Vascular Graft Infections

Walter R. Wilson, M.D.
Professor of Medicine
Edward C. Rosenow, III, M.D. Professorship in the Art of Medicine

Mayo Clinic

Division of
INFECTIOUS DISEASES

Mayo Clinic Infectious Diseases Subspecialties Update
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Vascular Graft Infection

- History
- Definition
  - Extracavitary
  - Intracavitary
- Diagnosis
  - Clinical presentation
  - Imaging
- Management
  - Medical
  - Surgical
- Prognosis

Vascular Graft Infections

- Synthetic material first used in 1950s
  - France 1951
  - DeBakey – 1953
  - Early infection rate 30-80%

VAH HOSPITAL HOUSTON 1950’S

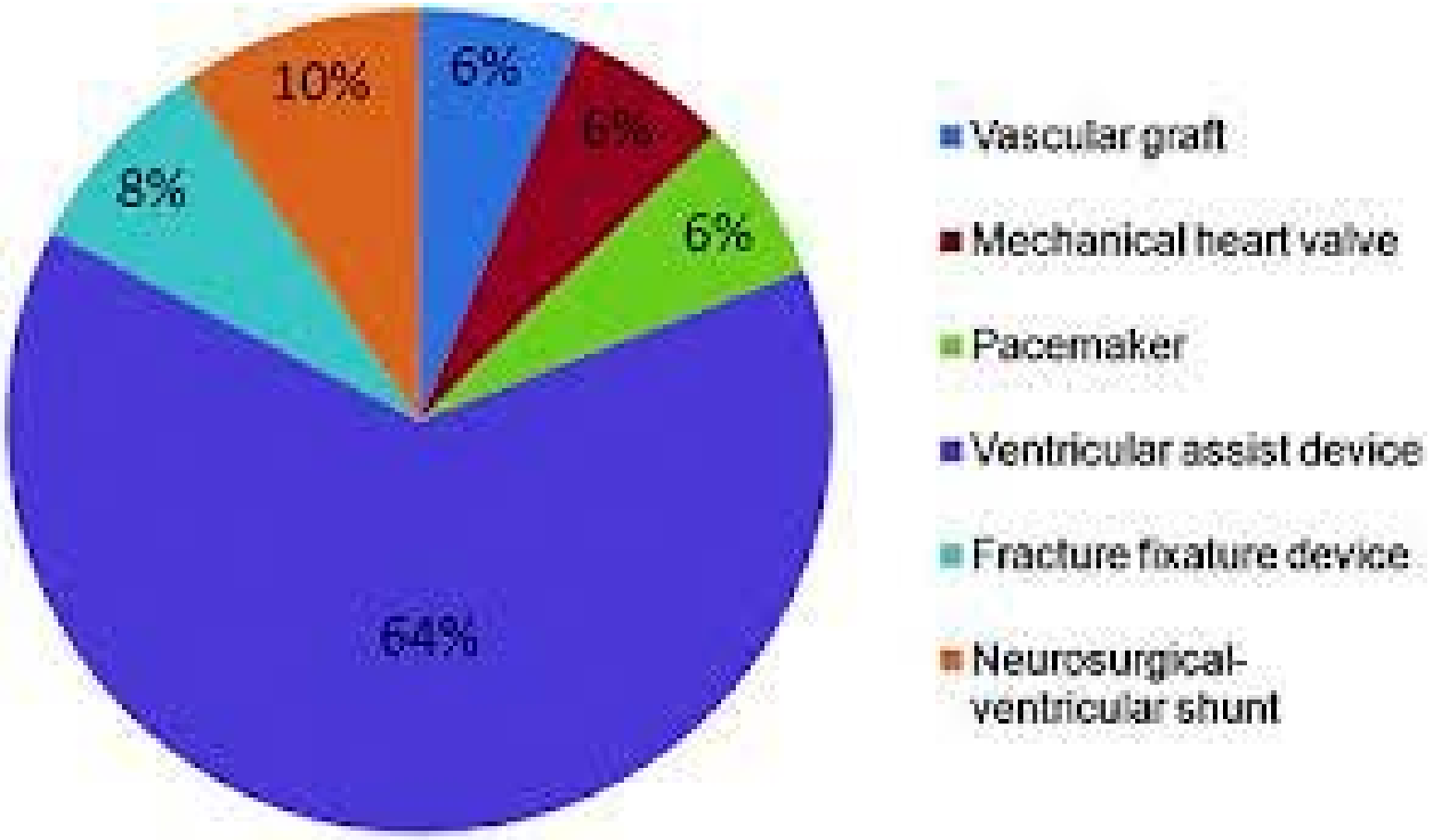
Vascular Graft Infections Definition

- Extracavitary
  - Groin 80%
  - Peripheral 20%
- Intracavitary
  - Intra-abdominal 70%
  - Intrathoracic 30%

Vascular Graft Infections

- Frequency
  - Extracavitary 1.5-2%
    - Groin 3-6%
  - Intracavitary 1-5%
    - Duodenal – aorta fistula 1-2% with aortic reconstruction

PERCENTAGE INFECTION PROSTHESES



Vascular Graft Infections Microbiology

- Extracavitary
  - Coag-neg Staph. 40%
  - S. aureus 30%
  - Gram-negative bacillus 10%; Pseudomonas most common
- Intracavitary
  - Coag-neg Staph. 30%
  - S. aureus 30%
  - Gram-negative, polymicrobial 35%

Vascular Graft Infections Pathogenesis

- Extracavitary
  - Wound infection in groin
  - Intraoperative contamination
- Intracavitary
  - Intraoperative contamination 50%
  - Enteric fistulae; duodenum 30%, rarely colon
  - Contiguous spread 10-15%
  - Bacteremia infection 5-10%

Vascular Graft Infections
Diagnosis – General Principles

- Index suspicion
- Different clinical presentations
  extracavitary, intracavitary
- Time of onset postop
- Physical findings
- Laboratory tests, cultures, draining sinus, perigraft fluid, surgical specimens
- Imaging

Vascular Graft Infections
Extracavitary - Diagnosis

- Clinical Presentation
  - Early onset - <2 months postop
    - Sepsis
    - Wound erythema
    - Sinus tract
    - Distal ischemia
    - Septic emboli
    - Graft rupture

Vascular Graft Infections
Extracavitary - Diagnosis

- Clinical Presentation
  - Late onset - >2 months
    - Less often present with sepsis
    - Indolent; groin erythema
    - Sinus tract
    - Erosion graft through skin
    - Pseudoaneurysm - rupture

Vascular Graft Infections
Extracavitary – Samson Classifications (Group 1-5)

Group	
1	No deeper than dermis
2	Subcutaneous tissue No direct contact with graft
3	Body of graft but not anastomosis
4	Exposed anastomosis, no bleeding, no bacteremia
5	Anastomosis involved bleeding, bacteremia

*Samson et al: J Vas Surg 8:147, 1988

Vascular Graft Infections
Extracavitary - Diagnosis

- Imaging
  - Individualize
  - Combination often required
  - Sinograms – only in select patients; risk of introduction of infections, less useful than other imaging
  - Angiography – Not useful for diagnosis, used to define anatomy for revascularization; CTA used more commonly now

Vascular Graft Infections
Extracavitary – Diagnosis

- Local swelling groin; no drainage – Samson 1 or 2

Ultrasound

- Dermis only
  - Samson 1
- Subcutaneous abscess
- Does not extend to graft
- Ultrasound nondiagnostic
- CT/MRI
- I&D
- No graft involvement
  - Samson 2

Vascular Graft Infections
Extracavitary – Treatment

- Samson 1 – antibiotic therapy alone
- Samson 2 – I&D, antibiotic therapy
- Antimicrobial therapy 2-4 weeks

Vascular Graft Infections
Extracavitary – Diagnosis

- Open draining wound groin, sinus tract
  - Ultrasound, CT, MRI, PET/CT, Indium scan
  - I&D

Graft involved but not anastomosis No bleeding from anastomosis	Infection surrounds graft Anastomosis exposed No bleeding BC negative	Anastomosis involved bleeding Pseudoaneurysm BC positive
Samson 3	Samson 4	Samson 5

Vascular Graft Infections
Extracavitary – Treatment
Samson 3

- Aggressive I&D, irrigation
- Surgery
  - Preservation; in situ reconstruction
  - Wound coverage , VAC, flap
- Antimicrobial therapy 4-6 weeks

Vascular Graft Infections
Extracavitary – Diagnosis

- Open draining wound groin, sinus tract
  - Ultrasound, CT, MRI, PET/CT, Indium scan
  - I&D

Graft involved but not anastomosis No bleeding from anastomosis	Infection surrounds graft Anastomosis exposed No bleeding BC negative	Anastomosis involved Bleeding Pseudoaneurysm BC positive
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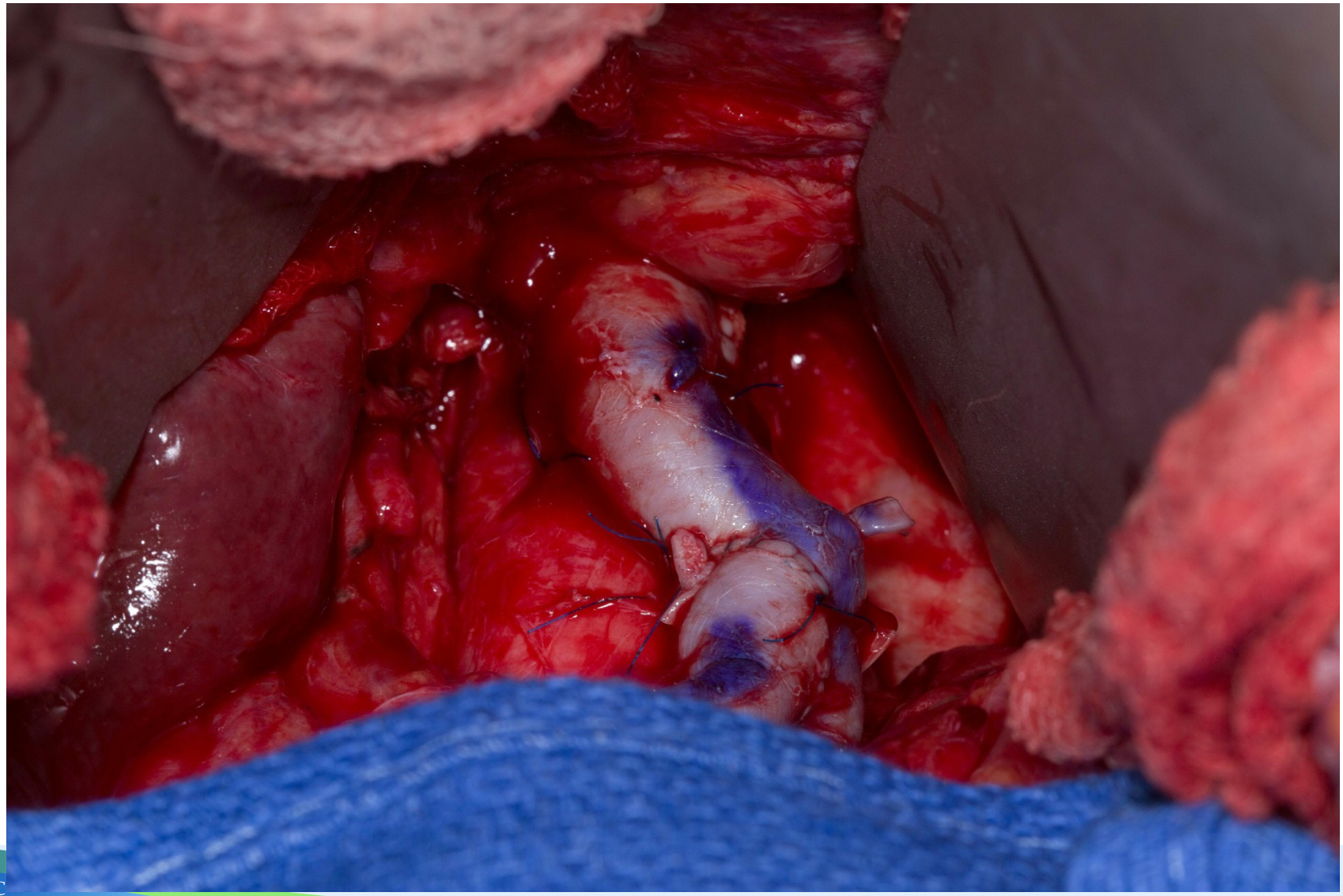
Samson 4



Vascular Graft Infections
Extracavitary – Treatment
Samson 4

- Aggressive I&D, irrigation
- Surgery
  - Preservation; in situ reconstruction
  - Wound coverage , VAC, flap
- Antimicrobial therapy 4-6 weeks

Vascular Graft Infections
Extracavitary – Diagnosis

- Open draining wound groin, sinus tract
  - Ultrasound, CT, MRI, PET/CT, Indium scan
  - I&D

Graft involved but not anastomosis No bleeding from anastomosis	Infection surrounds graft Anastomosis exposed No bleeding BC negative	Anastomosis involved bleeding Pseudoaneurysm BC positive
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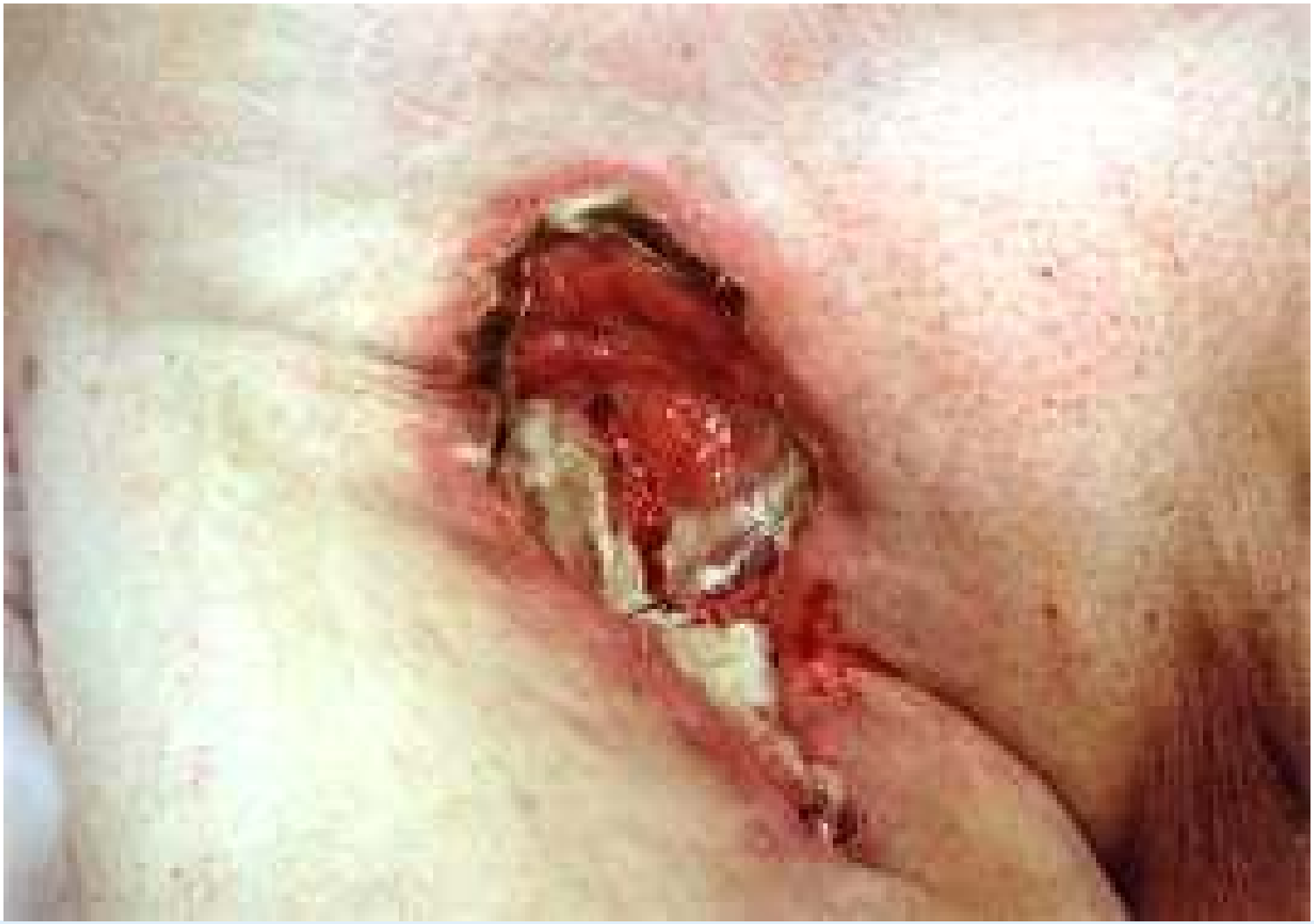
SAMSON 5



Samson 5

Vascular Graft Infections
Extracavitary – Treatment
Samson 5

- Control bleeding
- Pseudomonas, MRSA, poor prognosis
- Surgery
  - Extravascular reconstruction
  - Graft excision
  - Wound coverage, VAC, flap
- Antimicrobial therapy 4-6 weeks, lifelong suppressive selected patients

Vascular Graft Infections
Extracavitary Prognosis

- Samson 1, 2 – excellent
- Samson 3-5
  - Operative mortality – 1-18%; Samson 5 – 15-18%
  - Amputation
    - Samson 3 – 1-2%
    - Samson 4 – 10-15%
    - Samson 5 – 15-18%
  - Recurrence infection – Depends on Samson classification
    - Samson 1, 2 – 1-2%
    - Samson 3-5 – 15-20%

*Calligaro et al: J Vasc Surg 22:680, 1995

Vascular Graft Infections Definition

- Extracavitary
  - Groin 80%
  - Peripheral 20%
- Intracavitary
  - Intra-abdominal 70%
  - Intrathoracic 30%

Vascular Graft Infections Intracavitary

- Intra-abdominal
  - Enteric fistulae
- Intrathoracic

Vascular Graft Infections Microbiology

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Vascular Graft Infections
Intra-abdominal – Diagnosis

- Clinical presentation
  - May present months to years postop
  - Abdominal pain; sepsis
  - Duodenal fistulae – mixed polymicrobial, intermittent, bacteremia
  - GI bleeding – subtle or massive
  - Peripheral ischemia, emboli

Vascular Graft Infections
Intra-abdominal – Diagnosis

Clinical Presentation
Sepsis Syndrome

Monomicrobial bacteremia

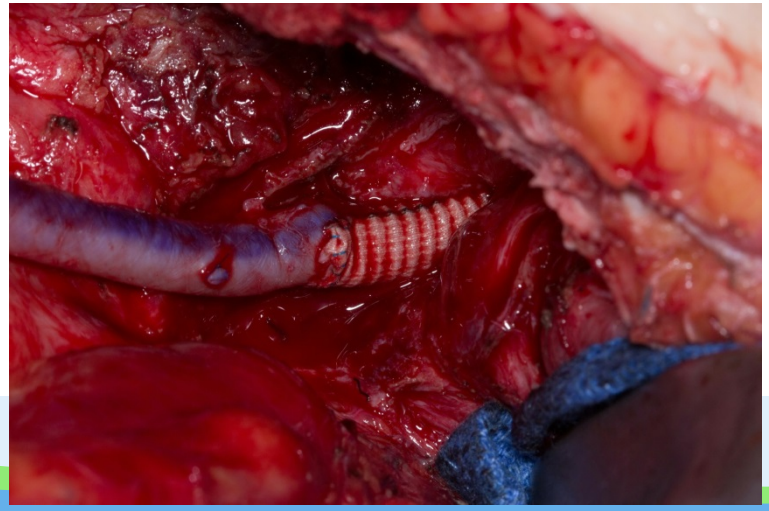
CT first choice

- PET/CT
- Indium scan

Polymicrobial bacteremia; GI bleeding

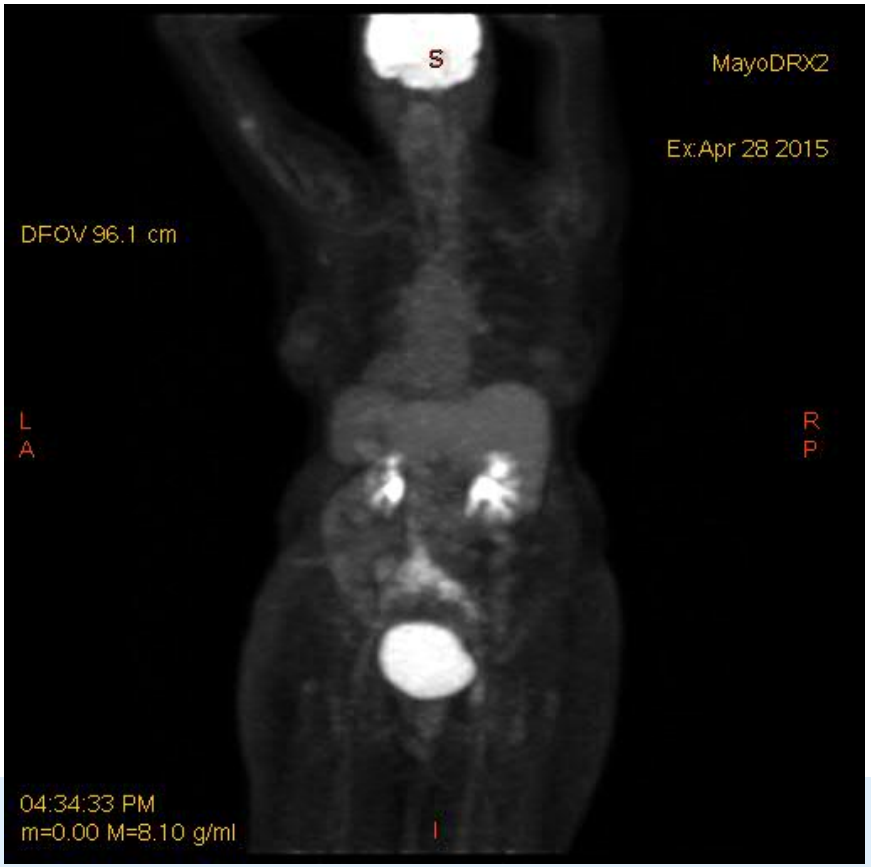
EGD – duodenal fistulae

- MRI/PET/CT
- Indium scan



Vascular Graft Infections
Intra-abdominal – Diagnosis

Imaging	Sensitivity	Specificity (%)
• CT	85-100	85-94
• MRI	68-85	97-100
• PET/CT	78-96	70-93
• Indium scan	67-73	87



Vascular Graft Infections
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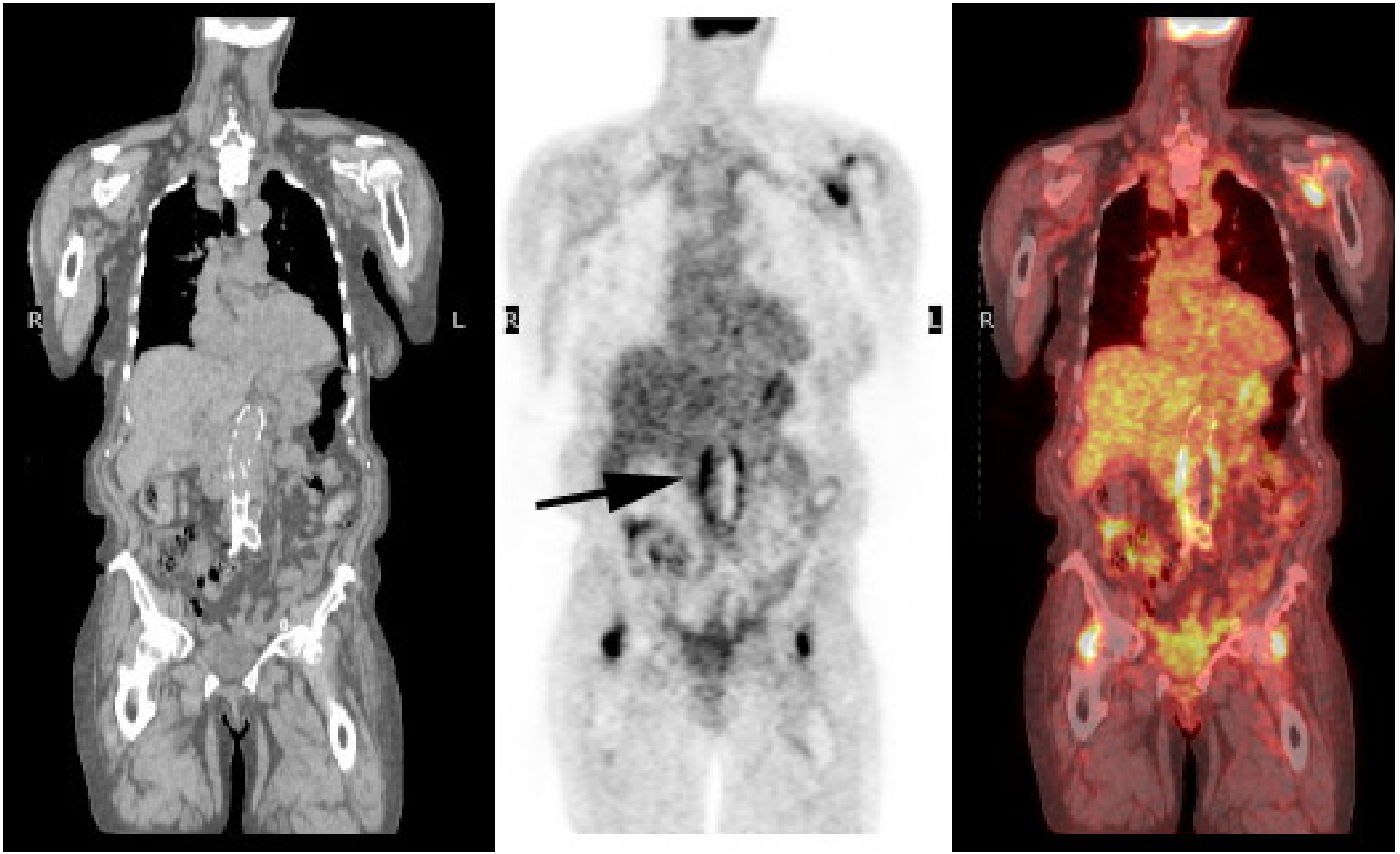
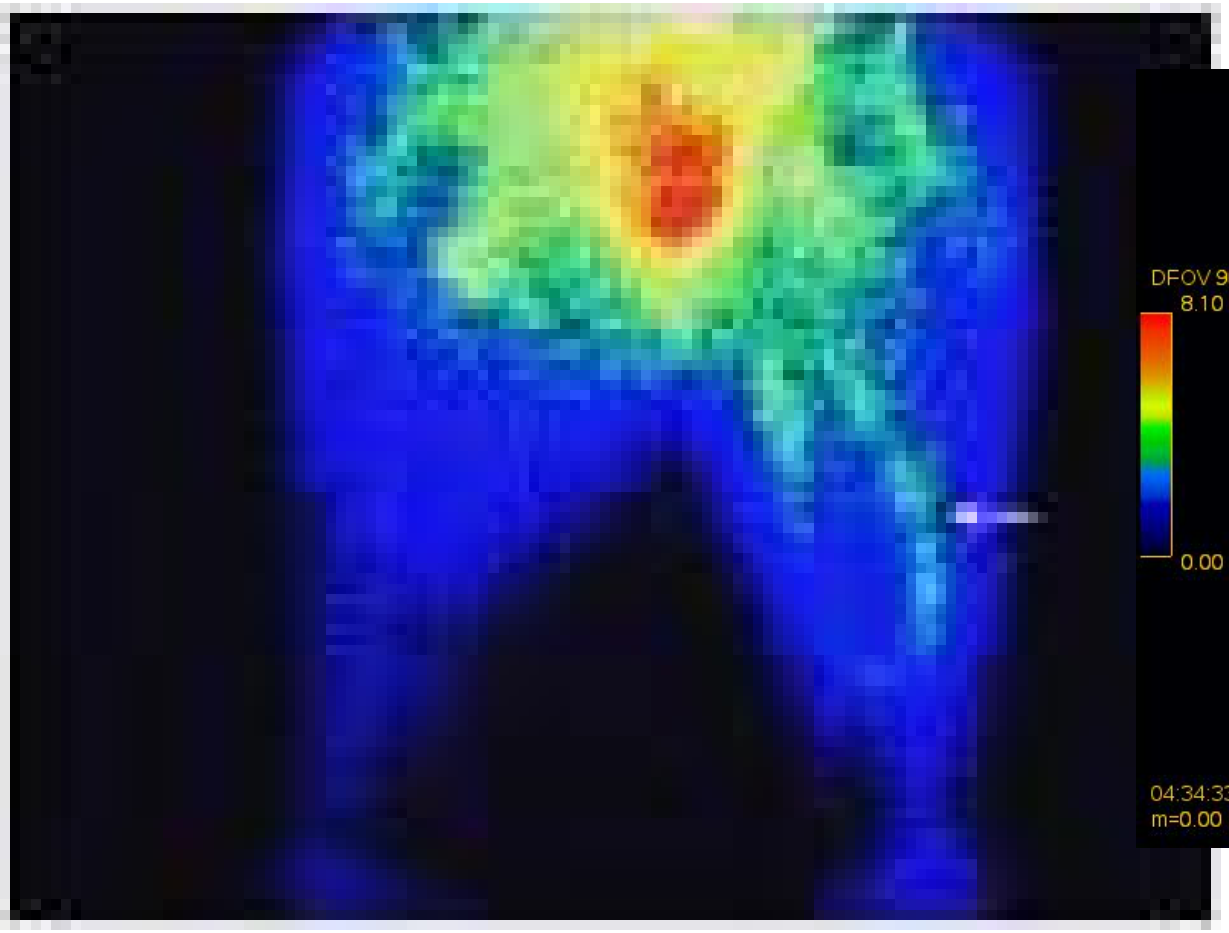
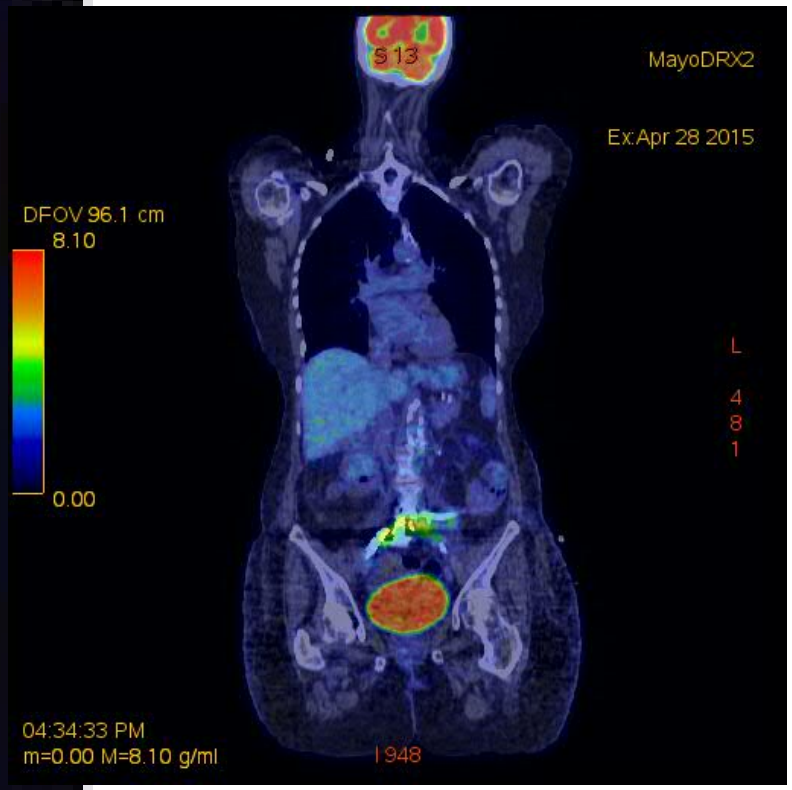
*Sah et al: Eur J Vas Endovas Surg 49:455, 2015

PET-CT



PET-CT

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Vascular Graft Infections
Intra-abdominal – Diagnosis

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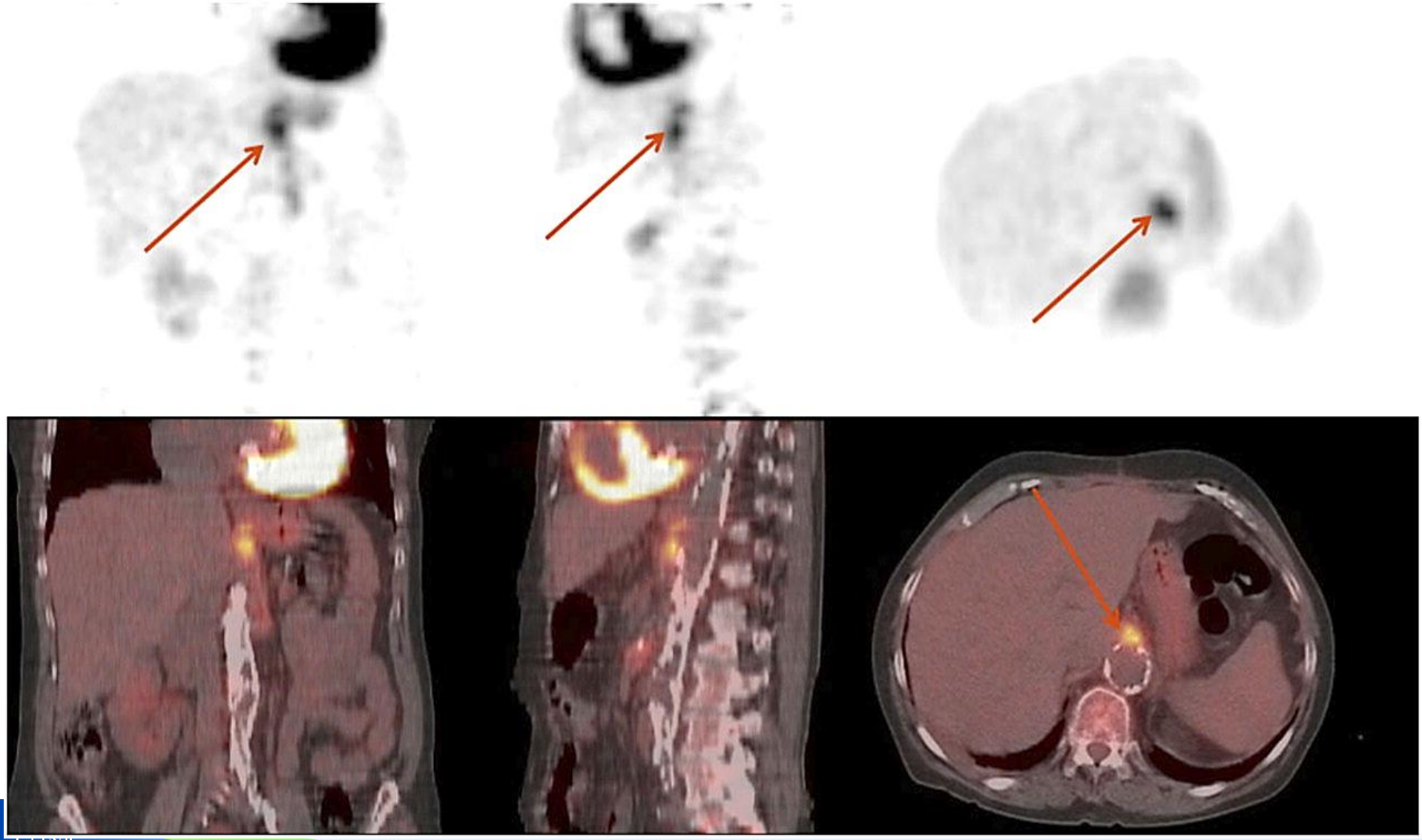
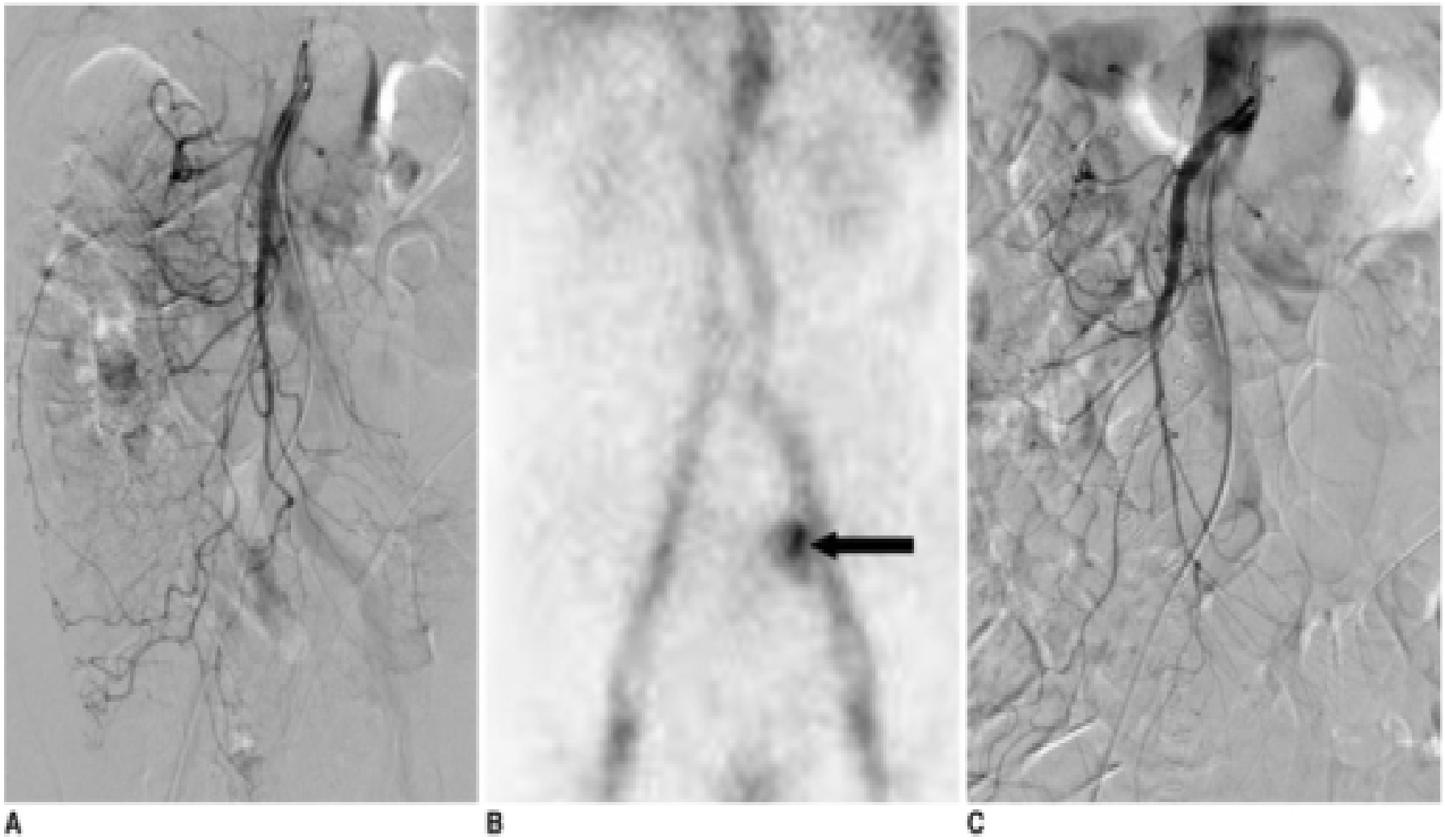
PET-CT; Indium Scan




A
B
C

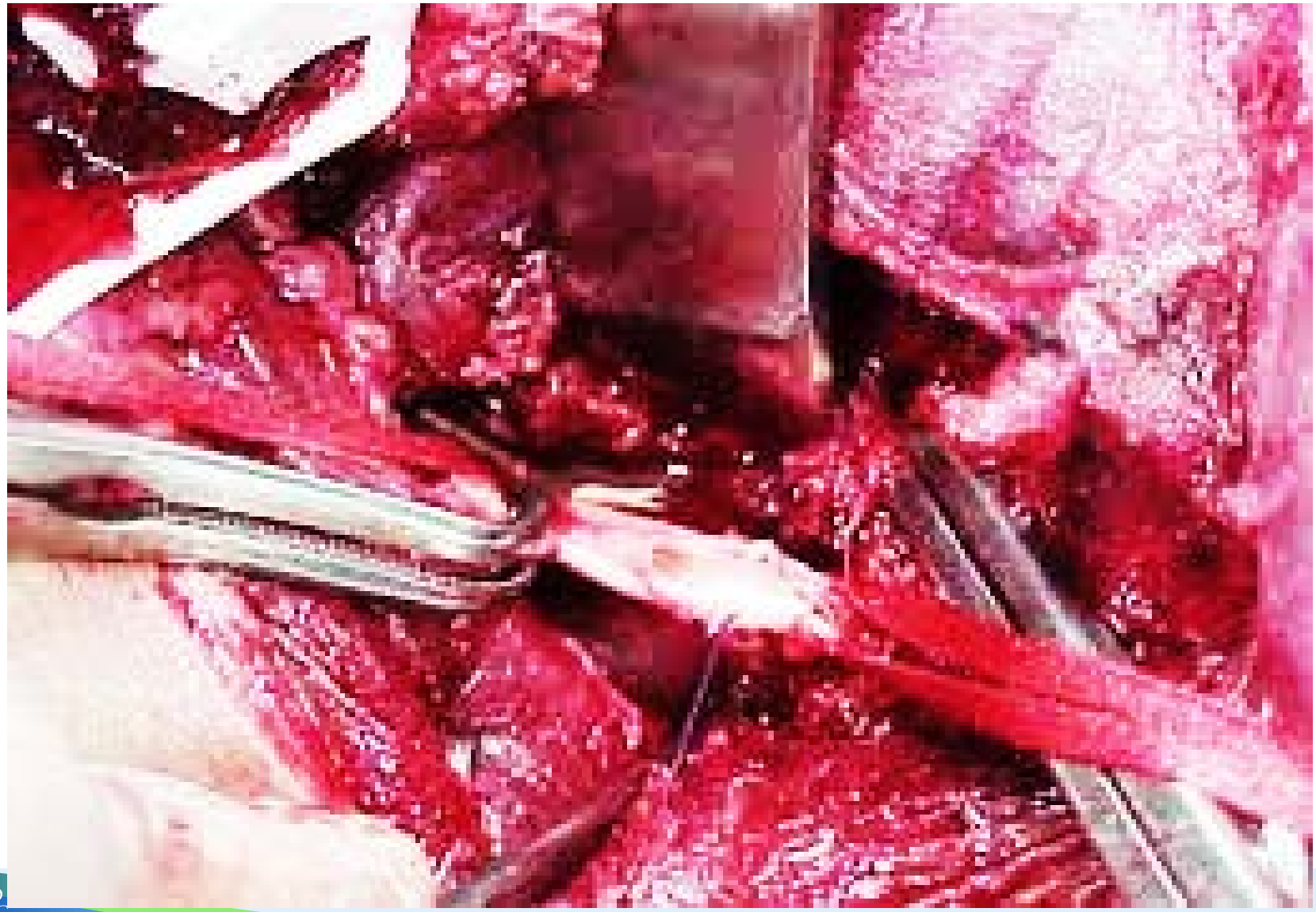
Vascular Graft Infections
Intra-abdominal - Management

- Surgery
  - Graft excision; in situ reconstruction
    - Cryopreserved arterial allograft
    - Autogenous venous graft
    - Rifampin or silver coated grafts
  - Extra-anatomic reconstruction; then graft excision

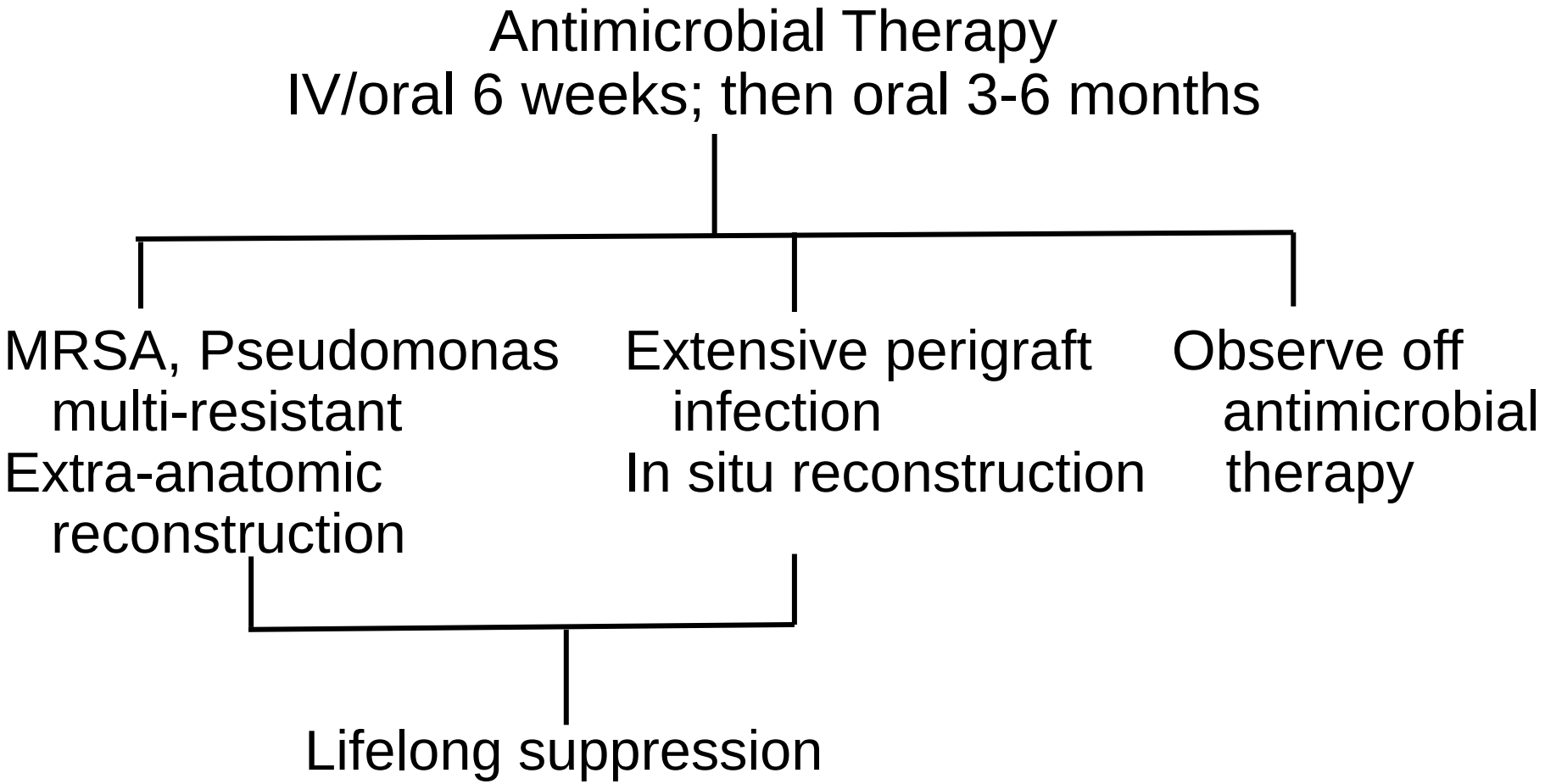
Vascular Graft Infections
Intra-abdominal – Management

- Surgery
  - Aorto-enteric fistulae
    - Excision, in situ reconstruction
  - MRSA, Pseudomonas, multiply drug resistant
    - Extra-anatomic reconstruction; graft excision

Intra-Abdominal In Situ Reconstruction



Vascular Graft Infections
Intra-abdominal – Management



Vascular Graft Infections
Intra-abdominal – Prognosis

- In situ
  - Perioperative mortality – 13-15%
  - Two; five year survival – 97%; 82%
- Extra-anatomic
  - Perioperative mortality 20%
  - Amputation rate 5%
  - Early graft failure 20%
  - 30 month survival, with no amputation 50-60%

Vascular Graft Infections
Intrathoracic – Diagnosis

- Clinical presentation
  - Present like IE or PVE
  - Sepsis
  - Chest pain
  - Rupture with massive bleeding

Vascular Graft Infections
Intrathoracic – Diagnosis

Clinical Presentation

IE/PVE

- TEE
  - Nondiagnostic or extensive infection
- CT/MRI, PET/CT

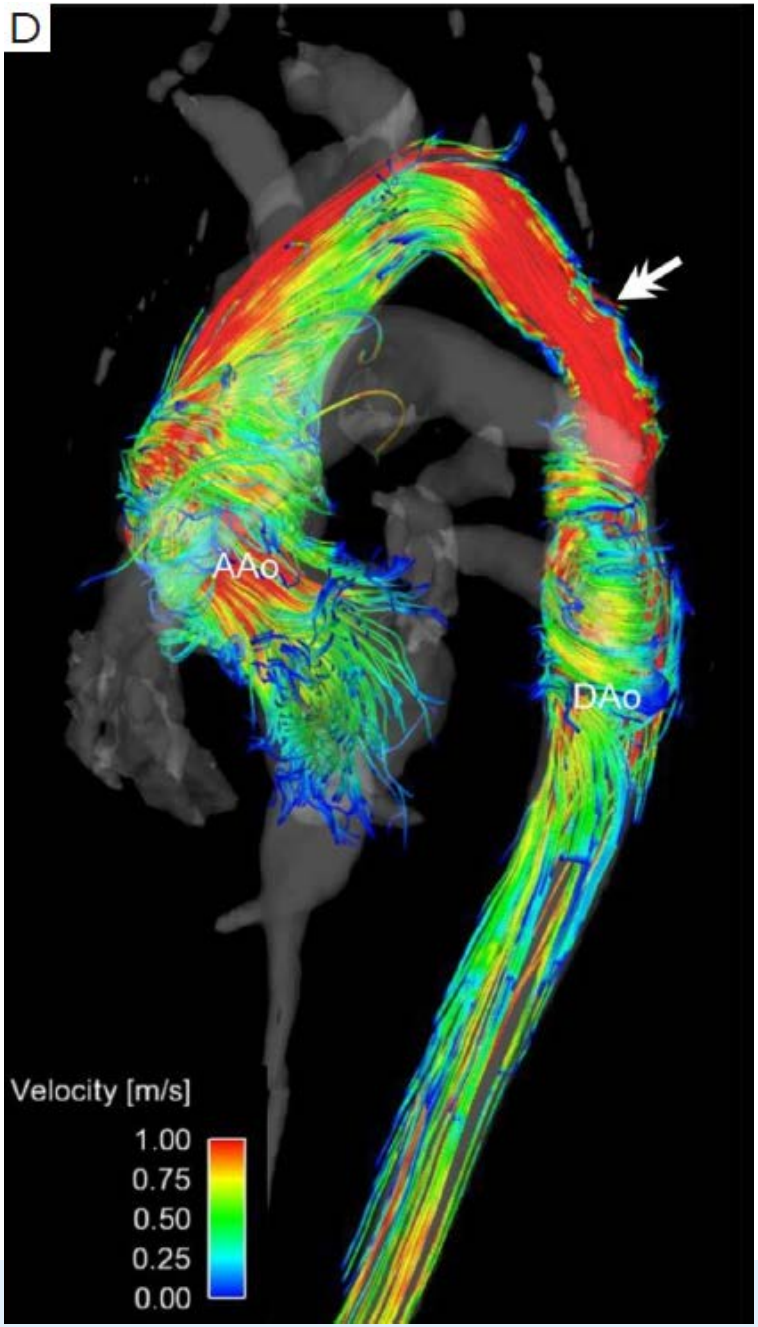
Aortic Graft

- CT/MRI
  - Inconclusive
- TEE, PET/CT
- PET/CT/MRI

Vascular Graft Infections Intrathoracic – Diagnosis

Clinical Presentation

IE/PVE	Aortic Graft
• TEE	• CT/MRI
• Nondiagnostic or extensive infection	• Inconclusive
• CT/MRI, PET/CT	• TEE, PET/CT • PET/CT/MRI



Vascular Graft Infections
Intrathoracic – Management

- Treat complications of IE, PVE
- In situ arterial allograft preferred
- Less experience with venous autograft
- Avoid rifampin synthetic graft because of risk infection
- Antimicrobial therapy 4-6 weeks; then 3-6 months, lifelong suppression in selected patients

Staphylococcus aureus Bacteremia: A Wolf that May Arrive in Sheep's Clothing

Daniel J. Sexton MD FACP

Professor, Department of Medicine

Director, Duke Infection Control Outreach Network

Duke University Medical Center

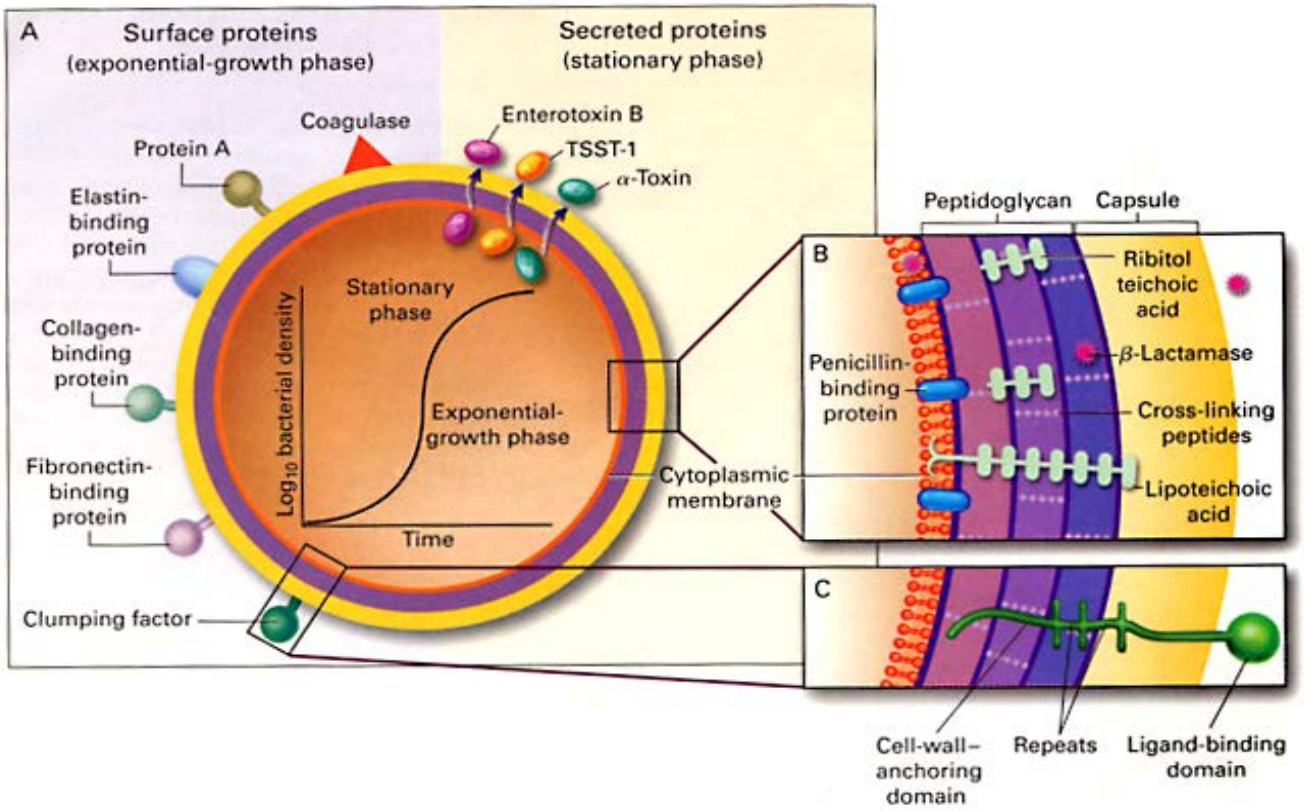
Goals of This Talk

- To discuss relevant old and new literature
- To discuss general principles of management
- To discuss a few ongoing unresolved clinical and scientific questions
- **To instill or reconfirm a sense of great respect for this frequently lethal sometimes curable infection**

The Big Picture

- SAB is common and becoming more frequent
- SAB is lethal without proper treatment and outcomes are often poor even with proper treatment.
- The management of SAB requires careful bedside evaluation(s), knowledge about its natural history and pitfalls and clinical skill in therapy. (i.e. effective treatment is NOT simply a matter of matching the bug with a a drug or treating for one moon cycle)

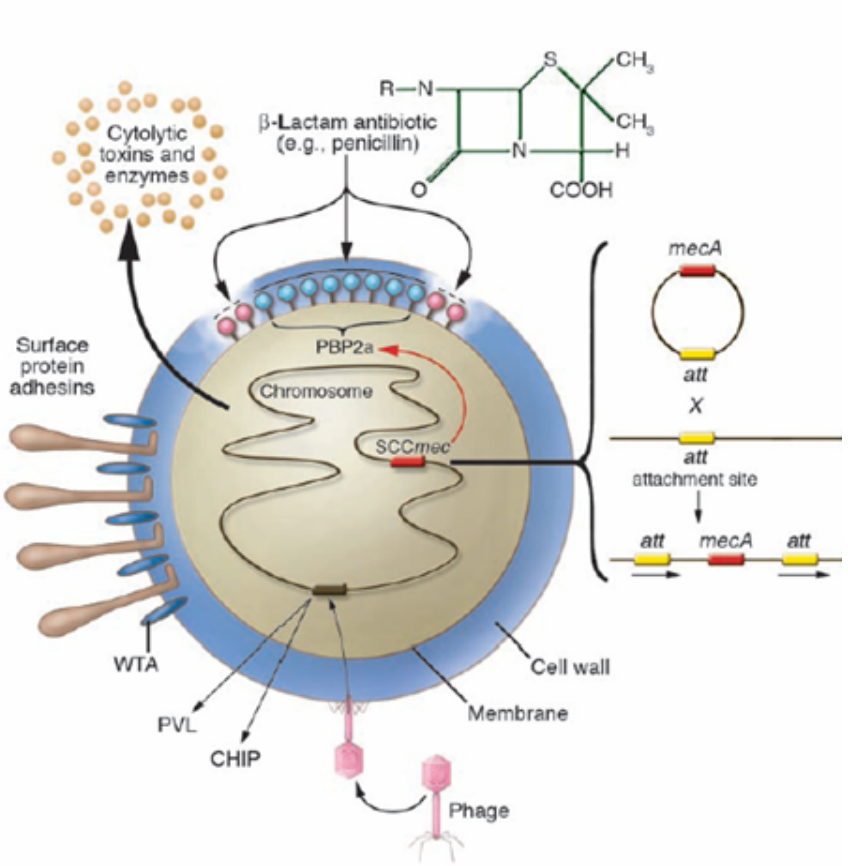
S. aureus
A Unique Organism



Lowy, NEJM 1998.

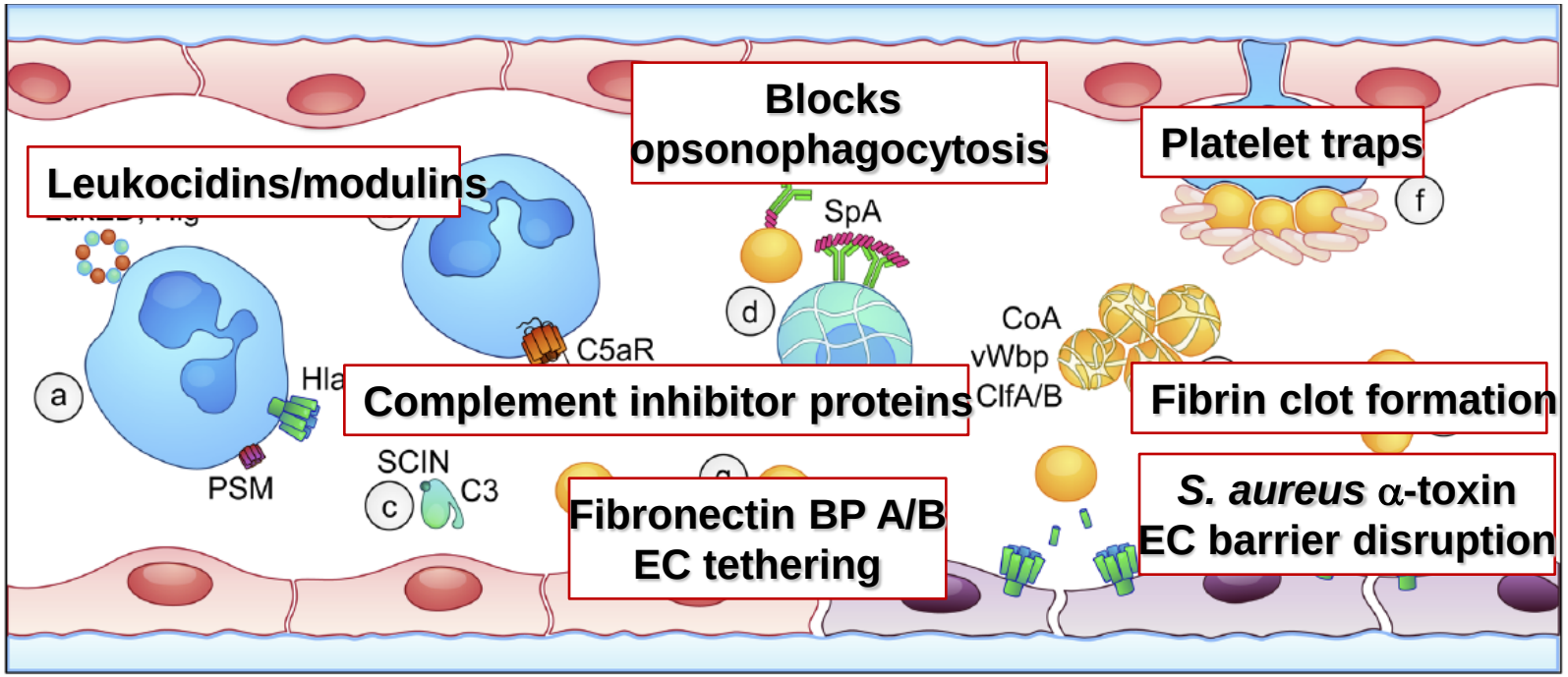
Cellular Composition of *S. aureus*

- Cell Wall
  - Peptidoglycans
  - Teichoic acid
  - Adhesins
  - Potential for "slime layer"
- Genes
  - SCC/mecA
  - Enzymes
    - Catalase/Coagulase
    - Beta-lactamases
- Virulence Factors
  - α, β, γ, δ, TSST toxins
  - Leukocidin (PVL)
  - Chemotaxis inhibitory protein



WTA=wall teichoic acid; PVL=Panton-Valentine leukocidin; CHIP=chemotaxis inhibitory protein.

Severe Sepsis— *S. aureus* Tissue/BSI virulence factors

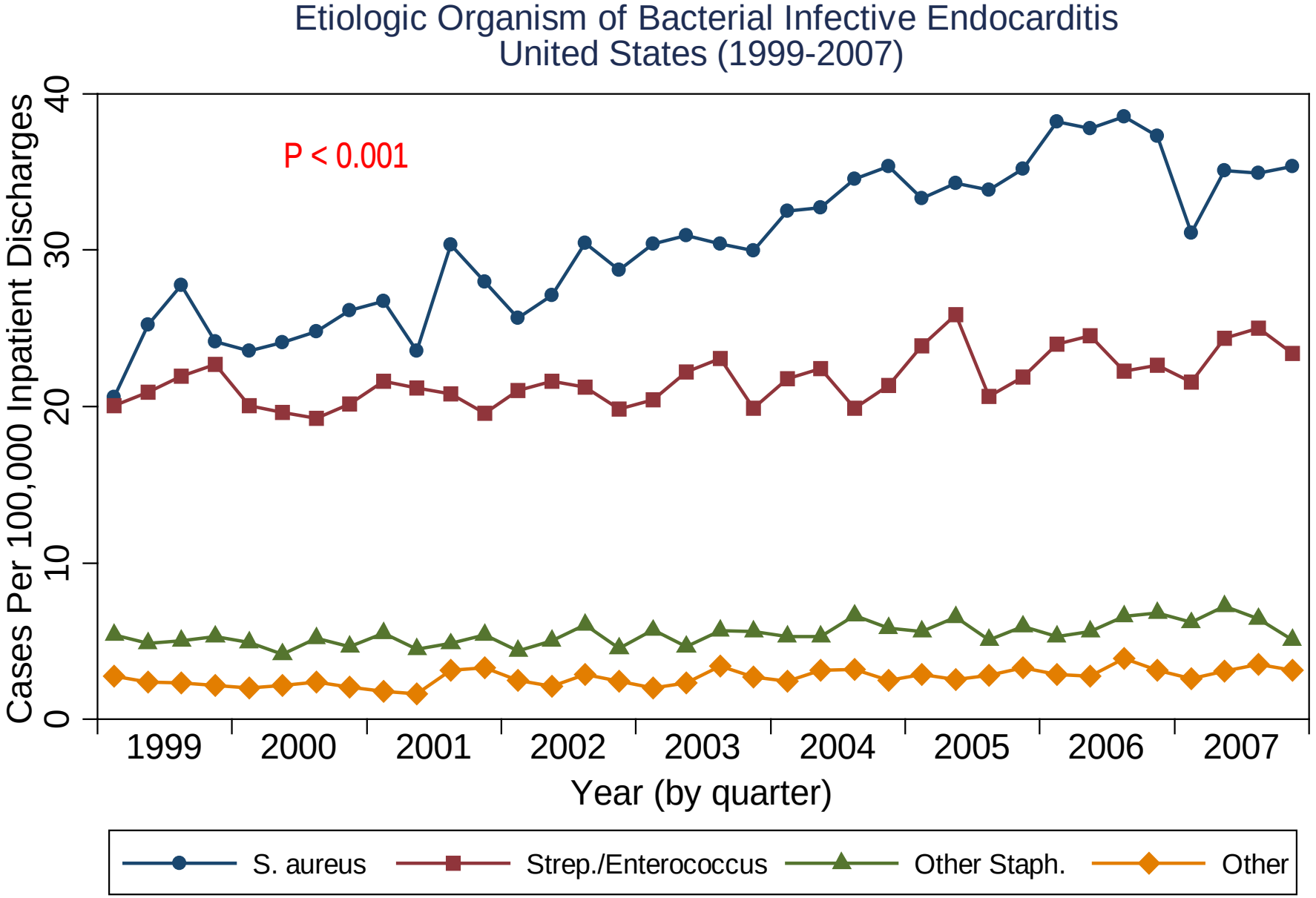


Powers ME, Wardenburg JB (2014) Igniting the Fire: Staphylococcus aureus Virulence Factors in the Pathogenesis of Sepsis. PLoS Pathog 10(2): e1003871. doi:10.1371/journal.ppat.1003871
http://www.plospathogens.org/article/info:doi/10.1371/journal.ppat.1003871

PLOS | PATHOGENS

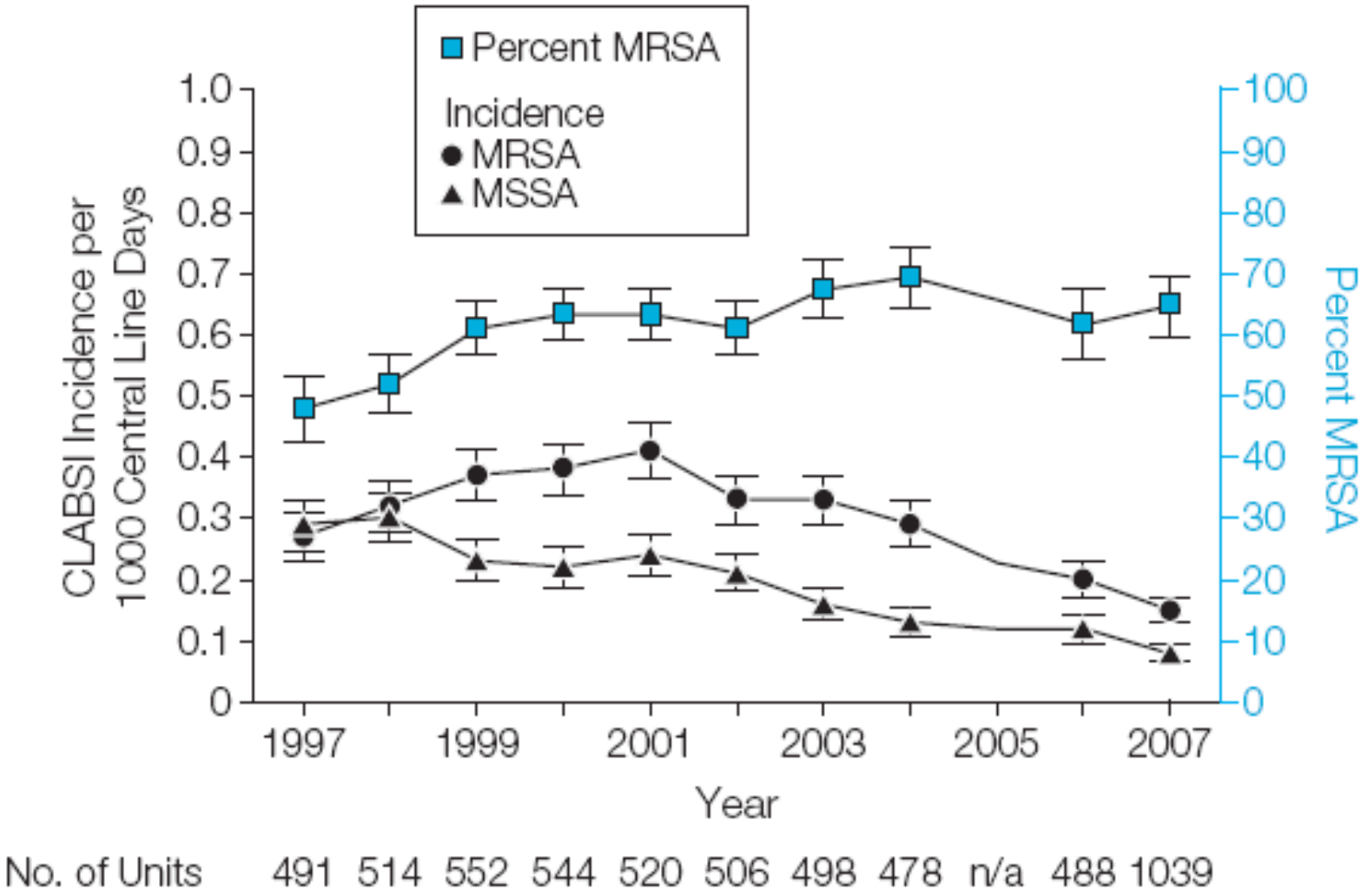
SAB: Epidemiology

- S. aureus is the leading cause of bacteremia in the US and in most community and tertiary care hospitals
- Good rule of thumb: 1/3rd of all cases of SAB are true community-onset; 2/3rd are healthcare-associated or hospital-onset



Federspiel et al *Arch Intern Med* , In press

Decreasing Rates of Central-Line Associated *S. aureus* Bacteremia



Deron et al. JAMA. 2009;301(7):727-736

SAB is BAD

- Mortality of S aureus IE in the preantibiotic era=100%
- Mortality of SAB in the pre-antibiotic era was ~80% [Skinner, D. and Keefer, C. S. *Arch.Intern.Med*. 68, 851-75. 1941]
- Mortality of SAB in the antibiotic era: 11-43%--recent evidence shows that proper management leads to better outcomes
- ***Mortality rate of IE due to S aureus largely unchanged from 1981-2015***

S. aureus Bacteremia Is A Bad Disease: 724 Prospectively Identified Patients at DUMC (Fowler et al, CID 2005)

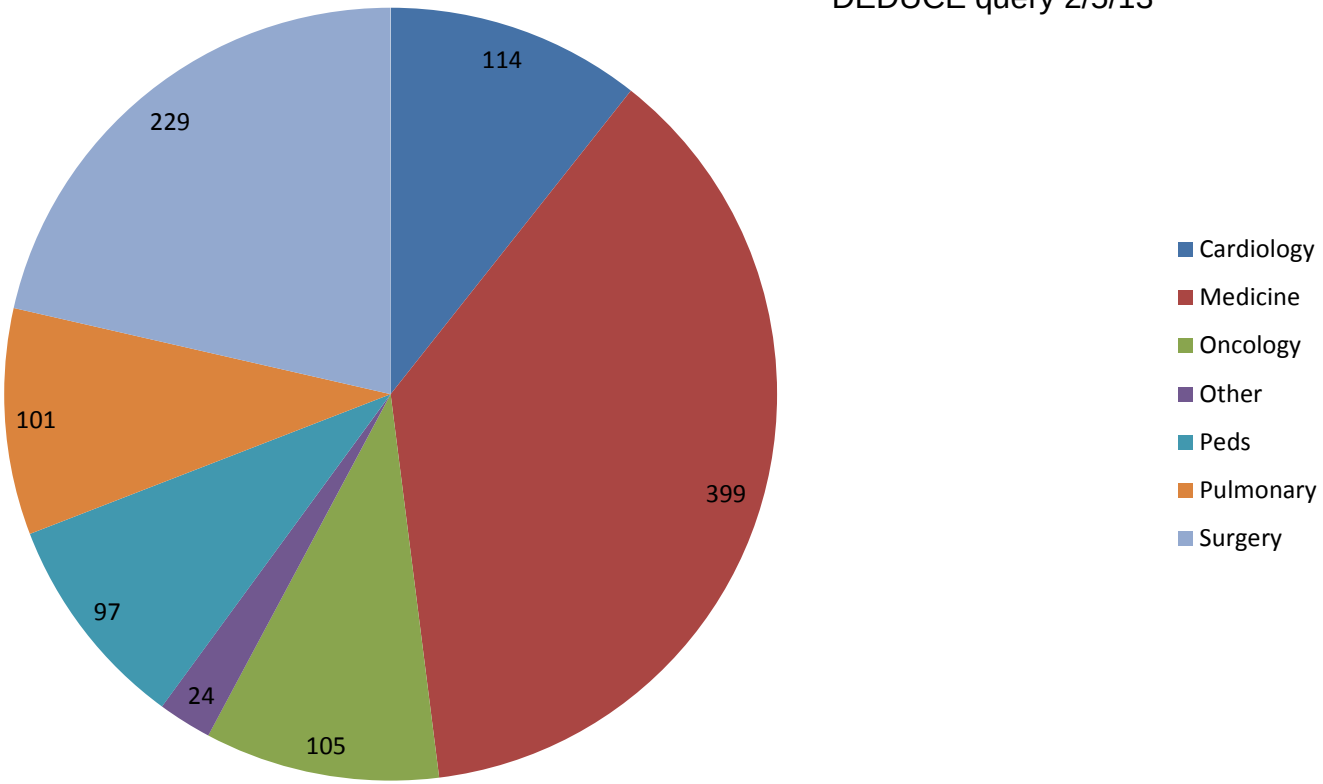
- Overall 12-week mortality: **24%**
- Metastatic infectious complication: **34%**
- IE: **12.2%**
- Relapse: **10%**

S. Aureus bacteremia cases, Duke Hospital, 2009-2013*

N = 1069**

**unique patients

*DEDUCE query 2/5/13



The Status Quo

- Failure to correctly treat SAB both empirically (before cultures return) and with directed therapy (after cultures return) is a common important problem in the US.
- Our treatment options for SAB in general are suboptimal.
- Many patients with SAB do poorly even with seemingly appropriate treatment. WHY?

The Deadly Toll of Invasive MRSA Infections (Kaye et al 2008)

- 1 in 3 patients with MRSA bacteremia (n=564) died during their initial hospitalization
- 57% were dead within a year of their bacteremia and
- 36% of survivors were re-hospitalized within 90 days of their MRSA bacteremia
- The mean duration of hospitalization for 374 patients with SAB who survived their initial hospitalization was 17.3 days
- Not surprisingly those who initially received effective therapy less often died (OR 3.2 $p<0.001$). ***Note: only 38% of patients with SAB rec'd effective Rx during the 24 hr period after blood cultures were drawn***.

Key Principle

Is SAB complicated or uncomplicated?

Uncomplicated SAB

Uncomplicated SAB: Definition

- Endocarditis excluded (often by echocardiography)
- Fever gone within 72h
- Follow-up blood cultures negative after 72h
- No prosthetic material (pacer, valve, arthroplasty)
- No evidence of metastatic infection

TREATMENT: **at least 2 weeks with an appropriate agent**

Clinical Infectious Diseases 2011;1–38

Use of a Simple Criteria Set for Guiding Echocardiography in Nosocomial *S. aureus* Bacteremia

Kaasch AJ, Fowler, VG, et al. Clin Infect Dis. 2011; 53:1–9

Table 2. Clinical Prediction Criteria Associated With Increased Risk of Infective Endocarditis (IE) in Patients With Nosocomial *Staphylococcus aureus* Bacteremia.

Clinical prediction criterion	No. (%) of Patients, by Study						
	INSTINCT- Europe				SABG - USA		
	All patients (n = 304)	Patients without IE (n = 291)	Patients with IE (n = 13)	P [a]	All patients (n = 432)	Patients without IE (n = 392)	Patients with IE (n = 40)	P
Prolonged bacteremia (>4							
Documented prolonged bac							
Possible prolonged bactere							
Permanent intracardiac dev							
Prosthetic heart valve							
Pacemaker/cardioverter-def							
Hemodialysis dependency							
Spinal infection or nonverte osteomyelitis							
No criteria fulfilled	83 (27.3)	83 (28.5)	0		125 (28.9)	124 (31.6)	1 (2.5)	
≥1 criterion fulfilled	221 (72.7)	208 (71.5)	13 (100)		307 (71.1)	268 (68.4)	39 (97.5)	

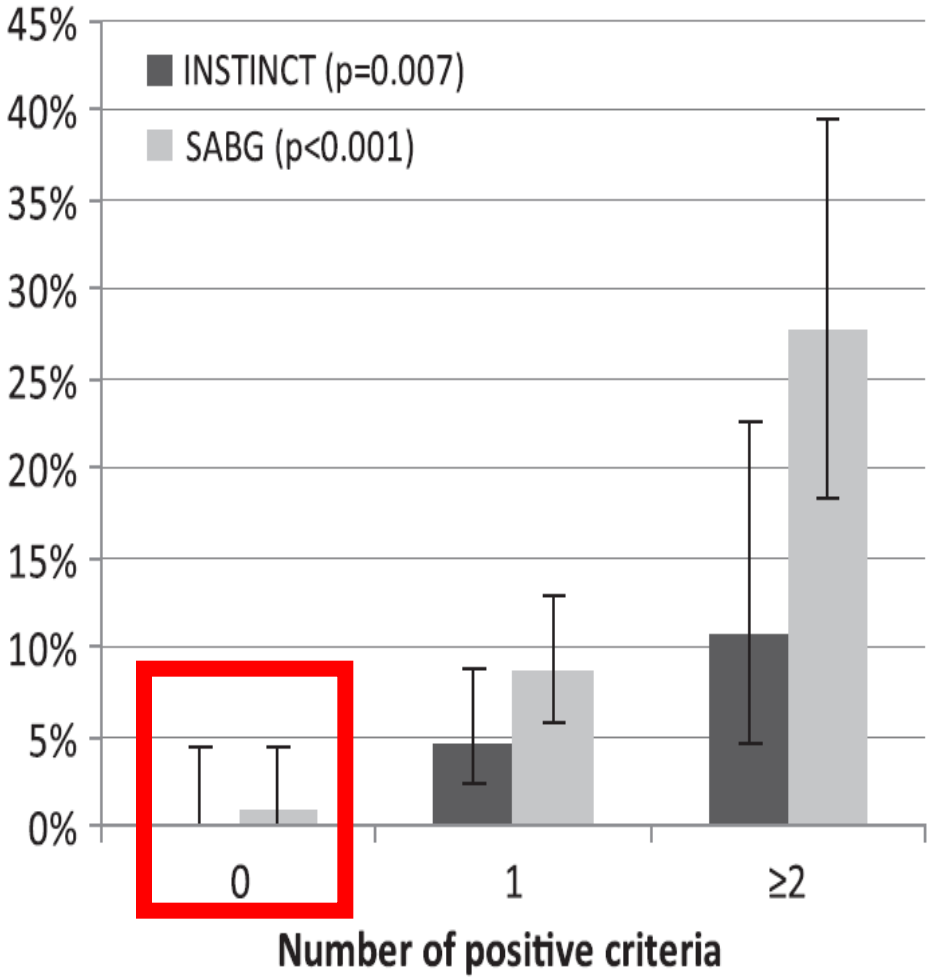
- Prolonged bacteremia >4 days
- Intracardiac devices (PV, ICD, PCM)
- Hemodialysis dependence
- Spinal infection/nonvertebral osteomyelitis

NOTE. Data are shown for 304 patients in the Invasive *S. aureus* Infection Cohort (INSTINCT) and 432 patients in the *S. aureus* Bacteremia Group (SABG) with complete follow-up. More than 1 criterion may be present.

[a] Determined using the 2-sided Fisher exact test.

Relative frequency of infective endocarditis by number of positive criteria in patients with nosocomial SAB

Kaasch AJ, Fowler, VG, et al. Clin Infect Dis. 2011; 53:1–9



TAKE HOME PAY:
Uncomplicated SAB

- If you think someone has it and if you treat someone for it, be sure you are right.

Complicated MRSA Bacteremia

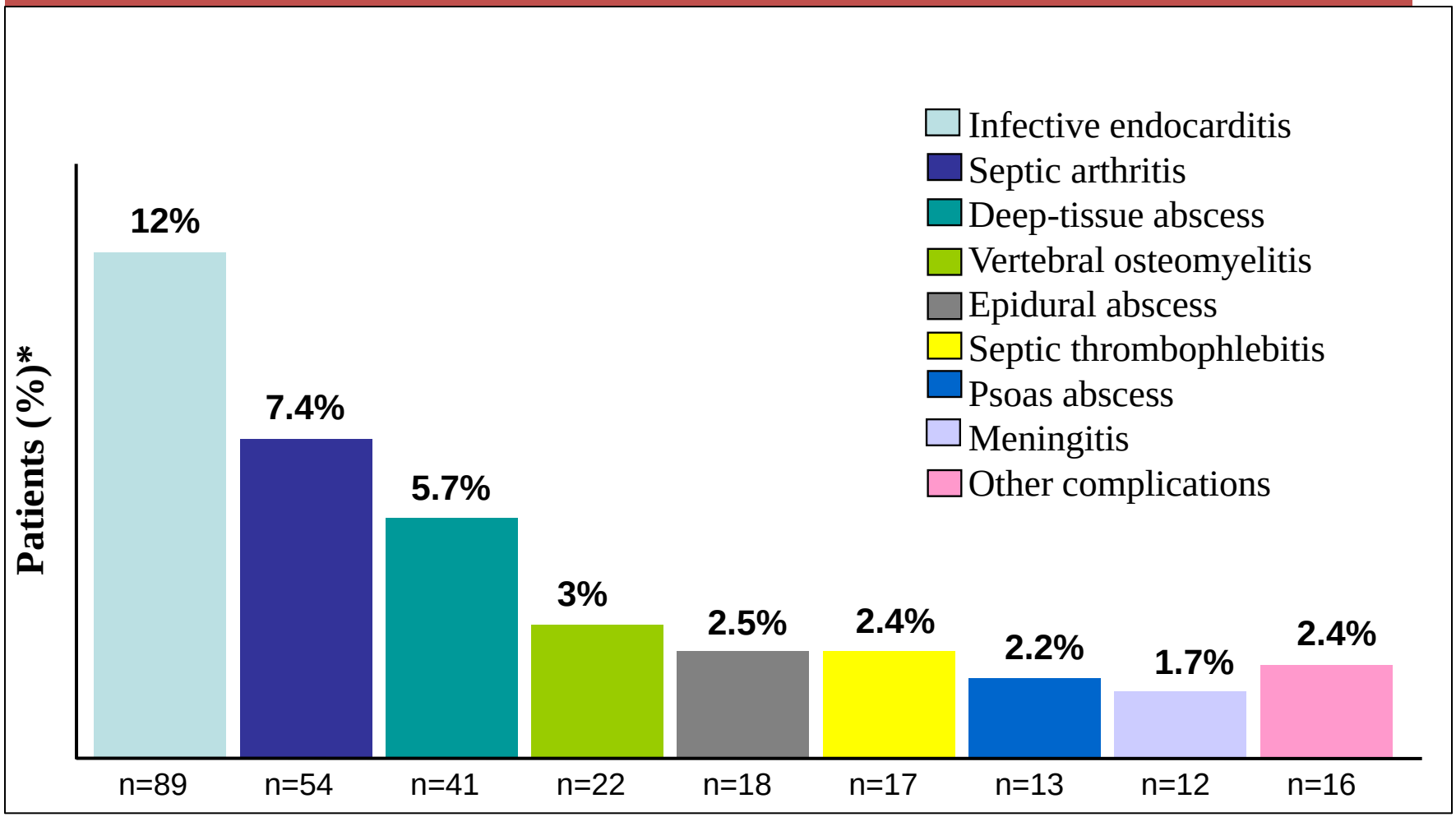
Complicated SAB is Common

Frequency in 724 consecutive Duke patients with SAB

43%

Fowler, et al. *Arch Intern Med*. 2003;163:2066-2072.

Complicated SAB is Complicated

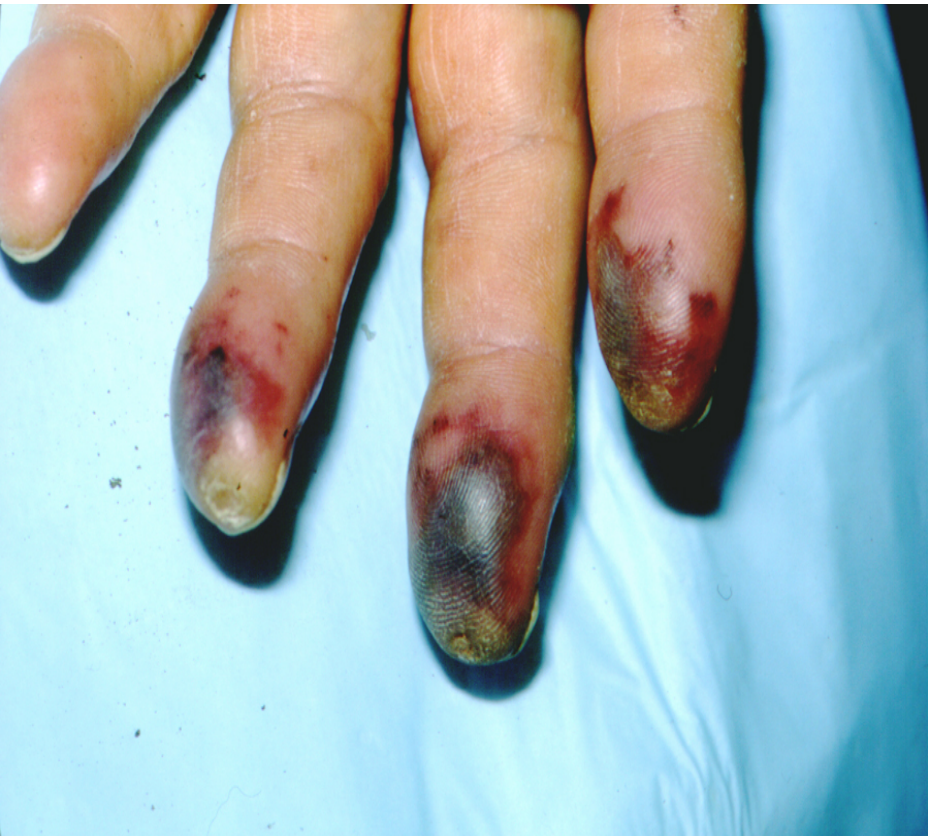


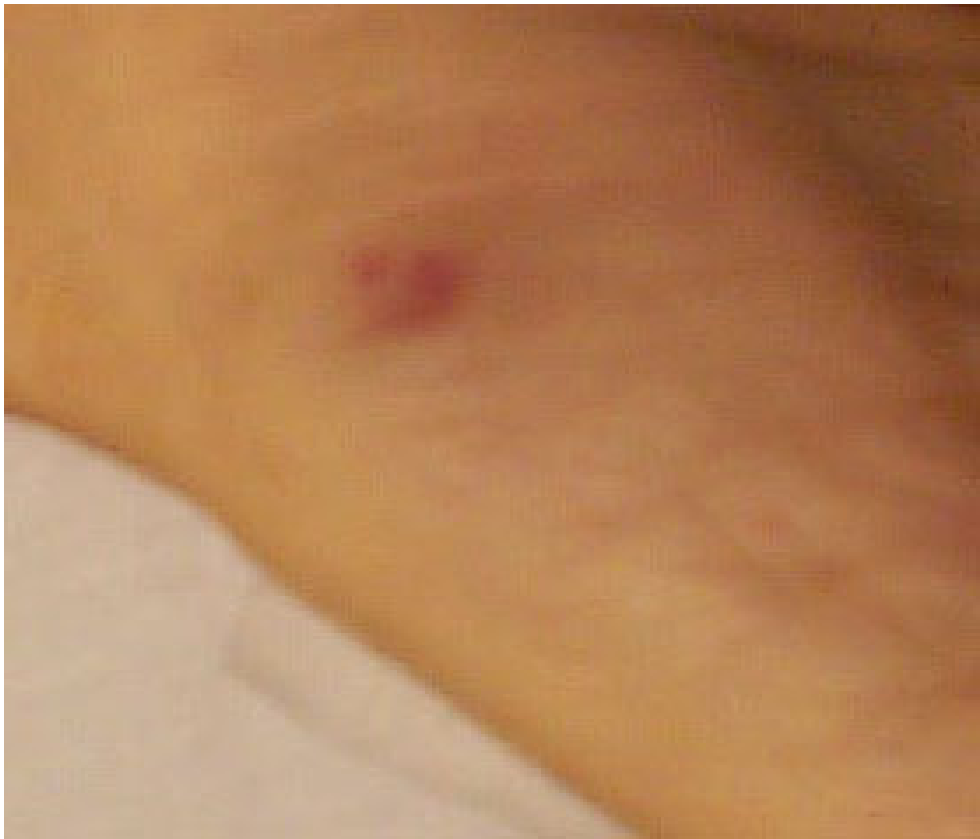
Fowler, et al. *Arch Intern Med*. 2003;163:2066-2072.

Identifying Complicated *S. aureus* Infection

Identifying Complicated SAB:
Physical Exam Matters

- **Helpful when Present**
- **Not Always Present**





Factors Associated With Complications in Patients with SAB

- **Fever > 72 hours** *Clin Infect Dis* 1992
- **Positive follow-up blood cultures** *Clin Infect Dis* 1992
- **Pain**
- **Abnormal Echocardiogram (especially TEE)**

  Arch Intern Med 87, *J Am Coll Cardiol* 97
- **Presence of prosthetic device**

Independent Predictors of Complicated SAB

- Positive follow-up blood culture OR 5.6
- Community-onset OR 3.1
- Persistent fever @ 72 hrs OR 2.2
- Skin lesions OR 2.0

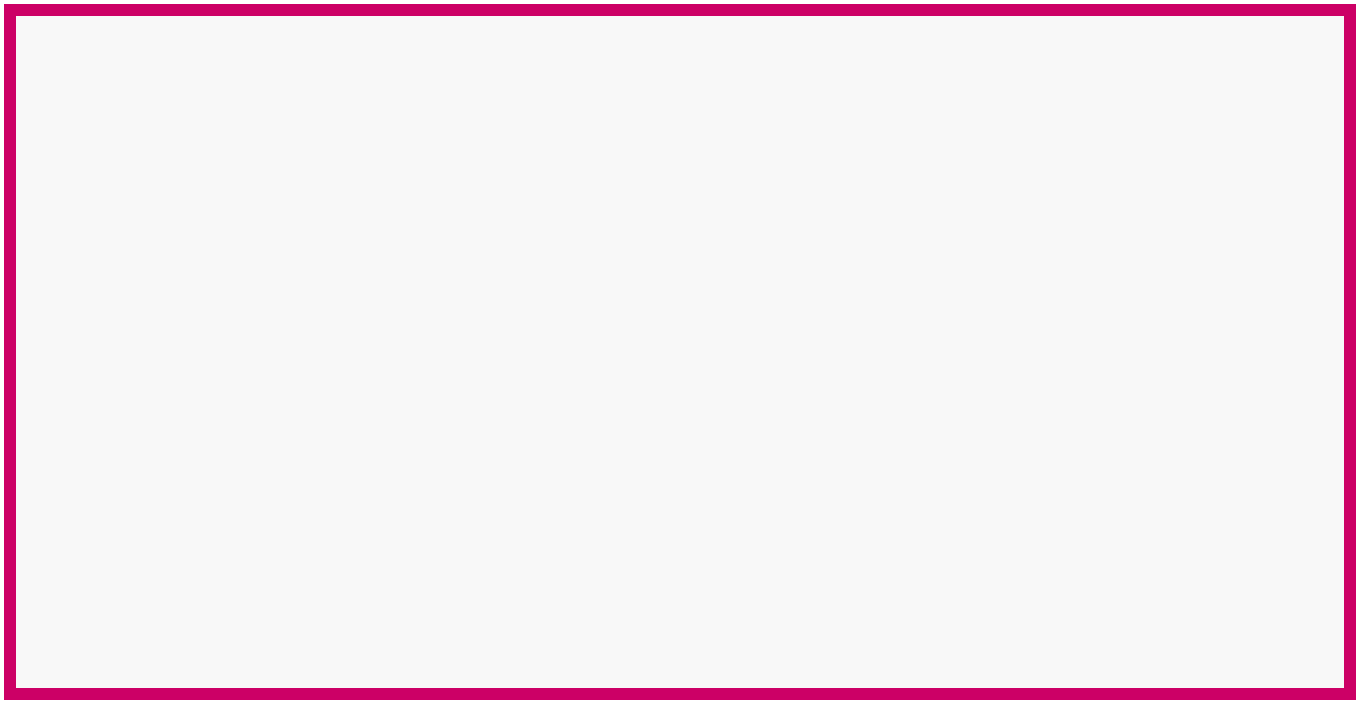
Risk factors for complications* in SAB

- Community acquisition:
  - Risk of complications 43% in CASAB vs 21% in noso SAB (CID 1993:16:567) [retrospective study n=281]
- Absence of an identifiable focus
  - Risk of complications was 51% without an identifiable focus vs 24% with a known focus (CID above)

*complications=metastatic infection, IE, relapse, or death

Identifying Complicated SAB

Scoring Systems Matter



1 point Community-acquired
Skin examination suggesting acute systemic infection
Persistent fever at 72 hours

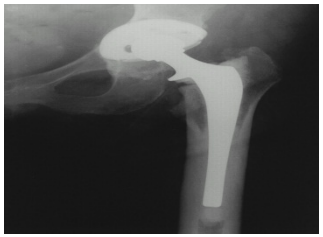
2 points Positive follow-up blood cultures at 48-96 hours

Fowler, *Arch Intern Med*, 2003;163:2066-72.

Identifying Complicated SAB

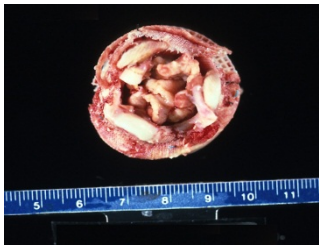
Clinical Context Matters

S. aureus Bacteremia + Prosthesis = Trouble



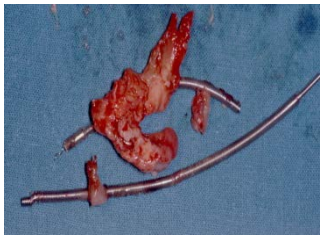
SAB + Arthroplasty = 28% Joint Infection

Murdoch et al *Clin Infect Dis* 2001; 32:647-9.



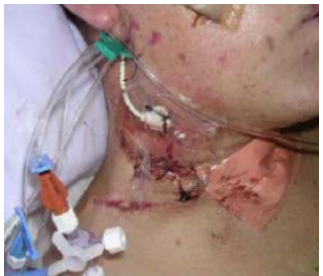
SAB + Prosthetic Valve = 51% Valve Infection

El-Adhab *Am J Med* 2005; 118:225-9.



SAB + Pacemaker/ICD = 45% Device Infection

Chamis *Circulation* 2001; 104: 1029



SAB + Central Catheter = 71% Thrombophlebitis

Crowley *Crit Care Med* 2008;36:385-90

Lessons Learned:
Clinical Identifiers of Complicated SAB

- Things to bank on:
  All SAB is Complicated SAB until Proven otherwise
- Things to always do:
  Get Follow-up Blood cultures
  Get an Echo
- Things to look for:
  Persistent Bacteremia
  Persistent Fever
  Community acquisition
  Clinical Evidence of complications
  Post-operative State
- Things to Fear:
  Pain
  Prostheses

Expertise Matters

ID Consultants Improve Outcome of S. aureus Bacteremia

Fowler *Clin Infect Dis* 1998; 27(3):478-86. Prospective cohort of 244 patients Compliance with IDC associated with less recurrent SAB (P<0.01)

Jenkins *Clin Infect Dis*. 2008;46:1000-8. Institutional IDC for SAB- 234 patients 4 standards of care more frequent with routine IDC (p<0.001).

Lahey *Medicine* 2009; 88: 263-7. Retrospective cohort of 241 patients with SAB IDC associated with lower mortality (hazard 0.46; p = 0.03)

Reig *J Infection* 2009; 59: 232-9. Retrospective cohort of 521 German SAB patients IDC associated with lower mortality (OR 0.6, CI 0.4-1.0)

Honda *Am J Med* 2010; 123: 631-7. Prospective cohort of 341 patients with SAB IDC associated with lower mortality (adj hazard: 0.44; 95% CI, 0.22-0.89)

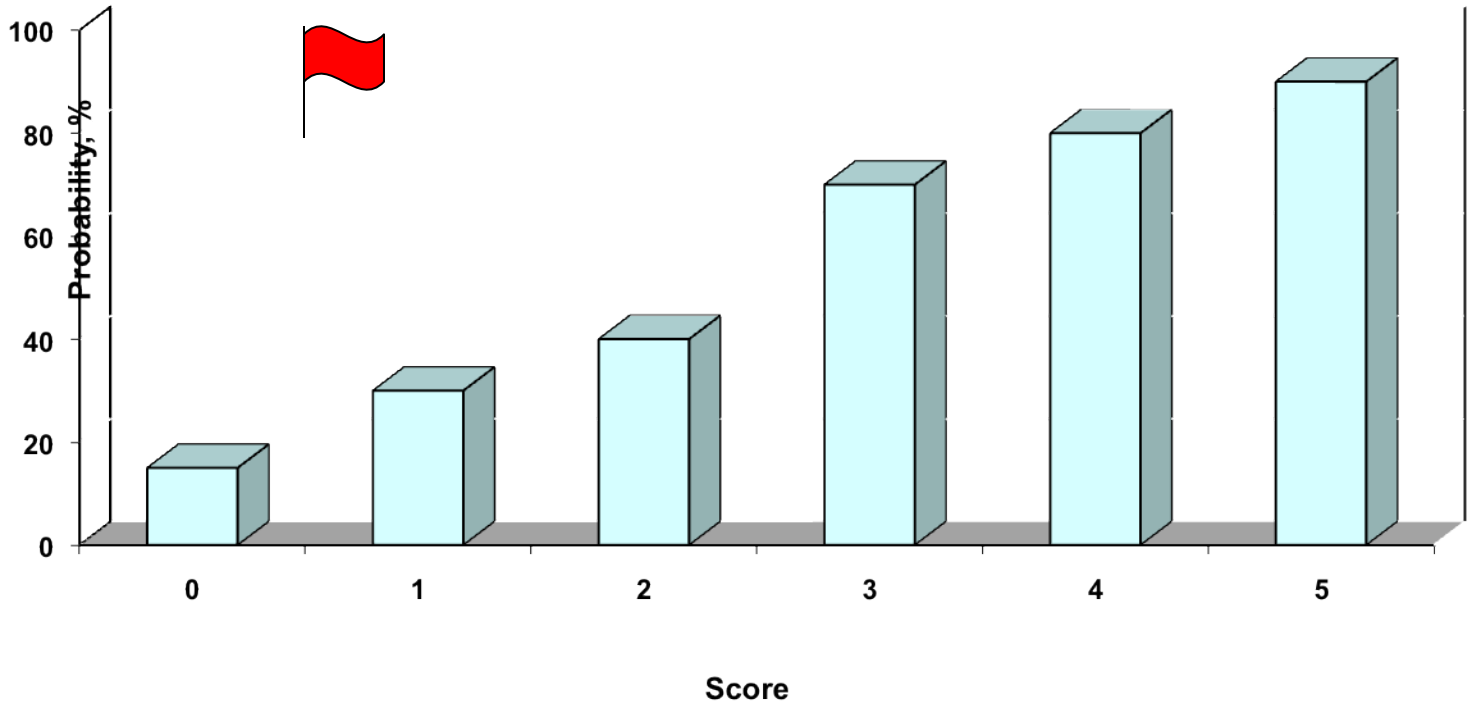
What about telephone consultation?

- Forsblom *Clin Infect Dis* 2013; 56:527-35. in 342 Finnish patients with MSSA bacteremia (all MRSA patients excluded…. N=5).
  - 72% formal IDC, 18% phone, 10% no consultation
  - Deep focus of infection identified in 78% formal, 53% phone, 29% no consult cases
  - In regression analysis, factors independently associated with death were pneumonia, steroid use, ICU care, no ID consult, and phone consultation (OR 2.31, 95% CI 1.22-4.38)

  - From the accompanying editorial:

"Most ID clinicians lack sufficient time or motivation to provide comprehensive advice when they receive an unsolicited call from another physician who intends to manage a problem as complex as SAB without a formal bedside consultation. Such calls are not rare even in tertiary care centers."

What is the risk of a poor outcome?



1 point each for skin findings, fever > 72h, community onset
4 points for positive blood culture @ 48-96h

Fowler, et al, Arch Intern Med 163:2066, 2003

SAB Therapy: General Comments

- Antibiotics are like golf clubs: good clubs won't keep a bad player from shooting a bad score
- Rx usually starts as empiric treatment; later it becomes directed treatment.
- Even appropriate Rx may fail. However, treatment failure and complications are much more likely with inappropriate Rx
- Little details (about Rx) can have big consequences (e.g. validity of allergy history, MIC, dose)

Delayed Antibiotic Treatment of Hospital-Acquired SAB (CID 2003)

- 167 Patients with SAB studied in a Detroit hospital
- Delayed Rx was defined as >45 hours from the time the first BC was obtained and the institution of effective Rx
- Infection-related death occurred in 16/48 (33%) patients with delayed Rx vs 23/119 (19%) with "early Rx" [p=0.05]
- Mean LOS after SAB was 17.6 days in delayed Rx group vs 14.9 days in early Rx group (NS)
- Note: 42 of 46 patients with delayed Rx had MRSA

The Deadly Toll of Invasive MRSA Infections (Kaye et al 2008)

- 1 in 3 of 564 patients with MRSA bacteremia died during their initial hospitalization
- 57% were dead within a year of their bacteremia and
- 36% of survivors were re-hospitalized within 90 days of their MRSA bacteremia

Impact of Methicillin Resistance on Outcome of *S. aureus* Bacteremia:

WORSE OUTCOME

Romero-Vivas *Clin Infect Dis* 1995

Conterno *Infect Control Hosp Epidemiol* 1998

Gonzalez *Clin Infect Dis* 1999

NO CHANGE IN OUTCOME

Harbarth, *Arch Intern Med* 1998

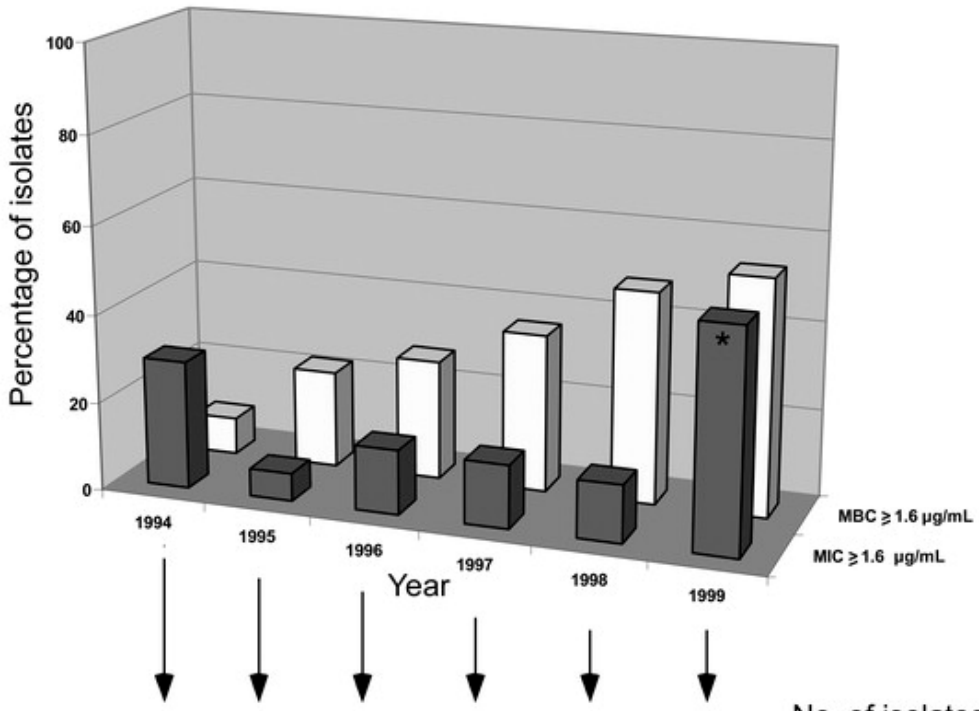
Mylotte *Infect Control Hosp Epidemiol* 1996

Soraino *Clin Infect Dis* 2000

SAB: Treatment Options

- Semi-synthetic penicillins (Nafcillin, Oxacillin)
- Penicillin-Penicillinase Inhibitors (Augmentin, Unasyn, Zosyn,)
- Cephalosporins
- Vancomycin
- Daptomycin
- Linezolid
- TM/SXT
- Tetracycline (minocycline, tigecycline)

Decreasing Susceptibilities to Vancomycin over Time



2	7	13	5	12	16	No. of isolates with an MBC > 1.6 µg/mL
24	32	48	14	23	30	Total no. of isolates
8	22	27	36	48	53	Percentage of isolates

$\chi^2_{trend} = 15.46$; df = 1; $P < .001$

Rhee Y et al. CID 2005; 40:1705-1706.

Relationship Between Vancomycin MIC and Outcome of MRSA Bacteremia (AAC 2008)

- Retrospective study of 92 hospitalized adult patients with hospital-onset MRSA bacteremia
- 66/92 patients had MIC of 1.5 or greater; 26 had MRSA strains with MICs of 1 or less
- 30-day mortality: 18.2% v 11.5%
- Microbiologic failure: 9% v 0
- Recurrence within 60 days: 17% v 4%
- Mean hospital LOS: 21 days v 11.5 days

What does an elevated MIC to Vancomycin really mean?

- It is true that patients with high MICs to vancomycin do worse on vancomycin than those with low MICs
- However, patients with MSSAB who have a high vancomycin MIC who are treated with B-lactams also do worse than patients with a low vancomycin MIC who are treated with B-lactams

Managing SAB: Critical Steps

1. First give empirical therapy pronto
2. Determine extent of the Staphylococcal infection
3. Be sure to order an appropriate drug and route of administration
4. Assess response to treatment
5. Give therapy for an appropriate length of time (while continuing to assess response)

SAB: A Suggested Approach

- Perform a careful clinical assessment when SAB is detected:
  - Do a careful clinical exam:
    - Cardiac assessment for murmurs
    - Look for signs of metastatic infection/emboli
    - **Carefully evaluate any pain(s)**
    - Percuss the spine
    - Examine/assess any IV lines
    - Assess vital signs
    - Determine if prosthetic material is in the patient
    - Prior history of S aureus infection?

SAB: A Suggested Approach-2

- Reassess antimicrobial Rx (drug, dose, route) when sensitivity results return
- If an IV catheter is present assess whether it can or should be removed
- Arrange for follow-up blood cultures
- At 72-96 hrs decide upon the duration of Rx:
  - Assess clinical response (repeat exam)
  - Assess need for an echocardiogram
- At the end of treatment: decide if post treatment follow-up is needed

Key Historical Points

- Setting in which bacteremia was acquired
- Previous endocarditis
- Recent IV procedures, line placement
  - Dialysis (huge risk)
- Heart structure/valve abnormalities
- Presence of hardware
  - Intravascular
  - Other (>25% of pts with prosthetic joints and SAB have PJI)
  - Removeable, removed

Murdoch DR, et al. CID 32: 647, 2001

Key Physical Exam Findings

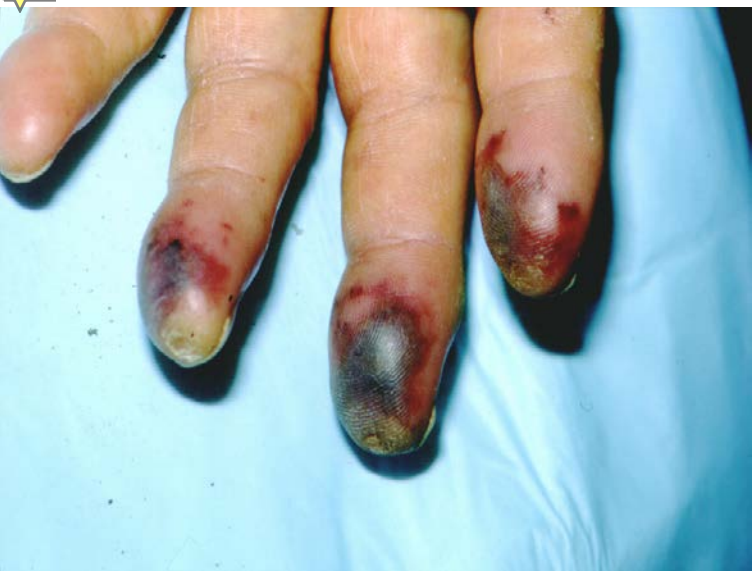
- Skin
- Eyes
  - Fundi
  - Conjunctivae
- Heart
- Other – *S. aureus* can infect any tissue
  - Lungs
  - Bones/Muscles/Joints
  - Kidneys
  - Liver/Spleen
  - Other

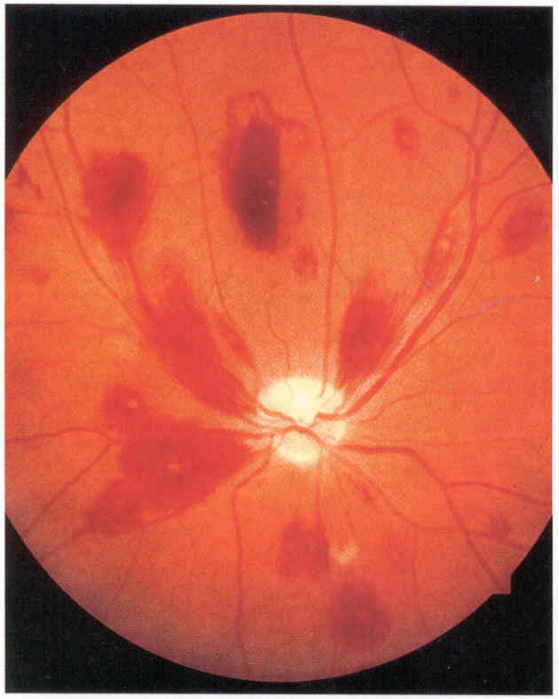
Key Laboratory Tests

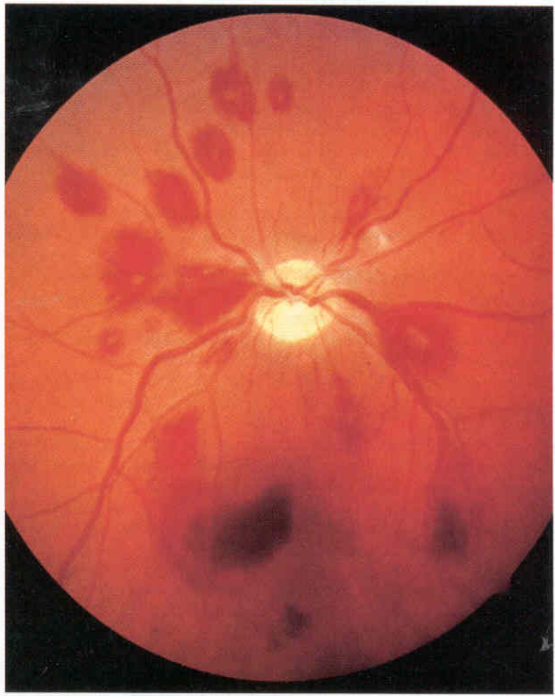
- Remember the primary objective:
  - Differentiate uncomplicated from complicated *S. aureus* bacteremia
- Urinalysis in patients without a Foley catheter
- Follow-up Blood Culture

Other Imaging

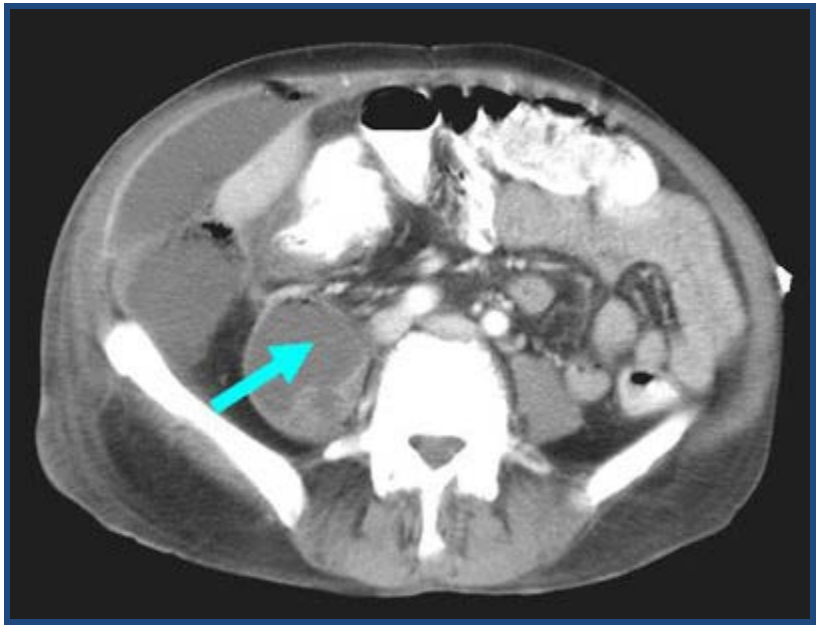
- Xrays
  - Chest
  - Bone
- CT
  - Very useful for abscess/osteo/other
  - Many more emboli than clinically apparent
    - Usefulness of these data unclear
- Imaging
  - MRI
  - 3D echo

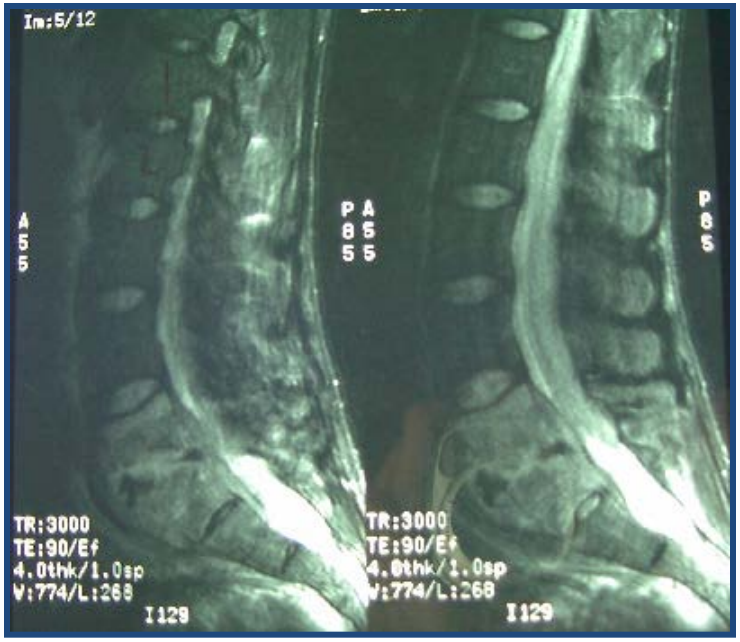






Courtesy of Drs Chip Chambers, Vance Fowler





Identifying *S. aureus* IE: TTE

*Curr ID Reports ’99

- Sensitivity: 57%*
- Specificity: 97%*

*447 patients in 11 studies

Echocardiograms

- TTE vs TEE
  - Important (often ignored) factors
    - Physical impediments to clear images
    - Technical expertise of physician
- Rosen: TEE cost effective

Rosen A et al Ann Int Med 130: 810, 1999

Cost-effectiveness of TEE to Determine Duration of Therapy for Patients With Vascular Catheter Associated SAB

Intern Ann Med 1999;130:810-820

"Within the limitations of existing empirical data, these data suggest that for patients with clinically uncomplicated catheter-associated S. aureus bacteremia, the use of TEE to determine therapy duration is a cost-effective alternative to 2 or 4 week empirical therapy."

Length of Treatment

2 weeks in well-defined patients with ALL of the following

- Catheter-associated bacteremia / catheter removed
- Follow-up BC negative
- Patient is afebrile within 72 hours of starting Rx
- TEE normal (not negative)
- No prosthetic material in joints or intravascular space
- No evidence of thrombophlebitis
- No symptoms suggestive of metastatic infection

Progressive Algorithm

	n	Cure n (%)	Recurrence n (%)	Attributable mortality n (%)	Non-*S. aureus* related mortality n (%)
a) ANY SAB	1282	804 (63)	131 (10)	135 (11)	150 (12)
b) a + non community-acquired	598	348 (58)	50 (8)	79 (13)	95 (16)
c) b + no prosthetic device	357	223 (62)	26 (7)	47 (13)	51 (14)
d) c + catheter-associated	167	132 (79)	8 (5)	9 (5)	17 (10)
e) d + ≤ 14 d parenteral Ab Rx	105	80 (76)	4 (4)	8 (8)	13 (12)
f) e + defervesce within 72h	72	55 (76)	3 (4)	4 (6)	10 (14)
g) f + neg f/u blood cx at d 2-4	50	43 (86)	2 (4)	0 (0)	5 (10)
h) g + any echo	36	31 (86)	2 (6) (1 reinfection)	0 (0)	3 (8)
i) h + TEE	26	23 (88)	1 (4) (1 reinfection)	0 (0)	2 (8)

Vancomycin v Nafcillin for MSSA

- Vancomycin is inferior:
  - Less rapidly bactericidal in vitro
  - Longer duration of bacteremia after Rx is started
  - More complications in patients with MSSA IE
  - Short duration Rx of MSSA right-sided IE fails with vancomycin but is successful with nafcillin

What antibiotic should be used?

Outcomes of dialysis pts with MSSA bacteremia:

	Vancomycin	Cefazolin
Failure	24%	6%
Death	8%	2%
Recurrence	16%	4%

Stryjewski et al. CID 2007

A Few Words about Daptomycin

- Studies have shown it to be equivalent to Vancomycin and Nafcillin (not better)
- Prior Rx with Vancomycin may lead to higher MICs to Daptomycin
- Resistance to Daptomycin may occur in selected patients
- Not effective in S aureus pneumonia
- Controversy exists about the optimal dose
- Toxicity can be severe (muscle, lung)

A Few Words About Linezolid

- Studies have shown it is “not inferior” to Vancomycin
- A recent open-labeled randomized trial of Linezolid v Vancomycin or Nafcillin in patients with catheter-associated SAB was discontinued prematurely
- Prolonged therapy with Linezolid can lead to hematologic and neurolgic toxicity

Avoidable Mistakes in Patients with SAB

- Leaving "removable foci" of infection in place during treatment (e.g PCs, CVCs, pacemakers)
- Giving therapy for too short a time period
- Assuming that long-term Rx will cure all metastatic infections and any prosthetic-related Staphylococcal infection
- Wrong route of Rx
- Assuming clinical response can be a surrogate for microbiologic response or assuming a good clinical response means short-term Rx is fine
- Not assuring follow-up after Rx has been completed
- Failure to diagnose concurrent or subsequent IE and its secondary complications

SAB: Odds and Ends

- Disseminated staphylococcal infections may occur in the absence of IE
- Disciitis commonly manifests *after* SAB is detected; ditto for other metastatic infections
- Prolonged SAB may occur in patients who look and feel surprisingly good
- Not knowing that a complication of SAB has occurred can lead to preventable further complications (e.g. paralysis, embolism)
- *Doing right is more important than being right*

SAB: Odds and Ends-2

- Late relapses may be due to the presence of biofilms (on devices) and/or the formation of small colony variants
- Strains of S aureus associated with invasive disease and/or relapse appear to have important genetic differences from strains associated with uncomplicated bacteremia
- Healthy previously well patients who develop SAB can end up dead or badly damaged

Clinical Pearls

- Pay close attention to any complaints of pain (pain is the diagnostician's friend)
- Remember Hickum's Dictum, but be highly suspicious that a poor response to Rx means there is a complication due to Staphylococcus
- Metastatic infections sometimes first manifest late in the course of illness or after even a long-course of Rx has been completed

Clinical Pearls

- Always inform patients about the possibility of relapse at the completion of treatment. Ask them to stay alert and seek care if ANYTHING goes wrong in the following 90 days—longer if a pacemaker is present.
- If recurrent bacteremia occurs in the next 90-180 days immediately suspect a RELAPSE rather than a reinfection

SAB: Speculations about the Future

- Vancomycin will become less useful and less commonly used
- Daptomycin and Linezolid resistance will become bigger problems
- We will eventually understand why some patients with SAB have complications and others don't. The answer will be more in the bug than the host
- Better diagnostic methods will be developed

Take Home Pay

- Respect and understand the enemy (SAB)
- Look for complications early AND during Rx-- Do serial assessments while on Rx (and during followup after Rx)
- Be sure you have the right drug, the right dose, right route and right duration of Rx
- Educate your patient about the possibility of early or late relapse **Make no warranties**

MAYO CLINIC

Infective Endocarditis in Adults

Diagnosis, Management, and Prevention

Financial Disclosures

- UpToDate, Inc.
  - Authorship
- Massachusetts Medical Society
  - Editor-in-Chief (NEJM Journal Watch Infectious Diseases)
- Email address: baddour.larry@mayo.edu

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2015 AHA Statement

- Update for 2005 Statement
  - Start up call date – 8/16/2012
  - Reviewed by AHA (SACC) and IDSA (endorsement)
  - Embargoed currently
- Other AHA-related Statements
  - “IE Prophylaxis” – 2007
  - “CIED Infections” – 2010
  - “IE in Pediatrics” - 2015

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Infective Endocarditis

2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease

Nishimura RA, et al. JACC 2014;63:e57-185

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Size of Treatment Effect

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	Class I	**Class IIa**	**Class IIb**	**Class III *No Benefit* *or* CLASS III *Harm***
	Benefit >>> Risk Procedure/Treatment **SHOULD** be performed/ administered	Benefit >> Risk Additional studies with focused objectives needed **IT IS REASONABLE** to perform procedure/ administer treatment	Benefit ≥ Risk Additional studies with broad objectives needed; additional registry data would be helpful Procedure/Treatment **MAY BE CONSIDERED**	**Procedure/ test** / **Treatment** COR III: no benefit — Not Helpful / No proven Benefit COR III: Harm — Excess cost w/o benefit or harmful / Harmful to pts
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	• Recommendation that procedure or treatment is useful/effective • Sufficient evidence from multiple randomized trials or meta-analyses	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from multiple randomized trials or meta-analyses	• Recommendation's that procedure or treatment is not useful/effective and may be harmful • Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	• Recommendation that procedure or treatment is useful/effective • Evidence from single randomized trial or nonrandomized studies	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from single randomized trial or nonrandomized studies	• Recommendation's usefulness/efficacy less well established • Greater conflicting evidence from single randomized trial or nonrandomized studies	• Recommendation's that procedure or treatment is not useful/effective and may be harmful • Evidence from single randomized trial or nonrandomized studies
LEVEL C Vey limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	• Recommendation that procedure or treatment is useful/effective • Only expert opinion, case studies, or standard of care	• Recommendation's usefulness/efficacy less well established • Only diverging expert opinion, case studies, or standard of care	• Recommendation's usefulness/efficacy less well established • Only diverging expert opinion, case studies, or standard of care	• Recommendation that procedure or treatment is not useful/effective and may be harmful • Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/ effective/beneficial	is reasonable can be useful/ effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/ effectiveness is unknown/unclear/ uncertain or not well established	**COR III: No Benefit** / **COR III: Harm** is not recommended / potentially harmful is not indicated / causes harm should not be performed/ administered/ other / associated with excess morbid-ity/mortality is not useful/ beneficial/ effective / should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended /indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated

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IDSA Guidelines

~ 55% are consensus-based

- Khan AR, et al. CID 2010;51:1147-56
- Deresinski S. CID 2010;51:1157-59
- Lee DH, Vielemeyer O. Arch Intern Med 2011;171:18-22
- Deresinski S, File TM. Arch Intern Med 2011;171:1402-3

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Infective Endocarditis

Prospective, randomized trials since 2005

- Fowler VG, Jr, et al. Daptomycin versus Standard Therapy for Bacteremia and Endocarditis Caused by Staphylococcus aureus. NEJM 2006;355:653-65
  - ~22% of cases were IE (predominately right-sided)
  - Cosgrove SE, et al. Initial Low-Dose Gentamicin for Staphylococcus aureus Bacteremia and Endocarditis is Nephrotoxic. CID 2009;48:718-21
- Kang, D-H, et al. Early Surgery versus Conventional Treatment for Infective Endocarditis. NEJM 2012; 366:2466-73

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Infective Endocarditis
Team Management

- Protocol development
  - Standardized care
    - Labs
    - Medical
    - Surgical
    - Other
- Multispecialty involvement in each case
- “Tumor Board” approach

Botelho-Nevers E, et al. Arch Intern Med 2009;169:1290-8
Chirillo F, et al. Am J Med 2013;112:1171-6
Carrasco-Chinchilla F, et al. Rev Esp Cardiol 2014;67:380-6

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Infective Endocarditis
Diagnosis

- Duke criteria – 1994
  - Durack DT, et al. Am J Med 1994; 96:200-209
  - Initially drafted for use in trials and epi studies
    - Used in individual patient management
- Modified – 2002
  - Li JW, et al. CID 2000;30:633-638

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Infective Endocarditis
Diagnosis

- Modified Duke criteria
  - Li JS, et al. CID 2000;30:633-8
  - Molecular screening – criterion??
- TTE and TEE are complementary
  - TTE more readily available in some centers (as compared to TEE)
  - Right-sided lesions, prosthetic aortic valve
  - Quantifying:
    - Hemodynamic dysfunction manifested by valvular dysfunction
    - Ventricular dysfunction
    - L and R elevated filling pressures and PA pressure

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Infective Endocarditis
Microbiology

- "The Big Three"
  - All 3 groups are gram-positive cocci
    - Viridans group streptococci
    - *Staphylococcus* species
    - *Enterococcus* species
- Other pathogens
  - Broad range of bacteria and fungi

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Infective Endocarditis
Enterococcal

Combination therapy

- Amp/PCN plus gentamicin
- Amp plus ceftriaxone (high dose)
  - 6 weeks in 2 non-randomized trials
- Amp/PCN plus gentamicin
  - 2 weeks of gentamicin
    - Swedish/Danish studies
      - Olaison L, and Schadewitz K, et al. CID 2002;34:159-66
      - Dahl A, et al. Circulation 2013;127:1810-7
      - Danish Cardiology guidelines - 2007

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Infective Endocarditis
VRE

- Few cases
- No defined optimal regimen

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Infective Endocarditis
Streptococcal

VGS common pathogen

- Ceftriaxone vs. PCN
  - High cure rates
  - Broad vs. narrower spectrum
  - Convenience
  - Cost
  - Adverse events
- PCN resistance

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Infective Endocarditis
VGS IE

- 1999 – 2013 (Olmsted County, MN)
  - 96.3% (26/27 isolates) were sensitive (MIC ≤0.12 µg/mL) to penicillin
- DeSimone D, et al. Unpublished data

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Infective Endocarditis
Staphylococcal

Native valve

- Gentamicin x 3-5 days
  - Avoid
  - Cosgrove SE, et al. Initial Low-Dose Gentamicin for *Staphylococcus aureus* Bacteremia and Endocarditis is Nephrotoxic. CID 2009;48:718-21
- Aqueous crystalline penicillin G
  - Avoid
  - Clinical labs are not able to confirm penicillin susceptibility

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Infective Endocarditis
Culture-Negative Endocarditis

- "Empirism begets empirism"
  - Common - recent antimicrobial use
- Conundrum – "optimal" treatment
  - Focus on epidemiology
- Operative tissue, if available
  - "Send out" for 16S rRNA gene sequencing

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Infective Endocarditis
Early Surgery

W/in 48 hours s/p randomization

- Inclusions
  - Native, left-sided, >10 mm veg, severe valve disease
- Exclusions
  - Prosthetic, mod-severe HF, heart block, annular or aortic abscess, destructive lesions requiring urgent surgery, fungal, >80 y/o, coexisting major embolic stroke with hemorrhagic risk, serious co-existing disease

Kang D-H, et al. NEJM 2012;366:2466-732

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Infective Endocarditis
Early Surgery

Limitations

- N = 76
- Mean age ~47 years
- ~60% streptococcal
- ~11% *S. aureus*
- ~22% CNE

Kang D-H, et al. NEJM 2012;366:2466-73

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Clinical End Points

Outcome	Conventional treatment (n=39)	Early surgery (n=37)	P value
Primary end point – no. (%)			
In-hospital death or embolic event at 6 weeks	9 (23)	1 (3)	0.01
In-hospital death	1 (3)	1 (3)	1.00
Embolic event at 6 weeks			
Any	8 (21)	0	0.005
Cerebral	5 (13)	0	
Coronary	1 (3)	0	
Popliteal	1 (3)	0	
Splenic	1 (3)	0	
Secondary end points at 6 months – no. (%)			
Any	11 (28)	1 (3)	0.003
Death	2 (5)	1 (3)	1.00
Embolic event	8 (21)	0	0.005
Recurrence of infective endocarditis	1 (3)	0	1.00

Kang D-H et al. N Engl J Med 2012;366:2466-2473

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Infective Endocarditis
Early Surgery – PVE – *S. aureus*

- W/in the first 60 days of hospitalization
- Left-sided, no IDU
- N=168 patients (ICE- Prospective Cohort Study)
  - 74 (44.3%) underwent surgery
    - 1-year mortality unchanged – risk ratio, 0.67 [95% CI, .39-1.15; P=.15]

"The decision to pursue EVS should be individualized for each patient……"

Chirouze C, et al. CID 2015;60:741-9

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Infective Endocarditis
Surgery

Prospective cohort – ICE-PLUS

- 1,296 patients with left-sided IE (25% PVE)
- 9/1/08 – 12/31/12
- 52% - hospital transfers
- 57% underwent surgery w/in 7 days (median)
- 24% w/o surgery – though with an indication
  - Nonsurgical cohort
    - Mod/severe liver disease
    - Stroke before surgical decision
    - *S. aureus*

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Chu V, et al. Circulation 2015;131:131-40
Erbel R. Circulation 2015;131:121-3

Infective Endocarditis
Management

- Short-term follow-up
  - Drug adverse events
  - PICC removal
  - Monitor for IE relapse
    - Importance of fever
    - BCs for fever and not as “routine”
    - New baseline echocardiography
- Long-term follow-up
  - Ongoing dental care
  - BCs for fever, systemic manifestations

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Infective Endocarditis
Transcatheter Valve Replacement

- “Valvulation”
- Aortic
- Pulmonic
- IE
  - Early (< 1 year)
  - TAVR – Enterococci
  - Surgical management – TPVR>>TAVR
  - Mortality – TAVR>>TPVR

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IE Prophylaxis
Advocated for > 50 Years

- No prospective trial data
- Cochrane Database review (2005)
  - "… no evidence that antibiotic prophylaxis is either effective or ineffective….".
- # of editorials > # of EBD trials
- "Emotive", "litigious", "controversial"

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IE Prophylaxis – AHA Guidelines

Year	Regimens (dental)
1955, 1957, 1960	Antibiotics for five days
1965, 1972	Antibiotics for three days
1977	Three doses antibiotics
1984	Two doses antibiotics
1990	Two doses antibiotics
1997	One dose

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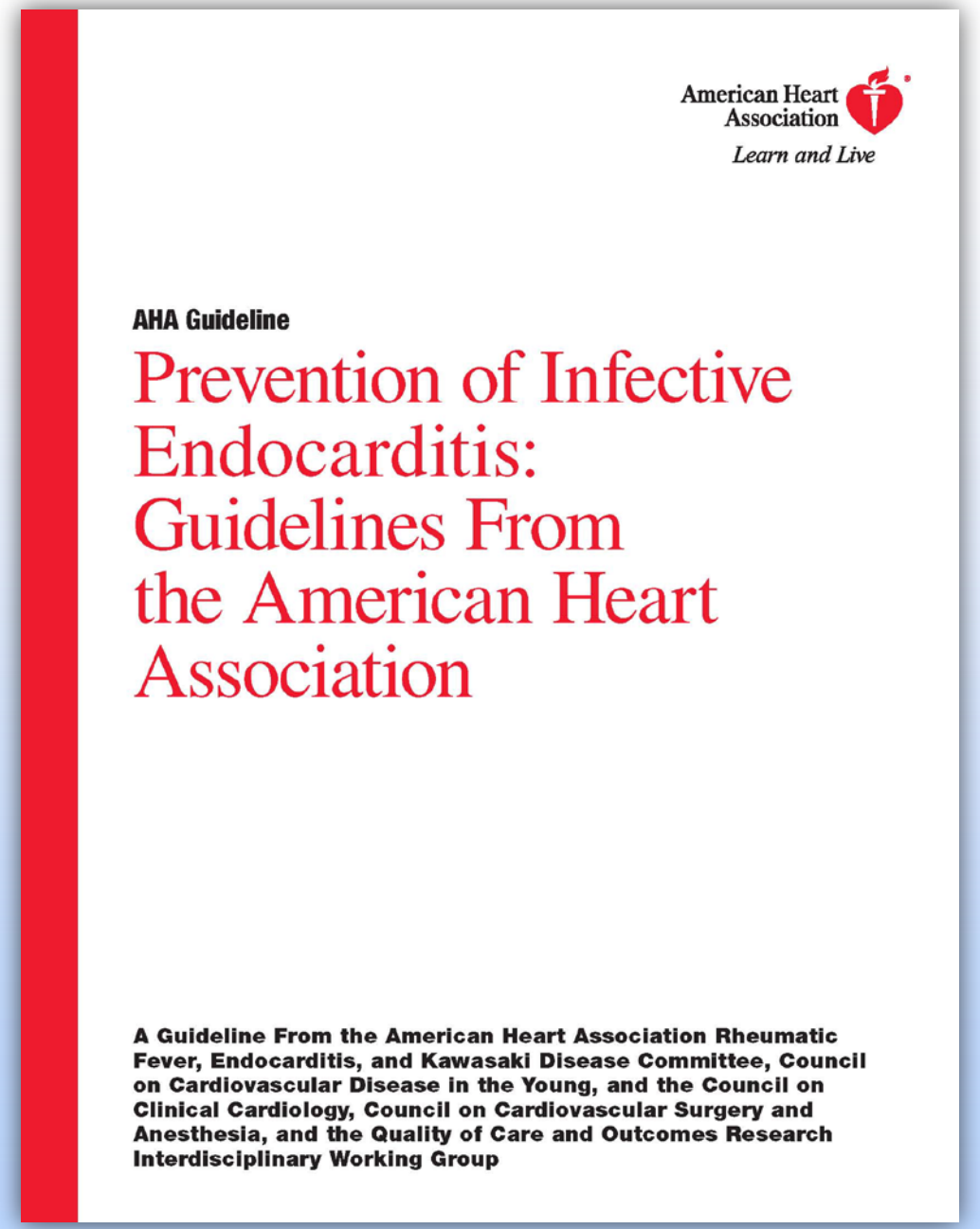

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AHA Guidelines 2007

Impact

Favorable

- ~90% reduction in antibiotic prophylaxis use
- Simplify guidelines

Unfavorable

- Endocarditis epidemic

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AHA Guidelines – 1997
Moderate-Risk Category

- Most other congenital cardiac malformations (other than above and below)
- Acquired valvar dysfunction (eg, rheumatic heart disease)
- Hypertrophic cardiomyopathy
- Mitral valve prolapse with valvar regurgitation and/or thickened leaflets[1]

Dajani AS, et al. Circulation. 1997; 96: 358-366

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AHA Guidelines 2007
Prevention

- Focus on oral health
- Limitations of antibiotic administration for prophylaxis
  - $$
  - Adverse drug events
  - Selection for resistance
  - “Ripple Effect”

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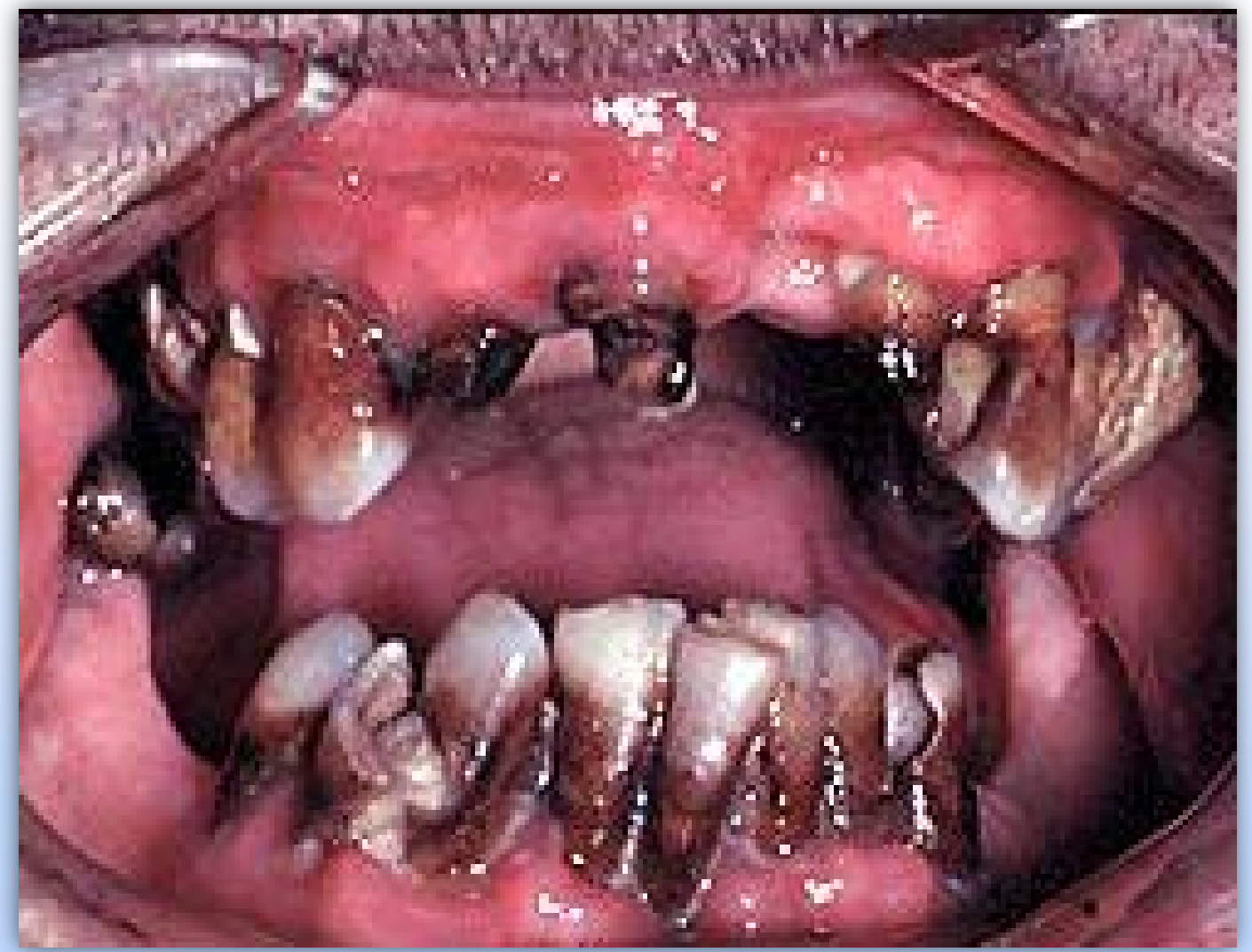

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IE Prophylaxis
Oral Health Importance

Oral hygiene and gingival bleeding

- Mean plaque and calculus scores
- Conclusion:
  - “Bacteremia after toothbrushing is associated with poor oral hygiene and gingival bleeding.”

Lockhart PB, et al. JADA 2009;140:1238-44

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IE Prophylaxis
"Ripple Effect"

Prosthetic total joint replacement

- ADA/AAOS (1997; updated 2003) "Advisory Statement"
  - With an accompanying legal perspective
- AAOS 2009 "Information Statement"
- ADA/AAOS 2013 "Clinical Practice Guideline"

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IE Prophylaxis
"Ripple Effect"

- Electrophysiologic devices
- Breast implants
- Vascular (prosthetic) grafts
- Tunneled catheters
- CSF shunts
- Penile implants

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IE Prophylaxis
Microbiologic Issues

Not addressed in 2007 AHA document

- Impact on development of resistance
  - PCN
  - Macrolides
  - Clindamycin

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IE Prophylaxis
Antibiotic Costs – Dental Prophylaxis

- Estimates for 15 medical conditions and devices
- Annual, United States
  - ~20,000,000 people
  - Estimated cost – between $19,880,279 and $143,685,823

Lockhart PB, et al. Oral Surg Oral Med Oral Path 2013;115:345-53

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IE Prophylaxis – Dental Procedures

- Prosthetic cardiac valve
- Previous infective endocarditis

Wilson W, et al: *Circulation* 2007;116;1736-1754

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IE Prophylaxis – Dental Procedures
Congenital Heart Disease (CHD)*

- Unrepaired cyanotic congenital heart disease, including those with palliative shunts and conduits
- Completely repaired CHD with prosthetic material or device either by surgery or catheter intervention during the first six 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 transplantation recipients who develop cardiac valvulopathy

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Dental Procedures

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

*The following procedures and events **do not need** routine prophylaxis: 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.

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IE Prophylaxis Regimens

Situation	Agent	Regimen – Single dose 30-60 min before procedure	
		Adult	**Children**
Oral	**Amoxicillin**	2 gm	50 mg/kg
Unable to take oral medication	Ampicillin OR Cefazolin or ceftriaxone	2 g IM or IV* 1 g IM or IV	50 mg/kg IM or IV 50 mg/kg IM or IV

*IM – intramuscular; IV – intravenous

**or other first or second generation oral cephalosporin in equivalent adult or pediatric dosage.

†Cephalosporins should not be used in an individual with a history or anaphylaxis, angioedema, or urticaria with penicillins or ampicillin

Wilson W, et al: Circulation; 116; 1736, 2007

IE Prophylaxis Regimens

Situation	Agent	Regimen – Single dose 30-60 min before procedure	
		Adult	**Children**
Allergic to penicillins or ampicillin (Oral)	**Cephalexin**†** OR **Clindamycin** OR **Azithromycin or Clarithromycin**	2 g 600 mg 500 mg	50 mg/kg 20 mg/kg 15 mg/kg
Allergic to penicillins or ampicillin (unable to take oral meds)	Cefazolin Ceftriaxone† OR Clindamycin	1 g IM or IV 600 mg IM or IV	50 mg/kg IM or IV 20 mg/kg IM or IV

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GI or GU Tract Procedures

The administration of prophylactic antibiotics solely to prevent endocarditis is **not** recommended for patients who undergo GU or GI tract procedures.

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IE Prophylaxis
AHA Guidelines

Future Considerations

"Studies are necessary to monitor the effects, if any, of these recommended changes in IE prophylaxis."

Wilson W, et al. Circulation 2007;116:1736-1754

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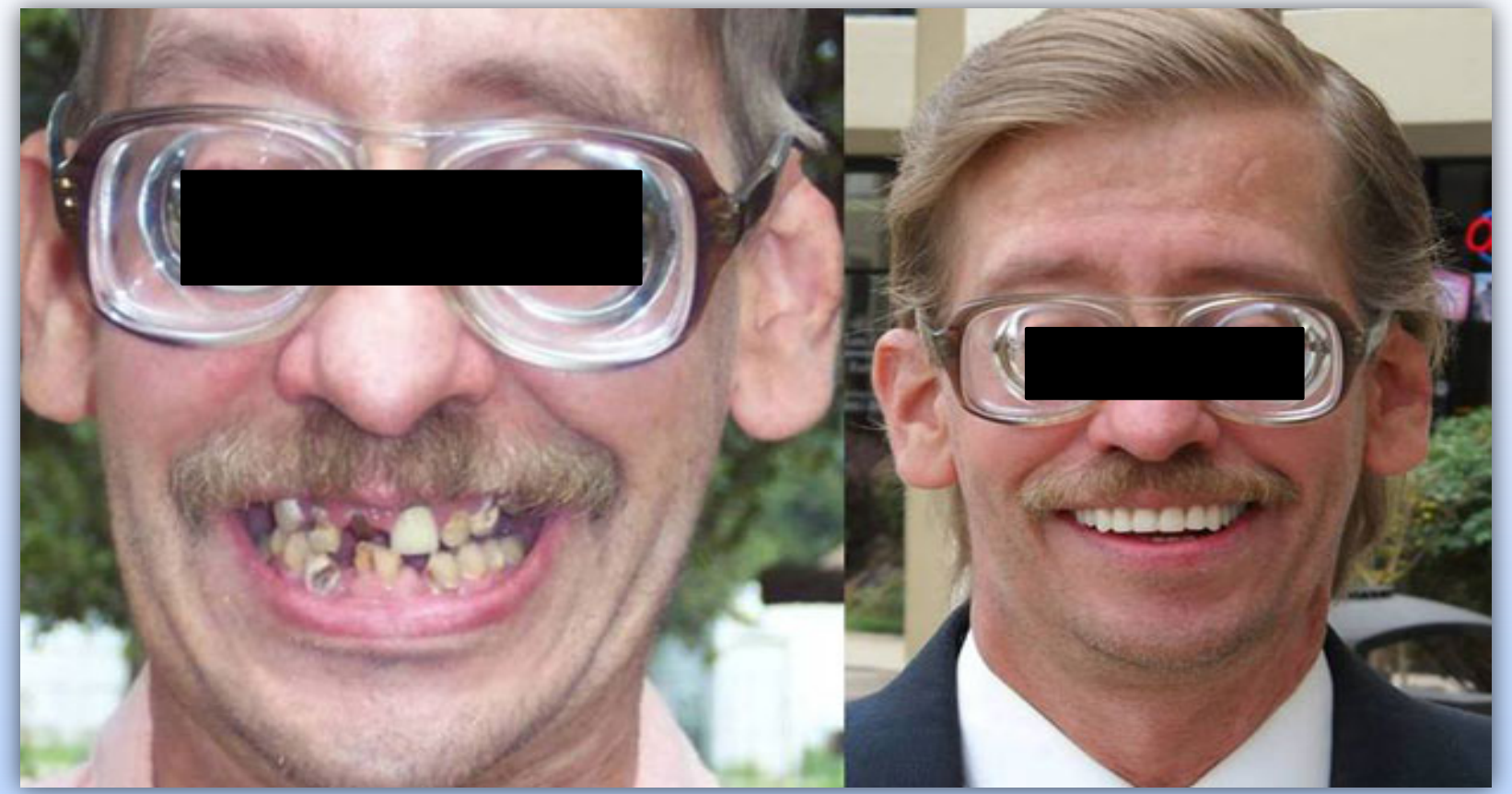
Infective Endocarditis

"Before and After Studies"



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Infective Endocarditis

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Infective Endocarditis

Three Countries

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IE Prophylaxis

- "NICE" impact
  - March 2008 guidelines (dental)
    - NO ANTIBIOTIC FOR ANY PATIENT
    - "Before and after study" – England
- January 2000 – April 2010
  - 78.6% reduction in prescribing of prophylaxis
  - No increase in IE cases (oral strep)

Thornhill MH et al. BMJ 2011;342:d2392

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IE Prophylaxis

- "NICE" impact
  - March 2008 guidelines (dental procedures)
    - NO ANTIBIOTIC FOR ANY PATIENT
    - "Before and after study" – England
- Updated analysis
  - Jan 1, 2004 – March 31, 2013

Dayer MJ, et al. Lancet 2015;385:1219-28

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Figure 1

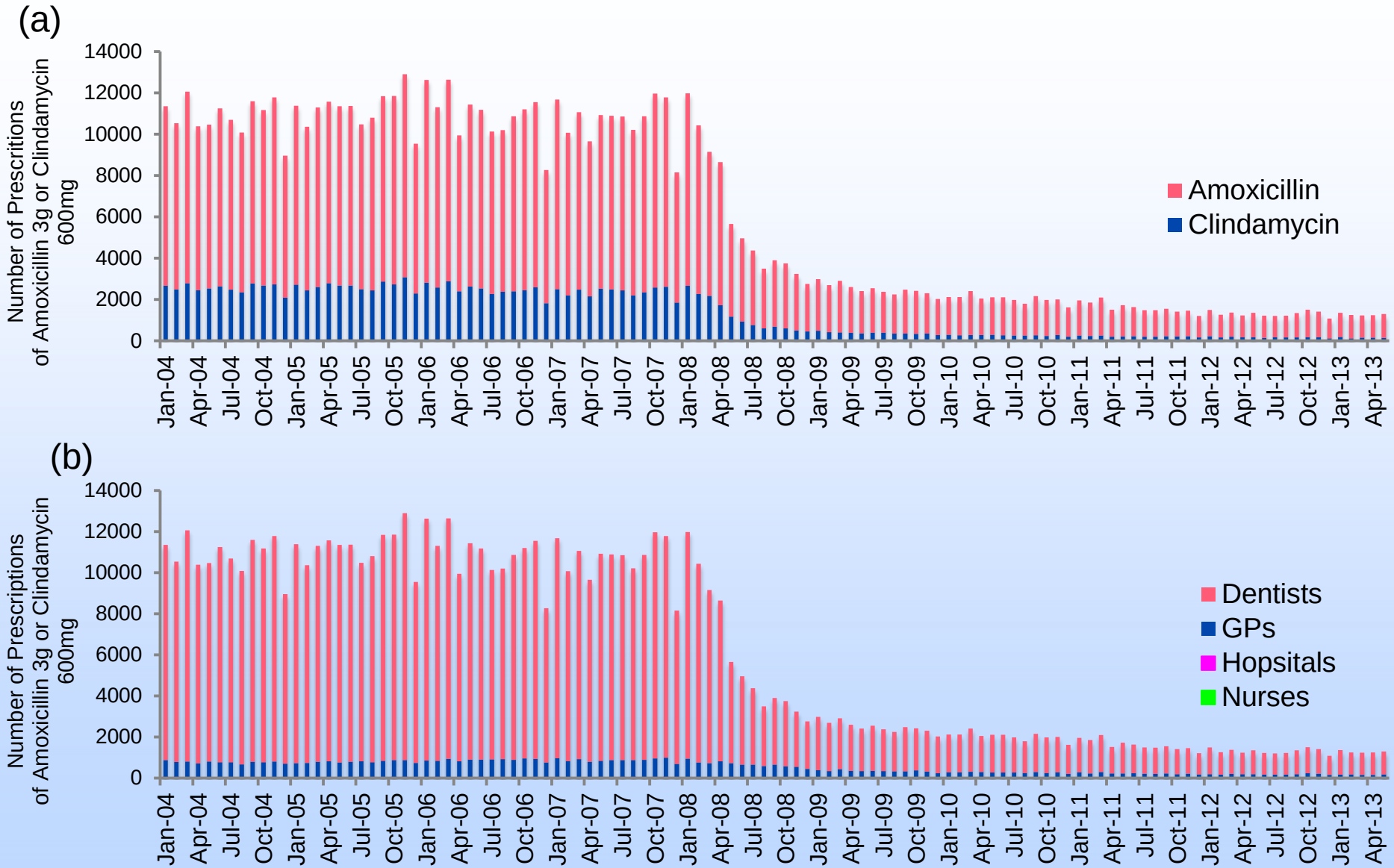

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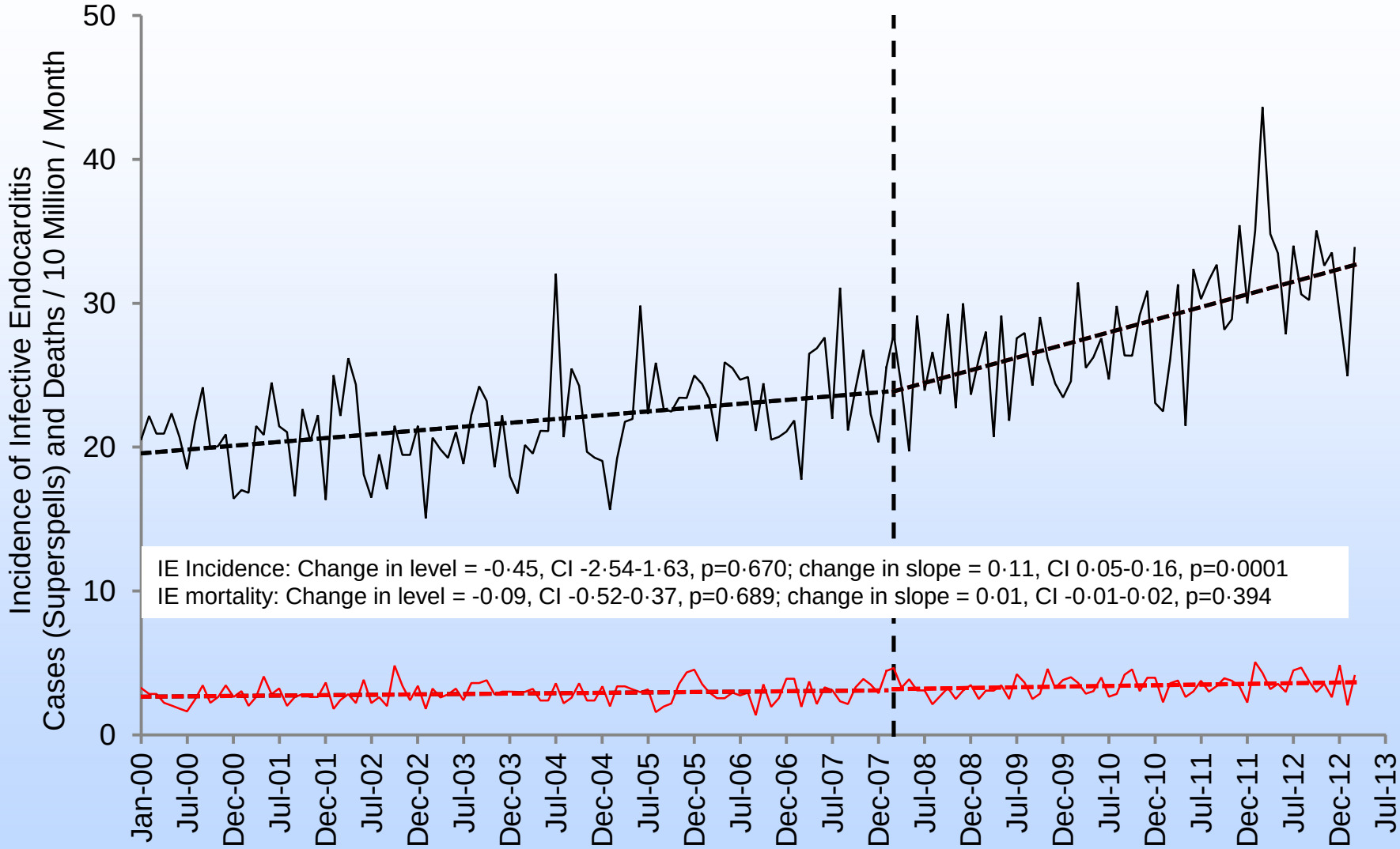
Figure 2



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IE Prophylaxis

- **Adverse events**
  - England
    - **Amoxicillin – 3 gm oral dose**
      - 0 fatal reactions/1,000,000 scripts
      - 22.62 non-fatal/1,000,000 scripts
    - **Clindamycin – 600 mg oral dose**
      - 13 fatal reactions/1,000,000 scripts
      - 149 non-fatal reactions/1,000,000 scripts

Thornhill MH, et al. JAC 2015.

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IE Prophylaxis

- 2002 French prophylaxis guidelines
  - Restricted use
- Population-based surveys
  - 1991, 1999, 2008
    - (24% of population, ≥20 years of age)
    - Overall IE incidence – stable
    - Oral streptococcal IE incidence – stable
    - Increase in staphylococcal IE
      - In those w/o known native valvulopathy

Duval X, et al. J Am Coll Card 2012;59:1968-76

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IE Prophylaxis
2007 AHA Guidelines

- Population-based (Olmsted County, MN) survey
  - Before and after 2007
    - 1999 through 2010, ≥18 years of age
- Nationwide Inpatient Sample database
  - 1999 through 2009
  - ~20% of stratified sample – US community hospitals
  - ICD-9-CM codes

DeSimone DC, et al. Circulation 2012;126:60-64

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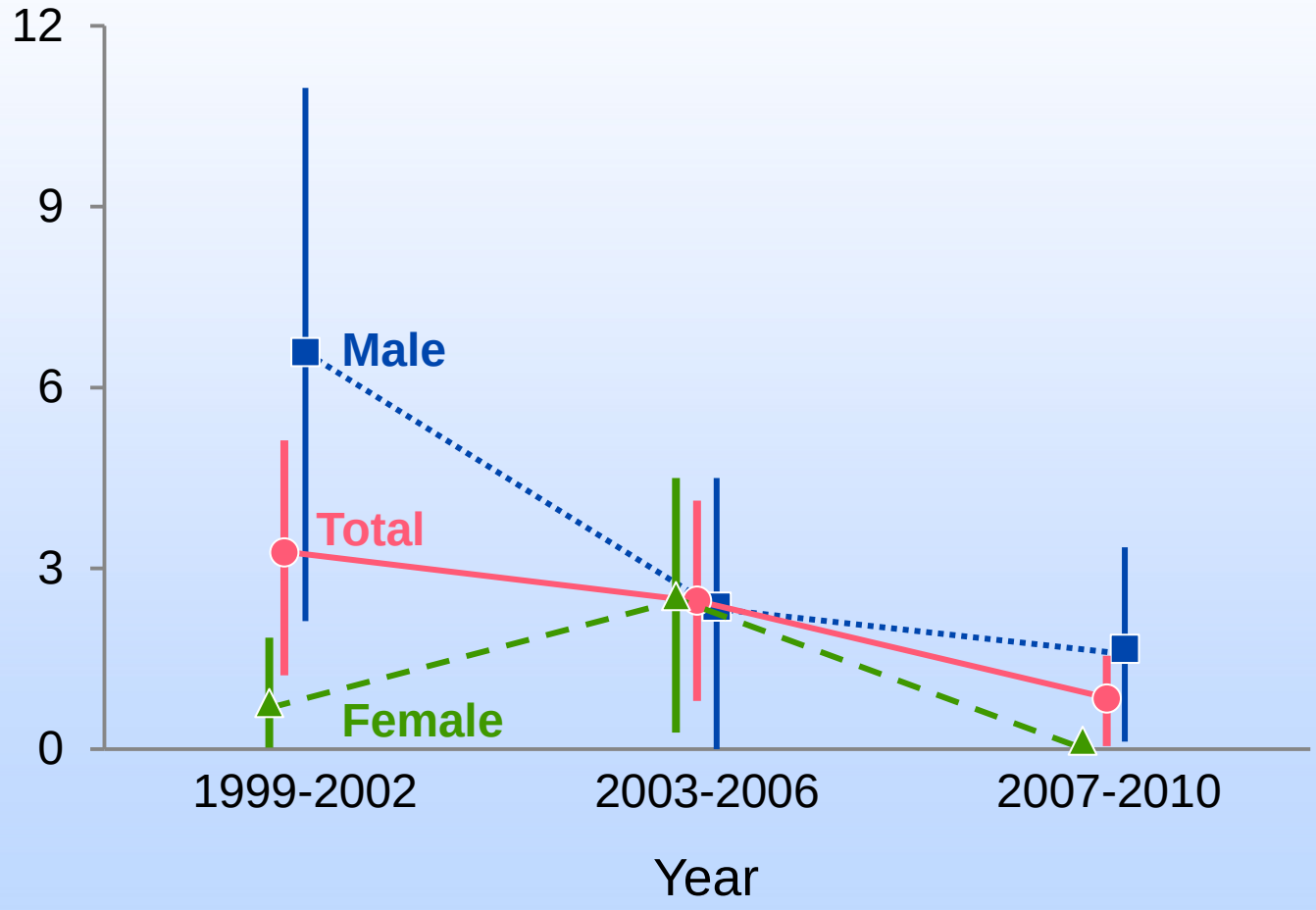

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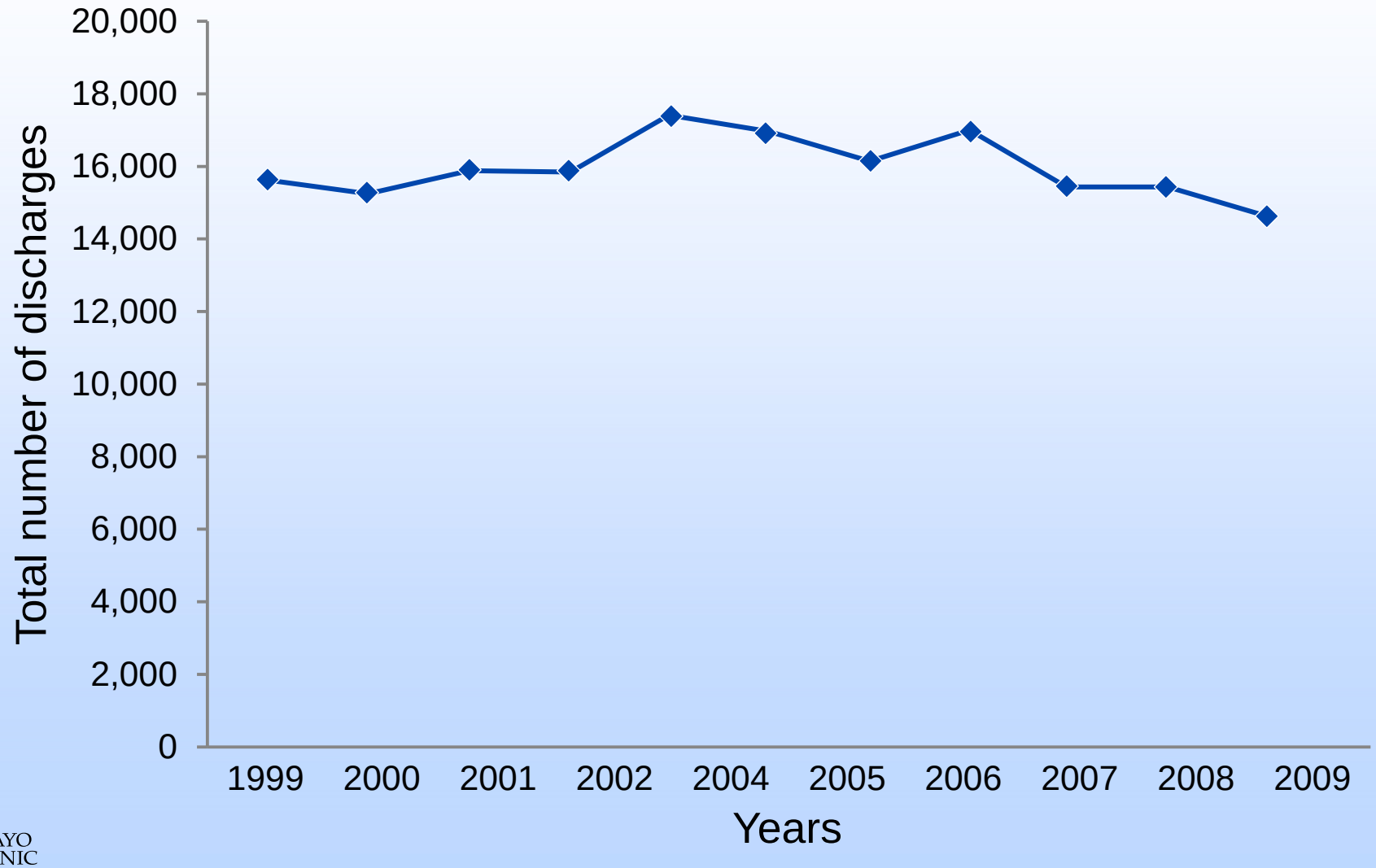
NIS Database – VGS IE



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IE Prophylaxis
Olmsted County, MN

Update

- 2011-2013
- No VGS incidence increase
- Limitation
  - ~150,000 population
  - Small # of IE cases/year

DeSimone D, et al. Unpublished data

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IE Prophylaxis
2007 AHA Guidelines

Pediatric Health Information Systems Database

- 37 centers, 2003-2010
- 1157 IE cases
- 68% had CHD
- Results
  - Oral streptococci – trend (P=0.05) toward decreased hospital admissions over time

Pasquali SK, et al. Am Heart J 2012;163:894-9

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IE Prophylaxis
2007 AHA Guidelines

- Medicare database (1999-2010)
- Principal or secondary dx of IE
- Hospitalizations
  - Per 100,000 person-years
- 30-day and 1-year mortality rates

Bikdeli B, et al. J Am Coll Cardiol 2013;62:2217-26

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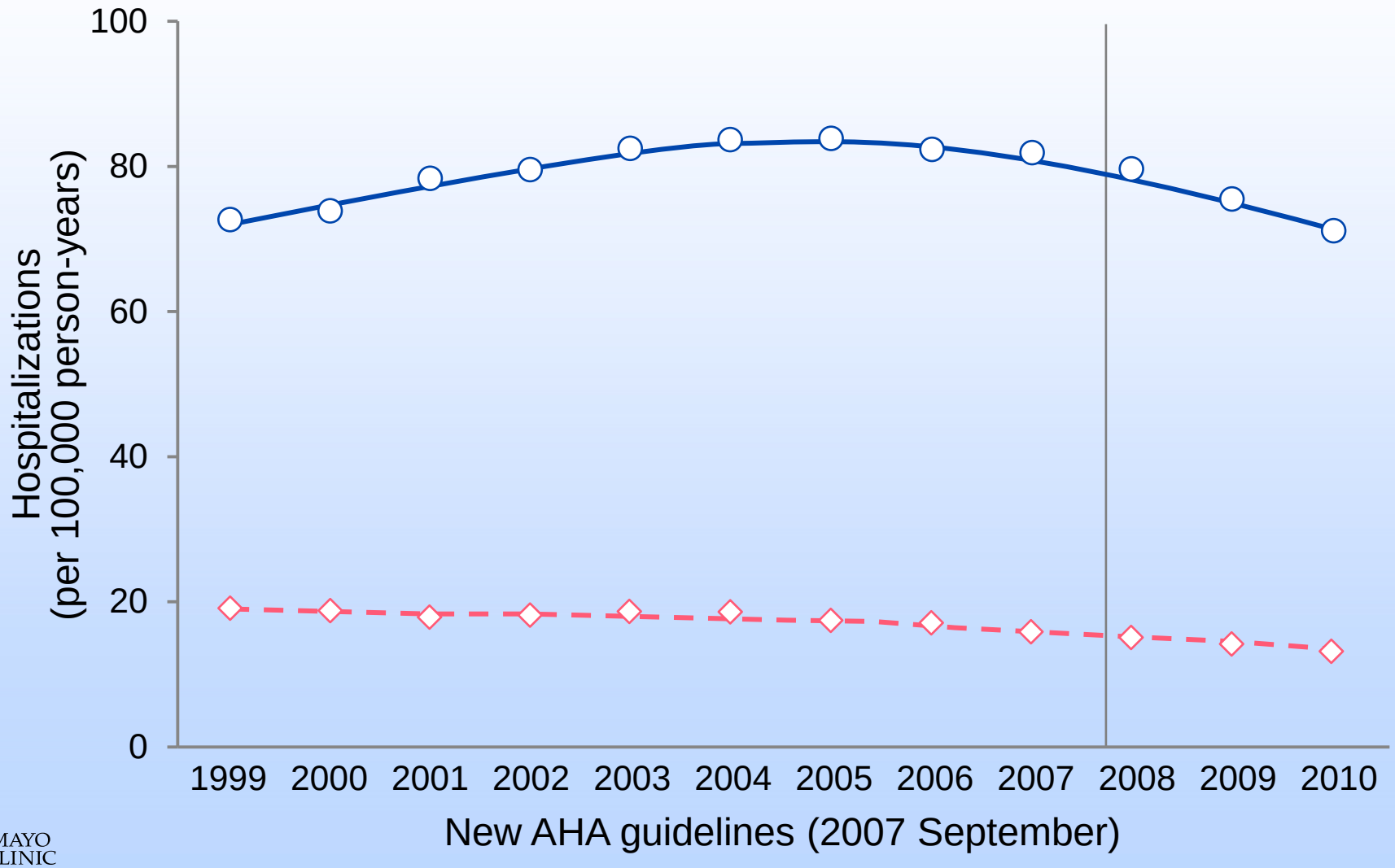
IE Prophylaxis – Medicare database (JACC 2013)



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IE Prophylaxis
Clinician Survey

“NICE guideline 64”

- 99% of respondents aware of guideline
- 36% of dentists have provided prophylaxis
- 1/3 of dentists have cases in whom prophylaxis was prescribed by other clinicians

Dayer MJ, et al. Q J Med 2013; ePub January 3, 2013

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IE Prophylaxis
AVERT

Silzone™ coating – mechanical valve

- 4400 patients in 17 centers
- July 1998 – recruitment
- January 21, 2000 – stopped
  - Perivalvular leak
    - Inhibited normal fibroblast response
  - Rates of IE in both groups – same

Schaff H, et al. J Heart Valve Dis 1998;8:131-139

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Infective Endocarditis
Conclusions

Many areas of controversy

- MRI brain – For all?
- Optimal timing of surgery?
- Daptomycin vs. vancomycin – MRSA/MRSE left-sided IE?
- Wholesale adoption of double beta-lactam therapy for enterococcal IE?
- Role of newer agents
  - Oritavancin, dalbavancin?
- Benefit of dental prophylaxis?
- Clinical trials are needed

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