5. Toxins produced:
   a) **Tetanolysin**: $O_2$- & heat-labile
   b) **Tetanospasmin**: $O_2$-stable but heat-labile neurotoxin (essential pathogenic product)
   c) A 3rd toxin: non-spasmogenic, **peripherally active** neurotoxin

6. Pathogenesis:

Wound contamination with *C. tetani* spores

*Germination & toxin production* take place only in wounds with low redox potential

Released *toxin* binds to *peripheral MN terminal* & enters *axon*

Transported to nerve *cell body* in CNS via retrograde intraneuronal transport

*Migrates across synapses* to *presynaptic terminals*

*Binds to gangliocyte receptors* & blocks inhibitory NT (GABA) release from vesicles via *tetanoplasmin* (a Zn metalloprotease)

Abolition of spinal inhibition causes *uncontrolled spreading* of impulses initiated anywhere in CNS

*Muscle rigidity & spasm* (due to simultaneous contraction of agonists & antagonists in absence of reciprocal inhibition)

*Involves cleavage of synaptobrevin* (protein essential in proper functioning of synaptic vesicle release apparatus)
17. Lab diagnosis:

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimens</td>
<td>Uneaten food, serum</td>
</tr>
<tr>
<td>Gram staining</td>
<td>*Gram (+) bacilli</td>
</tr>
<tr>
<td></td>
<td>*Subterminal, oval bulging spores</td>
</tr>
<tr>
<td></td>
<td>*Motile</td>
</tr>
<tr>
<td>Culture</td>
<td>*Strict anerobe</td>
</tr>
<tr>
<td></td>
<td>*Optimum temperature: 35°C</td>
</tr>
<tr>
<td></td>
<td>*Spores produced when grown in alkaline glucose gelatin medium (at 20 – 25°C)</td>
</tr>
<tr>
<td>Mice inoculation</td>
<td>Death (unless protected by antitoxin)</td>
</tr>
</tbody>
</table>

18. Botulism:

1. Types: food-borne, infant, wound

2. Bioterrorism-related botulism is the potential result of intentional dispersal (as aerosol/ contaminant in ingested material) of the (most potent bacterial) toxin

3. Infant botulism:
   a) Microbe grows in gut & produces toxin
   b) Source: ingestion of contaminated honey
   c) Infant develops weakness/ paralysis & may need respiratory support, but usually recovers spontaneously (by contrast, it is usually fatal in adults)

*Differential diagnosis (involves ruling out of...*)
SUB-PART EB 01 (A): INTRODUCTION

1. Poliovirus:
   
   1. Family: picornaviridae
   2. Group: enterovirus
   3. Non-enveloped
   4. Icosahedral nucleocapsid
   5. Acid-stable
   6. +ve sense ssRNA
   7. Natural infections occur only in humans
   8. Antigenic types (PV1, 2, 3)

SUB-PART EB 01 (B): PATHOGENESIS

2. Transmission & epidemiology:
   
   a) Transmitted via fecal-oral route
   b) Distribution: Pakistan, Afghanistan, Nigeria

3. Pathogenesis proper:

   Incubation period: 10 – 14 days  
   Replicates in oropharynx & GIT (may be transported to lymphoid tissue)  
   Viremia takes it to CNS

   LMN lesion  
   (Anterior horn) cell death  
   Replicates in MNs in anterior horn (of spinal cord)

*Encephalitis primarily involves brainstem
6. Pathogenesis:

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modes of transmission</td>
<td>*Contact with saliva from infected animals (i.e. bites, scratches, licks on broken skin &amp; mucus membrane)</td>
</tr>
<tr>
<td></td>
<td>*Airborne (aerosol) in bat rabies</td>
</tr>
<tr>
<td></td>
<td>*Iatrogenic (corneal transplants)</td>
</tr>
<tr>
<td>Pathogenesis Proper</td>
<td>Bite/other modes → Incubation period: 1 – 3 months → Attaches to ACh receptor → Spreads to nerves in CNS (via retrograde axonal transport) → Reaches peripheral nerves at NMJ → Multiply in muscle/connective tissue → Spreads thru nerves to other organs #</td>
</tr>
<tr>
<td></td>
<td>Multiplication in brain (encephalitis) → Spread to nerves to other organs #</td>
</tr>
</tbody>
</table>

#e.g. salivary glands, muscles, retina, cornea, adrenals, skin

*NO viremia* is observed

7. Clinical rabies:

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prodromal phase (2 – 4 days)</td>
<td>*Malaise, fever, headache</td>
</tr>
<tr>
<td></td>
<td><em>Discomfort</em> at site of bite</td>
</tr>
<tr>
<td>Clinical forms</td>
<td><em>Furious</em> rabies (encephalitic form, leads to seizures)</td>
</tr>
<tr>
<td></td>
<td><em>Dumb</em> rabies (paralytic form)</td>
</tr>
</tbody>
</table>
8. Lab diagnosis:

1. Done ante-mortem

2. Involves rabies Ag & NA detection

3. Fluorescent Ig technique (FAT)/ DFA on corneal smear:
   a) FAT on skin biopsy
   b) RT-PCR with saliva, CSF
   c) Ig detection in serum, CSF

4. Virus isolation (in adult/ suckling mice)

5. Cell culture (in murine neuroblastoma/ BHK 21 cells)

9. Negri bodies:
   a) Present in brain tissue (detected post-mortem)
   b) Eosinophilic intra-cytoplasmic bodies with basophilic inner granules
   c) Seen in about 60 – 70 % cases only
   d) Simple, rapid & specific marker (of rabies)
   e) Observed via direct impression smears from brain/ after-sections, or Seller’s staining on fresh brain

10. Vaccines:

   Encephalitic form (80%)
   - Hydro-/ aero-/ photo-phobia
   - Respiratory arrest
   - Seizures
   - Coma & death

Paralytic rabies (20%)
   - Ascending paralysis
   - Bladder involvement
   - Cardio-respiratory arrest (eventually)
   - Coma & death
CHAPTER EE: PRIONS

1. Features & their differences from conventional infectious agents:

1. Have proteinaceous infectious particles but NO DNA/ RNA

2. Composed of single glycoprotein

3. Extremely resistant to heat, disinfectants & irradiation

4. Inactivated by hypochlorite, NaOH and autoclaving

5. Slow replication rate (incubation period up to 35 years)

6. Cannot be cultured → elicit no immune responses (as there is no Ag presentation)

7. Comparison between PrP\(^C\) & PrP\(^SC\)

<table>
<thead>
<tr>
<th></th>
<th>PrP(^C)</th>
<th>PrP(^SC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shape</td>
<td>Linear</td>
<td>Globular</td>
</tr>
<tr>
<td>Susceptibility to proteases</td>
<td>Susceptible</td>
<td>Resistant</td>
</tr>
<tr>
<td>Predominant 2° structure</td>
<td>α-helices</td>
<td>β-pleated sheets</td>
</tr>
<tr>
<td>Others</td>
<td>May function in signal transduction</td>
<td>Aggregates to form filaments</td>
</tr>
</tbody>
</table>

8. For a prion (PrP\(^SC\)) to infect a host, the host must have a recognizable cellular form (PrP\(^C\)) of that prion

9. The closer the phylogenetic relationship between donor host & the recipient, the greater the chance for infection & the more rapidly symptoms occur

10. Transmission is thru ingestion, blood transfusion, iatrogenic
2. E.g. prion disorders: [Refer Part ED 02, #3]

3. CJD & kuru:

<table>
<thead>
<tr>
<th></th>
<th>CJD</th>
<th>Kuru</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmission</td>
<td>Iatrogenic (e.g. corneal transplants &amp; growth hormone injections)</td>
<td>Ingestion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*Thru cuts (wounds)</td>
</tr>
<tr>
<td>Clinical features</td>
<td>*Dementia</td>
<td>*Progressive tremors</td>
</tr>
<tr>
<td></td>
<td>*Myoclonic seizures</td>
<td>*Ataxia w/o dementia</td>
</tr>
<tr>
<td></td>
<td>*Ataxia, aphasia, visual loss, hemiparesis</td>
<td></td>
</tr>
</tbody>
</table>
22. Treatment: penicillin G

23. Prophylaxis:
   a) Rifampicin, ciprofloxacin
   b) Vaccines for capsular polysaccharides (A, C, Y, W-135) for soldiers/travellers

SUB-SUB-PART GA 01 (B 3): HEMOPHILUS INFLUENZAE

24. Transmission: airborne (throat carriage)

25. Predisposing factor: children (6 months to 5 years) – H. influenzae is present in respiratory tract of infants & young children

26. Virulence factors:
   a) Capsule: PRP (polyribosylribitol) Ag induces IgG, M & A (which are bactericidal, opsonic & protective)
   b) Pili
   c) IgA protease
   d) Endotoxin
   e) Outer membrane proteins

*N. meningitidis* has 6 serotypes (a – f), but invasions like meningitis is caused by type “b” (hence, the vaccine for it is Hib)

27. Pathogenesis
<table>
<thead>
<tr>
<th>Gram staining</th>
<th>*Gram (-) coccobaccilli</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>*Pleomorphic:</td>
</tr>
<tr>
<td></td>
<td>a) <strong>Coccobacilli</strong> in sputum</td>
</tr>
<tr>
<td></td>
<td>b) Long, bacillary, filamentous in CSF with meningitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CSF changes</th>
<th>*Turbid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>*Cells/ mL 200 – 20 K (neutrophils)</td>
</tr>
<tr>
<td></td>
<td>*Protein (mg%): High (&gt; 100)</td>
</tr>
<tr>
<td></td>
<td>*Glucose (mg%): &lt; 45</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Culture</th>
<th><em>Fastidious</em> (requires either X/ V factors/ both which are present in blood):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a) X factor is a hemin (for aerobic respiration)</td>
</tr>
<tr>
<td></td>
<td>b) V factor is a coenzyme @ NAD/ NADP (H+ acceptor)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Biochem</th>
<th><em>Catalase &amp; oxidase</em> +ve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>Ferments</em>* glucose &amp; xylose** (with acid only)</td>
</tr>
<tr>
<td></td>
<td><em>Satelitism</em> test +ve</td>
</tr>
</tbody>
</table>

| Ag detection | LAT/ FAT/ Quellung’s test/ countercurrent immunoelectrophoresis |

#Satelitism:
Usually above waist for HSV-1 & below waist for HSV-2

57. Pathogenesis:
   a) HSV-1 becomes latent in trigeminal ganglia while HSV-2 lumbar & sacral ganglia
   b) During latency, most of viral DNA is located in cytoplasm rather than integrated (into nuclear DNA)

58. HSV encephalitis:
   1. Is the commonest severe sporadic encephalitis
   2. Forms:
      a) Following 1st & generalized infection in infancy
      b) In adults due to virus reactivation in trigeminal ganglia, then infection passes back to temporal lobe (of brain)
   3. Herpetic skin mucosal lesions may be present
   4. Diagnosis is indicated by clinical signs of space-occupying lesion in temporal lobe & CT/ radioactive brain scan
   5. Clinical findings:
      a) Acute onset, with fever & focal neurological symptoms
      b) Demonstration of HSV DNA in CSF by PCR (sensitive in acute stage)

#Previously, brain biopsy was done

59. HSV meningitis:
   a) Is a self-limiting disease
   b) CSF shows lymphocytic pleocytosis & may yield virus in culture

#Is a neurological condition in which a patient has migraine-type headache & also has lymphocytes present in spinal fluid

60. Lab diagnosis:
**Space-occupying lesions**

*Headache, vomiting, seizures/ epilepsy, cysticercotic encephalopathy

**Eye**

*Uveitis, retinitis

*Larvae visualized floating in vitreous humor

82. Lab diagnosis:

1. **Subcutaneous nodule biopsy**: shows cysticerci
2. **X-ray** of skull/ soft tissue: shows **calcified cysticerci**
3. **CT/ MRI scan** (to **locate cyst**)
4. **DLC**: eosinophilia
5. **Sero logical tests** (to demonstrate specific Igs in serum), e.g.
   a) **IHA** (indirect hemagglutination)
   b) **IFA** (indirect fluorescent Ig)
   c) **ELISA**

83. Treatment:
   a) Praziquantel
   b) Albendazole
   c) Purgative

*For such patients washing hands after defecation & safe disposal of feces for ≥ 4 days following therapy are must
PART GB 02: URTIs

SUB-PART GB 02 (A): COMMON COLD

5. Causative agents:
   a) Rhino, corona, adeno, echo
   b) Coxsackie A
   c) Influenza, parainfluenza
   d) RSV
   e) *Mycobacterium pneumoniae*
   f) *Chlamydia pneumoniae*

6. Etiology & epidemiology:

   1. Caused by > 200 types of viruses
   2. 90% are due to viruses
   3. Distributed worldwide
   4. Seen mostly during winter
   5. Rhinoviruses are the most common agents (10 – 25%)

SUB-PART GB 02 (B): RHINOVIRUS

7. About:
   a) Small, non-enveloped with icosahedral nucleocapsid & +ve ssRNA
   b) NOT inactivated by lipid solvents
   c) Replicates better at 33°C than at 37°C
   d) No vaccine (as there are > 100 immunologically-distinct types)
   e) High infection frequency in childhood
   f) Humans are natural hosts
| M protein (protein Ag) | *Anti-phagocytic  
*Antigenic  
*80 types of M protein are recognized |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>C polysaccharide</td>
<td>Has toxic effect on <strong>connective tissue</strong></td>
</tr>
<tr>
<td>Fimbriae</td>
<td>For <strong>attachment</strong> to <strong>surface epithelium</strong> (via lipoteichoic acid)</td>
</tr>
</tbody>
</table>
| Hemolysins (responsible for β-hemolysis) | *Streptolysin ‘O’ (O₂ labile)  
*Streptolysin ‘S’ (O₂ stable) |
| Exotoxins             | *Exotoxin A (erythrogenic toxin, pyogenic)  
*Exotoxin B |
| Others                | *Streptokinase (fibrinolysin)  
*Hyaluronidase  
*Deoxyribonucleases (streptodornase, DNAase)  
*Nicotinamide adenine dinucleotidase (NADase) |

21. Pathogenesis:

Glycoprotein **fibronectin** on epithelial cell serves as **lipoteichoic acid ligand**

Virulent group A streptococci adhere to **pharyngeal epithelium** by means of **lipoteichoic acid** covering the surface pili

**Localization** favoured by **hypersensitivity** (due to prior contact)

**Pharyngitis** (sore throat)

22. Clinical features:
<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
</table>
| Rheumatic fever       | *Igs formed to Ags (in streptococcal cell wall) cross-react with sarcolemma of heart & other tissues  
*Granulomas formed in heart (Aschoff's nodules — see diagram below)  
*Patient develops myo-/ peri-carditis, which may be associated with…  
a) subcutaneous nodules  
b) polyarthritis  
c) chorea (results from streptococcal Igs reacting with neurones) |
| Rheumatic heart disease | *Immune-mediated disease  
*Due to repeated attacks of Strep. pyogenes with different M protein types  
*Lead to damage to heart valves |
| Acute glomerulonephritis | *Igs to streptococcal components combine with them to form circulating immune complexes (Ag-Ig complexes) → deposited in glomeruli, to which autoIgs to glomerular components.  
*Complement & coagulation systems activated → local inflammation  
*Blood appears in the urine (RBCs, protein)  
*Signs of acute nephritis syndrome (edema, hypertension) present  
*ASO (anti-streptolysin O) Igs are usually ↑ |
| Otitis media           |                                                                                                                                                                                                           |
| Sinusitis/ mastoiditis |                                                                                                                                                                                                           |
| Ludwig’s angina        |                                                                                                                                                                                                           |
| Suppurative adenitis   |                                                                                                                                                                                                           |
| Meningitis             |                                                                                                                                                                                                           |
### 28. Pathogenesis

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td><em>Infection in children &amp; adults are asymptomatic (EXCEPT in the immunocompromised)</em>&lt;br&gt;*1° site of latency: monocytes&lt;br&gt;*Others: kidneys (for years)/ cervix</td>
</tr>
<tr>
<td><strong>Reactivation</strong></td>
<td>*Occurs when CMI ↓&lt;br&gt;*Reactivation in cervix $\rightarrow$ infection of newborn when passing thru birth canal</td>
</tr>
<tr>
<td><strong>Pathogenesis proper</strong></td>
<td>*CMV infection occurs via immunosuppressive effect (by inhibiting CTCs)&lt;br&gt;*Host defences: CMI (more important) &amp; circulating Iggs&lt;br&gt;&lt;br&gt;*Immune evasion mechanism (maintains long, latent state):&lt;br&gt;&lt;br&gt;Cells infected&lt;br&gt;&lt;br&gt;Unstable assembly of MHC c1-viral peptide complex&lt;br&gt;&lt;br&gt;No Ag presentation on cell surface&lt;br&gt;&lt;br&gt;No CTC killing of infected cells&lt;br&gt;&lt;br&gt;*CMV also encodes several microRNAs which prevent translation of mRNA $\rightarrow$ MHC c1 protein:&lt;br&gt;a) Again, there is no Ag presentation&lt;br&gt;b) No CTC killing of infected cells</td>
</tr>
</tbody>
</table>

**QUICK BYTZ**

CTCs cannot present Ags due to defective MHC c1, & this…<br>Very much ↓ CTC killing of infected cells

### 29. Clinical features:

<table>
<thead>
<tr>
<th>In the Immunocompromised</th>
<th>In the Immunocompetent</th>
</tr>
</thead>
</table>
33. About:

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification</td>
<td>*γ-herpesvirus&lt;br&gt;*Structurally similar to other herpesviruses, but antigenically different</td>
</tr>
<tr>
<td>Ags</td>
<td>*Viral capsid Ags (VCAs)&lt;br&gt;*EBV early Ags (EAs)&lt;br&gt;*EBV nuclear Ag (EBNA)&lt;br&gt;*Lymphocyte-determined membrane Ag&lt;br&gt;*Viral membrane Ag (this is the main target for neutralization)</td>
</tr>
<tr>
<td>Infection</td>
<td>*Humans are natural hosts&lt;br&gt;*Infects lymphoid cells (esp. B cells) &amp; epithelial cells of oropharynx → sore throat&lt;br&gt;*In latently-infected cells, EBV DNA no incorporate into cellular DNA&lt;br&gt;*Infects very young children (age 1 – 6) &amp; adolescents (age 14 – 20)</td>
</tr>
<tr>
<td>Subtypes</td>
<td>*EBV-1 (type A): present in Western countries&lt;br&gt;*EBV-2 (type B): less virulent</td>
</tr>
</tbody>
</table>

34. Transmission:

1. **Oral secretions** (saliva) – during kissing

2. Blood, **transplanted** organs (less common than CMV)

3. **Intrauterine** (rare, but if infected, no viral transmission to fetus or adverse fetal outcomes)

4. Miscellaneous
   a) **Asymptomatic** infection during 1st few years of life
   b) **Early infection** occurs in **lower socioeconomic** groups
   c) **High frequency** in those exposed later in life
<table>
<thead>
<tr>
<th>Component</th>
<th>Function and Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fimbria</td>
<td>*For bacterial attachment to respiratory epithelium&lt;br&gt;Also helps in serotyping</td>
</tr>
<tr>
<td>Filamentous HA</td>
<td>*Present on bacterial surface&lt;br&gt;Helps in attachment &amp; facilitates 2° infections&lt;br&gt;*Protective (produces immune response which protects host)</td>
</tr>
<tr>
<td>AC toxin</td>
<td>*Causes ↑ cAMP&lt;br&gt;*Inhibits bactericidal activity of phagocytes</td>
</tr>
<tr>
<td>Tracheal cytotoxin</td>
<td>*Is a peptidoglycan fragment&lt;br&gt;*Kills tracheal epithelial cells (due to inhibition of DNA synthesis)</td>
</tr>
<tr>
<td>Pertactin</td>
<td>Is an outer membrane protein (can be used as vaccine)</td>
</tr>
<tr>
<td>Endotoxin</td>
<td>*Is a LPS&lt;br&gt;(Along with tracheal cytotoxin,) ↑ IL-1 &amp; NO synthesis → cell damage</td>
</tr>
</tbody>
</table>

*Fimbrial agglutinogen & filamentous HA are adhesins.

70. Clinical features (phases & their features):

- **Catarrhal**
  - Mild symptoms
  - Highly infective stage

- **Paroxysmal**
  - Characterized by cough bouts → rushing of air into empty lungs → whoop

- **Convalescence**
  - Recovery phase

*Each phase lasts ≈ 2 weeks*
1. ≈ 2 B @ 1/3 of world’s population are affected with tubercle bacilli

2. Every year, 8 – 9 M new cases appear, with 3 M deaths

3. Majority cases & deaths are from poor nations (e.g. India)

4. In India, > 40% of the population is infected & 15 M suffer from TB. 0.5 M die from this every year

b) General:

1. TB is highly associated with poverty (TB has declined rapidly in rich nations due to ↑ living standards)

2. HIV & TB are closely related* in which HIV infections can cause...
   a) reactivation of latent TB infections
   b) worsening of TB
   c) treatment of TB to be ineffective

3. Emergence & spreading of MDRTB worsens the situation (WHO once declared TB as a global emergency)

*TB in turn may hasten development of HIV infection into active disease

76. Transmission:

1. Source of bacteria: open case of TB

2. Transmitted via droplets during sneezing, coughing, talking

3. Tiny droplets remain suspended in air for long & get access to terminal air passages

4. Direct inhalation of aerosolized bacilli in droplet nuclei of expectorated sputum → infection

5. Spread occurs among household/ prolonged contact with open cases

*Majority of inhaled bacilli are arrested in URT
98. Predisposing factors:
   a) Alcoholism
   b) Patients on ventilators
   c) Immunocompromised
   d) DM

99. Virulence factors:
   a) Adhesins
   b) Pili
   c) Capsular- & lipo-polysaccharide

100. Pathogenesis & clinical features:

101. Lab diagnosis:

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimens</td>
<td>Sputum</td>
</tr>
<tr>
<td>Gram staining</td>
<td>Gram (-) bacilli, capsulated</td>
</tr>
<tr>
<td>Culture</td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>MA (McConkey agar): <strong>pink mucoid</strong> colonies</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Biochem tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Catalase, citrate, urease</em> +ve</td>
</tr>
<tr>
<td><em>Reduces NO₃</em></td>
</tr>
<tr>
<td><em>TSI test: A/A</em> (yellow slant &amp; butt)</td>
</tr>
<tr>
<td><em>Ferments</em> sugars (+)</td>
</tr>
<tr>
<td><em>Non-motile</em></td>
</tr>
<tr>
<td><em>Oxidase –ve</em></td>
</tr>
</tbody>
</table>

**SUB-SUB-PART GB 03 (E 4): 1° ATYPICAL PNEUMONIA**

**102. Definition:**

a) “1°” refers to pneumonia occurring as a new event (not 2° to influenza)

b) “Atypical” refers to the fact that *Strep. pneumoniae* is not isolated from sputum of such patients; symptoms are often general & respiratory-related; pneumonia fails to respond to penicillin or ampicillin

**103. Etiological agents:**

a) *Mycoplasma pneumoniae*

b) *Legionella pneumophila*

c) *Coxiella burnetti*

d) *Chlamyphila pneumoniae/ psittaci*
SUB-PART GB 03 (F): VIRAL PNEUMONIA

SUB-SUB-PART GB 03 (F 1): INFLUENZA

106. General
   a) Belong to Myxovirus family (interact with mucins), Orthomyxoviridae subfamily
   b) Enveloped RNA viruses
   c) Have ability to adsorb on mucoprotein receptors of RBCs, causing hemagglutination

107. Structure:

   1. **Enveloped**, spherical virus
   2. Contains **segmented** –ve ssRNA
   3. Has RNA-dependent RNA Pol
   4. **Helical nucleocapsid**, surrounded by M (matrix/ membrane) layer (which is protein in nature)
   5. **Outer lipid bilayer** is derived from **host membrane** during budding

   **QUICK BYTZ**

   Influenza has no matching properties:

   **Influenza – RNA – Helical nucleocapsid**

108. Antigenic structure:

   a) Major Ags: internal Ags (RNP & M proteins) & envelope Ags (HA & NA)
   b) RNP & M layer are group-specific Ags. They are stable (no show any antigenic variation)
   c) **Envelope Ags** are host-specific
**SARS**

*Family: Coronavirus*
- Non-segmented, +ve ssRNA genome
- Enveloped, with helical nucleocapsid
- No virion polymerase
- Incubation period ranges from 2 – 10 days (average 5)

*Severe atypical pneumonia* (characterized by fever ≥ 38°C)
- Dyspnea
- Hypoxia → diffuse edema
- Non-productive cough
- Chills
- Rigors
- Malaise
- Headache
- Sore throat
- Coryza (rhinorrhea, runny nose)

*Most adenovirus infections resolve spontaneously*

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**SUB-SUB-PART GB 03 (F 3): MEASLES**

119. Complications (with respect to 2° bacterial pneumonia):

- Virus replicates in epithelium of nasopharynx, middle ear & lung
- Interferes with host defences & enables bacteria (e.g. pneumo-/staphylo-/meningo-cocci) to establish 2° infections
- Virus replication continues unchecked (in children with severely impaired immune responses)
- Giant cell (2°) pneumonia (rare & usually fatal)
120. General properties:

1. Important cause of pneumonia in immunocompromised individuals

2. Medically, it is thought of as a protozoa because...
   a) it appears as cyst in tissue
   b) its cysts resemble those of protozoa

3. Subsequent analysis of mitochondrial DNA & various enzymes support the idea that it is a fungus. However,...
   a) it has no ergosterol in its membrane as fungi should have (it has cholesterol instead)
   b) it NO grow in fungal media
   c) anti-fungal drugs are ineffective on them

4. Found in domestic animals (horse, sheep, variety of rodents), but they are NOT reservoirs for human infection

5. Has major surface glycoproteins (hence, exhibit significant antigenic variation)

6. Has multiple genes encoding these surface proteins (but only 1 expressed at a time)

121. Morphology:

<table>
<thead>
<tr>
<th>Trophozoite</th>
<th>Pre-cyst</th>
<th>Cyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Thin wall</td>
<td></td>
<td>*Thick wall</td>
</tr>
<tr>
<td>*Irregular shape</td>
<td>*Is an intermediate stage of sexual phase</td>
<td>*Spherical</td>
</tr>
<tr>
<td>*Size: 1 – 5 mm</td>
<td>*Size: 5 – 8 mm</td>
<td>*Contains up to 8 intracystic bodies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*Size: up to 8 mm</td>
</tr>
</tbody>
</table>
SUB-SUB-PART GB 03 (G 2): ASPERGILLUS FUMIGATUS/ FLAVIUS

125. General properties:

1. Are **filamentous fungi/ molds**
2. Have **septate hyphae** (multicellular) forming V shape (dichotomous branches)
3. **Cell walls** are (more or less) **parallel**
4. **Conidia** form **radiating chains**
5. **Reproduce** by **spore** formation (asexually), but some undergo **sexual** reproduction
6. Appearance:
   a) Macroscopic: surface texture is **cottony/ wooly/ velvety/ granular, pigmentation** may be observed from the reverse
   b) Microscopic: thread-like **filamentous hyphae** (in tissues & culture)
7. Cause **opportunistic mycoses**
8. Infect immunocompromised patients (due to immunosuppressive drugs, DM, HIV) by various mechanisms

126. Transmission: **inhalation** of spores (sub in e droplets)

127. Clinical features:

<table>
<thead>
<tr>
<th>Feature</th>
<th>About</th>
<th>Sub-features</th>
</tr>
</thead>
<tbody>
<tr>
<td>(ABPA) allergic broncho-</td>
<td>Allergic response due to aspergillus</td>
<td><em>Asthma</em> (due to type I hypersensitivity) – occurs in atopic individuals following sensitization to inhaled spores</td>
</tr>
<tr>
<td>pulmonary aspergillosis</td>
<td>Ags in lungs</td>
<td><em>Extrinsic alveolitis</em> (type III hypersensitivity)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Eosinophilia</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>*High IgE titre</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*Expectorate: brownish <strong>bronchial plugs</strong> containing <strong>hyphae</strong></td>
</tr>
</tbody>
</table>
| Invasive aspergillosis | Causes pneumonia, then disseminates to involve other organs (brain, kidney, heart) | *Extreme tiredness  
*Excessive weakness  
*Severe headache  
*Delirium  
*Hemiplegia |
|-----------------------|---------------------------------------------------------------------------------|--------------------------|
| Aspergilloma | *Aspergilli colonize cavities in lungs (due to pre-existing lung cavities)  
*They grow & produce a fungal ball (aspergilloma = a mass of entangled hyphae), invading lung airways | *Massive hemoptysis  
*Bronchitis  
*Dyspnea  
*Fever  
*Chest pain |
| Superficial infections | Aspergilli colonize & invade abraded skin, wounds, burns, cornea, external ear, paranasal air sinuses | Fungal sinusitis |

128. Lab diagnosis:

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimens</td>
<td>*Sputum, tissue sections (biopsy/ post-mortem material)</td>
</tr>
</tbody>
</table>
| Staining | *Septate hyphae demo:  
 a) PAS staining  
 b) Wet mount of sputum (in 10% KOH)  

*Septate hyphae & conidiophores* demo:  
 a) LPCB staining  
 b) Conidiophores show swollen, rounded ends (vesicles)  
 c) Spores in chains on elongated cells (sterigmata) |