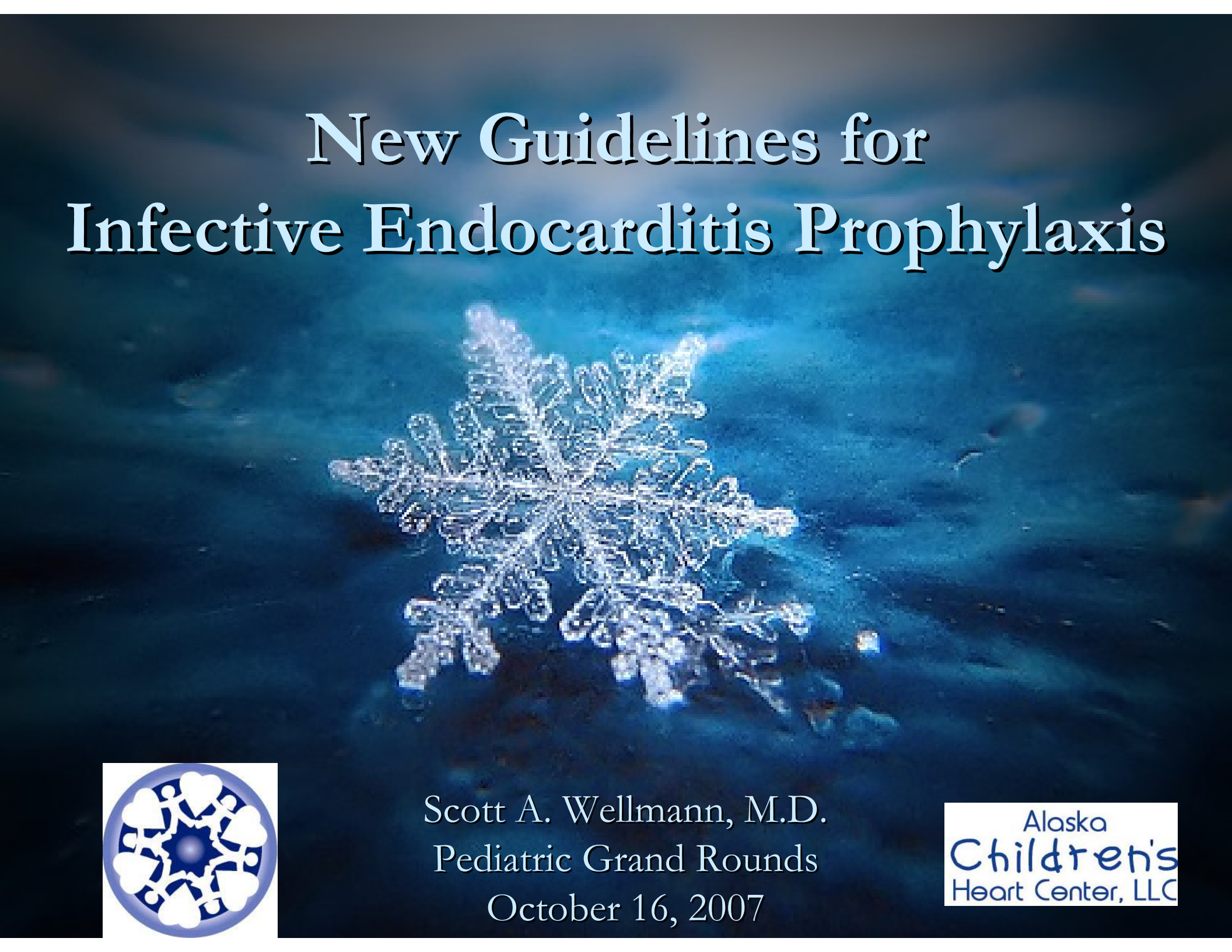
New Guidelines for Infective Endocarditis Prophylaxis



Scott A. Wellmann, M.D.
Pediatric Grand Rounds
October 16, 2007

Alaska Children's Heart Center, LLC

"It is of use from time to time to take stock, so to speak, of our knowledge of a particular disease, to see exactly where we stand in regard to it, to inquire to what conclusions the accumulated facts seem to point, and to ascertain in what direction we may look for fruitful investigations in the future."

- Sir William Osler

Introduction to first of three seminal lectures on endocarditis to the Royal College of Physicians of London in 1885.

-Lancet 1885;1:415-418.

History of American Heart Association Recommendations for the Prevention of Infective Endocarditis

- **1955**: IM PCN 30 minutes before.
- **1957**: Oral PCN 2 days before and 2 days after.
- **1960**: IM PCN daily 2 days before, twice on day of procedure and daily for 2 days after. Pediatric patients included.
- **1965**: IM PCN daily for 3 days starting day of procedure.
- **1972**: Same as 1965 with dose change for day of procedure.
- **1977**: IM PCN 30-60 minutes before procedure with 8 oral doses of PCN every 6 hours after.
- **1984**: Oral PCN 1 hour before and 6 hours after first dose.
- **1990**: Oral Amoxicillin 1 hour before and 6 hours after first dose.
- **1997**: Pre-procedure antibiotic dose reduced and eliminated the second dose. No prophylaxis for "negligible risk" category.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Fundamental Principles Driving Formulation and Revisions of AHA Guidelines

- IE is Uncommon but life-threatening infection.
- Certain underlying cardiac conditions predispose to IE.
- Bacteremia with organisms known to cause IE occurs commonly with invasive dental, GI, GU procedures.
- High morbidity and mortality in spite of advances in diagnostics, antimicrobial therapy and surgical techniques.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Fundamental Principles Driving Formulation and Revisions of AHA Guidelines

- Most cases of IE result from randomly occurring bacteremias from routine daily activities.
- Antimicrobial prophylaxis efficacy proven in animals.
- Antimicrobial prophylaxis ***thought to be effective*** in humans.
- Large number of poorly documented case reports implicated a dental procedure as a cause of IE.
- Previous guidelines not well supported by evidence.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Infective Endocarditis: Rationale for Revision of Guidelines

- IE is much more likely to result from frequent exposure to random bacteremias associated with daily activity than from bacteremia caused by a dental, GI tract or GU tract procedure.
- Prophylaxis may prevent an exceedingly small number of cases of IE, if any, in individuals who undergo a dental, GI tract or GU tract procedure.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Infective Endocarditis: Rationale for Revision of Guidelines

- The risk of antibiotic-associated adverse events exceeds the benefit, if any, from prophylactic antibiotic therapy.

- Maintenance of optimal oral health and hygiene may reduce the incidence of bacteremia from daily activities and is more important than prophylactic antibiotics for a dental procedure to reduce the risk of IE.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Methods for Formulation of Latest Revision of AHA Guidelines

- Review of the collective body of EVIDENCE published in numerous studies over the past 2 decades.
- Collective wisdom of experts on IE.
- International review.
  - British Society for Antimicrobial Chemotherapy IE prophylaxis recommendations (2006)
    - Previous Infective Endocarditis
    - Cardiac Valve Replacement
    - Surgically constructed Pulmonary Shunt or Conduit

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Potential Consequences of Substantive Changes in Recommendations

- Violation of Long-standing Expectations and Practice Patterns.
- Substantially Fewer Patients Eligible/Recommended for IE Prophylaxis.
- Reduction in Malpractice Claims Related to IE Prophylaxis.
- Stimulation of Prospective Studies on IE Prophylaxis.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Infective Endocarditis: Rationale for Revision of Guidelines

- "The Committee believes that recommendations for IE prophylaxis must be evidence based."
- "A placebo-controlled, multicenter, randomized, double-blinded study to evaluate the efficacy of IE prophylaxis in patients who undergo a dental, GI or GU tract procedure has not been done."

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Pathophysiology of Infective Endocarditis

- Development of IE is net result of complex interaction of bloodstream pathogen with matrix molecules and platelets at sites of endocardial cell damage.
- Many clinical manifestations of IE emanate from host immune response to infecting microorganism.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Pathophysiology of IE: Sequence of Events Resulting in IE

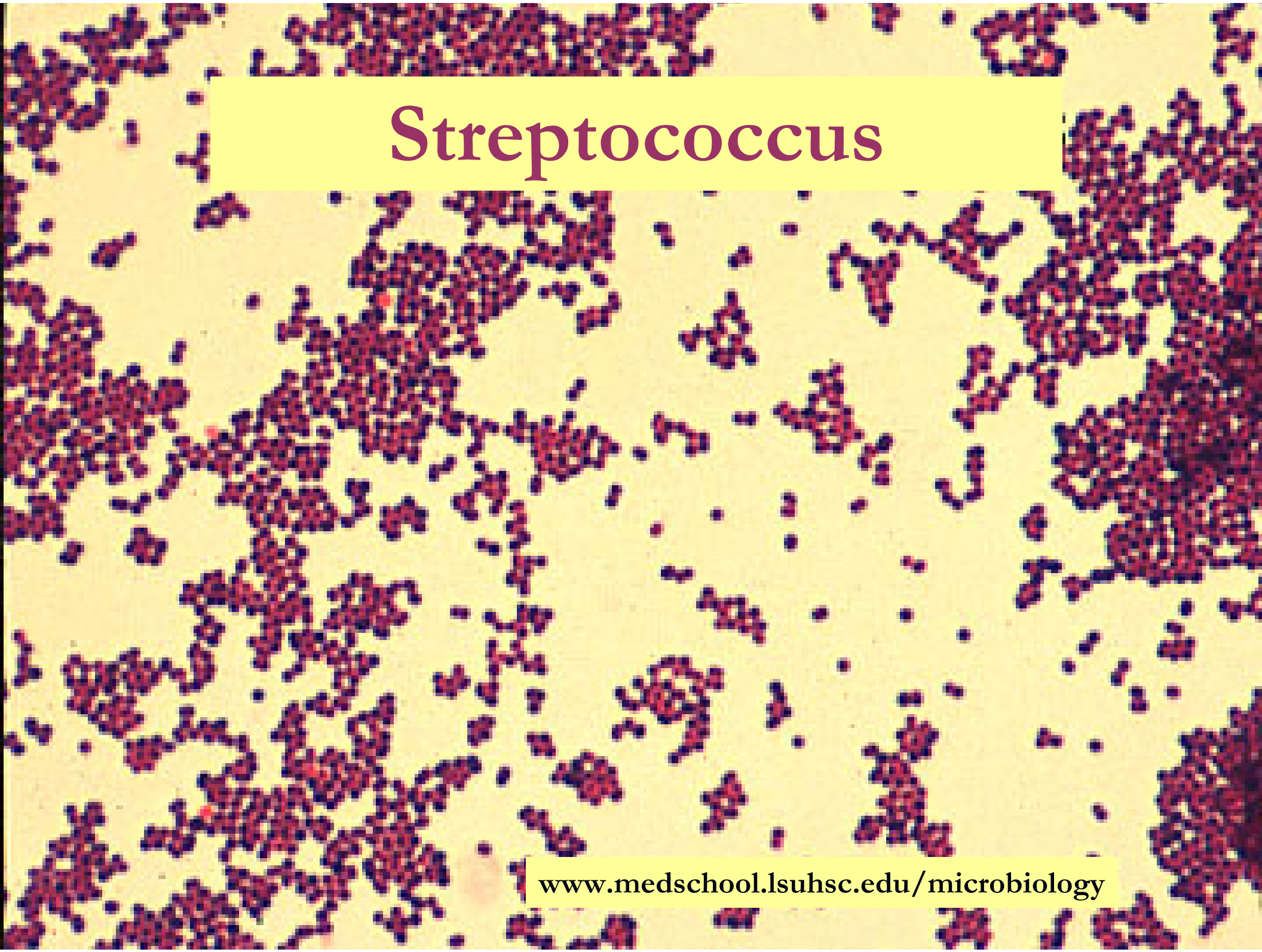
- Formation of Non-Bacterial Thrombotic Endocarditis (NBTE) on surface of cardiac valve or site of endothelial damage
  - Turbulent blood flow from certain congenital cardiac lesions tramatizes endothelium
  - Traumatized endothelium predisposed to deposition of platelets and fibrin on endothelial surface resulting in NBTE
- Bacteremia with potentially pathogenic organism
- Adherence of bacteria in bloodstream to NBTE
- Proliferation of bacteria within a vegetation

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Etiologic Agents of Infective Endocarditis in Infants & Children

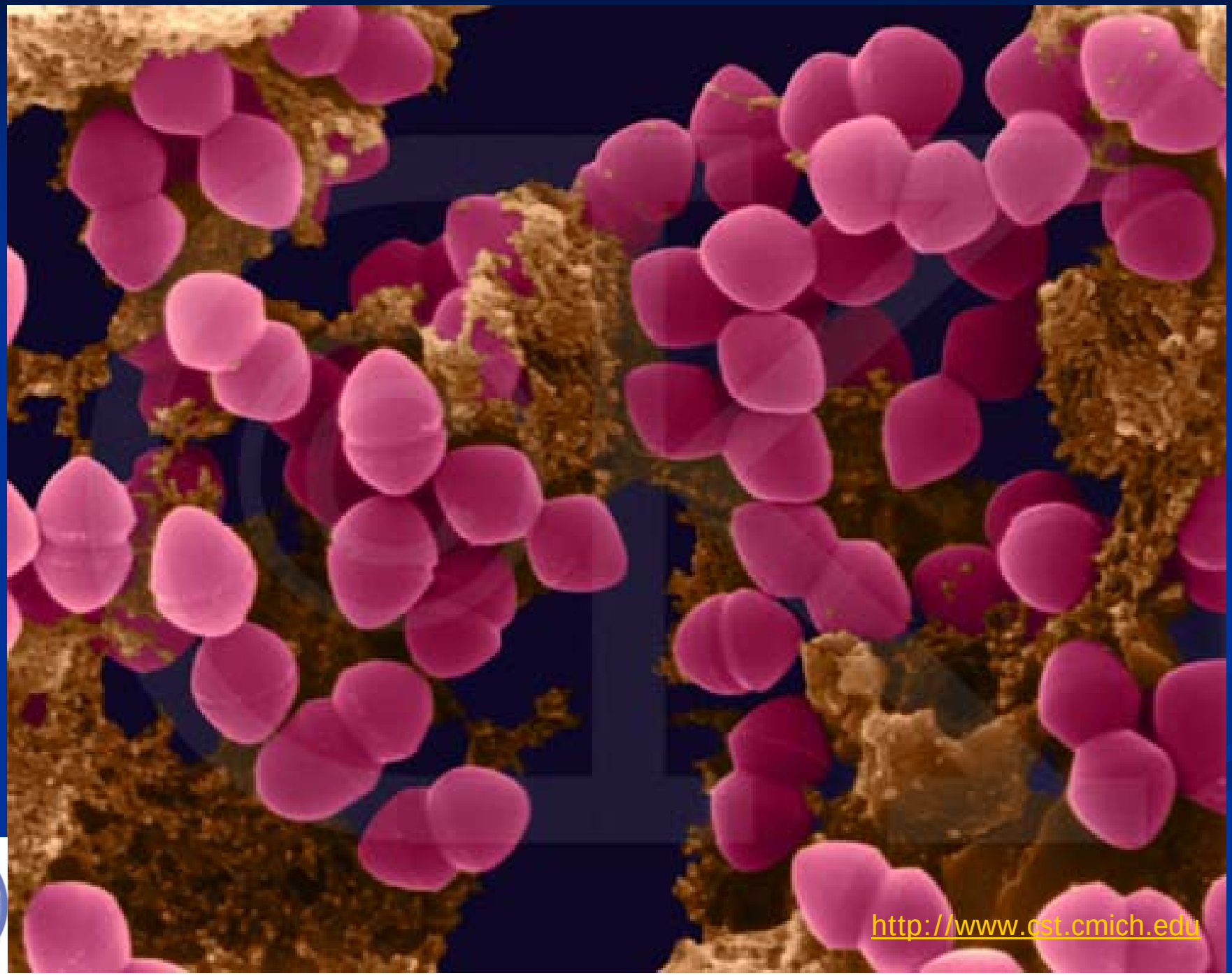
- Streptococci
  - Alpha-hemolytic — Most common
  - Beta-hemolytic — Uncommon
  - Enterococci — Rare
  - Pneumococci — Rare
- Staphylococci
  - *S. aureus* — Second most common
  - Coagulase negative — Uncommon, but increasing
- Gram-Negatives — All Rare
  - Enterics, *Pseudomonas* species, *Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella, Neisseria* species
- Fungi
  - Candida species — Uncommon
  - Others — Rare

Streptococcus



www.medschool.lsuhsc.edu/microbiology

Streptococcus mutans, a viridans streptococcus



Infective Endocarditis Types

- Acute Bacterial Endocarditis (ABE)
  - Fulminant and severe course
  - Death is Frequent
  - Organisms: *Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae*
- Subacute Bacterial Endocarditis (SBE)
  - Indolent, slower and less severe course over months
  - Organisms: *Streptococcus viridans*

Pathophysiology of Infective Endocarditis

- Frequency and intensity of bacteremia believed to be related to:
  - Nature and magnitude of tissue trauma
  - Density of microbial flora
  - Degree of inflammation or infection at site of trauma
- Venturi Effect: Bacteria/organisms accumulate on the low pressure side of a high pressure jet.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Eddy Currents

Pathophysiology of Infective Endocarditis

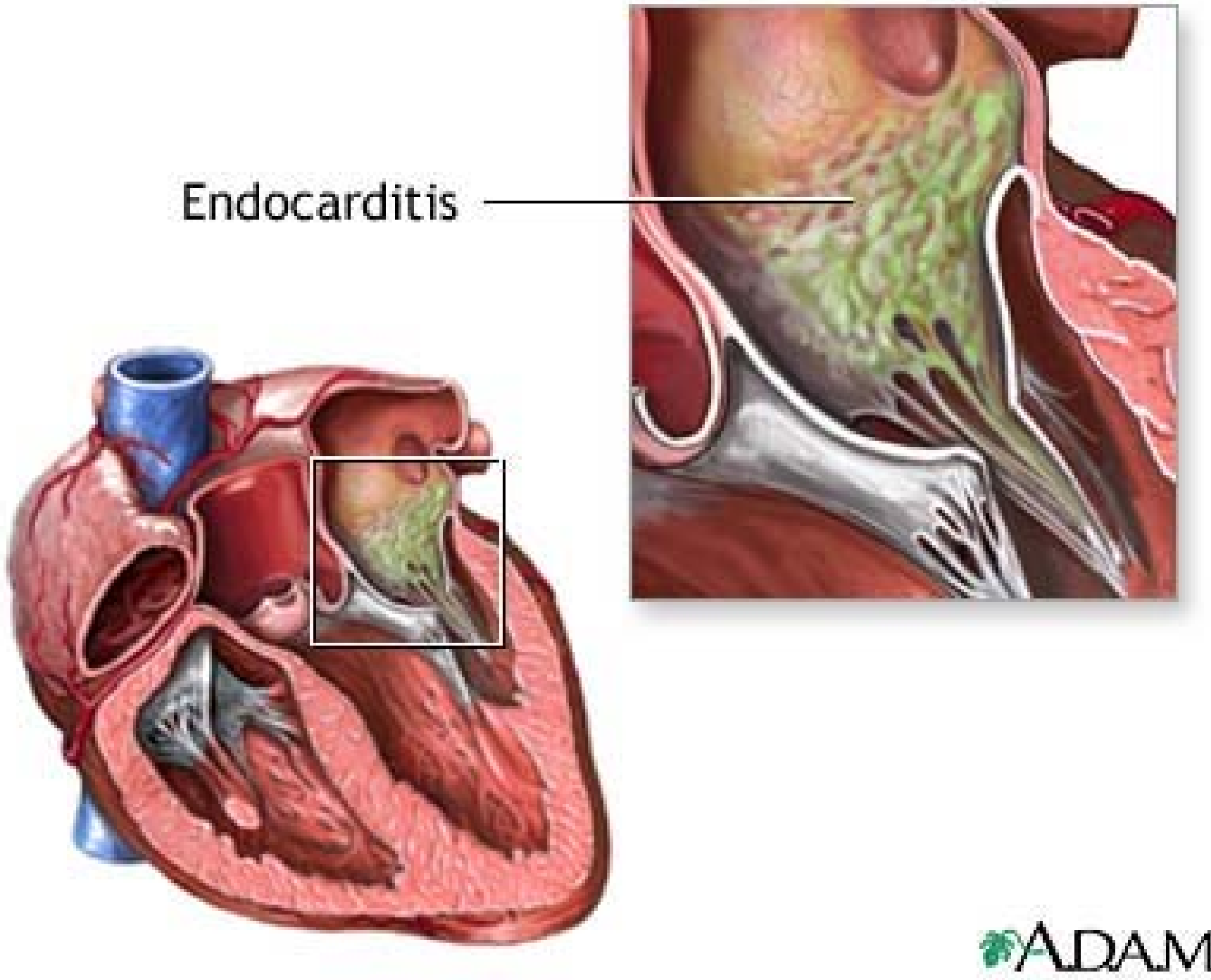
- Mediators of bacterial adherence serve as virulence factors in pathogenesis of IE.
- FimA protein is a lipoprotein receptor antigen I (LraI)
  - A major adhesin to fibrin platelet matrix
- Adhesins are immunogenic
- Vaccines prepared against FimA provide some protective effect against experimental IE caused by viridans group streptococci and staphylococci.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

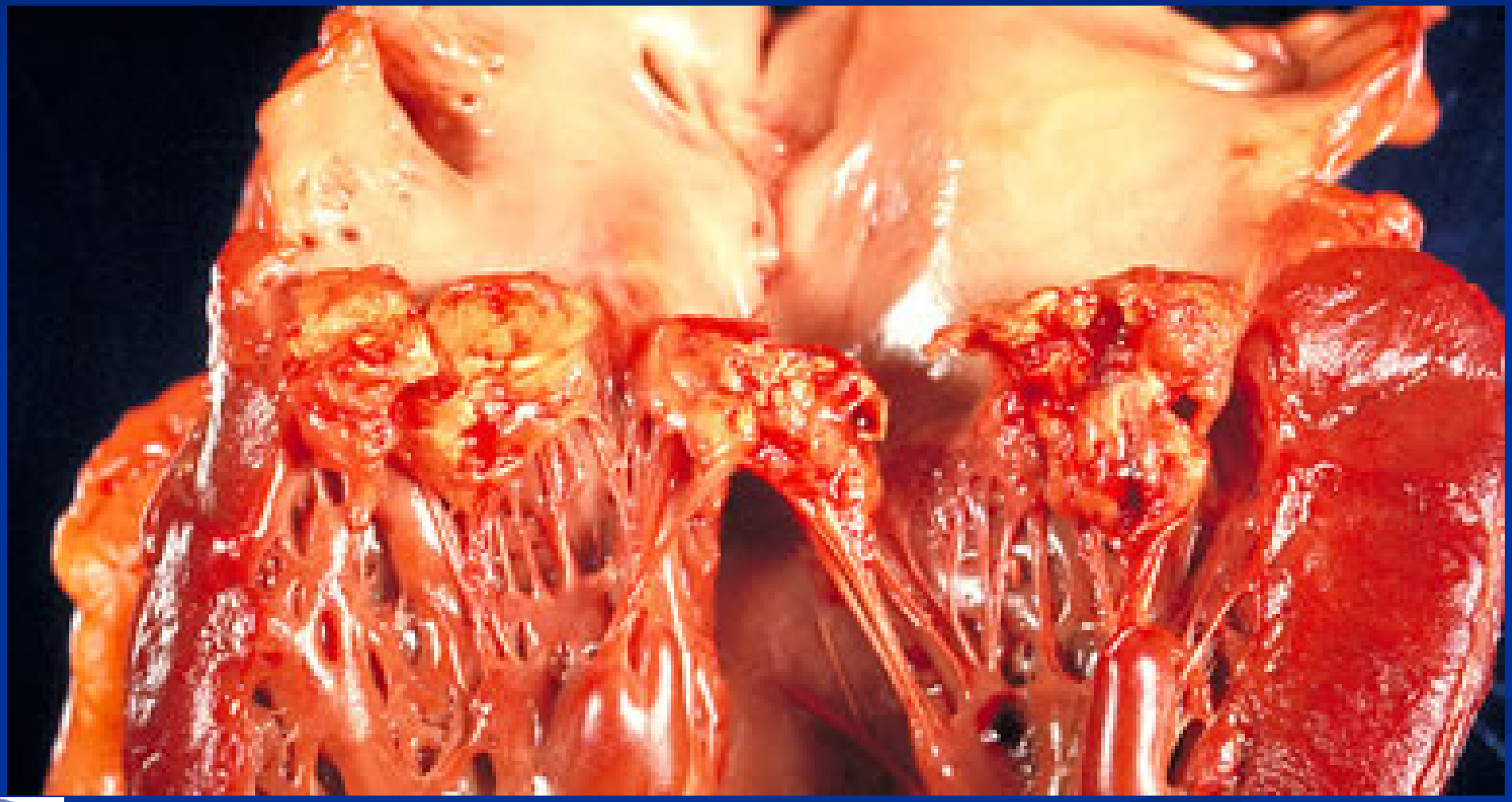
Pathophysiology of IE: Proliferation of Bacteria within a Vegetation

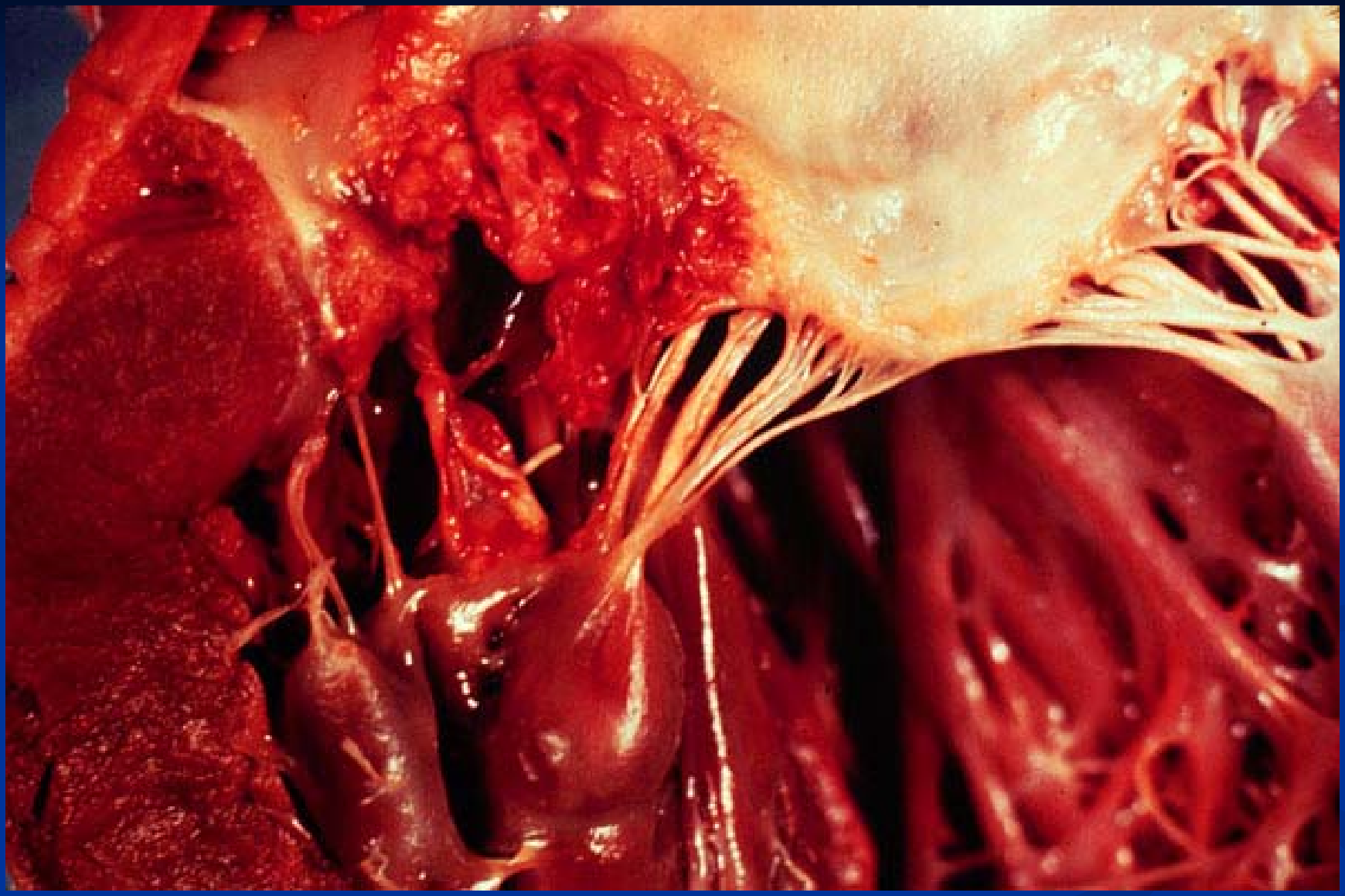
- Microorganisms adherent to vegetation stimulate further deposition of fibrin and platelets on their surface
- Buried microorganisms multiply as rapidly as bacteria in broth culture to reach 10^8-10^{11} colony-forming units/gram of vegetation on left side of heart.
- Vegetations of right heart have lower bacterial densities
- Presumed due to differences in host defense mechanism efficacy on left vs. right heart
- >90% microorganisms in mature vegetation are metabolically inactive

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

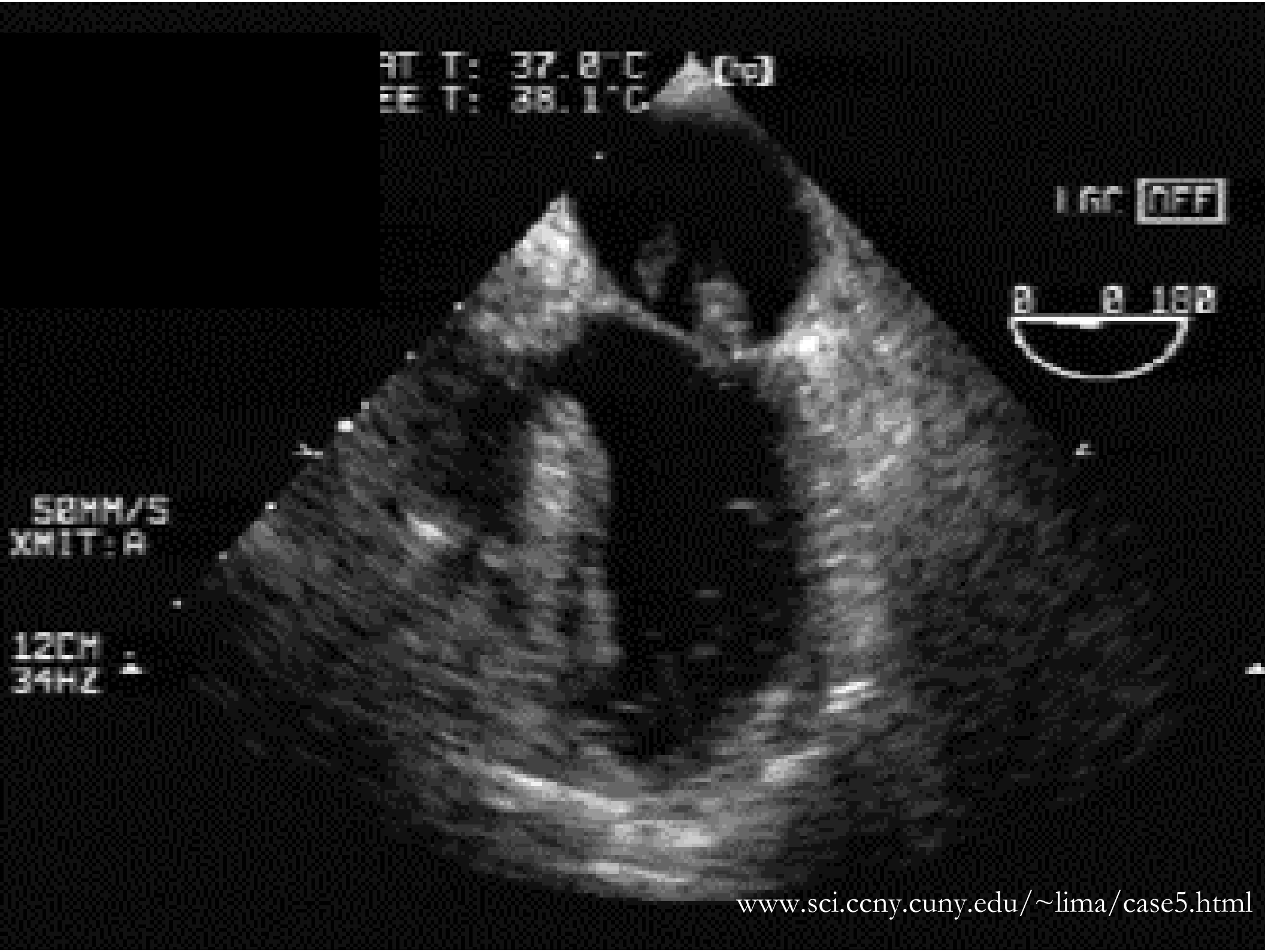

Endocarditis

Infectious Endocarditis Affecting the Mitral Valve: Destruction of the Mitral Valve Fibrin Due to *Haemophilus parainfluenzae* Bacterial Infection.





Akutni bakterijski endokarditis. Vegetacije na mitralnoj valvuli su udružene s razaranjem zaliska.


AT T: 37.8°C
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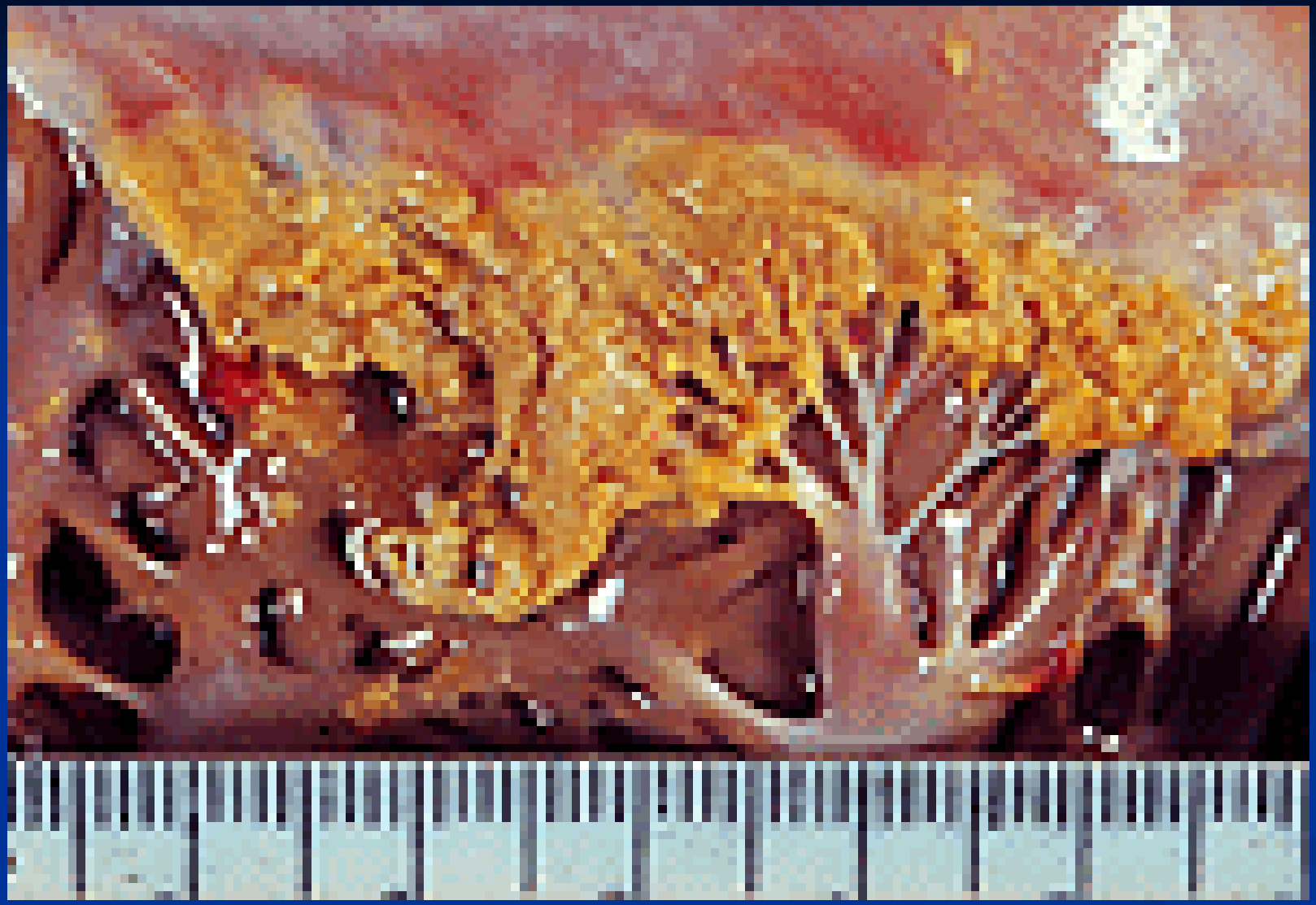
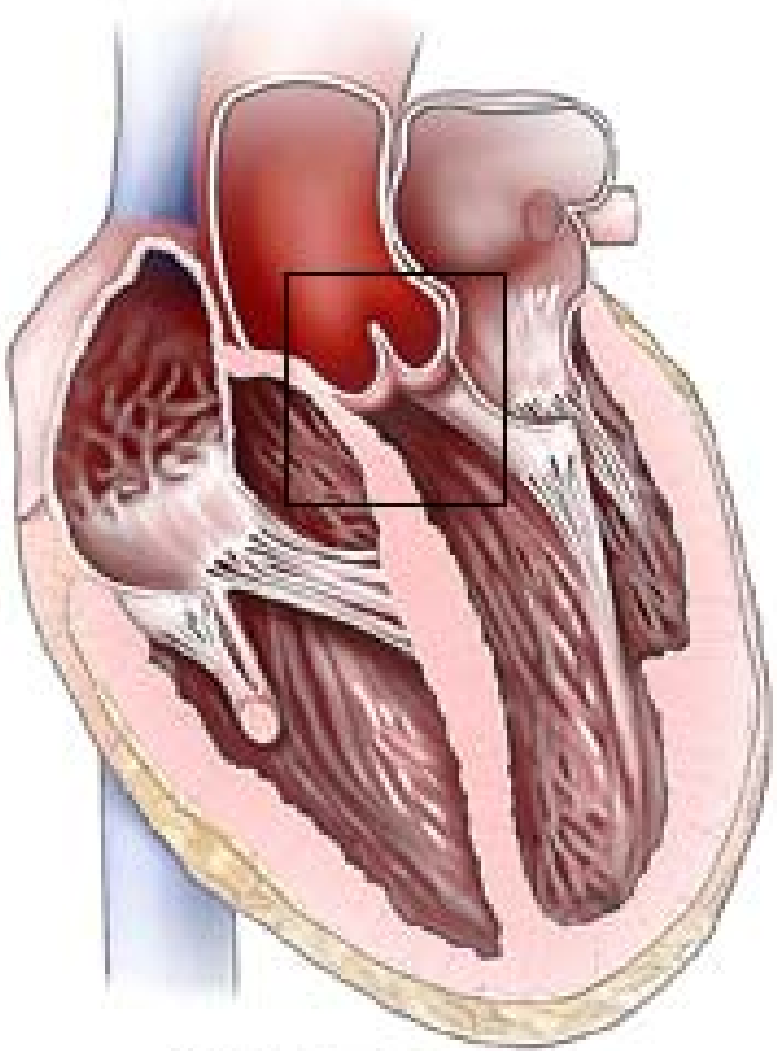
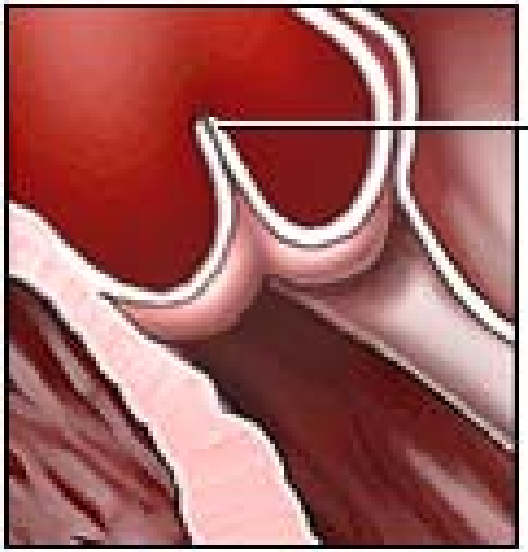
www.sci.ccny.cuny.edu/~lima/case5.html



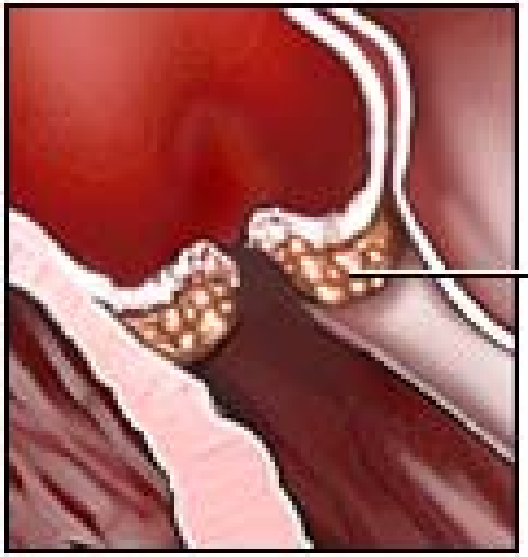
Endocarditis bacteriana aguda forma úlcero-trombótica, de la tricúspide.



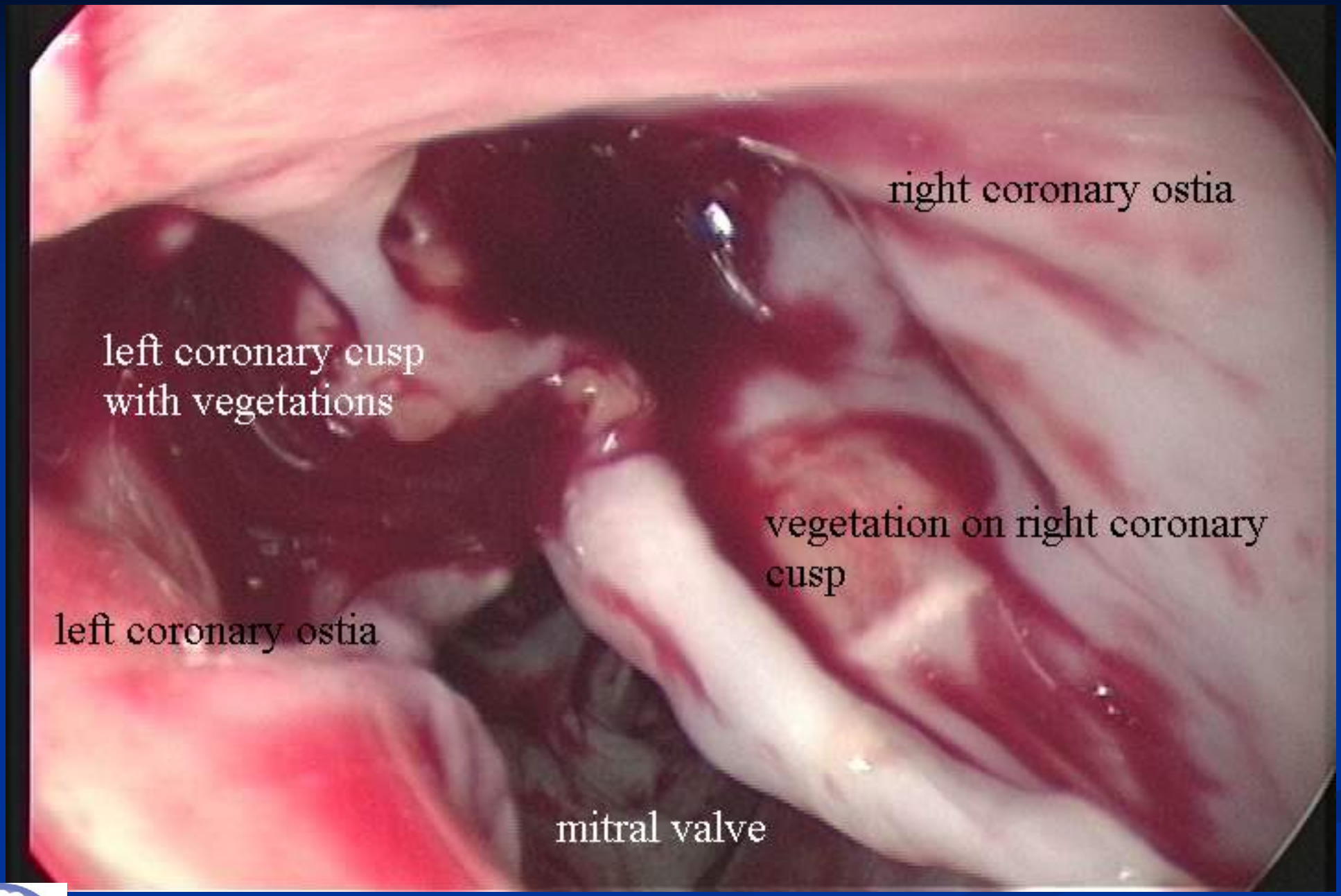
Cross section of the heart

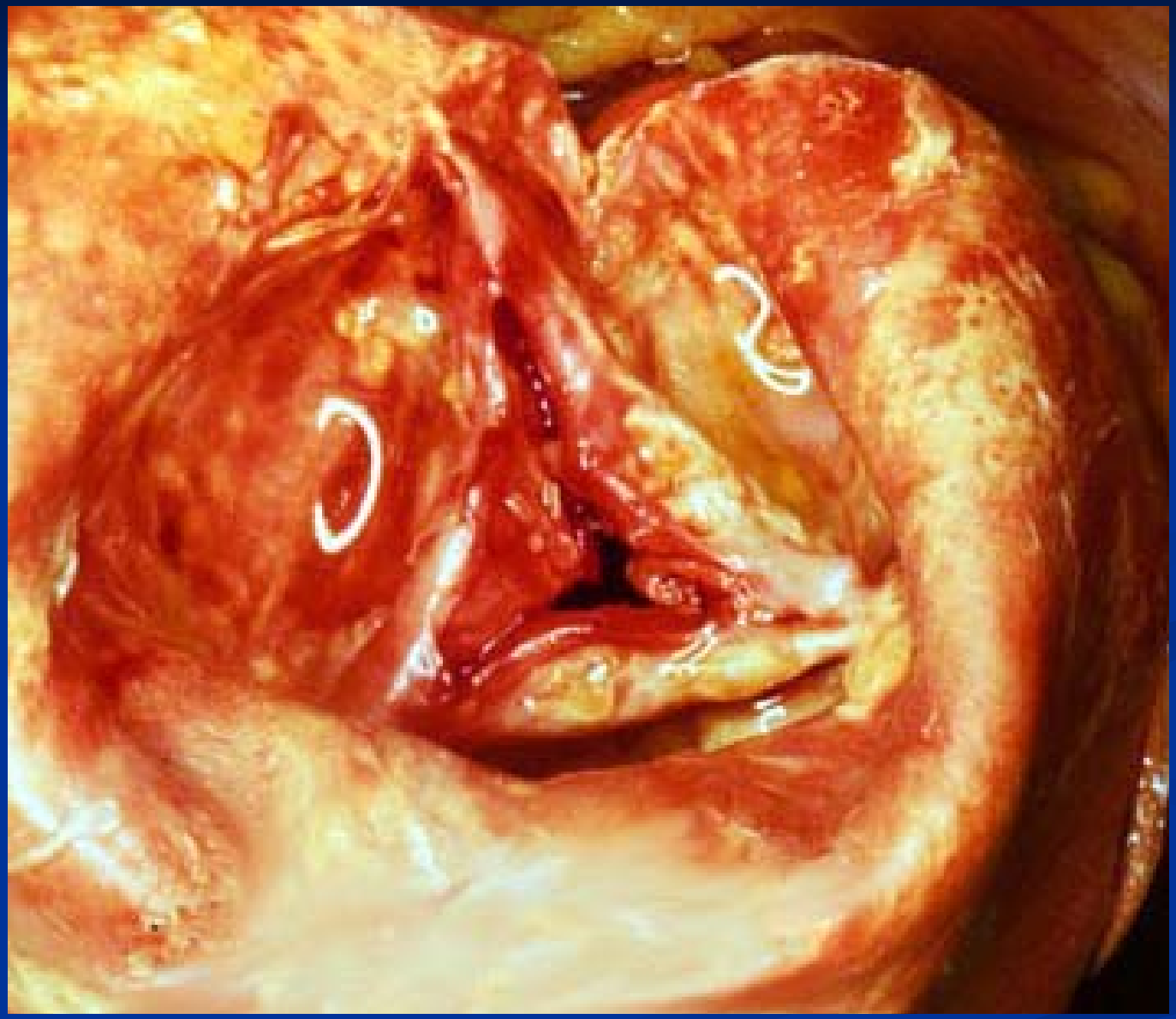


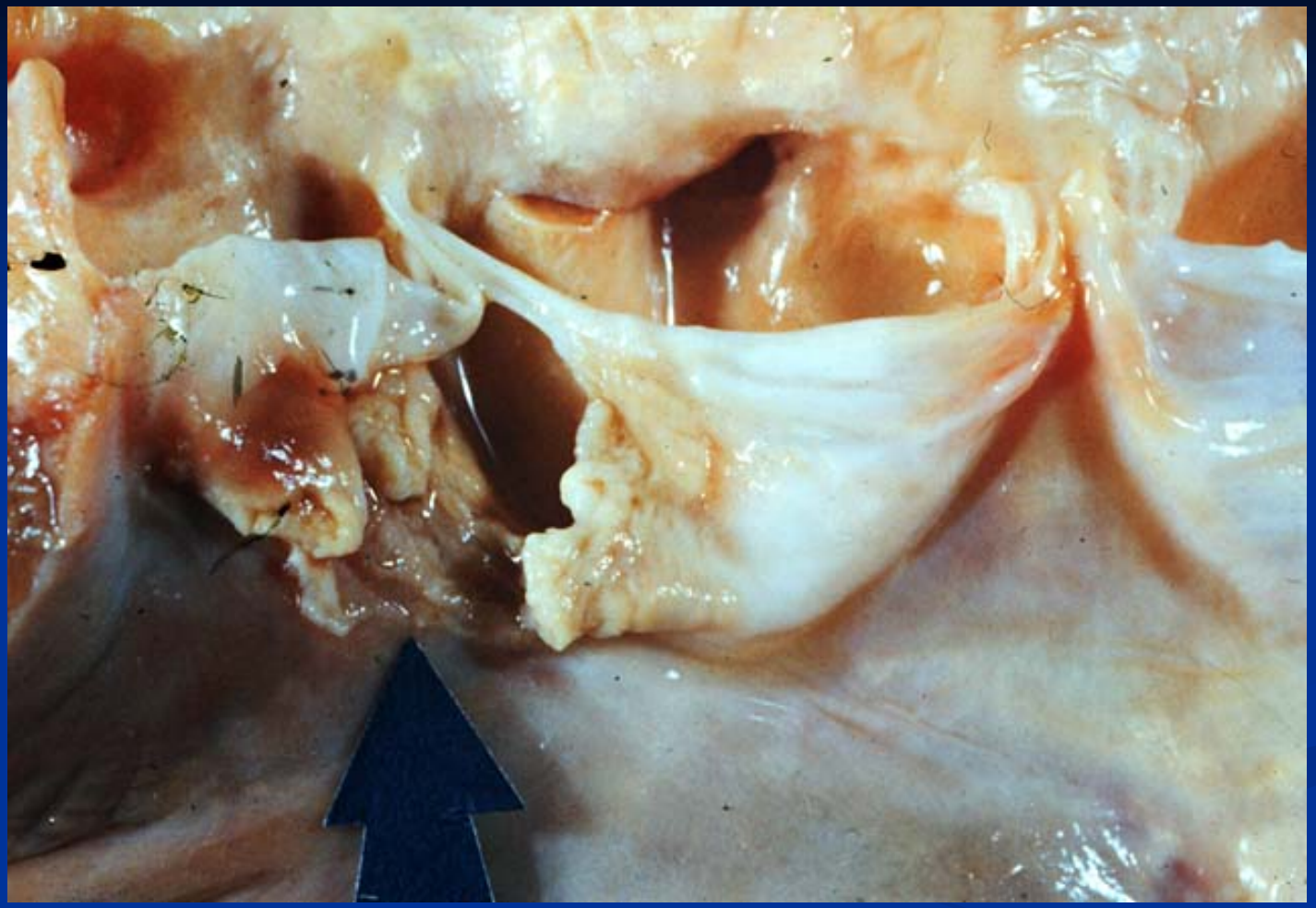
Normal aortic valve



Area of infection on the aortic valve

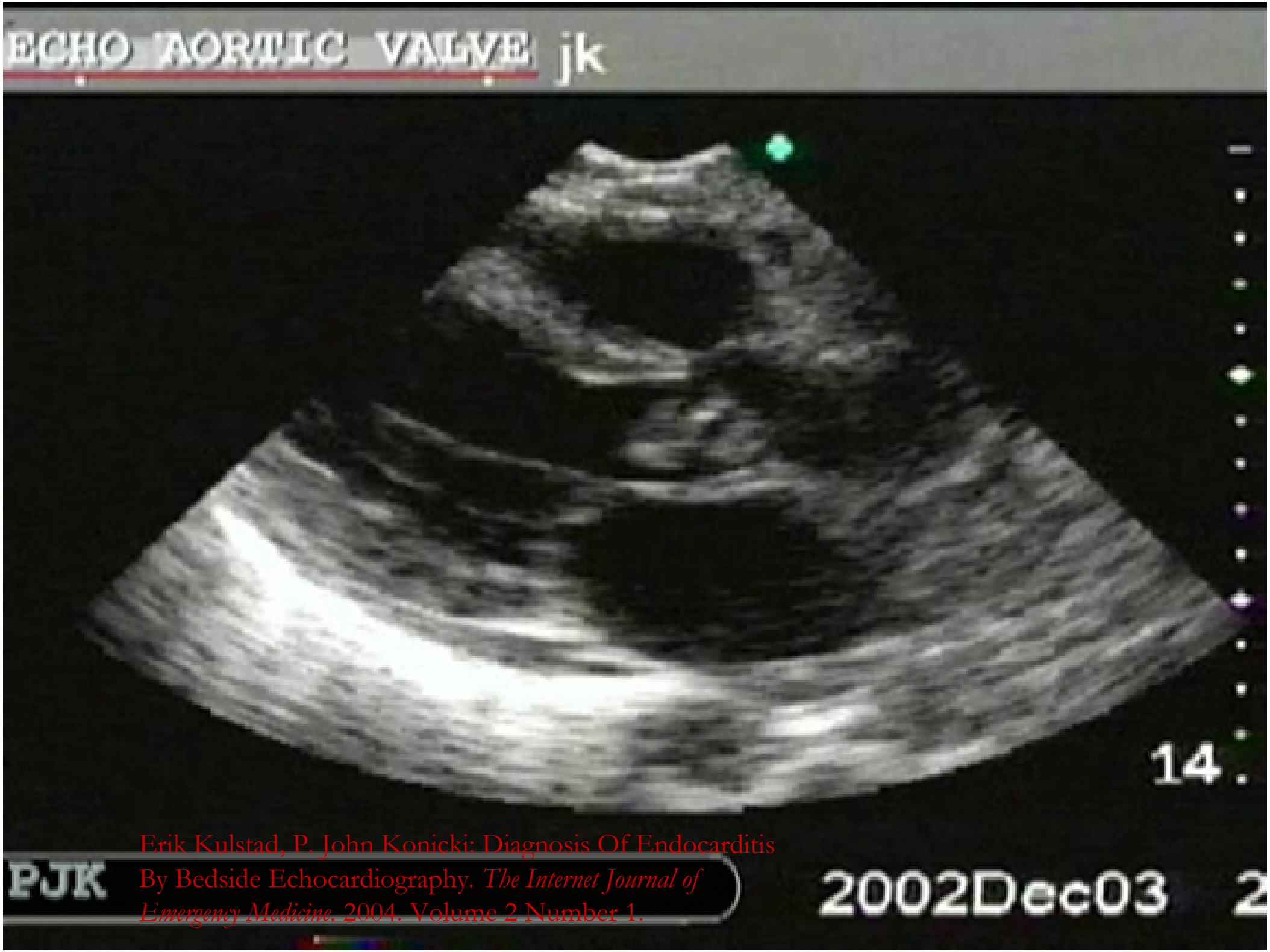

right coronary ostia
left coronary cusp
with vegetations
vegetation on right coronary
cusp
left coronary ostia
mitral valve





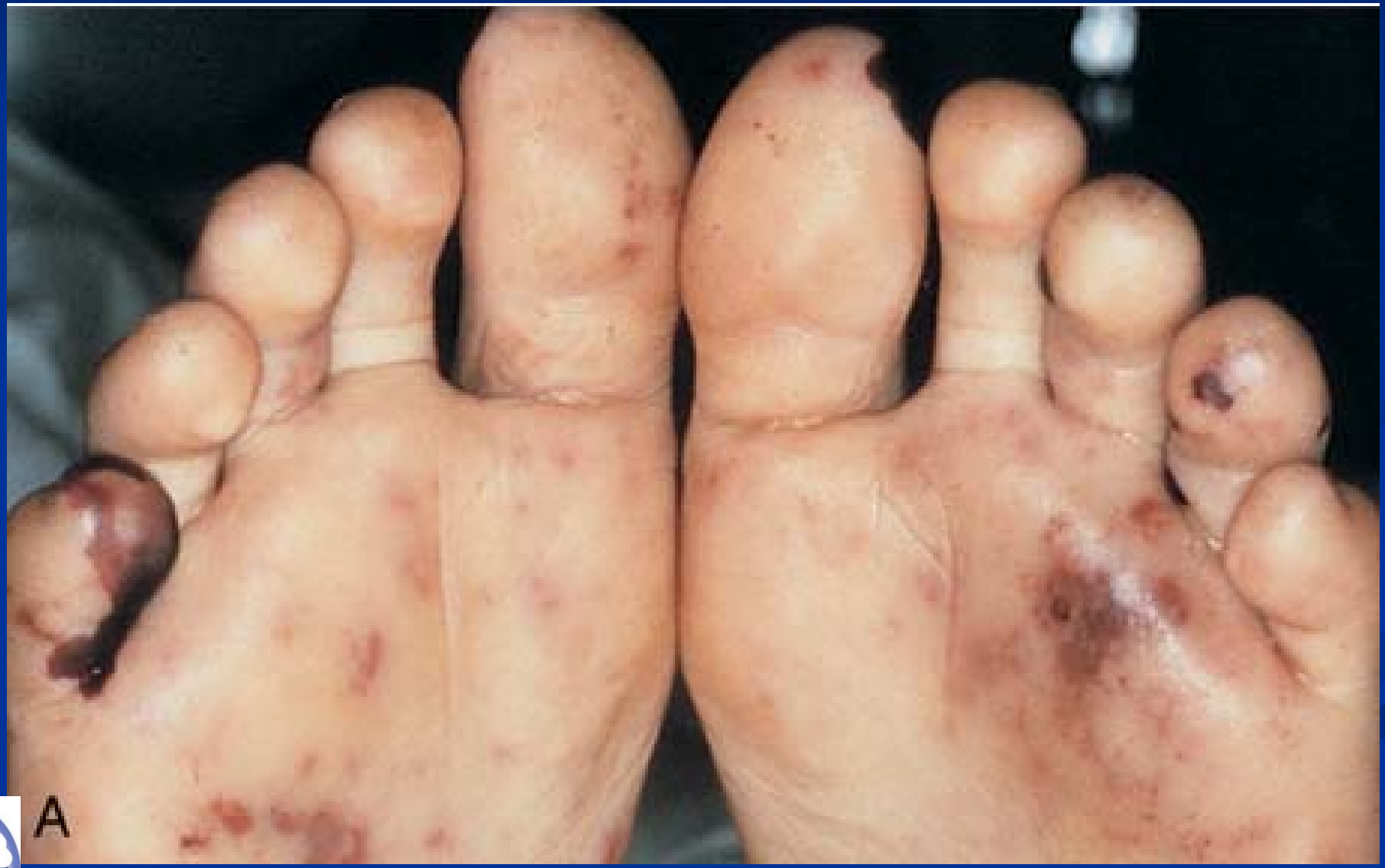
Endocarditis bacteriana aguda forma ulcerosa.

Extensa perforación del velo aórtico derecho.

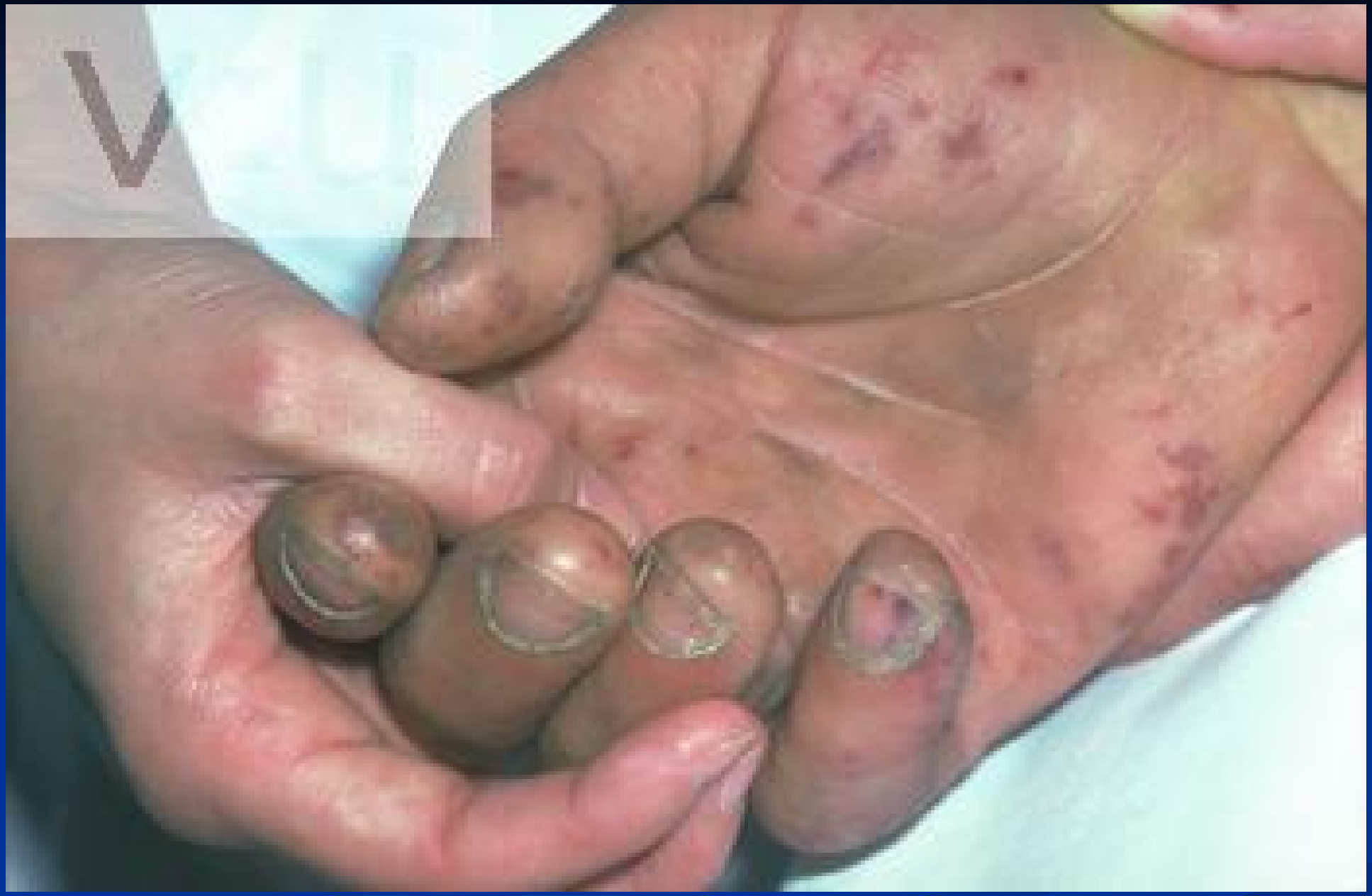


Erik Kulstad, P. John Konicki: Diagnosis Of Endocarditis By Bedside Echocardiography. *The Internet Journal of Emergency Medicine*. 2004. Volume 2 Number 1.

Hemorrhagic Lesions in a Patient with Acute Bacterial Endocarditis



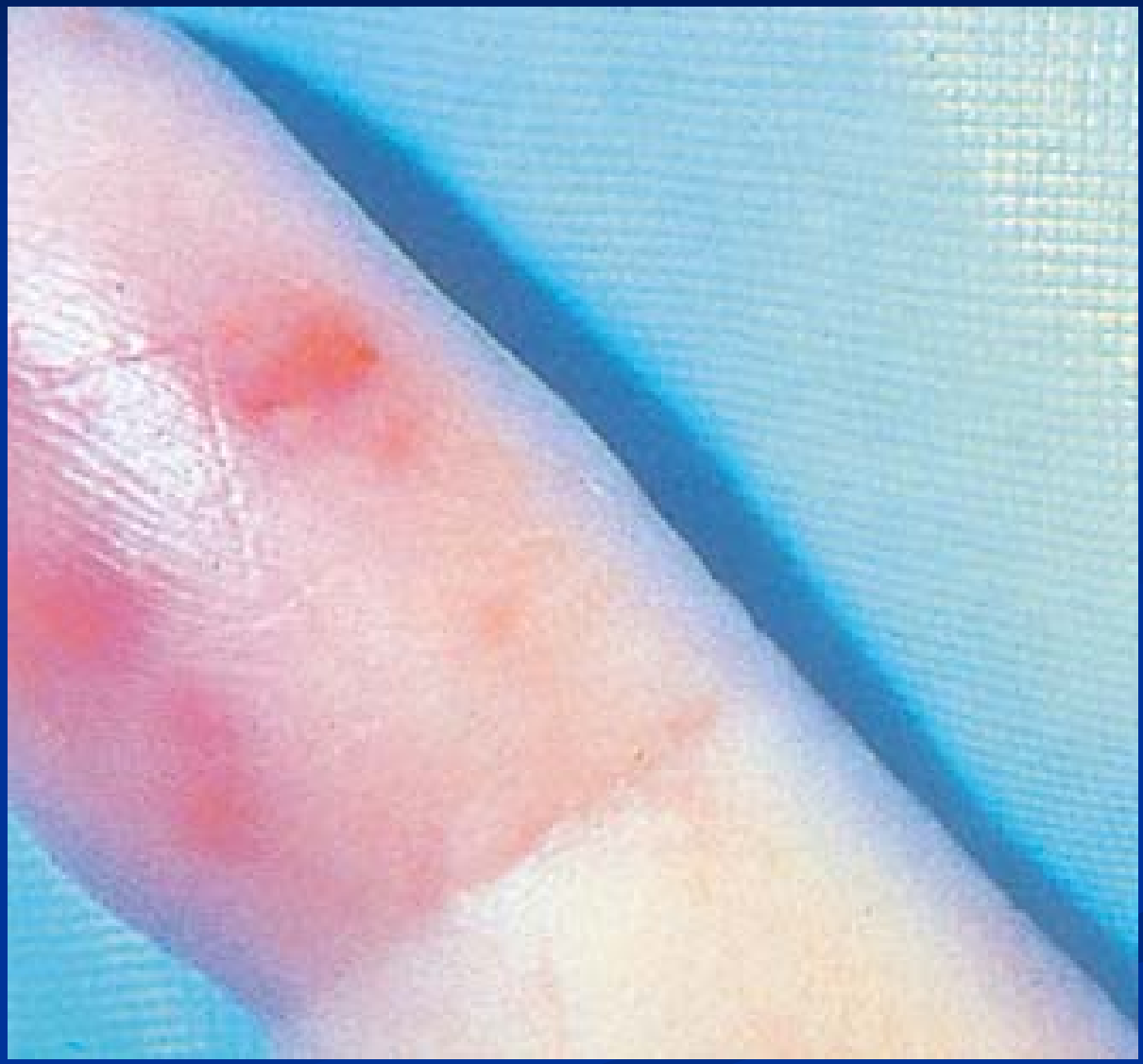
Zitelli & Davis, Pediatric Physical Diagnosis Electronic Atlas, Mosby 2004



Subungual Splinter Hemorrhages

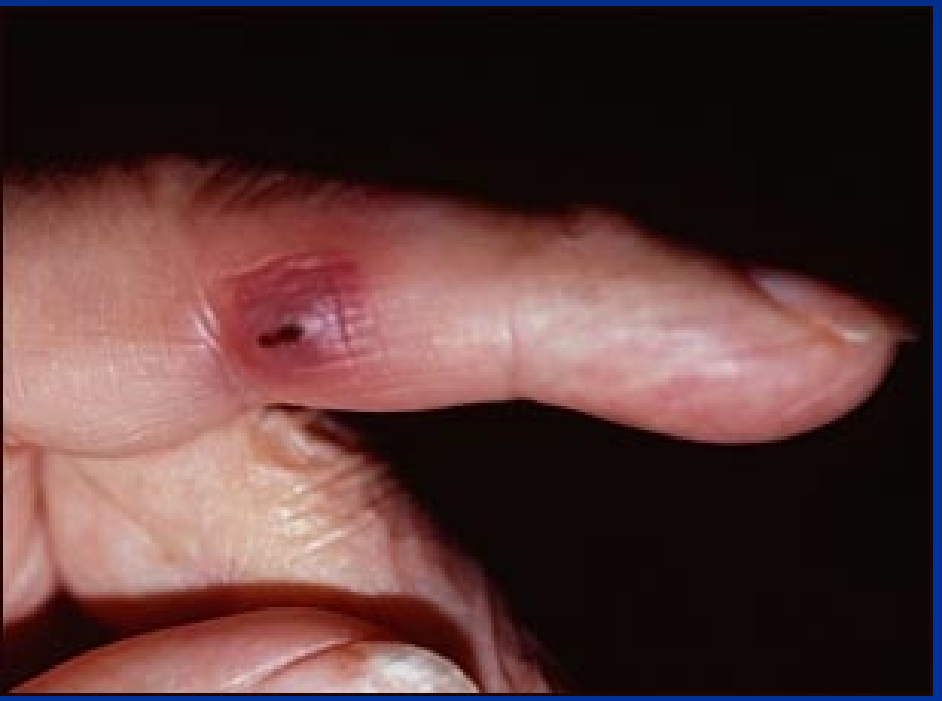
Zitelli & Davis, Pediatric Physical Diagnosis Electronic Atlas, Mosby 2004

Osler's Nodes: Painful erythmatous nodular lesions resulting from infective endocarditis



Zitelli & Davis, Pediatric Physical Diagnosis Electronic Atlas, Mosby 2004

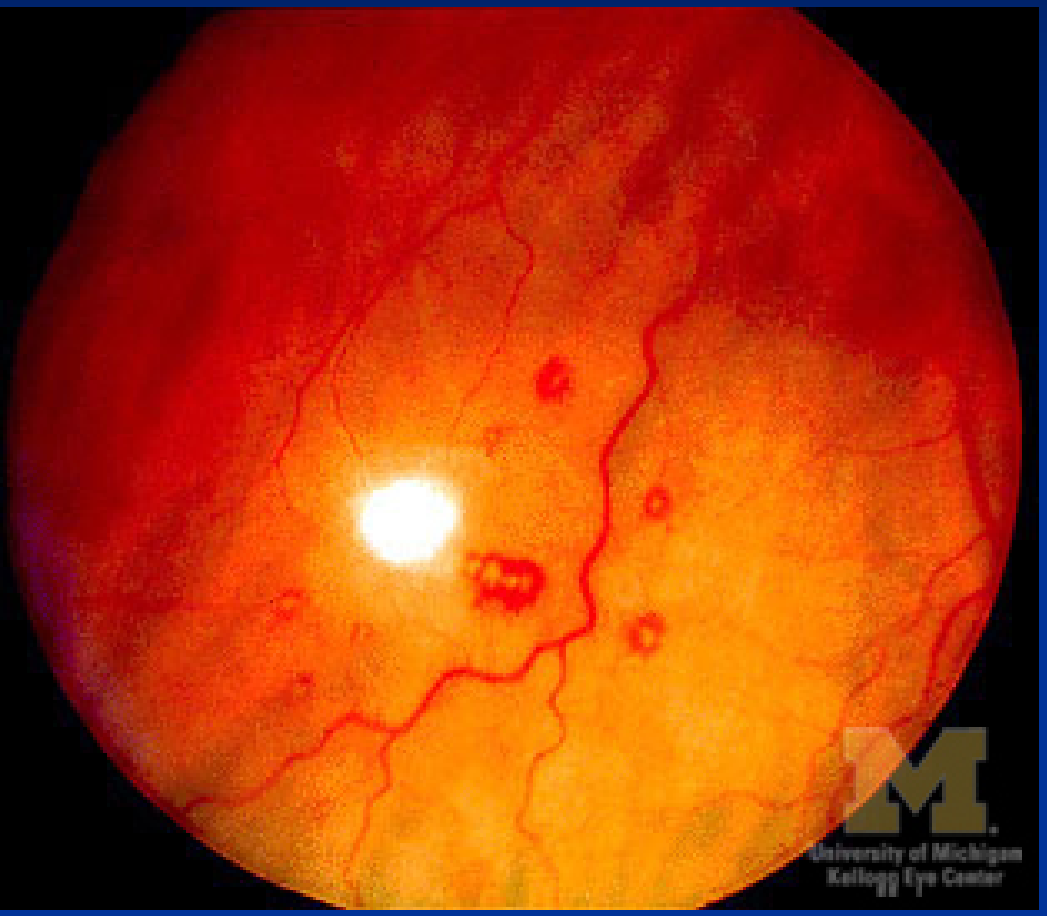
Janeway Lesions



- Non-tender, small erythematous or hemorrhagic macules or nodules in the palms or soles, which are pathognomonic of infective endocarditis.
- The pathology is due to a type III hypersensitivity reaction.

www.nlm.nih.gov/medlineplus/ency/imagepages/2455.htm

Roth Spots



- "White-centered" hemorrhages, originally described in patients with bacterial endocarditis.

- Non-specific for endocarditis, but discovering them in a patient who has other suggestive features of endocarditis constitutes strong support for the diagnosis.

- Probably reflect microinfarcts, just like cotton wool spots. Occur in a litany of disorders, including essential hypertension, HIV, connective tissue disease, severe anemia, Behçet's disease, viremia, and hypercoagulable states.

- Do not interfere with vision.

Estimated Incidence of Infective Endocarditis from Dental Procedures

- Overall US population: 1/14 million procedures
- Mitral Valve Prolapse: 1 case/ 1.1 million
- Congenital Heart Disease: 1/ 475,000
- Rheumatic Heart Disease: 1/ 142,000
- Prosthetic Cardiac Valve: 1/114,000
- Previous Infective Endocarditis: 1/ 95,000

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Bacteremia Risk Related to Dental Procedures

- Estimated cumulative exposure of 5370 minutes of bacteremia/ month related to chewing food and oral hygiene measure Vs. 6-30 minutes of bacteremia associated with single tooth extraction (Guntheroth 1984).
- Tooth brushing twice daily for 1 year has estimated IE risk 154,000 times greater than single tooth extraction (Roberts, 1999).
- Cumulative exposure to bacteremia over 1 year may be as high as 5.6 million times greater than that from a single tooth extraction (Roberts, 1999)..

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Cardiac Conditions for which IE Prophylaxis Recommended for Dental Procedures

- Prosthetic Cardiac Valve
- Previous Infective Endocarditis
- Congenital Heart Disease (CHD)
  - Unrepaired Cyanotic CHD, Including Palliative Shunts and Conduits
  - Completely Repaired CHD with Prosthetic Material or Device, whether by Surgery or by Catheter Intervention, during the first 6 months after the procedure
  - Repaired CHD with Residual Defects at the Site or Adjacent to the Site of a Prosthetic Patch or Prosthetic Device (which Inhibit Endothelialization)
- Cardiac Transplant Recipients who Develop Valvulopathy

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Infectious Bacterial Endocarditis Prophylaxis No Longer Recommended for the Following Conditions

- Ventricular Septal Defect
- Ostium Primum Atrial Septal Defect
- Pulmonary Stenosis
- Aortic Stenosis/Insufficiency
- Mitral Valve Prolapse with Valve Regurgitation
- Patent Ductus Arteriosus
- Coarctation of Aorta
- Rheumatic Heart Disease
- Hypertrophic Cardiomyopathy

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Endocarditis Prophylaxis NOT Recommended: Negligible-risk Category (No greater risk than the general population)

- Isolated secundum atrial septal defect
- Surgical repair of atrial septal defect, ventricular septal defect, or patent ductus arteriosus (without residua beyond 6 mo)
- Previous coronary artery bypass graft surgery
- Mitral valve prolapse without valvar regurgitation
- Physiologic, functional, or innocent heart murmurs
- Previous Kawasaki disease without valvar dysfunction
- Previous rheumatic fever without valvar dysfunction
- Cardiac pacemakers (intravascular and epicardial) and implanted defibrillators

American Heart Association SBE Guidelines- JAMA 1997;277:1794

Endocarditis Prophylaxis NOT Recommended:

- "Probably Innocent Murmur" never evaluated by cardiologist but getting SBE prophylaxis "just in case."

Dental Procedures for which Endocarditis Prophylaxis IS Recommended in Patients with the Highest Risk Cardiac Conditions

- All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa.

Dajani AS, Taubert KA, Wilson W, et al, JAMA 1997;277:1797
and Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Dental Procedures for which Endocarditis Prophylaxis IS NOT Recommended in Patients with the Highest Risk Cardiac Conditions

- Routine anesthetic injections through non-infected tissue
- Taking dental radiographs
- Placement of removable prosthodontic or orthodontic appliances
- Adjustment of orthodontic appliances
- Placement of orthodontic brackets
- Shedding of deciduous teeth
- Bleeding from trauma to the lips or oral mucosa

Dajani AS, Taubert KA, Wilson W, et al, JAMA 1997;277:1797
and Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Antibiotic Prophylaxis Administered Solely for the Prevention of Infective Endocarditis is No Longer Recommended for Genitourinary or Gastrointestinal Tract Procedures.

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

Common Procedures for which Endocarditis Prophylaxis is NOT Recommended

- Circumcision
- Ear/Body Piercing
- Tattooing
- Vaginal Delivery
- Hysterectomy

Recommendations for IE Prophylaxis for Respiratory Tract Procedures

- IE Prophylaxis May be Considered:
  - Invasive procedure of respiratory tract involving incision or biopsy of respiratory mucosa
  - Tonsillectomy & Adenoidectomy
- IE Prophylaxis Not Recommended:
  - Bronchoscopy unless procedure involves incision of respiratory mucosa

Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

IE Prophylaxis Dosing for Dental Procedure

- **Oral:** Administer 30-60 minutes prior to procedure.
  - **Amoxicillin*:** 50 mg/kg (maximum 2 grams)
  - Clindamycin: 20 mg/kg (maximum 600 milligrams)
  - Cephalexin or equivalent 1st/2nd Generation Cephalosporin: 50 mg/kg (max. 2 grams)
  - Azithromycin or Clarithromycin: 15 mg/kg (max. 500 mg)
- **IVor IM:** Administer 30-60 minutes prior to procedure.
  - **Ampicillin*:** 50 mg/kg (maximum 2 grams)
  - **Cephazolin or Ceftriaxone*:** 50 mg/kg (maximum 1 gram)
  - Clindamycin: 20 mg/kg (maximum 600 mg)

*First choice unless allergic.

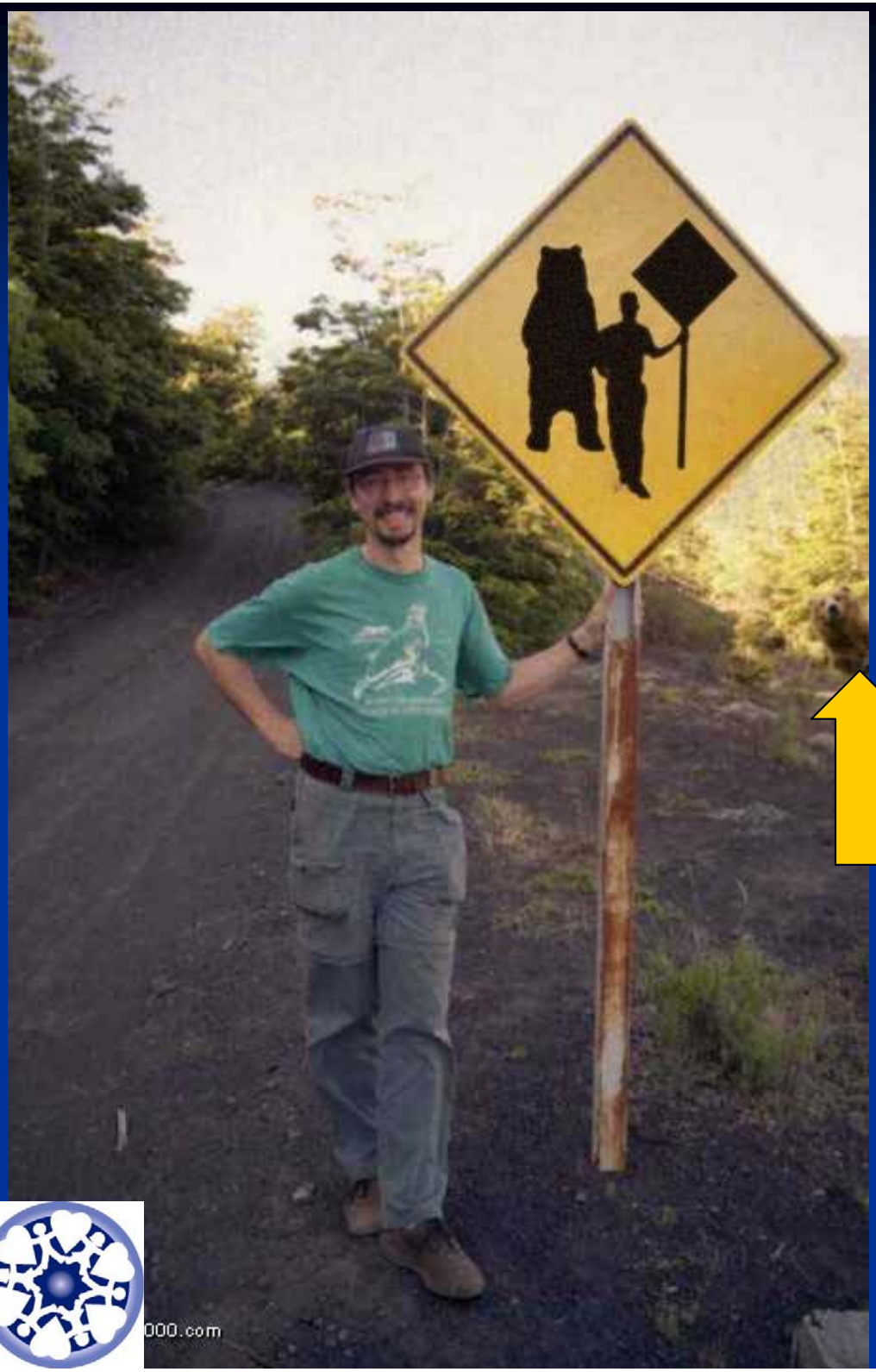
Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

IE Prophylaxis Dosing for Dental Procedure- What Changed?

- **Oral:** Administer (previously 1 hour) 30-60 minutes before procedure.
  - **Amoxicillin*:** 50 mg/kg (maximum 2 grams)
  - Clindamycin: 20 mg/kg (maximum 600 milligrams)
  - Cephalexin or Cefadroxil replaced with any equivalent 1st/2nd Generation Cephalosporin: 50 mg/kg (max. 2 grams)
  - Azithromycin or Clarithromycin: 15 mg/kg (max. 500 mg)
- **IVor IM:** Administer (30 minutes) 30-60 minutes prior.
  - **Ampicillin*:** 50 mg/kg (maximum 2 grams)
  - Cephazolin or Ceftriaxone (add *): 50 mg/kg (maximum 1 gram)
  - Clindamycin: 20 mg/kg (maximum 600 mg)

*First choice unless allergic.

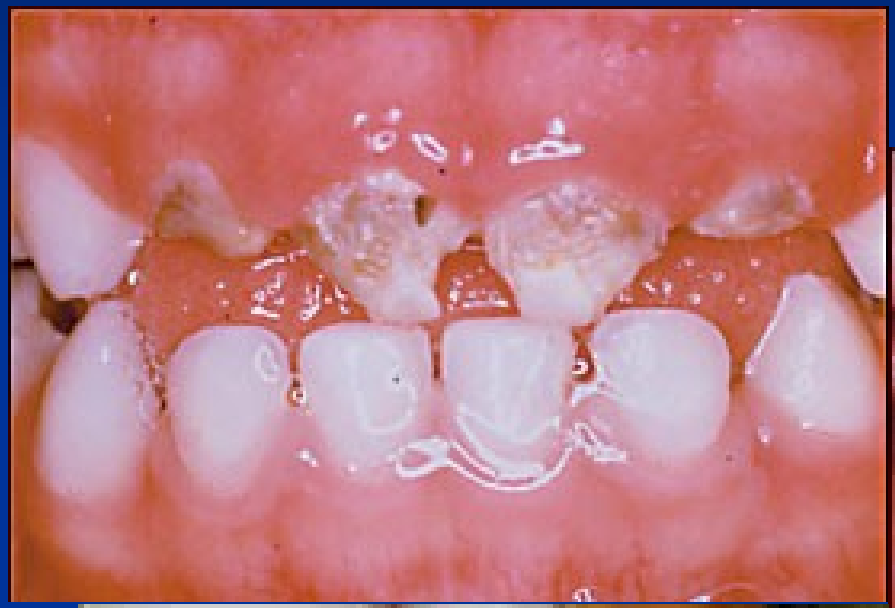
Wilson W, Taubert KA, Gerwitz M, et al. Circulation. 2007;115.

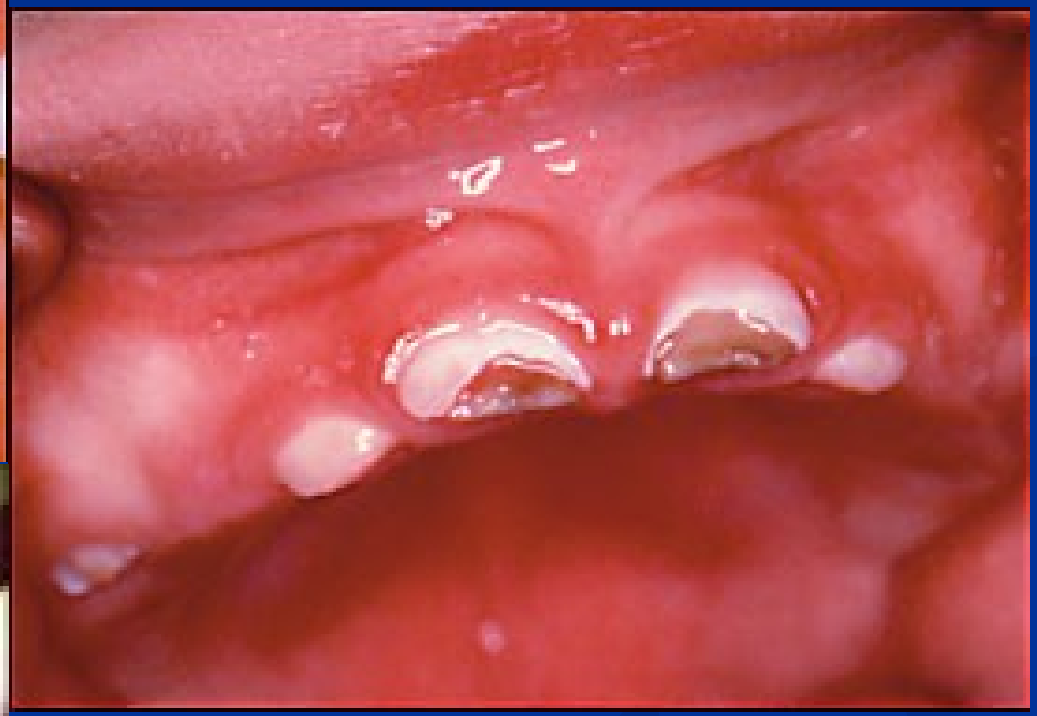


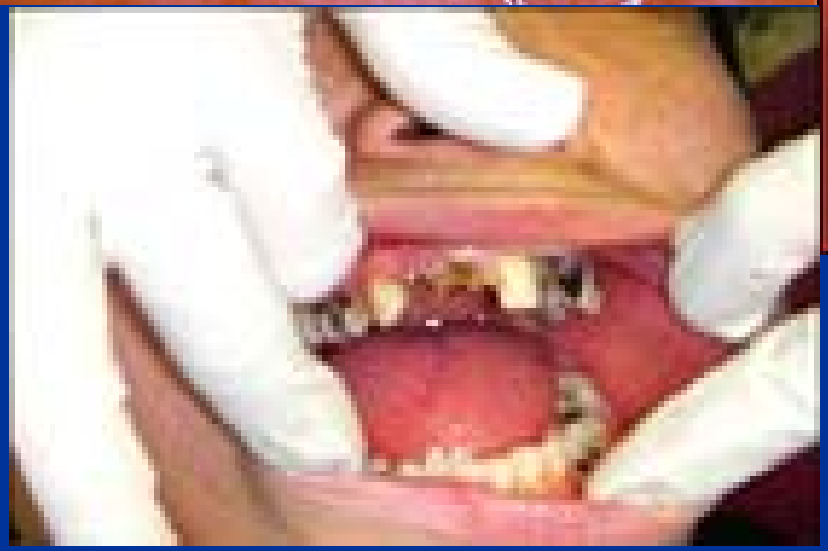
Signs Suggest Potential Danger Ahead

New Guidelines Emphasize Importance of Good Oral Hygiene

What Happens to the Risk of IE for Kids with Cavities?







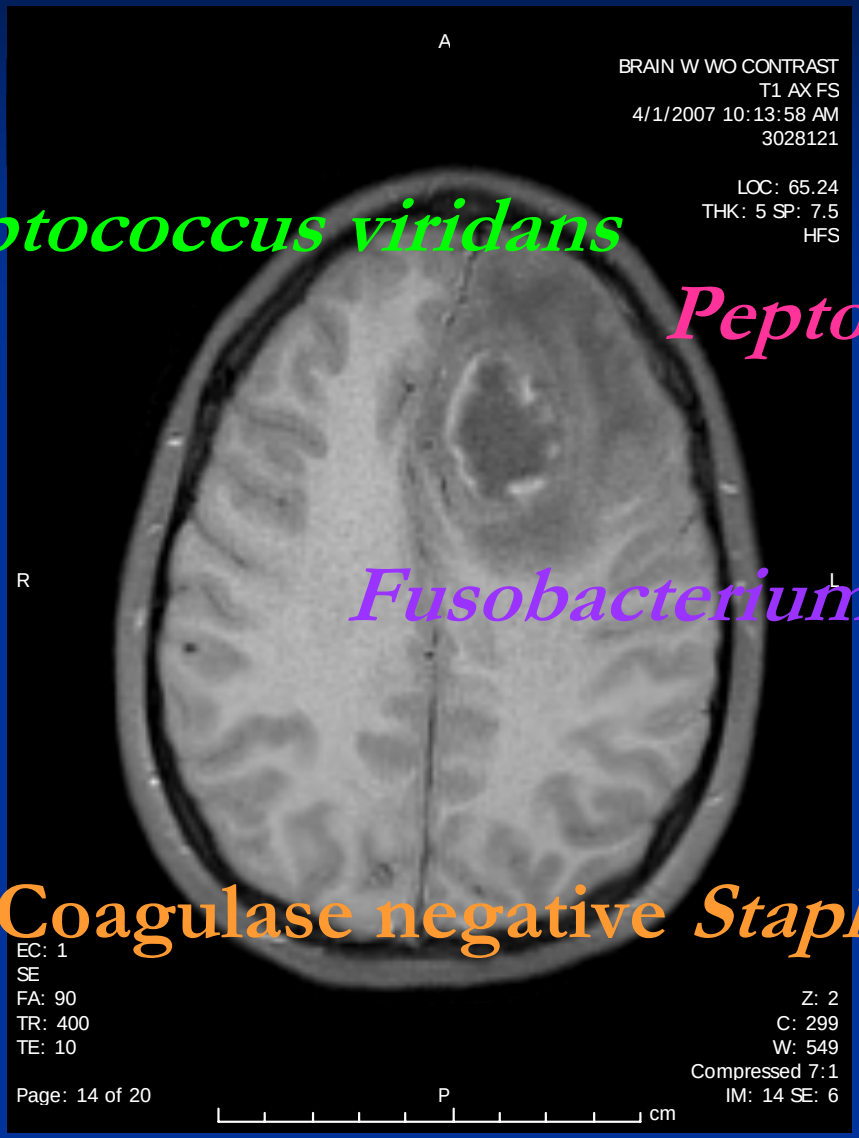
www.asu.edu/courses/css335/caring.htm

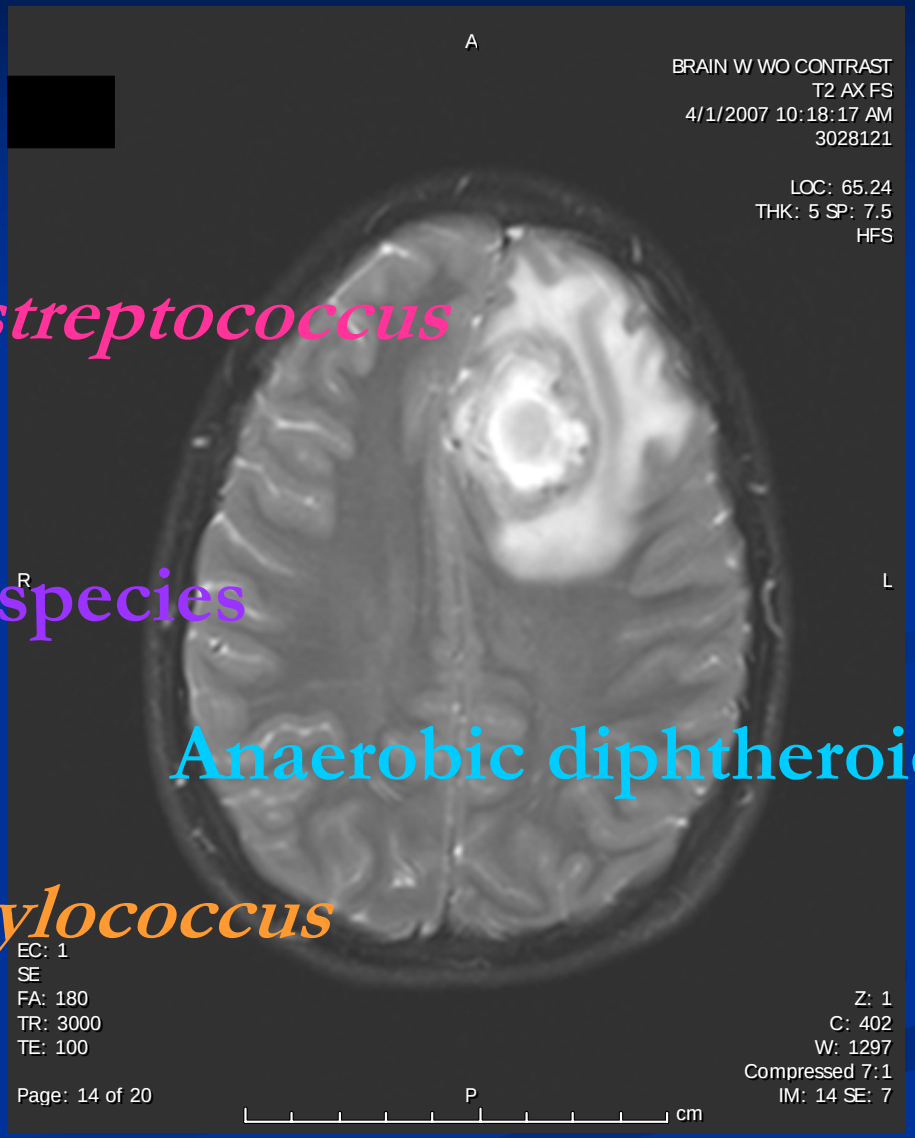
www.ada.org/prof/advocacy/legal/alaska/media.asp

Case: 15 year-old Generally Healthy Female

- History: Nausea, Vomiting, Photophobia and Headache with associated Aura for one week.
- Recent extensive dental work.
- Previous history of persistent hypoxia on room air following pneumonia 11/02 (Arterial pO_2-67 on room air and 66 on FiO_2-100%). Previous evaluation included cardiac catheterization which did not detect any right to left shunting.

MRI





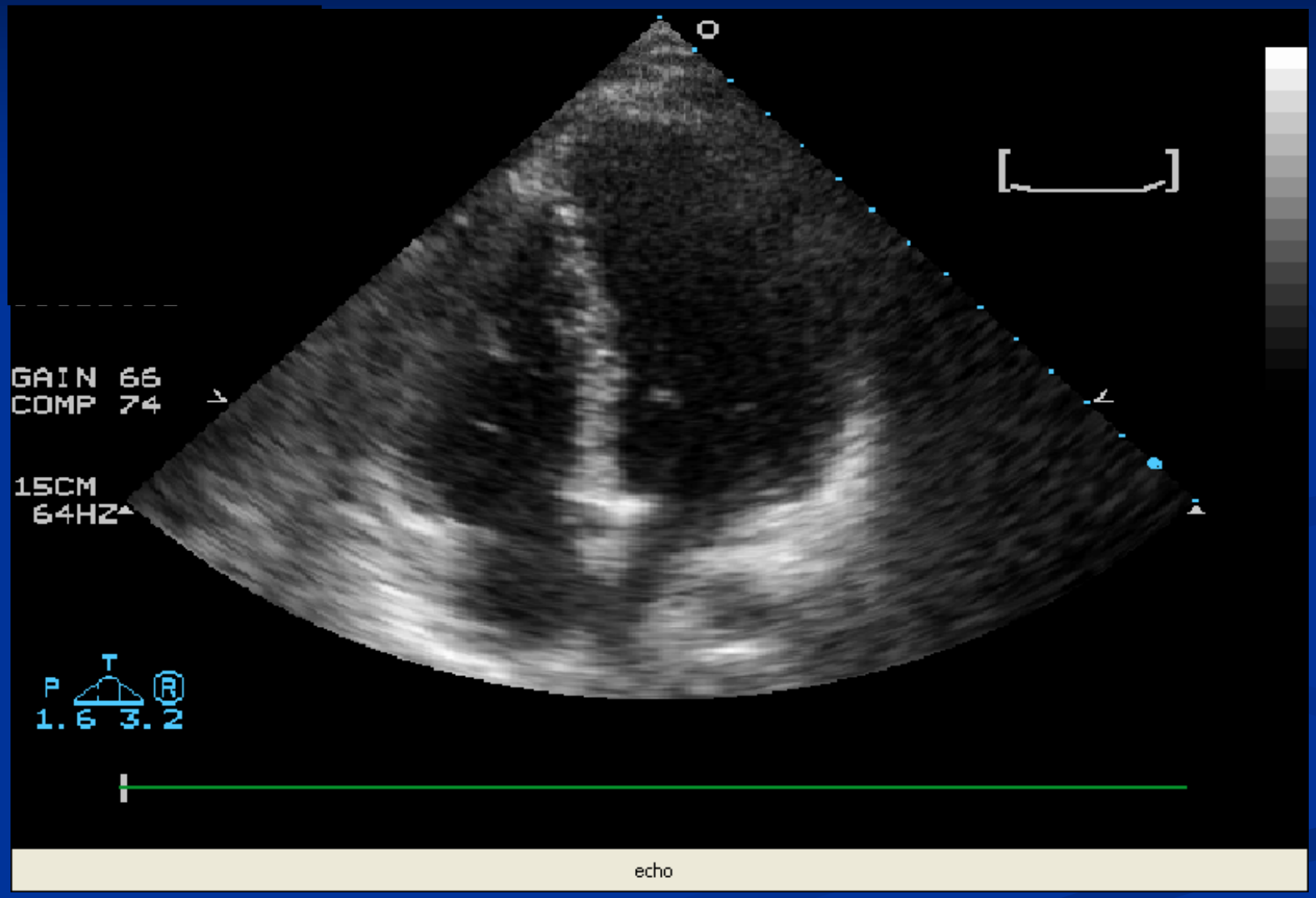
Streptococcus viridans

Peptostreptococcus

Fusobacterium species

Anaerobic diphtheroids

Coagulase negative *Staphylococcus*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15CM
64HZ
P
T
1.6
3.2
echo