



# ***Antibiotic Prophylaxis for Dental Treatment of Patients with Cardiovascular Disease: When and Why?***

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# Introduction

## *Antibiotic prophylaxis*

- Patients with heart conditions ➡ **INFECTIVE ENDOCARDITIS**
- Patients with total joint replacement ➡ **PROSTHETIC JOINT INFECTIONS**



# Infective Endocarditis

## Definition

- Endocarditis: inflammation of the endocardial surfaces
- Infective endocarditis (IE): microbial infection of endocarditis lesions (“vegetations”)



# Infective Endocarditis

## Epidemiology

- Incidence: 1-5 cases in 100 000 persons/year
- Overall mortality rate: ~20%
- Men more susceptible than women (1.2 to 3 times)
- Median age: over 55 years
  - Reduced incidence of rheumatic heart disease
  - Increased rates of cardiac damage and repair with age
- Increased incidence in patients with no known previous cardiac disease
  - Young children (up to the age of 2 years)
  - Intravenous drug users

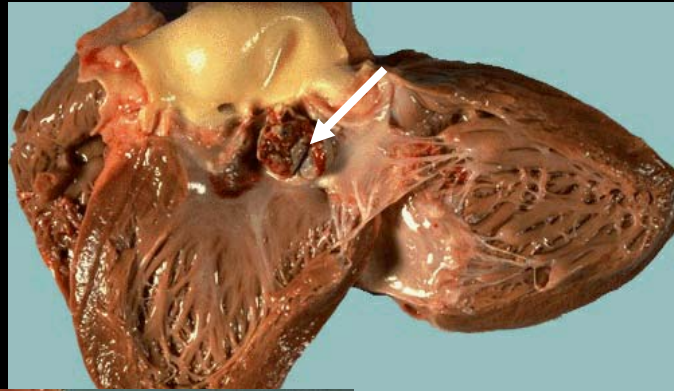


# Infective Endocarditis

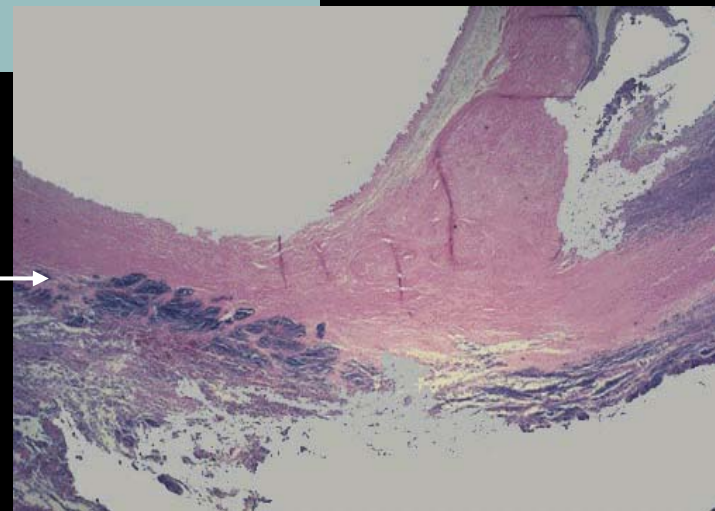
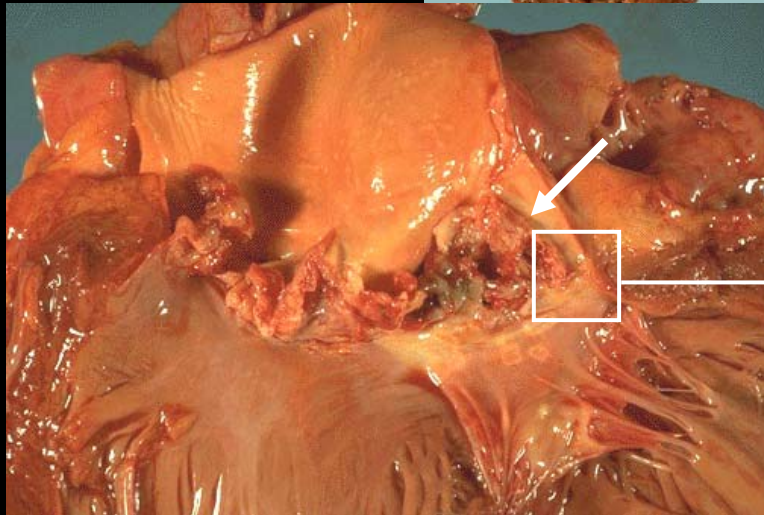
## Pathogenesis

- Formation of non-bacterial thrombotic vegetations (NBTV)
- Endocardial lining damaged by certain pre-existing heart conditions (e.g. congenital or acquired valvular dysfunction, history of previous IE, prosthetic heart valves, etc.)
- Deposition of fibrin and platelets
- Adherence of circulating microorganisms (during an episode of bacteremia) to NBTV
- Conversion of the NBTV to IE

# Infected Vegetations

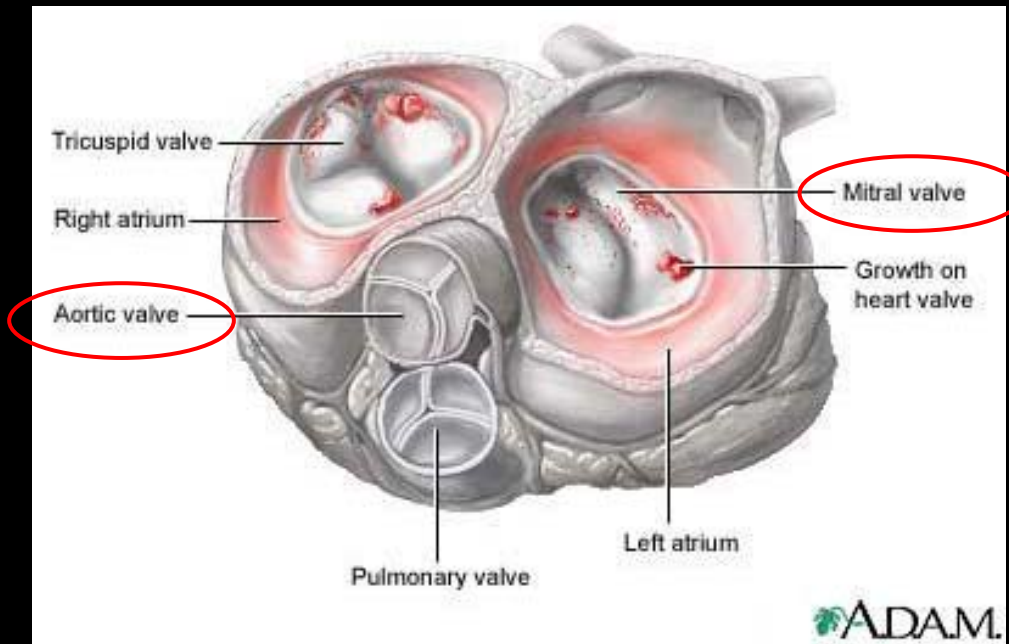


- microorganisms
- fibrin
- platelets
- inflammatory infiltrate

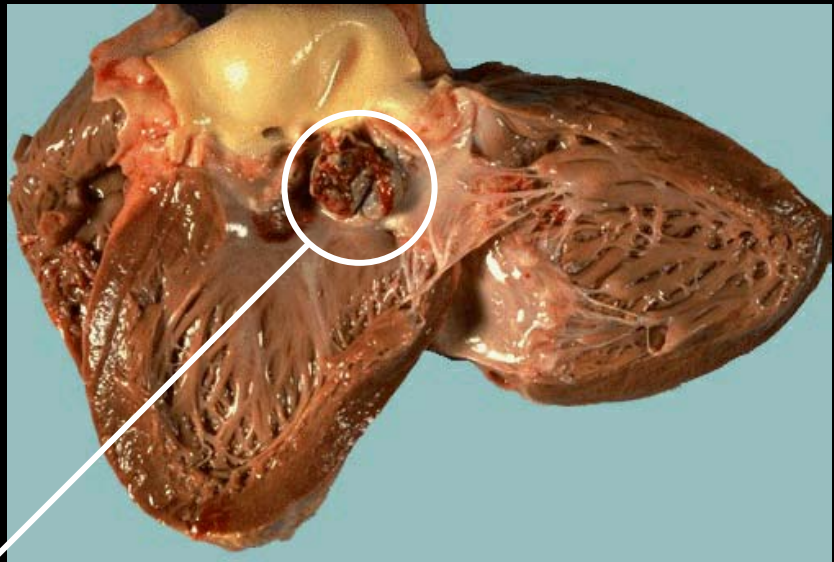


# Infected Vegetations

- Heart valves
- Endocardium



# Infected Vegetations



- Embolize and occlude blood vessels and valvular orifices
- Decrease cardiac output
- Induce congestive cardiac failure





# Conditions associated with risk of Infective Endocarditis (American Heart Association (AHA) Guidelines, 1997)

## High-risk category

- Prosthetic cardiac valves
- History of previous IE
- Complex cyanotic congenital heart disease
- Surgically constructed shunts/conduits

## Moderate-risk category

- Most other congenital cardiac malformations
- Acquired valvular dysfunction
- Hypertrophic cardiomyopathy
- Mitral valve prolapse (MVP) with valvular regurgitation and/or thickened leaflets

**PROPHYLAXIS RECOMMENDED**



# Conditions associated with risk of Infective Endocarditis (American Heart Association (AHA) Guidelines, 1997)

## **Negligible-risk category**

- Isolated secundum atrial septal defect
- Surgical repair of atrial or ventricular septal defect or patent ductus arteriosus of more than 6 months duration
- Previous coronary artery bypass graft surgery
- Physiological or functional heart murmur
- Previous Kawasaki disease without valvular dysfunction
- Cardiac pacemakers
- Implanted defibrillators

**PROPHYLAXIS NOT RECOMMENDED**



# Conditions associated with risk of Infective Endocarditis (British Society for Antimicrobial Chemotherapy (BSAC) Guidelines, 2006)

- History of previous IE
- Prosthetic cardiac valves
- Surgically constructed shunts/conduits
- Complex congenital heart disease
- Complex LV outflow abnormalities (aortic stenosis, bicuspid aortic valves)
- Acquired valvulopathy and MVP with substantial leaflet pathology and regurgitation

**PROPHYLAXIS RECOMMENDED**

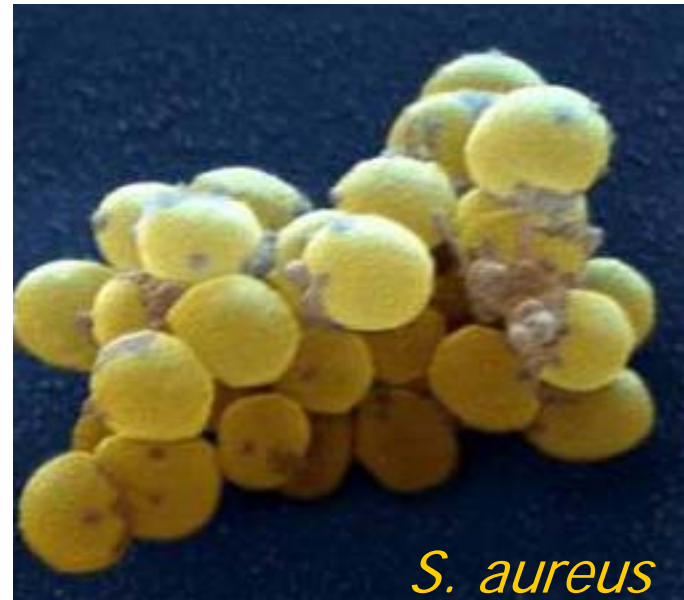
**NON-DENTAL PROCEDURES**



# Infective Endocarditis

## Microbiology

- Streptococci: recognized etiological agents of IE (Bayliss *et al*, 1983; Douglas *et al*, 1993)
- *Staphylococcus aureus*: leading cause of IE (Fowler *et al*, 2005; Miro *et al*, 2005; Cabell *et al*, 2002)
  - Overall worsening of the clinical course
  - Increased number of serious complications
  - Higher mortality rates





# Infective Endocarditis

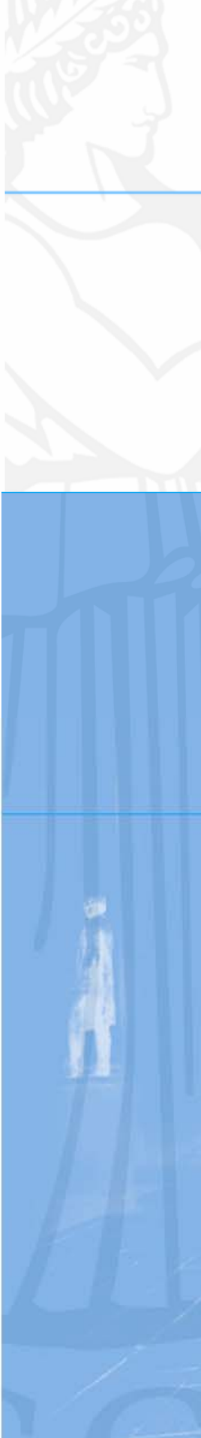
## Microbiology

- HACEK group bacteria (*Haemophilus* spp., *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella* spp.): 5-10% cases
- Fungi, *Mycobacterium* spp., chlamydiae, and *Mycoplasma* spp.: low frequency



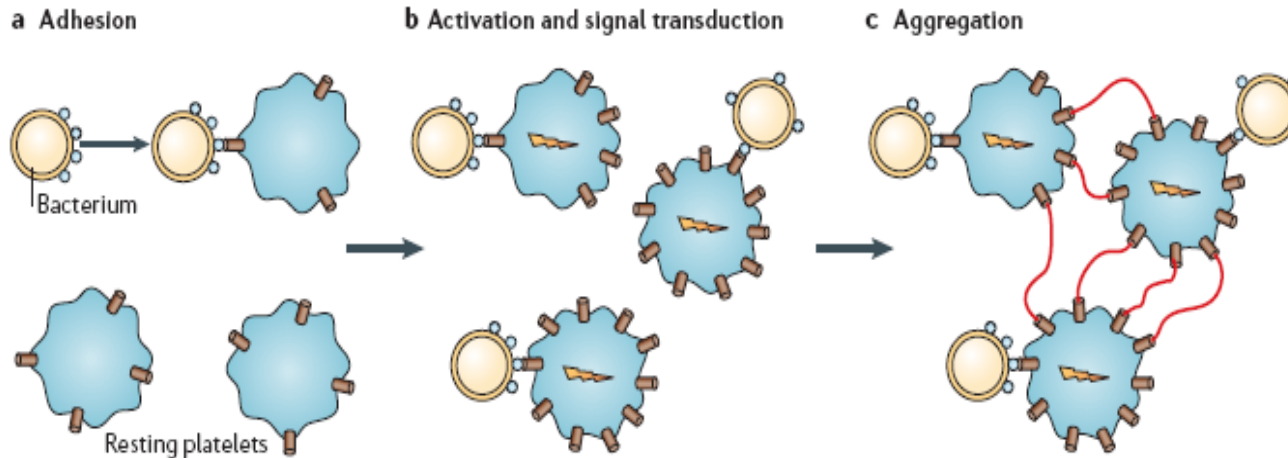
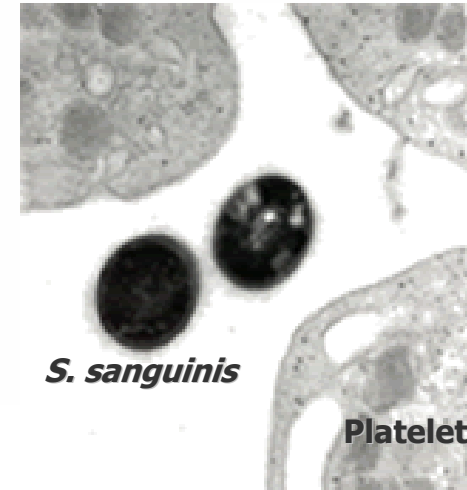
# Bacterial Virulence Factors

→ Adherence to the vegetations



# Bacterial Virulence Factors

- Adherence to the vegetations
- Promotion of thrombus formation
  - *S. sanguinis*: Platelet aggregation-associated protein (PAAP)

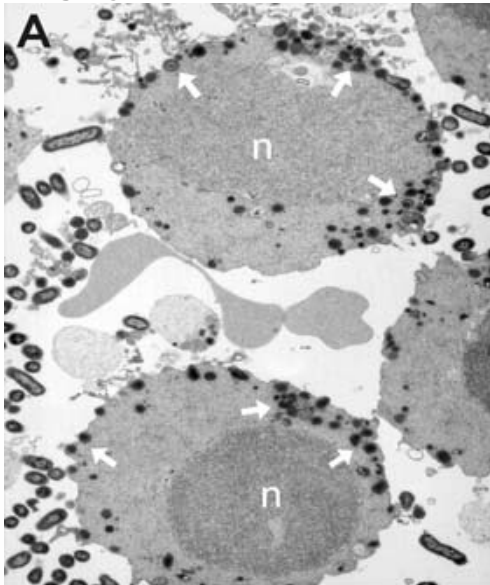


Nat Rev Microbiol. 2006

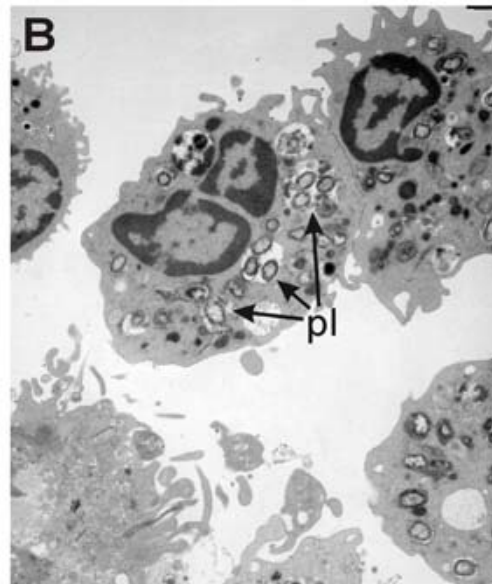
# Bacterial Virulence Factors

- Adherence to the vegetations
- Promotion of thrombus formation
- Resistance to phagocytosis and killing by PMNs
  - *S. gordonii*
  - *A. actinomycetemcomitans*

*A. actinomycetemcomitans*  
highly leukotoxic strain



*A. actinomycetemcomitans*  
low leukotoxic strain







# Prevention of Infective Endocarditis by Antibiotic Prophylaxis

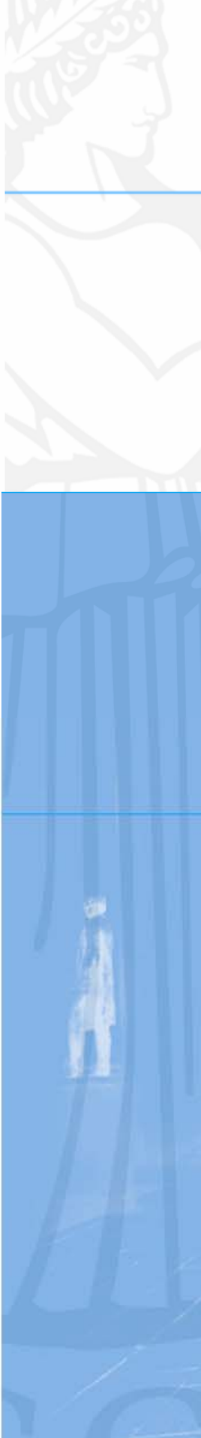
- The exact mechanisms behind antibiotic prophylaxis are unknown
- Efficacy of antibiotic prophylaxis: animal studies and clinical experience



# Prevention of Infective Endocarditis by Antibiotic Prophylaxis

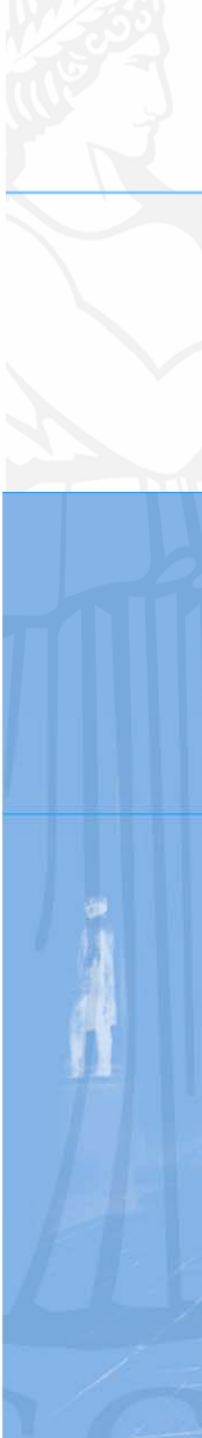
Mechanisms of Antibiotic Prophylaxis (animal models)

- I. Reduction of the incidence and magnitude of bacteremia
- II. Prevention of adherence to the vegetations
- III. Inhibition of bacterial growth on the vegetations



# Bacteremia after Antibiotic Prophylaxis in Humans

→ Conflicting results



# Bacteremia after Antibiotic Prophylaxis in Humans

Bacteremia after Oral Surgical Procedures  
and  
Antibiotic Prophylaxis

Gunnar Hall



Stockholm 1998

- Investigated the incidence and magnitude of postextraction bacteremia
- Healthy patients randomly assigned to receive active drug or placebo
- Test groups: Penicillin V, Amoxicillin, Erythromycin, Clindamycin and Cefaclor
- Blood samples: lysis-filtration technique
- Antibiotic prophylaxis did not reduce the incidence or magnitude of bacteremia after dental extraction
- The absence of reduction in bacteremia in the prophylaxis was not due to high bacterial resistance



# Bacteremia after Antibiotic Prophylaxis in Humans

- The protective effect of prophylaxis must be the result of interference with crucial steps in the development of IE

Bacteremia after Oral Surgical Procedures  
and  
Antibiotic Prophylaxis

Gunnar Hall



Stockholm 1998



# Prevention of Infective Endocarditis by Antibiotic Prophylaxis

## Mechanisms of Antibiotic Prophylaxis (humans)

- I. Reduction of the incidence and magnitude of bacteremia
- II. Prevention of adherence to the vegetations
- III. Inhibition of bacterial growth on the vegetations



# Oral Bacteria, Dental Treatment and Infective Endocarditis

- Oral bacteria and IE: a century of association
- Bacteremia of oral origin
  - Transient type
  - Various magnitudes

Table 1. Prevalence of bacteremia after various types of dental procedures

Procedure	Prevalence
<b>Extractions</b>	
● single	51%
● multiple	68-100%
<b>Periodontal surgery</b>	
● flap procedure	36-88%
● gingivectomy	83%
<b>Scaling and root planing</b>	8-80%
<b>Periodontal prophylaxis</b>	0-40%
<b>Endodontics</b>	
● intracanal instrumentation	0-31%
● extracanal instrumentation	0-54%
<b>Endodontic Surgery</b>	
● flap reflection	83%
● periapical curettage	33%
<b>Toothbrushing</b>	0-26%
<b>Dental flossing</b>	20-58%
<b>Interproximal cleaning with toothpicks</b>	20-40%
<b>Irrigation devices</b>	7-50%
<b>Mastication</b>	17-51%





# Oral Bacteria, Dental Treatment and Infective Endocarditis

- Are dentists the real culprits for IE?
  - A number of studies reporting IE after dental procedures
  - High frequency of bacteremia after oral invasive procedures
  - High recovery rate of oral streptococci in IE cases



# Oral Bacteria, Dental Treatment and Infective Endocarditis

- ➔ Are dentists the real culprits for IE?
  - Bacteremia from dental procedures: low intensity compared to ID<sup>90</sup>
  - Bleeding is a poor predictor of dental-induced bacteremia
  - Dental procedures: no risk of cumulative bacteremia
  - Cumulative exposure to bacteremia from daily activities may be up to  $10^6$  greater than operative dental procedures (Roberts, 1999)
  - Less than 4% of all IE cases are related to dental treatment-induced bacteremia (Guntheroth, 1984; Strom *et al*, 1998)



# Dental Procedures Considered for Antibiotic Prophylaxis in Risk Patients (AHA, 1997)

- Dental extractions
- Periodontal procedures, including surgery, scaling, root planing and probing
- Dental implant placement, reimplantation of avulsed teeth
- Endodontic instrumentation or surgery only beyond the apex
- Subgingival placement of antibiotic fibers or strips
- Initial placement of orthodontic bands
- Intraligamentary local anesthetic injections
- Prophylactic cleaning of teeth or implants with anticipated bleeding
- Incision and drainage or other procedures involving infected tissues

Table II. AHA Guidelines for Antibiotic Prophylaxis

<b>Situation</b>	<b>Agent</b>	<b>Regimen</b>
<b>Standard general prophylaxis</b>	<b>Amoxicillin</b>	<b>Adults: 2.0 g; children: 50 mg/kg Orally 1 hour before procedure</b>
<b>Unable to take oral medications</b>	<b>Ampicillin</b>	<b>Adults: 2.0 g; children: 50 mg/kg Intramuscularly (IM) or intravenously (IV) within 30 min before procedure</b>
<b>Allergic to penicillin</b>	<b>Clindamycin</b>	<b>Adults: 600 mg; children: 20 mg/kg Orally 1 hour before procedure</b>
	<b>OR</b>	
	<b>Azithromycin or clarithromycin</b>	<b>Adults: 500 mg; children: 15 mg/kg Orally 1 hour before procedure</b>
<b>Allergic to penicillin and unable to take oral medications</b>	<b>Clindamycin</b>	<b>Adults: 600 mg; children: 50 mg/kg IV within 30 min before procedure</b>

Dajani *et al*, 1997

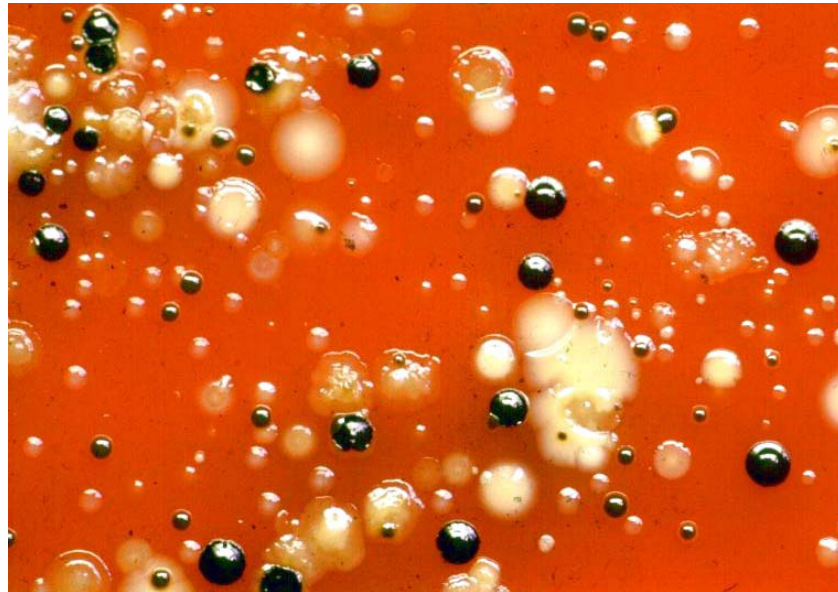


## Dental Procedures Not Recommend for Antibiotic Prophylaxis (AHA, 1997)

- Restorative dental procedures with or without retraction cord
- Intracanal endodontic procedures, post placement and buildup
- Local anesthetic injections
- Placement of rubber dams
- Postoperative suture removal
- Placement of removable prosthodontic or orthodontic appliances, and orthodontic appliance adjustment
- Taking oral impressions
- Fluoride treatments
- Taking oral radiographs
- Shedding of primary teeth

# Endodontics

- Pulp and periapical disease: microbial infection (Kakehashi *et al*, 1965; Sundqvist, 1976; Möller *et al*, 1981)
- Polymicrobial



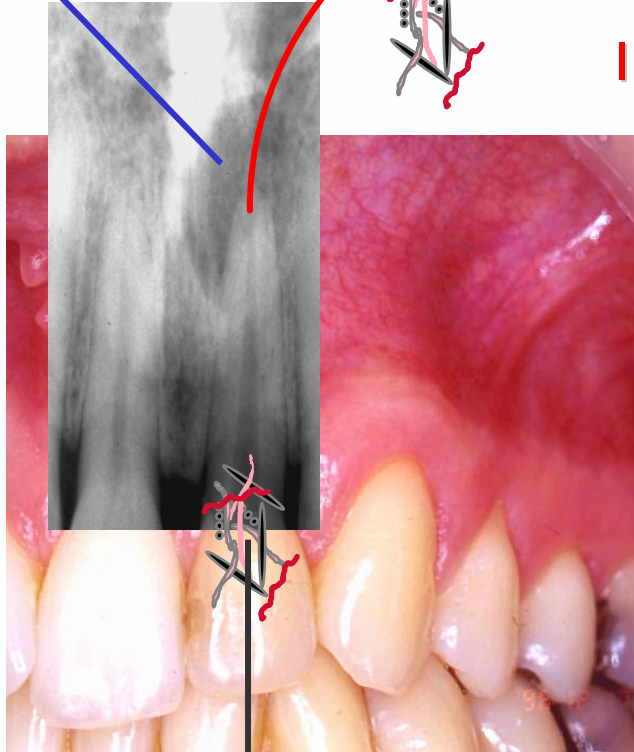


# Endodontics

- Pulp and periapical disease: microbial infection (Kakehashi *et al*, 1965; Sundqvist, 1976; Möller *et al*, 1981)
- Polymicrobial
- Bacteremia
  - Non-existent (Bender *et al*, 1960 and 1963; Baumgartner *et al*, 1976)
  - Sampling, transport and culture methods ???



Teeth with asymptomatic apical periodontitis



**Bacteremia**

Intracanal instrumentation: 31%

Instrumentation beyond the apex: 54%



Application of rubber dam

Endodontic therapy

Debelian, GJ. 1997. Bacteremia and Fungemia in Patients Undergoing Endodontic Therapy. Thesis, University of Oslo





# Antibiotic Prophylaxis for Dental Procedures in High-Risk Patients (BSAC, 2006)

## Dental procedures requiring antibiotic prophylaxis

- All dental procedures involving dento-gingival manipulation
- Endodontics

## High-risk cardiac conditions requiring antibiotic prophylaxis

- History of previous IE
- Prosthetic cardiac valves
- Surgically constructed shunts/conduits

Table II. Antibiotic Prophylaxis for Dental Procedures (BSAC)

Population	Age		
	>10 years	≥5 to <10 years	<5 years
<b>General</b>	<b>Amoxicillin 3 g 1 h pre-procedure</b>	<b>Amoxicillin 1.5 g 1 h pre-procedure</b>	<b>Amoxicillin 750 mg 1 h pre-procedure</b>
<b>Allergic to penicillin</b>	<b>Clindamycin 600 mg 1 h pre-procedure</b>	<b>Clindamycin 300 mg 1 h pre-procedure</b>	<b>Clindamycin 150 mg 1 h pre-procedure</b>
<b>Allergic to penicillin and unable to swallow capsules</b>	<b>Azithromycin 500 mg oral suspension 1 h pre-procedure</b>	<b>Azithromycin 300 mg oral suspension 1 h pre-procedure</b>	<b>Azithromycin 200 mg oral suspension 1 h pre-procedure</b>
<b>Intravenous regimen expedient</b>	<b>Amoxicillin 1 g IV just before procedure</b>	<b>Amoxicillin 500 mg IV just before procedure</b>	<b>Amoxicillin 250 mg IV just before procedure</b>
<b>Intravenous regimen expedient and allergic to penicillin</b>	<b>Clindamycin 300 mg IV at least 10 min before procedure</b>	<b>Clindamycin 150 mg IV at least 10 min before procedure</b>	<b>Clindamycin 75 mg IV at least 10 min before procedure</b>



## Reasons to promote the use of prophylactic regimens for IE prophylaxis

- IE results in high morbidity and mortality
- Prophylaxis is a long-standing medical practice
- IE prophylaxis follows logical principles (limited targeted population/procedures, limited pathogens, short-course regimens, reasonably safe and inexpensive)
- Animal models support prophylaxis
- Medico-legal concerns



## Reasons for challenging the use of prophylactic regimens for IE prophylaxis

- IE prophylaxis has not resulted in a decreased incidence of the disease
- No published, controlled clinical trials in humans
- Transient bacteremias are common events
- Individuals at-risk for IE are not easily identified
- False sense of security for patient and healthcare provider
- Potential for increasing antimicrobial resistance and adverse effects of antibiotics
- Poor compliance by patient and healthcare provider



# Conclusions

- The use of antibiotics does not guarantee prevention of IE in all cases
- Prevention of IE by antibiotic prophylaxis has been proven to be effective in experimental animal models, but not always in humans
- Antibiotic prophylaxis prior to dental treatment in high-risk patients remains reasonable and prudent, although evidence for its efficacy is currently lacking
- Greater emphasis should be placed on improving oral health, especially in high-risk patients