Overview of Antibiotics Treatment: Is 6 Weeks the Norm? What About Suppression?

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Disclosure Information

- I have no financial relationship to disclose.

- Is 6 Weeks the Norm?
- Yes (IDSA Guideline, 2012)
- What About Suppression?
- Yes, we do it – will discuss DAIR… (IDSA Guideline, 2012)

Principle of ABX therapy

- Antibiotic stewardship promotes "**optimal antibiotic drug regimen** including **dosing, duration of therapy**, and **route of administration**"
  – Clinical Infectious Diseases ; 2016 ; 62 : 51 -77

PJI treatment Goal of therapy

- Long term pain-free functional joint which can be accomplished by eradication of infection

Inf Disease Soc. of America PJI Guideline- Dec 2012 Multidisciplinary committee from Europe & Europe

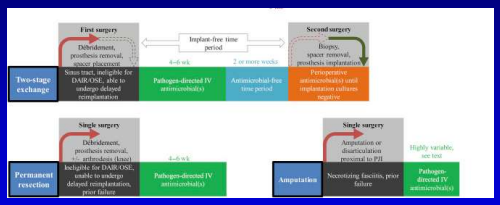
- Each section begins with a specific clinical question and is followed by recommendations evidence in support of the recommendations.

Table 1. Strength of Recommendation and Quality of Evidence

Category/Grade	Definition
Strength of recommendation	
A	Good evidence to support a recommendation for or against use.
B	Moderate evidence to support a recommendation for or against use.
C	Poor evidence to support a recommendation.
Quality of evidence	
I	Evidence from >1 properly randomized, controlled trial.
II	Evidence from >1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments.
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Management of Prosthetic Joint Infection

Inf Dis Clin North Am v31p 237 2017



TSE- T stage Explant

- Most patients receive a 4 to 6-week course of pathogen-directed IV abx
- The expected success rate > 85% for both hip and knee PJI based on several systematic reviews and studies reporting results 5 or more years after treatment (Inf Dis Clin North ; 2017)

Duration of IV Antimicrobial Therapy

- Retrospective data
- No randomized control trials
- Most USA investigators have reported outcome data on 6 wks of IV abx therapy

- Insall et al. J Bone J Surg. 65A:1087-1098, 1983.
- Zimmerli, NEJM, 2004
- IDSA guideline, CID: 2012

S. aureus Prosthetic Joint Infection Treated with Prosthesis Removal and Delayed Reimplantation Arthroplasty Duration of intravenous antibiotic therapy

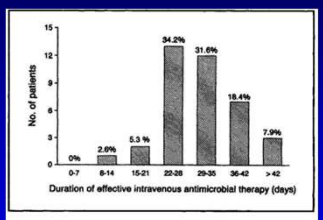


Figure 1. Duration of effective intravenous antimicrobial therapy for *Staphylococcus aureus* prosthetic joint infection treated with prosthesis removal and delayed reimplantation arthroplasty.

- Brandt et al.; Mayo Clin Proc. 1999;74:553-558.

Transition to oral antibiotic

References	IV	Total oral
Spanish Guideline (SEIMIC)2017	7- 14 days	6 weeks
French guideline 2009	14 days gram + 21 days P aer.	6 weeks
Zimmerli Swiss Med Wley 2005	2 weeks	6 weeks
IDSA 2012	4- 6 weeks	--

What About Suppression?

- PSAT is an option for patients with Surgical & medical contraindication
- Pt who refuses surgery
- Elderly patients
- Multiple previous revision
- etc

PSAT for PJI in the elderly:
a national multicenter cohort stuty

- 77 centers, France, 5 yrs.
- 136 patients, median age 86
- *S aureus* 41%
- Survival rate over 2 yrs 61%

- Prendki, Eur J Clin Micro Inf Dis 2017

Chronic Suppression for PJI CCF study

- 1999 – 2010, Cleveland, USA
  655 Hip and knee includingDAIR and TSE
  - 120 SAT ---- 92 eligible
  - 535- non suppresser -- 276 eligible
- Patients treated with PSAT after DAIR had an increased 5-year infection-free survival rate (64.7% vs. 30 %) compared with the non-suppression group p < 0.0001)
- - Patients who ahd DAIR & S. aureus infection had the greated benefit of suppression

Siqueira et al.; J Bone Joint Surg Am. 2015

Chronic Suppression for PJI CCF study

Limitations—
- Retrospective study
- Small study – 92 patiens
- Most patients who received DAIR did not received RIFAMPIN

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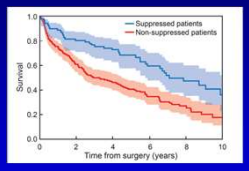
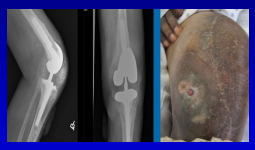


Siqueira et al.; J Bone Joint Surg Am. 2015

PSAT

Case 1

Case 2



The DAIR question…

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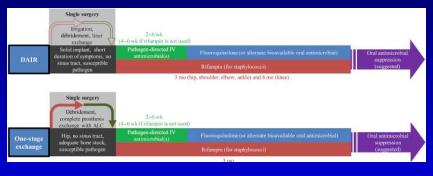

DAIR IDSA- candidates

- Have an early post-surgical - Age of IMPLANT- < 3 months
- or hematogenous infection (A-II), with a stable implant, and surrounding skin and soft tissues in good condition.
- b) ACUTE ≤3 weeks of symptoms (B-II).
- c) Can be treated with rifampin (staphylococcal infections) or fluoroquinolones (infections caused by GNB) (A-II).
- 2. Some patients who do not strictly meet the above criteria may still benefit from this strategy, but its implementation should be considered on an individualized basis, since there is a higher likelihood of failure (B-II).

DAIR IDSA PJI –guideline, 2012

Chronic Oral Antimicrobial Suppression

The panel could not agree on the use and duration of chronic suppression following the induction course of intravenous antimicrobial therapy in nonstaphylococcal PJI or following the 3- to 6-month course of quinolone or other companion drug/rifampin in staphylococcal PJI treated with debridement and component retention. Some members of the panel (D. L., W. Z.) would never use chronic suppression after

Short Communication

Short- versus long-duration levofloxacin plus rifampicin for acute staphylococcal prosthetic joint infection managed with implant retention: a randomised clinical trial ☆

S aureus PJI, THA & Knees

- An open-label, multicentre, (RCT)
- Patients with an early post-surgical or haematogenous staphylococcal PJI, managed with DAIR
- Levo +R ; randomised to receive 8 wks vs. 3 months (THA) or 6 months TKA PJI
- The primary endpoint was cure rate.

Prosthetic Joint Infection Group of the Spanish Network for Research in Infectious Diseases—REIPI.Int J Antimicrob Agents. 2016

Short Communication

Short- versus long-duration levofloxacin plus rifampicin for acute staphylococcal prosthetic joint infection managed with implant retention: a randomised clinical trial ☆

- 63 were included (52% women; med, 72 yrs)
- 33 patients (52%) LONG; 30 (48%) SHORT
- Median follow-up : 540 days
- ITT - cure rates were 58% Long vs 73% Short schedules (difference -15.7%, 95% CI -39.2% to 7.8%).
- This is the first RCT suggesting that 8 weeks of L+R could be non-inferior to longer standard treatments for acute staphylococcal PJI managed with DAIR.

Prosthetic Joint Infection Group of the Spanish Network for Research in Infectious Diseases--REIPI;J Antimicrob Agents. 2016

Consensus statement

Executive summary of management of prosthetic joint infections. Clinical practice guidelines by the Spanish Society of Infectious

DAIR

- What is the optimal duration of the antimicrobial treatment?
- •For acute staphylococcal PJI managed with rifampin and levofloxacin**, an 8-week schedule** of treatment after debridement appears sufficient for most patients (B-I).
  - Enferm Infecc Microbiol Clin.2017

Consensus statement

Executive summary of management of prosthetic joint infections. Clinical practice guidelines by the Spanish Society of Infectious

- **DAIR**
- •For PJI caused by other microorganisms treated with antibiotics with good activity against biofilm-embedded bacteria (i.e. ciprofloxacin for PJI caused by GNB)**, 8 weeks** is also a reasonable duration (B-III).
- •In other clinical scenarios, the most appropriate duration of treatment remains uncertain. A variable period between **8 and 12 weeks** may be adequate (B-III).
  - •Monitoring of CRP during the follow-up is advisable; the persistence of high values is suggestive of treatment failure (B-II), but its total normalization must not be a condition for deciding the end of therapy (B-II).

Conclusions

- 6 Weeks is still the norm for TSE
- Suppression therapy for selected cases
- Discrepancy between European and IDSA guideline regarding duration of therapy after DAIR

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Thank you
3rd Biennal Arthroplasty Disaster