Primary Cast Episode 17 - Infectious Disease Pathology

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1. **Staph Aureus**

   Describe the virulence factors of s.aureus

   Surface protein - involved in adherence and binding to host cells as well as evading the immune response
   Secreted enzymes- to degrade proteins and enhance capacity for invasion
   Secreted toxins - to damage host cells i.e. alpha toxin, beta toxin, superantigens

   What diseases can be caused by staph aureus?

   - Skin and soft tissue infections - cellulitis, impetigo, abscesses, folliculitis, paronychia. Necrotising skin infections and scalded skin syndrome
   - Pneumonia
   - Endocarditis
   - Osteomyelitis

   What are the risk factors for toxic shock syndrome?

   - Use of tampons
   - Post operative wound infections
   - Postpartum period
   - Use of nasal packs
   - Staph or strep infections

   What are the clinical features of toxic shock syndrome

   - Hypotension
   - Acute renal failure
   - Coagulopathy
   - Respiratory failure
   - Soft tissue necrosis at the sight of infection
   - Generalised rash

2. **Streptococci**

   What is the microscopic appearance of streptococci?

   Gram positive cocci in pairs or chains

   What are some post-infectious syndromes caused by streptococcal infections?

   - Rheumatic fever
   - Immune complex glomerulonephritis

   What are some infections that can be caused by streptococci?

   - Mouth – dental caries caused by S. mutans
   - Skin – erysipelas (group A strep) or scarlet fever also s.pyogenes
   - Pharyngitis – s.pyogenes
   - Pneumonia – s.pneumoniae (pneumococcus)
   - CNS infections – meningitis S. agalactiae (group B strep) – also causes Neonatal sepsis
   - Endocarditis via S. viridans

3. **E.Coli**

Which bacterial class does e. Coli belong to?

E.coli is a gram negative rod which is a facultative anaerobe. It is a normal GIT commensal

List some types of infections that are commonly caused by e.coli?

- Urinary tract infections
- Prostatitis
- Epididymo-orchitis
- Infectious enterocolitis
- Cholecystitis
- Bacterial peritonitis

List the types of e.coli enteritis and their features (2010)

Enterotoxic e.coli (ETEC)

Food and water borne, travellers diarrhoea
LT Heat labile toxin, stimulates adenylyl cyclase increases cAMP increases Cl- secretion (cholera-like toxin)
ST Heat stable toxin, guanylyl cyclase increase in cGMP

Enterohaemorrhagic e.coli (EHEC)

Found in meat
O157:H7 toxin
Shiga like toxin
Responsible for large outbreaks, clinically causes bloody diarrhoea,
Can result in haemolytic uraemic syndrome or thrombotic thrombocytopaenic purpura in 2% of cases

Enteroinvasive e.coli (EIEC)

Present in food and water, can be spread from person to person
NO toxins, invades the mucosa and causes colitis

Enteroaggregative E.coli (EAEC)

Adheres via adherence fimbriae
Shigella like toxin and ETEC ST toxin
Non-bloody diarrhoea, seen in patients with acquired immunodeficiency syndrome

What is the difference between endotoxin and exotoxin?

- E**n**dotoxins are lipopolysaccharides in the outer membrane of the cell wall of gram **n**egative bacteria which cause injury via the host immune response
  E.g. E coli, shigella, pseudomonas, neisseria

- Exotoxins are proteins that are secreted by the bacteria and cause direct injury
  - tetanospasmin produced by Clostridium tetani.
  - botulinum toxin produced by *Clostridium botulinum*

4. **Neisseria Meningitidis**

How does Neisseria meningitidis cause infection

- Common coloniser of the oropharynx
- Spread by respiratory droplets
- Most people develop an immune response and clear it
- Invasive disease happens when there is exposure to a new serotype
- Invades via the respiratory epithelium then to the bloodstream
- Capsule helps the pathogen evade immune response
- Mortality still approximately 10% even with abx cover

What are the consequences of Neisseria Meningitidis infection?

Sepsis, meningitis, seizures, SIADH, stroke, hearing loss, cognitive impairment, death

Apart from neisseria, what else can cause meningitis?

- Other bacteria - e.coli, group B strep (infants), strep pneumoniae, listeria, haemophilus, listeria
- Viral: enterovirus, measles
- Other: TB, rickettsial, carcinoma, autoimmune, chemical

5. **Gastroenteritis**

What are the common causes of infective gastroenteritis?

VIRAL: rotavirus, enteric adenovirus

BACTERIAL:

- Ingestion of preformed toxin i.e. s.aureus, vibrio and chlostridium perfringens
- Toxogenic organism i.e. those that proliferate in the gut and release toxins: e.coli, vibrio cholera
- Enteroinvasive organisms: e.coli, shigella, salmonella

PARASITES: giardia lamblia, entamoeba histolytica

6. **Salmonella**

What type of bacteria is salmonella?

Gram negative bacillus, flagellated

Describe the pathogenesis of typhoid fever

- Caused by salmonella typhi and paratyphi
- Invades the epithelium
- Taken up by macrophages in the lymphoid tissue in the gut.
- Invades M cells causing reactive hyperplasia in lymph tissue
- Disseminates via the blood

What are the clinical features?

- Fever, anorexia, vomiting, bloody diarrhoea via gut wall inflammation
- BC positive in 90% of those with fevers
- Subsequent bacteraemia which can present with flu like symptoms

7. **CHOLERA**

What is the causative organism of cholera?

Vibrio cholera – a gram negative bacteria that is comma shaped

Describe the pathogenesis of cholera (prompt – describe how the toxin causes diarrhoea)

- A non invasive pathogen
- Flagella proteins for attachment and colonisation
- Release of a pre-formed enterotoxin (the cholera enterotoxin, which has 5 beta subunits and 1 alpha subunit)
- Alpha subunit goes into the cytoplasm and binds a G protein which stimulates adenylyl cyclase increase intracellular cAMP
- This opens the CFTR channel and results in release of Cl into the lumen
- This results in secretion of large amounts of HCO3, Na and water
- Clinically, it is seen as secretory diarrhoea (ricewater stools) which overwhelms the colonic resorption capacity

8. **Glandular fever**

Describe the pathogenesis of glandular fever

- EBV transmitted by close contact (saliva)
- B cells infected
- Viral infection begins in the oropharyngeal lymphoid tissue
- There can be lysis of infected cells with virion release or latent infections
- Symptoms appear with the activation of the host immune system
- Proliferation of T cells in spleen and liver causes organomegaly
- Can result in recovery or in development of B cell lymphomas

What are the classical features of glandular fever?

Fever, sore throat, lymphadenitis, splenomegaly, fatigue, hepatitis, rash

What are the possible outcomes of glandular fever?

- Recovery - usually takes 4-6 weeks, fatigue can be longer
- Hepatic dysfunction - jaundice, abnormal LFTs, appetite
- Splenomegaly and splenic rupture
- Transformation to lymphomas

9. **HSV**

Please give some examples of clinical herpes simplex infection

Cold sores, gingivostomatitis, encephalitis, genital herpes, keratitis, oesophagitis, pneumonia, hepatitis

After a primary HSV infection, how does reactivation occur?

- Viral nucleocapsids travel from the skin to the nucleus of the sensory neuron
- During the latent period, only viral mRNA is produced, no viral proteins
- Reactivation occurs via avoiding immune recognition and moving along the sensory nerve again

10. **Varicella**

What are the 2 clinical conditions caused by this virus

Chicken pox and shingles

Describe the pathogenesis and clinical course of infection with this virus including chicken pox and shingles

- Starts with aerosol or direct contact spread
- Heamatogenous dissemination
- Vesicular skin lesions
- Vesicles rupture, crust over and then heal;
- Some virus lies dormant in the dorsal root ganglia and are reactivated later with immunosuppression
- Characterised by vesicular eruption along the dermatome of one or more sensory nerves
- May also cause nerve dysfunction i.e. ramsay hunt syndrome

What are the complications of chicken pox?

- Lung – interstitial pneumonia
- Nervous system – transverse myelitis, encephalitis
- Skin – shingles, bacteria superinfection
- Gut – necrotising visceral lesions

Describe the pathogenesis of varicella zoster

- Patient has an exposure to varicella zoster virus either chickenpox or subclinical
- Virus evades immune defences and infects the sensory neurons in and around the dorsal root ganglia
- Able to remain latent here for many years
- Uswually a single episode of recurrence in the form of shingles
- Reactivation often occurs in the elderly or immunocompromosed

11. **Influenza**

Describe the structure of the influenza virus

Single stranded RNA

What are the types and subtypes in influenza?

- Types A, B and C - determined by a nucleoprotein
- Subtypes depend on differences in the Hemagglutinin and neuraminidase proteins on the envelope

What is the pathological basis of pandemics and epidemics?

- This only occurs in influenza A
- Antigenic shift - for pandemics, H and N antigens are replaced by recombination of RNA with those from animal viruses
- Antigenic drift - for epidemics, mutation in H and N proteins over time allowing for escape from host antibodies

12. **Measles**

What type of virus is measles?

- Single stranded RNA virus
- Member of the paramyxovirus family

How is it spread
Respiratory droplet spread

Describe some of the clinical manifestations of measles infection

- Viral pneumonia
- Conjunctivitis and keratitis
- Acute measles encephalitis
- Longer term - subacute sclerosing panencephalitis
- Diarrhoea
- Immunosuppression
- Croup

What immune responses occur as a result of measles infection?
T cell mediated immunity controls the infection and produces the rash
Antibody mediated immunity protects against reinfection

13. **Malaria**

What organisms cause malaria?
Malaria is a protozoal infection and an intracellular parasite - plasmodium
The types are P. falciparum, P ovale, P vivax and P malariae

Describe the pathogenesis of malaria
Infectious stage (sporozoite) is found in saliva of female anopheles mosquito
Sporozoites are released into the blood and attach & invade hepatocytes
Multiply rapidly
Hepatocyte ruptures, releasing merozoites
These merozoites bind to the surface of RBCs and then grow in a vacuole
The RBCs lyse and spread further

How does P falciparum present clinically?
Fever, severe anaemia, cerebral symptoms, pulmonary oedema, DIC
Splenomegaly
Acute renal failure