Institute for Microbiology, Medical Faculty of Masaryk University
and St. Anna Faculty Hospital in Brno

Miroslav Votava
Lenka Černohorská

Agents of opportune infections

The last (15th) lecture for 3rd-year students of dentistry
10th December, 2010

Definition of nosocomial infections (NIs) – revision

Nosocomial (hospital-acquired) infections =

= infections occurring in connection with the stay in a medical institution (as opposed to community-acquired infections)

At least 5 % patients are afflicted, probably more

***Exogenous NIs*:**

source = other patients, environment, personnel

vector = mostly personnel's unwashed hands

***Endogenous NIs*:**

source = the patient himself/herself

Consequences of NIs – revision

- **Higher mortality (†) – almost 40 % higher (a conservative estimate in this country is hundreds of unnecessary deaths per year)**
- **Longer (by weeks) and more expensive hospitalization (by tens of thousands, even more CZK per case)**
- **Economic losses circa 1.5 billions CZK/year**
- **Additional ATB therapy (both higher costs and toxicity)**
- **Patients themselves = source of infection for others**

More than 1/3 of NIs can be prevented!

Main types of NIs – revision

1. Urinary tract infections in catheterized patients – up to 40 % of all NIs
2. Respiratory tract infections – about 20 %
   - Early ventilator-associated pneumonia
   - Late ventilator-associated pneumonia
   - Aspiration pneumonia
   - Other respiratory infections
3. Purulent infections of surgical wounds – about 20 %
4. Blood-stream infections (sepsis by inserted intravenous catheters) – at least 15 %

Etiology of nosocomial UTIs – revision

Escherichia coli	25 %
other enteric bacteria	20 %
enterococci	15 %
Pseudomonas aeruginosa	10 %
other G– nonfermenting rods	10 %
yeasts	5 %

Etiology of respiratory NIs I – revision

Early VAP:

Staphylococcus aureus	25 %
Streptococcus pneumoniae	20 %
Haemophilus influenzae	15 %
enteric bacteria	10 %
other aerobically growing bacteria	5 %
anaerobes	1 %

(monomicrobial etiology, agents originate in community)

Etiology of respiratory NIs II – revision

Late VAP:

Gram–negative nonfermenting rods (*P. aeruginosa, Acinetobacter baumannii*)	**40 %**
enteric bacteria (klebsiellae, *E. coli*, enterobacters)	**30 %**
staphylococci (mainly *S. aureus*)	**20 %**
yeasts	**5 %**

(some cases have polymicrobial etiology, agents are of hospital origin)

Etiology of respiratory NIs III – revision

***Nosocomial aspiration pneumonia*:**

Older studies emphasized anaerobes

Newer studies are discovering the same etiology as in VAP and put more emphasis on Gram-negative rods (non-fermenting rather than enteric ones)

***Pneumonia in febrile neutropenia*:**

Initial days: G+ cocci (staphylococci, pneumococci) occur twice more often than G– rods (enteric bacteria and pseudomonads)

Later on: ↓ G+ cocci, ↑ candidae and aspergilli

After allogenic transplantation of bone marrow: mainly CMV

Etiology of surgical wounds suppuration – revision

(depends on the terrain of the surgery)

Staphylococcus aureus

coagulase-negative staphylococci

Streptococcus pyogenes

enteric bacteria (*E. coli*)

bacteroids, prevotellae, peptostreptococci

Gram-negative non-fermenting rods

Clostridium perfringens

Etiology of sepsis during inserted i.v. catheter – revision

coagulase-negative staphylococci (>50 %)

– because of biofilm

enterococci – because of cephalosporins

Staphylococcus aureus

enteric bacteria (*E. coli*, klebsiellae)

Pseudomonas aeruginosa

***Acinetobacter* spp.**

***Candida* spp.**

Etiology of nosocomial virus infections – revision

influenza virus – mainly infants and older patients

RSV – newborns and suckling infants

adenoviruses – ophthalmologic wards

other respiratory viruses

CMV – after cytotoxic treatment

rubella virus – children (vaccination available now)

rotaviruses – mainly children

VHB – higher risk in longer hospitalization

HIV – in developing countries mostly

Predisposition to NIs – revision

Age – both extremes of age

Treatment – cytotoxic drugs, steroids, ATB

Underlying disease

- hepatic disease
- diabetes mellitus
- cancer
- renal failure
- skin disorders
- neutropenia

Trauma – incl. surgery and i.v. catheters

Prevention of NIs I – revision

Four main strategies:

- **Excluding sources of infection from the hospital environment**
- **Breaking the chain of infection from source to host**
- **Improving the host's ability to resist infection**
- **Investigating hospital infection**

Prevention of NIs II – revision

1. Exclusion of sources of infection from the hospital environment

- Sterile instruments, dressings, medicaments and intravenous fluids
- Using only blood screened for infectious agents
- Clean linen, uncontaminated food
- Preventing contact with infected staff – both acutely ill or carriers of pathogens

Prevention of NIs III – revision

2. Breaking the chain of infection

- **Facilities**
  - ventilation systems & air flow (air-conditioning: legionellae, construction works: aspergilli)
  - water systems (in particular warm water: legionellae)
  - patient isolation
    - to protect a particularly susceptible patient
    - to prevent the spread of pathogens from a patient to others
- **People**
  - facilitation of aseptic behavior of staff
  - the most important is effective hand washing

Prevention of NIs IV – revision

3. Improving the host's resistance

- **Immunization**
  - influenza (older patients)
  - pneumococcal infections (before transplantation or splenectomy)
  - VHB (in seronegative persons before hemodialysis)
  - varicella (zoster Ig in immunocompromised exposed to VZV)
- **Appropriate ATB prophylaxis**
  - in „dirty" surgery
  - In „super-clean" surgery (orthopaedics, neurosurgery)
- **Reducing the risk of postoperative infection**
  - correct operating technique
  - care of invasive devices and intravenous fluids
  - correct nursing techniques (prevention of pressure sores) and active physiotherapy

Prevention of NIs V – revision

4. Investigating hospital infections

- **Surveillance** (= regular monitoring) – allows early recognition of any change in the number or type of hospital infection
- **Investigation of outbreaks** from epidemiological and microbiological point of view
- **Establishment and monitoring of procedures** designed to prevent infection

…

Opportune infections: Definition and examples

Opportune infection = infection on a weakened terrain (in a lowered immunity)

Opportune infection is:

- **sometimes a secondary one during some other infection**
- **often a nosocomial one = hospital-acquired**
- **possibly a iatrogennic one = caused by a medical intervention**

Examples of opportune infections during a HIV infection:
CMV retinitis, CMV or candidal oesophagitis CMV, herpes zoster, cryptosporidial or microsporidial enteritis, cryptococcal meningitis, toxoplasmatic encephalitis, colibacillary and other sepsis

Causes of lowered immunity

Defects of the local barriers

Defects of the phagocytosis

Defects of the complement

Defects of the normal microflora

Defects of the humoral immunity

Defects of the cellular immunity

Defects of local barriers – I

Burns

Other injuries incl. surgical wounds

Foreign bodies *in situ*

- **urinary catheters**
- **i.v. catheters and cannulae**
- **arteficial prostheses**

Cystic fibrosis

Defects of local barriers – II

Burns

Not only a direct impairment of barriers, but also a defect in neutrophil function and burned tissue as a culture medium for bacteria

Little invasive infection limited to the eschar (scab)

Invasive infection → destruction of all skin layers → invasion of lymphatic vessels → sepsis

Agents: mainly *P. aeruginosa*, furthermore *S. aureus*, enterobacteria, *S. pyogenes* and other streptococci and enterococci

Defects of local barriers – III

Other injuries

See one of previous lectures

Surgical wounds - I

Staphylococcus aureus

coagulase-negative staphylococci (mainly *Staphylococcus epidermidis*)

enterobacteria (*Escherichia coli, Proteus mirabilis*)

Streptococcus pyogenes

anaerobes (*Peptostreptococcus anaerobius, P. micros, Bacteroides fragilis*)

Defects of local barriers – IV

Surgical wounds – II

Infection *during* a surgery:

- **preparing the operating field**
- **terrain (clean versus contaminated one)**
- **level of asepsis**
- **surgical technique**

Infection *after* a surgery:

- **slip (e.g breach of asepsis) during dressings**

In general: dangerous is the non-sterile touch, much less the non-sterile environment (but be careful during implantation of artificial devices)

Defects of local barriers – V

Foreign bodies in situ ***(coated by the biofilm)***

Urinary catheters: after >48 hrs quite commonly G– rods (periurethral and bowel flora – but transmission by hands also possible)

I.v. cannulae: >50 % *S. epidermidis* & other coagulase-negative staphylococci (from the skin), because of the biofilm resistant to ATB, infection not eradicable except by the removing the cannula

Artificial valves, joints, pacemakers, vascular prostheses, shunts: dtto

Cystic fibrosis

Impairment of ciliary function & production of mucus

After *S. aureus* and *H. influenzae* *Pseudomonas aeruginosa* (mucous strains producing alginate slime) and *Burkholderia cepacia* continue

Defects of phagocytosis – I

Neutropenia

- in haematologic malignities
- in recipients of bone marrow
- in recipients of transplanted solid organs

Chronic granulomatous disease

Asplenia

Defects of phagocytosis – II

Neutropenia:

No circulating leukocytes → sepsis (the first sign or the result of cytotoxic chemotherapy)

Febrile neutropenia

Agents:

- **fromerly G– rods (*E. coli, P. aeruginosa* etc.)**
- **now G+ cocci (staphylococci, streptococci, enterococci) and yeasts (in particular if the neutropenia persists)**

Defects of phagocytosis – III

Chronic granulomatous disease (CGD):

Defect of NADPH-oxidase → none H_2O_2

leukocytes in CGD cannot kill staphylococci and other catalase-positive bacteria → these microbes cause chronic deep abscesses

Asplenia:

Encapsulated bacteria (pneumococci, hemophilli) are not cleared from blood

Defects of complement

Relatively rare conditions

Resistance lowered against infections caused by neisseriae (mainly by meningococci)

Defects of normal flora

Problems mostly in intestinal microflora

After some antibiotics (clindamycin, cefoxitin, amoxicillin/clavulanic acid) *Clostridium difficile* multiplies excessively

Defects of humoral immunity

In particular agents of pyogenic infections and enteroviruses

Defects of cellular immunity

In particular infections by intracellular microbes:

- **viruses (mainly CMV, VZV, HSV)**
- **mycobacteria (not only *M. tbc*, but also atypical as *M. avium-intracellulare*), *Nocardia asteroides*, *Listeria monocytogenes***
- **fungi (candidae, aspergilli, *Pneumocystis jirovecii*, *Cryptococcus neoformans*)**
- **parasites (*Toxoplasma gondii*, *Cryptosporidium parvum*, *Isospora belli*, *Strongyloides stercoralis* and other)**

Homework 15

The third part of the cycle mentioned in the 13th lecture

Answer and questions

The solution of the homework and possible questions please mail (on Monday Dec. 12th at 6.30. at the latest) to the address

mvotava@med.muni.cz

Thank you for your attention

Merry Christmas!

Good luck in the examination!