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# G – rods (Enterobacteriaceae II.)

key points of the lecture

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# All *Enterobacteriaceae*

- Gram negative rods
- Oxidase negative - dif.dg.from other G - rods
- Biochemical active – fermentation of lactose pos. or neg.
- Facultative anaerobic
- Motile except *Shigella* and *Klebsiella*
- Non-fastidious
- Non-sporing
- Commonly present in large intestine, some are non-pathogenic, a few are highly pathogenic
- Some commensals turn out to be pathogenic (UTI after catheterization)

# Cultivation media used to distinguish between groups

- ENDO agar
- DC agar
- MacConkey agar
- TSI agar
- CIN agar

# *Yersinia*

- *animal pathogens that, under certain conditions, are transmissible*
- Non motile (*Y.pestis*)
- Motily when grown at 22°C (*Y.pseudotuberculosis*)
- Non sporing
- Facultative anaerobic
- GRAM negative cocobacilli

- belong to the *Enterobacteriaceae*
- includes cause of human plague and non-pathogenic environmental species
- three closely related pathogenic species
- Infections:
  - Human plague
  - Uncomplicated gastrointestinal infection usually self-limiting
  - acute enteritis, acute ileitis and mesenteric lymphadenitis
  - *Transmission: directly, or indirectly through*
    - *food*
    - *water or*
    - *via insect vectors*

# *Yersinia* - antigens

- O antigen / somatic antigen – LPS – endotoxin activity
  - K antigen / capsular antiphagocytic activity
  - H antigen / flagellar antigen – in motile *yersinia*
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- The various antigens of *yersinia* are numbered with Arabic numerals

# Medical important species

*Yersinia pestis*

*Yersinia pseudotuberculosis*

*Yersinia enterocolitica*

# *Yersinia pestis*

- plague bacillus,
- essentially a parasite of rodents
- may be transmitted **by fleas** to susceptible animals such as rats
- **wild or sylvatic plague**
- **urban plague**



# *Yersinia pestis* characteristic

- Non motile
- Non sporing
- Gram negative
- Singly or in pairs
  
- grows aerobically or anaerobically at 0–37°C (optimum 27°C)
- Small non hemolytic colonies
- Cin agar
- CHROM agar

# Pandemics

- Outbreaks of human plague, following epidemics in rats, have in the past sometimes developed into pandemics.
- Bubonic plague
- Pneumonic plague
- Septicaemic plague

# Bubonic plague

- the lymph nodes draining the area of the flea bite become affected
- Result: adenitis produces intensely painful swellings or **buboes** in the inguinal, axillary or cervical regions (depending on the position of the bite).
- the plague bacilli may spread to all parts of the body
- Complications:
  - bronchopneumonia,
  - septicaemia
  - meningitis.

# Pneumonic plague

- can develop in patients with bubonic or septicaemic plague
- as a primary infection by inhalation of droplets infected with *Y. pestis* usually from an individual with pneumonic disease
- severe bronchopneumonia develops
- the sputum becomes thin and blood stained

# Septicaemic plague

- This may occur as:
  - a primary infection or
  - as a complication of bubonic or pneumonic plague
- The bacilli spread rapidly throughout the body and the outcome is almost fatal, even in treated cases.
- Purpura may develop in the skin (**'Black Death'**), and disseminated intravascular coagulation is usually present.

# Laboratory diagnosis

- Sputum,
  - Exsudate
  - Fluid from buboes or local skin lesions
  - Blood
- 
- Post mortem : wide range of tissues, especially spleen, lung and lymph nodes
  - Cultivation on selective media
  - Giemsa stain
  - Serology
  - PCR

# Treatment

- *Y. pestis*
- **sensitive** to many antibiotics, including aminoglycosides, fluoroquinolones, chloramphenicol, co-trimoxazole and tetracyclines,
- **resistant** to penicillin
  
- !!! Antibiotic therapy should be started without waiting for confirmation of the diagnosis!!!

# *YERSINIA PSEUDOTUBERCULOSIS*

- disease in many species of wild and domesticated animals and birds
- Transmission - usually through contaminated food or water, raw milk, raw pork, person to person transmission also occurs
- motility when grown at 22°C
- O Ag
- H Ag



# Clinical disease

- acute ileitis and mesenteric lymphadenitis usually accompanied by fever, diarrhoea and pain simulating acute or subacute appendicitis
- Infection occasionally results in a severe typhoid-like illness with fever, purpura and enlargement of the liver and spleen, which is usually fatal.
- immunological sequelae such as erythema nodosum or reactive arthritis develop in some patients.

# Epidemiology and lab dg

- Many animal species suffer from the infection, but there is little proof of direct transmission to man.
- Most human infections probably result from the ingestion of contaminated water, vegetables or other food.
- Isolation in culture from blood, local lesions, or nodes
- Serological methods – ELISA, hemagglutination

# Treatment

- PNC
- Aminoglycosides
- Tetracyclines,
- Co-trimoxazol
- Fluoroquinolons

# *YERSINIA ENTEROCOLITICA*

- Gram negative
- Morphologically and culturally resembles other yersinia
- O Ag
- H Ag

# Clinical disease

- primarily infects the lymphoid tissue of the small intestine and ileocaecal junction
  - enteritis,
  - mesenteric lymphadenitis
  - terminal ileitis
- septicaemia is often fatal - most common in the elderly or in patients with predisposing conditions such as cirrhosis, iron overload or immunosuppression
- In young children the infection may lead to fever, diarrhoea, abdominal pain and vomiting. The symptoms may last for several weeks.
- Post-infectious complications
  - erythema nodosum, polyarthritits, Reiter's syndrome and thyroiditis

# Laboratory diagnosis

- Sample
  - Blood
  - Contaminated sources
  - Faeces
  - Lymph nodes
- Cultivation on BA, MacConkey agar
- Serology – agglutination tests

# Treatment

- Sensitive to aminoglycosides, chloramphenicol, cotrimoxazole, fluoroquinolones and tetracyclines,
- resistant to penicillin. Sensitivity to other  $\beta$ -lactam antibiotics is variable.
- Uncomplicated gastrointestinal infection is usually self-limiting
- treatment is indicated only in severe cases - tetracycline is probably the drug of choice.

# *Campylobacter* and *Helicobacter*

- *Campylobacter* and *Helicobacter* are phylogenetically related, spirally shaped, flagellate bacteria
- *Campylobacter jejuni* is the most frequently identified cause of acute infective diarrhoea, causing much morbidity and economic loss.
- *Helicobacter pylori* is essentially the cause of 'idiopathic' peptic ulceration, and a notable risk factor for the development of gastric cancer.



# *Campylobacter*

- Small, spiral, Gram-negative rods with a single flagellum at one or both poles
- sensitive to oxygen
- microaerobic and capnophilic conditions must be provided for their cultivation
- grow best at 37–42°C = ‘thermophilic campylobacters’
- Oxidase positive
- Catalase positive

# Lab dg

- Sample
  - Faeces
- Cultivation on selective media with the oxygen tension lowered to 5–15% and carbon dioxide raised to 5–10% at 42-43 °C for 48 hours
  - Charcoal-based blood-free agar (Karmali agar)
- Serology: if aseptic arthritis or Guillain–Barré syndrome (polyneuropathy) occurring after diarrhoea that was not investigated

# Medical important species

*Campylobacter jejuni*

*Campylobacter coli*

# Sources and transmission

- the bacteria from wild birds and other animals into the surface water of lakes, rivers and streams, in which campylobacters can survive for many weeks at low temperatures.
- **Farm animals** are often infected from such sources and flies have also been implicated in spread.
- Cattle are commonly infected, and **raw milk** often becomes contaminated.
- Raw or **inadequately pasteurized milk** and **untreated water**
- **chickens**

# Clinical manifestation

- Properly cooked food do not pose a risk, but cross-contamination to other foods, such as bread and salads, probably accounts for many infections
- Most infections are sporadic
- The spread of infection between individuals is of minor importance
- **Campylobacter enteritis** = the most common form of acute infective diarrhoea with high fever, malaise, painfull muscles, abdominal cramps, vomiting is not common
- The disease occurs among all age groups (especially young adults), shows a pronounced **summer peak** and is **often associated with travel**.

# Treatment

- Campylobacteriosis is usually self-limiting
- fluid and electrolyte replacement
- Antimicrobial treatment reserved for patients with severe or complicated infections connected with high fever and prolonged clinical symptoms
- Ciprofloxacin (and other fluoroquinolons) - !!!resistance rates are rising!!!
- Macrolides – ERY, AZI

# *HELICOBACTER*

- Gram-negative
- spirally shaped bacterium
- unipolar flagella
  
- strictly micro-aerophilic
- Urease positive

# Medical important species

*Helicobacter pylori*

*Helicobacter heilmannii*

*Helicobacter cinaedi*



# Pathogenesis

- The gastric antrum is the most favoured site,
- other parts of the stomach may be colonized,
- especially in patients taking an acid-lowering drug, or in subjects with a natural lower acid output
- are non-invasive, present in the mucus overlying the mucosa
- gastric acid is potentially destructive to *H. pylori*, protection is provided by its powerful urease activity and generation ammonia that may neutralize acid around *H.pylori*

# The course of infection

- mild attack of **acute achlorhydric gastritis** with symptoms of abdominal pain, nausea, flatulence and bad breath
- infection and **chronic active gastritis** persist - progression to **atrophic gastritis** and **intestinal metaplasia**

# Associated disease

- Gastric and duodenal ulcers – peptic ulcer disease
- Non-ulcers dyspepsia
- Gastric malignancies
- Other disease – iron deficiency anemia, increased rates of esophageal cancer, allergy, asthma

# Laboratory diagnosis

- Screening
- Definitive tests - finding *H. pylori* in specimens of gastric mucosa obtained by biopsy

# Lab dg – non-invasive tests

- **Serology**
- **Urea breath test**
- **Faecal antigen test**
- **PCR**

# Lab dg – invasive tests

- **Collection of specimens**

- Mucosal biopsy specimens are taken from the gastric antrum

- **Biopsy urease test**

- A biopsy specimen is placed into a small quantity of urea solution with a phenol red, which detects alkalinity resulting from the formation of ammonia

- **Histopathology and microscopy**

- **Culture**

# Treatment

- **sensitive to** most  $\beta$ -lactam antibiotics, macrolides, tetracyclines and nitroimidazoles,
- **resistant to** trimethoprim
- 4 main antibiotics: amoxicillin, clarithromycin, tetracycline and metronidazole.
- It is also sensitive to bismuth subcitrate or subsalicylate
- partially sensitive to the acid-lowering proton pump inhibitors omeprazole and lansoprazole.

# Eradication of *H. pylori* infection

- Triple therapy
  - macrolide clarithromycin, + amoxicillin + omeprazole
- Quadruple therapy
  - Tetracycline + metronidazole + bismuth subsalicylate + omeprazole



# Sources

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