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Enterobacteriaceae I.

key points of the lecture

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All *Enterobacteriaceae*

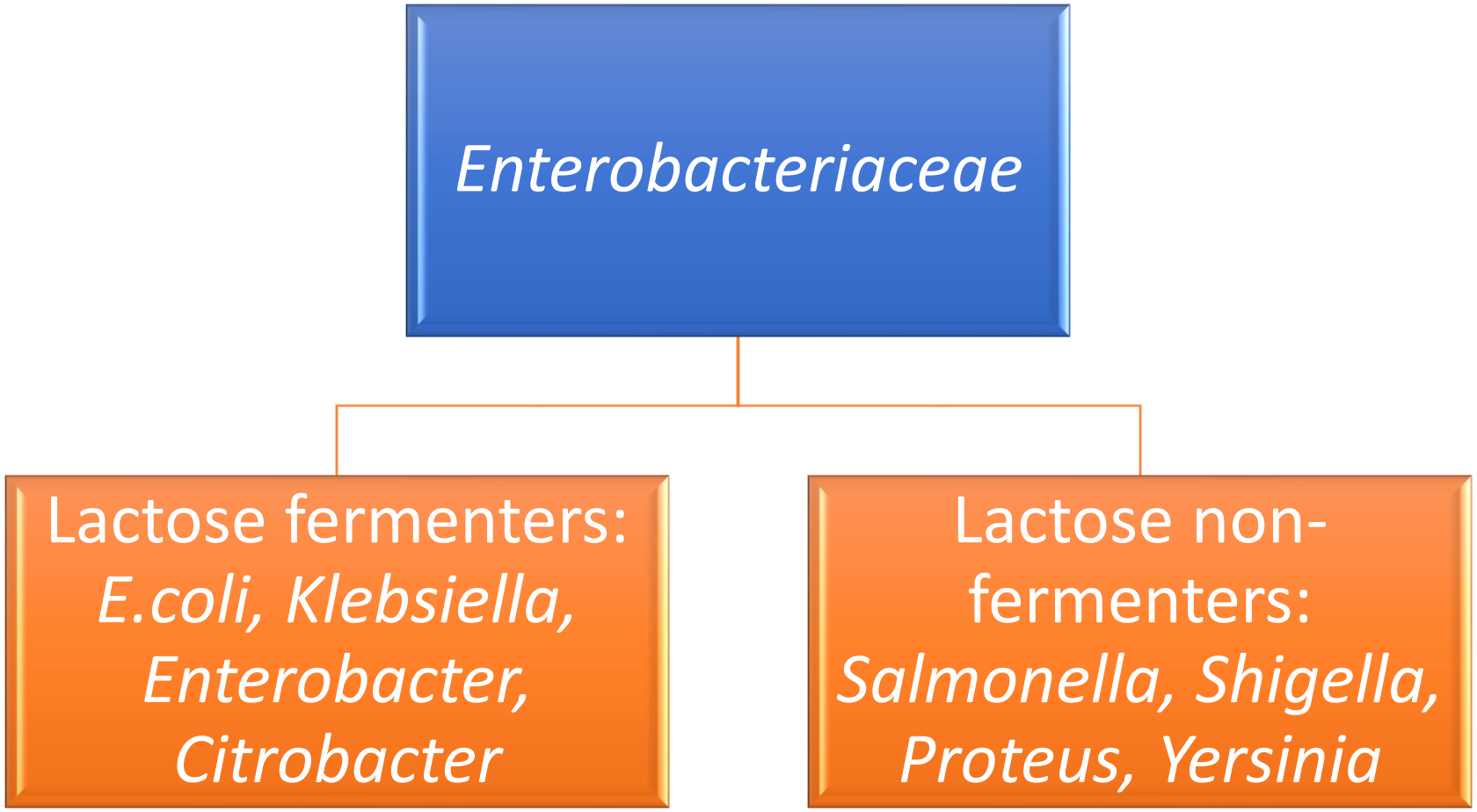
- Gram negative rods
- Oxidase negative - dif.dg.from other G - rods
- Biochemical active – fermentation of lactose pos. or neg.
- Facultative anaerobic
- Motile except *Shigella* and *Klebsiella*
- Non-fastidious
- Non-sporing
- Commonly present in large intestine, some are non-pathogenic, a few are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

All *Enterobacteriaceae*

- Widest and most heterogenous group of medically important bacteria
  - differentiation is based on biochemical properties, antigen characteristics, on DNA homology and ATB susceptibility
- Commonly present in nature (soil, water, plants)
- Commonly present in large intestine, parts of physiological flora of colon, some are non-pathogenic, a few are highly pathogenic
  - Obligatory pathogenic (*Yersinia pestis, Salmonella, Shigella*)
  - Oportunistic pathogens (*Klebsiella, E. coli, Proteus*)
  - Some commensals turn out to be pathogenic (UTI after catheterization)

  - Transmission:
    - from annimals (*Salmonella*),
    - from human carrier (*S. typhi*),
    - endogenous infection (*E.coli*) - after breaking of immune barriers, transmitted from GIT ascendently

Classification of *Enterobacteriaceae*



Cultivation media used to distinguish between groups

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

3 groups of antigens:

- somatic **O antigen**
  - most important antigen of cell wall, heat resistant, part of LPS
  - composed of 3 parts (O polysaccharide, core polysaccharide and lipid A) with endotoxin activity
- capsular **K antigen**
  - heat susceptible
- flagellar **H antigen**
  - termosusceptible

Salmonella

- Over 2000 different antigenic types – represent serotypes (serovars) of *Salmonella enterica*
- Certain serotypes are a major cause of food-borne infections
- Highly motile
- Facultative anaerobic

- Infections:
  - Relatively benign and restricted to the intestinal tract with diarrhoea
  - Life-threatening systemic diseases – *S.typhi, S.paratyphi*

Salmonella - antigens

- O antigen / somatic antigen – LPS – located in the outer membrane
  - Structural heterogeneity of LPS – is responsible for the large number of serotypes
- H antigen / flagellar antigen –
- Vi antigen /virulence antigen *S. typhi*

- The various O-antigens of *salmonellae* are numbered with Arabic numerals
- The Kauffmann–White classification

- Pathogenic to man are serotypes of *S. enterica*.
- Most serotypes of *S. enterica* (enteritidis...) cause **food-borne gastroenteritis** and have animal reservoirs.
- *S. enterica* serotypes Typhi and Paratyphi cause **typhoid fever**.
- Infective dose:
  - For human infections, the number of bacteria that must be swallowed in order to cause infection is uncertain and varies with the serotype.
- Many factors influence the infective dose:
  - variation in virulence of strains
  - The vehicle of ingestion - organisms ingested in water and other drinks may be carried through the stomach relatively rapidly, and evade the effect of gastric acid.
  - the administration of antacids, or the effects of gastric resection, reduces the infective dose.
- Host factors are also important, particularly the nutritional and immune status of the host.

CLINICAL SYNDROMES

- there are 4 major syndromes
  - enteric fever
  - gastroenteritis
  - bacteraemia with or without metastatic infection
  - the asymptomatic carrier state

Enteric fever

- is caused by strains of *S. Typhi* or *S. Paratyphi* A, B or C
- The clinical features tend to be more severe with *S. Typhi* (**typhoid fever**).
  - After penetration of the ileal mucosa the organisms pass via the lymphatics to the mesenteric lymph nodes,
  - after a period of multiplication they invade the bloodstream - primary bacteremic phase in the first 7–10 days of the incubation period.
  - After multiplication - a second and heavier bacteremia, the onset coincides with fever and other signs of clinical illness.
  - Peyer's patches and other gut lymphoid tissues become involved in an inflammatory reaction, followed by necrosis, sloughing and the formation of characteristic typhoid ulcers occurs.

Gastroenteritis and food poisoning

- Strains of S. enterica commonly cause food poisoning worldwide
- Diarrhoea, headache, malaise and nausea. The incubation period is usually 8–48 h, the clinical course is short and self-limiting
- Symptoms vary from the passage of 2 or 3 loose stools to a severe illness with the frequent passage of watery, green, offensive stools, fever, shivering, abdominal pain and, in the most cases, dehydration leading to hypotension, cramps and renal failure. Vomiting is rarely a prominent feature of the illness
- In most cases the acute stage is over within 2–3 days, although it may be more prolonged. Persistent or high fever suggests bacteremia, possibly with metastatic infection.

Bacteremia and metastatic disease

- Bacteremia is a constant feature of enteric fever caused by strains of *S. Typhi* and *Paratyphi* A and C.
- dissemination of the bacilli throughout the body results in the establishment of one or more localized foci of persisting infection
- Osteomyelitis
- Suppurative arthritis
- Meningitis
- Abscess formation

The prolonged carrier state

- Most people infected with salmonella continue to excrete the organism in their stools for days or weeks after complete clinical recovery
- A few patients continue to excrete the salmonellae for prolonged periods.
- The term **chronic carrier** is reserved for those who excrete *salmonellae* for a year or more.
- The bacilli are most commonly present in the gall bladder, less often in the urinary tract

LABORATORY DIAGNOSIS

- Cultivation on selective and diagnostic media
  - Blood
  - Stool
  - Urine
- Biochemical tests
- Serological tests
  - Widal agglutination test
  - ELISA
  - Immunoblotting

Therapy and prevention

- Typhoid and other serious systemic salmonella infections are treated with amoxicillin, co-trimoxazole, ciprofloxacin or chloramphenicol.
- Antibiotics have no place in the management of salmonella gastroenteritis unless invasive complications are suspected.
- Drugs that impair gut motility should be avoided!!!

- Clean water, sanitation and hygienic handling of foodstuffs are the keys to prevention.

To reduce the incidence of food poisoning, whether due to *salmonellae* or to other bacteria, two basic precepts must be observed:

- Raw foodstuffs of animal origin must never have direct or indirect contact with cooked foods.
- Foodstuff thought to be contaminated should be treated or held under temperature conditions that prevent the organisms from growing.
- Cooked foods should be served and eaten immediately after cooking or cooled rapidly and held at refrigerator.

Shigella

- Gram-negative bacilli
- non-motile
- non-capsulate
- Lactose non-fermenter
- Facultative anaerobic
- Microscopically are indistinguishable from other enteric Gram-negative bacilli

Medical important species

Shigella dysenteriae
Shigella flexneri
Shigella boydii
Shigella sonnei

CLINICAL FEATURES

- Bacillary dysentery
  - the frequent passage of bloodstained mucopurulent stools
  - caused by members of the genus *Shigella*,
  - is prevalent in many countries with temperate climates
- The incubation period
  - usually between 2 and 3 days, but may be as long as 8 days
- the initial symptom is abdominal colic
- followed by the onset of watery diarrhea
- accompanied by fever, headache, malaise and anorexia

- progress to abdominal cramps, tenesmus and the frequent passage of small volumes of stool, predominantly consisting of bloody mucus.
- The symptoms typically last about 4 days, but may continue for 14 days or more.
- Infection may affect the nervous system resulting in seizures and encephalitis.

- Shigellosis is occasionally associated with the development of Reiter's syndrome (reactive arthritis)

Pathogenic mechanisms

- lipopolysaccharide - a role in virulence by preventing the effects of serum complement.
- lipid A - implicated in causing localized cytokine release
- *Shiga toxin*
  - AB toxin
  - The A subunit possesses the biological activities of the toxin, and the B subunits mediate specific binding
- Haemolytic uraemic syndrome - caused by the action of *Shiga toxin* on kidney tissues
- neurotoxic properties

LABORATORY DIAGNOSIS

- Cultivation DC agar, ENDO agar, Mac Conkey agar
  - The faeces
- Biochemical tests
- Agglutination tests – serotyping
- PCR

TREATMENT

- mild forms do not require antibiotic therapy
- good nutrition is essential and symptomatic treatment
  - hydration by use of oral rehydration salt solution
- As with salmonella infections, drugs that impair gut motility should be avoided!!!
- Treatment with a suitable antibiotic is necessary in the very young, the aged or the debilitated, and in those with severe infections (ciprofloxacin, ceftriaxone. Ampicillin, tetracyclines and trimethoprim are suitable alternatives, but resistance is common.

Escherichia coli

- Gram negative bacili
- Facultative anaerobic
- Motile
- Non-sporing
- Lactose fermenter

Antigenic structure

- O Ag - somatic lipopolysaccharide (LPS)
- H Ag - flagellar
- K Ag - capsular

CLINICAL SYNDROMES

- *E. coli* is normally present in the gut as a harmless commensal

- Urinary tract and septic infections
- Diarrhoea
- Neonatal meningitis and septicaemia
- Sepsis in operation wounds
- Abscesses in a variety of organs

Urinary tract infection

- occurs more frequently in women than in men because the shorter, wider, female urethra appears to be less effective in preventing access of the bacteria to the bladder.

- Most urinary tract infections are caused by organisms originating from the patient's own faecal flora. – endogenous origin
- Therapy:
  - Uncomplicated cystitis usually responds to oral agents such as trimethoprim or nitrofurantoin
  - More serious infections require specific antimicrobial therapy based on laboratory results

Diarrhoea

- 5 groups, each associated with specific serotypes and with different pathogenic mechanisms:

1. Enteropathogenic E. coli (EPEC), which cause infantile enteritis, especially in tropical countries.
2. Enterotoxigenic E. coli (ETEC), which are responsible for community-acquired diarrhoeal disease in areas of poor sanitation and are the most common cause of travellers' diarrhoea.
3. Enteroinvasive E. coli (EIEC), which cause an illness resembling shigella dysentery in patients of all ages.
4. Verocytotoxin-producing E. coli (VTEC), which cause symptoms ranging from mild, watery diarrhoea to haemorrhagic colitis and haemolytic uraemic syndrome.
5. Enteroaggregative E. coli (EAggEC), which cause chronic diarrhoeal disease in certain developing countries.

Laboratory diagnosis

- Cultivation DC agar, ENDO agar, Mac Conkey agar
  - Rectal swab
- Biochemical tests
- Agglutination tests – serotyping

Treatment

- early administration of fluid and electrolytes
- Antimicrobial drugs play a minor role
- Clean water, sanitation and hygienic handling of foodstuffs are the keys to prevention.
- Travellers to countries with poor hygiene, especially in the tropics, should select eating places with care and, if possible, should consume only hot food and drinks, or bottled water.
- Self-peeled fruits are probably safe, but salads should be avoided.
- Unheated milk should always be considered unsafe.

Klebsiella

- non-motile
- capsulate
- Gram negative bacilli
- Facultative anaerobic

- Antigenic structure:
  - capsular (K) antigens
  - somatic (O) antigens

CLINICAL SYNDROMES

- urinary tract infections
- bronchopneumonia
- Septicaemia
- hospital-acquired infections
- Soft tissue infections
- Endocarditis
- central nervous system infections

- *Klebsiella pneumoniae*
  - pneumonia
  - Necrotic destruction of alveolar spaces.
  - Bloody sputum.
  - Infections of wounds, soft tissues and urinary tract.
- *K. rhinoscleromatis* - Rhinoscleroma is a chronic upper respiratory tract disease
  - lesions occur in the nose, larynx, throat and, to a lesser extent, the trachea, and consist of granulomatous infiltrations of the submucosa
- *K. ozaenae* – atrofic disease of nasal epitelium

TREATMENT

- resistant to ampicillin and amoxicillin,
- but combinations of these drugs with β-lactamase inhibitors such as clavulanic acid are usually effective
- susceptible to cephalosporins such as cefuroxime and cefotaxime, and to fluoroquinolones

Proteus

- **Highly motile**
- Gram negative bacilli (Rauss phenomenon)
- *P. mirabilis, vulgaris* –infections of urinary tract, hospital-acquired infections
  - production of urease (lysis of urea, alcalinisation, increased possibility for calculli formation, toxicity for epitelium)
- *Proteus vulgaris*: indol+
- *Proteus mirabilis*: indol-

- Therapy: ATB susceptibility testing
- Often resistant strains

Sources

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