

# Lectures 5,6

- Physiological - indigenous flora of skin and mucous membranes - distribution, importance, changes
- Pathogenicity and virulence
- Pathogenetic force of bacteria
- Infection - disease caused by microorganismi, conditon of establishment, ways of transmission, types of diseases

# Indigenous physiological flora of humans

## IPF

- Colonisation after delivery (environment, food intake)
- Persistent parasitism
- Composition differs between species
  - establish according to ecological relations
  - is relatively constant in species and individual

# Microbes in health and in disease

- Study of interaction of man and microorganism
- Microbes
  - involved in diseases
  - play key role in surviving and immunity

# Relation between man and indigenous human flora

- IF is a part of ecological relations between man and pathogens
- IF - can become pathogen if immunity is compromised
- 
- - interferes with pathogens in colonisation and invasion (competitive struggle for receptors, nutrients)
- - immunises host against pathogens via similar or cross reacting antigens
- production of bacteriocins
- can be confused or misidentified as ethiological agents (morphological resemblance, present on mucous membranes)

# IF $\neq$ carriage

- Normal physiological microflora - a standard tool of healthy host (*Staphylococcus aureus* on skin)
- Transient flora, carriage of pathogens - *Salmonella typhi* - pathogen long time present on mucous of a man after the disease thanks to partial acquired immunity without distinct harm in that period - source or quill of infection

# Distribution of IF

- Probably parts of bacterial surfaces are responsible for typical distribution of IF together with environment where they are residing
- Depends on age, hormonal activities, food intake and its composition - new borne, fertility period
- Is influenced by diseases -achlorhydria of stomach, - therapy - antacides

# Skin

- *Staphylococcus aureus* coagulase+
- *Staphylococcus epidermidis*, coagulase-
- *Propionibacterium acnes* (sebaceous glands, hair follicles)
- *Corynebacterium* (diphtheroids)
- *Clostridium*
- *Candida* sp.

# Conjunctiva

- Haemophilus sp., non hemolytical streptococci, coagulase-negat. staphylococci  
- when sampling - possibility of contamination from adjacent skin



# Nose - nasal cavity

- Staphylococcus epidermidis and coagulase -,  
Staphylococcus aureus,
- Corynebacterium sp.
- Haemophilus sp., Neisseria sp.,  
Str. pneumoniae
- Moraxella catarrhalis
- Streptococcus mitis, salivarius, viridans  
possibility of contamination from adjacent  
skin during sampling

# Oral cavity

- Staphylococcus epidermidis, Streptococcus salivarius, Lactobacillus acidophilus, Corynebacterium sp., Actinomyces bifidus, Leptotrichia buccalis, Treponema dentium, Mycoplasma sp., Spirillum sp. Streptococcus mutans, anaerobe micrococci, Streptococcus mitis, anaerobe streptococci, Neisseria sp., Bacteroides sp., Actinomyces israeli, Fusobacterium sp., Candida albicans, Moraxella catarrhalis, Veillonella alcalescens, Kingella, Eikenella

# Pharynx

- Streptococcus salivarius, Neisseria sp., Corynebacterium sp., Fusobacterium sp., Treponema dentium, Klebsiella aerogenes, Proteus sp., Moraxella catarrhalis, Streptococcus mitis, anaerobe streptococci, Veillonella alcalescens, Bacteroides sp., Vibrio sputorum, Actinomyces israeli, Haemophilus sp.

# Colon

- Number of bacteria is increasing in downward direction  
 $10^{10}$ /g of feces
- In breast feeding - lactobacillus
- In mixed food - E. coli, Bacteroides, Clostridia, Enterococcus
- Streptococcus mitis, Enterococcus faecalis, Lactobacillus sp., Escherichia coli, Pseudomonas aeruginosa, Bacteroides sp., Mycoplasma sp., Candida albicans, Bifidobacterium bifidum, anaerobe micrococci, Streptococcus salivarius, Clostridium sp., Alcaligenes faecalis, Klebsiella aerogenes, Fusobacterium sp., Eubacterium sp, Citrobacter sp., Proteus sp.

# External genitals

- Staphylococcus epidermidis, Enterococcus faecalis, Escherichia coli, Bacteroides sp., Mycobacterium smegmatis, Fusobacterium sp., Corynebacterium sp. - diphtheroids, Streptococcus sp., anaerobe streptococci, Spirillum sp, Treponema dentium, Candida albicans, Mycoplasma sp.,

# Vagina

- Anaerobe micrococci, Neisseria sp., Haemophilus sp., Treponema dentium, Lactobacillus vaginalis, Streptococcus viridans, Corynebacterium sp.,
- colonisation with lactobacilli soon after birth + staphylococcus, enterococcus, diptheroids
- with onset of puberty - lactobacilli are evidently responsible for acidity of vaginal secretions in child bearing age via chemical changes of glycogen
- postmenopausa - like in prepuberty

# Urinary tract

- Lower third of uretra can be contaminated by physiological flora from adjacent skin or external genitals
- Significant bacteriuria - the quantity of bacteria in 1ml that is very significant for infection ( $10^5$  of bacteria in 1 ml of urine)

- IF is physiological only in defined environment
- when microbes are inoculated in other place with other composition of IF or in place physiologically sterile - it can cause the disease - is pathogenic (*Escherichia coli* - IF in colon - pathogen in urinary tract)



# Benefits from IF

- Mutual control of composition based on:
  - the supervision of colonisation and implantation of pathogens (*Bifidobacteria* in colon of breast fed child interferes with colonisation by enteric pathogens, *streptococcus viridans* - blocs colonisation by *Candida* in mouth
- producton of viatmins (K,B) - avitaminis in atb therapy
- competition for sources of energy
- immunostimulation

# Possible risks from IF

- Facultative pathogens - in immunosuppression
- Endotoxin- producing bacteria- constant intoxication
- Bacteroides - mutagen production - Ca of colon
- PNC-ase producing Staphylococci can interfere with therapy (PNC in eradication of gonococci )
- Streptococci in mouth - oral cavity - active role in dental carries forming

# Changes in IF

- **Dysmicrobia** - changes in delicate equilibrium in composition of microflora - broad spectrum of atb
- overflow of on species from IF
- colonisation by pathogens in distinct environment (*Staf. aureus* in hospital, *Neisseria meningitidis* in military crowds)

# Sites steril in physiological conditions

- Respiratory tract downward from pharynx
- GIT from oesofagus - (transiently microbes present in food or saliva) - down to colon
- Urinary tract - (seldom IF in low third of uretra )
- Internal genitals
- Inner ear
- Inner tissues
- Structures of nervous systems
- Blood

# Sampling materials normally without bacteria

- Punctures - paranasal sinuses, soft tissues, joints, pleural, pericardial
- sputum, aspiration from pulmon, middle ear aspirates
- CSF
- Blood
- Urine
- Samples from endoscopy

# Interpretation of findings

- Isolation of nonpathogens consistent with IF (*Str. viridans* in mouth)
- Isolation of facultative pathogens consistent with IF (*Haemophilus influenzae* from nasopharynx)
- Isolation of nonpathogens not consistent with IF (*E. coli* from nose or lower third of uretra)
- Isolation of any bacteria from sites physiologically sterile (! Contamination)

Organisms living in or on another bigger organism - the former is **parasit**, the latter is **host**

**symbiosis** - living of 2 beings without distinct benefits or harm

**parasitism** - benefit for parasit, for host it can be or harmful or indifferent or benefit

## Microorganism

Nonpathogen - genetically determined situation in relationship between species vzt'ahu k druhu

Pathogens - highly virulent - cause disease in otherwise healthy persons

vaccination → grey zone → surviving

Opportunistic, facultative pathogens - low-virulent, cause disease in persons with apparently disturbed immunity. Often part of IF

# Phases in establishing infection

- Adherence and colonisation of host - adhesins, pilli - superficial structures
- Parasitismus
  - pathogens or non-pathogens (IF-endogenous, external microbes)
  - pathogenicity, virulence
- Reaction of macroorganism- immunity



# Infection 1

- Invasion of human by pathogen followed by disease
- Way of acquirement of infection - **inhalation, ingestion, inoculation**
- Infectivity of microbes depend on its ability to **adhere and attack the tissue**
  - first contact - passive electrostatic forces
  - tight irreversible chemical compositions - adhesins, pili of microbe and receptors on epithelial human cells
- colonisation - persistent presence of vital microbe on or in the host tissue without any harm**

# Infection 2

- With the exception of inoculation every infection starts with colonisation of mucous membrane

# Colonisation 3

- Soon after delivery
- Can be permanent or transient
- Influenced by environment (hospital, military camp)
- Is not disease, but is its first step
- Consequencies depend on resistence of the host

# Localisation or dissemination 4

- **Infection of epithelium withou penetratiione** *rhinovirises* - infection -disease of nose mucous membrane
- **Transmission via epithelium**, reaching of subepitelial space - tissue. Penetrátion and dissemination - extracelular enzymes - lipase, colagenase, hyaluronidase...
- **Spread** directly (per continuitatem) or via lymphatics or blood vessels

# Conditions for multiplication and growth in host 5

- Differences in growth in vivo and in vitro
- Change of virulence
- Disponibility of nutrients (free iron)
- Biofilm

# Patogenetical ways 1

- Microbes can induce tissue damage via.:
  - induction of inflammation - surface antigens attract chemically neutrophils
  - change or damage of cell structure or metabolism (toxins)
  - immunomodulation rhinovirusmi
- **Damage is frequently caused by immunological reaction to pathogens**

# Pathogens 2

- Able to cause disease in healthy non immune persons
- Have natural host and overcome its tools of resistance - immunity and cause the disease or carriage state
- Steady state in environment with surviving of the genus of host
- Infection of non natural host or via non natural way

# Protection of the host

- Innate immunity
- Acquired immunity



# Predisposing factors from the site of host

- Disruption of intact skin (burns)
- Failure of splashing function (urolithiasis)
- Dysmicrobia caused by antibiotic intake
- Therapy agranulocytosis following radiotherapy or corticosteroids intake, cytostatics treatment
- Hypogammaglobulinaemia, asplenia (encapsulated bacteria)
- Other - underlying disease - cirrhosis, diabetes, alcohol abuse
- Indwelling devices, permanent catheters, - biofilm
- Vascular occlusion, disturbance of microcirculation

# Outcomes of the parasit-host interaction

- Not each attempt of microbes to infect the host is successful:
- Microorganism
  - cannot overcome outer barriers-intact skin
  - after invasion is eliminated - cough, or establish the steady symbiotal state - immunity
- **Infection** - attenuated,
  - progressive reversible or irreversible changes
  - chonical
  - death

# Sequellae for the host

- 1) **No infection** -low virulence and elimination of the parasit
- 2) **Colonisation** establishment, not disease
- 3) **Inapparent disease** - host is not clinically ill, but immune reaction with protective effect is present of carriage state is established
- 4) **Klinically apparent disease** - classical disease
- 5) **Death** cause by tissue damage by infection, by immune reaction, by non infectious sequellae or by underlying conditions

# Conditions changing relationship

- Relationship of dynamic equilibrium host (immunity) and parasites in environmental conditions of IF
- Can be changed:
  - in contact with pathogens with very high virulence
  - in immune deficiency - opportunistic infections
- Non stability of both

# Nonstability of the parasit

- Phenotype or genotype changes
- Quick passage in epidemics - enhanced virulence
- Selection of immune population

# Changes of the host

- Genetically determined characteristics sickle cell anemia and malaria
- Age (hypogamaglobulinaemia in elderly)
- Nutrition (avitaminosis, hypogamaglobulinaemia)
- Hormonal conditions
- Persistet stress