**PART BJ 01: DEFINITION**

1. State in which ↓ CO/ effective circulating blood volume impairs tissue perfusion → cellular hypoxia.

**PART BJ 02: TYPES**

2. Types:

<table>
<thead>
<tr>
<th>Type</th>
<th>Mechanism</th>
<th>Clinical E.g.</th>
</tr>
</thead>
</table>
| Cardiogenic           | ![Intrinsic myocardial damage](image) Extrinsic compression Outflow obstruction Failure of myocardial pump ↓ cardiac output | *MI  
*Pulmonary embolism  
*Ventricular rupture  
*Arrhythmia  
*Cardiac tamponade |
| Hypovolemic           | ![Massive fluid loss](image) hemorrhage ↓ blood/plasma volume ↓ O$_2$ perfusion                     | *Fluid loss (hemorrhage, diarrhea)                                                                |
| Septic#               | ![Microbe causes activation of macrophages, neutrophils, dendritic & endothelial cells & soluble compartment of innate immune system](image) ↓ Initiate inflammatory responses that interact with complex ↓ Septic shock & multi-organ dysfunction | *Immunocompromised hosts due to...  
a) chemotherapy  
b) immunosuppression  
c) advanced age  
d) HIV |
| Shock associated with systemic inflammation | ![Cytokine cascade activation](image) ⟷ Peripheral vasodilation & pooling WBC-induced damage Endothelial activation DIC | *Overwhelming microbial infections  
*SuperAgs  
*Trauma  
*Burns |
5. 2nd phase complications: renal insufficiency \(\rightarrow\) **progressive** ↓ in urine output, severe fluid & electrolyte imbalance

<table>
<thead>
<tr>
<th>Septic</th>
<th><strong>Warm &amp; flushed skin</strong> (initially)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>Rapidly followed by…</em></td>
</tr>
<tr>
<td></td>
<td>a) cardiac, cerebral &amp; pulmonary dysfunction</td>
</tr>
<tr>
<td></td>
<td>b) electrolyte disturbances</td>
</tr>
<tr>
<td></td>
<td>c) <strong>metabolic acidosis</strong></td>
</tr>
</tbody>
</table>
### CHAPTER BL: PATHOLOGIC CALCIFICATION

### PART BL 01: ABOUT

1. Is the deposition of **Ca$^{2+}$ salts** (along with smaller amounts of Fe, Mg & other mineral salts) on abnormal tissue

2. Common process, occurring in a variety of pathologic conditions

### PART BL 02: TYPES

3. Types of calcification:

<table>
<thead>
<tr>
<th></th>
<th>Dystrophic</th>
<th>Metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td><em>Local precipitation</em> of <strong>Ca$^{2+}$ salts</strong></td>
<td>*Less common than dystrophic calcification</td>
</tr>
<tr>
<td></td>
<td><em>Serum Ca$^{2+}$ normal</em></td>
<td>*↑ serum Ca$^{2+}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Widespread calcification</em></td>
</tr>
<tr>
<td><strong>Occurrence</strong></td>
<td><strong>Tissues already affected by disease</strong></td>
<td><strong>Normal tissues</strong></td>
</tr>
<tr>
<td><strong>E.g.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>**Conditions/</td>
<td>*Atheromatous plaques</td>
<td><strong>Hyperparathyroidism</strong></td>
</tr>
<tr>
<td>Causes**</td>
<td><em>Congenitally bicuspid aortic valves</em></td>
<td>PTH liberates Ca$^{2+}$ (from bone) → hyperCa$^{2+}$emia</td>
</tr>
<tr>
<td></td>
<td><em>Calcification of mitral valve ring</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>*Old TB lesions</td>
<td><strong>HyperCa$^{2+}$emia of malignancy</strong></td>
</tr>
<tr>
<td></td>
<td>*Fat necrosis</td>
<td>*Skeletal metastasis → extensive bone erosion → hyperCa$^{2+}$emia</td>
</tr>
<tr>
<td></td>
<td>*Breast lesions</td>
<td>*PTH-related peptide</td>
</tr>
<tr>
<td></td>
<td>*Calcinosis cutis</td>
<td></td>
</tr>
<tr>
<td><strong>Morphology</strong></td>
<td>*Ca$^{2+}$ appear macroscopically as <strong>fine, white granules/clumps</strong> &amp;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>have <strong>gritty</strong> feeling</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*Sometimes, a TB lymph node is virtually converted to stone</td>
<td></td>
</tr>
</tbody>
</table>

*PTH* - parathyroid hormone
SUB-PART BM 02 (D): HYPOALBUMINEMIC EDEMA

9. Pathogenesis:

SUB-PART BM 02 (E): PULMONARY EDEMA

10. Is the edema of lungs:

11. Causes:
   a) ↑ hydrostatic pressure (due to LVF – the usual cause)
   b) Alveolar capillary wall injury (during infections, e.g., pneumonia, or liquid aspiration of gastric contents/during near-drowning)

12. Lungs are heavy & wet (water oozes when they are squeezed)

13. Pulmonary congestion:
   a) Is a passive process
   b) Due to ↓ blood outflow

14. Chronic venous congestion:
   a) Occurs in LVF (esp. mitral stenosis)
   b) Lungs have tough consistency & are brownish (“brown induration of lungs”)
   c) Alveoli walls are thickened (due to fibrosis during chronic disease) → no fluid leaks out when lung is pressed
*There are 2 other modes of spread as well: direct contact & iatrogenic

SUB-SUB-PART CC 01 (B 2): TB MENINGITIS

10. Methods of spread:

1. **Hematogenous** spread from 1°/ 2° complex in lungs
2. **Direct spread** from a spinal vertebral body → meninges

11. Gross changes:
   a) **Thick, gelatinous exudate** around basal cisterns & within cerebral sulci
   b) Grey tubercular exudate (contains granulomas) adjacent to vessels

SUB-PART CC 01 (C): VIRAL MENINGITIS

12. About:
16. About:
   a) Mild, self-limiting
   b) Rabies, HSV type I infections lead to extensive destruction & are often fatal
   c) ALL virus infections of brain & spinal cord produce similar pathological changes in CNS

17. Pathological findings:

   1. Lymphocytes, macrophages & plasma cells infiltration
   2. Perivascular cuffing (usually extends into parenchyma)
   3. Cell lysis (cytolytic viral infection) & phagocytosis of cell debris by macrophages
   4. Reactive hypertrophy & hyperplasia of astrocytes & microglia
   5. Edema
   6. Inclusion bodies in infected neurones/ glial cells:
      a) Negri bodies in rabies
      b) Owl-eye inclusion bodies in CMV

*Bitemporal encephalitis is assumed to be caused by HSV until proven otherwise
a) Cerebral HIV infection (causing progressive dementia)
b) Multiple opportunistic infections (e.g. toxoplasma, fungi)
c) Other viral infections (e.g. CMV, papova)
d) 1° cerebral lymphoma

SUB-PART CC 01 (F): SYPHILLIS
19. Effects:
   a) Meningitis
   b) Meningeal thickening
   c) Cranial nerve palsies
   d) Tabes dorsalis
   e) Gummas (small, soft swellings characteristic of late stages of syphilis)
   f) General paralysis of the insane (neuropsychiatric disorder affecting the brain, caused by late-stage syphilis)

SUB-PART CC 01 (G): CEREBRAL ABSCESS
20. About:

   - Usually develops from acute suppurative encephalitis following...
     1. Direct spread: via paranasal sinuses/middle ear
     2. Septic sinus thrombosis: mastoid cavities of middle ear via sigmoid sinus
     3. Hematogenous: bronchiectasis/infective endocarditis

   *Hematogenous abscesses occur in parietal lobe & are often multiple

21. Morphology:
   a) Pus formation with local tissue destruction (liquefactive necrosis)
   b) Capsule formation around abscess (contains granulation tissue & reactive astrocytes)
   c) Adjacent brain is markedly edematous
   d) Perivascular inflammatory lymphocyte & plasma cells infiltration
   e) Abscess (frequently) enlarge & become multiloculate
11. Diagnosis:

Symptoms may be severe at beginning of stroke, or they may progress/ fluctuate for the 1st day or 2

Once there's no further deterioration, stroke evaluation is considered complete

12. Prevention:

a) Screen BP at least every 2 years (esp if have family history of hypertension)
b) Cholesterol check
c) Treat hypertension, diabetes, high cholesterol & heart disease (if present)
d) Follow low-fat diet
e) Quit smoking
f) Exercise regularly
g) Lower weight (if overweight)
h) Avoid alcohol overuse
PART CC 05: ALZHEIMER'S DISEASE

1. Clinical features:

   1. Age ≈ 60 years
   2. Lasts 2 – 8 years
   3. Forgetfulness, memory disturbances (memory loss)
   4. Loss of language, math, speech & motor skills
   5. Rigidity development
   6. Patients wander aimlessly
   7. Death usually due to bronchopneumonia

2. Morphology:

<table>
<thead>
<tr>
<th>Gross</th>
<th>Microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ brain weight (often to 1 100 g, due to</td>
<td>neuritic plaques (β amyloid plaques)</td>
</tr>
<tr>
<td>neuronal loss)</td>
<td>See in amygdala, hippocampus &amp; cerebral abscess</td>
</tr>
<tr>
<td>Cortical atrophy (marked in frontal &amp;</td>
<td>* Are focal, spherical collections of dilated pre</td>
</tr>
<tr>
<td>temporal lobes)</td>
<td>synaptic neuritic processes around a diffuse</td>
</tr>
<tr>
<td>Loss of cortical grey &amp; white matter</td>
<td>aggregate of amyloid</td>
</tr>
<tr>
<td>Compensatory dilation of ventricles → 2°</td>
<td>* Later, plaques enlarge &amp; develop amyloid core</td>
</tr>
<tr>
<td>hydrocephalus</td>
<td>Reactive astrocytes &amp; microglia are present at</td>
</tr>
<tr>
<td>Changes seen mostly in limbic system,</td>
<td>periphery (of plaque)</td>
</tr>
<tr>
<td>temporal &amp; frontal areas</td>
<td></td>
</tr>
<tr>
<td>Structures of medial temporal lobe (including</td>
<td></td>
</tr>
<tr>
<td>hippocampus, entorhinal cortex &amp; amygdala</td>
<td></td>
</tr>
<tr>
<td>are involved early) → severe atrophy</td>
<td></td>
</tr>
<tr>
<td>Normal cerebellum &amp; spinal cord</td>
<td></td>
</tr>
</tbody>
</table>
Cysts (4)

*Develop via dilation of acini & terminal ducts
*May be lined by squamous/ cuboidal/ columnar epithelium
*Secretions within it can calcify
*Can sometimes rupture → inflammation

Columnar cell change

*Comprises distended acini lined with prominent apical snouts
*Microcalcification is frequent (detectable by mammography)
*May show flat cellular atypia (acini lined by multiple layers of mildly pleomorphic cells)
*Often coexists with other atypical lesions (e.g. atypical ductal/ lobular hyperplasia)

Atypical hyperplasia

<table>
<thead>
<tr>
<th>Atypical Ductal Hyperplasia</th>
<th>Atypical Lobular Hyperplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Loss of cell polarity</td>
<td>• Partial acini distension by monomorphic population of small, non-cohesive cells</td>
</tr>
<tr>
<td>• Nuclear pleomorphism</td>
<td></td>
</tr>
<tr>
<td>• (Occasional) mitotic figures</td>
<td></td>
</tr>
</tbody>
</table>

Papillomatosis (2)

*Simple papillary processes project into lumens of dilated ducts/ small cysts
*Have fine connective tissue core & covered by 1/ 2 epithelial layers
*May branch

[Mnemonic: A SAFE C²AP]

8. Significance:
   a) Severe, periodic discomfort
   b) ↑ breast cancer risk
   c) Mimics breast cancer
<table>
<thead>
<tr>
<th>Microscopy</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ducts involved</em></td>
<td></td>
</tr>
<tr>
<td><em>↑ N/C ratio</em></td>
<td></td>
</tr>
<tr>
<td><em>Pleomorphism</em></td>
<td></td>
</tr>
<tr>
<td><em>Hyperchromasia</em></td>
<td></td>
</tr>
<tr>
<td><em>↑ &amp; abnormal mitotic figures</em></td>
<td></td>
</tr>
<tr>
<td><em>Microcalcification present</em></td>
<td></td>
</tr>
<tr>
<td><em>Patterns:</em></td>
<td></td>
</tr>
<tr>
<td>a) <em>Solid</em></td>
<td></td>
</tr>
<tr>
<td>b) <em>Comedo</em> (central necrosis)</td>
<td></td>
</tr>
<tr>
<td>c) <em>Cribriform</em></td>
<td></td>
</tr>
<tr>
<td><em>(Sometimes, can spread to lobules)</em></td>
<td></td>
</tr>
<tr>
<td><em>Acini involved</em></td>
<td></td>
</tr>
<tr>
<td><em>Relatively uniform cells</em></td>
<td></td>
</tr>
<tr>
<td><em>Lobule shape retained</em> (but enlarged)</td>
<td></td>
</tr>
<tr>
<td><em>Non-cohesive</em></td>
<td></td>
</tr>
<tr>
<td><em>Clear cytoplasm</em></td>
<td></td>
</tr>
<tr>
<td><em>No necrosis</em> (usually)</td>
<td></td>
</tr>
<tr>
<td><em>Relative</em></td>
<td></td>
</tr>
<tr>
<td><em>Acini involved</em></td>
<td></td>
</tr>
</tbody>
</table>

**Patterns:**

1. Solid
2. Comedo (central necrosis)
3. Cribriform

*(Sometimes, can spread to lobules)*

**Prognosis**

Good (if DCIS is completely excised)

---

**SUB-PART CD 05 (A): INVASIVE DUCTAL CA**

16. Occurs in both **pre- & post-menopause**

17. **Clinical features:**

1. 10 – 80 mm
2. Firm
3. **Tethers to skin/ muscle**
4. Dimpling
5. **Peau d’orange** (due to invasion of lymphatics)
6. **Nipple retraction** (intramammary ligaments involved)

*(L-R): Solid, comedo & cribriform (with microcalcification) DCIS*
4. Morphology:

<table>
<thead>
<tr>
<th>Gross</th>
<th>Microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Dilation</em> of bronchi &amp; bronchioles (usually of lower lobes)</td>
<td><em>Inflammatory infiltrate</em> (esp. neutrophils) in acute stage</td>
</tr>
<tr>
<td><em>Cylindrical/ saccular/ fusiform</em> shape</td>
<td><em>Bronchial wall fibrosis</em> (in later stages)</td>
</tr>
<tr>
<td><em>Honeycomb</em> appearance</td>
<td></td>
</tr>
</tbody>
</table>

5. Clinical features & complications:

- **Clinical features**
  - Dyspnea
  - Chronic cough
  - Copious foul-smelling sputum
  - Finger clubbing

- **Complications**
  - Pneumonia
  - Septicemia
  - Empyema
  - Remote abscesses
  - *Cor-pulmonale*#
  - Amyloid formation

#Is the abnormal enlargement of right side of heart due to disease of lungs/ pulmonary vessels.

6. Treatment:
   a) **Physiotherapy**
   b) **Antibiotics**
8. Clinical features:
   a) Dys-/ tachy-pnea
   b) Cyanosis
   c) Hypoxia
   d) Respiratory failure (type I)
   e) Bilateral opacities on chest X-ray
### Non-atopic

*Associated with **recurrent RTI** (due to rhino/ parainfluenza infection)
*Due to **vulnerability** of vagal receptors to irritants
*Not immunologically-mediated, inherited, responsive to skin test
*Bronchoconstriction occurs in unusually-reactive airways

### Drug-induced

*Cause: aspirin, NSAIDs
*Recurrent rhinitis, nasal polyps, urticaria
*Due to ↑ bronchoconstrictor LTs

### Occupational

*Hypersensitivity to an agent at work, e.g.
  a) **Fumes** (epoxy resins)
  b) Organic & chemical **dusts** (wood, cotton, Pt)
  c) **Gases** (methylbenzene)
  d) **Chemicals** (formaldehyde, penicillin products)

*Pathogenesis: type I & III hypersensitivities

### Allergic bronchopulmonary aspergillosis

*Inhalation of **spores** of *Aspergillus fumigatus*
*Pathogenesis: (immediate) type I & (delayed) type III hypersensitivities
*Hyphae of aspergilli seen in mucus plugs in bronchi (of asthmatic patients)

### Clinical features:

**Classic acute asthma attack**
- Lasts up to **several hrs**
- Persists at **low lvl** constantly

**Status asthmaticus**
- Severe acute paroxysm
- Persists for days/ weeks
- Airflow obstruction may occur → severe cyanosis → death

### Morphology:

<table>
<thead>
<tr>
<th>Gross (Status Asthmaticus)</th>
<th>Microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
10. Clinical features (pink puffer)

1. **Dyspnea** (insidious onset & progressive)
2. **Weight loss**
3. **Prolonged expiration**
4. **Productive cough**
5. **Barrel chest** (due to ↑ residual air volume in lungs)
6. Sits forward in a hunched-over (tripod) position
7. Breathing thru **pursed lips** (nostrils alone inspire insufficient air)
8. **Pink** appearance (as accessory muscles are used during respiration)
<table>
<thead>
<tr>
<th>Definition</th>
<th>[See #1 above]</th>
<th>[See #1 above]</th>
</tr>
</thead>
</table>
| **Pathogenesis & role of host resistance to TB** | [See below] | *Most cases involve reactivation of old 1° infection*  
*Occur when there’s some degree of immune dysfunction (e.g. age, underlying malignancy, steroid therapy)* |
| **Lung involvement** | **Small, mid-zone lesion with hilar nodes involvement** | Always located in lung apices (sometimes bilaterally) |
| **Histology** | *Granuloma with central necrosis surrounded*  
(by epithelioid histiocytes, Langhan’s cells & lymphocytes)  
*Also seen in nodes that drain affected portion of lung* | Granulomas, most having central necrosis |
| **Complications** | *May progress with systemic spread*  
*Death (in some cases)* | *Progression depends on balance between host sensitivity & organism virulence*  
*Complications can ensue* |
| **Sequelae** | *Usually, 1° lesion will organize & heal as immune reaction develops, leaving fibrocalcific nodule in lung*  
*Tubercle bacilli may still be present within scarred foci & may persist as viable organism for years* | *Most lesions converted to fibrocalcific scars* |
**Silicosis**

- Silica particles (diameter < 2 mm) enter terminal respiratory units
- Ingested by macrophages (but silica is toxic to macrophages)
- Macrophages die, release proteolytic enzymes & undigested silica particles (which are ingested by other macrophages & the cycle continues)
- Released enzymes cause local tissue destruction and subsequent fibrosis
- Nodules form (along with fibrosis)
- Pulmonary function test reveals restrictive defects (interstitial lung disease)

*Some patients develop reactivation of TB (2° TB)*

**Asbestosis**

- Asbestos causes tissue bleed
  - Hb degradation (in RBCs)
  - Hemosiderin formation
  - Hemosiderin coats asbestos (asbestos bodies formed)

*2 types of asbestos which are most harmful are serpentine & amphibole*

*Histology (Lower lobes are more affected):*
  - a) Large areas of fibrosis
  - b) Honeycomb lung
  - c) Asbestos bodies

*Finger clubbing*
5. Clinical features:

1. Pain
2. Movement limitations
3. Morning stiffness
4. Audible **creaking** of joints (palpable crepitus due to loose, calcified debris @ joint mice)
5. *All lab investigations are normal*

6. Treatment: **joint replacement** (with **prosthesis**)
PART CE 04: BONE TUMORS
SUB-PART CE 04 (A): CLASSIFICATION

1. Classification:

SUB-PART CE 04 (B): 1° TUMORS
SUB-SUB-PART CE 04 (A 1): OSTEOSARCOMA

1. Classical osteosarcoma:

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histogenesis (origin)</td>
<td>Osteoblasts</td>
</tr>
<tr>
<td>Risk factors</td>
<td>*Radiation exposure</td>
</tr>
<tr>
<td></td>
<td>*Defective p53 &amp; Rb genes</td>
</tr>
<tr>
<td></td>
<td>*Paget's disease (of bone)</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td>*Age: 10 – 20</td>
</tr>
<tr>
<td></td>
<td>*Site: metaphysis</td>
</tr>
<tr>
<td></td>
<td>*Pain, swelling, pathological fractures</td>
</tr>
</tbody>
</table>
| Mixed | *Osteoclasts persist*
|       | *Most bone surfaces are lined by prominent osteoblasts*
|       | *Marrow is replaced by loose connective tissue which contains osteoprogenitor cells & vessels*
|       | *Newly-formed bone may be woven/ lamellar (but eventually, lamellar bone becomes predominant)*

| Sclerotic | *Mosaic/ jigsaw puzzle pattern of lamellar bone*
|          | *Bone becomes a caricature of itself*
|          | *Soft, porous & lack structural stability*
|          | *Pathological fractures*
3. **Pathogenesis:**

![Pathogenesis Diagram]

4. **Clinical features:**

<table>
<thead>
<tr>
<th>Site</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Anemia/ leucopenia/ thrombocytopenia</td>
</tr>
</tbody>
</table>