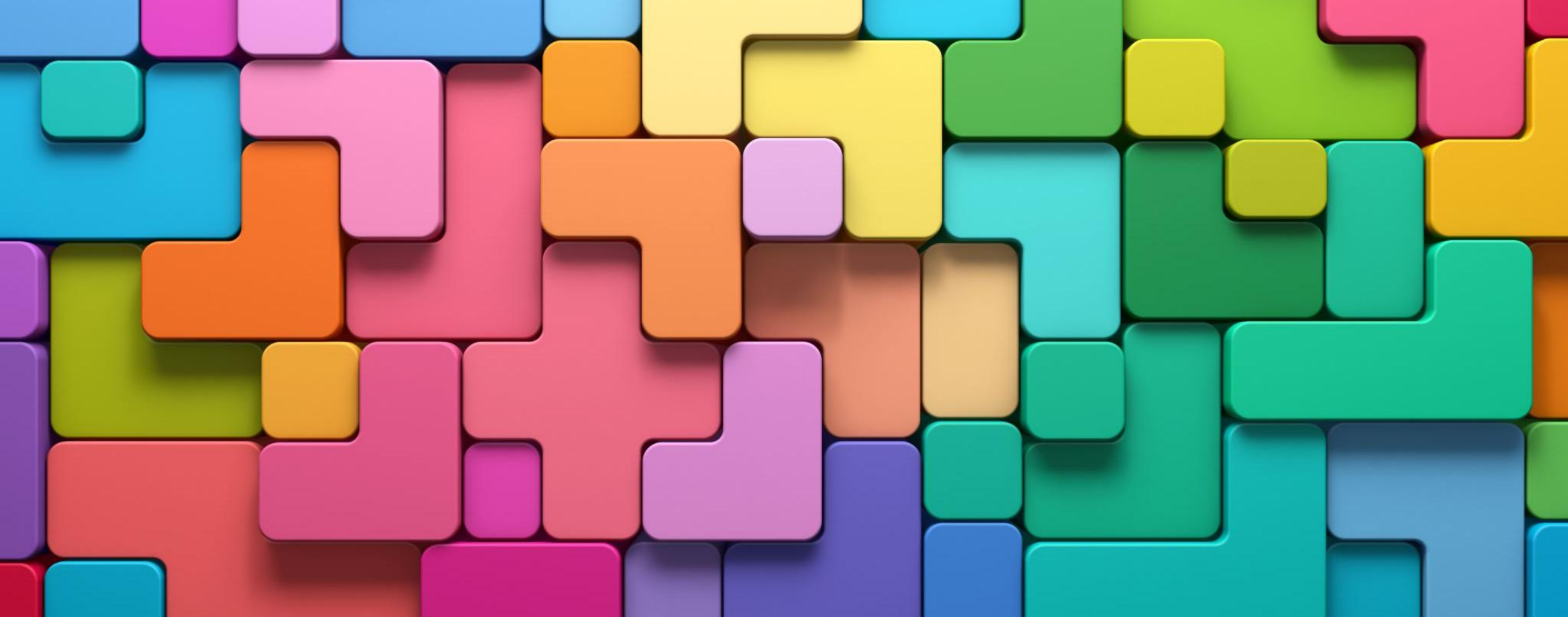


Biofilm – skutečný vrah neno jen fantom?

DAN MAREK

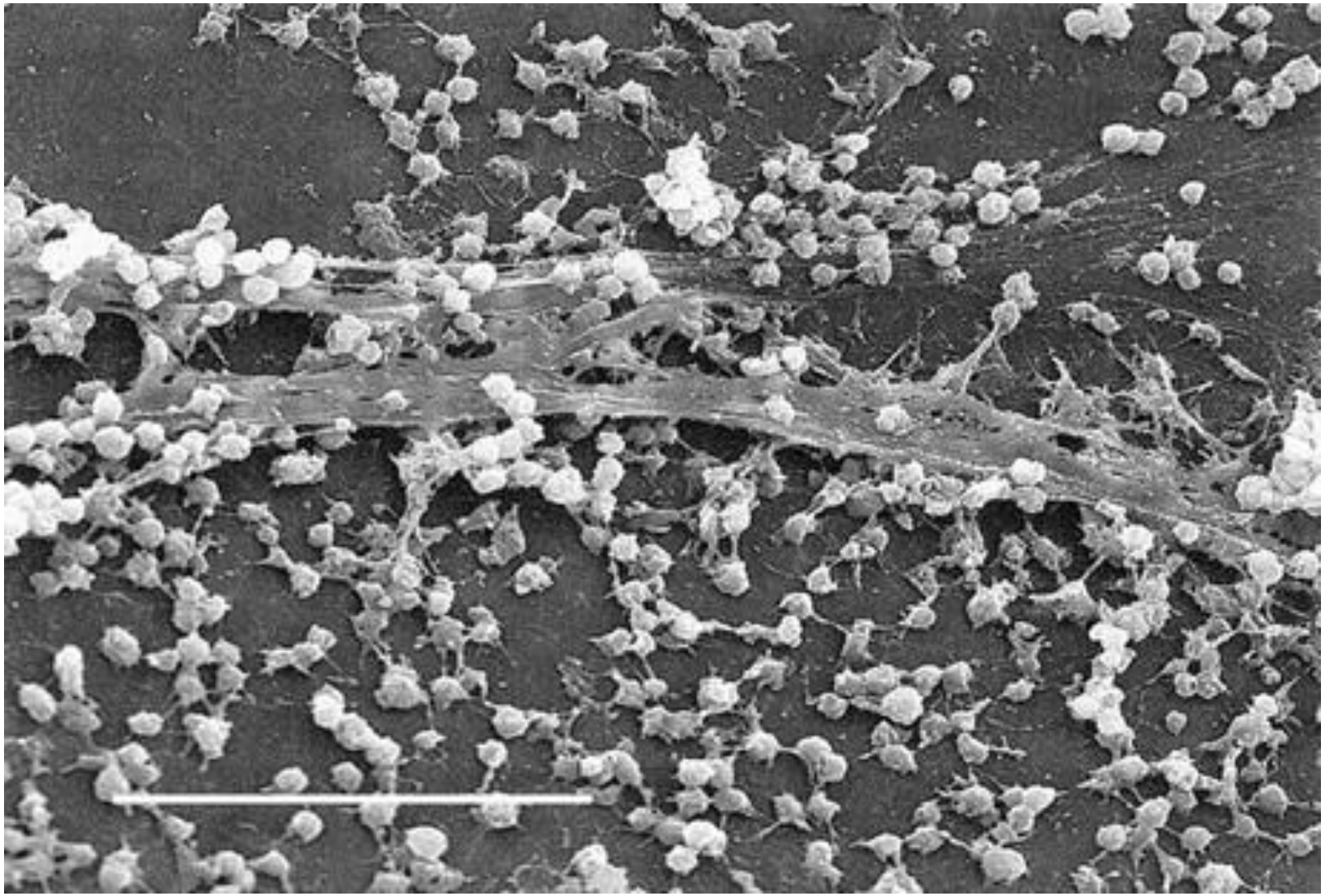
Nemocnice Agel Přerov

FN Olomouc

Co je biofilm?

- A biofilm has been defined as “a structured community of bacterial cells enclosed in a self-produced polymeric matrix and adherent to an inert or living surface”.*
- PM, PV, ale i periodontický film, katetry, chronické rány…
- European Society of Clinical Microbiology and Infectious Disease (ESCMID) Study Group for Biofilms (ESGB)

* **Costerton, J. W., P. S. Stewart, and E. P. Greenberg.** 1999. Bacterial biofilms: a common cause of persistent infections. Science **284:**1318-1322.



Scanning electron micrograph of a staphylococcal biofilm on the inner surface of an indwelling medical device. Bar-20 microns. (Photograph by Janice Carr of the Hospital Infections Program of CDC, Atlanta, GA.)

Nemocnice AGEL Přerov

I. INTERNÍ KLINIKA KARDIOLOGICKÁ
FAKULTNÍ NEMOCNICE OLOMOUC

Mikrobiální tolerance

- mikrobi sice nejsou resistentní k ATB,
- bakterie původem z biofilmu kultivované na agaru jsou totiž stejně citlivé jako ty z hemokultur, ale
- tyto bakterie rostoucí v biofilmu jsou 100-1000x méně citlivé na dané ATB než ty stejné volně rostoucí*
- a tak v biofilmu nedojde ke „killing“ bakterií

* **Donlan, R. M.** 2000. Role of biofilms in antimicrobial resistance. ASAIO J. S47-S52.

Mikrobiální tolerance – nejen zpomalený metabolismus

suprese růstu mikrobů v biofilmu = spíše příčina tolerance než následek léčby

- ? existuje taktilní receptor na bakteriích – indukce genu zpomalujícího růst
- ? polymerová vrstvá brání přístupu kyslíku, tedy zpomalen metabolismus
- ? polymer je chrání před průnikem ATB
- ? a kolektivní ochrana před fagocytózou

Mikrobiální tolerance a relaps

- dormantní bakterie v biofilmu (případně vegetacích,) na cizích tělesech (protetické chlopně, elektrody…) nebo v ráně mohou být vysvětlením pro relapsy bakteriemie/infekce rány po ukončení ATB léčby

Revised recommendations (11)

Možná endokarditida

2015	Class	Level	2023	Class	Level
Recommendations for cardiovascular implanted electronic device-related infective endocarditis (continued)					
HK přetrvávající G+, F Complete hardware removal should be considered on the basis of occult infection without another apparent source of infection. **HK přetrvávající G-**	IIa	C	In cases of possible CIED-related IE or occult Gram-positive bacteraemia or fungaemia, complete system removal should be considered in case bacteraemia/fungaemia persists after a course of antimicrobial therapy.	IIa	C
			In cases of possible CIED-related IE with occult Gram-negative bacteraemia, complete system removal may be considered in case of persistent/relapsing bacteraemia after a course of antimicrobial therapy.	IIb	C

2023 ESC Guidelines for the management of endocarditis
(European Heart Journal; 2023 – doi: 10.1093/eurheartj/ehad193)

Revised recommendations (10) Valvulární endokarditida

2015	Class	Level	2023	Class	Level
Recommendations for cardiovascular implanted electronic device-related infective endocarditis (continued)					
In patients with NVE or PVE and an intracardiac device with no evidence of associated device infection, complete hardware extraction may be considered.	IIb	C	Complete CIED extraction should be considered in case of valvular IE, even without definite lead involvement, taking into account the identified pathogen and requirement for valve surgery.	IIa	C

Antimicrob Agents Chemother. 2006 Jan; 50(1): 55–61.
doi: 10.1128/AAC.50.1.55-61.2006
PMCID: PMC1346774
PMID: 16377667

Multiple Combination Bactericidal Testing of Staphylococcal Biofilms from Implant-Associated Infections

Raphael Saginur,[1,2,*] Melissa StDenis,[2,3] Wendy Ferris,[2,3] Shawn D. Aaron,[1,2] Francis Chan,[2,3] Craig Lee,[1,2] and Karam Ramotar[1,2]

ABSTRACT

Na biofilm může dobře působit Rifampicin

Standardized susceptibility testing fails to predict in vivo resistance of device-related infections to antimicrobials. We assessed agents and combinations of antimicrobials against clinical isolates of *Staphylococcus epidermidis* and *S. aureus* (methicillin-resistant *S. aureus* and methicillin-sensitive *S. aureus*) retrieved from device-associated infections. Isolates were grown planktonically and as biofilms. Biofilm cultures of the organisms were found to be much more resistant to inhibitory and bactericidal effects of single and combination antibiotics than planktonic cultures ($P < 0.001$). Rifampin was the most common constituent of antibiotic combinations active against staphylococcal biofilms. Other frequently effective antimicrobials were vancomycin and fusidic acid. Susceptibility testing involving biofilm-associated bacteria suggests new options for combination antibiotic therapy.

For many patients, surgical implantation of bioengineered medical devices such as valvular prostheses, vascular prostheses, ventricular assist devices, or ventricular shunts can be life saving. However, implantation of these foreign bodies carries risk of infection. Although the risk of infection of these devices is in general only between 1 and 7%, the impact of implant-associated infection is major (3). Implant-associated infections are associated with considerable morbidity, repeated surgeries, and prolonged antibiotic therapy. Mortality of prosthetic valve endocarditis ranges up to 30%, and mortality rates

Clinical Infectious Diseases

MAJOR ARTICLE

Is Rifampin Use Associated With Better Outcome in Staphylococcal Prosthetic Valve Endocarditis? A Multicenter Retrospective Study

Audrey Le Bot,[1] Raphaël Lecomte,[2] Pierre Gazeau,[3] François Benezit,[1] Cédric Arvieux,[1] Séverine Ansart,[3] David Boutoille,[2] Rozenn Le Berre,[4] Céline Chabanne,[5] Matthieu Lesouhaitier,[1] Loren Dejoies,[6,7] Erwan Flecher,[5] Jean-Marc Chapplain,[1] Pierre Tattevin,[1,7,8] and Matthieu Revest[1,7,8]; Pour le Groupe d'Epidémiologie et Recherche en Infectiologie Clinique du Centre et de l'Ouest (GERICCO)

[1]Infectious Diseases and Intensive Care Unit, Pontchaillou University Hospital, Rennes, France, [2]Department of Infectious Diseases, CIC UIC 1413 INSERM, University Hospital, Nantes, France, [3]Infectious Diseases and Tropical Medicine, La Cavale Blanche University Hospital, Brest, France, [4]Department of Internal Medecine and pneumology, La Cavale Blanche University Hospital, Brest, France, [5]Department of thoracic and cardiovascular surgery, Pontchaillou University Hospital, Rennes, France, [6]Department of bacteriology, Pontchaillou University Hospital, Rennes, France, [7]University of Rennes, Inserm, BRM (Bacterial Regulatory RNAs and Medicine), UMR_1230, France, and [8]CIC-Inserm 1414, Pontchaillou University Hospital, Rennes, France

Background. International guidelines recommend rifampin-based combinations for staphylococcal prosthetic valve endocarditis (PVE). However, no robust clinical data support this recommendation, and rifampin tolerability is an issue. We aimed to evaluate the impact of rifampin for the treatment of staphylococcal PVE.

Methods. An observational retrospective cohort study of all adults with staphylococcal PVE (modified Duke criteria) was conducted in 3 referral centers for endocarditis, during years 2000–2018. Primary outcome measurement was 1-year mortality.

Results. We enrolled 180 patients with PVE due to *Staphylococcus aureus* (n = 114, 63.3%), or coagulase-negative staphylococci (n = 66, 36.7%), on bioprosthesis (n = 111, 61.7%), mechanical valve (n = 67, 37.2%), or both (n = 2). There were 132 males (73.3%), and mean age was 70.4 ± 12.4 years. Valvular surgery was performed in 51/180 (28.3%) cases. Despite all isolates were susceptible to rifampin, only 101 (56.1%) were treated with rifampin, for a median duration of 33.0 days, whereas 79 (43.9%) received no rifampin. Baseline characteristics were similar in both groups. One-year mortality was, respectively, 37.6% (38/101), and 31.6% (25/79), in patients treated with, or without, rifampin ($P = .62$). Relapse rates were 5.9% (6/101), and 8.9% (7/79), $P = .65$. Patients treated with rifampin had longer hospital length-of-stay: 42.3 ± 18.6 vs 31.3 ± 14.0 days ($P < .0001$). On multivariate analysis, only cerebral emboli (odds ratio [OR] 2.95, 95% confidence interval [CI], 1.30–6.70, $P = .009$), definite endocarditis (OR 7.15, 95% CI, 1.47–34.77,

257.Le Bot A, Lecomte R, Gazeau P, Benezit F, Arvieux C, Ansart S, *et al.* Is rifampin use
258.associated with better outcome in staphylococcal prosthetic valve endocarditis? A multicenter retrospective study. *Clin Infect Dis* 2021;**72**:e249–e255.

Suma sumarum

- biofilm existuje
- na CIED/PV
- může být zdrojem relapsu teplot/infekce/sepse
- nemůžeme ho nijak prokázat in vivo
- blbě se léčí (rifampicin?)

Fantom nebo vrah: Máme u konkrétního pacienta s možnou IE (pozitivní hemokultury + něco) extrahovat CIED?

- i když u něj nemáme žádný průkaz osídlení mikroby, ale jeho implantát může být teoreticky pokryt biofilmem?

Kdo vraždil jednou, nemusel nutně vraždit teď

- přestože možná existence biofilmu neznamená, že tento biofilm je původcem klinických potíží?

Něčí přítomnost na místě činu z něj vraha ještě nedělá

Hlasování pléna

1. Ano

2. Ne