





we care and cure

The public health and economic burden of bone and joint infections, improvement areas

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I am infectious disease physician (with a PhD)



Some major emerging problems



Referral center for the management of DE LA SANTÉ ET DE LA PRÉVENTION complex bone and joint infections (BJI)



Égalité



Different clinical settings of BJI

Hematogenous BJI



Different clinical settings of BJI

Fracture-related infections (FRI) Trauma-related fracture Accident in general population War for soldiers (and potential civilians) Post-trauma osteomyelitis

Hematogenous BJI



Prosthetic joint infection (PJI)



Significant burden

REGULAR ARTICLE

Acta Pædiatrica 2013

Paediatric bone and joint infections are more common in boys and toddlers: a national epidemiology study

L Grammatico-Guillon (leslie.guillon@univ-tours.fr), Z Maakaroun Vermesse, S Baron, S Gettner, E Rusch, L Bernard Tours University Hospital, Tours, France

- By using the French National Hospital Discharge Database,
- Bone and joint infection (BJI) prevalence rate of 22 per 100 000 in child <15 years
- Estimated that the cost of paediatric BJI care is approximately €16 million per year
- The mean hospital stay was 8.6 days, costing approximately €5200 per BJI stay
- Rehospitalization rate was 9.7%

National epidemiological study reveals longer paediatric bone and joint infection stays for infants and in general hospitals

E Laurent (e.laurent@chu-tours.fr)^{1,2}, L Petit^{1,3}, Z Maakaroun-Vermesse^{3,4}, L Bernard^{4,5}, T Odent^{5,6}, L Grammatico-Guillon^{1,5}





Figure 3 Number of microorganisms coded in paediatric bone and joint infections by age. France, 2013.

The role of Kingella kingae in pre-school aged children with bone and joint infections $\stackrel{\scriptscriptstyle \diamond}{\scriptscriptstyle \sim}$



Journal of Infection 83 (2021) 321-331













Implant-associated bone and joint infections (BJI)

- Infrequent in elective surgery such as ARTHROPLASTY (1-2%, but increase to 30% in particular population such as in smokers, obese and diabetic patients)
- <u>More frequent</u> in TRAUMA surgery (up to 30-50%)
- Iterative surgeries (i.e. the number): significant risk factor for acquisition of an infection
- Infection considerably influence the outcome, especially in patients for whom a reconstruction is done (such as big prosthesis or bone graft)

Chronic or persistent from <u>native</u> BJI

The two bacterial lives after reaching bone

Replicative state





Dormant state



Largely unknown As it is microscopic

Bacteria are living as a community in biofilm





in a child.

Acute infection

Intensive bacterial replication Suppurative infection Vascular congestion

Chronic infection

Ischaemic bone tissue **Bone sequestrum** Slowing the bacterial growth **Bacterial persistence in biofilm** THE NEW ENGLAND JOURNAL OF MEDICINE

Jan.

MEDICAL PROGRESS

OSTEOMYELITIS: A REVIEW OF CLINICAL FEATURES, THERAPEUTIC CONSIDERATIONS AND UNUSUAL ASPECTS (First of Three Parts)* FRANCIS A. WALDVOGEL, M.D., GERALD MEDOFF, M.D., AND MORTON N. SWARTZ, M.D.





Fractured Biofilm on electronic microscopy at sequestrum surface Evans et al. *Clin Orthop* 1998: 243-249









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Prosthesis loosening with infiltration of PMNs in bone

T. Ferry et al. Chapter in the book "Infection in Knee Replacement" on behalf of Springer and ISAKOS, 2021





The two bacterial lives after reaching bone

Replicative state





Dormant state



Largely unknown As it is microscopic









Bourgeon charnu





Observational Study

Hematogenous osteomyelitis in childhood can relapse many years later into adulthood

A retrospective multicentric cohort study in France

Axelle Clerc, MD^{a,b,*}, Valerie Zeller, MD^c, Simon Marmor, MD^c, Eric Senneville, MD, PhD^d, Bruno Marchou, MD, PhD^e, Frederic Laurent, PharmD, PhD^{b,f}, Frederic Lucht, MD, PhD^g, Nicole Desplaces, MD, PhD^h, Sebastien Lustig, MD, PhDⁱ, Christian Chidiac, MD, PhD^{a,b}, Tristan Ferry, MD, PhD^{a,b}



• 37 patients

- Median time between osteomyelitis in childhood and the relapse in adulthood was 26 years (13–45)!
- Surgical debridement, microbiological diagnosis and effective antimicrobial therapy during 12 weeks
- All patients had a favorable outcome



Similar concepts

Pathophysiology	Diagnosis		
Bacteria reach	Clinical eviden	се	
Slow-growing bacteria			
Biofilm			
Perforn microb			

Similar concepts

Pathophysiology	Diagnosis	
Bacteria reach the bone	Clinical evidence	
Slow-growing bacteria	Suspect low grade infection	
Biofilm	hone sampling for	

microbiological diagnosis

Prosthesis loosening

Actuel

ital de la Croix Rou

oom :0.4

Pain with no fistula No fever Low CRP

Chronic infection due to *Cutibacterium acnes*

Radiographies du ba

10-05-201 09:08 AM



Bone samples

Collected during surgery (individual sterile tubes) Lot of caution to avoid bacterial contamination!



Synovial fluid

Collected during puncture or during surgery Lot of caution to avoid bacterial contamination!



Courtesy Dr. T. Roussel-Gaillard	Microbiological diagnosis	
· · · · · · · · · · · · · · · · · · ·	4 mL	
1 mL	-	
Vacutainer collection tube	Biomérieux BactAlert	
	Pediatric bottles (blood culture)	

1 mL



EDTA Tube Cell count
Microbiological analysis

- 1. Pre analytical process
- Before sampling
 - Avoid antimicrobial therapy before sampling
- Sample collection
 - Special indications -Date & time of collection / localization
 - Transportation Transportation time & storage conditions after collection



Set up of bone Microbiologcal diagnosis in Armenia



Microbiological analysis

2. Analytical process

- Equipment
- Microbiological safety station
- Homogenization before cultivation
- Appropriate culturing media
- Atmosphere conditions / CO2 /anaerobic
- Incubation time & temperature
- Susceptibility testing





Prolonged Bacterial Culture to Identify Late Periprosthetic Joint Infection: A Promising Strategy

Peter Schäfer,¹ Bernd Fink,² Dieter Sandow,¹ Andreas Margull,¹ Irina Berger,³ and Lars Frommelt⁴

¹Ambulatory Healthcare Center, Labor Ludwigsburg, Ludwigsburg, ²Clinic of Joint Replacement, General and Rheumatic Orthopaedics, Orthopaedic Clinic Markgröningen, Markgröningen, ³Institute of Pathology, Klinikum Kassel, Kassel, and ⁴ENDO-Klinik, Hamburg, Germany

Clin Infect Dis. 2008, 47(11):1403-9.



Microbiological analysis

3. Post -analytical process

- Reporting results
 - Interpret antibiogram
 - Comment in case of possible contamination to help physician and surgeon decision





Actuel

inital de la Croix Rou

oom :0.4

Pain with no fistula No fever Low CRP All positive in culture *C. acnes* After 14 days of incubation



Radiographies du ba

10-05-201 09:08 AM

Chronic infection due to *Cutibacterium acnes*





MINISTÈRE DE LA SANTÉ ET DE LA PRÉVENTION Liberté Égalité Fratemité

Referral center for the management of complex bone and joint infections (BJI)





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Referral center for the management of complex bone and joint infections (BJI)



Orthopaedic surgeon Plastic surgeon Infectious diseases physician **Microbiologist** Pharmacist Pharmacologist

Epidemiology / Hygene

MINISTÈRE DE LA SANTÉ ET DE LA PRÉVENTION Libené Égalité Fraternité

Referral center for the management of complex bone and joint infections (BJI)





to my plastic surgeons colleagues!





Different clinical settings of implant-associated BJI



Prosthetic joint infection (PJI)



Different clinical settings of implant-associated BJI

Fracture-related infections (FRI)

Prosthetic joint infection (PJI)

EB The European Bone & Joint Infection Society JIS https://ebjis.org/

Fracture-related Infection Consensus Meeting 2018

First short guide: EBJIS FRI Guidelines 2018

The European Medicines Agency has released for public consultation a draft concept paper on preparation of a revised guideline on the evaluation of medicinal products indicated for treatment of bacterial infections.

This concept paper proposes the development of a single guideline on the clinical evaluation of medicinal products indicated for treatment of bacterial infections. The development of this single guideline is intended to merge, revise and add to the guidance that is currently included in two separate documents as follows: guideline on the evaluation of medicinal products indicated for treatment of bacterial infections (CPMP/EWP/558/95 Rev. 2), adopted in 2011 and in force since 2012 and the addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections, (CPMP/EWP/558/95 Rev. 2), adopted in 2011 and in force since 2012 and the addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections (EMA/CHMP/351889/2013), adopted in 2013 and in force since 2014.

The concept paper is available by clicking here.

The EBJIS definition of periprosthetic joint infection (PJI)

• For more information please download both documents here and here

We are pleased to announce that the British Infection Association (BIA) has endorsed our EBJIS Definition of Prosthetic Joint Infection (Bone Joint J 2021; 103-B(1): 18-25). Members of the EBJIS Executive Committee took part in the recent Federation of Infection Societies Conference with a session on our 'European guidelines for the management of septic arthritis' and a lecture on 'Importance of cross-specialty working; lessons from bone and joint infection clinical care and research'. It is always a pleasure to develop relationships with new Societies and Institutions who are interested in infection. This endorsement adds to our previous collaborations with EFORT, MSIS and ESCMID.





Conservative approach: DAIR: 'Debridement, Antibiotics and Implant Retention'



Prosthesis exchange (1-stage or 2-stage) And antibiotics



Management of Bone and joint infections

• Implementation of bone diagnosis of infection (microbiology)

- Sampling in operating room
- To not contaminate the sample
- Culturing in dedicated media for 14 days

Implementation of empirical antimicrobial therapy

- Just after surgery
- Pending the results of culture
- Oral or intravenous, depending on the clinical situation
- Implementation of the use of PICC line (if IV required)
 - Implantation under sonography
 - Management for the outpatient setting
- Adapt the antimicrobial therapy depending on the surgical strategy and on the pathogen(s) involved



Diagram showing a PICC line © CancerHelp UK



Elastomedic infusor

Vancomycin or ceftazidime

For continuous infusion during 24h











Bone and joint infection



- Medical care in patients with complex bone and joint infections
 - The concept of biofilm and latent infection
 - Bacteria is the enemy, the enemy is vicious (pioning)
 - Absolute need to be a second to be a secon
 - Need for loss the benefit of surgery
 Need for loss the benefit of surgery antibiotics that need to be charged adequatly depending on the enemy profile
 - **Prolonged** antimicrobial therapy targeted the enemy (3 months)

Could help to keep the function (bone healing) and avoid occurrence of more complex situations, and amputation





Online multidisciplinary meetings





DIRECTION GÉNÉRALE DE L'OFFRE DE SOINS DE SOINS

Useful for multidisciplinary teams outsite our hospital to share clinical cases and decisions

At CRIOAc Lyon, several types of multidisciplinary team (MDT) meetings are organised to best meet the demand :

- "Bedside-care MDT meetings", involving multidisciplinary day-hospital healthcare professionals specialising in "Septic Orthopaedic Infection" take place at the Croix-Rousse Hospital. Orthopaedic surgeons, plastic surgeons and bacteriologists also attend this day-long meeting.
- Cases are discussed through video conference MDT meetings with orthopaedic surgeons of the Lyon Sud Hospital (Wednesdays 6pm to 8pm)
- Hospitals from all over the region can present cases during a video conference MDT meeting (Mondays 5:30pm to 6:30pm)
- MDT meetings dedicated to complex facial BJI (certain Tuesdays 6pm to 7pm)
- MDT meetings dedicated to BJIs of the spine and the skull (certain Mondays 5:30pm to 7pm)
- International MDT meetings dedicated to BJIs in middle-income countries (certain Wednesday 5:30pm to 7pm)





+ Google Agenda



- 44% **+**

International multidisciplinary team (IMDT) meetings France-Armenia

Complex BJI





Reference centre for the management of complex BJI



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Imaging



d:DCM / Lin:DCM / Id:ID

- <u>« Slow growing »</u>state of bacteria
- Biofilm production
- Need for identification
- Antimicrobial treatment
- Has to be <u>started</u> at the time of explantation (empirical treatment)
- Has to be <u>adapted</u> (targeted treatment)
- Has to be prolonged 3 months
- <u>To avoid a failure</u> (contamination of the <u>next prosthesis</u>)

Conclusion







- A better understanding the disease is one of the key
- <u>Accept</u> that the patient is infected, <u>the surgeon is not the culprit</u>!
- <u>Suspect</u>, <u>recognize</u> and <u>diagnose</u> implant-associated infection is crucial for the patient prognosis
- <u>Multidisciplinary management</u> is complex to set up, but <u>essential</u> for the patient management (enjoy to understand your colleague's position and share point of views!)

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There is a huge place for ID/pediatricians/microbiologists to participate to the patient care, as the medical management of the patient should not be the surgeon's job and responsibility

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There is a huge place for ID/pediatricians/microbiologists to participate to the patient care, as the medical management of the patient should not be the surgeon's job and responsibility

• The standard of care if patients with complex BJI is:

- Surgical expertise (orthopaedics, plastic surgery)
- Multidisciplinar discussions (physical and on line)
- Bone sampling with adequate methodology for culturing
- Empirical antibiotics (IV with piccline) with development of outpatient program to make it possible
- Active oral antibiotics during several months

We are learning from each other! We are stronger together to improve the patient care!

Post graduate course 'Bone and joint infections'

Orthopaedic surgeon

Microbiologist

Infectious diseases physician





Lyon BJI Study group

Coordinator: Tristan Ferry

Infectious Diseases Specialists – Tristan Ferry, Florent Valour, Thomas Perpoint, Florence Ader, Sandrine Roux, Agathe Becker, Claire Triffault-Fillit, Anne Conrad, Cécile Pouderoux, Pierre Chauvelot, Paul Chabert, Johanna Lippman, Evelyne Braun Surgeons – Sébastien Lustig, Elvire Servien, Cécile Batailler, Stanislas Gunst, Axel Schmidt, Elliot Sappey-Marinier, Quentin Ode, Michel-Henry Fessy, Anthony Viste, Jean-Luc Besse, Philippe Chaudier, Lucie Louboutin, Adrien Van Haecke, Marcelle Mercier, Vincent Belgaid, Aram Gazarian, Arnaud Walch, Antoine Bertani, Frédéric Rongieras, Sébastien Martres, Franck Trouillet, Cédric Barrey, Ali Mojallal, Sophie Brosset, Camille Hanriat, Hélène Person, Samuel Prive, Philippe Céruse, Carine Fuchsmann, Arnaud Gleizal; Anesthesiologists – Frédéric Aubrun, Mikhail Dziadzko, Caroline Macabéo, Dana Patrascu; Microbiologists – Frederic Laurent, Laetitia Beraud, Tiphaine Roussel-Gaillard, Céline Dupieux, Camille Kolenda, Jérôme Josse; Imaging – Fabien Craighero, Loic Boussel, Jean-Baptiste Pialat, Isabelle Morelec; PK/PD specialists – Michel Tod, Marie-Claude Gagnieu, Sylvain Goutelle; Clinical research assistant and database manager– Eugénie Mabrut

PHAGE*in***LYON**

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Aram Gazarian Armenian colleagues French ambassy and healthcare autority













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