Clinical Design Mastermind Session

BACTERIOPHAGE THERAPY SUMMIT

Clinical considerations to perform phage therapy clinical trials in patients with prothetic joint infection

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Prosthetic joint infection

NIH U.S. National Library of Medicine

ClinicalTrials.gov

- **Osteomyelitis: 68**
- **Prosthetic-joint inf**
- Meningitis: 348
- Urinary tract infectior
- Tuberculosis: 915
- Influenza: 2'152

Few patients per surgeon or per hospital

Rate of infection after arthroplasty ~1-2%

"Patients are scattered"

Why and **How** considering phage therapy?

Various surgeries

- Implant retention
- 1-stage exchange
- 2-stage exchange

Various antibiotics

- Combination?
- Duration?

Evaluation of the outcome at 1 or 2 years

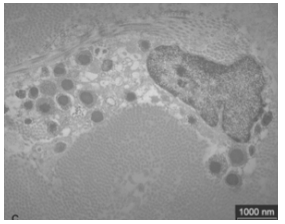
"The negleted infectious disease of industrialized countries"

"A complex disease that needs medicosurgical treatment and a prolonged follow-up"

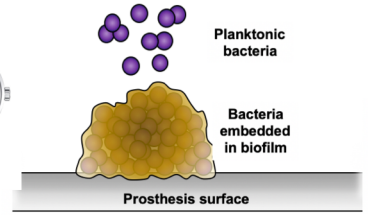
Why?

Prosthetic joint infection

- One of the **most difficult-to-treat** ID
- Bacterial mechanisms of **persistence**
- **Intracellular survival** (*S. aureus*)
- **Implant surface** (biofilm)



Sendi et al.
Clin Infect Dis
2006

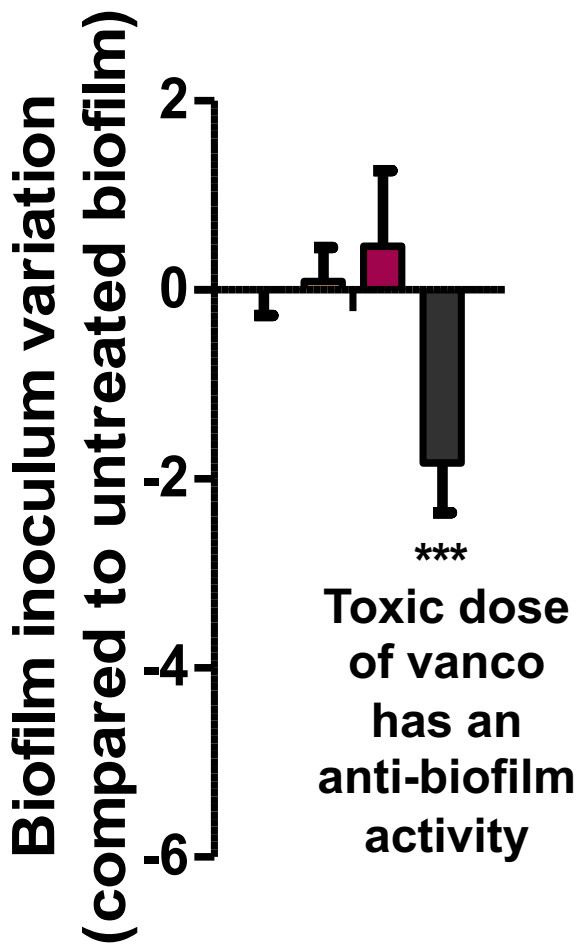


Josse et al.
Front Microb
2019

Positive infectious outcome in only 20 to 80%
Risk for relapse and microbiological persistence
Risk for superinfection (new infection)

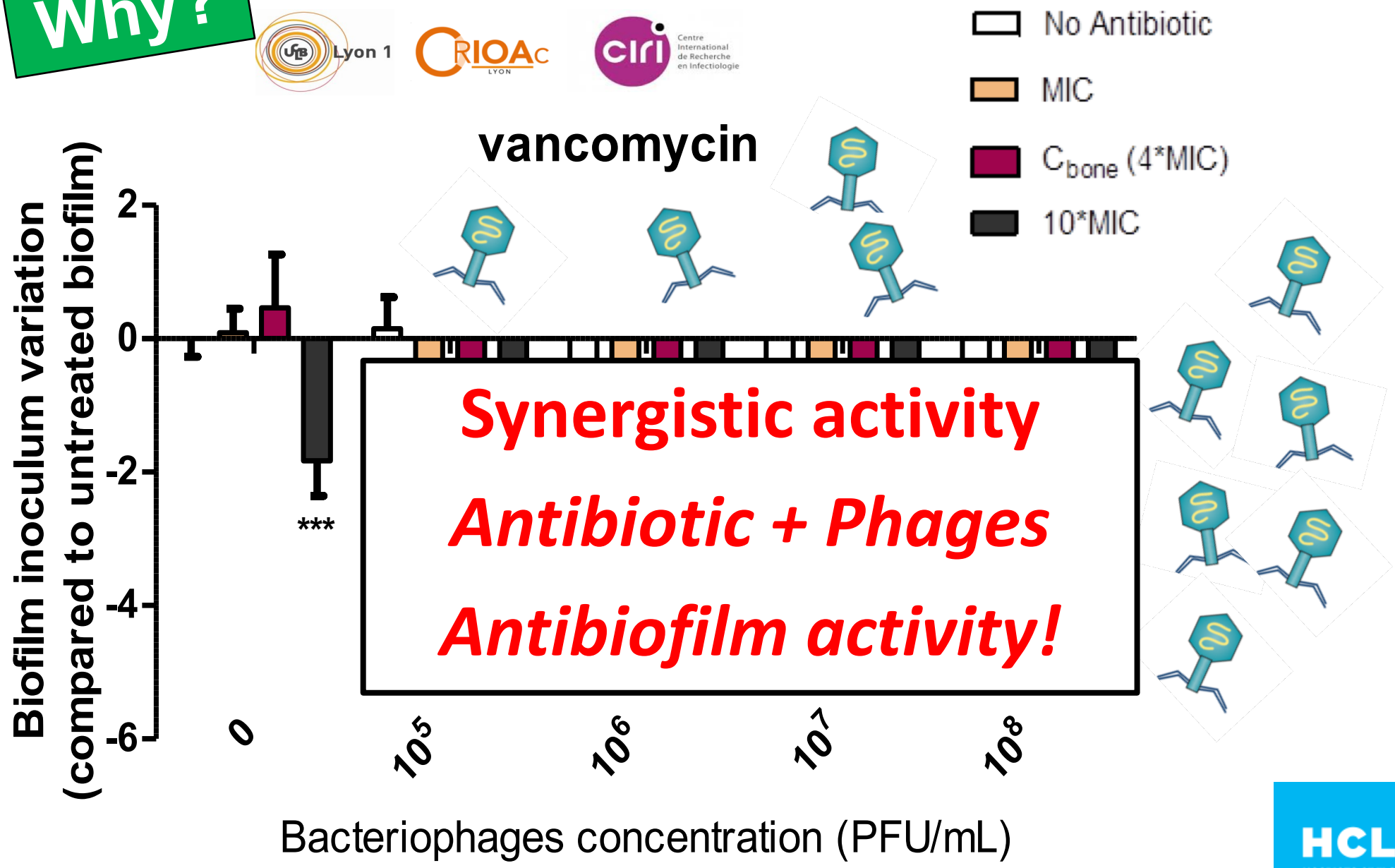
Why?

C. Kolenda et al. Antimicrob Agents Chemother 2019



Why?

C. Kolenda et al. Antimicrob Agents Chemother 2019

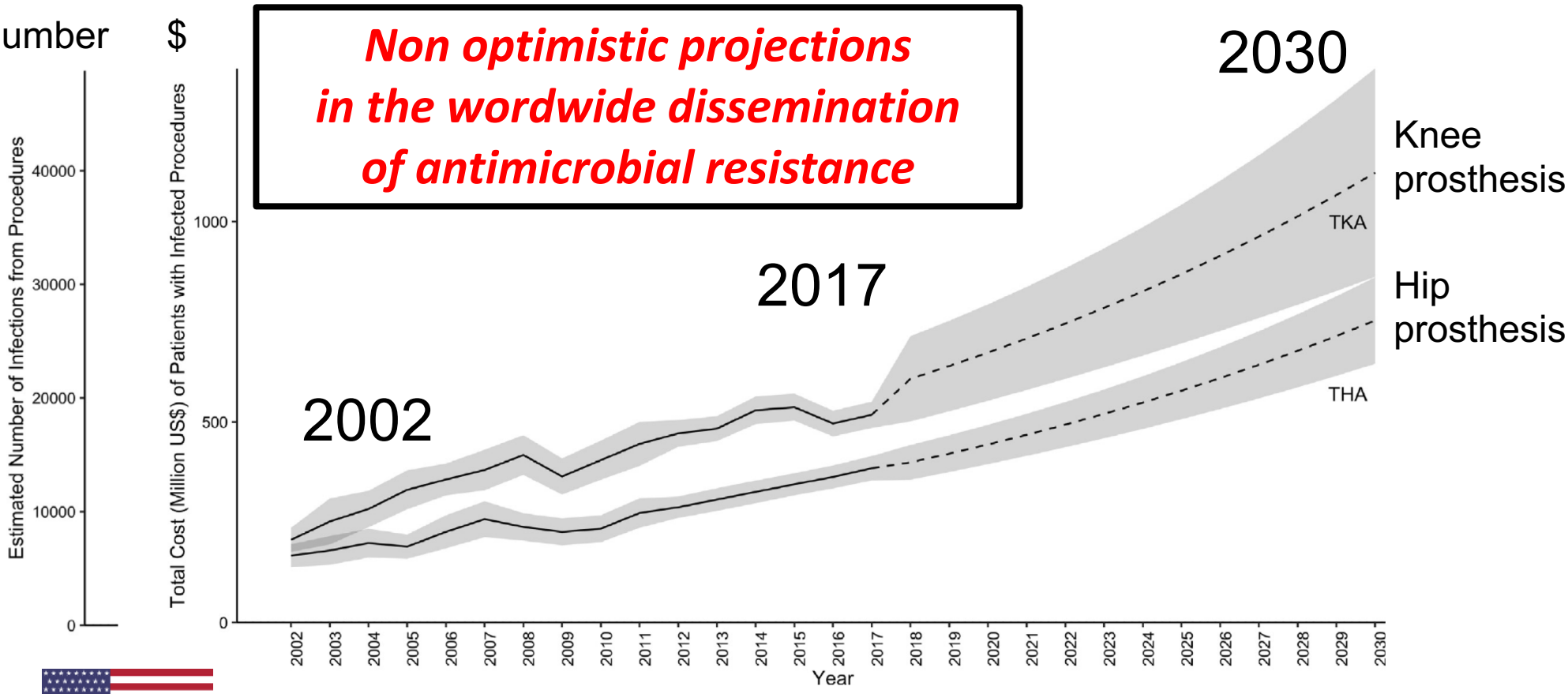


Why?

Projected Economic Burden of Periprosthetic Joint Infection of the Hip and Knee in the United States

Ajay Premkumar, MD, MPH [a,*], David A. Kolin, MSc [b], Kevin X. Farley, BS [c], Jacob M. Wilson, MD [d], Alexander S. McLawhorn, MD, MBA [a], Michael B. Cross, MD [a], Peter K. Sculco, MD [a]

Non optimistic projections in the wordwide dissemination of antimicrobial resistance



J Arthroplasty 2020

Why?

antibiotics 2020

MDPI

Case Report

Salvage Bacteriophage Therapy for a Chronic MRSA Prosthetic Joint Infection

James B. Doub [1,*], Vincent Y. Ng [2], Aaron J. Johnson [2], Magdalena Slomka [1], Joseph Fackler [3], Bri'Anna Horne [3], Michael J. Brownstein [3], Matthew Henry [4], Francisco Malagon [4] and Biswajit Biswas [4]

Clinical Infectious Diseases

MAJOR ARTICLE 2020

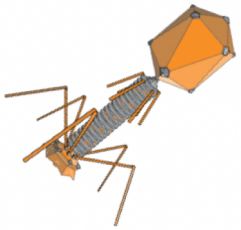
IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Phage Therapy for Limb-threatening Prosthetic Knee *Klebsiella pneumoniae* Infection: Case Report and In Vitro Characterization of Anti-biofilm Activity

Edison J. Cano,[1,2] Katherine M. Caflisch,[2,3] Paul L. Bollyky,[4] Jonas D. Van Belleghem,[4] Robin Patel,[1,2,5] Joseph Fackler,[6] Michael J. Brownstein,[6] Bri'Anna Horne,[6] Biswajit Biswas,[7] Matthew Henry,[7,8] Francisco Malagon,[7] David G. Lewallen,[9] and Gina A. Suh[1]

Open Forum Infectious Diseases

BRIEF REPORT



Salvage Debridement, Antibiotics and Implant Retention ("DAIR") With Local Injection of a Selected Cocktail of Bacteriophages: Is It an Option for an Elderly Patient With Relapsing Staphylococcus *aureus* Prosthetic-Joint Infection?

2018

The Potential Innovative Use of Bacteriophages Within the DAC® Hydrogel to Treat Patients With Knee Megaprosthesis Infection Requiring "Debridement Antibiotics and Implant Retention" and Soft Tissue Coverage as Salvage Therapy

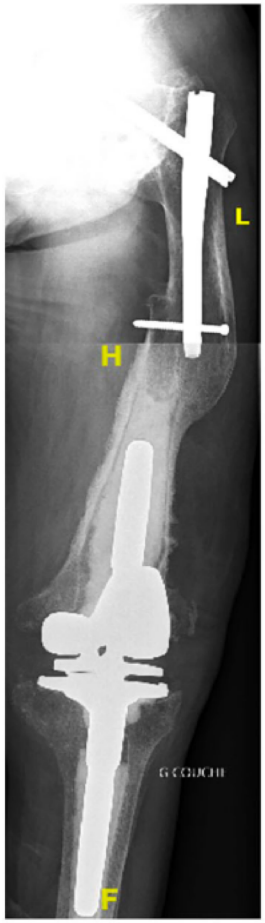
2020

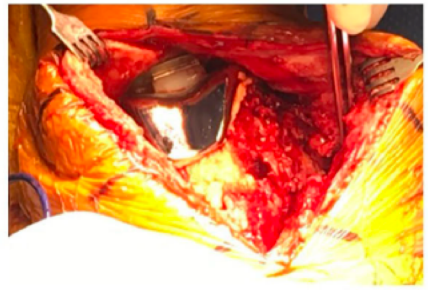
Tristan Ferry[1,2,3,4], Cécile Batailler[2,3,5], Charlotte Petitjean[6], Joseph Chateau[7], Cindy Fevre[6], Emmanuel Forestier[8], Sophie Brosset[7], Gilles Leboucher[9], Camille Kolenda[2,3,4,10], Frédéric Laurent[2,3,4,10] and Sébastien Lustig[2,3,5] on behalf of the Lyon BJI Study Group*

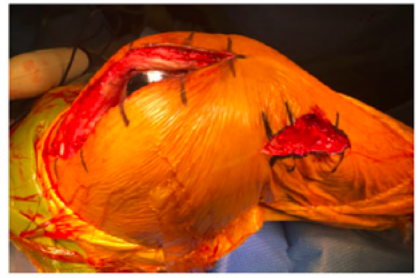
Why?

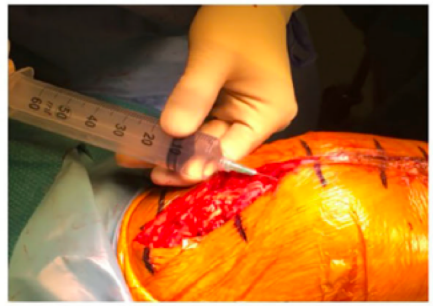
Phage Therapy as Adjuvant to Conservative Surgery and Antibiotics to Salvage Patients With Relapsing *S. aureus* Prosthetic Knee Infection

Tristan Ferry[1,2,3,4], Camille Kolenda[2,3,4,5], Cécile Batailler[2,3,6], Claude-Alexandre Gustave[2,3,4,5], Sébastien Lustig[2,3,6], Matthieu Malatray[3,6], Cindy Fevre[7], Jérôme Josse[2,3,4,5], Charlotte Petitjean[7], Christian Chidiac[1,2,3,4], Gilles Leboucher[8] and Frédéric Laurent[2,3,4,5] on behalf of the Lyon BJI Study group*









frontiers in Medicine

2021

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BUT

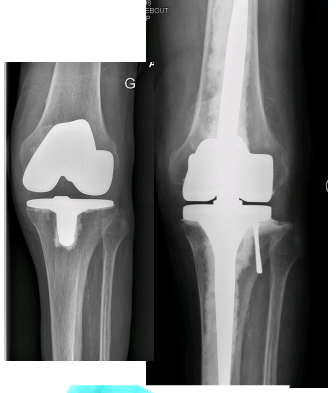
Only case reports with a positive outcome are usually published

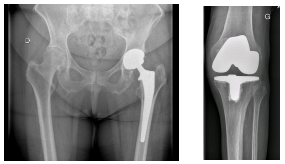
We also have to learn a lot from patients who experienced a failure

Accumulating data from compassionate cases is crucial

BUT

Prosthetic joint infection

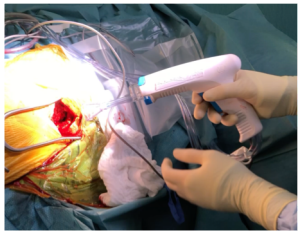


Type of prosthesis Hip/knee  Primary/Revision

Type of infection  Acute (biofilm +)  Chronic (biofilm ++++) 

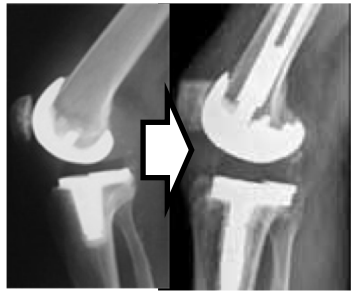
Pathogen 

S. aureus *E. coli* *K. pneumoniae* *P. aeruginosa* …
CoNS *Streptococcus spp.* *Enterococcus spp.* *C. acnes*

Surgical treatment DAIR 

1-stage exchange 2-stage exchange

Mechanical eradication of biofilm



Antibiotics  SOC Rifampin Fluoroquinolone

Antibiotic duration ≤ 6 weeks 8 weeks 12 weeks SAT

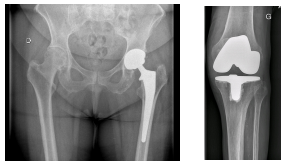
DAIR = Debridement Antibiotics and Implant Retention; SAT = Suppressive Antimicrobial Therapy

How?

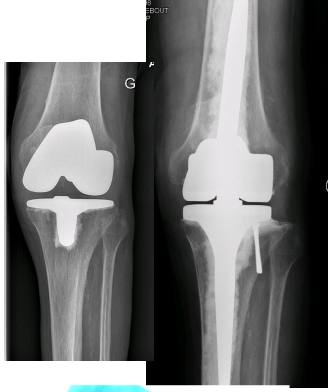
Prosthetic joint infection

Type of prosthesis

Hip/knee



Primary/Revision



Type of infection

Acute (biofilm +)

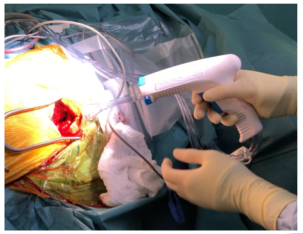
Chronic (biofilm ++++)

Pathogen

S. aureus *E. coli* *K. pneumoniae* *P. aeruginosa* …
CoNS *Streptococcus spp.* *Enterococcus spp.* *C. acnes*

Surgical treatment

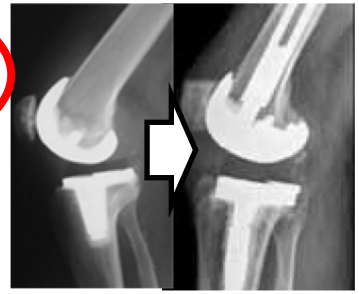
DAIR



1-stage exchange

2-stage exchange

Mechanical eradication of biofilm



Antibiotics

SOC Rifampin Fluoroquinolone

Antibiotic duration

≤ 6 weeks 8 weeks 12 weeks SAT

Select an homogenous clinical condition

How?

Determine the best way of phage administration

Local injections?

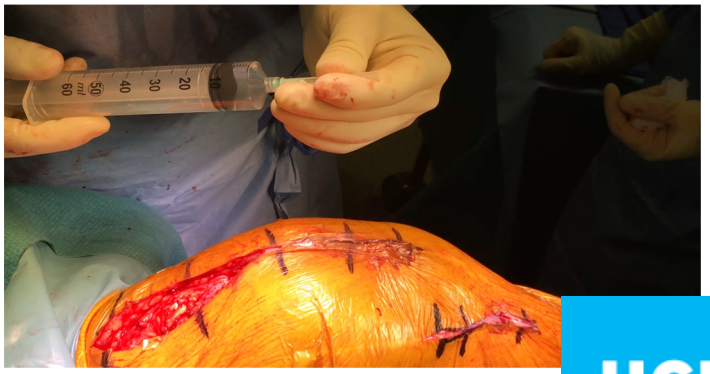
Before

Concentration?

During **Surgery?**

After

Number of Administrations?



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Intravenous administrations?

How?

Empirical of targeted Phage therapy?

Empirical

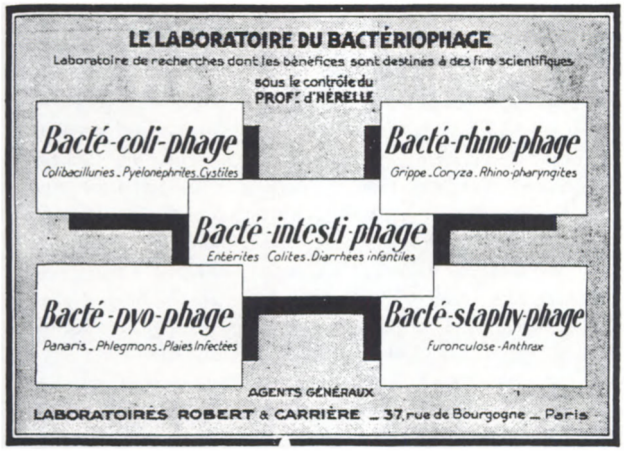
Fixed cocktail targeting bacteria?

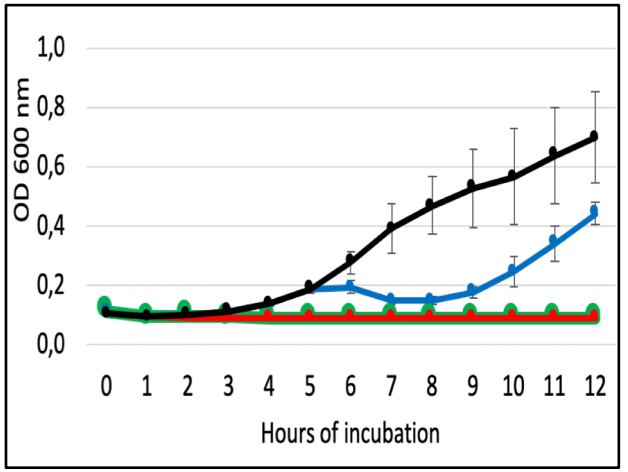
Targeted

Fixed cocktail?

Phagogram-based cocktail?

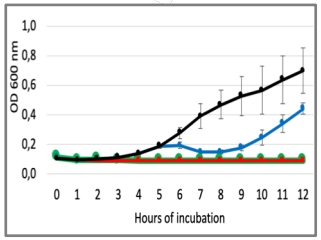
Empirical followed by targeted?





Conclusion

- Real **rationale** for the use of phage therapy in patients with PJI
  - Phage target biofilm
  - Severe disease
  - Increasing incidence and cost
- But PJI is a **complex** and **heterogenous** infection
- With several simultaneous interventions
  - Surgery
  - Antibiotics
- Phage therapy clinical trials are required
- Choosing the **most relevant clinical situation** is required to demonstrate the adding value of Phage



Lyon BJI Study group

Coordinator: Tristan Ferry

Infectious Diseases Specialists – Tristan Ferry, Florent Valour, Thomas Perpoint, Florence Ader, Sandrine Roux, Claire Triffault-Filit, Agathe Becker, Anne Conrad, Marielle Perry, Cécile Pouderoux, Nicolas Benech, Pierre Chauvelot, Johanna Lippman, Evelyne Braun, Christian Chidiac

Surgeons – Sébastien Lustig, Elvire Servien, Cécile Batailler, Stanislas Gunst, Axel Schimdt, Matthieu Malatray, Elliot Sappey-Marinier, Michel-Henry Fessy, Anthony Viste, Jean-Luc Besse, Philippe Chaudier, Lucie Louboutin, Quentin Ode, Adrien Van Haecke, Marcelle Mercier, Vincent Belgaid, Arnaud Walch, Sébastien Martres, Franck Trouillet, Cédric Barrey, Ali Mojallal, Sophie Brosset, Camille Hanriat, Hélène Person

Microbiologists – Frederic Laurent, Céline Dupieux, Laetitia Berraud, Camille Kolenda, Jérôme Josse, Tiphaine Roussel-Gaillard

Nuclear Medicine – Isabelle Morelec, Marc Janier, Francesco Giammarile

PK/PD specialists – Michel Tod, Marie-Claude Gagnieu, Sylvain Goutelle

Clinical Research Assistant – Eugénie Mabrut

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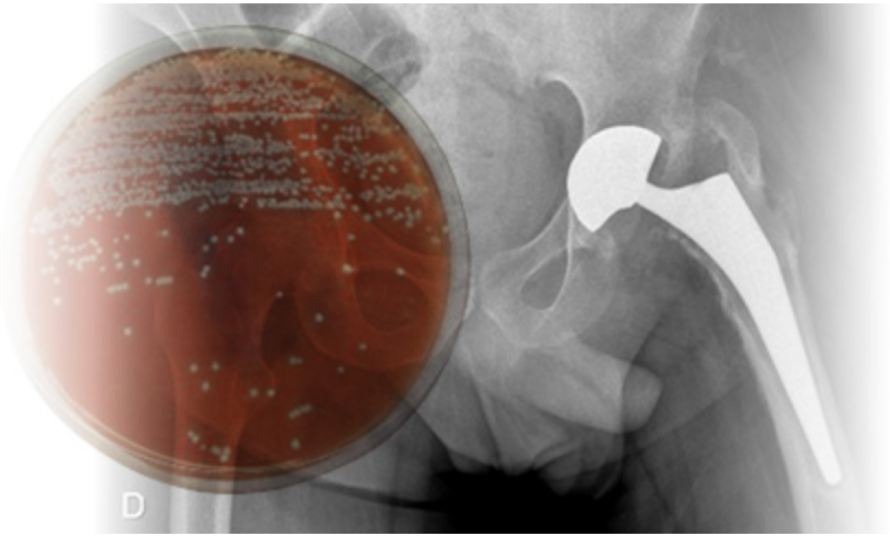

- Published cases
- Open acces studies in pdf
- All thesis in pdf
- All recommendations
- **Newsletter**

YouTube

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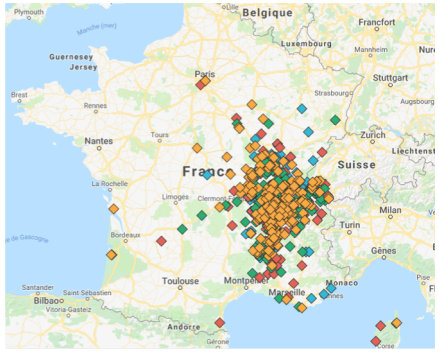

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