# THE GENUS *STREPTOCOCCUS*

The genus *Streptococcus* obtains Gram-positive cocci, nonmotile, nonsporeforming, arranged mostly in chains or in pairs.
Most species are facultative anaerobes.
Some of streptococci are encapsulated.

- The single scheme for differentiation of streptococci is used in practise:
  - streptococci with complete (β) hemolysis
  - streptococci with incomplete (α) hemolysis (s.c. viridans streptococci)
  - streptococci without hemolysis

# Streptococci

- facultative anaerobe
- Gram-positive
- chains or pairs
- catalase negative

- Streptococci are widely distributed in nature.
- Some are members of the normal human microflora, other are associated with important human diseases attributable in part to infection by streptococci, in part to sensitization to them.
- Streptococci produce a variety of extracellular substances and enzymes.

- The differentiation of streptococci according to serological properties

  (Lancefield groups A to V).

  - Streptococci, classified into different groups, possess group-specific antigens which are either cell wall carbohydrates (s.c. C polysaccharides) or teichoic acid.

- Other possibilities of differentiation of streptococci – according to biochemical properties or clinical presentations.

# Chemical structure and antigens

- Cell wall polysaccharide C
- Peptidoglycan
- Lipoteichoic acid
- M-protein
- T substance and R protein
- Capsule
- F protein

# M protein

- This substance is  major virulence factor of *S. pyogenes*.
- When M protein is present, the streptococci are virulent, and in the absence of M type–specific antibodies, they are able to resist phagocytosis by polymorphonuclear leukocytes.
- M protein also promotes adherence to host epithelial cells.
- *S. pyogenes* strains that lack M protein are not virulent.

# T substance

- This antigen has no relationship to virulence of streptococci.
- Unlike M protein, T substance is acid-labile and heat-labile.
- It is obtained from streptococci by proteolytic digestion.
- T substance permits differentiation of certain types of streptococci by agglutination with specific antisera.
- Another surface antigen has been called R protein.

# Extracellular products

- Erythrogenic toxin (pyrogenic toxin)
- Streptolysin O
- Streptolysin S
- Hyaluronidase (spreading factor)
- Streptokinase
- Streptodornase

  (streptococcal deoxyribonuclease)
- other

# Erythrogenic toxin (pyrogenic toxin)

- This toxin is soluble and it is destroyed by boiling for 1 hour.
- It causes the rash that occurs in scarlet fewer. Only *S. pyogenes* strains elaborating this toxin can cause scarlet fewer.
- A non-toxigenic strain, after lysogenic conversion will produce erythrogenic toxin.
- Erythrogenic toxin is antigenic.
- Superantigen.

# Streptolysin O

- Streptolysin O is a protein that is hemolytically active in the reduced state, but rapidly inactivated in the presence of oxygen.

- ASLO – appear in human following infection with any streptococci that produce streptolysin O.

# Streptolysin S

- Streptolysin S is the agent responsible for the hemolytic zones around streptococcal colonies growing on the surface of blood agar.
- It is not antigenic.

# Hyaluronidase

- Hyaluronidase splits hyaluronic acid, an important component of the ground substance of connective tissues.
- Thus, hyaluronidase aids in spreading of infecting microorganisms (spreading factor).
- Hyaluronidases are antigenic and specific for each bacterial or tissue source.

# Streptodornase (streptococcal deoxyribonuclease)

- Streptococcal deoxyribonuclease depolymerizes DNA.

- The enzymatic activity can be measured by the decrease in viscosity of known DNA solutions.

# Streptokinase (fibrinolysin)

- Streptokinase is produced by many strains of group A beta-hemolytic streptococci.
- It transforms the plasminogen of human plasma into plasmin, an active proteolytic enzyme that digests fibrin and other proteins.
- Streptokinase has been given intravenously for treatment of pulmonary and of coronary artery and venous thromboses.

# Classification of streptococci of particular medical interest

- *Streptococcus pyogenes*
- *Streptococcus agalactiae*
- beta-hemolytic streptococci C, F, G
- *Streptococcus pneumoniae*
- *Streptococcus anginosus*
- viridans streptococci
- *Peptostreptococcus* species

# The species *Streptococcus pyogenes*

- Gram-positive spherical cocci, 1.0 micrometer in diameter arranged in chains (especially in liquid media and pathological specimens).
- *S. pyogenes* likely as other streptococci does not produce catalase (in contrast to staphylococci).
- This species does not split ribose (in contrast to other streptococci).
- It grows in white regular colonies about 1 mm in diameter, with a large zone of β-hemolysis on blood agar after 24 hours of incubation.

# The species *Streptococcus pyogenes*

- The metabolism of *S. pyogenes* is fermentative; the organism is a catalase-negative aerotolerant anaerobe (facultative anaerobe), and requires enriched medium containing blood in order to grow.

- Group A streptococci typically have a capsule composed of hyaluronic acid and exhibit beta (clear) hemolysis on blood agar.

- Group A streptococci are parasites of humans, and *Streptococcus pyogenes* is one of the most frequent pathogens of humans.
- It is estimated that between 5-15% of normal individuals harbor *Streptococcus pyogenes*, usually in the respiratory tract, without signs of disease.
- When the host defenses are compromised, or when the microorganism is able to exert its virulence, or when it is introduced to vulnerable tissues or hosts, an acute infection occurs.

- *Streptococcus pyogenes* owes its major success as a pathogen to its ability to colonize and rapidly multiply and spread in its host while evading phagocytosis and confusing the immune system.

- **Acute diseases** associated with *Streptococcus pyogenes* occur chiefly in the **respiratory tract**, **bloodstream**, or the **skin**. Streptococcal disease is most often a respiratory infection (pharyngitis or tonsillitis) or a skin infection (pyoderma). *S. pyogenes* is the leading cause of uncomplicated bacterial pharyngitis and tonsillitis.

- *S. pyogenes* infections can also result in sinusitis, otitis, mastoiditis, pneumonia, joint or bone infections, necrotizing fasciitis and myositis, meningitis or endocarditis.
- *S. pyogenes* also infects the skin. Infections of the skin can be superficial (impetigo) or deep (cellulitis).
- Scarlet fever and streptococcal toxic shock syndrome are systemic responses to circulating bacterial toxins.
- Two post streptococcal sequelae (rheumatic fever following respiratory infection and glomerulonephritis following respiratory or skin infection), occur in 1-3% of untreated infections.

- **The most frequent etiologic agents of bacterial tonsillitis and tonsillopharyngitis are *Streptococcus pyogenes* strains (80-90 %).**

# Initial antibiotic therapy of bacterial tonsillitis and tonsillopharyngitis

- **Antibiotics of I. choice**
  - penicillin (3-4 x daily)
  - macrolides (in patients with allergy to penicillins)

# Etiology and treatment of peritonsillar and tonsillar abscess

- **Etiology:**
  - ***Streptococcus pyogenes***
  - anaerobic microbes (*Peptostreptococcus* sp.)
- **ATB of I. choice:**
  - penicillin
- **Alternative ATB:**
  - clindamycin

# Diagnostic methods

- microscopy
- cultivation
- biochemical tests
- serological examination
- others

# *Streptococcus pneumoniae*

- Pneumococci are alfa-hemolytic.
- Their growth is inhibited by optochin.
- The pneumococci are Gram-positive diplococci, often lancet-shaped or arranged in chains, possessing a capsule of polysaccharide that permits typing with specific antisera.

- ***Streptococcus pneumoniae* is very important etiologic agent of pneumonia**
- Pneumonia
  - typical pathogens
  - atypical pathogens
- Pneumonia
  - community-acquired
  - hospital-acquired (nosocomial)

# Etiology of pneumonia CAP

typical pathogens

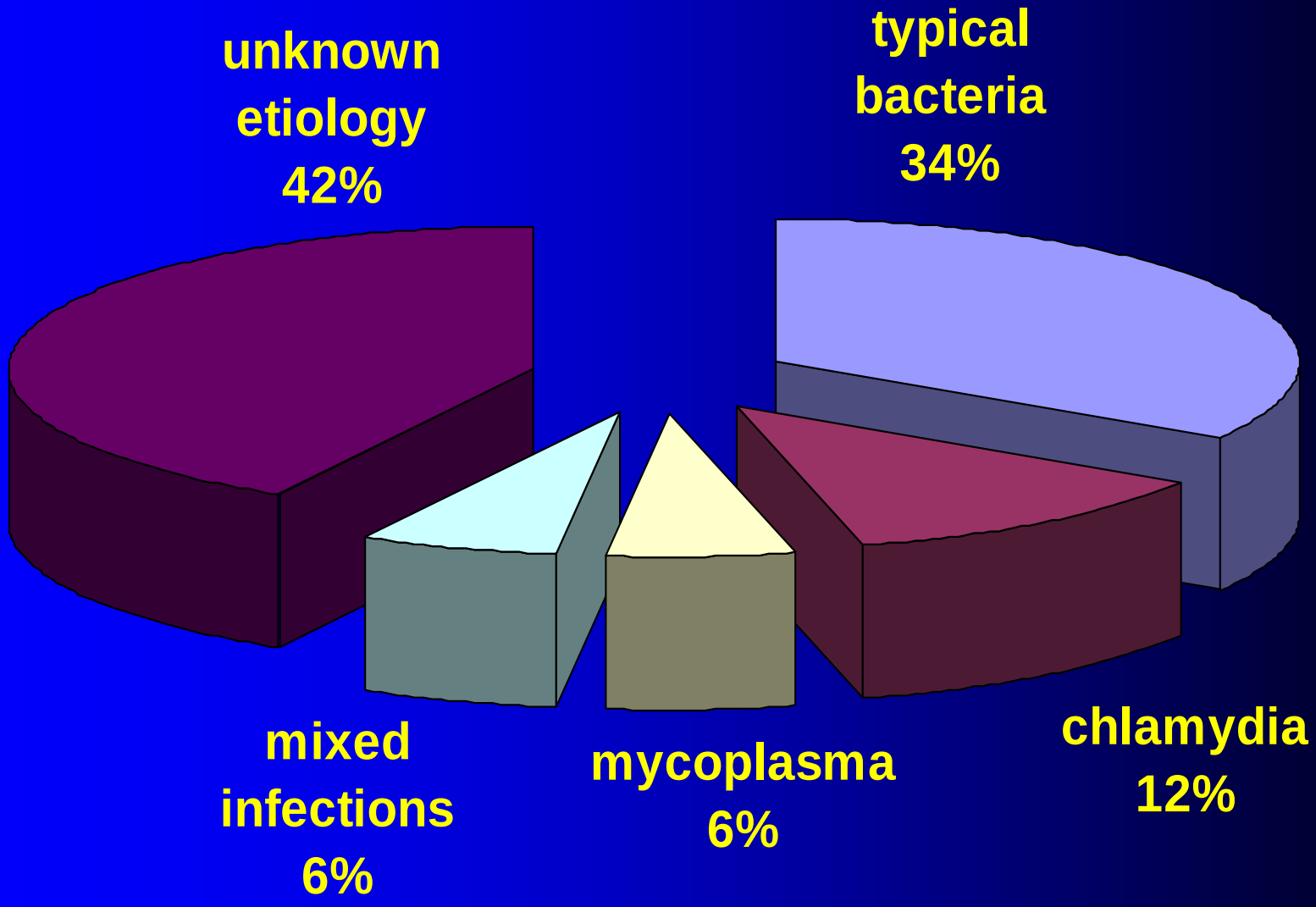
- ***Streptococcus pneumoniae***
- *Haemophilus influenzae*
- *Moraxella (Branhamella) catarrhalis*
- *Staphylococcus aureus*
- *Klebsiella pneumoniae*
- other

# Etiology of pneumonia CAP

atypical pathogens

- *Chlamydophila pneumoniae*
- *Chlamydophila psittaci*
- *Mycoplasma pneumoniae*
- *Legionella pneumophila*
- others

# Etiology of pneumonia in olomouc region (CAP)



# Initial antibiotic therapy of community-acquired pneumonia

- **Drug of I. choice**
  - amoxicillin
- **Alternative antibiotics**
  - macrolides (e.g. clarithromycin, azithromycin)
  - doxycycline (in adults and children older than 12 years)

# Etiology and treatment of otitis media acuta

- **Etiology:**
  - ***Streptococcus pneumoniae***
  - *Haemophilus influenzae*
  - *Moraxella (B) catarrhalis*

- **Antibiotic of I. choice:**
  - amoxicillin

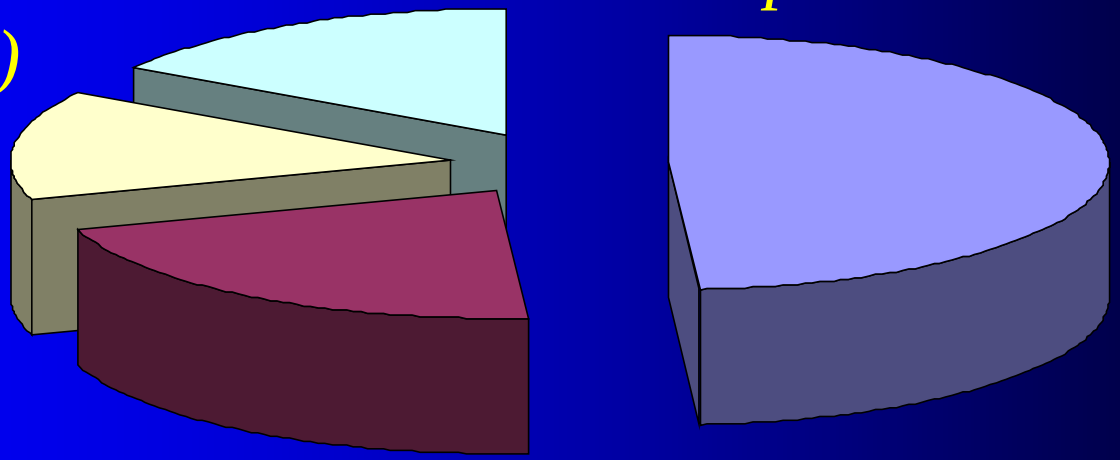
- **Alternative antibiotic:**
  - amoxicillin/clavulanic acid
  - ampicillin/sulbactam
  - cephalosporins II. gen. (cefuroxime, cefprozil)
  - in patients with allergy to penicilllins - macrolides

# Bacterial etiology of acute otitis media in olomouc region

others - 16%

*Streptococcus pneumoniae* - 49%

*Moraxella (B) catarrhalis* - 14%



*Haemophilus influenzae* - 21%

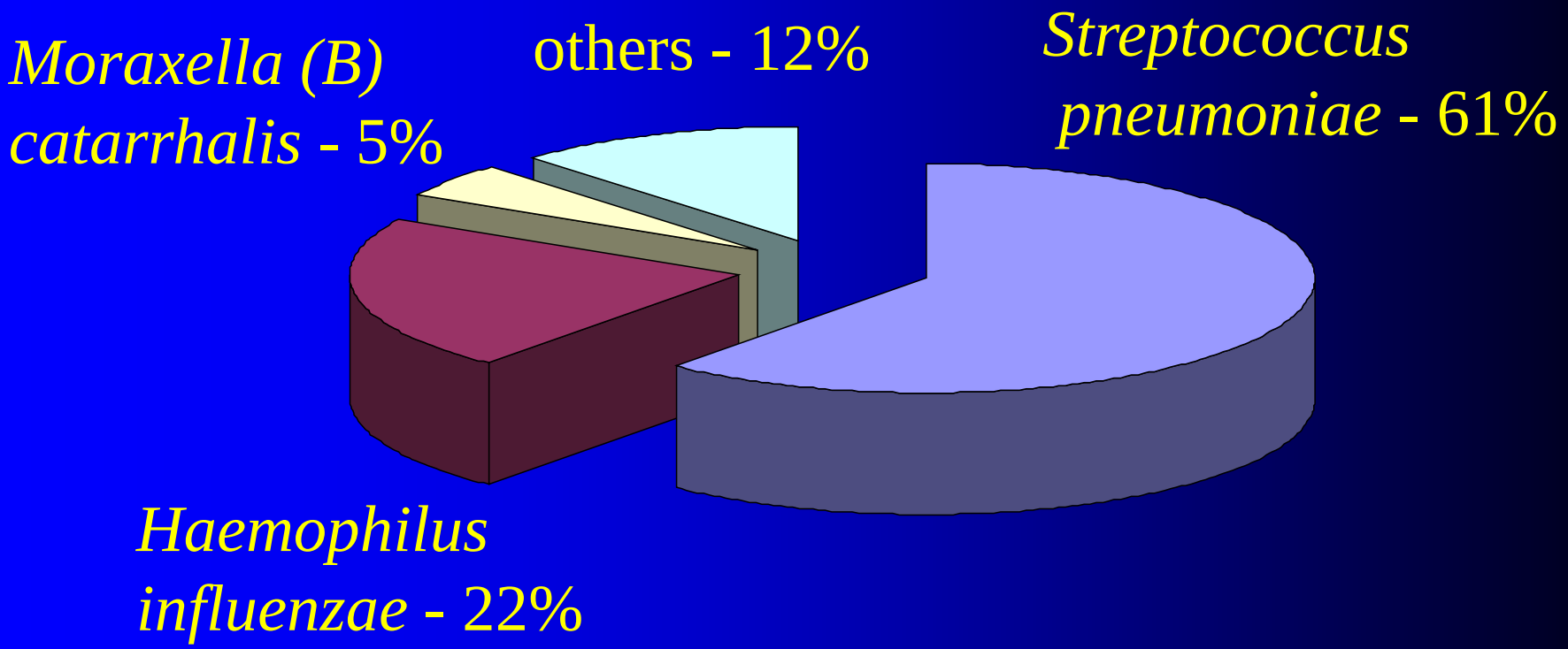
# Etiology and treatment of sinusitis acuta

- **Etiology:**
  - ***Streptococcus pneumoniae***
    *Haemophilus influenzae*
  - *Moraxella (B) catarrhalis*

- **Antibiotic of I. choice:**
  - amoxicillin

- **Alternative antibiotic:**
  - amoxicillin/clavulanic acid
  - ampicillin/sulbactam
  - cephalosporins II. gen. (cefuroxime, cefprozil)
  - in patients with allergy to penicilllins - macrolides

# Bacterial etiology of acute sinusitis in olomouc region



# *Streptococcus agalactiae*

- These are the group B streptococci.
- They are members of the normal flora of the female genital tract and an important cause of neonatal sepsis and meningitis.
- They typically are beta-hemolytic.
- They have positive CAMP test.

- Basing on results obtained in Neonatal department of Teaching Hospital in Olomouc, the most frequent bacterial pathogens of neonatal sepsis are *Escherichia coli*, *Klebsiella pneumoniae*, *Streptococcus agalactiae*, *Enterococcus* spp. and *Staphylococcus aureus*.
- Based on their resistance to antibiotics it can be concluded that ampicillin in combination with gentamicin/netilmicin is first choice regimen.
- In case of persisting signs of infection, it is necessary to consider the etiological role of chlamydia, mycoplasma and ureoplasma and the therapy is to be changed by adding of macrolide.
- After the identification od bacterial pathogens and the resistance to antibiotics the therapy should be focused on the aimed (causal) one.

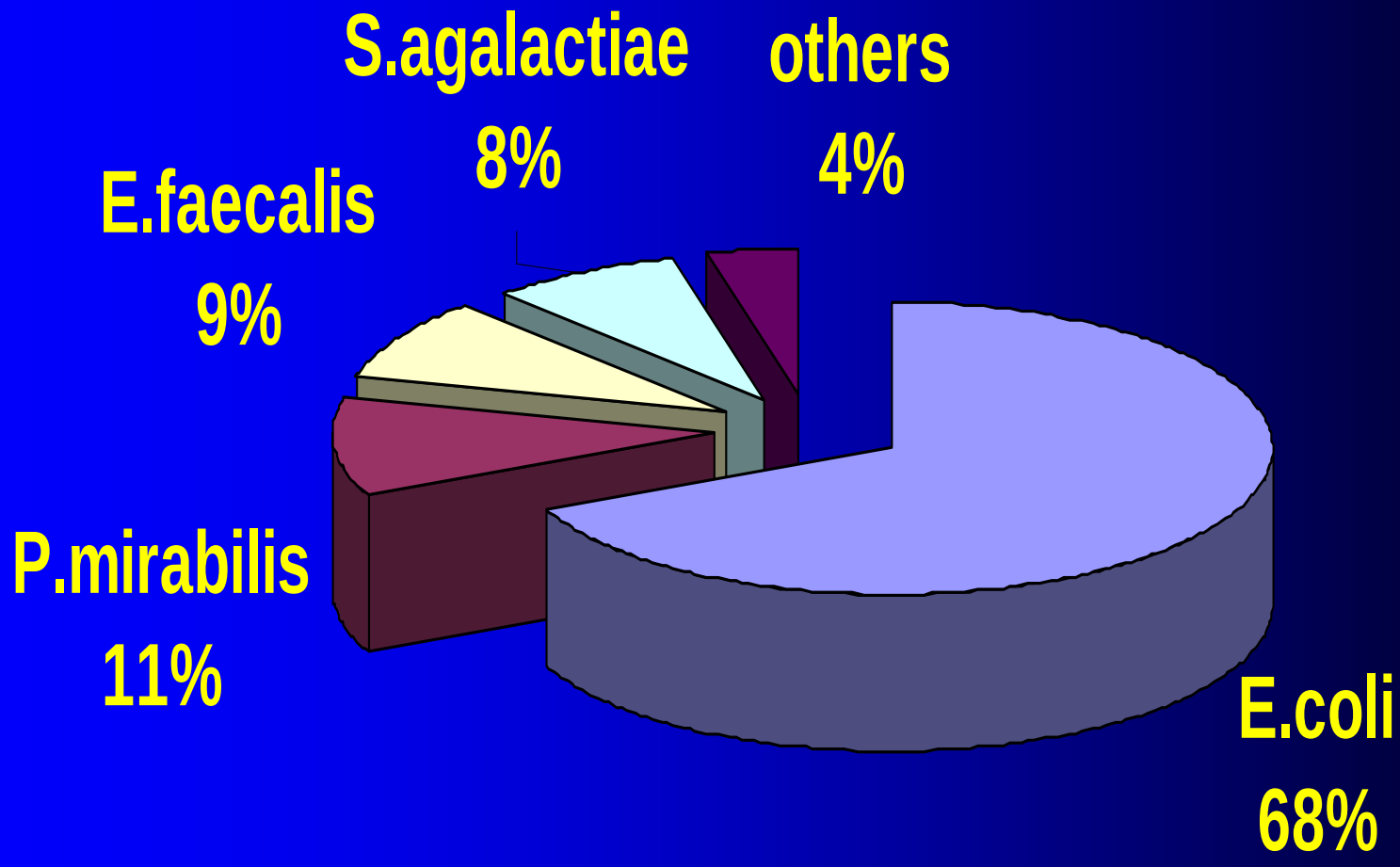
# Etiology of neonatal infections in Teaching Hospital in Olomouc

| | | |
|---|---|---|
| **Gram-negative bacteria** | | 53 % |
| *Escherichia coli* | 19 % | |
| *Klebsiella pneumoniae* | 16 % | |
| *Pseudomonas aeruginosa* | 7% | |
| *Enterobacter cloacae* | 6 % | |
| *Acinetobacter baumannii* | 5 % | |
| **Gram-positive bacteria** | | 43 % |
| ***Streptococcus agalactiae*** | 15% | |
| *Enterococcus* sp. | 13 % (84 % is *E. faecalis*) | |
| *Staphylococcus aureus* | 9 % | |
| *Staphylococcus* sp. (coagulase-negative) | 6 % | |
| *Candida* sp. ( 87 % is *C. albicans*) | | 4 % |

# Etiology of community-acquired urinary tract infections

- *Escherichia coli*
- *Proteus mirabilis*
- *Enterococcus faecalis*
- *Streptococcus agalactiae*
- others

# Bacterial etiology of community-acquired urinary tract infections in olomouc region



# Initial antibiotic therapy of community-acquired urinary tract infections

- **Drug of I. choice**
  - nitrofurantoin, cotrimoxazol, trimethoprim
- **Alternative antibiotics**
  - amoxicillin/clavulanic acid
  - ampicillin/sulbactam
  - cephalosporins II. gen. (cefuroxime, cefprozil)

# *Streptococcus milleri group*

- *S. anginosus*
- *S. intermedius*
- *S. constellatus*
- These streptococci are part of the normal flora (oral cavity and gastrointestinal tract) with the ability to cause abscesses and systemic infections
- They may be beta, **alpha** or non-hemolytic

# Viridans streptococci

- Viridans streptococci include *S. mitis*, *S. mutans*, *S. salivarius*, *S. sanquis* and other.
- Typically they are alpha-hemolytic, but they may be non-hemolytic.
- The viridans streptococci are the most prevalent members of normal microflora of the upper respiratory tract and are important for healthy state of mucous membranes there.
- They may reach the bloodstream as a result of trauma and are a principal cause of endocarditis on abnormal heart valves.

# *Peptostreptococcus* species

- These streptococci grow only under anaerobic conditions and variably produce hemolysins.
- They are part of the normal microflora of the mouth, upper respiratory tract, bowel, and female genital tract.
- They often participate with many other bacterial species in mixed anaerobic infections in the abdomen, pelvis, lung, or brain.