Foreign Body Infections Orthopedic Devices

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Pathogenesis of Device Infection

- Direct introduction of pathogen at surgery with use or manipulation
- Device erosion into contaminated area
- Direct extension of adjacent infection
- Hematogenous seeding
- Depressed local host defenses: C', PMNs
- Biofilm – Embedded organisms stationary phase and resist action of many antibiotics

Microbiology Spine Implant Infection

Microbiology	Early* (N=30)	Late† (N=51)
S aureus	13	15
Coag-neg staph	6	13
Gram-neg bacilli	10	1
Streptococci	5	11
Peptostreptococci	2	1
Corynebacteria	2	2
P acnes	2	9
Candida	---	3
Lactobacillus	---	1
Culture negative	1	8

*7 polymicrobial.
†12 polymicrobial.   Kowalski et al. CID 2007;44(April 1).

Characteristics of Foreign Body Infections

- Relatively **infrequent events** (occasional exceptions – often percutaneous element: CAPD catheter, ventricular assist device)
- Often **caused by low inoculum exposure**
- May be cause by low virulence organism (high virulence too –relates to pathogenesis)
- Selected organisms implicated frequently, likely a **unique "tropism"** - **Staphylococci**
- Difficult to cure without **device removal**
- Cause significant **morbidity and mortality**

Outcome of Early Spine Implant Infection

Total		30
Implant removed	1	
Antibiotics only	1	
Debride - retain- antibiotic – no suppression		6
Fail	5 (83%)	
Debride – retain – antibiotic - suppression		22
Fail	5 (23%)	
Non-failure	17	
On suppression	7	
Off suppression 468 d (169-687)	10	
Antibiotic therapy IV 41 d (27-43)		
Oral 303 d (147-672)		

Kowalski et al. CID 2007;44(April 1).

Outcome of Late Spinal Implant Infection

Total		51
Antibiotics only	6	
Failed	4 (67%)	
Debride – retain – antibiotics	13	
Suppressed - failed/total	4/8	
Non-suppressed - failed/total	3/5	
Debride – remove – antibiotics	32	
Failed	7 (22%)	
New implant	10	
Cured	15	
Antibiotic therapy		
IV 42 d (36-44)		
Oral 410 d (61-667)	Kowalski et al. CID 2007;44(April 1).	

Prosthetic Joint Infection Clinical Presentations

- **Acute wound infection** extending to joint
  Post operative wound infection –
  days to 1 month- out to 3 months
- **Cryptic indolent infection** –Several months
  to 2 yrs post op. Major symptom is
  pain
- **Acute septic arthritis**
  > 2 yrs after joint replacement

Diagnosis of Prosthetic Joint Infection: Pre – Intra Operative Assessment

Diagnosis:
- **Preoperative joint aspirate: 2 or 3 pos of > 3 specimens -86% sensitvity,94% specificity**
- **Gram stain not useful**
- **At surgery obtain >/= 3 or 4 specimens (capsule, membrane at implant, suspicious tissue), multiple positive cultures**
- **≥ 5 PMN/hpf considered diagnostic (sensitivity ≥ 80%, specificity ≥ 90%)**

Atkins, J Clin Micro 1998; 36:2932

Prosthesis Sonication Provides Increased Sensitivity for Prosthetic Joint Infection

Add 400 ml Ringer's Solution (laboratory)

0.5 ml Aerobic & Anaerobic Culture Plates

Prosthesis Placed in Container (operating room) → Vortex 30 sec → Sonicate 5 min → Vortex 30 sec
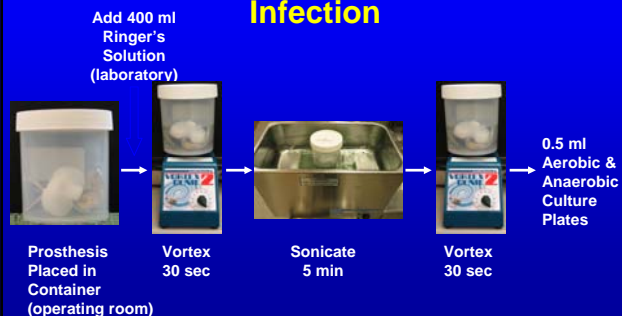
Trampuz et al. NEJM 2007;357:654

Sonication of Removed Hip and Knee Prostheses for Diagnosis of Infection (Aseptic Failure 252; PJI 79)

	Cultured Material		
	Sonicate*	Tissue**	Synovial Fluid
Sensitivity (%)	78.5	60.8	56.3
Specificity (%)	98.8	99.2	98.1

14/79 sonicate only positive: CN Staph 5, S. aureus 3, Enterococcus 2, Strep 1, Candida 1, Proprionibacteria 2

17 sonicate negative

* > 5 CFU/plate; ** = 2 specimens positive

PERFORMS BEST IF OFF RX 14 DAYS

Trampuz, et al., NEJM 2007; 357:654.

Prosthetic Joint Infection;Time to Detection in Culture
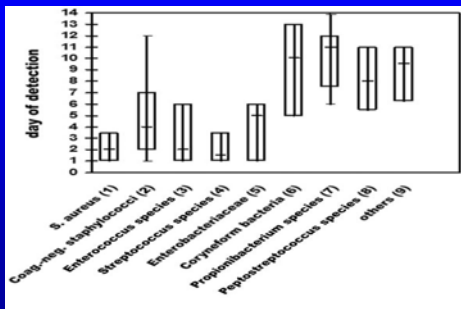
Schafer et al. CID 2008:47: 1403-9

Synovial Fluid for Diagnosis of Infected Prosthetic Knee Joint – 133 Failed TKR

	Aseptic N=99	Septic N=34	P Value
> 1 positive culture fluid/tissue	6 (6)	31 (91)	<0.001
WBC x 10³/µL	0.3 (0.1-16)	18.9 (0.3-178)	<0.001
Percent Neutrophils (range)	7 (0-79)	92 (55-100)	<0.001

Trampuz, et al., Am J Med 2004; 117:556-562.

Distribution of WBC Counts and Neutrophils in PJ Synovial Fluid Prosthetic Knee Joint – 133 Failed TKR

Trampuz et al Am J Med 2004;117:556-562

Diagnosis of Infected Joint Prostheses

Test	Sensitivity (%)	Specificity (%)
ESR >30 to 35 mm/hr	61-88	79-100
C reactive protein ≥ 10 mg/L	91-96	88-92
Technetium scan	High	Low
Gallium scan	High	Low
Indium WBC scan	38-100	41-100

NONE ARE DIAGNOSTIC but a normal ESR and CRP are strongly against PJI

Microbiology of 578 Prosthetic Joint Infections: Mayo Clinic 1992-1997

ORGANISM	NO (%)
Coagulase negative staphylococci	172 (30)
S.aureus	135 (23)
Polymicrobial	71 (12)
Unknown	64 (11)
Streptococci	51 (9)
Gram negative bacilli	32 (6)
Anaerobes	23 (4)
Enterococci	16 (3)
Others	14 (2)
TOTAL	578

Steckelberg and Osmond, 2000

Hematogenous Seeding of Prosthetic Joints: Organisms Isolated from Joint 36 Cases

S.aureus	12
S.epidermidis	3
Group A streptococci	2
Beta-hemolytic streptococci	4
Enterococci	1
Diphtheroid	1
E.coli	2
P.aeruginosa	2
Enterobacteriaceae	1
Other GNR	3
Bacteroides	2
Mixed Gr+/GR-	3

Infection of Orthopedic Devices After S. aureus Bacteremia

	Infected/Bacteremic (%)
Prosthetic joints: All	15/44 (34)
Knees	5/10 (50)
Hips	9/34 (26)
Devices	1/15 (7)

- 13 mos – 25 years after placement
- Diagnosis after bacteremia: 0-65 d (median 3)

Murdoch, et al., CID 2002; 32:647

Treatment of Foreign Body Infection

- **Goals of Therapy**

  ➢ Preserve Life
  ➢ Relieve Pain
  ➢ Eradicate infection with or without device removal
  ➢ Maintain device function or provide an alternative

Treatment of Infected Joint Prosthesis

- **Traditional approach – device removal**
- **Consider patient's general health**
- **Consider device function – pain/loosening**
- Options:
  - **Amputation**
  - **Arthrodesis**
  - **Resection arthroplasty**
  - **One stage revision: 80% success**
  - **Two stage revision: 85-91% success**
    - **Antibiotic impregnated cement may increase success rate**
  - **Debridement and Retention**

Treatment of Prosthetic Joint Infection

Prosthesis loose Mild tissue damage "Susceptible" organism	Prosthesis loose,Resistant organism, Mod/severe tissue damage
Debridement **One stage exchange** **Antibiotic therapy 3-6 mos**	**Debride/remove device** **Spacer- suscept organism** **No spacer- resist organism** **Antibiotic Therapy $\geq$6 wks**
	Assessment hiatus varies with pathogen **Reinsert prosthesis** **Antibiotic suppression**

Zimmerli et al. *NEJM* 2004;351:1645-1654.

Treatment of Infected Prosthetic Joints

Approach (year of publication)	No Recurrence
•Resection arthroplasty	
(1977-89)	236/301 THA (78%)
(1985-90)	25/32 TKA (78%)
•One step exchange (1978-89)	
Without antibiotic in cement	145/160 THA (90%)
With antibiotic in cement	915/1143 THA (80%)
•Two step exchange (1981-89)	
Without antibiotic in cement	115/202 THA (84%)
With antibiotic in cement	51/60 THA (85%)
Without antibiotic in cement	88/102 TKA (86%)
With antibiotic in cement	33/37 TKA (89%)
With antibiotic in cement plus spacer	53/58 TKA (91%)

Steckleberg & Osman, Infections Associated with Indwelling Devices, ASM Press 1994

Management
Reimplantation-THA Infection
One Stage vs. Two Stage Exchange
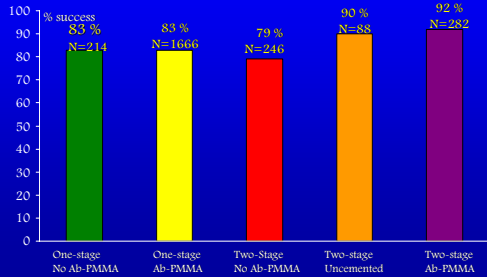
% success

Bar	Value
One-stage No Ab-PMMA	83 % N=214
One-stage Ab-PMMA	83 % N=1666
Two-Stage No Ab-PMMA	79 % N=246
Two-stage Uncemented	90 % N=88
Two-stage Ab-PMMA	92 % N=282

Steckelberg, J.M., Osmon, D.R. In Press. Prosthetic joint infections. In: Bisno, A. L., Waldvogel, F.A. *Infections Associated With Indwelling Medical Devices* .

Management
Reimplantation-TKA Infection
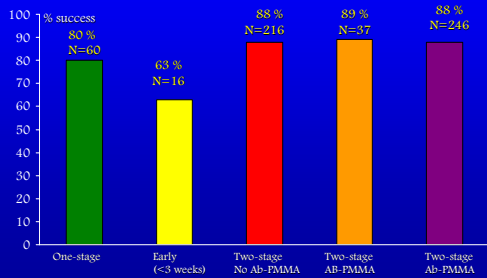
% success

Bar	Value
One-stage	80 % N=60
Early (<3 weeks)	63 % N=16
Two-stage No Ab-PMMA	88 % N=216
Two-stage AB-PMMA	89 % N=37
Two-stage Ab-PMMA	88 % N=246

Steckelberg, J.M., Osmon, D.R. In Press. Prosthetic joint infections. In: Bisno, A. L., Waldvogel, F.A. *Infections Associated With Indwelling Medical Devices* .

213 PJI Treated with Two Staged Exchange 1995-99

Kaplan –Meier Joint Survival
Cumulative Proportion of PJ Survival

P=0.03

AI absent (181)
AI present (23)

Survival Time (days)

Marculescu, et al , IDSA 2003 Abst #283

23 PJI with Acute Inflammation at Reimplantation Treated with and without Chronic Oral Antibiotics 1995-99:

Kaplan-Meier Cumulative Survival Plot
Cumulative Proportion of Survival

p=0.05

Survival Time (days)

♦ No oral chronic suppression

— Chronic oral suppression

Marculescu, et al , IDSA 2003 Abst #283

PJI in Patients with Rheumatoid Arthritis

Organism	Number (%) N=200	Joint Age – Months Median (25-75%)
S.aureus	74 (37)	31 (10, 84)
Coag-neg staph	25 (12)	22 (15, 48)
Anaerobes	16 (8)	52 (27-87)
Polymicrobial	30 (15)	12 (3-20)
Gram-neg bacilli	22 (11)	19 (11-50)
Enterococci	7 (4)	27 (6-108)
Sterile	19 (9)	36 (9-79)
Other	7 (4)	24 (8-36)

Berbari, et al., CID 2006; 42:216-223.

PJI in 200 Patients with Rheumatoid Arthritis

Receiving steroid Rx 84 (42%)
Synchronous joint infection: Common, S.aureus

Treatment	# (%)	5 Year Survival % (CI)
Debride/retain	46 (23)	32 (21-49%)
Two stage exchange	39 (19)	79 (66-93%)
Resection arthroplasty	74 (37)	61 (49-74%)
Other	41 (21)	54 (38-80%)

Debride/retain (5.9 OR), resection (2.5 OR), other (3.1 OR) vs.
2 stage exchange

Berbari, et al., CID 2006; 42:216-223.

Culture Negative Prosthetic Joint Infection in 60 (7%) of 897 Infections

- **Features: T° > 38-13 (22%); sinus – 6 (10%); purulence 27 (45%); pathology 47 (78%)**
- **Antibiotics within prior 3 months: 32 (53%); 14 ongoing**
- **Treatment:**
  - **Surgery: 2 stage 34 (57%); retain 12 (20%); resection 8 (13%); 1 stage 5 (7%); amputate 1 (2%)**
  - **Antibiotic: cephalosporins, vancomycin, median 28d (2-88)**
- **Outcome: 5 yr survival 82% (2 stage 94%; retention 71%, resection 51%)**

Berbari, et al., CID 2007; 45:1113-9.

Treatment of Enterococcal Prosthetic Joint Infection

Variable	Monotherapy (%) N=31	Combination Rx (%) N=19	P
Loosening Surgical Rx	11 (35)	15 (79)	0.004
2 stage	9 (29)	8 (42)	
Resection	14 (45)	9 (47)	
Retain	5 (16)	0	
Failure	5 (16)	7 (37)	0.2
Nephrotoxicity	2 (6)	5 (26)	0.09
CN VIII Toxicity	0	6 (32)	0.002
2 yr Infection Free	88% (77-100)	72 % (54-96)	0.1

Helou, et al., CID 2008; 47:903-909.

PJI - Debridment and Retention Potential Utilization

- Relatively avirulent organism (strep > staph)
- Susceptible to oral antimicrobials
- Well seated prosthesis (not loose)
- Short duration symptoms (< 2-3 wks, days)
- Debridement (? change liner)
- Not necessarily recent implant
- Long term suppressive therapy desirable ?
- Patient with increased surgical risks

Treatment of Prosthetic Joint Infection

Early onset or hematogenous

≤3 weeks

Stable device Intact soft tissue

Deep tissue – synovial culture

Debride and retain Antibiotic therapy 3-6 months
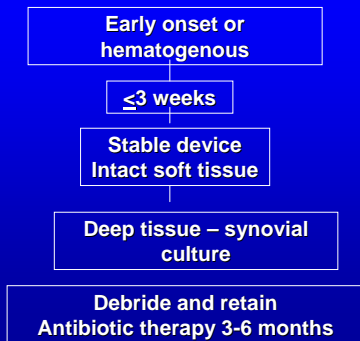
Zimmerli et al. *NEJM* 2004;351:1645-1654.

Outcome of PJI Treated with Debridement and Retention of Components 1995-99

- **Treated: 99/509 (19%) None loose intraop**
- **Staphylococci: 32% S. aureus; 23% CNS,14%strep**
- **IV Antibiotics: 28 d median (1-90)**
- **Suppression: 89% median 541 d (4-2673)**
- **Failure 53 pts median F/U 700 d (1-2779)**
- **Success 2 yrs: 60% (50-71% CI)**
- **Risk Failure: S. aureus [HR 5.1 (2.3-11.2)], sinus track [HR 2.8 (1.5-5.4)]; Sx > 8 d [HR 1.79 (1.04-3.09)]**

Marculescu, et al., CID 2006;42:471-8

Joint Survival for 99 PJI Episodes Treated with Debridement and Retention 1995-99

Kaplan-Meier Cumulative Survival Plot

Cumulative Proportion of Survival

P = 0.15

No suppression
suppression

Survival Time
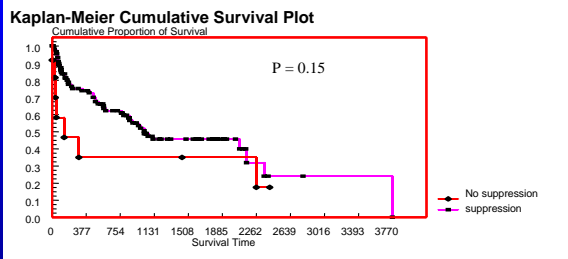
Marculescu, et al., CID 2006;42:471-8

Debridement and Retention of Prosthesis Penicillin Susceptible Streptococcal PJI

- **Attempted:** 19/232 episodes (13 TKA, 6 THA)
- **Mean Sx:** 4 d (1-10 d)
- **Duration PJ:** Mean 1.5 yr (0.15-13 yr)
- **Organisms:** 6 Gr G, 7 Gr B, 4 viridans, 2 Gr A
- **Fever:** 13 (68%), bacteremia 4 (21%)
- **Rx:** IV – median 28 d (14-37) β-lactams, 8 long term oral Rx
- **Outcome:** No relapse 17/19 (89%) at median F/U 3.9 yr (0.3-21.8yr); failure - 2 Gr B strep – not on oral Rx (3.8, 6.8 m)

Meehan, et al., CID 2003; 36:845-849.

Rifampin Treatment of Orthopedic Implant Related Staphylococcal Infection – Randomized Trial*

	Cipro-Rifampin**	Cipro-Placebo
Enrolled	18	15
Onset < 2 mos after surg	12	7
Success/treated	16/18	9/15
Success/completed Rx	12/12 (35 mos f/u)	7/12 (33 mos f/u)
Success retreated	5/7	1 /2
Resistance emerged (Cipro)		4/5
Median days infection (range)	5 (0-19)	4 (0-21)

*Early post -op or hematogenous infection, device stable
**2 wks parenteral combination therapy, then cipro 750 mg q 12 h, rifampin 450 mg q 12 h for 3 (hips) to 6 (knees) months

Zimmerli, et al., JAMA 1998; 279:1537

Treatment for Salvage of Staphylococcal Infected Orthopedic Device (PJI)

- **Select appropriate patient**
- **Although data is largely from regimens using a quinolone, reasonable to use other antistaphylococcal agents (B-lactam, TMP/SMZ, linezolid, fusidic acid)**
- **Rifampin is an important part of regimen for staphylococcal infections**
- **Reduce bacterial burden to avoid emergence of rifampin resistance**
- **Long courses of rx have been used, monitor for toxicity: >/=3 months (3hips,6 months knees)**

Clinical and Cost Effectiveness of Two-stage exchange vs. Debridement and Retention for THA infection in the Elderly

- A Markov model was used to simulate patients' projected lifetime clinical course in hypothetical cohorts of 65-year-old and frail 80-year-old men and women.

- Initial debridement and retention increased life expectancy 2.2-2.6 quality-adjusted life months and had a favorable cost-effectiveness ratio in all cohorts.

- Results were most sensitive to the annual rate of relapse after debridement and age at initial diagnosis of infection.

- In the absence of prospective clinical trials, debridement and retention is a reasonable strategy for treatment of older persons with staphylococcal or streptococcal infection and a non-loosened prosthesis.

Fisman DN. Reilly DT. Karchmer AW. Goldie SJ. Clinical Infectious Diseases. 32(3):419-30, 2001

Treatment of Prosthetic Joint Infection According to Current Recommendations

- 68 episodes: 6 early, 30 delayed, 32 late
- 39/68 (57%) success at 2 yrs F/U
- Risk for treatment failure:

Variable	Hazard Ratio (CI 95%)	P
Age	1.03 (0.99-1.1)	0.12
Charlson score	1.09 (0.89-1.3)	0.42
Duration of Sx	1.87 (0.66-5.3)	0.14
Infection score (mean)	1.29 (1.1-1.4)	<0.001*
Sinus tract	2.35 (1.1-5.0)	0.02
Inadequate antibiotics	3.45 (1.5-7.6)	0.002*
Surgical strategy not recommended	2.34 (1.1-4.7)	0.01*

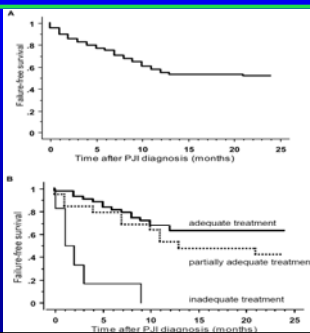*Significant in Cox regression analysis
Betsch, et al., CID 2008; 46:1221-1226.

Proportion of Patients whose Prosthesis Remained Infection Free

All patients

Patients by Treament Group

Bertsch et al.
CID 46(8):1221-1226

Surgical Treatment and Outcome of PJI

	No. Treated (%) [% Cured]			
	Hips N=63*	Knees N=40**	Hips or Knees N=68***	Total N=171
Debride/retain	14 (22) [57]	21 (53) [45]	12 (18) [50]	47 (27) [72]
One stage	16 (26) [93]	2 (5) [100]	4 (6) [0]	22 (13) [77]
Two stage	31 (49) [90]	13 (33) [85]	51 (75) [65]	95 (55) [76]
Other	2 (3) [50]	4 (10) [75]	1 (1) [0]	7 (4) [37]
By algorithm				
Yes	50 (79) [88]	26 (65) [92]		
No	13 (21) [62]	14 (35) [86]		

*Giulieri, et al., Infection 2004; 52:222.
**Laffer, et al., Clin Microbiol Infect 2006; 12:433.
***Betsch, et al., CID 2008; 46:1221.

Dental Procedures as Risk Factors for Prosthetic Hip or Knee Infection: A Hospital-Based Prospective Case-Control Study

Elie F. Berbari,[1] Douglas R. Osmon,[1] Alan Carr,[2] Arlen D. Hanssen,[3] Larry M. Baddour,[1] Doris Greene,[1] Leo I. Kupp,[6] Linda W. Baughan,[5] W. Scott Harmsen,[4] Jayawant N. Mandrekar,[4] Terry M. Therneau,[4] James M. Steckelberg,[1] Abinash Virk,[1] and Walter R. Wilson[1]

Departments of [1]Medicine, Division of Infectious Diseases, [2]Dental surgery, [3]Orthopedic Surgery, and [4]Biostatistics and Epidemiology, Mayo Clinic College of Medicine, Rochester, and [5]Department of Periodontics, Burnsville, Minnesota; and [6]Department of Endodontics, Virginia Commonwealth University, Richmond, Virginia

(See the editorial commentary by Zimmerli and Sendi, on pages 17–9.)

Background. The actual risk of prosthetic joint infection as a result of dental procedures and the role of antibiotic prophylaxis have not been defined.

Methods. To examine the association between dental procedures with or without antibiotic prophylaxis and prosthetic hip or knee infection, a prospective, single-center, case-control study for the period 2001–2006 was performed at a 1200-bed tertiary care hospital in Rochester, Minnesota. Case patients were patients hospitalized with total hip or knee infection. Control subjects were patients who underwent a total hip or knee arthroplasty but without a prosthetic joint infection who were hospitalized during the same period on the same orthopedic floor. Data regarding demographic features and potential risk factors were collected. Logistic regression was used to assess the association of variables with the odds of infection.

Results. A total of 339 case patients and 339 control subjects were enrolled in the study. There was no increased risk of prosthetic hip or knee infection for patients undergoing a high-risk or low-risk dental procedure who were not administered antibiotic prophylaxis (adjusted odds ratio [OR], 0.8; 95% confidence interval [CI], 0.4–1.6), compared with the risk for patients not undergoing a dental procedure (adjusted OR, 0.6; 95% CI, 0.4–1.1) respectively. Antibiotic prophylaxis in high-risk or low-risk dental procedures did not decrease the risk of subsequent total hip or knee infection (adjusted OR, 0.9 [95% CI, 0.5–1.6] and 1.2 [95% CI, 0.7–2.2], respectively).

Conclusions. Dental procedures were not risk factors for subsequent total hip or knee infection. The use of antibiotic prophylaxis prior to dental procedures did not decrease the risk of subsequent total hip or knee infection.

CID 2010;50:8-16

Summary

- **Increasing attempt at retention vs. 2 stage replacement (Europe > U.S.)**
- **Treatment according to algorithm improves outcome. Consider:**
  - Prosthesis function
  - Tissue damage – fistula, etc.
  - Organism susceptibility – available Rx
  - Long course of antimicrobials (> 3 months)
  - Biofilm targeted antimicrobials: rifampin, FQs
  - Patient general health/wishes
- **Post treatment management not resolved – stop antibiotics vs. prolonged suppression**