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Hospital infections and the principles of antimicrobial therapy

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Hospital-acquired infections

- Surgical site infection
- Clostridium difficile infection
- Pneumonia (incl. ventilator-associated pneumonia)
- Catheter-associated urinary tract infection
- Central venous catheter-related infection

Surgical site infection (SSI)

- Superficial surgical site infection occurs within 30 days after the surgery, involves only skin and the subcutaneous tissue in the incision site, and meets at least one of the following criteria:
 - 1. Purulent discharge from the incised cutaneous layers, without microbiological evidence
 - Bacteria have been isolated from the aseptic sampling of the incision site
 - **3.** At least one of the following symptoms is observed:
 - 1. Pain or tenderness
 - 2. Localized edema
 - 3. Redness or inflammation
 - 4. The surgeon decided to cut open the incision site (except when the wound culture is negative)
 - 4. The superficial SSI has been diagnosed by a doctor

Surgical site infection (SSI)

- Deep SSI occurs within 30 days after the surgery if no implants were used and within a year after the surgery in case of implanting. The infection seems to be surgery-related, involves deeper soft tissue (e.g. fascia, muscles) in the incision site, and meets at least one of the following criteria:
 - 1. Purulent discharge from the depth of the incision site, provided that it does not originate from the organ or space that were involved in the surgery
 - 2. The surgical wound opens itself or is cut open by the doctor, while the patient shows one of the following symptoms:
 - 1. Fever (>38°C / >100.4°F)
 - 2. Localized pain or inflammation (except when the wound culture is negative)
 - There is an abscess or the infection has been documented by a different method (incision, reoperation, histopathological examination or imaging)
 - 4. The deep SSI has been diagnosed by a doctor

Surgical site infection (SSI)

- Organ/space infection occurs within 30 days after the surgery if no implants were used and within a year after the surgery in case of implanting. The infection seems to be surgery-related, involves any anatomical part other than those in the incision site that has been opened or interfered with during the surgery, and meets at least one of the following criteria:
 - 1. Purulent discharge from a drain inserted in the operated organ/space
 - 2. Bacteria have been isolated from the aseptic sampling of exudate or tissue from the operated organ/space
 - 3. There is an abscess or the infection of the operated organ/space, which has been documented in the course of a direct examination, reoperation, histopathological examination or imaging
 - 4. The infection of the operated organ/space has been diagnosed by a doctor

SSI – antibiotic prophylaxis

- Recommendations for the administration of antibiotics according to the type of procedure performed (a list of procedures should be prepared, including the information whether the antibiotic treatment is necessary)
- Duration of the antibiotic treatment:
 - 1. In most procedures, a single dose will suffice
 - 2. The procedures that allow prophylaxis of longer duration include:
 - Open heart surgery: up to 24-48 hours
 - Joint replacement surgery: up to 24 hours
 - Limb amputation: up to 5 days
 - Extensive open fracture: up to 72 hours

SSI – antibiotic prophylaxis

Choice of an antibiotic:

- 1. Cefazolin is the antibiotic of choice in most procedures that involve surgical incisions
- Other antibiotics are applied to patients who are allergic to β-lactam antibiotics (clindamycin, vancomycin) and in procedures performed through mucous membranes:
 - Ophthalmology
 - Urology
- **3.** Application of metronidazole is recommended in procedures performed on the colon and in some procedures performed through the oral mucosa
- Time of administration of the antibiotic: cefazolin is administered up to 60 minutes before a surgical incision is made
- An additional dose of cefazolin should be administered in case of:
 - Heavy bleeding during surgery
 - Heavy transfusion of fluids
 - A surgical procedure longer than 2-3 hours

SSI – microbiological assessment

Recommendations:

- 1. When an antibiotic treatment is necessary (Gram staining of the wound exudate, the result of which affects the first-choice therapy)
- 2. In severe infections
- **3.** When the patient is allergic to first-choice antibiotics
- 4. When there is suspicion of a drug-resistant bacterial infection (e.g. patients who are often hospitalized or have been admitted to a unit where they remain at high risk of being infected with drug-resistant bacteria)

SSI – application of antibiotics

Antibiotic is not necessary:

- 1. There is a minimal inflammatory infiltration around the wound (the infiltrate does not exceed 5 cm)
- General symptoms of an infection do not occur (i.e. fever >38.5°C / >101.3°F, heart rate > 100/min)
- Antibiotic is recommended :
 - 1. There is an inflammatory infiltrate that exceeds 5 cm
 - General symptoms of an infection are observed (i.e. fever >38.5°C / 101.3°F, heart rate >100/min)
- The antibiotic therapy may be of short duration (48 hours from the wound's opening) if symptoms prove to be quickly resolving

SSI – application of antibiotics

- If there is suspicion of a staphylococcal infection, the following drugs may be applied:
 - 1. Cloxacillin
 - 2. Cefazolin
 - 3. Cefuroxime
- In units with the high rate of MRSA occurrences, it is justified to apply the following drugs in an empiric therapy:
 - 1. Glycopeptide
 - 2. Linezolid
- If there is suspicion of a Gram-negative bacterial infection, the following drugs may be chosen as the first-choice antibiotic:
 - 1. Cephalosporin (1st or 2nd generation)
 - 2. Fluoroquinolone

SSI – application of antibiotics

- If the SSI occurs within 48 hours after the surgery, the etiology of Streptococcus pyogenes or Clostridium spp. should be suspected. In such a case, penicillin with clindamycin may be applied, but the choice of antibiotics should be supported by the results of the direct Gram staining
- If the SSI is not related to a surgery performed on the gastrointestinal tract, the urinary tract or reproductive organs, the applied antibiotic should cover Staphylococcus aureus
- If the SSI occurs after a surgery performed on the gastrointestinal tract or reproductive organs, the applied antibiotic should cover the anaerobic bacteria
- If the SSI occurs after a surgery performed on the oral mucosa, the applied antibiotic or combination of antibiotics should be efficient against streptococci, staphylococci and anaerobics

Clostridium difficile infection

- The infection caused by the Clostridium difficile bacteria must meet at least one of the following criteria :
 - 1. Diarrhea-related loose stools or toxic megacolon and a positive result of the test for the presence of *C. difficile* toxin A or B in stool
 - 2. Features of the pseudomembranous colitis in the endoscopy of the lower gastrointestinal
 - 3. Features of the *C. difficile* infection (with or without diarrhea) in the histopathological examination of a sample collected during endoscopy, colectomy or autopsy
- If symptoms of the *C. difficile* infection occur within 28 days after the patient is discharged, the infection is defined as hospital-acquired

Clostridium difficile infection - microbiological assessment

Recommendations:

- Occurrence of diarrhea in a patient who has been or is still being treated with antibiotics, even 2-10 weeks earlier
- In a patient with loose stools of the potentially infectious causes, if the testing for the presence of other enteropathogens proves negative
- In all patients who suffered from diarrhea in the 48 hours following the hospital admission
- In patients with diarrhea who have been hospitalized in the last 3 months
- 5. In a patient with the hospital-acquired acute abdomen or obstructive symptoms without any other noticeable causes - in a patient who has been or still is being treated with antibiotics
- 6. In patients with the hospital-acquired leukocytosis (>20,000/μl), with no other noticeable causes

Clostridium difficile infection - microbiological assessment

- The routine procedures of the microbiological laboratory include:
 - 1. GDH antigen detection (glutamate dehydrogenase)
 - 2. *C. difficile* toxin A and/or toxin B detection
- The procedures of detecting GDH antigens and C. difficile toxin A and/or B are performed simultaneously and take approx. 1 hour
- If the toxin is present, the diarrhea has been most probably caused by the C. difficile infection
- The presence of the GDH antigen and the negative outcome the toxin A and/or toxin B test may have one of the two following causes:
 - 1. the patient is the carrier of a non-toxigenic strain or the diarrhea has other causes
 - 2. the diarrhea is caused by the presence of a toxigenic strain, but the limited sensitivity of the test makes it unable to detect the toxin
- If the GDH antigen is present and the toxin A and/or toxin B test comes out negative, the molecular testing should be considered

- The applied antibiotic should be discontinued and replaced with another one from the group of the lower risk of causing the *C. difficile* infection
- Do not administer drugs that inhibit peristalsis
- The orally administered metronidazole or vancomycin should be the firstchoice drug
- Do not administer both drugs simultaneously, except severe and complicated infection forms
- In all patients with severe and complicated infections, a surgical consultation should take place, and an abdominal CT scan is recommended

- The surgical intervention should be considered in the following cases:
 - 1. Hypotension requiring the application of vasopressors
 - 2. Sepsis with kidney and/or respiratory tract failure
 - 3. Occurrence of disorders of consciousness
 - 4. Growth of WBC to the amount of >50,000/µl
 - 5. Increase level of serum lactate >5 mmol/l
 - 6. No improvement is shown after 5 days of treatment

Mild/medium form

- Criteria:
 - 1. Diarrhea
 - 2. Deviations that do not meet the criteria for other form
- Treatment:
 - Metronidazole 3x500 mg administered orally for 10 days

Severe form

- Criteria albumins <3 g/dl and one of the following:</p>
 - 1. WBC >15,000/µl
 - 2. Abdominal tenderness
- Treatment :
 - Vancomycin 4x125 mg administered orally for 10 days

Severe and complicated form:

- Criteria one of the following:
 - 1. Admission to the Anesthesiology and Intensive Care Unit
 - 2. Drops of blood pressure
 - 3. Fever >38.5°C / 101.3°F
 - 4. Disorders of consciousness
 - 5. Intestinal occlusion or flatulence
 - 6. WBC ≥35,000/µl or <2,000/µl
 - 7. Serum lactate >2.2 mmol/l
 - 8. Multiple organ failure

Treatment:

- Vancomycin 4x500 mg administered orally
- Metronidazole 3x500 mg administered intravenously

First recurrence of infection:

- The patient may be treated with the same drug that was applied in the original infection
- If the recurrence is more severe, Vancomycin 4x125 mg should be administered orally for 10 days

Another recurrence of infection:

- The patient should be treated with the pulsed dosing of vancomycin:
 - 4x125 mg administered orally for 10 days, then 1x125-500 mg administered orally each second/third day for 3 weeks
 - 4x125 mg administered orally for 10 days, then 2x125 mg administered orally for 7 days, then 1x125 mg administered orally for 7 days, then 1x125 mg administered orally each second/third day for 2-8 weeks
- In case there is no improvement despite the treatment, the fecal microbiota transplant (also known as a stool transplant) should be considered

- Risk factors for recurrent infections:
 - Old age
 - Antibiotic treatment
 - Application of proton-pump inhibitors
 - Hypervirulent strain of *C. difficile*

Special cases:

- In pregnant and breast-feeding women, it is recommended to administer vancomycin 4x125 mg orally for 10 days
- In patients with impaired intestinal passage, the rectal administration of vancomycin 4x500 mg in 100-500 ml of 0.9% saline solution should be considered
- In patients who cannot be treated with orally administered medications:
- If the recurrence is more severe, vancomycin 4x125 mg should be administered orally for 10 days
 - Mild and medium form: metronidazole 3x500 mg intravenously for 10 days
 - Severe form: metronidazole 3x500 mg administered intravenously and vancomycin 4x500 mg administered rectally

Hospital-acquired pneumonia

 Hospital-acquired pneumonia – an infection contracted by a patient at least 48 hours after being admitted to hospital, the incubation period of which has not begun before admission

Diagnosis:

- Pneumonia has been confirmed on 2 or more serial thoracic images or CT scans, in case of the co-occurrence of cardiological or pulmonary disorders; in patients who do not suffer from any cardiological or pulmonary disorders, a single imaging examination should suffice
- At least one of the following symptoms:
 - Fever >38°C / >100.4°F with no other causes
 - Leukopenia (<4,000 WBC/mm³) or leukocytosis (> 12,000 WBC/mm³)

Hospital-acquired pneumonia - diagnosis

Diagnosis:

- At least one of the following symptoms:
 - Secretion of purulent sputum or change of properties of the already occurring one (color, smell, volume, consistency)
 - Cough, shortness of breath or rapid breathing
 - Auscultatory changes (respiratory murmurs, crackles, wheezes)
 - Worsening of gas exchange (drop in the arterial blood oxygen tension or the necessity to increase the concentration of oxygen in the breathing air or the respiratory effort)

Hospital-acquired pneumonia – diagnosis

It is recommended to precede the administration of antibiotics with microbiological assessment:

- Blood cultures should be collected from all patients with hospital-acquired pneumonia
- Respiratory tract cultures: sputum culture; if a tracheostomy tube has been inserted: tracheal aspirate or bronchoscopic sampling
- If the course of pneumonia involves excessive exudation or the patient shows symptoms of intoxication, it is recommended to perform thoracentesis with the collection of fluids for the purpose of conducting analysis and microbiological assessment

Hospital-acquired pneumonia – treatment

The choice of treatment depends on:

- severity of the patient's condition
- risk of hospital-acquired multi-resistant bacterial infections
- the result of Gram staining of the secretion collected from the lower resp.tract
- radiological imaging
- The risk of multi-resistant bacterial infections rises if:
 - the patient has already been hospitalized
 - the patient has been previously treated with antibiotics
 - the patient has been previously admitted to an Intensive Care Unit
- Low risk of multi-resistant bacterial infections:
 - ceftriaxone 1x2 g
 - ciprofloxacin 2x400 mg
- The risk of multi-resistant bacterial infection one of the following options:
 - ceftazidime 3x2 g iv, piperacillin/tazobactam combination 4x4.5 g iv, imipenem 4x0.5 g iv or 3-4x1 g, meropenem 3x1 g iv, cefepime 2-3x1-2 g iv

Ventilator-associated pneumonia – diagnosis

 Clinical criteria for diagnosing the ventilator-associated pneumonia (VAP):

- New inflammatory infiltration (radiograph) or the progression of lesions and
- Observation of at least two of the following three symptoms:
 - Fever >38.3°C / >100.9°F
 - Leukocytosis (>10,000/µl) or leukopenia (<4,000/µl)
 - Purulent respiratory discharge

Ventilator-associated pneumonia – assessment

- All patients with suspicion of VAP should have samples collected from the respiratory tract:
 - tracheal aspirate
 - bronchoalveolar lavage (BAL)
 - bronchial swab
- It is not recommended to collect samples from the respiratory tract if there is no clinical suspicion of VAP or tracheobronchitis
- A sterile culture sampled from the respiratory tract of a patient to whom no new antibiotics have been introduced in the last 3 days practically rules out the presence of a bacterial respiratory infection, except *Legionella spp.* and other atypical pathogens and viral infections

Ventilator-associated pneumonia – treatment

- While choosing the primary therapy, the differentation between early- and late-onset VAP should be taken into account. The most common etiological factors of VAP include S. aureus, S. pneumoniae, H. influenzae and the relatively antibiotic-sensitive strains of Gram-negative bacilli
- The choice of an antibiotic therapy in the early-onset VAP (<4 days of mechanical ventilation) in a patient who does not show any risk factors for multi-resistant bacterial infections: ceftriaxone 1x2 g iv or levofloxacin 1x750 mg iv
- The choice of an empirical antibiotic therapy in the late-onset VAP (>4 days of mechanical ventilation) should be based on the local epidemiological data

Ventilator-associated pneumonia – treatment

- The choice of antibiotics in the late-onset VAP or in a patient who shows risk factors for multi-resistant bacterial infections (hospitalization >5 days, antibiotic treatment in the last 90 days, hospitalization in the last 90 days, patient from a nursing home, chronic hemodialysis, home intravenous therapy, patient with chronic subcutaneous lesions, immunosuppression):
 - ceftazidime 3x2 g or piperacillin/tazobactam combination 4x4.5 g
 - severe condition: imipenem 4x0.5 g or 3-4x1 g or meropenem 3x1 g

Treatment duration:

- 8 days
- longer if the infection has been caused by *P. aeruginosa* or *S. aureus*

Urinary tract infection (UTI) – diagnosis

- Microbiologically confirmed symptomatic urinary tract infection:
 - The patient shows at least one of the following symptoms:
 - Fever (>38°C / >100.4°F)
 - Urinary urgency
 - Pollakiuria
 - Dysuria
 - Suprapubic tenderness s

and

 The urine culture proved positive (i.e. ≥10⁵ CFU/ml) with occurrence of not more than two bacterial species

- Symptomatic urinary tract infection without microbiological evidence:
 - The patient shows at least one of the following symptoms:
 - Fever (>38°C / >100.4°F)
 - Urinary urgency
 - Pollakiuria
 - Dysuria
 - Suprapubic tenderness

and

- At least one of the following criteria is met:
 - Positive paper-strip test for the presence of leukocyte esterase or nitrates

- At least one of the following criteria is met:
 - Pyuria ≥10 WBC/ml or ≥3 WBC/in the field of vision in the unspun urine
 - Bacteria noticeable in the preparation of the unspun Gram-stained urine
 - At least two positive urine cultures with isolation of the same uropathogen (Gram-negative bacteria or *S. saprophyticus*) with increase to ≥10² CFU/ml in urine
 - ≤10⁵ CFU/ml with isolation of a uropathogen (Gram-negative bacteria or *S. saprophyticus*) in a patient who is efficiently treated due to the urinary tract infection
 - The doctor diagnosed the urinary tract infection
 - The doctor administered the applicable treatment due to the urinary tract infection

Asymptomatic bacteriuria:

- The patient does not show any of the following symptoms:
 - Fever (>38°C/>100.4°F)
 - Urinary urgency
 - Pollakiuria
 - Dysuria
 - Suprapubic tenderness

and

- Does not meet any of the following criteria:
 - The Foley catheter was inserted within 7 days before the urine culture was collected

- Does not meet any of the following criteria :
 - The urine culture proved positive, i.e. ≥10⁵ CFU/ml of urine contains not more than two types of bacteria
 - The Foley catheter was not inserted within 7 days before the first positive urine culture

and

 At least two urine cultures proved positive with increase to ≥10⁵ CFU/mm³ of urine with two-time isolation of the same bacteria (not more than two types)

Catheter-associated UTI – diagnosis

Clinical symptoms:

- Symptoms of an infection occur merely in 10% of patients with the significant bacteriuria
- Symptoms of an urinary tract infection in catheterized patients are nonspecific: hypogastric pains, dysuria
- The symptoms are related to the presence of a catheter and occur as often in catheterized patients with urinary tract infections as in those who are not infected
- Bacteriuria related to the urinary tract occurs in 2% of patients with the significant bacteriuria
- The obstruction of urine passage in patients with bacteriuria may lead to the symptoms of urosepsis or even the septic shock
- Other risk factors for infection include procedures performed on the urinary tract, removal or replacement of a catheter, as well as the catheter being pulled out by a patient

Catheter-associated UTI – diagnosis

- It is not recommended to conduct microbiological assessment in patients who do not show symptoms of infection, except pregnant women and patients awaiting urological surgery
- Most patients with the asymptomatic bacteriuria also suffer from pyuria (>5 leukocytes in the microscope's field of vision at 400x magnification or >10/µl). Thus, the correct WBC value is more important diagnostically-wise since it is helpful in ruling out the urinary tract infection as the cause of the fever
- Apart from infections, pyuria may also be caused by the irritation from the catheter
- It is recommended to conduct the urine culture before introducing the treatment

Catheter-associated UTI – treatment

Recommendations:

- The asymptomatic catheter-associated urinary tract infection does not require treatment
- In older patients and chronically catheterized patients, the administration of antibiotics may be justified by the occurrence of at least one of the following symptoms:
 - Fever >37.9°C/>100.2°F
 - Loin tenderness
 - Chills
 - Mental confusion
- The urine culture should have at least 10⁵ CFU/ml
- In severe conditions, it is recommended to prescribe an antibiotic therapy while waiting for the culture testing results

Catheter-associated UTI – treatment

Asymptomatic bacteriuria in catheterized patients:

- The asymptomatic catheter-associated urinary tract infection does not require treatment
- The administration of a targeted antibiotic is recommended in the case of significant bacteriuria in patients awaiting urological surgery

Symptomatic infection treatment:

- The replacement of a catheter while beginning treatment results in the faster resolution of symptoms and decreases the risk of recurrences; thus, such a replacement is recommended if the catheter has been inserted more than 2 weeks earlier and it is still necessary
- Treatment duration: 10 days if the symptoms resolved quickly and 14 days if the resolution of symptoms was slow-paced
- It is not recommended to conduct the control urinary culture as the tool for evaluating the treatment's efficiency

Catheter-associated UTI – prophylaxis

- In chronically catheterized patients, it is not recommended to administer antibacterial drugs for the purpose of preventing infection
- In patients catheterized for short periods (e.g. before surgery), antibacterial drugs should not be administered as preventive medication
- The prophylactic administration of antibiotics should be considered in patients with bacteriuria after the urological surgery. In such cases, it is recommended to prescribe a single dose of ceftriaxone 1g iv 1-2 hours before removing the catheter

Central venous catheter-related infection - diagnosis

Laboratory-confirmed vascular bed infection:

- 1 positive blood culture with presence of a recognized pathogen
- The patient shows one of the following symptoms:
 - Fever (>38°C/>100.4°F)
 - Chills
 - Hypotension

and

 Two positive blood cultures with the isolated dermal flora (from two independent blood samples that have been usually collected within 48 hours)

Central venous catheter-related infection - diagnosis

Localized central venous catheter-related (CVC) infection:

- increase in the quantitative CVC culture CVC ≥10³ CFU/ml or the semiquantitative CVC culture >15 CFU and
- pus/inflammatory infiltrate in the venous catheter insertion spot or at the tunnel
- Generalized CVC-related infection:
 - increase in the quantitative CVC culture CVC ≥10³ CFU/ml or the semiquantitative CVC culture >15 CFU and
 - clinical improvement within 48 hours after removal of the venous catheter

Central venous catheter-related infection - diagnosis

Collection of urine cultures:

- in each patient with the CVC inserted who has a fever and there is suspicion of an infection, a single blood sample should be collected for testing purposes (blood culture) from at least two sources:
 - directly from a vein
 - from the CVC
- if there is no possibility of collecting a blood sample directly from a vein, blood should be sampled from at least two CVC channels
- if the quantity of bacteria is higher in the blood sample collected at least 2 hours earlier from the CVC than in the blood sampled from a vein, the risk of the catheter-related bloodstream infection is very high
- if the CVC is removed due to the suspicion of infection, the catheter's end (approx. 4 cm) should be kept for the purpose of microbiological testing (only semiquantitative or quantitative)

Central venous catheter-related infection – treatment

- The CVC should be removed/replaced every time the patients is diagnosed with the catheter-related bloodstream infection
- If the infection is caused by the coagulase-negative staphylococcus, it may be considered not to remove the CVC, prescribe the intravenous antibiotic therapy and rinse the line with that antibiotic

• Empiric antibiotic therapy:

- Glicopeptide should be administered if there is suspicion of the catheter-related bloodstream infection, if the infection is acquired in a unit with the high rate of MRSA occurrences or if there is a foreign body in the patient's vascular bed
- The supplementation of the glicopeptide with an antibiotic against Gram-negative bacteria is recommended in patients with neutropenia that show symptoms of sepsis or in patients whose organisms have been colonized by these bacteria

Central venous catheter-related infection – treatment

Empiric antibiotic therapy:

- the choice of an antibiotic against Gram-negative bacteria depends on the local epidemiological situation and the severity of infection
- in patients with catheters inserted into the femoral vein, the combination of glicopeptide, an antibiotic against Gram-negative bacteria and an antifungal medication should be administered
- in the empiric therapy, an antifungal medication should be prescribed to:
 - patients provided with parenteral nutrition and with the CVC inserted into their femoral veinj
 - patients who have been undergoing long-term treatment with broadspectrum antibiotics
 - patients with hematologic conditions and after a solid organ transplantation
 - patients with multi-site Candida spp. colonization

Central venous catheter-related infection – treatment

Treatment duration depends on etiology:

- coagulase-negative staphylococci: if the CVC was removed 5-7 days, if the CVC was not removed – 7-10 days
- Staphylococcus aureus: at least 14 days, treatment duration depends on potential complications
- Gram-negative bacteria: 7-14 days
- Candida spp.: at least 14 days from the last positive blood culture and the resolution of symptoms