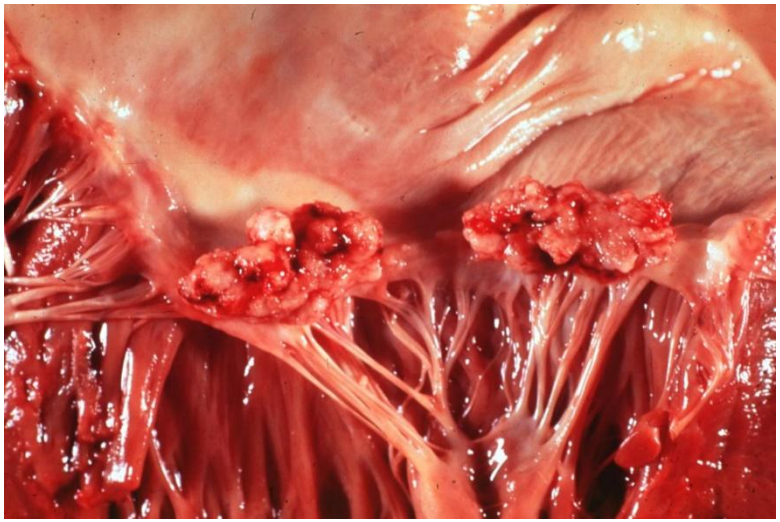
Základy ATB terapie IE

pro kardiology



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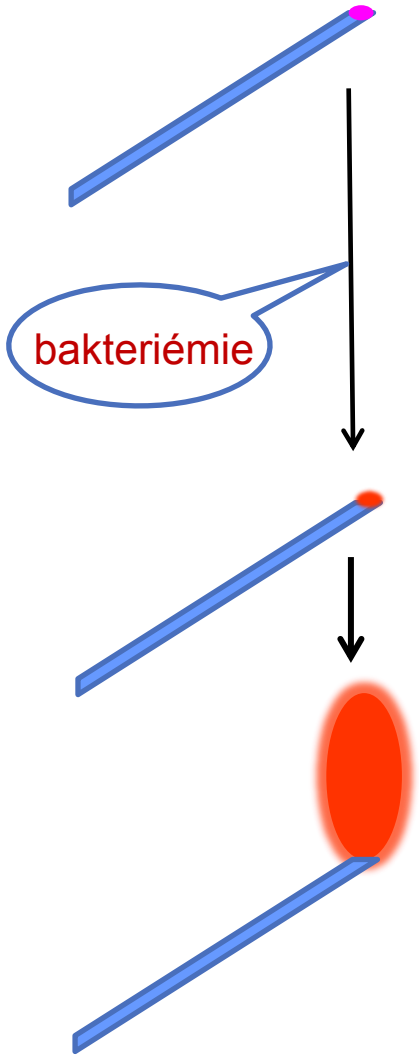
FN Bulovka, Praha

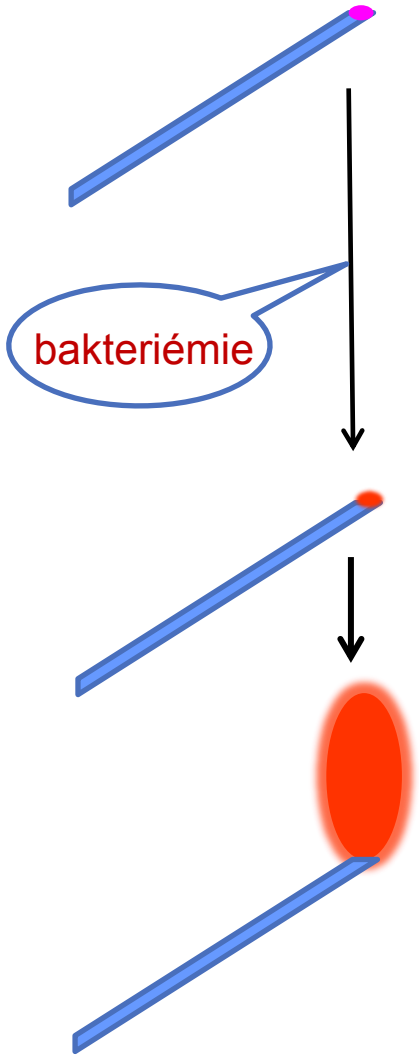
29.2.2024

Patogeneze infekční endokarditidy



- bakterie jsou obaleny sítí fibrinu a trombocytů, chráněny před PMN; imunita nemá vliv na průběh IE
- bakterie ve vysoké denzitě (10^9)
  – platí zvl. pro levostrannou IE
- bakterie málo metabolicky aktivní
- bakterie se trvale uvolňují do oběhu
- do oběhu se uvolňují i části vegetace

Důsledky pro ATB léčbu



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- bakterie málo metabolicky aktivní
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- do oběhu se uvolňují i části vegetace

Důsledky pro ATB léčbu

Vždy baktericidní ATB, v praxi stěnová ATB.
Vždy vysoké dávky, i.v. podávání.
Vždy dlouhodobá léčba.

- Pro volbu ATB je potřeba znát kvantitativní citlivost (MIC).
- β-laktamy působí rychleji a razantněji než vankomycin.
  (vyplývá z mechanismu účinku)
- Peniciliny působí na G+ bakterie lépe než cefalosporiny.
- U β-laktamů je žádoucí zajistit účinnou hladinu ATB po celou dobu dávkového intervalu. (hlídat biol. poločas!)
- Je nutné používat po celou dobu léčby baktericidní režim, na rozdíl od jiných infekcí nelze přejít na „doléčování“.
- Je nutné trvale monitorovat účinnost léčby (nejen klinicky).
- Je nutné být stále připraven na možnost komplikací. Endokarditidu nelze podceňovat.

ESC European Society of Cardiology

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ESC GUIDELINES

2023 ESC Guidelines for the management of endocarditis

Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC)

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Nuclear Medicine (EANM)

Authors/Task Force Members: Victoria Delgado *†, (Chairperson) (Spain), Nina Ajmone Marsan ‡, (Task Force Co-ordinator) (Netherlands), Suzanne de Waha‡, (Task Force Co-ordinator) (Germany), Nikolaos Bonaros (Austria), Margarita Brida (Croatia), Haran Burri (Switzerland), Stefano Caselli (Switzerland), Torsten Doenst (Germany), Stephane Ederhy (France), Paola Anna Erba [1] (Italy), Dan Foldager (Denmark), Emil L. Fosbøl (Denmark), Jan Kovac (United Kingdom), Carlos A. Mestres (South Africa), Owen I. Miller (United Kingdom), Jose M. Miro [2] (Spain), Michal Pazdernik (Czech Republic), Maria Nazarena Pizzi (Spain), Eduard Quintana [3] (Spain), Trine Bernholdt Rasmussen (Denmark), Arsen D. Ristić (Serbia), Josep Rodés-Cabau (Canada), Alessandro Sionis (Spain), Liesl Joanna Zühlke (South Africa), Michael A. Borger *†, (Chairperson) (Germany), and ESC Scientific Document Group

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[1] Representing the European Association of Nuclear Medicine (EANM)

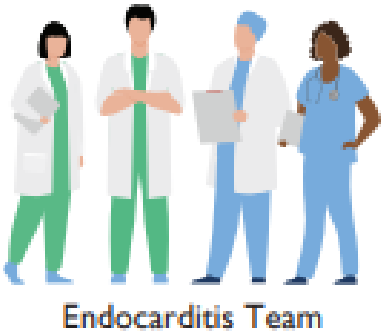
[2] Representing the European Society of Clinical Microbiology and Infectious Diseases (ESCMID)

[3] Representing the European Association for Cardio-Thoracic Surgery (EACTS)

Aktuální doporučené postupy

Delgado V, Marsan NA, de Waha S, Bonaros N, Brida M, Burri H, Caselli S, Doenst T, Ederhy S, Erba PA, Foldager D, Fosbø EL, Kovac J, Mestres CA, Miller OI, Miro JM, Pazdernik M, Pizzi MN, Quintana E, Rasmussen TB, Ristić AD, Rodés-Cabau J, Sionis A, Zühlke LJ, Borger MA, ESC Scientific Document Group.
2023 ESC Guidelines for the management of endocarditis.
European Heart Journal 2023 Oct 14; 44(39):3948-4042.

Preamble: *Členové této pracovní skupiny byli vybráni ESC, aby zastupovali lékaře zabývající se problematikou IE. Cílem výběrového řízení bylo zahrnout členy z celého regionu ESC, kteří se specializují (publikují) o IE. Pozornost bvla věnována diverzitě, zejména s ohledem na pohlaví a zemi původu.*



Victoria Delgado. Head of the department of Cardiovascular Imaging. Barcelona, Cataluña, España

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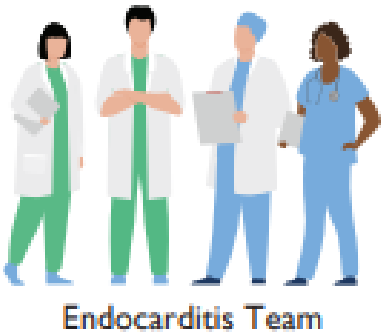
Table 7: Members of the Endocarditis Team

Core members
- Cardiologists
- Cardiac imaging experts
- Cardiovascular surgeons
- Infectious disease specialist
- Microbiologist
- Specialist in outpatient parenteral antibiotic treatment



Recommendation Table 7

Recommendations for antibiotic treatment of infective endocarditis due to oral streptococci and *Streptococcus gallolyticus* group

Recommendations		Class[a]	Level[b]
Penicillin-susceptible oral streptococci and *Streptococcus gallolyticus* group			
Standard treatment: 4-week duration in NVE or 6-week duration in PVE			
In patients with IE due to oral streptococci and *S. gallolyticus* group, penicillin G, amoxicillin, or ceftriaxone are recommended for 4 (in NVE) or 6 weeks (in PVE), using the following doses:[277,278]		I	B
Adult antibiotic dosage and route			
Penicillin G	12–18 million[c] U/day i.v. either in 4–6 doses or continuously		
Amoxicillin	100–200 mg/kg/day i.v. in 4–6 doses		
Ceftriaxone	2 g/day i.v. in 1 dose		
Paediatric antibiotic dosage and route			
Penicillin G	200 000 U/kg/day i.v. in 4–6 divided doses		
Amoxicillin	100–200[c] mg/kg/day i.v. in 4–6 doses		
Ceftriaxone	100 mg/kg/day i.v. in 1 dose		
Standard treatment: 2-week duration (not applicable to PVE)			
2-week treatment with penicillin G, amoxicillin, ceftriaxone combined with gentamicin is recommended only for the treatment of non-complicated NVE due to oral streptococci and *S. gallolyticus* in patients with normal renal function using the following doses:[277,278]		I	B
Adult antibiotic dosage and route			
Penicillin G	12–18 million[c] U/day i.v. either in 4–6 doses or continuously		
Amoxicillin	100–200 mg/kg/day i.v. in 4–6 doses		
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Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose or 3 equally divided doses[d]		
Allergy to beta-lactams			
In patients allergic to beta-lactams and with IE due to oral streptococci and *S. gallolyticus*, vancomycin for 4 weeks in NVE or for 6 weeks in PVE is recommended using the following doses:[292]		I	C
Adult antibiotic dosage and route			
Vancomycin[e]	30 mg/kg/day i.v. in 2 doses[e]		
Paediatric antibiotic dosage and route			
Vancomycin[e]	30 mg/kg/day i.v. in 2 or 3 equally divided doses[e]		
Oral streptococci and *Streptococcus gallolyticus* group susceptible, increased exposure or resistant to penicillin			
In patients with NVE due to oral streptococci and *S. gallolyticus*, penicillin G, amoxicillin, or ceftriaxone for 4 weeks in combination with gentamicin for 2 weeks is recommended using the following doses:[285–290]		I	B
Adult antibiotic dosage and route			
Penicillin G	24 million U/day i.v. either in 4–6 doses or continuously		
Amoxicillin	12 g/day i.v. in 6 doses		
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C citlivý
I intermediární
R rezistentní

C citlivý
I increased exposure
R rezistentní

HRUBÁ CHYBA !!

Dávkování u „C“
PEN G 12-18 MU/d
AMO 100-200 mg/kg
CTR 2 g/d ??

Paediatric antibiotic dosage and route			
Penicillin G	200 000 U/kg/day i.v. in 4–6 divided doses		
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Nebylo by lepší tuto část tabulky oddělit?

A specifikovat předěl mezi „C“ a „I“?
MIC ≤0,125 mg/l ??

Proč jsou dávky výše vztaženy na kg hmotnosti a zde ne?

Proč není zmíněno dávkování u dětí?
Redakční chyba?

Paediatric antibiotic dosage and route			
Penicillin G	200 000 U/kg/day i.v. in 4–6 divided doses		
Amoxicillin	100–200 mg/kg/day[c] i.v. in 4–6 doses		
Ceftriaxone	100 mg/kg i.v. in 1 dose		
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Serum concentrations should achieve 10-15 mg/L at pre-dose (trough) level, although some experts recommend to increase the dose of vancomycin to 45-60 mg/kg/day i.v. in 2 or 3 divided doses to reach serum trough levels (c_{min}) of 15-20 mg/L. However, vancomycin dose should not exceed 2 g/d unless serum levels are monitored and can be adjusted to obtain a peak plasma concentration of 30-45 µg/mL 1 h after completion of the i.v. infusion.

A co nasycovací dávka?

Recommendation Table 8

Recommendations for antibiotic treatment of infective endocarditis due to *Staphylococcus* spp.

Recommendations		Class[a]	Level[b]
IE caused by methicillin-susceptible staphylococci			
In patients with NVE due to methicillin-susceptible staphylococci, (flu)cloxacillin or cefazolin is recommended for 4–6 weeks using the following doses:[264,314,316–318]		I	B
Adult antibiotic dosage and route			
(Flu)cloxacillin[c]	12 g/day i.v. in 4–6 doses		
Cefazolin[e]	6 g/day i.v. in 3 doses		
Paediatric antibiotic dosage and route			
(Flu)cloxacillin[c]	200–300 mg/kg/day i.v. in 4–6 equally divided doses		
Cefazolin[e]	300–600 mg/kg/day in 3–4 doses		
In patients with PVE due to methicillin-susceptible staphylococci, (flu)cloxacillin or cefazolin with rifampin for at least 6 weeks and gentamicin for 2 weeks is recommended using the following doses:[264,314,316–318,320]		I	B
Adult antibiotic dosage and route			
(Flu)cloxacillin[c]	12 g/day i.v. in 4–6 doses		
Cefazolin	6 g/day i.v. in 3 doses		
Rifampin	900 mg/day i.v. or orally in 3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		
Paediatric antibiotic dosage and route			
(Flu)cloxacillin[c]	200–300 mg/kg/day i.v. in 4–6 equally divided doses		
Cefazolin	300–600 mg/kg/day in 3–4 doses		
Rifampin	20 mg/kg/day i.v. or orally in 3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		

Recommendation Table 8

Recommendations for antibiotic treatment of infective endocarditis due to *Staphylococcus* spp.

Allergy to beta-lactams			
In patients with NVE due to methicillin-susceptible staphylococci who are allergic to penicillin, cefazolin for 4–6 weeks is recommended using the following doses:[322–327]		I	B
Adult antibiotic dosage and route			
Cefazolin[e]	6 g/day i.v. in 3 doses		
Paediatric antibiotic dosage and route			
Cefazolin[e]	300–600 mg/kg/day in 3–4 doses		
In patients with PVE due to methicillin-susceptible staphylococci who are allergic to penicillin, cefazolin combined with rifampin for at least 6 weeks and gentamicin for 2 weeks is recommended using the following doses:[344]		I	B
Adult antibiotic dosage and route			
Cefazolin[e]	6 g/day i.v. in 3 doses		
Rifampin	900 mg/day i.v. or orally in 3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		
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Cefazolin[e]	300–600 mg/kg/day in 3–4 doses		
Rifampin	20 mg/kg/day i.v. or orally in 3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		

For penicillin-allergic patients with MSSA IE, penicillin desensitization can be attempted or cefazolin can be used since vancomycin is inferior to beta-lactams.[309]

Riziko desenzibilizace a/nebo zkřížené alergie je menší zlo než vankomycin?

309. Apellaniz G, Valdes M, Perez R, Martin-Luengo F, Garcia A, Soria F, *et al.* [Teicoplanin versus cloxacillin, cloxacillin-gentamycin and vancomycin in the treatment of experimental endocarditis caused by methicillin-sensitive *Staphylococcus aureus*]. *Enferm Infecc Microbiol Clin* 1991;**9**:208–210.

Abstract

Thirty-three rabbits, (12 in the control group and 21 treated, 5 with teicoplanin, vancomycin and cloxacillin-gentamycin and 6 with cloxacillin alone) with methicillin-sensitive *Staphylococcus aureus* (MSSA) experimentally induced endocarditis were studied to evaluate the efficacy of teicoplanin and its comparison with cloxacillin, vancomycin and cloxacillin-gentamycin. The rabbits were treated during three days. Mortality, blood cultures at 48 and 72 hours and the number of colonies forming units per gram of vegetation were then evaluated. There was statistically significantly differences between the control group and the 4 treated groups in respect of mortality (p less than 0.001), and blood culture's negativity at 48 and 72 hours (p less than 0.001), but not among the various groups of treatments. The CFU number of the vegetations were also significantly different between control and treatment groups (p less than 0.001). Cloxacillin and the combination cloxacillin-gentamycin lowered the CFU number more than teicoplanin and vancomycin (p less than 0.005). These results, allowed us to conclude than teicoplanin may be used as an alternative of standard treatments in infective endocarditis due to MSSA.

+ dávkování vankomycinu odpovídalo 30 mg/kg/den u člověka…

Zatratit vankomycin kvůli takové studii je HRUBÁ CHYBA !!

IE caused by methicillin-resistant staphylococci			
In patients with NVE due to methicillin-resistant staphylococci, vancomycin is recommended for 4–6 weeks using the following doses:[345]		I	B
Adult antibiotic dosage and route			
Vancomycin[h]	30–60 mg/kg/day i.v. in 2–3 doses		
Paediatric antibiotic dosage and route			
Vancomycin[h]	30 mg/kg/day i.v. in 2–3 equally divided doses		
In patients with PVE due to methicillin-resistant staphylococci, vancomycin with rifampin for at least 6 weeks and gentamicin for 2 weeks is recommended using the following doses:		I	B
Adult antibiotic dosage and route			
Vancomycin[h]	30–60 mg/kg/day i.v. in 2–3 doses		
Rifampin	900–1200 mg/day i.v. or orally in 2 or 3 divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		
Paediatric antibiotic dosage and route			
Vancomycin[h]	30 mg/kg/day i.v. in 2–3 equally divided doses		
Rifampin	20 mg/kg/day i.v. or orally in 2 or 3 divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 (preferred) or 2 doses		
In patients with NVE due to methicillin-resistant staphylococci, daptomycin combined with cloxacillin, ceftaroline or fosfomycin may be considered using the following doses:[335,345–349]		IIb	C
Adult antibiotic dosage and route			
Daptomycin	10 mg/kg/day i.v. in 1 dose		
Cloxacillin[c]	12 g/day i.v. in 6 doses		
OR	OR		
Ceftaroline[f]	1800 mg/day i.v. in 3 doses		
OR	OR		
Fosfomycin[g]	8–12 g/day i.v. in 4 doses		

Vankomycin je při alergii nevhodný, ale v léčbě MRSA IE je použitelný?

Recommendation Table 10

Antibiotic regimens for initial empirical treatment of IE

Recommendations		Class[b]	Level[c]
In patients with community-acquired NVE or late PVE (≥12 months post-surgery), ampicillin in combination with ceftriaxone or with (flu)cloxacillin and gentamicin should be considered using the following doses:[255]		IIa	C
Adult antibiotic dosage and route			
Ampicillin	12 g/day i.v. in 4–6 doses		
Ceftriaxone	4 g/day i.v. or i.m. in 2 doses		
(Flu)cloxacillin	12 g/day i.v. in 4–6 doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose		
Paediatric antibiotic dosage and route			
Ampicillin	300 mg/kg/day i.v. in 4–6 equally divided doses		
Ceftriaxone	100 mg/kg i.v. or i.m. in 1 dose		
(Flu)cloxacillin	200–300 mg/kg/day i.v. in 4–6 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 3 equally divided doses		

AMP + CTR
nebo
AMP+OXA+GEN

Jak to, že iniciální empirická ATB léčba nepostihuje stafylokoky?

HRUBÁ CHYBA !!

(*S. aureus* je častý původce NVE a IE mívá akutní průběh)

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ESC GUIDELINES

2023 ESC Guidelines for the management of endocarditis

Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC)

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Nuclear Medicine (EANM)

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- Hrubé chyby (riziko poškození i smrti)
- Četné menší odborné chyby
- Redakční zpracování: nepřehlednost, nedůslednost, nedbalost.

Endorsed by cardiac societies

Armenian Cardiologists Association, Azerbaijan Society of Cardiology, Belgian Society of Cardiology, Association of Cardiologists of Bosnia & Herzegovina, British Cardiovascular Society, Croatian Cardiac Society, Estonian Society of Cardiology, Egyptian Society of Cardiology, Finnish Cardiac Society, French Society of Cardiology , Georgian Society of Cardiology, German Cardiac Society, Hellenic Society of Cardiology, Hungarian Society of Cardiology, Irish Cardiac Society, Italian Federation of Cardiology, Kosovo Society of Cardiology, Kyrgyz Society of Cardiology, Lithuanian Society of Cardiology, Luxembourg Society of Cardiology, Maltese Cardiac Society, Moroccan Society of Cardiology, Polish Cardiac Society, Portuguese Society of Cardiology, San Marino Society of Cardiology, Cardiology Society of Serbia, Slovak Society of Cardiology, Spanish Society of Cardiology, Swiss Society of Cardiology, Turkish Society of Cardiology.

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A co dále?

Konzultace klinických mikrobiologů, infektologů a farmakologů/klinických farmaceutů

v ČR

v zahraničí

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