

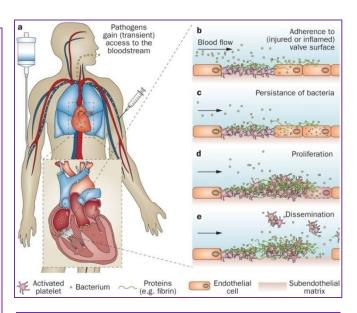


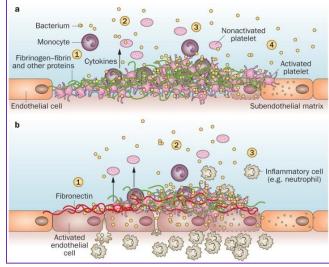
# İnfektif Endokardit 2015 Rehberi'nde neler değişti?

Dr. Özlem Kurt Azap Başkent Üniversitesi Tıp Fakültesi Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

# Sunum plani

- Rehberler
- "Avrupa" rehberi- yenilikler
- Profilaksi
- "Endokardit takımı"
- Tanı kriterleri- görüntüleme yöntemleri
- > Tedavi ve izlem
- Özel durumlar
- Özet

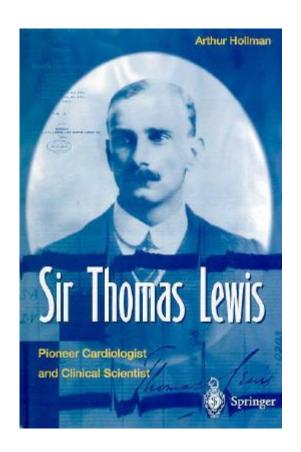




# Başlangıç...

1923- Br Heart J
 Dental girişimlerin
 endokardit için risk
 oluşturduğuna ilişkin ilk
 gözlem

1955- AHA, Circulation
 Endokardit profilaksisi için ilk rehber



### Endokardit Tanı/Tedavi- ABD 2005

#### **AHA Scientific Statement**

#### **Infective Endocarditis**

Diagnosis, Antimicrobial Therapy, and Management of Complications
A Statement for Healthcare Professionals From the Committee on Rheumatic
Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular
Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and
Cardiovascular Surgery and Anesthesia, American Heart Association

Endorsed by the Infectious Diseases Society of America

Larry M. Baddour, MD, Chair; Walter R. Wilson, MD; Arnold S. Bayer, MD; Vance G. Fowler, Jr, MD, MHS; Ann F. Bolger, MD; Matthew E. Levison, MD\*; Patricia Ferrieri, MD; Michael A. Gerber, MD; Lloyd Y. Tani, MD; Michael H. Gewitz, MD; David C. Tong, MD; James M. Steckelberg, MD; Robert S. Baltimore, MD†; Stanford T. Shulman, MD; Jane C. Burns, MD; Donald A. Falace, DMD‡; Jane W. Newburger, MD, MPH; Thomas J. Pallasch, DDS, MS; Masato Takahashi, MD; Kathryn A. Taubert, PhD

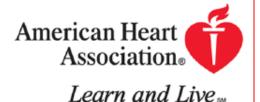
Background—Despite advances in medical, surgical, and critical care interventions, infective endocarditis remains a disease that is associated with considerable morbidity and mortality. The continuing evolution of antimicrobial resistance among common pathogens that cause infective endocarditis creates additional therapeutic issues for physicians to manage in this potentially life-threatening illness.

Methods and Results—This work represents the third iteration of an infective endocarditis "treatment" document developed by the American Heart Association under the auspices of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease of the Young. It updates recommendations for diagnosis, treatment, and management of complications of infective endocarditis. A multidisciplinary committee of experts drafted this document to assist physicians in the evolving care of patients with infective endocarditis in the new millennium. This extensive document is accompanied by an executive summary that covers the key points of the diagnosis, antimicrobial therapy, and management of infective endocarditis. For the first time, an evidence-based scoring system that is used by the American College of Cardiology and the American Heart Association was applied to treatment recommendations. Tables also have been included that provide input on the use of echocardiography during diagnosis and treatment of infective endocarditis, evaluation and treatment of culture-negative endocarditis, and short-term and long-term management of patients during and after completion of antimicrobial treatment. To assist physicians who care for children, pediatric dosing was added to each treatment regimen.

Conclusions—The recommendations outlined in this update should assist physicians in all aspects of patient care in the diagnosis, medical and surgical treatment, and follow-up of infective endocarditis, as well as management of associated complications. Clinical variability and complexity in infective endocarditis, however, dictate that these guidelines be used to support and not supplant physician-directed decisions in individual patient management. (Circulation. 2005; 111:e394-e433.)

### Endokardit Profilaksisi- ABD 2007





**JOURNAL OF THE AMERICAN HEART ASSOCIATION** 

Prevention of Infective Endocarditis: Guidelines From the American Heart Association: A Guideline From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group

Walter Wilson, Kathryn A. Taubert, Michael Gewitz, Peter B. Lockhart, Larry M. Baddour, Matthew Levison, Ann Bolger, Christopher H. Cabell, Masato Takahashi, Robert S. Baltimore, Jane W. Newburger, Brian L. Strom, Lloyd Y. Tani, Michael Gerber, Robert O. Bonow, Thomas Pallasch, Stanford T. Shulman, Anne H. Rowley, Jane C. Burns, Patricia Ferrieri, Timothy Gardner, David Goff, David T. Durack and The Council on Scientific Affairs of the American Dental Association has approved the guideline as it relates to dentistry. In addition, this guideline has been endorsed by the American Academy of Pediatrics, Infectious Diseases Society of America, the In Circulation 2007;116:1736-1754; originally published online Apr 19, 2007;

### Avrupa Rehberi- Türkçe çeviri 2009



European Heart Journal (2009) **30**, 2369-2413 doi:10.1093/eurheartj/ehp285

**ESC KILAVUZLARI** 

# Enfektif endokardit tanı, önleme ve tedavi kılavuzu (2009 güncellemesi)

Avrupa Kardiyoloji Derneği (ESC) Enfektif Endokardit Tanı, Önleme ve Tedavi Görev Grubu

Avrupa Klinik Mikrobiyoloji ve Enfeksiyon Hastalıkları Derneği (ESCMID) ve Uluslararası Enfeksiyon ve Kanser Kemoterapisi Derneği (ISC) tarafından desteklenmiştir

Türk Kardiyol Dern Arş Suppl 8, 2009

### Endokardit Tanı/Tedavi-İngiltere 2011

Journal of Antimicrobial Chemotherapy Advance Access published December 2, 2011

J Antimicrob Chemother doi:10.1093/jac/dkr450

Journal of Antimicrobial Chemotherapy

# Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy

F. Kate Gould<sup>1\*</sup>, David W. Denning<sup>2</sup>, Tom S. J. Elliott<sup>3</sup>, Juliet Foweraker<sup>4</sup>, John D. Perry<sup>1</sup>, Bernard D. Prendergast<sup>5</sup>, Jonathan A. T. Sandoe<sup>6</sup>, Michael J. Spry<sup>1</sup> and Richard W. Watkin<sup>7</sup>

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The BSAC guidelines on treatment of infectious endocarditis (IE) were last published in 2004. The guidelines presented here have been updated and extended to reflect developments in diagnostics, new trial data and the availability of new antibiotics. The aim of these guidelines, which cover both native valve and prosthetic valve endocarditis, is to standardize the initial investigation and treatment of IE. An extensive review of the literature using a number of different search criteria has been carried out and cited publications used to support any changes we have made to the existing guidelines. Publications referring to *in vitro* or animal models have only been cited if appropriate clinical data are not available. Randomized, controlled trials suitable for the development of evidenced-based guidelines in this area are still lacking and therefore a consensus approach has again been adopted for most recommendations; however, we have attempted to grade the evidence, where possible. The guidelines have also been extended by the inclusion of sections on clinical diagnosis, echocardiography and surgery.

## Endokardit Tanı/Tedavi- ABD 2015

#### **AHA Scientific Statement**

### Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

A Scientific Statement for Healthcare Professionals From the American Heart Association

Endorsed by the Infectious Diseases Society of America

Larry M. Baddour, MD, FAHA, Chair; Walter R. Wilson, MD; Arnold S. Bayer, MD;
Vance G. Fowler, Jr, MD, MHS; Imad M. Tleyjeh, MD, MSc;
Michael J. Rybak, PharmD, MPH; Bruno Barsic, MD, PhD; Peter B. Lockhart, DDS;
Michael H. Gewitz, MD, FAHA; Matthew E. Levison, MD; Ann F. Bolger, MD, FAHA;
James M. Steckelberg, MD; Robert S. Baltimore, MD; Anne M. Fink, PhD, RN;
Patrick O'Gara, MD, FAHA; Kathryn A. Taubert, PhD, FAHA; on behalf of the American Heart
Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on
Cardiovascular Disease in the Young, Council on Clinical Cardiology, Council on Cardiovascular
Surgery and Anesthesia, and Stroke Council

Background—Infective endocarditis is a potentially lethal disease that has undergone major changes in both host and pathogen. The epidemiology of infective endocarditis has become more complex with today's myriad healthcare-associated factors that predispose to infection. Moreover, changes in pathogen prevalence, in particular a more common staphylococcal origin, have affected outcomes, which have not improved despite medical and surgical advances.

Methods and Results—This statement updates the 2005 iteration, both of which were developed by the American Heart Association under the auspices of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease of the Young. It includes an evidence-based system for diagnostic and treatment recommendations used by the American College of Cardiology and the American Heart Association for treatment recommendations.

Conclusions—Infective endocarditis is a complex disease, and patients with this disease generally require management by a team of physicians and allied health providers with a variety of areas of expertise. The recommendations provided in this document are intended to assist in the management of this uncommon but potentially deadly infection. The clinical variability and complexity in infective endocarditis, however, dictate that these recommendations be used to support and not supplant decisions in individual patient management. (Circulation. 2015;132:1435-1486. DOI: 10.1161/CIR.00000000000000296.)

# Endokardit Rehberi- Avrupa 2015

European Heart Journal Advance Access published August 29, 2015



European Heart Journal doi:10.1093/eurheartj/ehv319 **ESC GUIDELINES** 

# 2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

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

### Rehberde...

#### 99 öneri mevcut

- Bir adet A düzeyinde öneri
- 48 adet B düzeyinde öneri (Yarısı antibiyotik tedavisi ile ilgili)
- 50 adet C düzeyinde öneri (13'ü antibiyotik tedavisi ile ilgili)

# Öneri Sınıflaması

#### Tablo 1 Tavsiye sınıfları

Tavsiye Sınıfları	Tanım		
Sınıf I	Belli bir tedavi veya işlemin kârlı, yararlı ve etkili olduğuna ilişkin kanıt ve/veya genel görüş birliği varlığı		
Sınıf II	Belli bir tedavi veya işlemin yararlı/etkili olduğuna ilişkin çelişkili kanıt ve/veya farklı görüşler		
Sınıf IIa	Kanıtların/görüşlerin ağırlığı yararlılık/etkililik yönünde		
Sınıf IIb	Kanıtlar/görüşler yararlılık/etkililiği daha az destekliyor		
Sınıf III	Belli bir tedavi ya da işlemin yararlı/etkili olmadığı, bazı durumlarda zararlı olabileceği yönünde kanıt ya da genel görüş birliği		

able I Classes of recommend	ations	
Classes or recommenda		Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness'efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

# Kanıt Düzeyleri

Tablo 2 Kanıt düzeyleri	
Kanıt Düzeyi A	Veriler birden çok rastgele yöntemli klinik çalışmadan ya da meta-analizden elde edilmiştir
Kanıt Düzeyi B	Veriler tek bir rastgele yöntemli klinik çalışmadan veya rastgele yöntem kullanılmayan büyük boyutlu çalışmalardan elde edilmiştir
Kanıt Düzeyi C	Uzmanların görüş birliği ve/veya küçük boyutlu çalışmalar, geriye dönük çalışmalar, kayıt çalışmaları

able 2 Levels of evidence			
Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.		
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.		
Level of evidence C	Consensus of opinion of the experts and/ or small studies, retrospective studies, registries.		

### Rehberde...

#### 99 öneri mevcut

- Bir adet A düzeyinde öneri
- 48 adet B düzeyinde öneri (Yarısı antibiyotik tedavisi ile ilgili)
- 50 adet C düzeyinde öneri (13'ü antibiyotik tedavisi ile ilgili)

## **Profilaksi**

# Risk durumu vs işlem

- Yüksek riskli hasta: Protez kapak..vb
- Orta-düşük düzey riskli: Mitral kapak prolapsusu..vb
- Saptanmış bir riski olmayan kişi
- >Günlük aktiviteler: Diş fırçalama, defekasyon..vb
- **≻**Tıbbi girişimler:

Dental girişimler: Jinjival işlemler..vb

Endoskopik girişimler

Perkütan invazif işlemler

Cerrahi işlemler

### Nonspesifik öneriler

#### Herkese önerilmeli; yüksek riskli hastalarda vurgulanmalı

### Table 4 Non-specific prevention measures to be followed in high-risk and intermediate-risk patients

### These measures should ideally be applied to the general population and particularly reinforced in high-risk patients:

- Strict dental and cutaneous hygiene. Dental follow-up should be performed twice a year in high-risk patients and yearly in the others.
- · Disinfection of wounds.
- · Eradication or decrease of chronic bacterial carriage: skin, urine.
- · Curative antibiotics for any focus of bacterial infection.
- · No self-medication with antibiotics.
- · Strict infection control measures for any at-risk procedure.
- · Discourage piercing and tattooing.
- Limit the use of infusion catheters and invasive procedure when possible. Favour peripheral over central catheters, and systematic replacement of the peripheral catheter every 3—4 days. Strict adherence to care bundles for central and peripheral cannulae should be performed.

### Yüksek riskli kardiyak durumlar

Table 3 Cardiac conditions at highest risk of infective endocarditis for which prophylaxis should be considered when a high-risk procedure is performed

Recommendations	Classa	Levelb
Antibiotic prophylaxis should be considered for patients at highest risk for IE:  (1) Patients with any prosthetic valve, including a transcatheter valve, or those in whom any prosthetic material was used for cardiac valve repair.  (2) Patients with a previous episode of IE.  (3) Patients with CHD:  (a) Any type of cyanotic CHD.  (b) Any type of CHD repaired with a prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains.	lla	С
Antibiotic prophylaxis is not recommended in other forms of valvular or CHD.	Ш	С

- Protez kapak
- Geçirilmiş İE
- Siyanotik konjenital kalp hastalığı
- Siyanotik kalp hastalığı cerrahisinden sonraki ilk 6 aylık dönem

# Yüksek riskli hastalarda **profilaksi önerilen dental** işlemler

Table 5 Recommendations for prophylaxis of infective endocarditis in the highest-risk patients according to the type of at-risk procedure

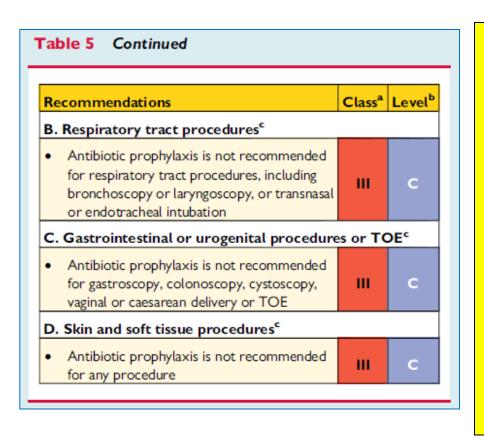
Recon	nmendations	Classa	Levelb
A. Dental procedures			
cor ma reg	tibiotic prophylaxis should only be nsidered for dental procedures requiring nipulation of the gingival or periapical gion of the teeth or perforation of the oral cosa	lla	U
for tiss ren or a ort the	tibiotic prophylaxis is not recommended local anaesthetic injections in non-infected sues, treatment of superficial caries, noval of sutures, dental X-rays, placement adjustment of removable prosthodontic or hodontic appliances or braces or following shedding of deciduous teeth or trauma to lips and oral mucosa	Ш	v

- Jinjival işlemler
- Periapikal işlemler
- Oral mukozada perforasyon

#### **ÖNERİLMEYENLER!**

- ➤ Lokal anestezi
- **≻**Dolgu
- ≻Film çekimi
- ➤ Prostodontik veya ortodontik işlemler

# Profilaksi önerilmeyen işlemler



Bronkoskopi, entübasyon

Gastroskopi, kolonoskopi, sistoskopi, TÖE, sezeryan, doğum

Deri ve yumuşak doku ile ilgili işlemler

### Profilaksi- antibiyotikler

#### Table 6 Recommended prophylaxis for high-risk dental procedures in high-risk patients

Situation	Antibiotic	Single-dose 30–60 minutes before procedure		
		Adults	Children	
No allergy to penicillin or ampicillin	Amoxicillin or ampicillin <sup>a</sup>	2 g orally or i.v.	50 mg/kg orally or i.v.	
Allergy to penicillin or ampicillin	Clindamycin	600 mg orally or i.v.	20 mg/kg orally or i.v.	

Journal of Antimicrobial Chemotherapy Advance Access published April 29, 2015

J Antimicrob Chemother doi:10.1093/jac/dkv115 Journal of Antimicrobial Chemotherapy

### Incidence and nature of adverse reactions to antibiotics used as endocarditis prophylaxis

Martin H. Thornhill<sup>1,2\*</sup>, Mark J. Dayer<sup>3</sup>, Bernard Prendergast<sup>4</sup>, Larry M. Baddour<sup>5</sup>, Simon Jones<sup>6</sup> and Peter B. Lockhart<sup>2</sup>

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Received 10 January 2015; returned 25 March 2015; revised 30 March 2015; accepted 1 April 2015

**Objectives:** Antibiotic prophylaxis (AP) administration prior to invasive dental procedures has been a leading focus of infective endocarditis prevention. However, there have been long-standing concerns about the risk of adverse drug reactions as a result of this practice. The objective of this study was to identify the incidence and nature of adverse reactions to amoxicillin and clindamycin prophylaxis to prevent infective endocarditis.

**Methods:** We obtained AP prescribing data for England from January 2004 to March 2014 from the NHS Business Services Authority, and adverse drug reaction data from the Medicines and Healthcare Products Regulatory Agency's Yellow Card reporting scheme for prescriptions of the standard AP protocol of a single 3 g oral dose of amoxicillin or a single 600 mg oral dose of clindamycin for those allergic to penicillin.

Results: The reported adverse drug reaction rate for amoxicillin AP was 0 fatal reactions/million prescriptions (in fact 0 fatal reactions for nearly 3 million prescriptions) and 22.62 non-fatal reactions/million prescriptions. For clindamycin, it was 13 fatal and 149 non-fatal reactions/million prescriptions. Most clindamycin adverse drug reactions were Clostridium difficile infections.

**Conclusions:** AP adverse drug reaction reporting rates in England were low, particularly for amoxicillin, and lower than previous estimates. This suggests that amoxicillin AP is comparatively safe for patients without a history of amoxicillin allergy. The use of clindamycin AP was, however, associated with significant rates of fatal and nonfatal adverse drug reactions associated with *C. difficile* infections. These were higher than expected and similar to those for other doses, durations and routes of clindamycin administration.

# Kısıtlı profilaksi sonrası durum

# Incidence of infective endocarditis in England, 2000–13: a secular trend, interrupted time-series analysis

Mark J Dayer, Simon Jones, Bernard Prendergast, Larry M Baddour, Peter B Lockhart, Martin H Thornhill

#### Summary

Background Antibiotic prophylaxis given before invasive dental procedures in patients at risk of developing infective endocarditis has historically been the focus of infective endocarditis prevention. Recent changes in antibiotic prophylaxis guidelines in the USA and Europe have substantially reduced the number of patients for whom antibiotic prophylaxis is recommended. In the UK, guidelines from the National Institute for Health and Clinical Excellence (NICE) recommended complete cessation of antibiotic prophylaxis for prevention of infective endocarditis in March, 2008. We aimed to investigate changes in the prescribing of antibiotic prophylaxis and the incidence of infective endocarditis since the introduction of these guidelines.

Methods We did a retrospective secular trend study, analysed as an interrupted time series, to investigate the effect of antibiotic prophylaxis versus no prophylaxis on the incidence of infective endocarditis in England. We analysed data for the prescription of antibiotic prophylaxis from Jan 1, 2004, to March 31, 2013, and hospital discharge episode statistics for patients with a primary diagnosis of infective endocarditis from Jan 1, 2000, to March 31, 2013. We compared the incidence of infective endocarditis before and after the introduction of the NICE guidelines using segmented regression analysis of the interrupted time series.

Findings Prescriptions of antibiotic prophylaxis for the prevention of infective endocarditis fell substantially after introduction of the NICE guidance (mean 10 900 prescriptions per month [Jan 1, 2004, to March 31, 2008] *vs* 2236 prescriptions per month [April 1, 2008, to March 31, 2013], p<0·0001). Starting in March, 2008, the number of cases of infective endocarditis increased significantly above the projected historical trend, by 0·11 cases per 10 million people per month (95% CI 0·05–0·16, p<0·0001). By March, 2013, 35 more cases per month were reported than would have been expected had the previous trend continued. This increase in the incidence of infective endocarditis was significant for both individuals at high risk of infective endocarditis and those at lower risk.

Interpretation Although our data do not establish a causal association, prescriptions of antibiotic prophylaxis have fallen substantially and the incidence of infective endocarditis has increased significantly in England since introduction of the 2008 NICE guidelines.

Lancet 2015; 385: 1219–28

### Dental işlemlerde profilaksinin etkinliği

### Antibiotics for the prophylaxis of bacterial endocarditis in dentistry (Review)

Glenny AM, Oliver R, Roberts GJ, Hooper L, Worthington HV

#### Key results

It is unclear whether taking antibiotics as a preventive measure before undergoing invasive dental procedures is effective or ineffective against bacterial endocarditis in people at risk.

No studies were located that assessed numbers of deaths, serious adverse events requiring hospital admission, other adverse events, or cost implications of treatment.

There is a lack of evidence to support previously published guidelines in this area. It is not clear whether the potential harms and costs of antibiotic administration outweigh any beneficial effect. Ethically, practitioners need to discuss the potential benefits and harms of preventive antibiotic treatment with their patients before a decision is made about prescribing it.

## THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library 2013, Issue 10

http://www.thecochranelibrary.com

# Cerrahi profilaksisi

Table 7 Recommendations for antibiotic prophylaxis for the prevention of local and systemic infections before cardiac or vascular interventions

Recommendations	Classa	Level <sup>b</sup>	Ref.c
Preoperative screening of nasal carriage of Staphylococcus aureus is recommended before elective cardiac surgery in order to treat carriers	1	A	46,47
Perioperative prophylaxis is recommended before placement of a pacemaker or implantable cardioverter defibrillator	ı	В	45
Potential sources of sepsis should be eliminated ≥2 weeks before implantation of a prosthetic valve or other intracardiac or intravascular foreign material, except in urgent procedures	lla	U	
Perioperative antibiotic prophylaxis should be considered in patients undergoing surgical or transcatheter implantation of a prosthetic valve, intravascular prosthetic or other foreign material	lla	С	
Systematic local treatment without screening of S. aureus is not recommended	Ш	С	

- Kardiyak cerrahi öncesi S.aureus taşıyıcılığının taranması
- ➤ Pil..vb öncesi profilaksi
- Protez kapak ameliyatından en az
   2 hafta önce enf odağının
   ortadan kaldırılması
- Protez kapak (transkateter dahil) yerleştirilmesinde profilaksi
- S.aureus taşıyıcılığı taranmadan lokal tedavi YOK!

### **Endokardit Takımı**

### Endokardit takımı/Referans merkez

#### Table 8 Characteristics of the 'Endocarditis Team'

#### When to refer a patient with IE to an 'Endocarditis Team' in a reference centre

- Patients with complicated IE (i.e. endocarditis with HF, abscess, or embolic or neurological complication or CHD), should be referred early and managed in a reference centre with immediate surgical facilities.
- Patients with non-complicated IE can be initially managed in a nonreference centre, but with regular communication with the reference centre, consultations with the multidisciplinary 'Endocarditis Team', and, when needed, with external visit to the reference centre.

#### Characteristics of the reference centre

- Inmediate access to diagnostic procedures should be possible, including TTE, TOE, multislice CT, MRI, and nuclear imaging.
- 2. Immediate access to cardiac surgery should be possible during the early stage of the disease, particularly in case of complicated IE (HF, abscess large vegetation neurological and embolic complications)
- Several specialists should be present on site (the 'Endocarditis Team'), including at least cardiac surgeons, cardiologists, anaesthesiologists, ID specialists, microbiologists and, when available, specialists in valve diseases, CHD, pacemaker extraction, echocardiography and other cardiac imaging techniques, neurologists, and facilities for neurosurgery and interventional neuroradiology.

#### Role of the 'Endocarditis Team'

- The 'Endocarditis Team' should have meetings on a regular basis in order to discuss cases, take surgical decisions, and define the type of follow-up.
- The 'Endocarditis Team' chooses the type, duration, and mode of follow up of antibiotic therapy, according to a standardized protocol, following the current guidelines.
- 3. The 'Endocarditis Team' should participate in national or international registries, publicly report the mortality and morbidity of their centre, and be involved in a quality improvement programme, as well as in a patient education programme.
- 4. The follow-up should be organized on an outpatient visit basis at a frequency depending on the patient's clinical status (ideally at 1, 3, 6, and 12 months after hospital discharge, since the majority of events occur during this period<sup>57</sup>).

#### Komplike endokardit

- > Kalp yetmezliği
- > Abse
- Embolik veya nörolojik komplikasyonlar
- > Konjenital siyanotik kalp hastalığı

#### Referans merkezde

- ➤TTE, TÖE, multislice BT, MR, nükleer inceleme
- ➤ Acil kardiyak cerrahi

# Tanı / Tanı kriterleri

### Modifiye Duke kriterleri

Enfektif endokardit tanı, önleme ve tedavi kılavuzu (2009 güncellemesi)

#### Tablo 11 Enfektif endokardit tanısında modifiye Duke ölçütleri (Li ve ark., 94 uyarlanarak yayımlanmıştır)

#### **MAJÖR ÖLÇÜTLER**

#### Kan kültürü EE açısından pozitif

 İki ayrı kan kültüründe EE ile uyumlu tipik mikroorganizmalar:
 Viridans streptokoklar, Streptococcus bovis, HACEK grubu, Staphylococcus aureus; ya da Birincil odak olmaması koşuluyla, toplumdan edinilmiş enterokoklar

ya da

Pozitif olmaya devam eden kan kültürlerinde EE ile uyumlu mikroorganizmalar:

>12 saat arayla alınmış en az iki kan kültüründe pozitif sonuç alınması; ya da

Üç ayrı kan kültürünün hepsinde ya da 4 ayrı kan kültürünün çoğunda (birinci ve son örnekler arasında en az 1 saat olması koşuluyla) pozitif sonuç alınması

ya da

Coxiella burnetii için tek bir pozitif kan kültürü ya da faz I IgG antikor titresinin >1:800 olması

#### Endokardiyal tutulum kanıtları

Ekokardiyografi EE için pozitif
 Vejetasyon - Apse - Protez kapakta yeni ortaya çıkan kısmi ayrışma (dehisens)

Yeni valvüler yetersizlik

#### MİNÖR ÖLÇÜTLER

- Yatkınlık: yatkınlık oluşturan kalp sorunu, damardan madde kullanımı
- Ateş: vücut sıcaklığının >38°C olması
- Vasküler olaylar: majör arteriyel emboli, septik pulmoner enfarkt, mikotik anevrizma, intrakraniyal hemoraji; konjunktival hemoraj, Janeway lezyonları
- · İmmünolojik olaylar: glomerülonefrit, Osler nodülleri, Roth lekeleri, romatoid faktör
- Mikrobiyolojik kanıtlar: kan kültürü pozitiftir, ancak majör ölçütler yoktur ya da EE ile uyumlu bir mikroorganizma ile aktif enfeksiyonu gösteren serolojik kanıtlar

Şunlar varsa EE tanısı kesindir:

2 majör ölçüt ya da

1 majör ölçüt ve 3 minör ölçüt ya da

5 minör ölçüt

Şunlar varsa EE tanısı mümkündür:

1 majör ve 1 minör ölçüt ya da

3 minör ölçüt

#### **EKO-1**

#### Table 10 Role of echocardiography in infective endocarditis

Re	commendations	Classa	Levelb	Ref.c
Α.	Diagnosis			
•	TTE is recommended as the first-line imaging modality in suspected IE.		В	64,65
•	TOE is recommended in all patients with clinical suspicion of IE and a negative or non-diagnostic TTE.	1	В	64, 68–71
•	TOE is recommended in patients with clinical suspicion of IE, when a prosthetic heart valve or an intracardiac device is present.	1	В	64,71
•	Repeat TTE and /or TOE within 5–7 days is recommended in case of initially negative examination when clinical suspicion of IE remains high.	1	υ	
•	Echocardiography should be considered in Staphylococcus aureus bacteraemia.	lla	В	66,67
	TOE should be considered in patients with suspected IE, even in cases with positive TTE, except in isolated right-sided native valve IE with good quality TTE examination and unequivocal echocardiographic findings.	lla	υ	
В.	Follow-up under medical therapy	у		
•	Repeat TTE and/or TOE are recommended as soon as a new complication of IE is suspected (new murmur, embolism, persisting fever, HF, abscess, atrioventricular block).	1	В	64,72

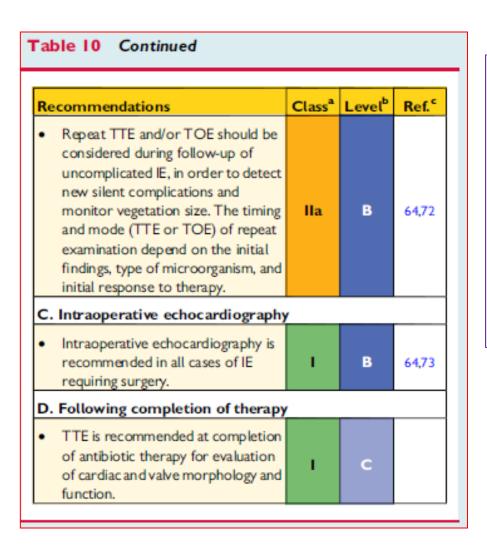
Continued

- >TTE: ilk tetkik
- **≻TÖE** 
  - TTE negatif ise veya tanısal değil ise
  - Protez kapak var ise

İzole sağ kapak endokarditi dışındaki **tüm olgularda TÖE** öneriliyor

- Klinik şüphe durumunda TTE ve/veya
   TÖE 5-7 gün içinde tekrarlanmalıdır
- S.aureus bakteriyemisinde EKO yapılabilir

### **EKO-2**

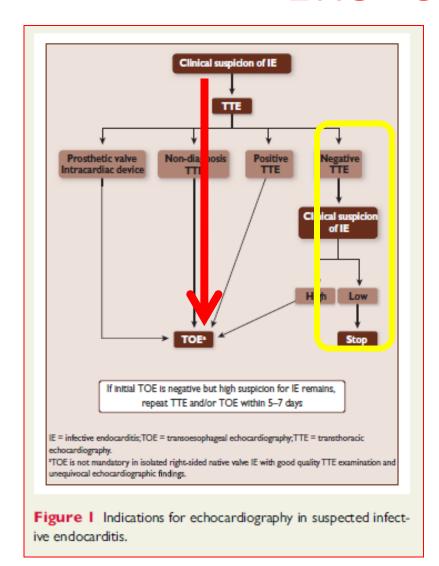


İzlemde TTE veya TÖE

İntra-operatif EKO

Tedavi bitiminde TTE

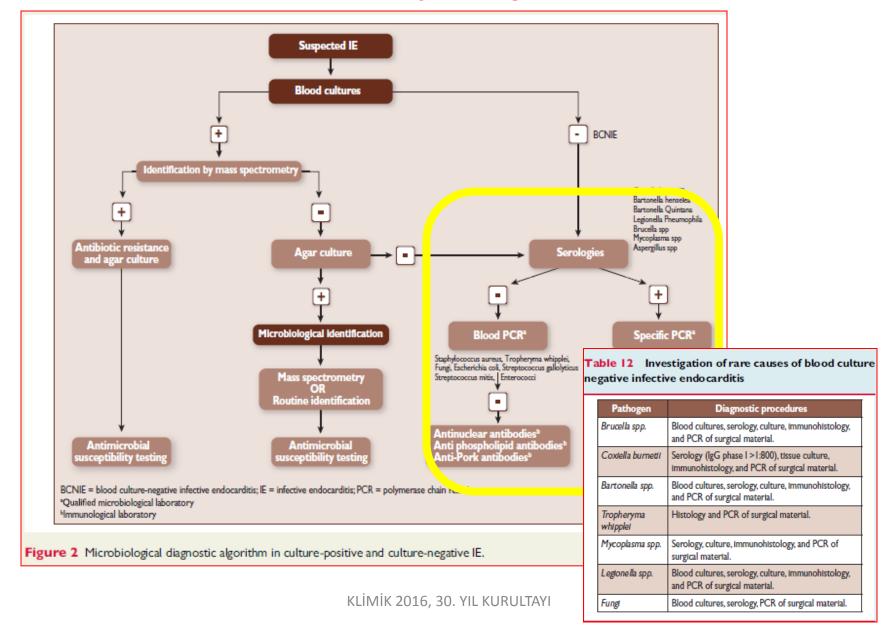
### **EKO-3**



Aort kapağı

Soi Soi Kulakcık

# Mikrobiyolojik tanı

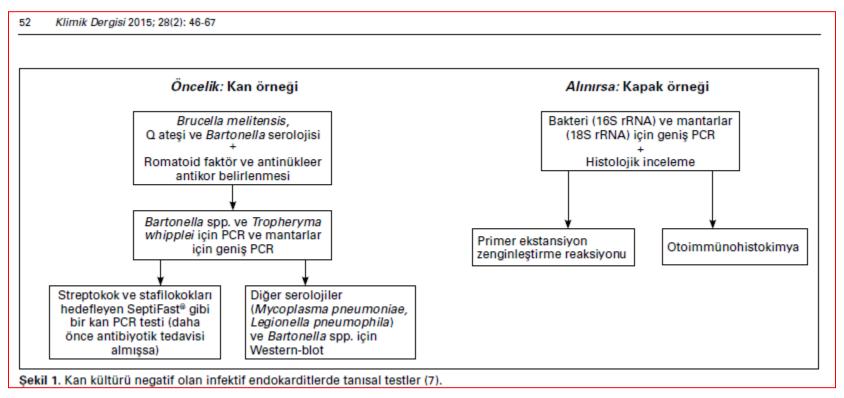


### Kültür negatif endokardit

#### İnfektif Endokardit: Güncel Bilgiler

Infective Endocarditis: An Update

Serap Şimşek-Yavuz İstanbul Üniversitesi, İstanbul Tıp Fakültesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, İstanbul, Türkiye



### Tanı kriterleri

- Duke Kriterleri- Durack DT, Am J Med, 1994
- Modifiye Duke kriterleri, Li JS Clin Infect Dis, 2000
- 2015-ESC(Avrupa Kardiyoloji Derneği)
   Modifiye Duke kriterleri'ne ek öneriler

Given the recent published data, the Task Force proposes the addition of three further points in the diagnostic criteria (Table 14):

- (1) The identification of paravalvular lesions by cardiac CT should be considered a major criterion.
- (2) In the setting of the suspicion of endocarditis on a prosthetic valve, abnormal activity around the site of implantation detected by <sup>18</sup>F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leucocyte SPECT/ CT should be considered a major criterion.
- (3) The identification of recent embolic events or infectious aneurysms by imaging only (silent events) should be considered a minor criterion.

#### Table 14 Definitions of the terms used in the European Society of Cardiology 2015 modified criteria for the diagnosis of infective endocarditis

#### Major criteria

#### 1.Blood cultures positive for IE

- Typical microorganisms consistent with IE from 2 separate blood cultures:
- Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus, or
- Community-acquired enterococci, in the absence of a primary focus; or
- Microorganisms consistent with IE from persistently positive blood cultures:
- ≥2 positive blood cultures of blood samples drawn > 12 h apart; or
- All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or
- c. Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre >1:800

#### 2. Imaging positive for IE

- a. Echocardiogram positive for IE:
- Vegetation;
- Abscess, pseudoaneurysm, intracardiac fistula;
- Valvular perforation or aneurysm;
- New partial dehiscence of prosthetic valve.

Abnormal activity around the site of prosthetic valve implantation detected by <sup>18</sup>F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.

Definite paravalvular lesions by cardiac CT.

#### Minor criteria

- Predisposition such as predisposing heart condition, or injection drug use.
- Fever defined as temperature >38°C.
- Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycodc)
  aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and
  Janeway's lesions.
- Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
- Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

CT = computed tomography, FDG = fluorodeoxyglucose; HACEK = Haemophilus parainfluenzae, H. aphrophilus, H. paraphrophilus, H. influenzae, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae, and K. denitrificans; IE = infective endocarditis; Ig = immunoglobulin; PET = positron emission tomography, SPECT = single photon emission computerized tomography. Adapted from Li et al. 87

### Tanı

Table 13 Definition of infective endocarditis according to the modified Duke criteria (adapted from Li et al. 87)

#### Definite IE

#### Pathological criteria

- Microorganisms demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or
- Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis

#### Clinical criteria

- 2 major criteria; or
- · I major criterion and 3 minor criteria; or
- 5 minor criteria

#### Possible IE

- · I major criterion and I minor criterion; or
- 3 minor criteria

#### Rejected IE

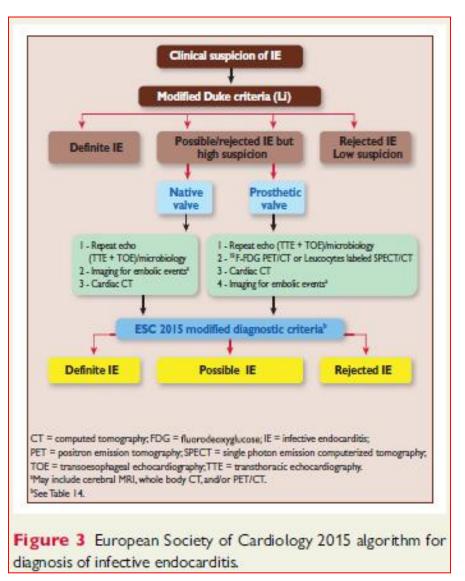
- · Firm alternate diagnosis; or
- Resolution of symptoms suggesting IE with antibiotic therapy for ≤4 days; or
- No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days; or
- · Does not meet criteria for possible IE, as above

#### Majör kriterlere ek:

Görüntüleme tetkikleri bulguları Minör kriterlere ek:

Görüntüleme tetkikleri bulguları

### Tanı için önerilen algoritma



# Tedavi ve İzlem

### Tedaviye başlarken prognostik değerlendirme önemli!

Endokardit mortalitesi: %15-30

kalp yemezliği
periannüler komplikasyon — % 79
etken *S.aureus* 

#### Table 15 Predictors of poor outcome in patients with infective endocarditis

#### Patient characteristics

- Older age
- Prosthetic valve IE
- Diabetes mellitus
- Comorbidity (e.g., frailty, immunosuppression, renal or pulmonary disease)

#### Clinical complications of IE

- Heart fallure
- Renal fatture
- >Moderate area of ischaemic stroke
- · Brain haemorrhage
- Septic shock

#### Microorganism

- Staphylococcus aureus
- Fungt
- Non-HACEK Gram-negative bacilli

#### Echocardiographic findings

- · Pertannular complications
- · Severe left-sided valve regurgitation
- · Low left ventricular ejection fraction
- · Pulmonary hypertension
- Large vegetations
- · Severe prosthetic valve dysfunction
- Premature mitral valve closure and other signs of elevated diastolic pressures

### Referans merkez- Ne zaman?

Komplike olgu
Referans merkezinde izlenmeli

➤ Kan kültürü, antibiyotiğin 48.-72. saatinde pozitif olanlar da prognoz kötü!

# Empirik tedavi

Table 20 Proposed antibiotic regimens for initial empirical treatment of infective endocarditis in acute severely ill patients (before pathogen identification)<sup>a</sup>

Antibiotic	Dosage and route	Classb	Levelc	Comments
Community-acq	uired native valves or late p	rosthet	ic valve	es (≥12 months post surgery) endocarditis
Ampicillin with (Flu)cloxacillin or oxacillin with Gentamicin	12 g/day i.v. in 4–6 doses 12 g/day i.v. in 4–6 doses 3 mg/kg/day i.v. or i.m. in 1 dose	lla	С	Patients with BCNIE should be treated in consultation with an ID specialist.
Vancomycin <sup>d</sup> with Gentamicin <sup>d</sup>	30-60 mg/kg/day i.v. in 2-3 doses 3 mg/kg/day i.v. or i.m. in 1 dose	ΠЬ	С	For penicillin-allergic patients
Early PVE (<12 r	months post surgery) or no	socomi	al and n	on-nosocomial healthcare associated endocarditis
Vancomycin <sup>d</sup> with Gentamicin <sup>d</sup> with Rifampin	30 mg/kg/day i.v. in 2 doses 3 mg/kg/day i.v. or i.m. in 1 dose 900-1200 mg i.v. or orally in 2 or 3 divided doses	ПЬ	С	Rifampin is only recommended for PVE and it should be started 3–5 days later than vancomycin and gentamicin has been suggested by some experts. In healthcare associated native valve endocarditis, some experts recommend in settings with a prevalence of MRSA infections >5% the combination of cloxacillin plus vancomycin until they have the final S. aureus identification

#### Streptokok, stafilokok, enterokok, HACEK için tedavi önerileri mevcut!

Antibiotic	Dosage and route	Duration (weeks)	Class <sup>b</sup>	Level <sup>c</sup>	Ref.d	Comments		
Strains penicil	lin-susceptible (MIC $\leq$ 0.125 mg/L) oral and digestive strepto	cocci						
Standard treat	ment: 4-week duration							
Penicillin G r	12–18 million U/day i.v. either in 4–6 doses or continuously	4	1	В	6,8, 135-	Preferred in patients > 65 years or with impaired renal or VIII (vestibulocochlear) cranial nerve functions. 6-week therapy recommended for patients with PVE		
Amoxicillin <sup>e</sup> r	100-200 mg/kg/day i.v. in 4-6 doses	4	1	В	139			
Ceftriaxonef	2 g/day i.v. or i.m. in 1 dose	4	1	В				
	Paediatric doses <sup>g</sup> Penicillin G 200,000 U/kg/day i.v. in 4–6 divided doses Amoxicillin 300 mg/kg/day i.v. in 4–6 equally divided doses Ceftriaxone 100 mg/kg/day i.v. or i.m. in 1 dose							
tandard treat	ment: 2-week duration							
Penicillin G r	12–18 million U/day i.v. either in 4–6 doses or continuously	2	1	В	6,8, 127, 135- 138	Only recommended in patients with non-complicated NVE with normal renal function.		
Amoxicillin <sup>e</sup> r	100-200 mg/kg/day i.v. in 4-6 doses	2	1	В				
Ceftriaxone <sup>f</sup>	2 g/day i.v. or i.m. in 1 dose	2	1	В				
Gentamicin <sup>h</sup>	3 mg/kg/day i.v. or i.m. in 1 dose	2	1	В				
Netilmicin	4–5 mg/kg/day i.v. in 1 dose	2 <b>I</b>		В		Netilmicin is not available in all		
Paediatric doses: <sup>g</sup> Penicillin G, amoxicillin, and ceftriaxone as above Gentamicin 3 mg/kg/day i.v. or i.m. in 1 dose or 3 equa					- European countries.			
n beta-lactam	allergic patients							
ancomycin <sup>j</sup>	30 mg/kg/day i.v. in 2 doses	4	1	С		6-week therapy recommended for patients with PVE		
	Paediatric doses: <sup>g</sup> Vancomycin 40 mg/kg/day i.v. in 2 or 3 equally divided doses							

# Enterokok endokarditi

Table 18 Antibiotic treatment of infective endocarditis due to Enterococcus spp.									
Antibiotic	Dosage and route	Duration, weeks	Class <sup>g</sup>	Levelh	Ref.	Comments			
Beta-lactam	and gentamicin-susceptible strains (fo	or resistant i	solates	see a,b,c)	)				
Amoxicillin*	200 mg/kg/day i.v. in 4-6 doses	4-6	1	В	6,8, 129,	6-week therapy recommended for patients with >3 months symptoms or PVE			
Gentamicin <sup>d</sup>	3 mg/kg/day i.v. or i.m. in 1 dose	2-6**	1	В	135, 136, 186				
	Paediatric doses: <sup>e</sup> Ampicillin 300 mg/kg/day i.v. in 4–6 equally divided doses Gentamicin 3 mg/kg/ day i.v. or i.m. in 3 equally divided doses								
Ampicillin with	200 mg/kg/day i.v. in 4–6 doses	6	1	В	183– 185	This combination is active against Enterococcus faecalis strains with and without HLAR, being the			
Ceftriaxone	4 g/day i.v. or i.m. in 2 doses	6	1	В		combination of choice in patients with HLAR  E faecalis endocarditis.			
	Paediatric doses: <sup>e</sup> Amoxicillin as above Ceftriaxone 100 mg/ kg/12 h i.v. or i.m.					This combination is not active against E. faecium			
Vancomycin <sup>f</sup> with	30 mg/kg/day i.v. in 2 doses	6	1	С					
Gentamicin <sup>d</sup>	3 mg/kg/day i.v. or i.m. in 1 dose	6	1	С					
	Paediatric doses: <sup>e</sup> Vancomycin 40 mg/kg/day i.v. in 2–3 equally divided doses. Gentamicin as above								

### Kültür negatif endokarditler için tedavi

Table 19 Antibiotic treatment of blood culture-negative infective endocarditis (adapted from Brouqui et al. 193)

Pathogens	Proposed therapy <sup>a</sup>	Treatment outcome			
Brucella spp.	Doxycycline (200 mg/24 h) plus cotrimoxazole (960 mg/12 h) plus rifampin (300–600/24 h) for ≥3–6 months <sup>b</sup> orally	Treatment success defined as an antibody titre <1:60 Some authors recommend adding gentamicin for the first 3 weeks.			
C. burnetil (agent of Q fever)	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h) <sup>c</sup> orally (>18 months of treatment)	Treatment success defined as anti-phase I IgG titre <1:200, and IgA and IgM titres <1:50.			
Bartonella spp.d	Doxycycline 100 mg/12 h orally for 4 weeks plus gentamicin (3 mg/24 h) i.v. for 2 weeks	Treatment success expected in ≥90%.			
Legionella spp.	Levofloxacin (500 mg/12 h) l.v. or orally for ≥6 weeks or clarithromycin (500 mg/12 h) l.v. for 2 weeks, then orally for 4 weeks plus rifampin (300–1200 mg/24 h)	Optimal treatment unknown.			
Mycoplasma spp.	Levofloxacin (500 mg/12 h) Lv. or orally for ≥6 months <sup>c</sup>	Optimal treatment unknown.			
T. whipplei (agent of Whipple's disease) <sup>f</sup>	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h) <sup>c</sup> orally for ≥18 months	Long-term treatment, optimal duration unknown.			

# Tedavide yenilikler

The indications and pattern of use of aminoglycosides have changed. They are no longer recommended in staphylococcal NVE because their clinical benefits have not been demonstrated, but they can increase renal toxicity; 128 when they are indicated in other conditions, aminoglycosides should be given in a single daily dose to reduce nephrotoxicity. 129

Rifampin should be used only inforeign body infections such as PVE after 3–5 days of effective antibiotic therapy, once the bacteraemia has been cleared. The rationale supporting this recommendation is based on the likely antagonistic effect of the antibiotic combinations with rifampin against planktonic/replicating bacteria, <sup>130</sup> the synergy seen against dormant bacteria within the biofilms and prevention of rifampin-resistant variants. <sup>131</sup>

Although a consensus was obtained for the majority of antibiotic treatments, the optimal treatment of staphylococcal IE and the empirical treatment are still debated.

- ➤ Aminoglikozitlerle ilgili
- > Rifampisinle ilgili
- ➤ Empirik tedavi?

### Cerrahi Tedavi

Table 22 Indications and timing of surgery in left-sided valve infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)

Indications for surgery	Timinga	Classb	Level <sup>c</sup>	Ref. <sup>d</sup>	
1. Heart failure					
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock	Emergency	1	В	111,115, 213,216	
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance	Urgent	-	В	37,115, 209,216, 220,221	
2. Uncontrolled infection					
Locally uncontrolled infection (abscess, false an eurysm, fistula, enlarging vegetation)	Urgent	1	В	37,209, 216	
Infection caused by fungi or multiresistant organisms	Urgent/ elective	1	С		
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci	Urgent	lla	В	123	
PVE caused by staphylococci or non-HACEK gram-negative bacteria	Urgent/ elective	110			
3. Prevention of embolism		Acil	: 24 s	aat içir	ide
Aortic or mitral NVE or PVE with persistent vegetations > 10 mm after one or more embolic episode despite appropriate antibiotic therapy				7 gün	
Aortic or mitral NVE with vegetations > 10 mm, associated with severe valve stenosis or regurgitation, and low operative risk	Urgent	Elel	ktif: 1-	-2 hafta	ı içi
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm)	Urgent	lla	В	113	
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery <sup>e</sup>	Urgent	Шь	С		

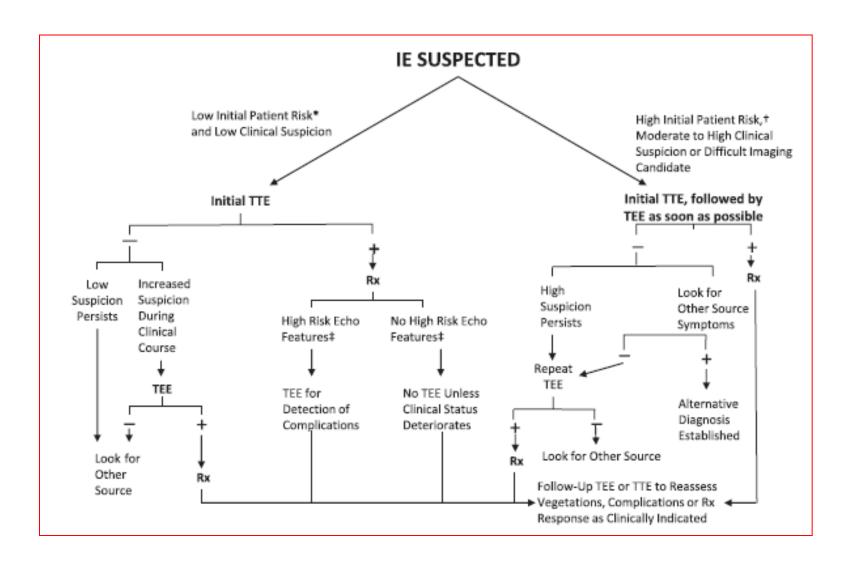
# Relaps için risk faktörleri

# Table 24 Factors associated with an increased rate of relapse

- Inadequate antibiotic treatment (agent, dose, duration)
- Resistant microorganisms, i.e. Brucella spp., Legione lla spp., Chlamydia spp., Mycoplasma spp., Mycobacterium spp., Bartonella spp., Coxiella Burnetii, fungi
- Polymicrobial infection in an IVDA
- Empirical antimicrobial therapy for BCNIE
- Perlannular extension
- Prosthetic valve IE
- Persistent metastatic foci of infection (abscesses)
- · Resistance to conventional antibiotic regimens
- Positive valve culture
- · Persistence of fever at the seventh postoperative day
- Chronic dialysis

# "Spesifik" Durumlar

- İmplante edilen kardiyak cihazlar
- YBÜ'de infektif endokardit
- Sağ kalp endokarditi
- Konjenital kalp hastalıklarında İE
- Gebelikte İE
- İnfektif endokarditte anti-trombotik tedavi
- Non-bakteriyel trombotik endokardit
- Kanser hastalarında endokardit



Profilaksi endikasyonları önemli!

"Endokardit takımı" önemli!

> 30 dakika ara ile 3 set kan kültürü almak önemli!

Klinik şüphe durumunda ve sonrasında komplikasyonlar için TÖE yapılması önemli!

➤ Hastayı prognostik faktörler yönünden değerlendirmek ve gerekirse konsülte/refere etmek önemli!

> Tedavi sırasında 48.-72. saatte kan kültürü almak önemli!

➤ Tedavi süresini doğru belirlemek için operasyon sırasında kapak kültürü istenmesi önemli!

- Mikrobiyoloji laboratuvarları ile iletişim halinde olmak ve tanı kapasitesini arttırmak önemli!
- ➤ Görüntüleme yöntemleri için radyoloji ve Nüklere tıp ile iletişim halinde olmak önemli!

Toksisite nedeniyle aminoglikozitleri daha az kullanmak ve kullanırken de günde tek doz kullanmak önemli!

Rifampisini doğru zamanda doğru durumlarda başlamak önemli!

> Tedavi bitiminde EKO önemli!

- > Etken spesifik tedaviyi netleştirmek önemli!
- > Empirik tedaviyi netleştirmek önemli!



