
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</tbody>
</table>

| Need | Bacteria 3 | Atypical 1 | Viral 1 |

<table>
<thead>
<tr>
<th>2. How do atypical pneumonias differ from classical (typical) bacterial pneumonias</th>
<th>PROMPT; how do the lung changes differ?</th>
<th>Moderate amount sputum</th>
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<tbody>
<tr>
<td></td>
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<td>No physical findings of consolidation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Only moderate elevation of WCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No alveolar infiltrate</td>
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<td></td>
<td><strong>Patchy inflammatory changes</strong> largely confined to alveolar septa and pulmonary interstitium ie interstitial nature of the inflammation of alveolar exudates in classical pneumonia</td>
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<td><strong>Different clinical presentation:</strong> few localising signs, cough often absent, typical symptoms are fever, headache, myalgia,</td>
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<td></td>
<td></td>
<td><strong>Lower mortality cf bact pneumonia</strong></td>
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<td></td>
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<td>(severe disease uncommon)</td>
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</tbody>
</table>

| Lung changes to pass | Water related |

<table>
<thead>
<tr>
<th>3. How is legionella pneumonia contracted?</th>
<th>Artificial <strong>aquatic environment</strong> eg water cooling tower, water supply tubing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Inhalation of aerosolised droplets</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Or aspiration</strong> of contaminated drinking water</td>
</tr>
</tbody>
</table>

| Water related |
| **Question 5.** | **Osteomyelitis** | **1. Describe the pathogenesis of osteomyelitis** | 3 basic methods of infection  
• **blood borne** (haematogenous)  
• **local infection** (extension contiguous site)  
• **trauma/surgery** (direct implantation) | 2/3 |
|----------------|-------------------|-----------------------------------------------|-----------------|
|                |                   | **3. What Bacterial organisms cause osteomyelitis?** | **S. Aureus**  
• Gp B strep (neonatal)  
• S. Aureus (> 80%)  
Surgery/open fractures  
mixed  
Patient with UTI or IV drug user  
• E. Coli, Pseudomonas, Klebsiella | S. Aureus and 1 other |
|                |                   | **2. What are the changes in the bone that occur in osteomyelitis** | **New bone around area of necrosis**  
• Involucrum  
• Abscesses  
• Sclerosis  
• Deformity  
• Sequestrum  
• Draining sinus | 3 items |

**COMMENTS_______________________________________________________________________________________________________________________________________________________________**

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<table>
<thead>
<tr>
<th>TOPIC</th>
<th>QUESTION</th>
<th>ESSENTIAL KNOWLEDGE</th>
<th>PASS CRITERIA / COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question 1. Atrophy</td>
<td>1. What is atrophy?</td>
<td>Shrinkage in the size of an organ or tissue due to decrease in cell size and number.</td>
<td>Must know</td>
</tr>
</tbody>
</table>
| | 2. What are the causes of atrophy? | • Disuse  
• Denervation  
• Diminished blood supply  
• Inadequate nutrition  
• Loss of endocrine stimulation  
• Pressure | At least 4 |
| | 3. Give some examples of atrophy | • Fracture disuse  
• damage to nerves causing muscle atrophy  
• breast/reproductive organs from oestrogen lack | At least 2 |
| Question 2. Normal Haemostasis | 1. List the sequence of events in normal haemostasis after vascular injury | 1. **Transient vasoconstriction** [Neurogenic & humoral factors (include endothelin – endothelium derived vasoconstrictor)]  
2. **Primary haemostatic plug - platelet.**  
3. **Secondary haemostatic plug:** coagulation cascade activated by tissue factor and platelet phospholipids, fibrin polymerization “cementing” platelets  
4. **Limit spread:** tissue plasminogen activator & thrombomodulin | 3 of 4 bold |
| | 2. Describe the creation of the Primary Haemostatic Plug? | **Platelets** bind via  
1. glycoprotein lb (GpIb) receptors to  
2. von Willebrand factor (vWF) on  
3. exposed extracellular matrix (ECM) are  
4. activated undergo  
5. shape change and  
6. granule release: adenosine diphosphate (ADP) and thromboxane A<sub>2</sub> (TxA<sub>2</sub>)  
7. additional platelet aggregation through platelet GpIIb-IIIa receptor binding to fibrinogen | 3 of 7 (plus must say platelets) |
### Question 3. Tuberculosis

<table>
<thead>
<tr>
<th>1. What is secondary tuberculosis?</th>
<th>Pattern of disease that arises in a previously sensitised host</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. How may infection occur in secondary tuberculosis?</td>
<td>1. May follow shortly after primary infection (&lt;5%)&lt;br&gt;2. Reactivation of latent organisms&lt;br&gt;   • Typically in areas of low disease prevalence&lt;br&gt;3. Reinfection&lt;br&gt;   • Typical in regions of high prevalence</td>
</tr>
<tr>
<td>3. Describe the pathological features in the lung of secondary infection with TB.</td>
<td>• Locale - apical UL in secondary&lt;br&gt;• Area of inflammation / granuloma / multinucleate giant cells&lt;br&gt;• Central caseous necrosis&lt;br&gt;• Cavitation&lt;br&gt;• Healing with fibrosis and calcification&lt;br&gt;• +/- Complications include tissue destruction, erosion of blood vessels, miliary spread, pleural effusion, empyema, fibrous pleuritis</td>
</tr>
</tbody>
</table>

### Question 4. Chronic gastritis

| 1. What are the causes of chronic gastritis? | H Pylori<br>• Chronic bile reflux<br>• NSAIDS<br>• Autoimmune<br>• Allergic response<br>• Infections<br>• Radiation | Mechanical<br>• Psychological stress<br>• Chronic irritants (coffee, alcohol, caffeine )<br>• Systemic disease<br>• (Crohns, amyloid, graft vs host) |
| 2. Describe the features of H pylori induced chronic gastritis | Most common cause<br>• predominantly antral<br>• High acid production<br>• Hypogastrinaemia<br>• Generates ammonia (specific test)<br>• Disruption normal mucosal defence mechanisms |
| 3. What are the complications of gastric ulcer? | Bleeding (15-20%)<br> • Accounts for 25% of ulcer deaths<br>• Perforation<br>• Obstruction<br>• Gastric adenocarcinoma (complication of chronic H. Pylori pangastritis) |
1. **What is the most frequent cause of subarachnoid haemorrhage?**

   - **Rupture of an aneurysm**
     - (less common causes include ext of traumatic haem, H/T intracerebral bleed into ventricular system, AVM, bleeding disorders, tumour)

2. **Where are saccular aneurysms commonly located?**

   - **Most** near major arterial branch points along the circle of Willis or a major vessel just beyond (= anterior cerebral circulation)
     - 40% ant comm art
     - 34% middle cerebral art
     - 20% int carotid/PICA
     - 4% Basilar/Posterior Cerebral

3. **What are the genetic risk factors for saccular aneurysms?**

   - Generally unknown, not ‘congenital’
   - Some genetic risk
     - Polycystic kidney
     - Ehlers Danlos type 4
     - Neurofibromatosis type 1
     - Marfan’s
     - Fibromuscular dysplasia
     - Aortic coarctation

4. **What are the pathological consequences of subarachnoid haemorrhage?**

   - **Early**
     - vasospasm and additional ischemic injury
     - increased intracranial pressure
   - **Late**
     - meningeal fibrosis & scarring
     - CSF obstruction

<table>
<thead>
<tr>
<th>Question 5. Subarachnoid Haemorrhage</th>
<th>Prompt for “Late”</th>
<th>Need 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rupture of an aneurysm to pass</td>
<td>At least anterior circulation and 1 other to pass</td>
<td>2/6</td>
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<td>Comments:________________________________________________________________________</td>
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</tbody>
</table>
| **Question 1.**
Cell Death / Necrosis | 1. Describe the cellular changes in necrosis
PROMPT
Start with the cellular features. | • Usually irreversible injury  
• Often adjacent inflammation  
• **Swollen cells**  
• Increased eosinophilia  
• Myelin figures (whorls of cell membrane bits)  
• Nucleus fades (karyolysis), may shrink (pyknosis) and then fragments (karyorrhexis)  
• Organelle disruption → amorphous mass  
• **Cell membrane disrupted**, contents released  
• Swelling  
• Disruption of cell integrity. | |
| | 2. What are the patterns of tissue necrosis?  
PROMPT
What are the different macroscopic appearances of necrotic tissues? | • **Coagulative** (architecture preserved)  
• **Liquefactive** (digestion → liquid viscous mass)  
• Caseous (friable white)  
• "Gangrenous (usually applied to limb. Typically coagulative. Superimposed liquefaction from infection → 'wet gangrene')  
• "Fat necrosis (focal areas of fat destruction)  
• Fibrinoid (microscopic feature of Ag-Ab complexes in vessel walls from immune mediated) | Coagulative  
Liquefactive
Prompt with names needs to describe difference  
*these terms clinical not true pathology terms |
| **Question 2.**
Cell derived mediators of inflammation | 1. Which mediators of inflammation are derived from cells? | • Preformed  
  o **Vasoactive amines**  
    ▪ Histamines  
    ▪ Serotonin  
  • Newly synthesized  
    o **Arachidonic metabolites**  
      ▪ Prostaglandins  
      ▪ Leukotrienes  
      ▪ Lipoxins  
    o Reactive Oxygen Species  
    o Platelet activating factors  
    o Nitric Oxide  
    o Cytokines (TNF, IL1)& Chemokines | Pass = bold + 1 other |
| | 2. Which cells release histamine? | Widely distributed in tissues, richest sources:  
• **Mast cells**  
• **Basophils**  
• **Platelets** | Pass =/> 2 |
| | 3. What are the effects of histamines in an inflammatory response? | • Dilation of the arterioles  
• **Increased vascular permeability of the venules**  
• Can cause constriction of large arteries | Pass = bold (2) |
**Question 3. Measles**

1. Describe the pathogenesis of measles
   - PROMPTS: What type of virus is measles? What is the mode of transmission?
   - 1. Paramyxovirus (single stranded RNA)
   - 2. Respiratory droplet spread
   - 3. Multiples in upper respiratory tract epithelial cells
   - 4. >lymphoid tissue where it replicates in mononuclear cells
   - 5. Haematogenous spread
   - 6. Preventable by vaccination as only single strain.
   - 7. Epidemics amongst un-vaccinated individuals

2. What type of immune responses occur in measles?
   - 1. T cell mediated immunity controls infection + causes rash
   - 2. Antibody mediated protects against re-infection
   - 3. Epidemics in unvaccinated hosts

3. Describe some of the systemic features of measles virus infection.
   - Prompt: What are some complications of measles infection?
   - 1. Rash – blotchy, red/brown. Skin hypersensitivity reaction
   - 2. Oral mucosal ulceration – Koplik’s spots
   - 3. Croup
   - 4. Interstitial pneumonia
   - 5. Conjunctivitis, Keratitis, scarring and visual loss
   - 6. Encephalitis; - plus SSPE, measles inclusion-body encephalitis
   - 7. Diarrhoea with protein losing enteropathy
   - 8. Immunosuppression
   - 9. Secondary bacterial infection

**Question 4. Ischaemic bowel disease**

1. What conditions can lead to infarction of bowel?
   - PROMPT; by what mechanisms do these conditions cause injury
   - 1. Acute vascular obstruction
      - atherosclerosis (esp. origin major vessels)
      - aortic aneurysm
      - hypercoagulable states
      - OC use
      - embolism
   - 2. Intestinal hypoperfusion
      - cardiac failure
      - shock
      - dehydration
      - vasoconstrictive drugs
   - Systemic vasculitis
      - Henoch-Schlein purpura
      - Wegener’s granulomatosis
   - Mesenteric venous thrombosis
      - hypercoagulable states
      - invasive neoplasms
      - cirrhosis
      - trauma
      - abdominal masses

2. Describe the intestinal response to an acute ischaemic insult.
   - Prompt: what is the mechanism by which ischaemic bowel injury occurs?
   - 1. Initial hypoxic injury
   - 2. Secondary reperfusion injury
      - major injury in this phase
      - free radical production, neutrophil infiltration, inflammatory mediator release
   - 3. Magnitude of response determined by
      - vessels affected
      - timeframe over which ischaemia develops

3. Which parts of the bowel are most susceptible to acute ischaemic injury and why?
   - Watershed zones
      - splenic flexure, sigmoid colon and rectum
      - located at end of arterial supply
   - Must know that it is predominantly a reperfusion type injury

Surface epithelium: Villi more at risk than crypts
-intestinal caps run from crypts up villi to surface

Must be able to explain why watershed zones are most susceptible to injury.
**Question 5. Hepatic Failure**

| 1. What are the causes of acute liver failure? | Drugs and toxins: Paracetamol, halothane, rifampicin, mushrooms, CCL4  
Infections: hepatitis A, B and (rarely) C.  
Mechanism: direct toxic eg paracetamol, mushrooms  
Or toxicity and/or immune mediated eg Hepatitis virus | 3 causes - at least 1 drug and 1 infection |
| 2. What are the clinical features of liver failure? | Jaundice  
Ascites  
Hypoalbuminaemia  
Hyperammonemia → encephalopathy  
Coagulopathy  
Portal hypertension  
Foetor hepaticus  
Spider naevi  
Palmar erythema  
Hypogonadism + gynaecomastia | At least 5 features |
| OPTIONAL (Good candidates) What do you understand by hepato-renal syndrome? | Renal failure in pt with severe chronic liver disease with no obvious cause for the renal failure. Features include:  
Na retention  
Impaired free water excretion  
Decreased renal perfusion and GFR | Any features |

Comments: ____________________________________________________________
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