

TREATMENT CONCEPTS OF PROSTHETIC JOINT ASSOCIATED INFECTIONS

International Conference on Surgical Infections (ICSI)
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- Introduction
- What are the treatment options?
- Role of rifamycins
- Treatment algorithm
- Clinical studies
- Conclusions

DEFINITIONS

Exogenous Infection

- Implantat-associated infection is mainly introduced during surgery or before complete wound healing
- Early (<3 months) or delayed (3-24m) infection in case of bridging symptoms starting after surgery

Hematogenous Infection

- New signs and symptoms during/after bloodstream or focal infection with hidden bacteremia

Probable hematogenous Infection

- All late infection (> 2 y) after free interval

TREATMENT OPTIONS OF PROSTHETIC JOINT ASSOCIATED INFECTION

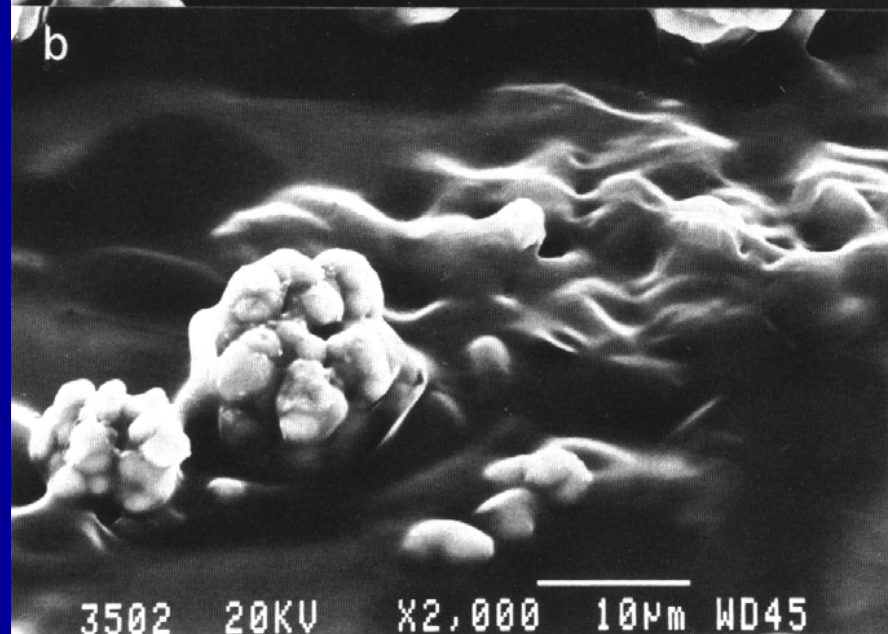
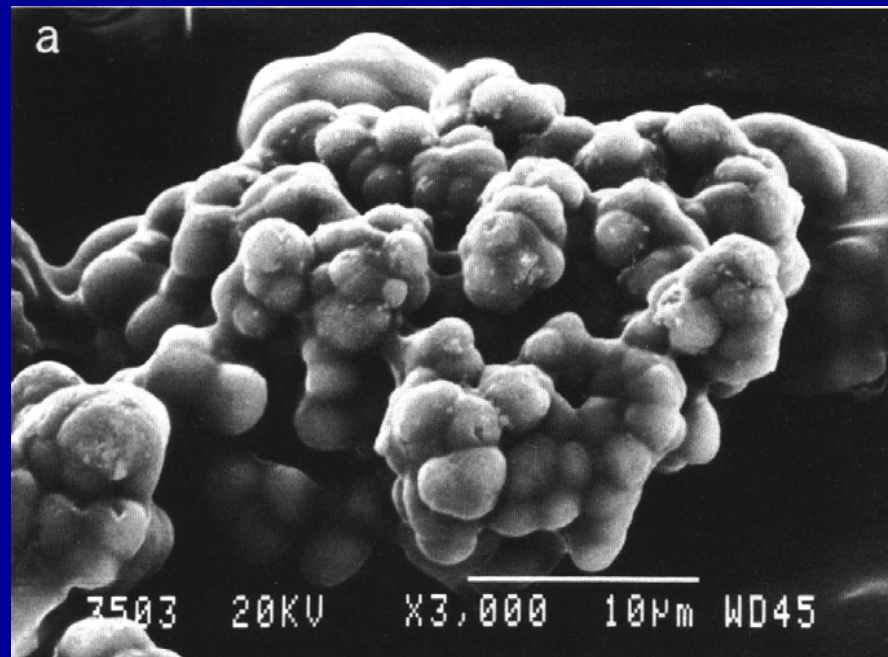
- 2-stage replacement
- 1-stage replacement
- Débridement with retention
- Removal without replacement
- Suppressive therapy

2-STAGE EXCHANGE FOR EVERYBODY: WHY SHOULD WE BEND THIS RULE?

- **The least invasive possible intervention should be chosen, since each surgery results in tissue destruction**
- **Débridement or 1-stage exchange allows resolution of the problem during one single hospital stay**

→ However, less invasive surgery should not be paid with poorer results

ROLE OF RIFAMYCINS IN THE TREATMENT OF PJI



PERSISTENCE OF INFECTION IN THE VICINITY OF AN IMPLANT

It is a general clinical observation that infection around a foreign body cannot be cured.

⇒ What is the reason that bacterial clearance cannot be predicted by the routine susceptibility testing?

GUINEA PIG MODEL TO TEST THE EFFICACY OF A 4-DAY ANTIBIOTIC TREATMENT

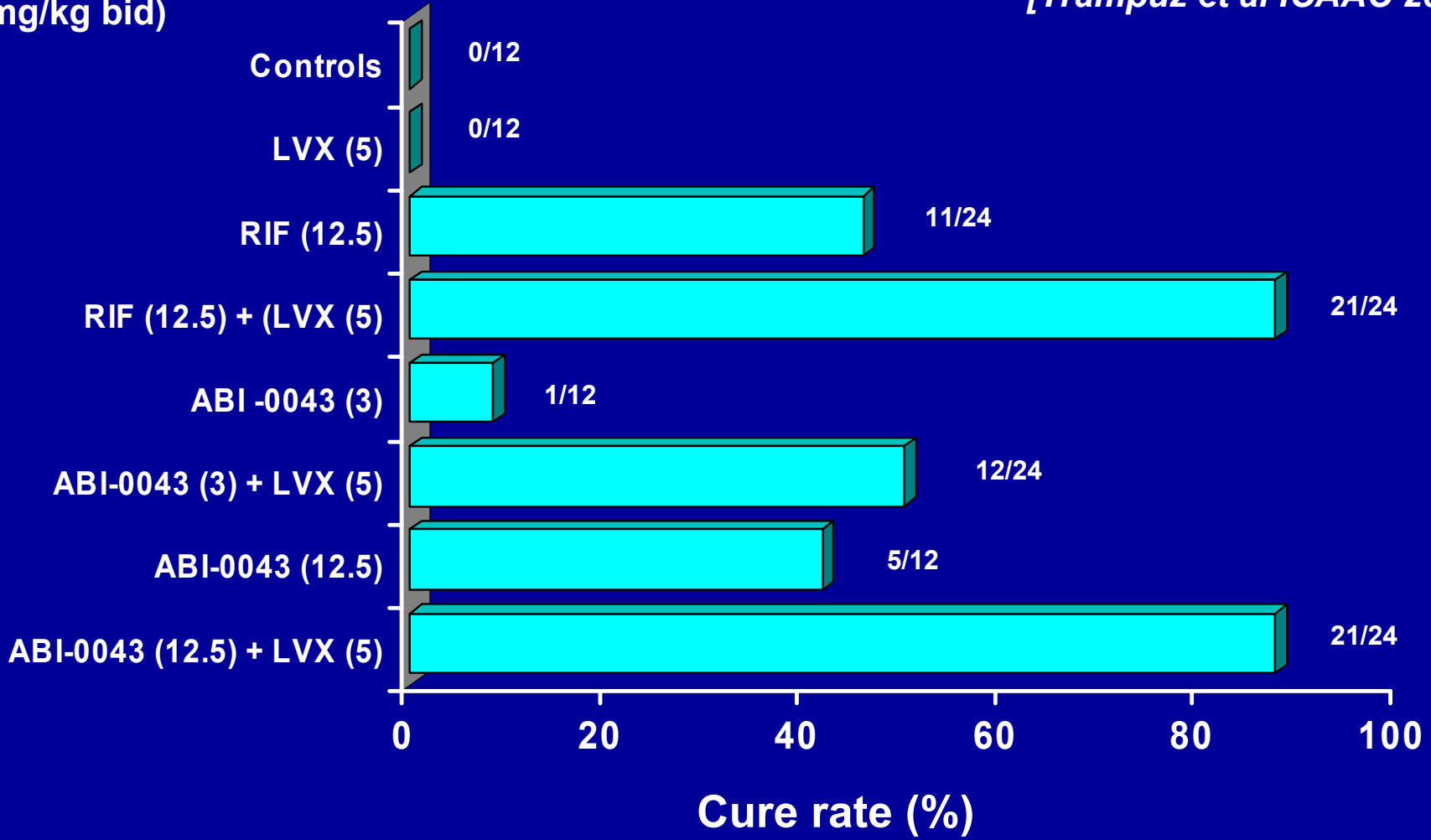


- Perforated cylinders (subcutaneous tissue cages) were directly inoculated with 10^4 cfu *S. aureus*
- Treatment was started 24h later with different bid-regimens by the intraperitoneal route

Efficacy of RIFAMPIN and a novel RIFAMYCIN ABI-0043 against *S. aureus* ATCC 29213 in the tissue-cage model

Antibiotic regimen (mg/kg bid)

[Trampuz et al ICAAC 2005]



PROPERTIES OF MICROORGANISMS INVOLVED IN DEVICE-RELATED INFECTIONS

Microorganisms involved in device-related infections are typically:

- in stationary-phase of growth**
- surface-adhering instead of planktonic**
- in biofilm formation**

Minimal bactericidal concentration in different growth phases (local peak level)

Strain <i>S.aureus</i>	Rifampin (8.3 mg/l)		Ciprofloxacin (0.95 mg/l)	
	MBC _{log} mg/l	MBC _{stat}	MBC _{log} mg/l	MBC _{stat}
KE89	1.8	3.6	0.8	133
ZP89	2.2	7.0	1.3	175
FB90	1.3	9.4	0.5	75
JJ89	0.7	5.1	0.8	133
EW90	0.7	1.8	1.1	113
HM92	1.7	1.7	0.8	150

ROLE OF RIFAMPIN IN IMPLANT-RELATED BONE INFECTIONS: A randomized controlled trial

Treatment: Initial débridement and antibiotics:

2 weeks iv

**Flucloxacillin or Vancomycin plus
Rifampin or Placebo**

followed by:

3-6 months p.os

Ciprofloxacin plus Rifampin or Placebo

Zimmerli et al. JAMA 279:1537-41,1998

STUDY POPULATION (2)

	Placebo- combination (n=15)	Rifampin- combination (n=18)
Microbiology:		
- <i>S. aureus</i> (0/26 methicillin-resistant)	11	15
- <i>S. epidermidis</i> (2/7 methicillin-resistant)	4	3
Initial iv-treatment:		
- Flucloxacillin	13	13
- Vancomycin	2	5
Follow-up (months) (median,range)	33 (15-41)	35 (24-46)

RESULTS

	CIP+PLACEBO	CIP+RIF
Cure (ITT)	9/15 (60%)	16/18 (89%)
Cure (as treated)	7/12 (58%)	12/12 (100%)*
Drop-out	3/15	6/18
Follow-up (months)	33 (15-41)	35 (24-46)

***p=0.019 (Fisher's exact test)**

ROLE OF RIFAMYCINS IN IMPLANT-RELATED BONE INFECTIONS: Summarized evidence

- *In vitro*: Rifamycins are able to kill stationary-phase staphylococci which is a prerequisite for the efficacy in device-related infection.
- *Animal model*: Rifamycins are more efficacious than other antimicrobial agents in a guinea pig model for device-related infection.
- *Controlled trial*: Among patients with a stable orthopedic implant, a long-term treatment with rifampin-ciprofloxacin combined with débridement surgery was highly efficacious without removal of the device.

PJI: TREATMENT ALGORITHM

CURRENT CONCEPTS

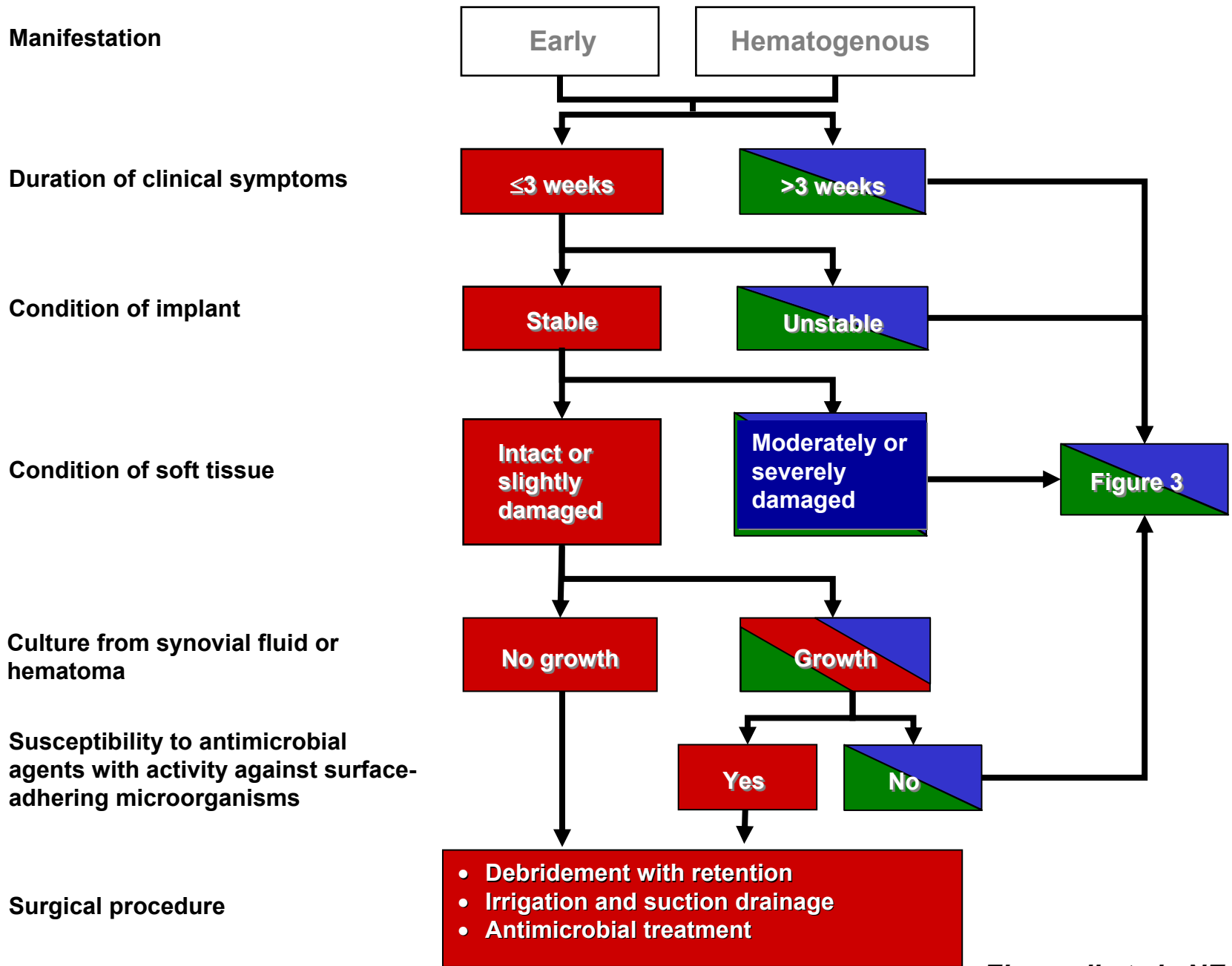
REVIEW ARTICLE

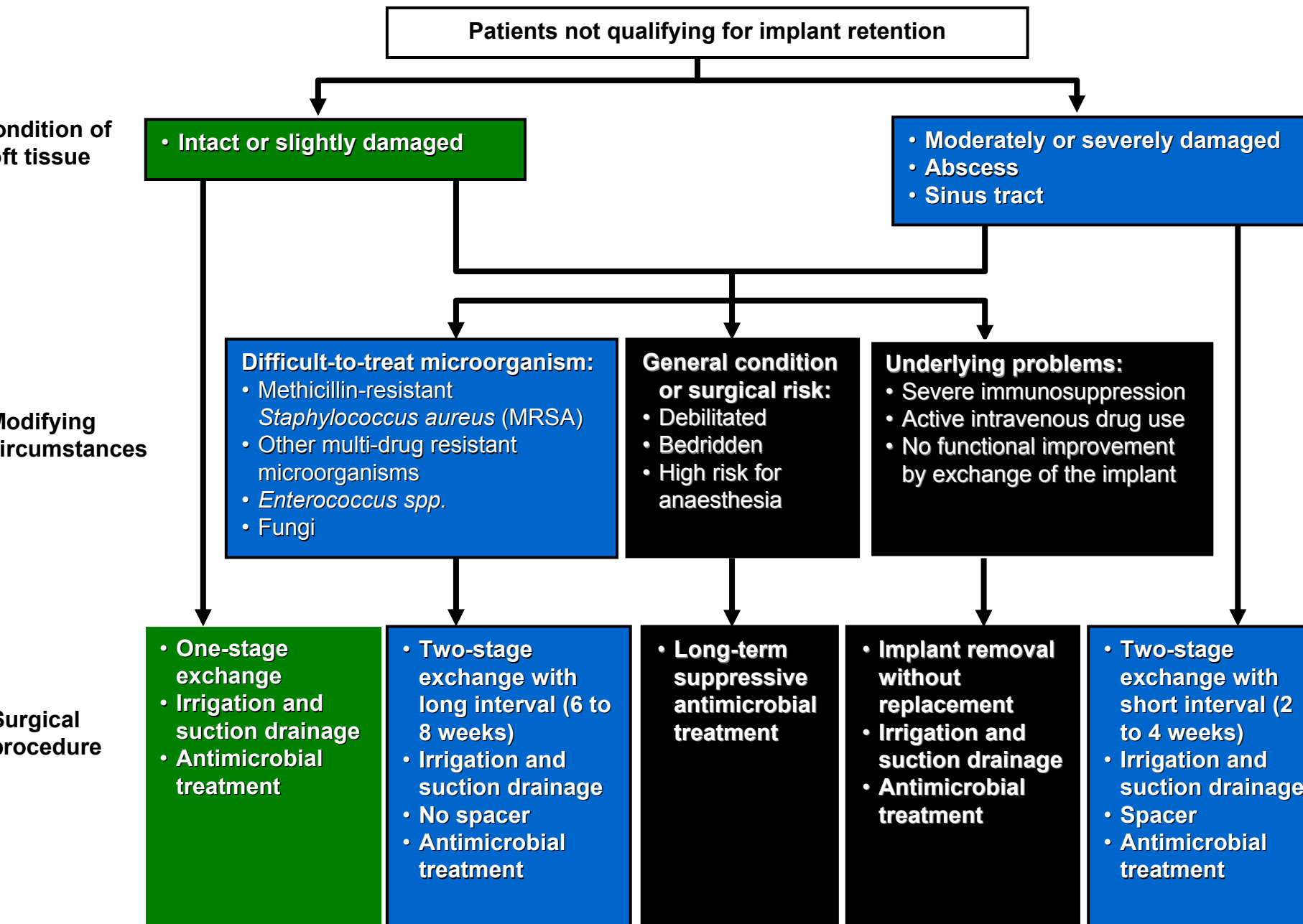
CURRENT CONCEPTS

Prosthetic Joint Infections

Werner Zimmerli, M.D., Andrej Trampuz, M.D., and Peter E. Ochsner, M.D.

N Engl J Med 351:1645-54, 2004





PJI:
CLINICAL COHORT STUDY

Validation with a cohort study in patients with TKA-associated infection: PATIENTS' CHARACTERISTICS

- **Number of episodes:** 40 (35 patients)
 - own patients 13 (36%)
 - referred patients 22 (64 %)
- **Median age:** 70.1 y (43-90)
- **Sex (F/M)** 51%/49%
- **Median follow-up** 28 months

[Laffer R et al. Clin Microbiol Infect Dis 12:1537-9 2006]

MICROORGANISMS

No. (%)

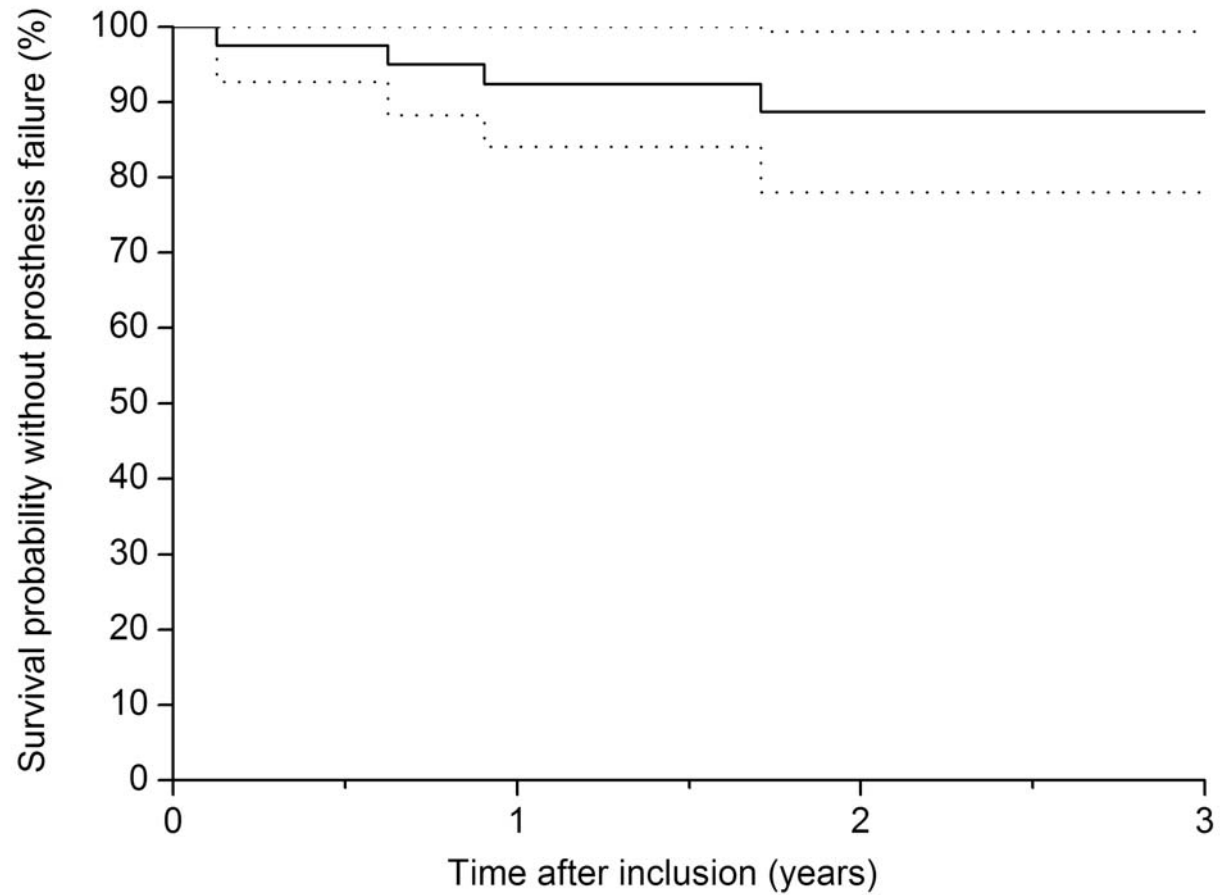
<i>Staphylococcus aureus</i>	14	(33.3)
Coagulase-negative staphylococci	9	(21.4)
<i>Streptococcus</i> species	5	(11.9)
Gramnegative rods	5	(11.9)
<i>Enterococcus faecalis</i>	3	(7.1)
<i>Peptostreptococcus</i> species	1	(2.4)
<i>Propionibacterium acnes</i>	1	(2.4)
<i>Hafnia alvei</i>	1	(2.4)
<i>Granulicatella adiacens</i>	1	(2.4)
No growth	2	(4.8)

2 mixed infections: *S. aureus* plus *Enterococcus faecalis*, and *S. aureus* plus coagulase-negative *Staphylococcus*

OUTCOME AFTER FIRST TREATMENT

- **Successful outcome** **36/40 (90%)**
with a follow-up of 877 d
(range 236-5'879 d)
- **Failures** **4/40 (10%)**
 - **first year** **3**
 - **second year** **1**
- **Success in patients with > 2y of follow-up:**
25/27 (92.8%)

KAPLAN-MEIER ESTIMATE OF SURVIVAL



No. at risk: 40 39 32 27 21 17 15

SUCCESS RATE ACCORDING TO SURGICAL THERAPY

Type of surgery	Success rate, No. (%)
Débridement with retention	20/21 (95.2)
One-stage exchange	2/2
Two-stage exchange	11/13 (84.6)
Arthrodesis	3/3
Amputation ^a	0/1

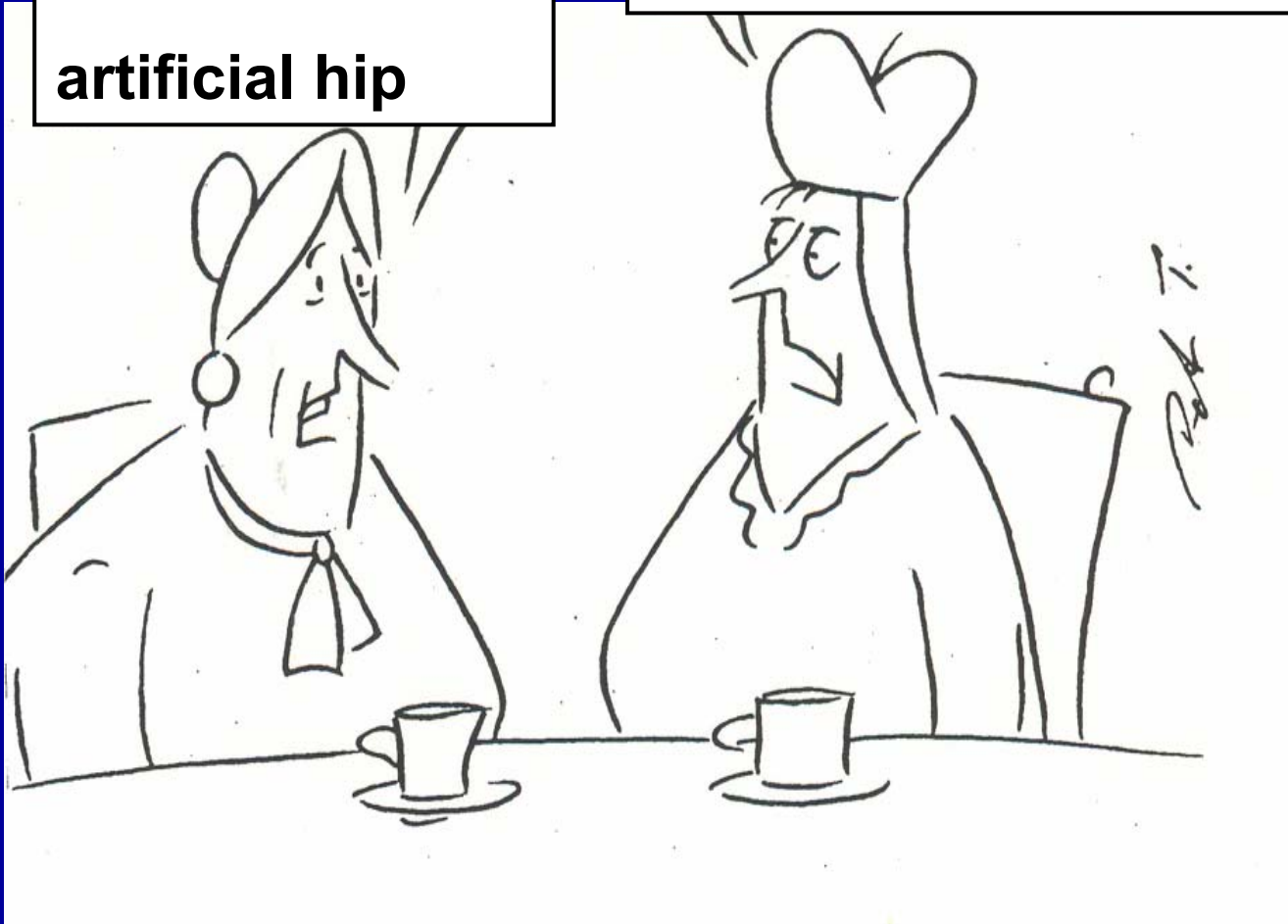
^aEarly death due to sepsis and comorbidity

CONCLUSIONS

- **Different surgical procedures result in similar success rates, provided that the type of infection, the pathogen, the stability of the implant, and the local skin and soft tissue conditions are considered**
- **Adherence to an algorithm defining a rational surgical and antibiotic treatment strategy contributes to the favorable outcome**

I got an
artificial hip

Didn't you have money
for a natural one?



Thank you for your attention