

Endocarditis

February 22, 2008

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Topics to be covered

- Epidemiology
- Microbiology
- Clinical presentation
- Physical Exam Findings
- Diagnostic Imaging
- Overview of Treatment
- Complications
- Indications for Surgery
- Prognosis
- Prophylaxis
- Pearls for the Boards

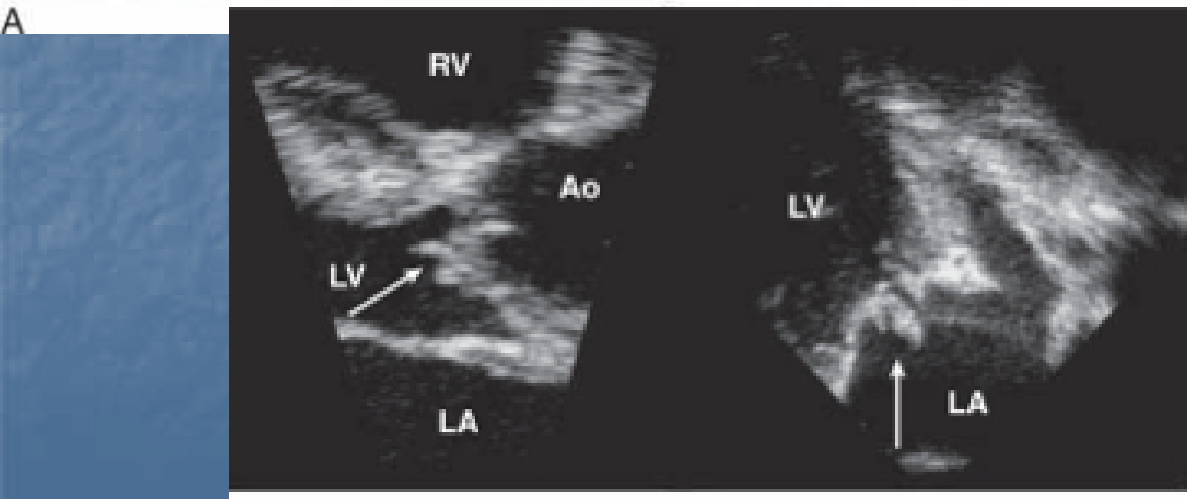
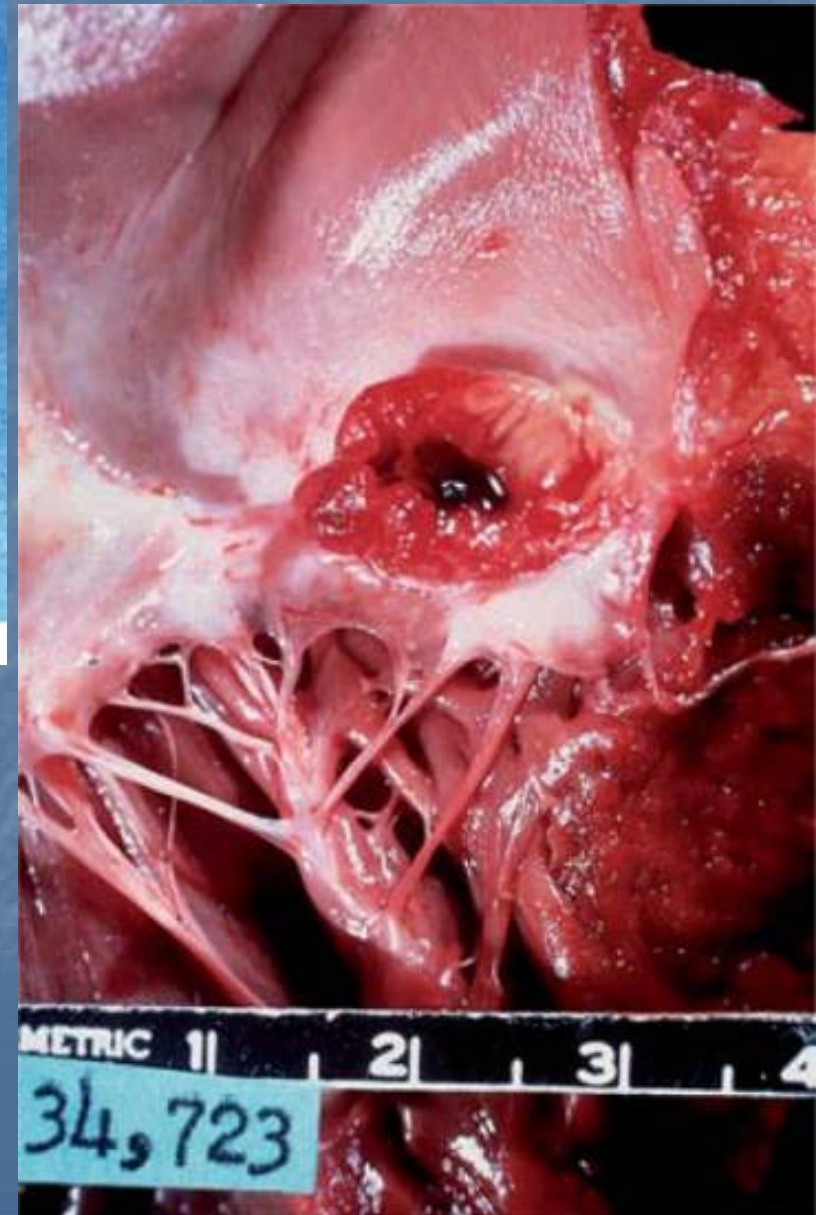
Endocarditis is...

- An infection of the heart, typically involving valve leaflets
 - May also involve
 - Chordae tendinae
 - Mural endocardium
 - Site of a septal defect
 - Arteriovenous shunts
 - Patent ductus arteriosus
 - Intracardiac hardware

A vegetation is...

- A collection of
 - Platelets
 - Fibrin
 - Bacteria
 - Inflammatory cells

Endocarditis looks like...



Epidemiology

- Incidence of 2.4-11.6 per 100,000 patient years
- Stable or increasing in incidence
- Higher incidence in urban populations
- Elderly at 4-6x risk
- Median age 47-69
- Male:Female ratio of about 2:1
- Up to 75% of patients with native valve involvement have identifiable risk factors

Time course of endocarditis

- Acute
 - Typically *Staphylococcus aureus*
 - Toxic
 - Progresses over days to weeks
 - Valvular destruction
 - Metastatic infection
- Subacute
 - Less toxic
 - Weeks to months
 - Pathogens
 - Viridans streptococci
 - Enterococci
 - Coagulase-negative staphylococci
 - Gram-negative coccobacilli

Risk factors for native valve endocarditis

- Rheumatic heart disease
- Congenital heart disease
- Mitral valve prolapse
- Degenerative heart disease
- Asymmetrical septal hypertrophy
- Intravenous drug abuse

Mitral Valve Prolapse

- High prevalence
 - 2-4% of general healthy population
 - 20% of young women
- 7-30% of Native valve endocarditis without IVD
- Incidence
 - 4.6 per 100,000 patient years without murmur
 - [0.004%/year]
 - 52 per 100,000 patient years with murmur
 - [0.05%/year]

Rheumatic Heart Disease

- Declining in incidence
 - 20-25% of endocarditis cases in 1970's
 - 7-18% of endocarditis cases in 1980's
- Commonly involves
 - Mitral valve in women
 - Aortic valve in men
- Absolute risk 380-440 per 100,000 patient-years [0.4%/year]

Congenital Heart Disease

- Accounts for
 - 10-20% of endocarditis cases in young adults
 - 8% of cases in older adults
- Common lesions
 - Patent ductus arteriosus
 - Ventricular septal defect
 - Bicuspid aortic valve

Intravenous drug use

- Risk of endocarditis 2-5 per 100 patient years
 - Higher risk than rheumatic disease or prosthetic valve
- 65-80% of IVD endocarditis population is male
- Average age 27-37
- Commonly involves tricuspid valve (46-78% of cases)
- *S. Aureus* involved in over 50% of cases

Prosthetic Valves

- Account for 10-30% of all endocarditis cases
- Risk is greatest in first 6 months after implant
 - “Early” endocarditis occurs in first 60 days
- Incidence about 5% at 5 years
- Risk declines over time
- Mechanical valve has higher risk than bioprosthesis initially
- After 1 year bioprosthesis is more risky than mechanical valve

Microbiology in a nutshell

- Any pathogen can cause endocarditis
- Common organisms
 - *Strep viridians* – 28%
 - *Staph aureus* – 28%
 - Other *Strep* species – 23%
 - Coag negative *Staph* – 7%
 - Gram-negatives – 4%
 - Other – 5%
 - No growth – 5%
- Drug resistance seen commonly in IV drug use
- *Staph aureus* incidence appears to be rising

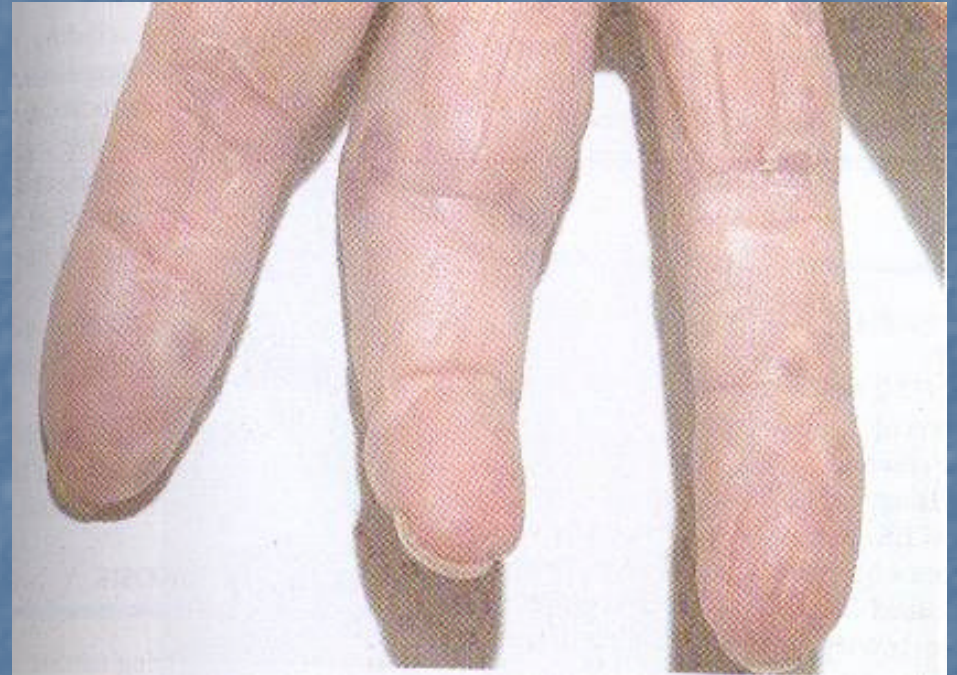
Clinical presentation

Nonspecific symptoms and signs

- Fever
- Mitral or aortic regurgitation murmurs
- Splenomegaly (50% of cases)
- Microscopic hematuria
- Sepsis – especially in acute infective endocarditis
- Joint arthritis and arthralgias
- Chronic wasting –in subacute endocarditis
- Cutaneous signs are infrequent

Osler's Nodes

- Tender violaceous nodules in pulp of fingers or toes
- Due to infective emboli or immune complex deposits



Petechial Lesions

- Petechiae may appear on extremities, chest, or mucous membranes



Splinter Hemorrhage

- Due to rupture of fine subungual capillaries
- Usually 2-3mm long in long axis of nail
- Initially blue-purple in color, change to brown or black in 1-2 days
- Move distal with nail growth
- Trauma is the most common cause; 20% of population have them



Splinter Hemorrhage



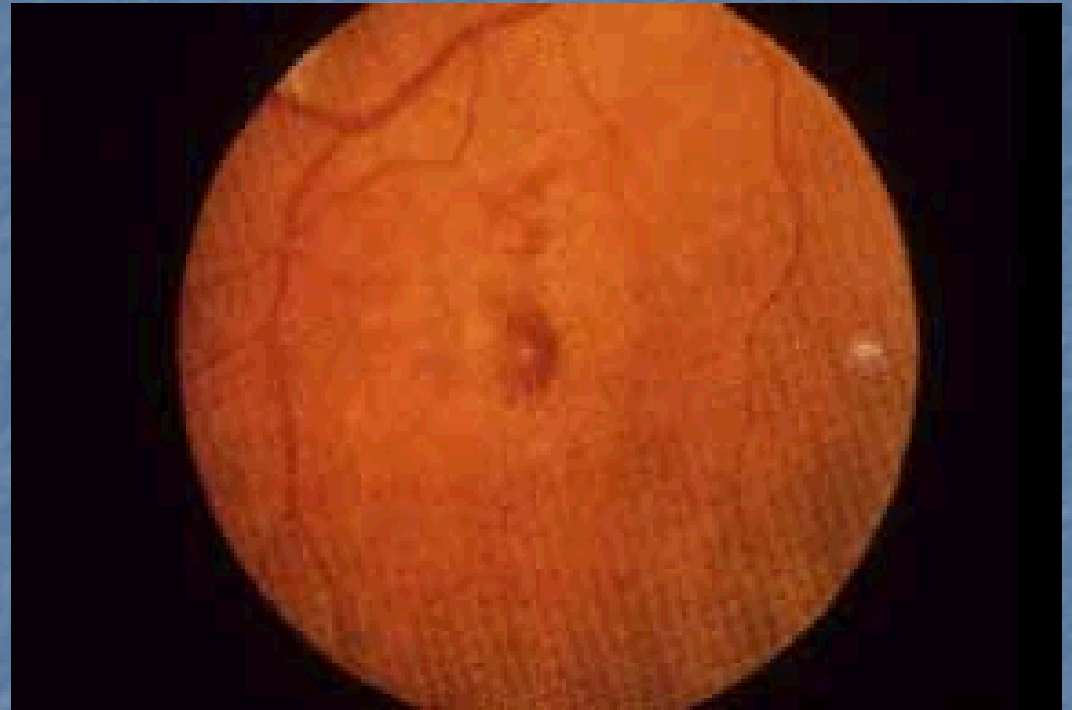
Janeway Lesions



- Nontender
- Small hemorrhagic macules or nodules
- Commonly on palms or soles

Roth Spots

- Red retinal hemorrhage
- Pale center



Clinical Presentation

Cardiac signs and symptoms

- Heart failure – especially unexplained in young pt
- Pericarditis – uncommon, often the result of abscess or fistulous tract formation
- Abnormal echocardiogram

Clinical Presentation

Complications of endocarditis

- Septic pulmonary emboli
 - Commonly in tricuspid valve endocarditis due to IV drug use
 - May cause chest pain and dyspnea
 - Pulmonary fleeting patchy infiltrates on chest xray
- Stroke – due to embolism of vegetation or thrombus
- Renal failure – rare complication due to sepsis, embolism, or immune complex reaction
- Peripheral vascular embolism

Endocarditis and Embolism

- Up to 75% of embolic events occur prior to diagnosis or treatment
- 50-65% of clinically evident emboli involve the CNS, especially in middle cerebral artery distribution
- Embolism risk decreases after 1 week of antibiotics
- Surgery indicated for 2 or more embolic events

Prosthetic Valve Endocarditis

- Early endocarditis occurs within 60 days of surgery
 - More common in patients needing reoperation or long ventilator support
 - Commonly involves *S. aureus* or fungal species
 - Acute presentation, 65% mortality
- Late endocarditis occurs more than 60 days postop
 - Subacute presentation
 - Typical subacute organisms
- Prosthetic valve endocarditis can cause mechanical failure due to abscess, valve dehiscence, paravalvular leaks

Duke Criteria - Diagnosis

- Definite Endocarditis
 - Positive histology or culture from vegetation
 - Two major criteria
 - One major and three minor criteria
 - Five minor criteria
- Rejected
 - Firm alternative diagnosis
 - Resolution after ≤ 4 days of antibiotics
- Possible Endocarditis

Duke criteria - Major

- 1) More than one positive blood culture typical for endocarditis
- 2) Evidence of endocardial involvement
 - New regurgitation murmur
 - Echocardiogram with oscillating mass, abscess or valve dehiscence

Major Criteria

- Positive blood culture
 - Typical microorganism for infective endocarditis from two separate blood cultures
 - Viridans streptococci, *Streptococcus bovis*, HACEK group *or*
 - *Staphylococcus aureus* or community-acquired enterococci in the absence of a primary focus, *or*
 - Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from:
 - Blood cultures (≥ 2) drawn more than 12 hr apart, *or*
 - All of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hr apart
 - Single positive blood culture for *Coxiella burnetii* or antiphase I IgG antibody titer $>1:800$
- Evidence of endocardial involvement
 - Positive echocardiogram (TEE advised for PVE or complicated infective endocarditis)
 - Oscillating intracardiac mass, on valve or supporting structures, *or* in the path of regurgitant jets, *or* on implanted material, in the absence of an alternative anatomical explanation, *or*
 - Abscess, *or*
 - New partial dehiscence of prosthetic valve, *or*
 - New valvular regurgitation (increase or change in preexisting murmur not sufficient)

Duke criteria - Minor

- 1) Cardiac risk factor including IV drug use
- 2) Fever $\geq 100.4^{\circ}$ F
- 3) Vascular manifestation
- 4) Immunologic phenomena
- 5) Echocardiogram consistent with endocarditis but not meeting major criterion
- 6) Positive blood culture not meeting major criterion or serologic evidence of organism

Minor Criteria

- Predisposition: predisposing heart condition *or* intravenous drug use
- Fever $\geq 38.0^{\circ}\text{C}$ (100.4°F)
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions
- Immunological phenomena: glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor
- Microbiological evidence: positive blood culture but not meeting major criterion as noted previously[*] *or* serologic evidence of active infection with organism consistent with infective endocarditis

Diagnostic Imaging

- Echocardiography
- Chest Xray
- CT
- MRI
- Nuclear

Chest Xray

- Nonspecific findings
- Cardiomegaly
- Nodular infiltrates
 - Tricuspid valve endocarditis causing septic emboli



CT and MRI

Still Mostly Experimental

- Primarily evaluate brain for complications
- Isolated CT case reports
 - Large aortic root abscess and AV fistula
- MRI can potentially diagnose complications of aortic root aneurysms or abscesses

Nuclear Imaging

- Tagged WBC scans have been used
 - Can identify vegetations
 - Nonspecific
 - High false negative
- Case reports suggest that positive scan can be used to detect local complications of endocarditis
- Useful to detect metastatic septic embolism

Echocardiography

- Major Duke criteria
- Diagnose and management of infective endocarditis
- Vegetations – detected in 67% of “definite” cases by Duke criteria
 - Irregular shape
 - Occur on low-pressure side of turbulent jet
 - Atrial side in mitral and tricuspid regurgitation
 - Ventricular side in aortic and pulmonic regurgitation
 - May occur on other nonvalvular locations

Vegetation characteristics

- Large vegetation (>10mm) has 3 times risk of embolization compared to small ones¹
- Prolapsing vegetations or extravalvular involvement carries higher risk of heart failure, brain embolization, need for valve replacement²

■ However, poor interobserver

reproducibility of these characteristics

¹Tischler M, Vaitkus P. The ability of vegetation size on echocardiography to predict complications: a meta-analysis. *J Amer Soc Echo* 1997; 10:562-8.

²Sanfillipo A, Picard M, Newell J, et al. Echocardiographic assessment of patients with infectious endocarditis: prediction of risk for complication. *J Am Coll Cardiol* 1991; 18:1191-9.

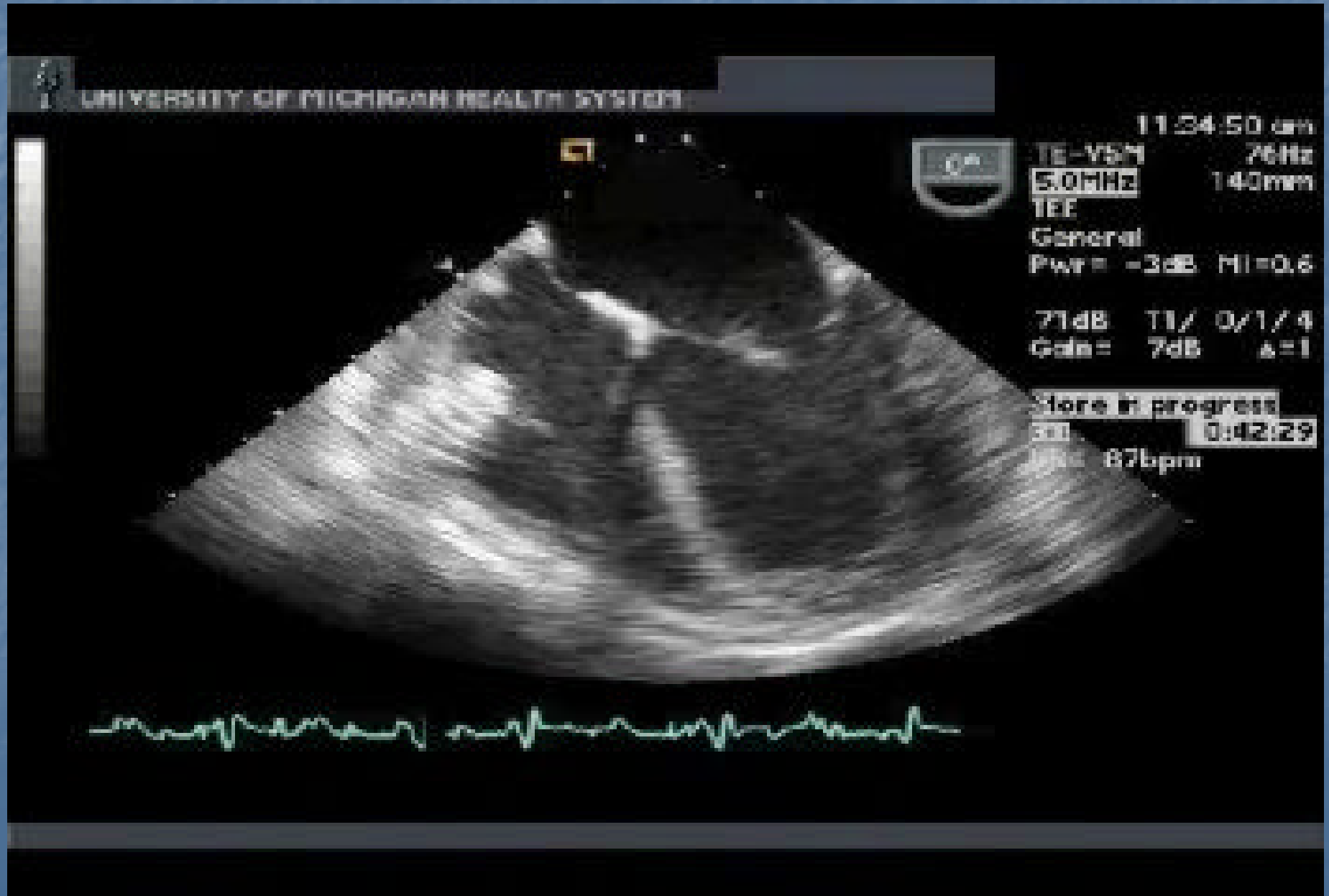
Valvular location

- Small series show 26% mortality of aortic location vs. 16% with mitral location
- Aortic valve endocarditis more resistant to antibiotic therapy, more likely to need surgery
- Mitral valve endocarditis, especially anterior leaflet, has highest incidence of embolization

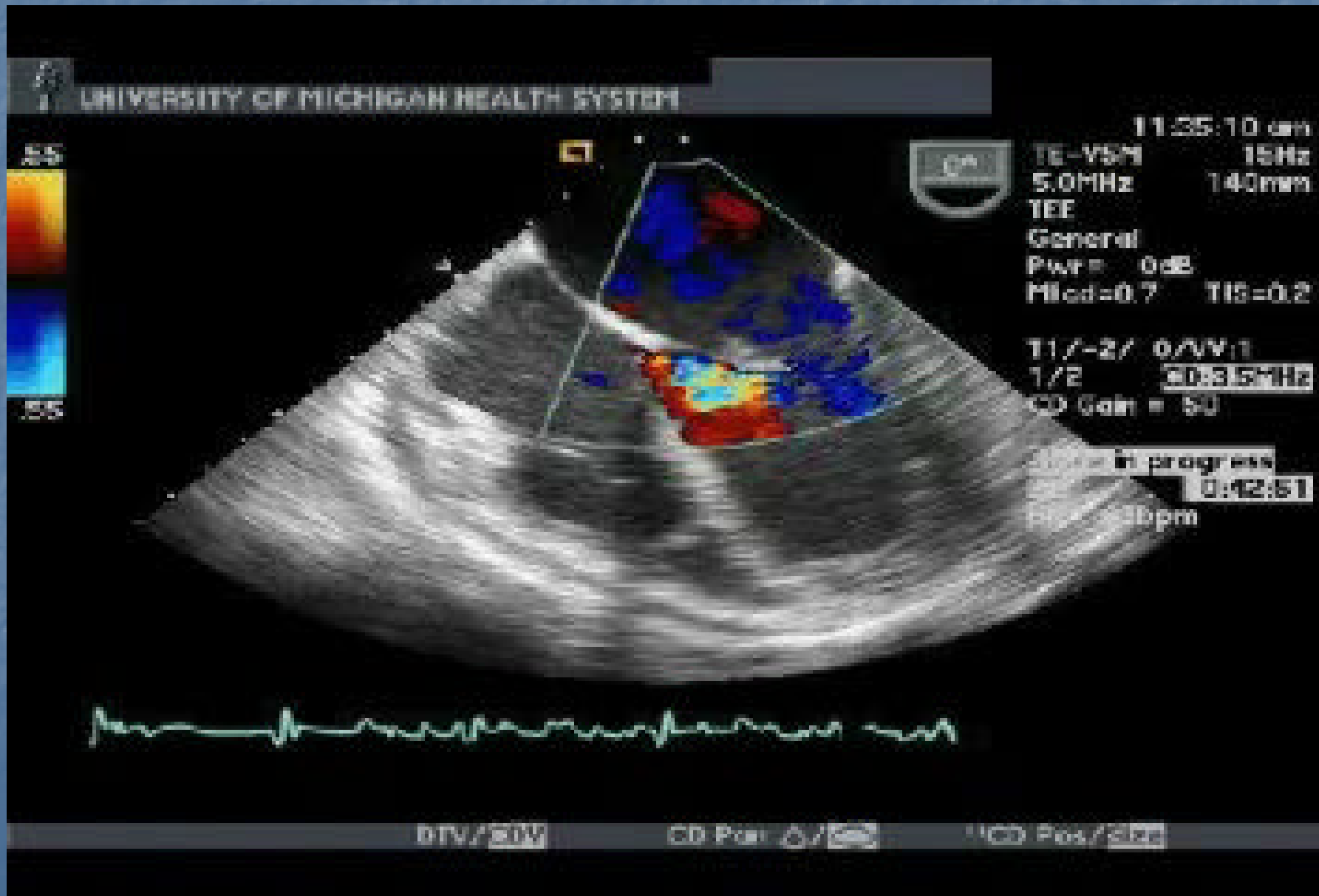
Mitral valve vegetation



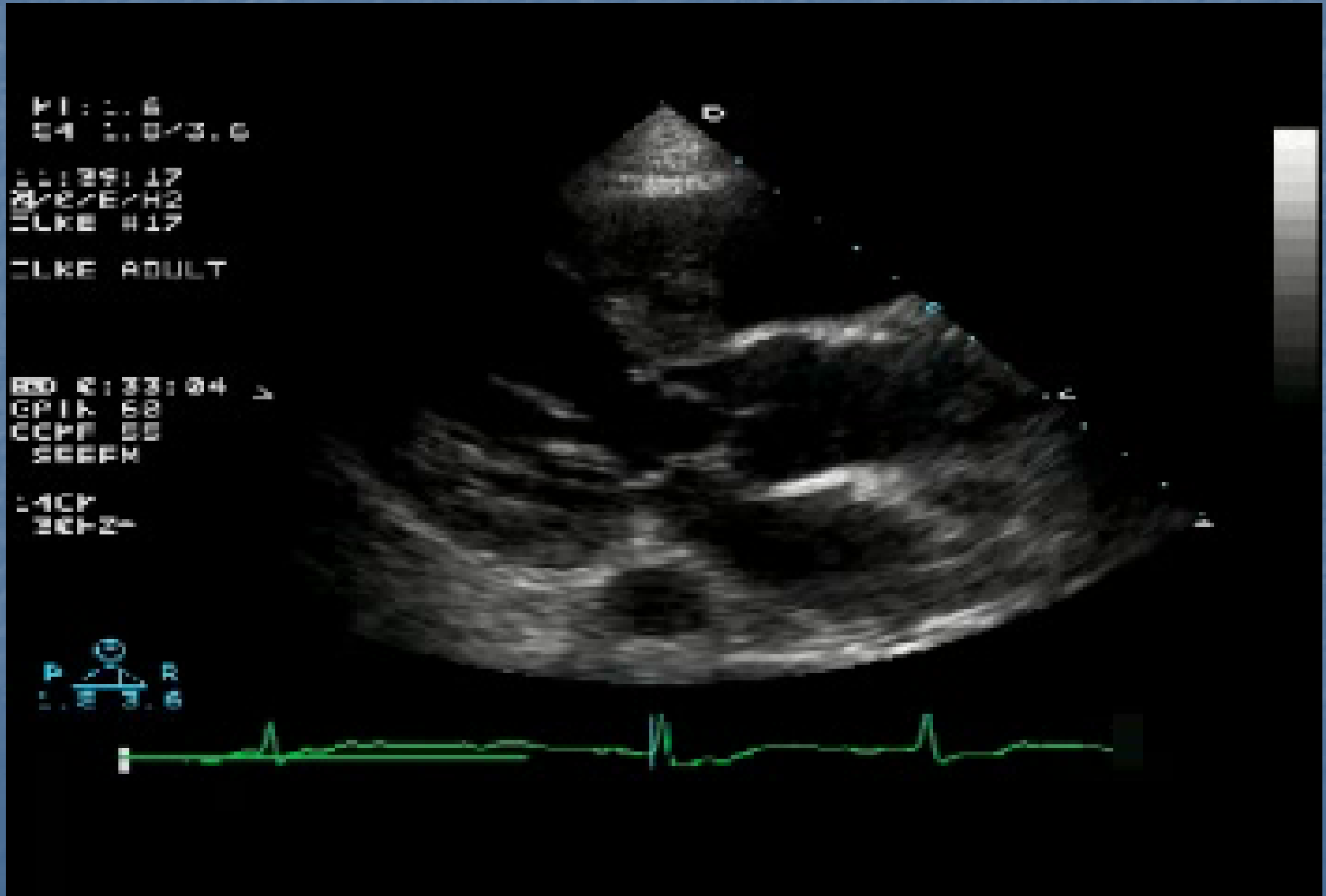
Mitral valve vegetation with perforation



Mitral valve vegetation with perforation



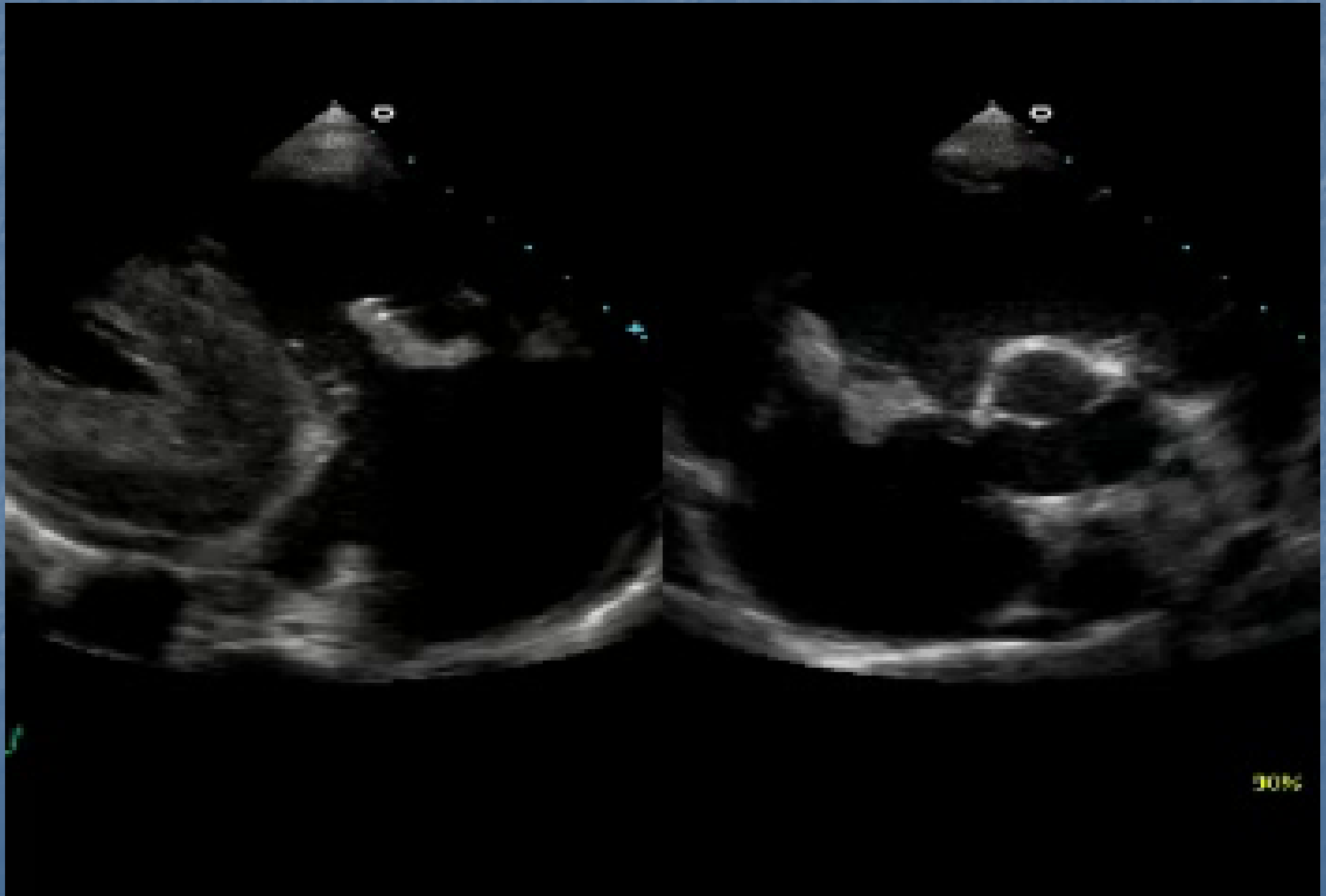
Aortic valve vegetation



Aortic valve vegetation



Tricuspid valve vegetation



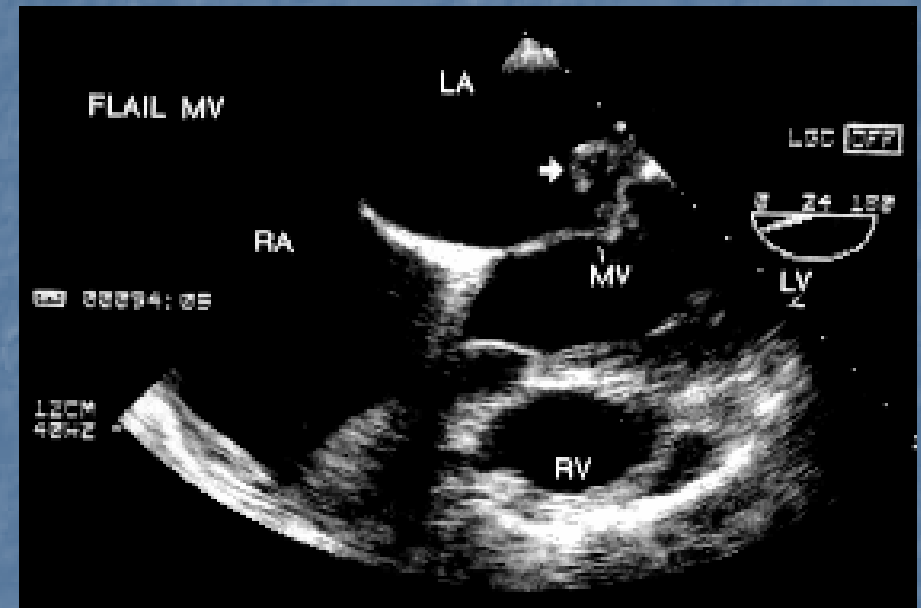
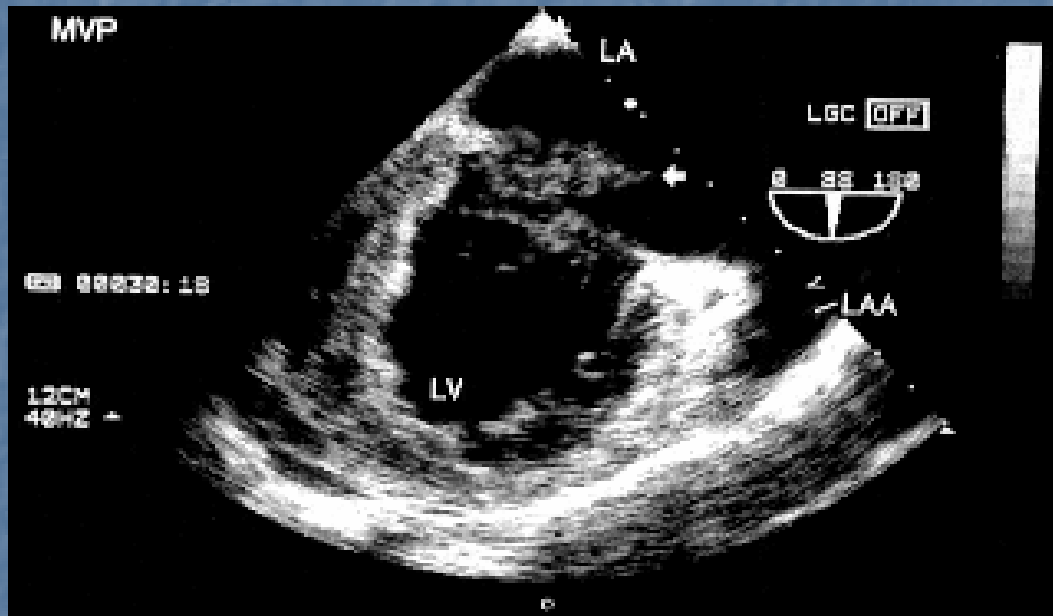
TEE Tricuspid vegetation



Echocardiographic mimics

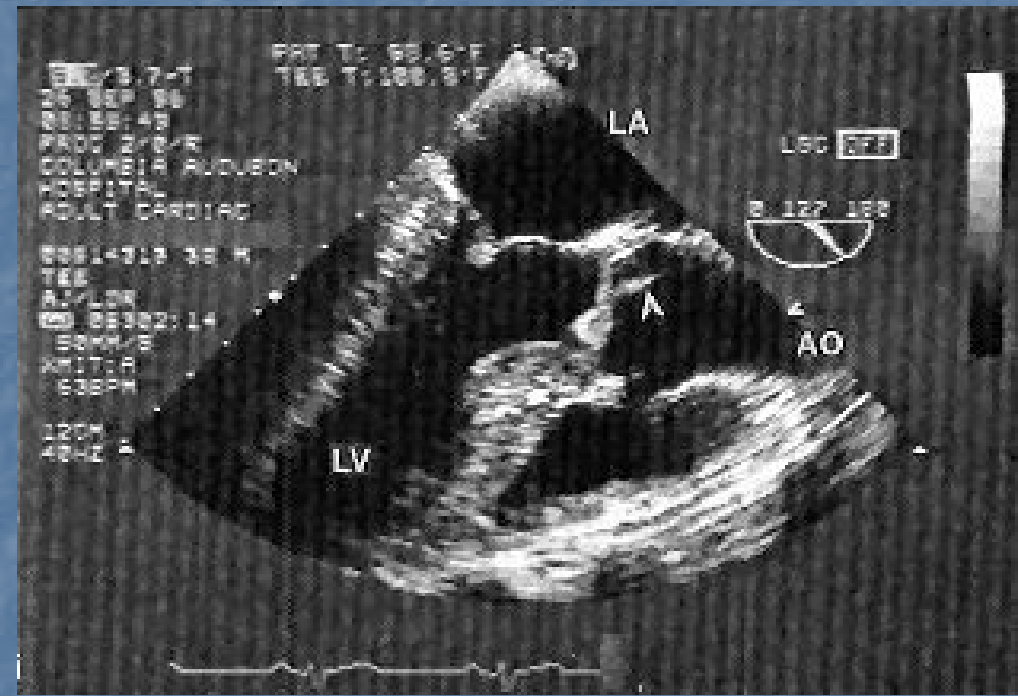
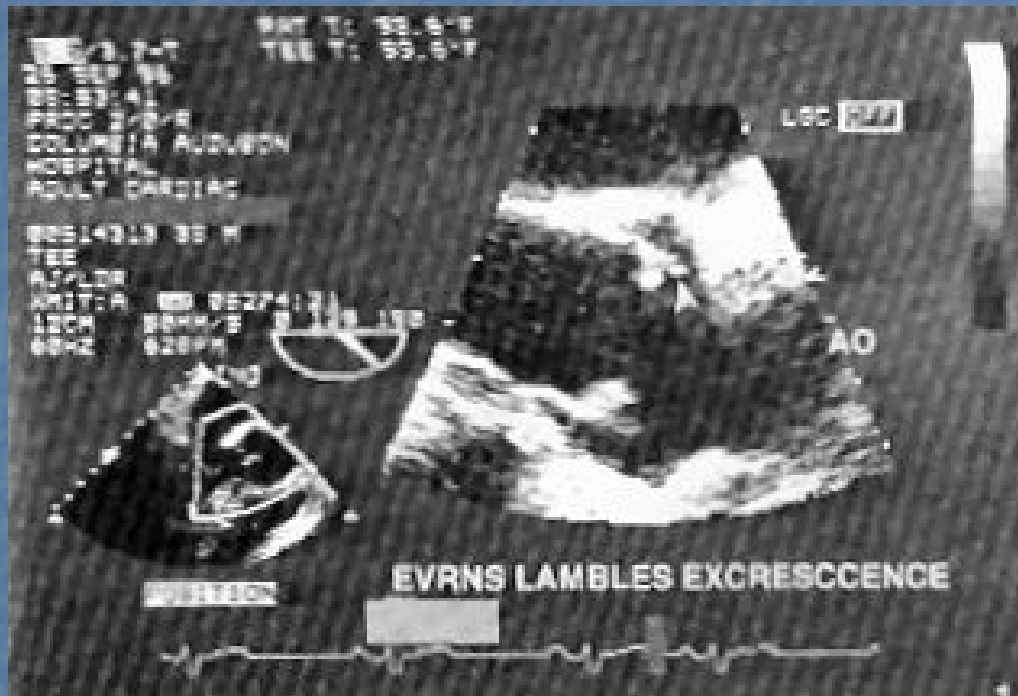
- Sterile vegetations (marantic endocarditis)
 - Libman-Sacks endocarditis
 - Systemic malignancy
- Myxomatous valves
- Cardiac tumors
- Degenerative thickening
- Lambl's excrescence – small, multiple filamentous tags on heart valves found in 70-90% of adults at autopsy

Myxomatous mitral valve



Flail myxomatous mitral valve prolapsing into left atrium

Lambli's Excrescence



Echocardiography

TTE vs. TEE

- Transthoracic
 - 18-63% sensitivity
 - Can rule out endocarditis only with good quality images and a low pre-test probability
 - Low sensitivity for detecting complications of endocarditis
- Transesophageal
 - 48-100% sensitive
 - Indicated in all cases of suspected prosthetic valve endocarditis

Nonbacterial Thrombotic Endocarditis

Libman-Sacks Endocarditis

- Etiology
 - Hypercoagulable state
 - Endothelial injury
- Found in 1.3% of patients at autopsy
 - Advanced age, malignancy, **lupus**, valvular heart disease, indwelling catheters are all risk factors
- Can convert to infective endocarditis

Device associated endocarditis



Catheter associated endocarditis



Overview of Medical Treatment

- Target therapy to blood culture
- Bactericidal antibiotics
 - β -lactam preferred
 - Monotherapy for MRSA with 1st generation cephalosporin is feasible
 - Vancomycin less bactericidal than penicillins
- Therapy for >4 weeks
 - Studies involving 2 week courses generally not as efficacious

Anticoagulation and Endocarditis

somewhat controversial

- Anticoagulation not indicated in native valve endocarditis
- In prosthetic valve endocarditis due to *Staph Aureus*, it may be beneficial to stop anticoagulation during the acute phase
- Aspirin therapy does not reduce embolic complications, and may increase bleeding

Indications for Surgery

- Heart failure refractory to medical treatment
 - NYHA class 3-4 due to endocarditis
 - Caused by aortic or mitral regurgitation (acute or subacute)
- Prosthetic valve endocarditis (most cases)
 - Medical management may suffice if
 - Late onset infection (>12 months after prosthesis)
 - Low virulence organism (viridians step, HACEK, enterococci)
 - No evidence of invasive infection
- Local invasive complications
 - Periannular extension, abscess, mycotic aneurysm, pseudoaneurysm, fistula
 - Heart block may herald local extension

Indications for Surgery

- 2 or more Major embolic events
 - A recent stroke presents higher operative risk (CVA extension)
 - Prefer to perform surgery at least 10-14 days after CVA
- Major valve dysfunction
 - Valve obstruction
 - Regurgitation
 - Leaflet perforation
- Resistance to antibiotic therapy
 - Persistent bacteremia after 7 days of antibiotics
 - Exclude extracardiac foci of infection
 - Recurrent fever is common, not necessarily an indication of antibiotic failure

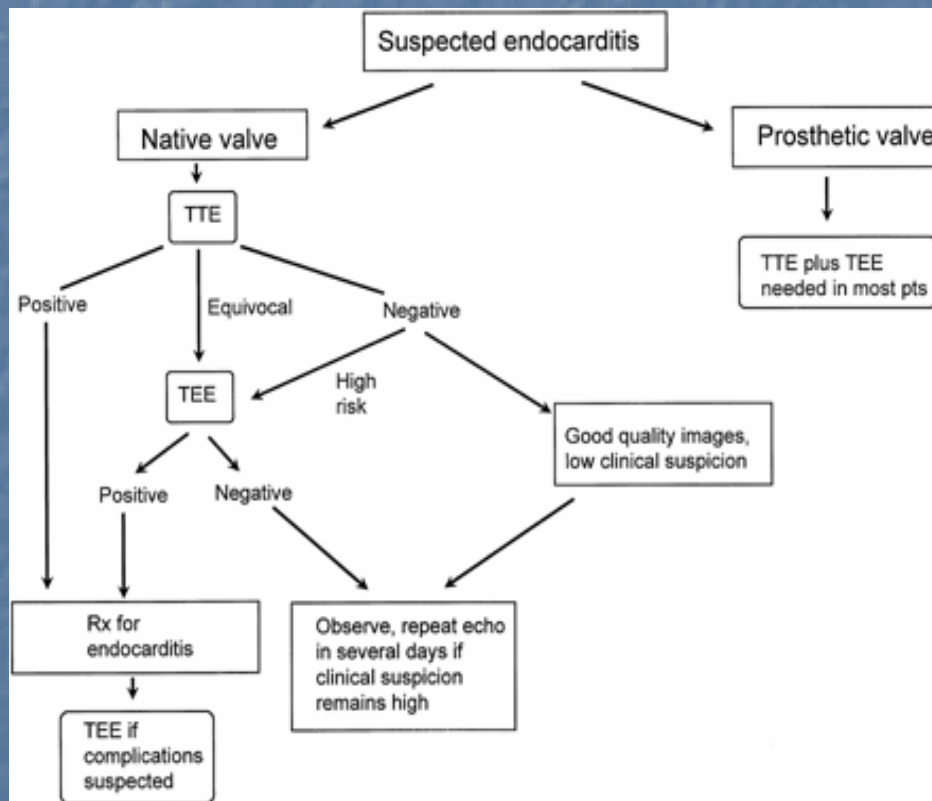
Surgical Considerations

- Surgery needed in 25-30% in acute phase, 20-40% in subacute phase
- No prerequisite for antibiotics before surgery
 - Equivalent mortality (8.5%) for patients having surgery before 10 days and after 10 days of antibiotics
- Consider early surgical intervention with aggressive pathogen (*Staph Aureus*, fungal sp.)
- Device removal almost always required for device related endocarditis

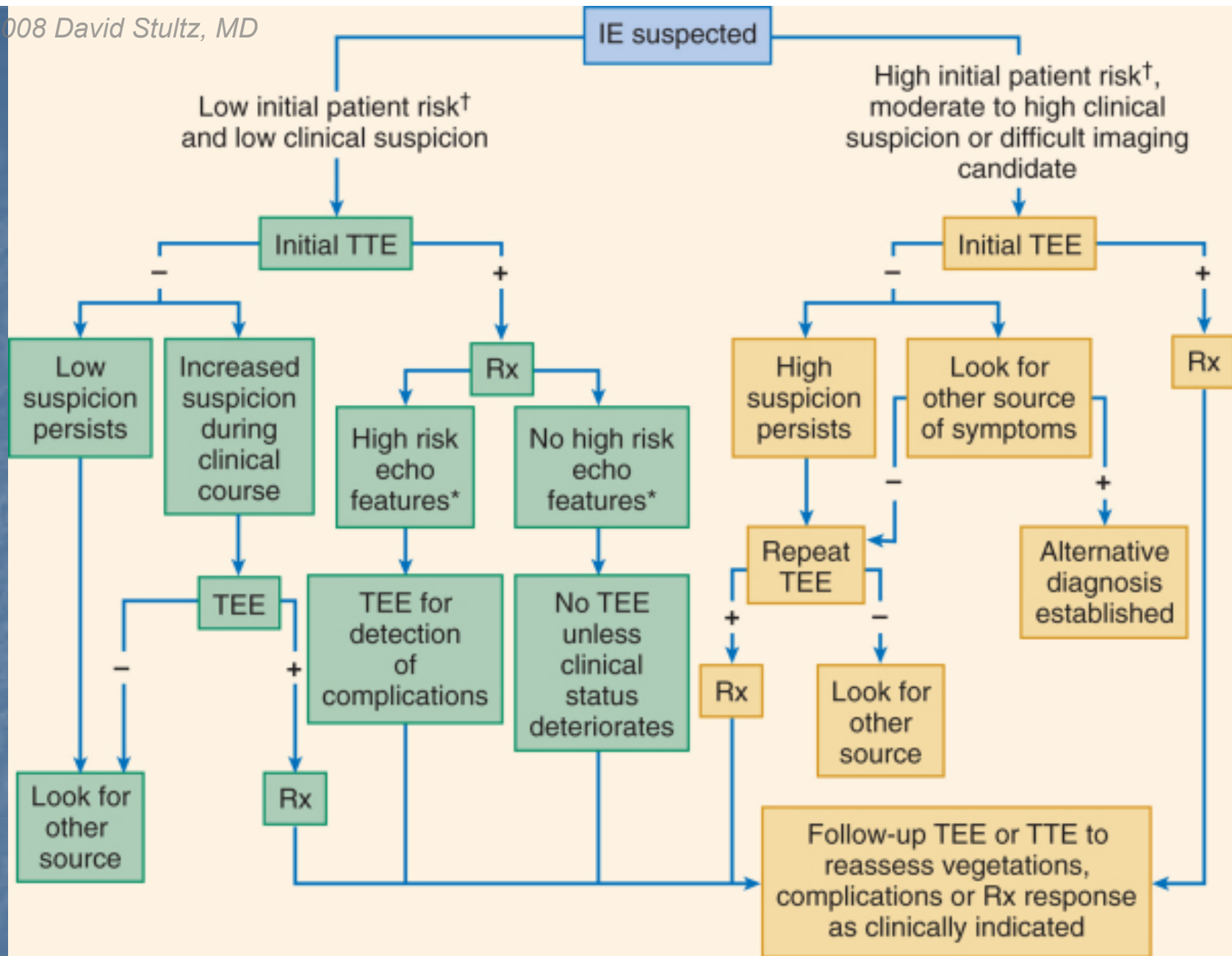
Prognosis

- Overall mortality of 20-25%
- Patients with surgical intervention have 61% survival at 10 years
- Risks of high mortality
 - Elderly
 - Aggressive pathogen (*S. Aureus*)
 - Presence of embolism
 - More extensive valve damage
 - Renal involvement
 - Longer duration of endocarditis

Diagnostic Algorithm



- TEE indicated for suspected prosthetic valve endocarditis
- TTE can rule in endocarditis
- TTE can only rule out endocarditis with good quality images and a low pre-test probability



Schematic approach to the diagnostic use of echocardiography. High-risk echocardiographic features include large vegetations, valve insufficiency, suggestion of perivalvular extension, or ventricular dysfunction. Patients with high initial risk include those with prosthetic heart valves, complex congenital heart disease, prior IE, new murmur, and heart failure. Rx indicates initiation of antibiotic therapy for IE. IE = infective endocarditis; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography. (Reproduced from Bayer AS, Bolger AF, Taubert KA, et al: Diagnosis and management of infective endocarditis and its complications. *Circulation* 98:2936-48, 1998.)

Endocarditis Prophylaxis

Endocarditis prophylaxis Redefined 2007

- Why update the guidelines?
- IE is much more likely to result from frequent exposure to random bacteremias associated with daily activities 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.
- 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.

Guidelines seek a balance

Why did they change them???

- Prophylaxis recommended for patients with highest risk of infection and/or highest risk of complications
- Risk of death from penicillin anaphylaxis is estimated at 15-25 per million (33% with known allergy)
- Estimated 5370 minutes of bacteremia per month in dentulous people (based on chewing, brushing teeth, flossing)
- Estimated 6 to 30 minutes of bacteremia from a tooth extraction

Endocarditis prophylaxis for dental procedures

Antibiotic prophylaxis with dental procedures is recommended only for patients with cardiac conditions associated with the highest risk of adverse outcomes from endocarditis, including:

- Prosthetic cardiac valve
- Previous endocarditis
- Congenital heart disease only in the following categories:
 - Unrepaired cyanotic congenital heart disease, including those with palliative shunts and conduits
 - Completely repaired congenital heart disease with prosthetic material or device, whether placed by surgery or catheter intervention, during the first six months after the procedure*
 - Repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)
- Cardiac transplantation recipients with cardiac valvular disease

**Prophylaxis is recommended because endothelialization of prosthetic material occurs within six months after the procedure.*

Which Dental procedures need prophylaxis?

- All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth, or perforation of the oral mucosa
- **Antibiotic prophylaxis is NOT recommended for the following dental procedures or events:**
 - routine anesthetic injections through noninfected tissue
 - taking dental radiographs
 - placement of removable prosthodontic or orthodontic appliances
 - adjustment of orthodontic appliances
 - placement of orthodontic brackets
 - shedding of deciduous teeth and bleeding from trauma to the lips or oral mucosa.

Other procedures

- Endocarditis prophylaxis no longer recommended for gastrointestinal and genitourinary procedures
- Prophylaxis is recommended for respiratory procedures (except routine bronchoscopy without biopsy)
- Recommended for procedures involving manipulation of *infected* skin, skin structure or musculoskeletal structure

Notable lesions no longer recommended for prophylaxis

- Rheumatic heart disease
- Valvular stenosis
- Valvular regurgitation

Prophylaxis Regimen

Regimen – Single dose 30–60 minutes before procedure

Situation

Agent

Adults

Children

Oral

Amoxicillin

2 gm

50 mg/kg

Unable to take oral medication

Ampicillin

2 g IM or IV*

50 mg/kg IM or IV

OR

Cefazolin or ceftriaxone

1 g IM or IV

50 mg/kg IM or IV

Allergic to penicillins or ampicillin – Oral regimen

Cephalexin**†

2 g

50 mg/kg

OR

Clindamycin

600 mg

20 mg/kg

OR

Azithromycin or clarithromycin

500 mg

15 mg/kg

Allergic to penicillins or ampicillin and unable to take oral medication

Cefazolin or ceftriaxone[†]

1 g IM or IV

50 mg/kg IM or IV

OR

Clindamycin

600 mg IM or IV

20 mg/kg IM or IV

Pearls for the Boards

- Association of *Strep. Bovis* with GI malignancy, especially colon cancer
- Identify patients who should and should not receive endocarditis prophylaxis
 - Prosthetic valves
 - Prior endocarditis
 - Cardiac transplant with valvular disease
 - Unrepaired cyanotic congenital heart disease
 - Completely repaired cyanotic CHD for 1st 6 months after repair
- Recognize that a prosthetic valve with endocarditis will most likely need surgical treatment

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