



Phage therapy: The basics and susceptibility testing for microbiologists

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Topics

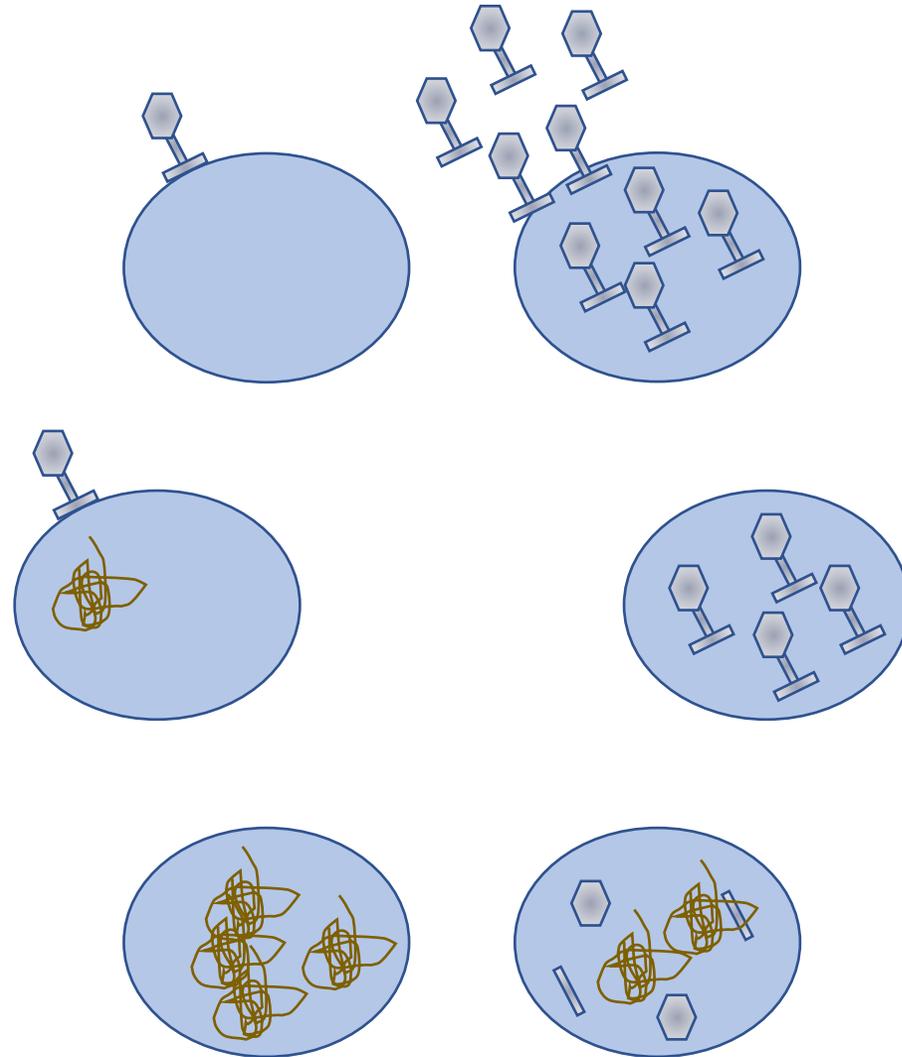
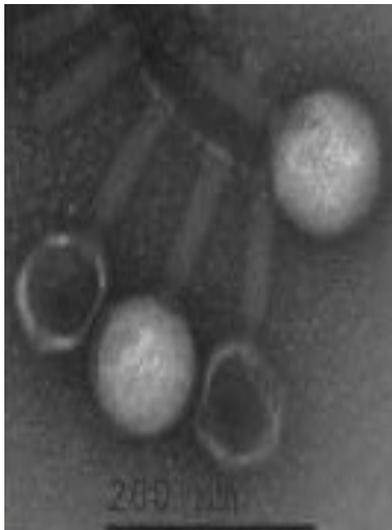
- Phages what are they?
- Phages for clinical therapy
- Clinical phage microbiology



Emerging of Antimicrobial Resistance



(Bacterio)Phages may serve as a solution



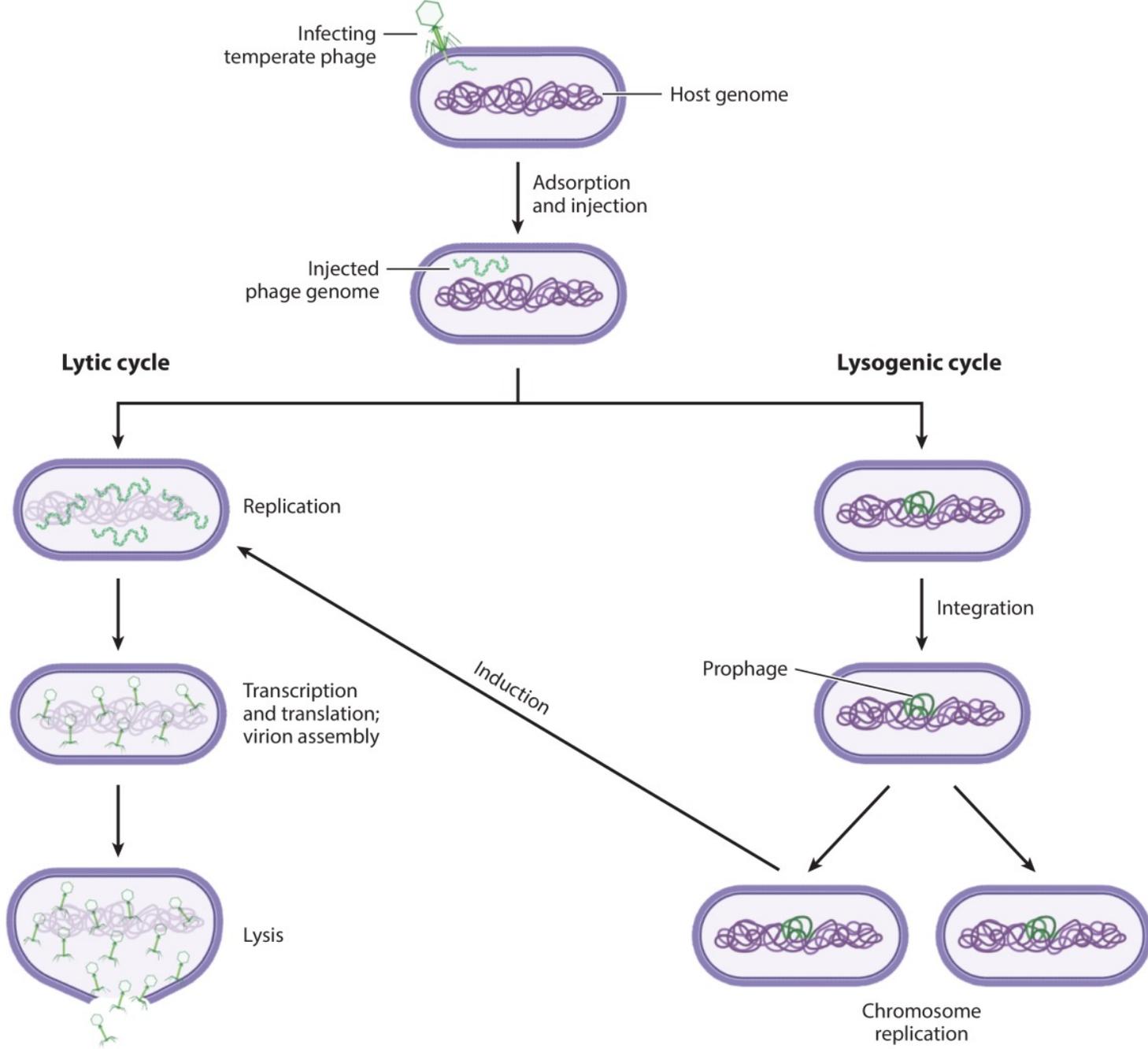
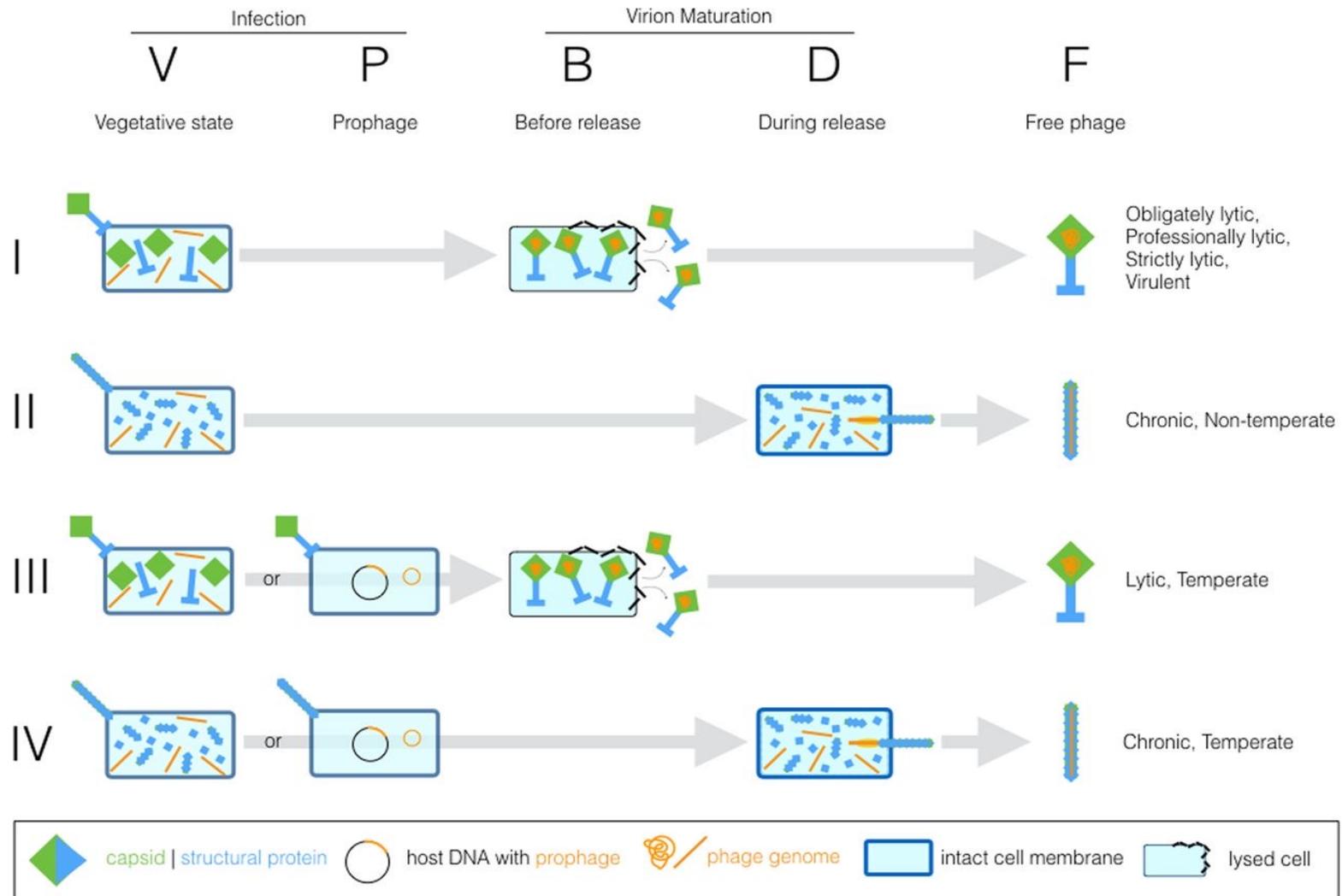
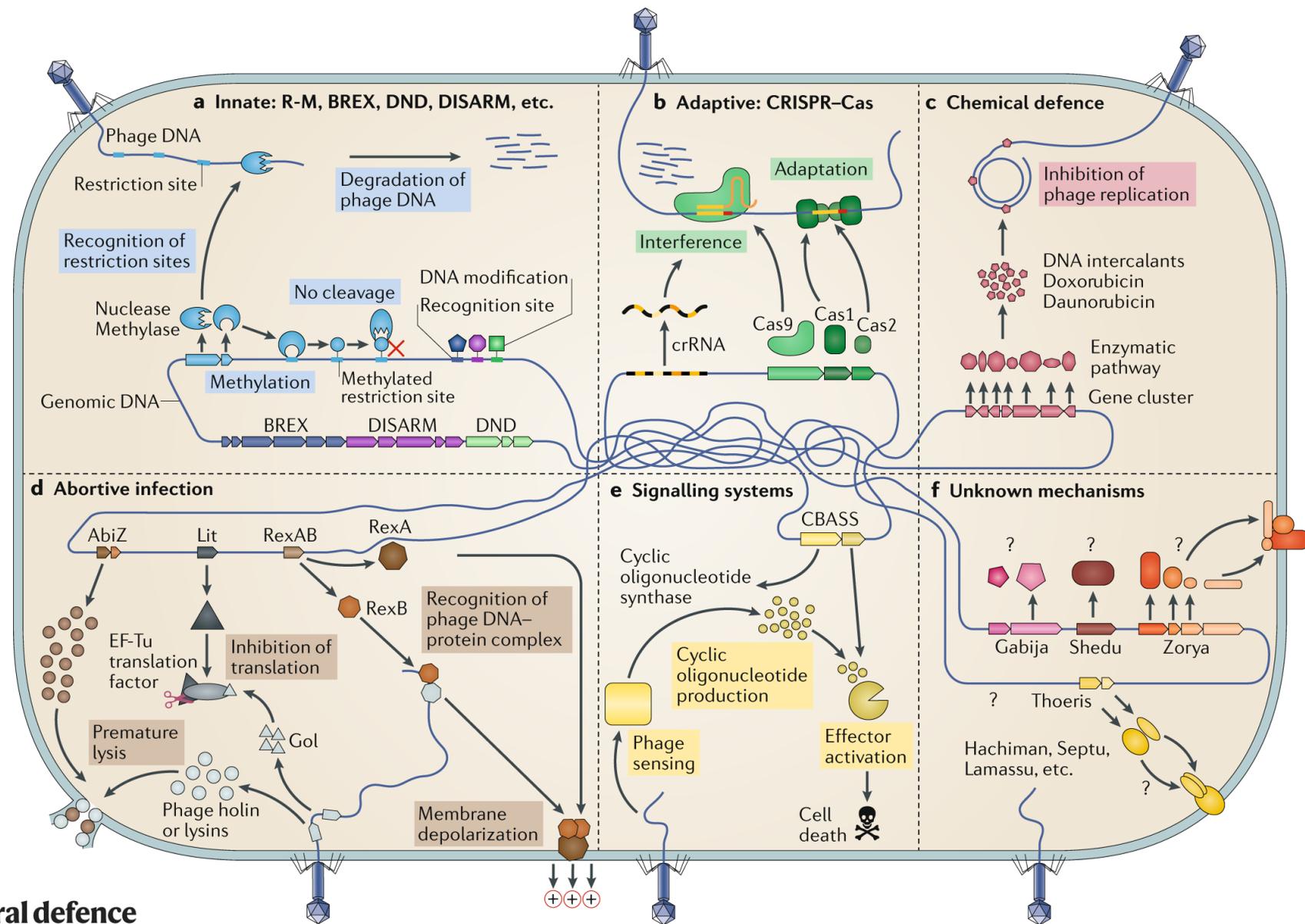


Figure 1. Distinguishing among phage states. Intracellularly and unencapsidated, phages can exist in Vegetative versus ...





The pan-immune system of bacteria: antiviral defence as a community resource

Aude Bernheim & Rotem Sorek [✉](#)

Nature Reviews Microbiology 18, 113–119 (2020) | [Cite this article](#)

The “previous” (old) concept of phage use



Felix d'Herelle



“... is a notable example of the negative impact an investigator's personality can have on the outcome of a discovery. Surely the prospects of phage therapy in the historical era would have been better served if d'Herelle had possessed some of the personality traits and scientific style of Pasteur”

Phage treatment and eradication of 2 MDR pathogens

Nir-Paz, Gelman, Khouri, et al, Successful Treatment of Antibiotic-resistant, Poly-microbial Bone Infection With Bacteriophages and Antibiotics Combination, *Clinical Infectious Diseases*, Volume 69, Issue 11, 1 December 2019, Pages 2015–2018, <https://doi.org/10.1093/cid/ciz222>

Phages against *Acinetobacter baumannii* and *K. pneumoniae* (5/6)

Before treatment (28/5)
Painful wounds are open (3 weeks), Secretions and Inflammation are observed.

ϕ AbKT21phi3 ϕ KpKT21phi1

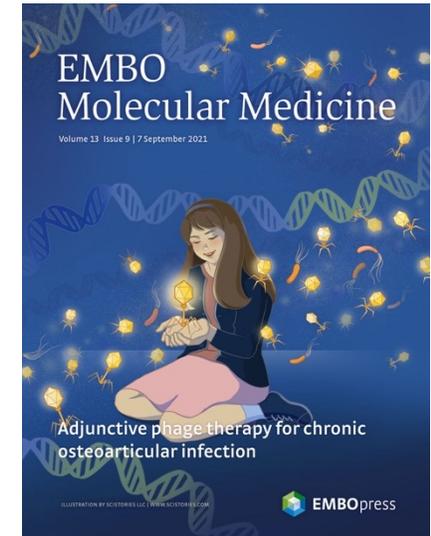
After treatment (19/6)
Wounds are close and dry with no secretion or pain

~2 weeks after treatment he was released from the hospital and **walked** to his home.

5/11/2018
(8 month after treatment)

Clinical cases @ Hadassah/Israel

- *Pseudomonas aeruginosa*
 - 5 In Israel
 - 4 abroad
- *Enterococcus faecalis*
 - 2 Israel
 - 1 Germany
- *Mycobacterium abscessus*
 - 2 Israel
- Acinetobacter and Klebsiella
 - Israel



Article

Bacteriophage Rescue Therapy of a Vancomycin-Resistant *Enterococcus faecium* Infection in a One-Year-Old Child following a Third Liver Transplantation

Kevin Paul ^{1,*}, Maya Merabishvili ², Ronen Hazan ^{3,*}, Martin Christner ⁴, Uta Herden ⁵, Daniel Gelman ³, Leron Khalifa ³, Ortal Yerushalmy ³, Shunit Copenhagen-Glazer ³, Theresa Harbauer ¹, Sebastian Schulz-Jürgensen ¹, Holger Rohde ⁴, Lutz Fischer ⁵, Saima Aslam ⁶, Christine Rohde ⁷, Ran Nir-Paz ⁸, Jean-Paul Pirnay ^{2,*}, Dominique Singer ^{1,†} and Ania Carolina Muntau ^{1,†}

Israeli phage bank

More than 300 phages against:

1. *E. faecalis*
2. *P. acnes* (~20)
3. *Shigella*
4. *Sallmonela*
5. *B. anthracis*
6. *P. aeruginosa* (~ 100 phages)
7. *S. aureus* (~10)
8. *E. coli*
9. *A. baumannii*
10. *S. mutans*
11. *M. abscessus*
12. *Burkholderia*
13. *Providencia*
14. And More....



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The Israeli Phage Bank (IPB)

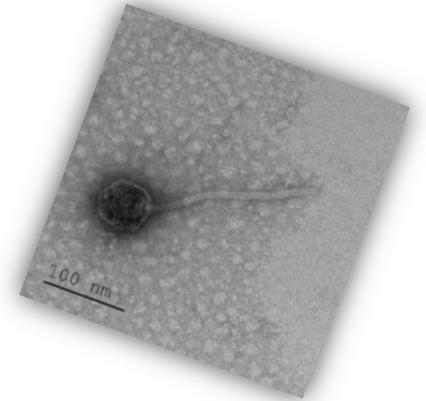
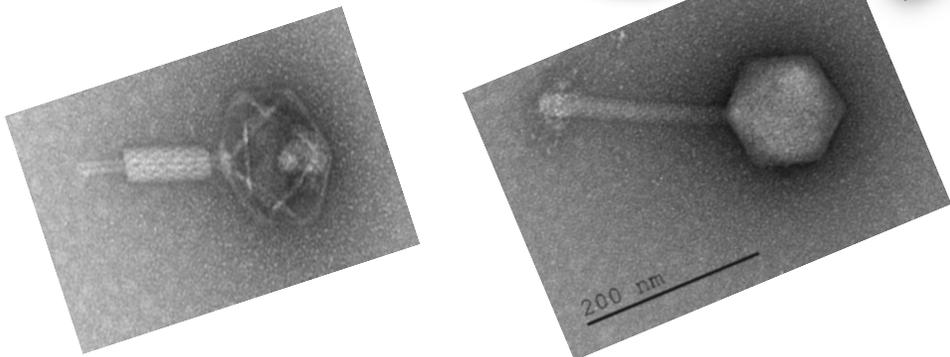
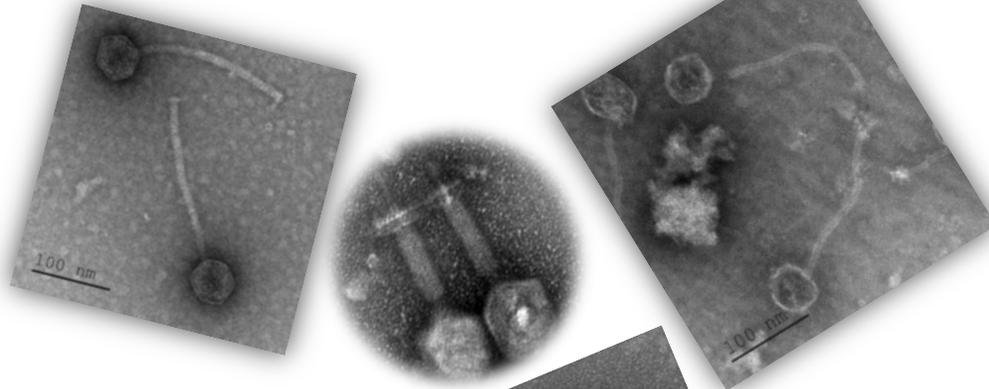
by [Ortal Yerushalmy](#)¹, [Leron Khalifa](#)¹, [Naama Gold](#)¹, [Chani Rakov](#)¹, [Sivan Alkalay-Oren](#)¹, [Karen Adler](#)¹, [Shira Ben-Porat](#)¹, [Reut Kraïtman](#)¹, [Niv Gronovich](#)², [Kerem Shulamit Ginat](#)², [Mohanad Abdalrhman](#)³, [Shunit Copenhagen-Glazer](#)¹, [Ran Nir-Paz](#)³ and [Ronen Hazan](#)^{1,*}

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³ Hadassah Medical Center, Department of Infectious Diseases, Jerusalem 91120, Israel

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Bacteria	Number of isolates in HMC and IHM	Number of bacteria to be screened in the current proposal	Current number of phages in our "Bank"
<i>Pseudomonas aeruginosa</i> (PA)	3030	900	~80
<i>Acinetobacter baumannii</i> (AB)	1387	900	14
<i>Klebsiella pneumoniae</i> (KP)	4884	900	14
<i>Staphylococcus aureus</i> (SA)	1056	900	8
<i>Enterococcus faecalis</i> (EF) and <i>Enterococcus faecium</i> (EM)	2500	900	29
<i>Mycobacterium abscessus</i> (MA) and <i>Mycobacterium tuberculosis</i> (MT)	> 500	500	1
<i>Providencia stuartii</i> (PS)	~50	50	1 (the first ever described)
Other (less relevant to the current proposal)	NA	NA	25

Worldwide status of Phage use

- Authorized in former soviet union:
 - Historical reasons
 - Georgia
 - Poland
 - Russia
- Europe
 - Belgium – magistral phage
 - Rest of Europe eIND
 - Clinical trials
- USA/Austrlia
 - eIND
 - Clinical trials



Ludwik Hirszfeld
Institute of Immunology and Experimental Therapy
Polish Academy of Sciences

Institute Structure Events PhD Studies Projects Contact

Phage Therapy Unit

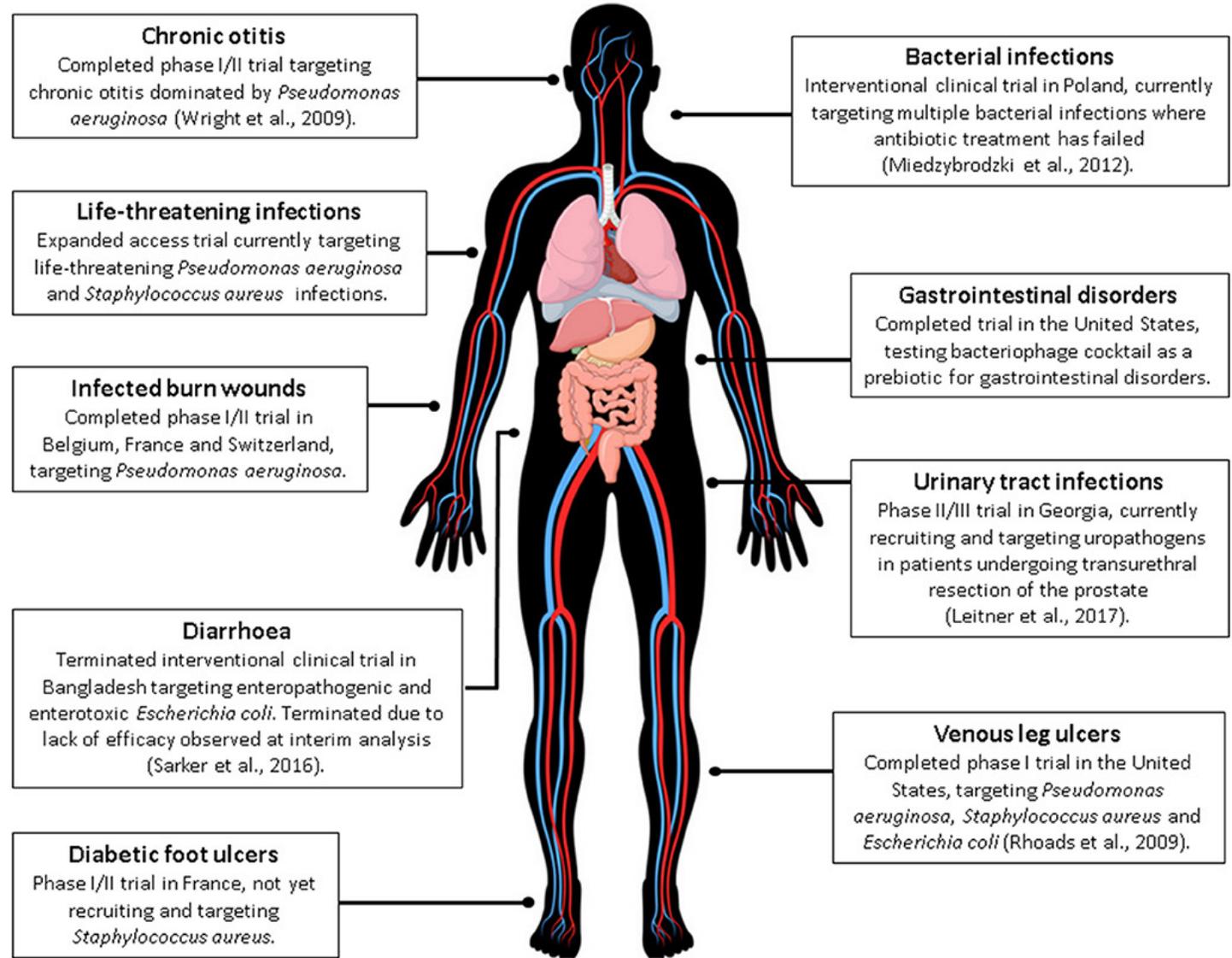
Phage Therapy Unit
of the Medical Centre
of the Institute of Immunology and Experimental Therapy PAS

Phage therapy is a method of treating bacterial infections which uses unique features of bacteriophages – bacterial viruses which attack only bacterial cells. Bacteriophages (or simply “phages”) are able to destroy different bacteria including those which are resistant to antibiotics and which cause life-threatening infections. It is this exceptional feature which determines the potential of phages in treating bacterial infections. This method has been known since the beginning of the 20th century. The Institute of Immunology and Experimental Therapy PAS in Wrocław (IET PAS) has been conducting research on the biological properties and the application of bacteriophages for several decades. It has all the disposal methods for isolating bacteriophages and for preparing phage formulations which have been provided for different hospitals in Poland for phage therapy coordinated by the institute since the 1970s.

To enable the application of phage therapy after Poland joined the European Union according to current regulations the institute opened its own Phage Therapy Unit (PTU) in 2008. Its aim is the admission of patients for treatment and its provision according to the protocol approved by an independent bioethics committee.

Phage Therapy Unit

List of studies



MINI REVIEW ARTICLE

Front. Cell. Infect. Microbiol., 23 October 2018 | <https://doi.org/10.3389/fcimb.2018.00376>



Bacteriophage Therapy: Clinical Trials and Regulatory Hurdles

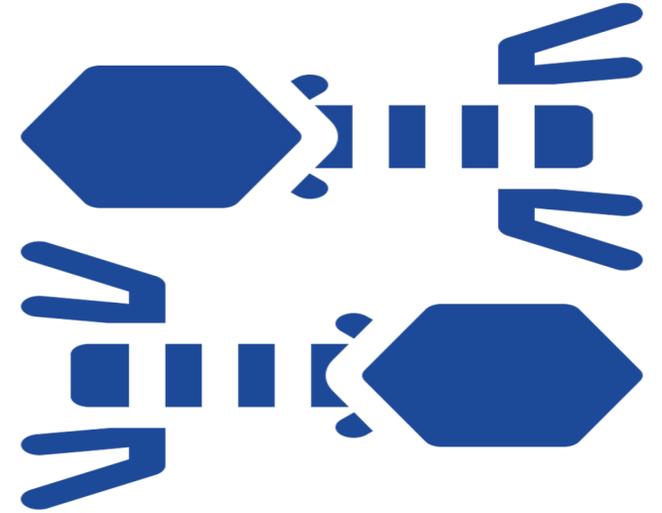
Lucy L. Furfaro¹, Matthew S. Payne¹ and Barbara J. Chang²

¹Division of Obstetrics and Gynecology, School of Medicine, The University of Western Australia, Crawley, WA, Australia

²The Marshall Centre for Infectious Diseases Research and Training, School of Biomedical Sciences, The University of Western Australia, Crawley, WA, Australia

Phage therapy

- Two major (contradicting) concepts:
 - Shelf product
 - Personalized approach
- Can we breach the gap?
- Medical community (infectious diseases) need to avoid study design related failing studies
- Combining industry and academics may help



HUMAN RANDOMIZED TRIALS

Outcome

Babalova et al	Bacterial dysentery directed prophylactic treatment in children	Zh Mikrobiol Epidemiol Immunobiol. 1968	3-4 fold reduction in dysentery
Carlton R.	PK and safety of an IV phage solution against VRE in healthy volunteers (Ia)	Personal communication	??
Bruttin et al	Oral T4 phages directed against E.coli in 15 healthy volunteers	Antimicrob Agents Chemother. 2005	Relatively safe
Wright et al	AB resistant Pseudomonas directed phages in patients with chronic otitis	Clin Otolaryngol. 2009	Safe and probably efficacious
Sarker et al	Impact of oral T4 phage cocktail on fecal microbiota in healthy volunteers	Virology. 2012	Safe
Brüssow et al	Safety of oral t4-like phage cocktails in children with E.coli diarrhea	Virology. 2012	Safe
McCallin et al	Safety of oral Microgenin® 5 adults and 5 10y-old children	Virology. 2013	



Review
Bacteriophages as Alternatives to Antibiotics in Clinical Care

Daniela Romero-Calle ¹, Raquel Guimarães Benevides ¹, Aristóteles Góes-Neto ¹ and Craig Billington ^{2*}

Wittebole St. Luc Bruxelles

Available from - https://www.ema.europa.eu/en/documents/presentation/presentation-current-clinical-evidence-therapeutic-use-bacteriophages-xavier-wittebole_en.pdf

4 major studies to learn from



Research Paper

Oral Phage Therapy of Acute Bacterial Diarrhea With Two Coliphage Preparations: A Randomized Trial in Children From Bangladesh

Shafiqul Alam Sarker^a, Shamima Sultana^a, Gloria Reuteler^b, Deborah Moine^c, Patrick Descomb Florence Charton^b, Gilles Bourdin^b, Shawna McCallin^b, Catherine Ngom-Bru^b, Tara Neville^b, Mahmuda Akter^a, Sayeeda Huq^a, Firdausi Qadri^a, Kaiser Talukdar^a, Mohamed Kassam^c, Michèle Chloe Loiseau^b, Ying Deng^b, Sahar El Aidy^b, Bernard Berger^b, Harald Brüssow^{b,*}

Interpretation: Oral coliphages showed a safe gut transit in children, but failed to achieve intestinal amplification and to improve diarrhea outcome, possibly due to insufficient phage coverage and too low E. coli pathogen titers requiring higher oral phage doses. More knowledge is needed on in vivo phage–bacterium interaction and the role of *E. coli* in childhood diarrhea for successful PT.

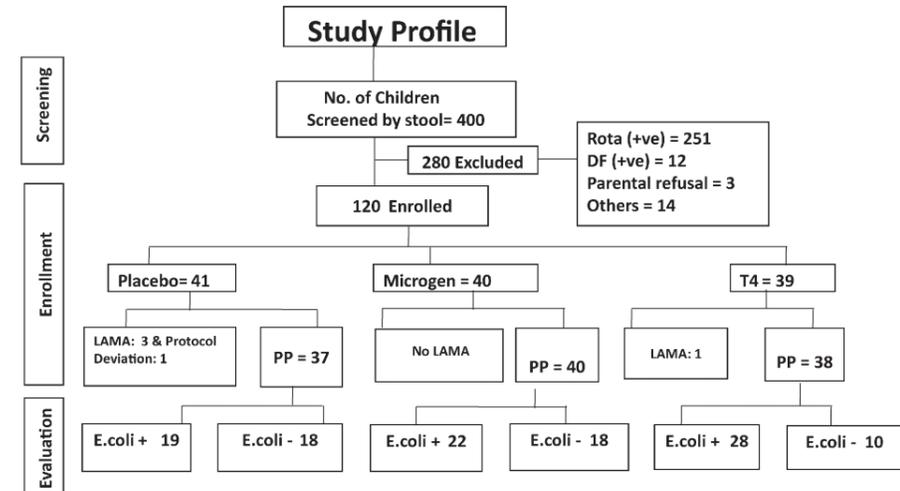


Fig. 1. Study flow chart. The numbers indicate the children with diarrhea who were screened, enrolled and evaluated. Rota(+ve), patients with rotavirus positive stool in ELISA; DF(+ve), patients with *V. cholerae* positive stool in dark field microscopy; others, patients meeting other exclusion criteria; Microgen, commercial ColiProteus phage cocktail from Microgen, Russia; T4, phage cocktail consisting of T4-like phages from NRC; LAMA, left the study against medical advice; PP, per protocol, *E. coli* +, patient displaying a pathogenic *E. coli* in the stool; *E. coli* - patient without a pathogenic *E. coli* in the stool.

In 2016, oral bacteriophage treatment of acute coliform diarrhoea in Bangladeshi children, using two coliphage preparations, showed safe gut transit but failed to improve diarrhoea outcomes over the level of standard care. This was explainable, at least in part, because the targeted *Escherichia coli* was found in smaller amounts than expected and the primary pathogen appeared instead to be *Streptococcus* spp, which was present in larger amounts but had not been tested before the trial.

Efficacy and tolerability of a cocktail of bacteriophages to treat burn wounds infected by *Pseudomonas aeruginosa* (PhagoBurn): a randomised, controlled, double-blind phase 1/2 trial



Patrick Jault, Thomas Leclerc, Serge Jennes, Jean Paul Pirnay, Yok-Ai Que, Gregory Resch, Anne Françoise Rousseau, François Ravat, Hervé Carsin, Ronan Le Floch, Jean Vivien Schaal, Charles Soler, Cindy Fevre, Isabelle Arnaud, Laurent Bretaudeau, Jérôme Gabard

Summary

Background Wound infections are the main cause of sepsis in patients with burns and increase burn-related morbidity and mortality. Bacteriophages, natural bacterial viruses, are being considered as an alternative therapy to treat infections caused by multidrug-resistant bacteria. We aimed to compare the efficacy and tolerability of a cocktail of lytic anti-*Pseudomonas aeruginosa* bacteriophages with standard of care for patients with burns.

Lancet Infect Dis 2019; 19: 35-45

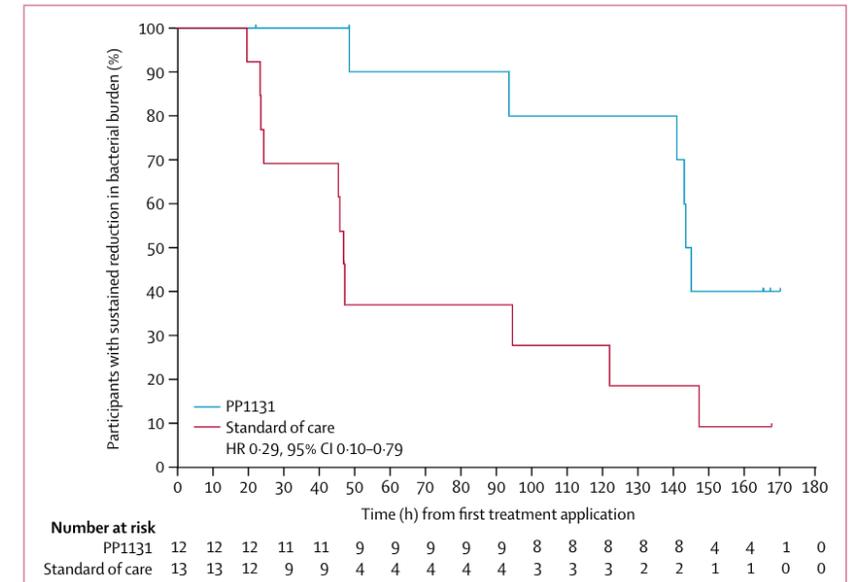
Published Online
October 3, 2018
[http://dx.doi.org/10.1016/S1473-3099\(18\)30482-1](http://dx.doi.org/10.1016/S1473-3099(18)30482-1)

In 2018, *The Lancet Infectious Diseases* published a report of the results of the PhagoBurn trial,³ investigating the efficacy and tolerability of a bacteriophage cocktail in topical treatments of *Pseudomonas aeruginosa* burn wound infections. Unfortunately, by the time the bacteriophage product was used, its titre had dropped several orders of magnitude.

	PP1131 (n=12)	Standard of care (n=13)
Age, years	61 (35-75)	37 (32-62)
Sex		
Male	8 (67%)	7 (54%)
Female	4 (33%)	6 (46%)
Burn severity		
TBSA (%)	19 (12-39)	35 (13-39)
Third degree burn TBSA (%)	6 (3-11)	23 (7-30)
Inhalation injury	3 (25%)	4 (31%)
At randomisation, time since injury, days	29 (21-43)	23 (23-36)
On active antibiotics on day 0	2 (17%)	2 (15%)

Data are median (IQR) or n (%). mITT population comprised patients with a burn wound infected with *Pseudomonas aeruginosa* who were given at least one application of PP1131 or standard of care. mITT=modified intention to treat. PP1131=cocktail of 12 natural lytic anti-*Pseudomonas aeruginosa* bacteriophages. TBSA=total body surface area.

Table 1: Baseline characteristics of mITT population



Intravesical bacteriophages for treating urinary tract infections in patients undergoing transurethral resection of the prostate: a randomised, placebo-controlled, double-blind clinical trial

Lorenz Leitner, Aleksandre Ujmajuridze, Nina Chanishvili, Marina Goderdzishvili, Irina Chkonia, Sophia Rigvava, Archil Chkhotua, Giorgi Changashvili, Shawna McCallin, Marc P Schneider, Martina D Liechti, Ulrich Mehnert, Lucas M Bachmann, Wilbert Sybesma, Thomas M Kessler

Summary

Background Urinary tract infections (UTIs) are among the most prevalent microbial diseases and their financial burden on society is substantial. In the context of increasing antibiotic resistance, finding alternative treatments for UTIs is a top priority. We aimed to determine whether intravesical bacteriophage therapy with a commercial bacteriophage cocktail is effective in treating UTI.

Procedures

Urine cultures and subsequent antibiotic sensitivity testing were done. For quantification and qualification of uropathogenic bacteria, the chromogenic UriSelect 4 media (BioRad Laboratories, Marnes-la-Coquette, France) was used. Positive urine cultures were microscopically assessed for Gram stain and morphology. If predefined pathogens potentially targeted by Pyophage were detected, urine cultures were sent for in-vitro sensitivity testing against the Pyophage cocktail with a bacterial cell lysis screening assay.¹⁷ In case of a positive in-vitro sensitivity test concluded within 24 h after receipt of the urine culture, patients were randomly assigned to a treatment group.

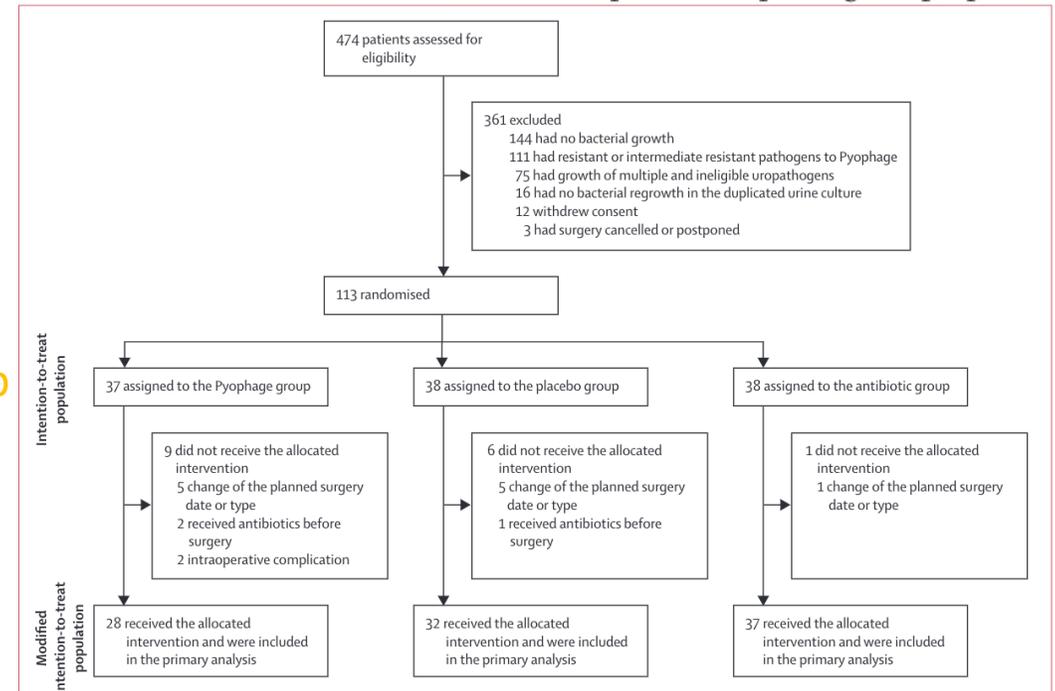


Lancet Infect Dis 2021; 21: 427-36

Published Online
September 16, 2020

Inclusion criteria for study participation were men (aged >18 years) scheduled for TURP, presenting with non-systemic and non-febrile UTI (including catheter-associated UTIs), defined as positive urine culture harbouring at least 10⁴ colony-forming units per mL, and acute intensification of symptoms such as urgency, frequency, or dysuria. All patient urine cultures must have been positive for pathogens covered by the Pyophage cocktail (ie, *Enterococcus* spp, *Escherichia coli*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus* spp, and *Streptococcus* spp) and been sensitive to bacteriophage in vitro. Patients harbouring other typical UTI pathogens, such as *Klebsiella* spp, were not eligible.¹⁷ Local application via intravesical instillation of Pyophage, rather than systemic application, was preferred to avoid potentially more frequent and relevant side effects. The common practice of placing a suprapubic

~40 each group



	n/N (%)	Unadjusted analysis			Adjusted analysis		
		OR	95% CIs	p value	OR	95% CIs	p value
Primary outcome: treatment success rate							
Pyophage	5/28 (18%)	1	Ref	..	1	Ref	..
Placebo	9/32 (28%)	1.80	0.52-6.19	0.35	1.60	0.45-5.71	0.47
Antibiotics	13/37 (35%)	2.49	0.77-8.10	0.13	2.66	0.79-8.82	0.11
Post-hoc analysis: reduction in colony-forming unit count per mL of urine culture post-treatment versus pre-treatment							
Pyophage	7/28 (25%)	1	Ref	..	1	Ref	..
Placebo	12/32 (38%)	1.80	0.59-5.49	0.30	1.62	0.51-5.12	0.41
Antibiotics	18/37 (49%)	2.84	0.97-8.29	0.056	2.98	1.00-8.84	0.049
Safety outcome: adverse events							
Pyophage	6/28 (21%)	1	Ref	..	1	Ref	..
Placebo	13/32 (41%)	0.39	0.13-1.25	0.12	0.36	0.11-1.17	0.089
Antibiotics	11/37 (30%)	0.65	0.21-2.03	0.45	0.66	0.21-2.07	0.47

Treatment success was defined as normalisation of urine culture (<10⁴ colony-forming units per mL) after treatment. Adjusted analysis included the baseline quality of life assessment, urinalysis parameters, and method of bladder emptying (ie, spontaneous vs indwelling catheter) as covariates. OR=odds ratio.

Table 2: Logistic regression of the primary and safety outcomes, as well as post-hoc analysis of quantitative urine culture parameters, in the modified intention-to-treat population

Added value of this study

To our knowledge, this study is the first randomised, placebo-controlled, double-blind trial investigating bacteriophages for treating urinary tract infections (UTIs). Bacteriophages were actively instilled into the bladder and compared with either bladder instillation of sterile bacteriophage buffer (placebo) in a double-blind manner or to systemically applied antibiotics as an open-label standard-of-care comparator. We observed non-inferiority of bacteriophages in terms of efficacy compared with antibiotics, and high tolerability and safety. However, superiority of bacteriophages over placebo was not observed, most likely because of a therapeutically relevant effect of the placebo treatment caused by unanticipated mechanical reduction of the bacterial load following repeated bladder irrigation over 7 days.



	Pyophage (n=28)	Placebo (n=32)	Antibiotics (n=37)
Age, years (SD)	69 (62-76)	68 (59-77)	68 (60-76)
International Prostate Symptom Score*			
Patients with symptoms	19 (13-25)	17 (8-26)	17 (9-25)
Patients with quality of life affected	5 (4-6)	4 (2-6)	4 (2-6)
Free uroflowmetry			
Maximum flow rate, mL/s	9 (6-12)	9 (5-13)	9 (6-12)
Post void residual, mL	165 (25-305)	200 (30-370)	125 (0-270)
Bladder diary			
Daytime frequency	6 (4-8)	6 (5-7)	7 (5-9)
Nighttime frequency	4 (3-5)	4 (3-5)	4 (3-5)
Mean voided volume, mL	180 (95-265)	165 (110-220)	180 (100-260)
Prostate volume, mL	72 (36-108)	76 (38-114)	79 (46-112)
PSA value, µg/L	6 (0-16)	4 (0-8)	6 (0-13)
Indwelling catheter before surgery	9 (32%)	14 (44%)	14 (38%)
Duration of catheterisation before surgery, days	31 (8-54)	37 (8-66)	24 (9-39)
Urinalysis			
Leucocytes	16 (57%)	20 (63%)	17 (46%)
Erythrocytes	12 (43%)	24 (75%)	22 (59%)
Nitrites	10 (36%)	9 (28%)	8 (22%)
Bacterial sampling			
Enterococcus spp	15 (54%)	14 (44%)	15 (41%)
Escherichia coli	5 (18%)	10 (31%)	10 (27%)
Proteus mirabilis	0	1 (3%)	2 (5%)
Pseudomonas aeruginosa	0	0	1 (3%)
Streptococcus spp	8 (29%)	7 (22%)	8 (22%)
Staphylococcus spp	0	0	1 (3%)
Colony-forming units per mL of preoperative urine culture			
10 ⁴ to <10 ⁵	0	1 (3%)	0
10 ⁵ to <10 ⁶	8 (29%)	9 (28%)	12 (32%)
10 ⁶ to <10 ⁷	15 (54%)	19 (59%)	14 (38%)
≥10 ⁷	5 (18%)	3 (9%)	11 (30%)
Surgical parameters			
Duration of surgery, min	50 (36-64)	54 (39-69)	56 (42-70)
Resected tissue, 10 ⁻³ kg	38 (23-53)	36 (27-45)	33 (16-50)
Histology			
Malignancy	1 (4%)	4 (13%)	0
Chronic prostatitis	10 (36%)	8 (25%)	11 (30%)
Benign prostate hyperplasia	17 (61%)	20 (63%)	26 (70%)

The modified intention-to-treat population included all patients who received at least one dose of the allocated treatment. Data are mean (95% CIs) or n (%), unless otherwise stated. *Used to determine prostate-related bladder storage and voiding symptoms.

Table 1: Baseline clinical characteristics of the modified intention-to-treat population

There are amendments to this paper

Safety of bacteriophage therapy in severe *Staphylococcus aureus* infection

Aleksandra Petrovic Fabijan ^{1,2,6}, Ruby C. Y. Lin ^{1,2,3,4,6}, Josephine Ho^{1,2}, Susan Maddocks^{1,2,3}, Nouri L. Ben Zakour^{1,3}, Jonathan R. Iredell ^{1,2,3} * and Westmead Bacteriophage Therapy Team⁵

In this single-arm non-comparative trial, 13 patients in an Australian hospital with severe *Staphylococcus aureus* infections were intravenously administered a good manufacturing practice-quality preparation of three Myoviridae bacteriophages (AB-SA01) as adjunctive therapy. AB-SA01 was intravenously administered twice daily for 14 d and the clinical, haematological and blood biochemical parameters of the recipients were monitored for 90 d. The primary outcome was the assessment of safety and tolerability (that is, pain and redness at the infusion site and systemic adverse reactions, such as fever, tachycardia, hypotension, diarrhoea or abdominal pain and the development of renal or hepatic dysfunction). No adverse reactions were reported, and our data indicate that AB-SA01 administered in this way is safe in severe *S. aureus* infections, including infective endocarditis and septic shock. Future controlled trials will be needed to determine the efficacy of AB-SA01 but no phage resistance evolved in vivo and the measurements of bacterial and phage kinetics in blood samples suggest that 12 h dosing of 10⁹ plaque-forming units may be a rational basis for further studies. Trial Registration: Westmead Hospital Human Research Ethics Committee HREC/17/WMEAD/275; ClinicalTrials.gov: [NCT03395769](https://clinicaltrials.gov/ct2/show/study/NCT03395769); Clinical Trials Notification (Australian Therapeutic Goods Association): CT-2018-CTN-02372-1.

Table 1 | Patient data

WMP ID (age (yr), gender) ^a	Diagnoses ^b	<i>S. aureus</i> sequence type ^c	EOP ^d	Predicted mortality (%) ^e			Antibiotics and phage therapy			CRP WBC ^h		Outcome	Comments ^k
				CCI	APACHE II (score)	IE	Principal antibiotics ^f	Time before therapy (d) ^g	Phage doses	Pre-therapy (24 h)	D14 ^j		
001 (65, M)	Septic shock, PVE (A, M)	15	143	23	25 (18)	87	FLU, CIP, RIF, MEM	(10)	28	171 24.5	47 16.2	Survived D28 Survived D90	-
003 (47, M)	Septic shock, IE (A, M)	340	23	23	40 (25)	68	FLU	(5)	5	ND 17.9	-	Died D3	Septic shock, valve failure
004 (43, F)	OM/epidural abscess	72	9	2	8 (6)	17	FLU	(6)	28	271 6.2	50 4.4	Survived D28 Survived D90	-
005 (39, M)	OM/epidural abscess	25	5	2	4 (3)	10	FLU	(6)	28	19 ⁱ 13	28 7.1	Survived D28 Survived D90	-
006 (87, M)	Possible PVE (A)	5	<1	98	40 (23)	74	FLU	(8)	4(W)	151 26.3	-	Died D6 (W)	Refused CRRT
007 (89, M)	OM/septic arthritis	109	116	98	40 (21)	35	FLU	(7)	24(W)	130 5.3	-	Died D15 (W)	Myelodysplastic syndrome, palliated D13
008 (36, F)	RIE (T), empyema	15 and 398	0 and 23	2	8 (7)	26	FLU, CLI	(7)	28	252 ⁱ 13.9	ND 9.6	Survived D28 Survived D90	2 months later: ST672 sepsis
009 (69, F)	PVE (A, M)	45	21	79	40 (25)	45	FLU, CIP, RIF	(8)	28	149 45.8	48 9.4	Survived D28 Died D90	Surgery D50
010 (21, M)	PVE (A)	5	28	2	25 (17)	40	FLU, CIP, RIF	(6)	28 × 2	79 16.1	241 22.9	Survived D28 Survived D90	Surgery D15; phage × 2 courses
011 (64, M)	Septic shock, pneumonia	(22)	0	10	40 (25)	45	VAN, CLI, MEM, AZI	(5)	5(w)	437 ⁱ 14.9	-	Died D7 (W)	ECMO, CRRT
012 (71, M)	Epidural abscess	93	15	23	15 (12)	35	CEF, CLI, FLU	(6)	28	164 9	15 7.4	Survived D28 Survived D90	-
013 (81, M)	PVE (A)	45	<1	100	25 (19)	50	FLU, CIP, RIF	(4)	27	156 15.2	96 12.7	Died D27	Respiratory failure
014 (70, M)	Possible IE (A)	188	83	47	8 (6)	40	CEF, FLU	(4)	28	327 ⁱ 6.9	19 5.2	Survived D28 Survived D90	Mycotic aneurysm

W, phage therapy withdrawn; AZI, azithromycin. ^aM, male; F, female. Nb. Pt WMP002 did not have staphylococcal infection and did not receive AB-SA01, and is reported elsewhere²¹. ^bM, mitral valve; A, aortic valve; IE, infective endocarditis; RIE, right-sided infective endocarditis; T, tricuspid valve; OM, osteomyelitis. ^cMRSA *S. aureus* are in parentheses. ^dEOP of AB-SA01 phages on *S. aureus* isolates (average values calculated from ≥ 2 biological replicates) relative to the reference *S. aureus* strain SA-5863. ^eCCI, Charlson comorbidity index (predicted one-year mortality percentage); APACHE II, acute physiology and chronic health evaluation (in-hospital mortality percentage), the absolute score is in parentheses. IE, infective endocarditis score (predicted six-month mortality percentage). ^fUsed for > 72 h; CEF, cefazolin; CIP, ciprofloxacin; CLI, clindamycin; FLU, flucloxacillin; MEM: meropenem; RIF, rifampicin; VAN, vancomycin. ^gNumber of days of effective anti-staphylococcal antibiotic therapy before starting bacteriophage therapy. ^hCRP, C-reactive protein (mg l⁻¹): reference value, ≤ 3 mg l⁻¹; WBC, white blood cells (×10⁹ l⁻¹): reference value, ≤ 3 mg l⁻¹; ND, not done. ⁱ48 h before phage-therapy administration. ^jEnd of phage therapy (± 48 h). ^kECMO, extra-corporeal membrane oxygenation; CRRT, continuous renal replacement therapy.

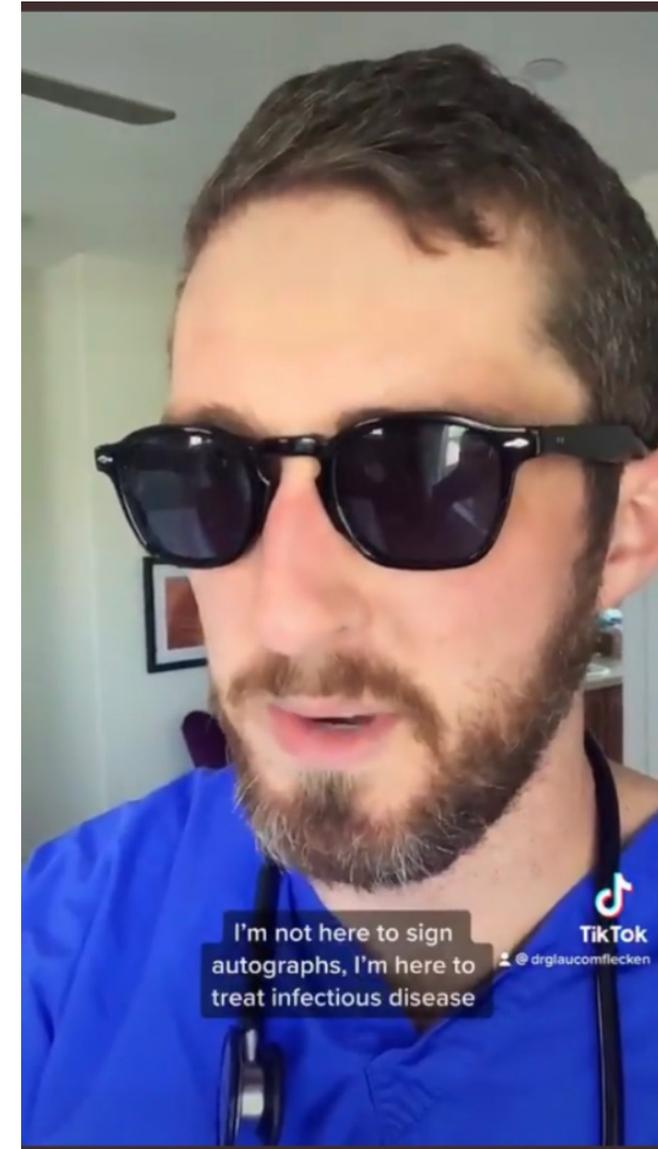
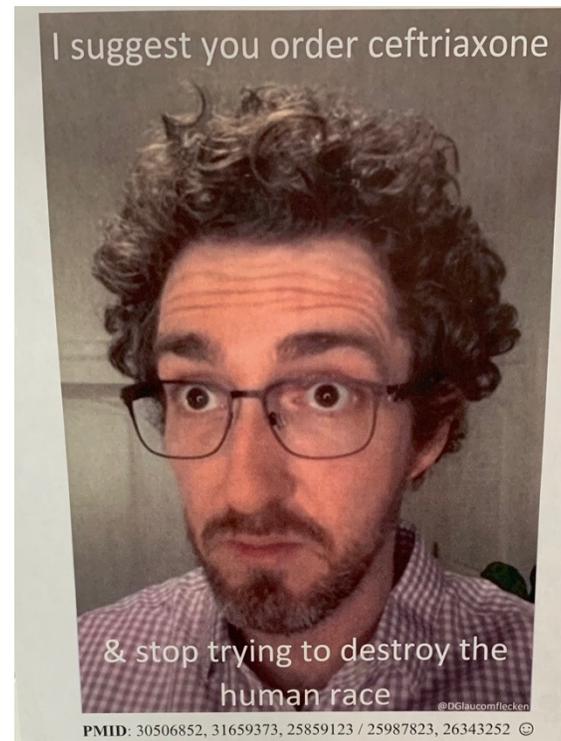
AB-SA01 (3 anti SA phages) safety and tolerability trial

- 13 cases (SA bacteremia)
 - All on conventional antibiotic treatment.
- Single phage cocktail
- Indications :
 - Endocarditis 8
 - Osteomyelitis/pneumonia/ epidural abscess – 1 each (+2 osteomyelitis)
- Outcome
 - **3 bacterial isolates resistant/ “less susceptible”**
 - 5 died during follow-up
 - Possibly improved outcome compared to risk.

Other patients were treated in other centers but not reported as part of this series

Antimicrobial susceptibility....

- A processes in which at the end we get an answer.
- But ID physicians while looking complex creatures....



Antimicrobial susceptibility....

- A set of processes in which at the end we get an answer

Guidance on reading EUCAST Breakpoint Tables

EUCAST Clinical Breakpoint Tables v. 12.0, valid from 2022-01-01

MIC determination (broth microdilution according to ISO standard 20776-1)
 Medium:
 Inoculum:
 Incubation:
 Reading:
 Quality control:

EUCAST methodology and quality control for MIC determination

Disk diffusion (EUCAST standardised disk diffusion method)
 Medium:
 Inoculum:
 Incubation:
 Reading:
 Quality control:

EUCAST methodology and quality control for disk diffusion

An arbitrary "off scale" breakpoint which categorises wild-type organisms as "Susceptible, increased exposure (I)".

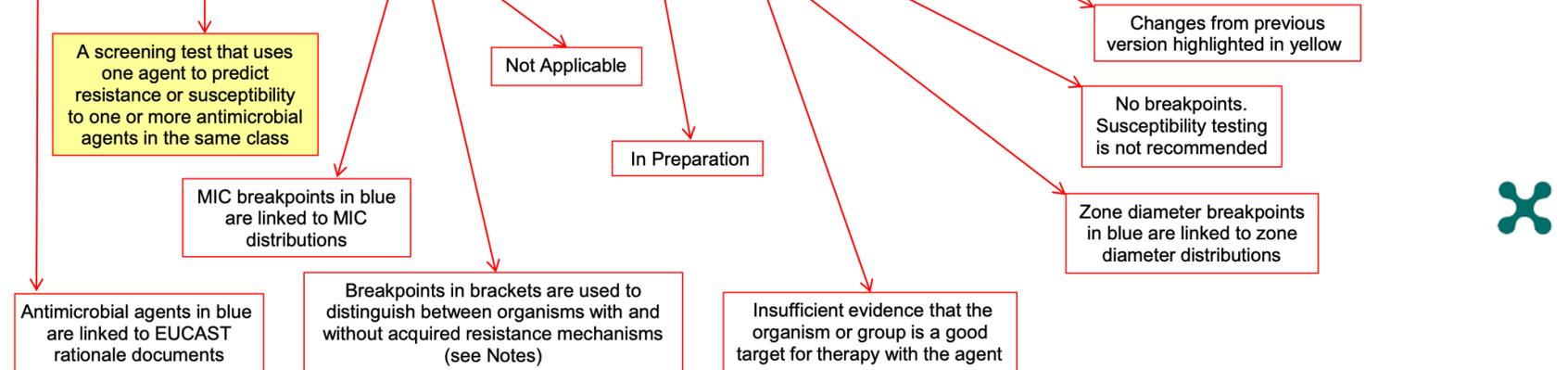
Breakpoints with a species name apply only to that particular species (in this example *S. aureus*)

The I category is not listed but is interpreted as the values between the S and the R breakpoints. If the S and R breakpoints are the same value there is no I category.

Agent A: No I category
 Agent B: I category: 4 mg/L, 23-25 mm
 Agent H: I category: 1-2 mg/L, 24-29 mm

Area of Technical Uncertainty
 See specific information on how to handle technical uncertainty in antimicrobial susceptibility testing.

Antimicrobial agent	MIC breakpoint (mg/L)			Disk content (µg)	Zone diameter breakpoint (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	
Antimicrobial agent A	1 ¹	1 ¹		X	20 ^A	20 ^A		Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method. 1. Notes that are general comments and/or relating to MIC breakpoints. 2. New comment Removed comment A. Comment on disk diffusion
Antimicrobial agent B	2 ²	4		Y	26	23		
Antimicrobial agent C	0.001	8		X	50	18		
Antimicrobial agent D, <i>S. aureus</i>	IE	IE			IE	IE		
Antimicrobial agent E	-	-			-	-		
Antimicrobial agent F	IP	IP			IP	IP		
Antimicrobial agent G (screen only)	NA	NA		Y	25	25		
Antimicrobial agent H	0.5	2		Z	30	24		
Antimicrobial agent I	(8) ¹	(8) ¹		30	(18) ^A	(18) ^A		



This Issue

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News From the Food and Drug Administration

February 19, 2019

FDA Approves Bacteriophage Trial

Rebecca Voelker, MSJ

JAMA. 2019;321(7):638. doi:10.1001/jama.2019.0510

The first US clinical trial of intravenously administered **bacteriophage therapy** has received FDA approval. Physician researchers at the University of California San Diego (UCSD) School of Medicine will conduct the trial in collaboration with AmpliPhi Biosciences Corporation, a San Diego-based biotechnology company.

Current active trails

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input checked="" type="checkbox"/>	Not yet recruiting NEW	Mayo Clinic Phage Program Biobank	<ul style="list-style-type: none"> Bacteriophage Therapy 		<ul style="list-style-type: none"> Mayo Clinic Rochester Rochester, Minnesota, United States
2	<input checked="" type="checkbox"/>	Not yet recruiting	Bacteriophage Therapy in Patients With Prosthetic Joint Infections Who Previously Failed Surgery for PJI	<ul style="list-style-type: none"> Prosthetic Joint Infection 	<ul style="list-style-type: none"> Drug: Bacteriophage Drug: Placebo 	
3	<input checked="" type="checkbox"/>	Not yet recruiting	Bacteriophage Therapy in First Time Chronic Prosthetic Joint Infections	<ul style="list-style-type: none"> Prosthetic Joint Infection Bacterial Infections 	<ul style="list-style-type: none"> Biological: Phage Therapy 	
4	<input checked="" type="checkbox"/>	Not yet recruiting	A Study of Topical BX005-A in Subjects With Moderate to Severe Atopic Dermatitis	<ul style="list-style-type: none"> Atopic Dermatitis 	<ul style="list-style-type: none"> Biological: BX005-A Other: Placebo 	
5	<input checked="" type="checkbox"/>	Not yet recruiting	Study Evaluating Safety, Tolerability, and Efficacy of Intravenous AP-SA02 in Subjects With S. Aureus Bacteremia	<ul style="list-style-type: none"> Bacteremia Staphylococcus Aureus Staphylococcus Aureus Bacteremia (and 2 more...) 	<ul style="list-style-type: none"> Biological: AP-SA02 Other: Placebo 	<ul style="list-style-type: none"> Rhode Island Hospital Providence, Rhode Island, United States
6	<input checked="" type="checkbox"/>	Not yet recruiting	Safety and Efficacy of the Bacteriophage Preparation, ShigActive™, in a Human Experimental Model of Shigellosis	<ul style="list-style-type: none"> Shigellosis 	<ul style="list-style-type: none"> Biological: bacteriophage Other: Placebo 	<ul style="list-style-type: none"> University of Maryland, Baltimore, University of Maryland School of Medicine, C and Global Health Baltimore, Maryland, United States
7	<input checked="" type="checkbox"/>	Recruiting	Bacteriophage Therapy in Patients With Diabetic Foot Osteomyelitis	<ul style="list-style-type: none"> Osteomyelitis Diabetic Foot Osteomyelitis 	<ul style="list-style-type: none"> Biological: Phage Therapy Other: Placebo 	<ul style="list-style-type: none"> Martin Foot and Ankle York, Pennsylvania, United States Futuro Clinical Trials, LLC McAllen, Texas, United States
8	<input checked="" type="checkbox"/>	Not yet recruiting	Nebulized Bacteriophage Therapy in Cystic Fibrosis Patients With Chronic Pseudomonas Aeruginosa Pulmonary Infection	<ul style="list-style-type: none"> Chronic Pseudomonas Aeruginosa Infection Cystic Fibrosis 	<ul style="list-style-type: none"> Drug: BX004-A Drug: Placebo 	
9	<input checked="" type="checkbox"/>	Not yet recruiting	Phage Therapy for the Prevention and Treatment of Pressure Ulcers.	<ul style="list-style-type: none"> Pressure Ulcer 	<ul style="list-style-type: none"> Combination Product: Bacteriophage-loaded Microcapsule Spray Combination Product: Placebo Procedure: Standard of Care 	
10	<input checked="" type="checkbox"/>	Recruiting	Bacteriophage Therapy TP-102 in Diabetic Foot Ulcers	<ul style="list-style-type: none"> Diabetic Foot Ulcer Pseudomonas Aeruginosa Infection Staphylococcus Aureus Infection Acinetobacter Infection 	<ul style="list-style-type: none"> Biological: TP-102 	<ul style="list-style-type: none"> Hadassah Medical Center, Ein Kerem Jerusalem, Israel
11	<input checked="" type="checkbox"/>	Withdrawn	Bacteriophage Therapy in Patients With Prosthetic Joint Infections	<ul style="list-style-type: none"> Prosthetic Joint Infection 	<ul style="list-style-type: none"> Biological: Phage Therapy Procedure: Two-Stage Exchange Arthroplasty 	<ul style="list-style-type: none"> Mayo Clinic Rochester, Minnesota, United States
12	<input checked="" type="checkbox"/>	Recruiting	Cystic Fibrosis bacterioPHage Study at Yale (CYPHY)	<ul style="list-style-type: none"> Cystic Fibrosis 	<ul style="list-style-type: none"> Drug: Standard Dose YPT-01 Other: Placebo 	<ul style="list-style-type: none"> Yale New Haven Hospital New Haven, Connecticut, United States
13	<input checked="" type="checkbox"/>	Not yet recruiting	Phage Safety Cohort Study	<ul style="list-style-type: none"> Prosthetic Joint Infection Bone and Joint Infection Implant Infection 	<ul style="list-style-type: none"> Other: Adverse event after injection of phages 	<ul style="list-style-type: none"> Hospices Civils de Lyon Lyon, France
14	<input checked="" type="checkbox"/>	No longer available	Personalized Phage Treatment in Covid-19 Patients With Bacterial Co-Infections Microbials for Pneumonia or Bacteremia/Septicemia	<ul style="list-style-type: none"> Covid19 Bacteremia Septicemia (and 3 more...) 	<ul style="list-style-type: none"> Other: Phage Therapy 	
15	<input checked="" type="checkbox"/>	Recruiting	Ph 1/2 Study Evaluating Safety and Tolerability of Inhaled AP-PA02 in Subjects With Chronic Pseudomonas Aeruginosa Lung Infections and Cystic Fibrosis	<ul style="list-style-type: none"> Cystic Fibrosis Pseudomonas Aeruginosa Pseudomonas (and 2 more...) 	<ul style="list-style-type: none"> Biological: AP-PA02 Other: Placebo 	<ul style="list-style-type: none"> Children's Hospital Los Angeles Los Angeles, California, United States University of South Florida Tampa, Florida, United States St. Luke's Cystic Fibrosis Center of Idaho Boise, Idaho, United States (and 13 more...)
16	<input checked="" type="checkbox"/>	Recruiting	The Effect of Supraglottic and Oropharyngeal Decontamination on the Incidence of Ventilator-associated Pneumonia	<ul style="list-style-type: none"> Trauma Injury Brain Injuries 	<ul style="list-style-type: none"> Drug: Control Drug: Antiseptic Solution 	<ul style="list-style-type: none"> Budgetary Healthcare Institution of Arkhangelsk Region "Severodvinsk City Clin Severodvinsk, Arkhangelsk Region, Russian Federation

16	<input checked="" type="checkbox"/>	Recruiting	The Effect of Supraglottic and Oropharyngeal Decontamination on the Incidence of Ventilator-associated Pneumonia	<ul style="list-style-type: none"> Trauma Injury Brain Injuries Abdominal Sepsis (and 5 more...) 	<ul style="list-style-type: none"> Drug: Control Drug: Antiseptic Solution Drug: Bacteriophage 	<ul style="list-style-type: none"> Budgetary Healthcare Institution of Arkhangelsk Region "Severodvinsk City Clin Severodvinsk, Arkhangelsk Region, Russian Federation
17	<input checked="" type="checkbox"/>	Not yet recruiting	Phage Therapy for the Prevention and Treatment of Wound Infections in Burned Patients	<ul style="list-style-type: none"> Wound Infection 	<ul style="list-style-type: none"> Biological: Bacteriophage cocktail spray Drug: Xeroform 	
18	<input checked="" type="checkbox"/>	Withdrawn	Assessing the Efficacy of Anti-staphylococcal Phages in the Management of Infected Foot Ulcers in Diabetes	<ul style="list-style-type: none"> Diabetes Diabetic Foot Diabetic Foot Infection 	<ul style="list-style-type: none"> Drug: Phage 	<ul style="list-style-type: none"> University Hospitals Derby and Burton NHS Foundation Trust Derby, Derbyshire, United Kingdom
19	<input checked="" type="checkbox"/>	Recruiting	Bacteriophage Therapy in Patients With Urinary Tract Infections	<ul style="list-style-type: none"> Urinary Tract Infection Bacterial 	<ul style="list-style-type: none"> Biological: Bacteriophage Therapy 	<ul style="list-style-type: none"> Universal Axon Clinical Research Doral, Florida, United States AMPM Research Clinic Miami Gardens, Florida, United States AdMed Research Miami, Florida, United States (and 5 more...)
20	<input checked="" type="checkbox"/>	Recruiting	Safety and Efficacy of EcoActive on Intestinal Adherent Invasive E. Coli in Patients With Inactive Crohn's Disease	<ul style="list-style-type: none"> Crohn Disease 	<ul style="list-style-type: none"> Biological: Placebo Biological: Bacteriophage preparation 	<ul style="list-style-type: none"> The Mount Sinai Hospital New York, New York, United States
21	<input checked="" type="checkbox"/>	No longer available	Individual Patient Expanded Access for AB-SA01, an Investigational Anti-Staphylococcus Aureus Bacteriophage Therapeutic		<ul style="list-style-type: none"> Biological: AB-SA01 	
22	<input checked="" type="checkbox"/>	No longer available	Individual Patient Expanded Access for AB-PA01, an Investigational Anti-Pseudomonas Aeruginosa Bacteriophage Therapeutic		<ul style="list-style-type: none"> Biological: AB-PA01 	
23	<input checked="" type="checkbox"/>	Not yet recruiting	Standard Treatment Associated With Phage Therapy Versus Placebo for Diabetic Foot Ulcers Infected by S. Aureus	<ul style="list-style-type: none"> Diabetic Foot Staphylococcal Infections 	<ul style="list-style-type: none"> Drug: Topical anti-Staphylococcus bacteriophage therapy Drug: Topical placebo corresponding to anti-Staphylococcus bacteriophage therapy 	<ul style="list-style-type: none"> CHU de Bordeaux - Hôpital Pellegrin Bordeaux, France CHRU de Nimes - Hôpital Universitaire de Réadaptation du Grau du Roi Le Grau du Roi, France CHU de Nantes - Hôtel Dieu Nantes Cedex 1, France (and 6 more...)
24	<input checked="" type="checkbox"/>	Completed	MicroPhage S. Aureus / MSSA / MRSA Blood Culture Beta Trial	<ul style="list-style-type: none"> Bacteremia Staphylococcal Infection Sepsis Infection 	<ul style="list-style-type: none"> Other: MicroPhage S. aureus / MSSA / MRSA Blood Culture Test (prototype) 	<ul style="list-style-type: none"> Evanston Northwestern Healthcare Research Institute Evanston, Illinois, United States University of Maryland Baltimore Baltimore, Maryland, United States Johns Hopkins Medical Institute Baltimore, Maryland, United States
25	<input checked="" type="checkbox"/>	Completed	A Prospective, Randomized, Double-Blind Controlled Study of WPP-201 for the Safety and Efficacy of Treatment of Venous Leg Ulcers	<ul style="list-style-type: none"> Venous Leg Ulcers 	<ul style="list-style-type: none"> Drug: Bacteriophage Drug: WPP-201 Bacteriophage Drug: Bacteriophages 	<ul style="list-style-type: none"> Southwest Regional Wound Care Center Lubbock, Texas, United States

Hurdles

- QA and stability of product
- Microbiological ITT: phages are specific (or too specific)
- Clinical ITT
- Or like the case reports/compassionate use,
 - we should aim on phage + antibiotics in clinical trials???

Clinical Phage Microbiology

Critical tool for

- Adopting the right phage to the patients' disease
- Understanding clinical trial efficacy and clinical efficacy in infected patients.

However, unlike antibiotics

- No standardization is available
- No knowledge on right methodology for each clinical application
- No streamlining of processes, thus testing may take time

Antimicrobial Stewardship

How would you define this: R/S/ ATU

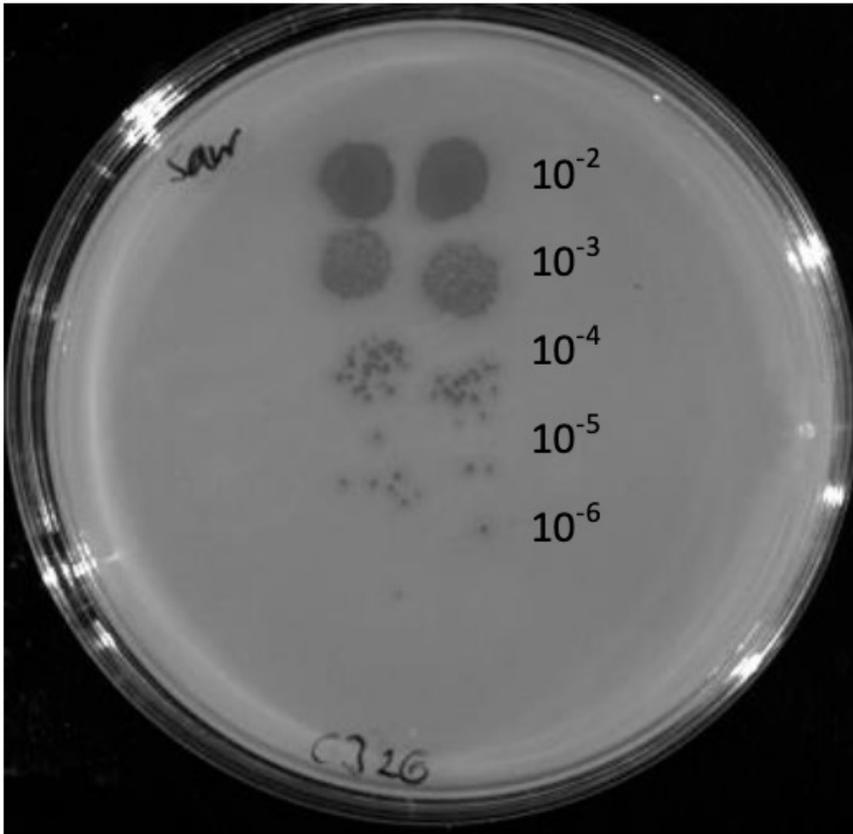


Fig. 1: Plaque assay test of SaW1Q0439ph1 phage on the patient's bacterial isolate (C326)

How would you define this: R/S/ ATU

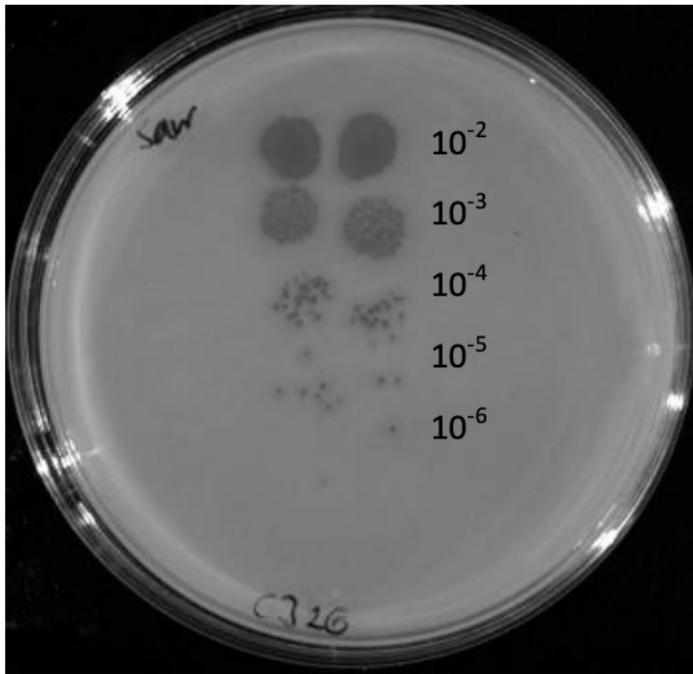
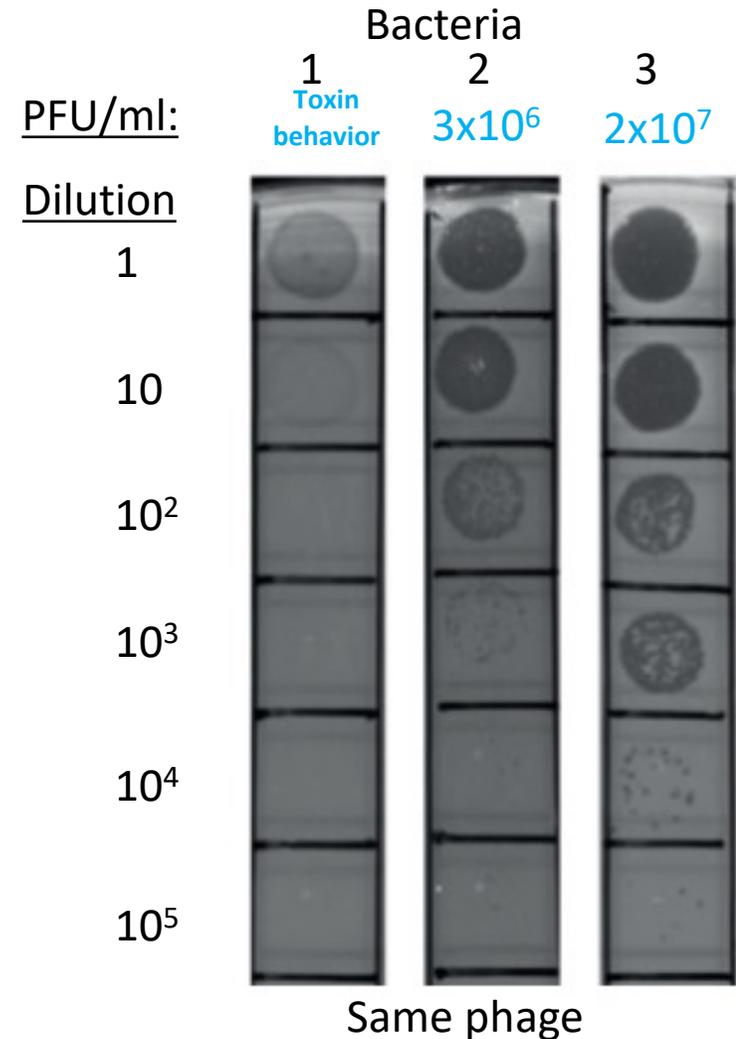


Fig. 1: Plaque assay test of SaWIQ0439ph1 phage on the patient's bacterial isolate (C326)



How would you define this: R/S/ ATU

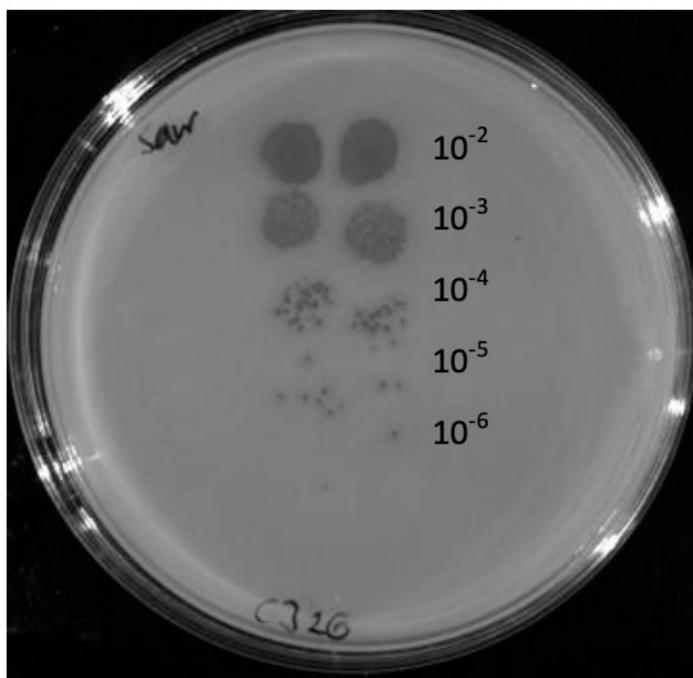


Fig. 1: Plaque assay test of SaWIQ0439ph1 phage on the patient's bacterial isolate (C326)

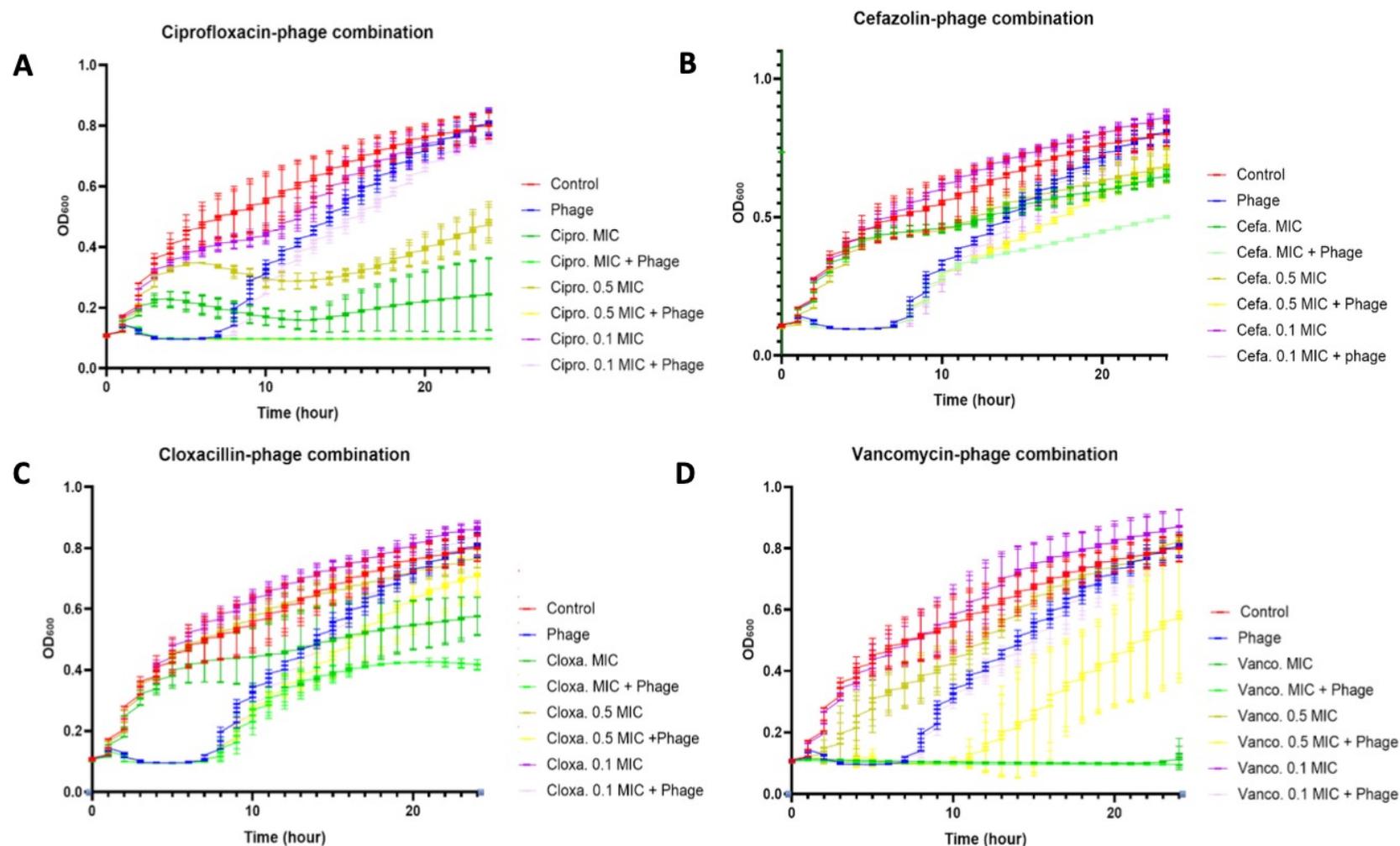


Fig. 2: Antibiotic-phage combinations checkerboard test 0.1-1 MIC. A) A synergistic effect was observed in all cipro. concentrations. B) A mild synergistic effect was observed in the highest concentration of cefazolin but not in the others. C) A mild synergistic effect was observed in the highest concentration of cloxacillin but not in the others. D) A synergistic effect was observed when using 0.5 MIC of vancomycin.

Phage clinical microbiology

- 2 major publications to date
- No harmonization/standards yet
- Not yet known consideration for dosage in clinical practice

Clinical Phage Microbiology: a suggested framework and recommendations for the in-vitro matching steps of phage therapy

Daniel Gelman, MD, Ortal Yerushalmy, MA, Sivan Alkalay-Oren, MA, Chani Rakov, MA, Shira Ben-Porat, MD, Leron Khalifa, MA, Karen Adler, MA, Mohanad Abdalrhman, BSc, Shunit Copenhagen-Glazer, PhD, Saima Aslam, MD, Prof Robert T Schooley, MD, Ran Nir-Paz, MD, Ronen Hazan, PhD

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MINIREVIEW
March 2022 Volume 66 Issue 3 e02071-21
<https://doi.org/10.1128/aac.02071-21>

Considerations for the Use of Phage Therapy in Clinical Practice

Gina A. Suh ^a, Thomas P. Lodise ^b, Pranita D. Tamma ^c, Jane M. Knisely ^d, Jose Alexander ^e, Saima Aslam ^f, Karen D. Barton ^g, Erica Bizzell ^d, Katherine M. C. Totten ^a, Joseph L. Campbell ^d, Benjamin K. Chan ^h, Scott A. Cunningham ^a, Katherine E. Goodman ⁱ, Kerryl E. Greenwood-Quaintance ^a, Anthony D. Harris ⁱ, Shayla Hesse ^d, Anthony Maresso ^j, Veronique Nussenblatt ^d, David Pride ^f, Michael J. Rybak ^k, Zoe Sund ^g, David van Duin ^l, Daria Van Tyne ^m, Robin Patel ^a, for the Antibacterial Resistance Leadership Group

Questions in the guidelines

QUESTION 6: UNDER WHICH CONDITIONS SHOULD PST BE USED TO SELECT PHAGES FOR THERAPEUTIC USE?

- **While it would be ideal to perform PST** before phage administration so that a phage or phages active against the infecting bacterium is or are selected for use, **standardized, accurate, and reproducible methods, reported with validated interpretive criteria are lacking** (see Question 7). Once such methods are available, their routine use is suggested before phage administration, when possible.

QUESTION 7: WHICH PARAMETERS SHOULD EMERGING PST PLATFORMS CONSIDER?

- The ARLG Phage Taskforce identified several laboratory testing strategies for assessing phage activity against individual bacterial isolates, with **no reference gold standard method identified**. Methods ideally need to be standardized, accurate, reproducible, rapid, test multiple phages at a time, and report out **using interpretive criteria that predict clinical activity; no such criteria yet exist**. The ARLG Taskforce suggests that methods that demonstrate lack of *in vitro* phage activity against the targeted bacterium be shown to correlate with unlikely *in vivo* activity.
 - double-layer agar method
 - The spot test
 - Liquid-based testing
 - **Stationary VS Logarithmic?**

QUESTION 8: WHICH PARAMETERS SHOULD TEST METHODS FOR ASSESSMENT OF PHAGE ACTIVITY IN COMBINATION WITH ANTIBIOTICS CONSIDER?

- As with PST, the ARLG Phage Taskforce found **no standard method for phage-antibiotic combination testing**. Such an assay may be helpful to predict effects of specific phage-antibiotic combinations on bacterial population reductions, addressing synergy and antagonism.

QUESTION 9: WHICH IMMUNE SYSTEM COMPONENTS ARE LIKELY TO IMPACT SAFETY AND EFFICACY OF PHAGE THERAPY, AND HOW CAN THESE BE TESTED?

- The ARLG Phage Taskforce is unable to recommend specific assessment of immunologic parameters that correlate with phage activity that should be assessed due to a significant knowledge gap in this area but suggests considering tests for neutralizing antibodies in the context of prolonged phage administration, with the recognition that standardized assays for such measurements are unavailable. As indicated in Question 3, monitoring of renal, liver, and hematologic function is recommended; it may also be reasonable to monitor an inflammatory marker (e.g., C-reactive protein).
- Should we think about MIC/MBC etc... PK/PK??

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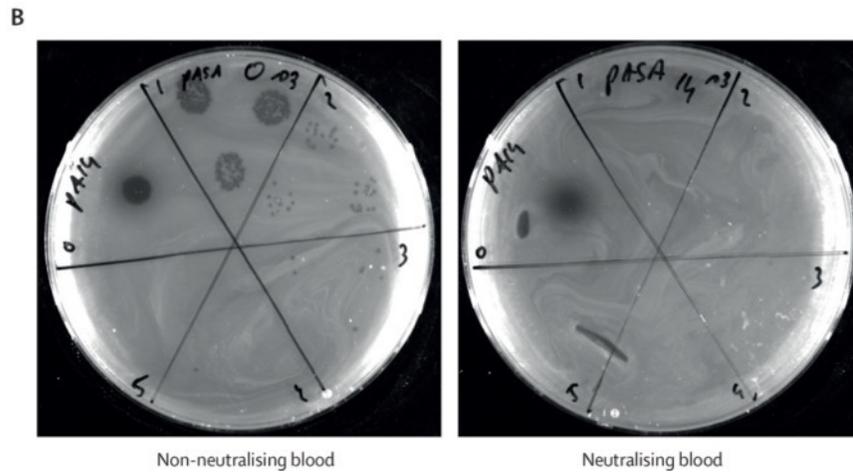
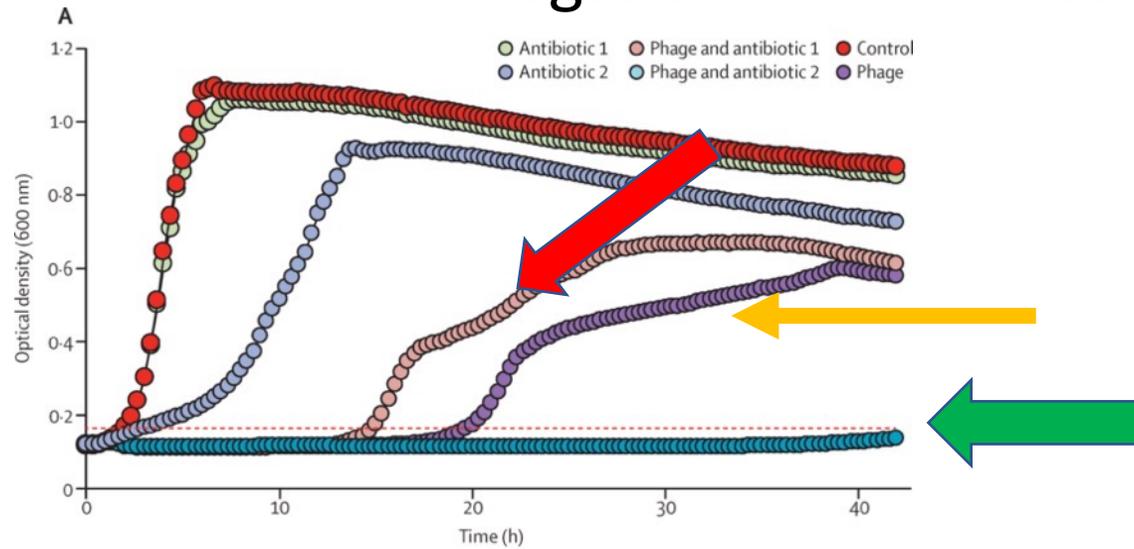
The Lancet Microbe

Volume 2 Issue 10 Pages e555-e563 (October 2021)

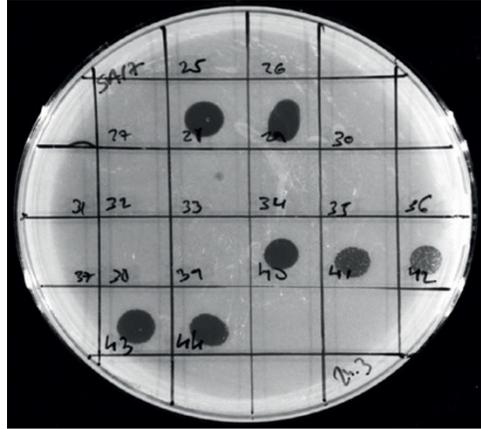
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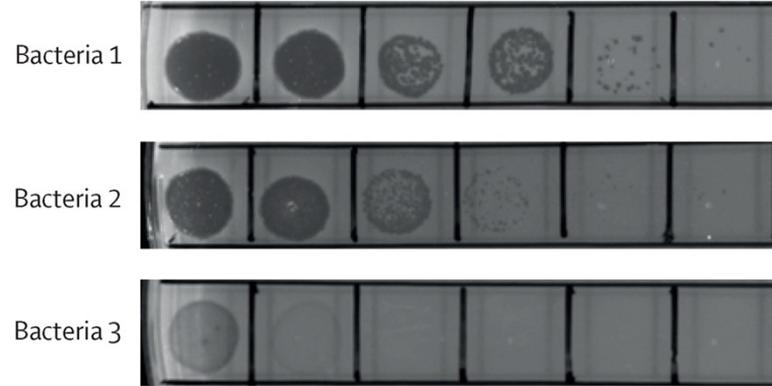
Phages and antibiotics – not simple to predict



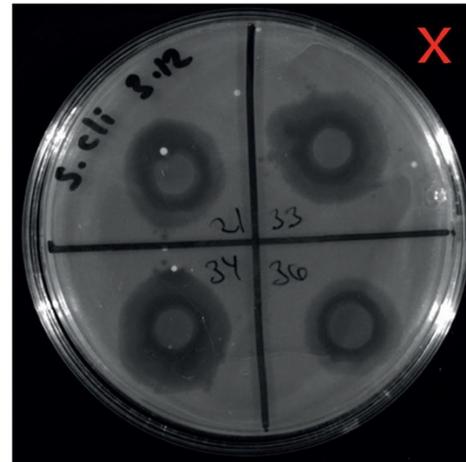
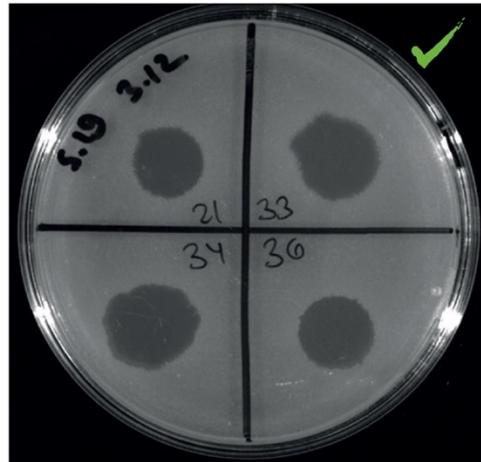
A



B



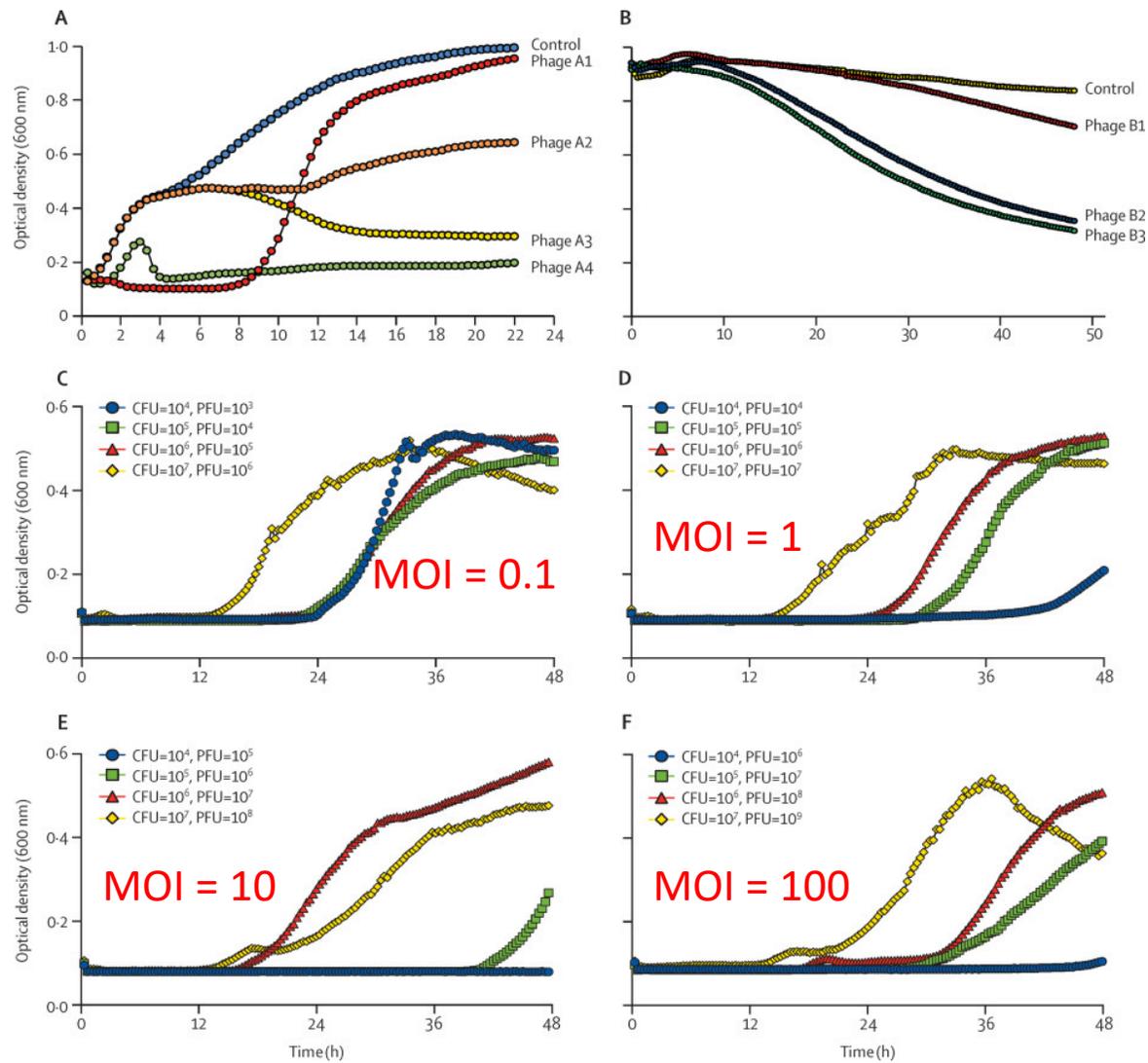
C



The game of MOI and initial bacterial load

Log phase

Stationary



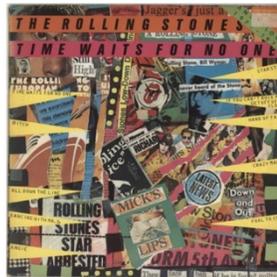
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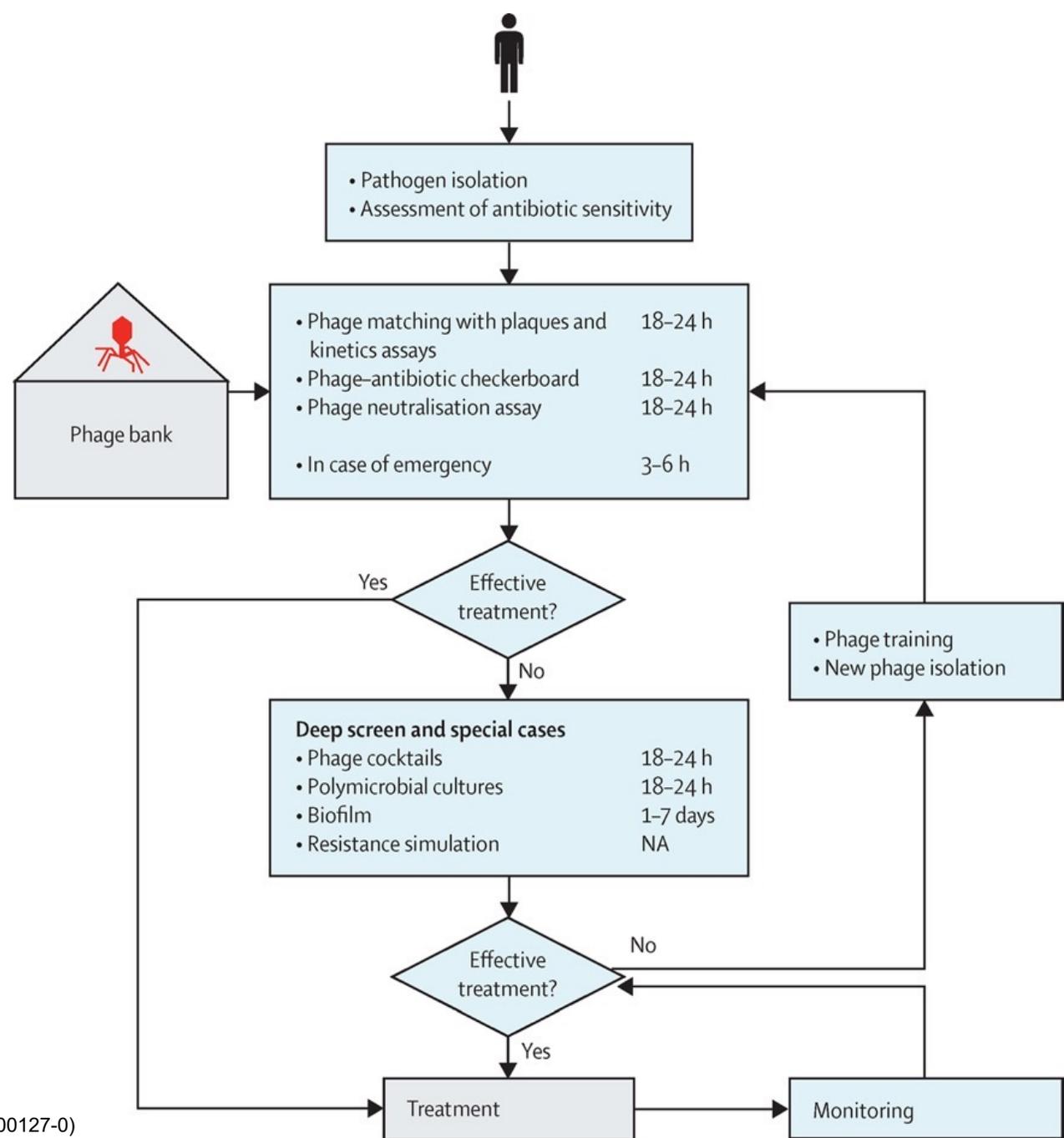
*“...Time waits for no one, no favors has he
Time waits for no one, and he won't wait for me....”*

Keith Richards / Mick Jagger



The Lancet Microbe 2021 2e555-e563DOI: (10.1016/S2666-5247(21)00127-0)

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How to put all together?

IPTC, Clinical Phage Microbiology Report

Hazan's Lab

11.05.2022

Spot assay	Plaque assay	Phage kinetic	Phage + antibiotic combination
C	S	S	NE

Table 4: Phage susceptibility in the different assays.

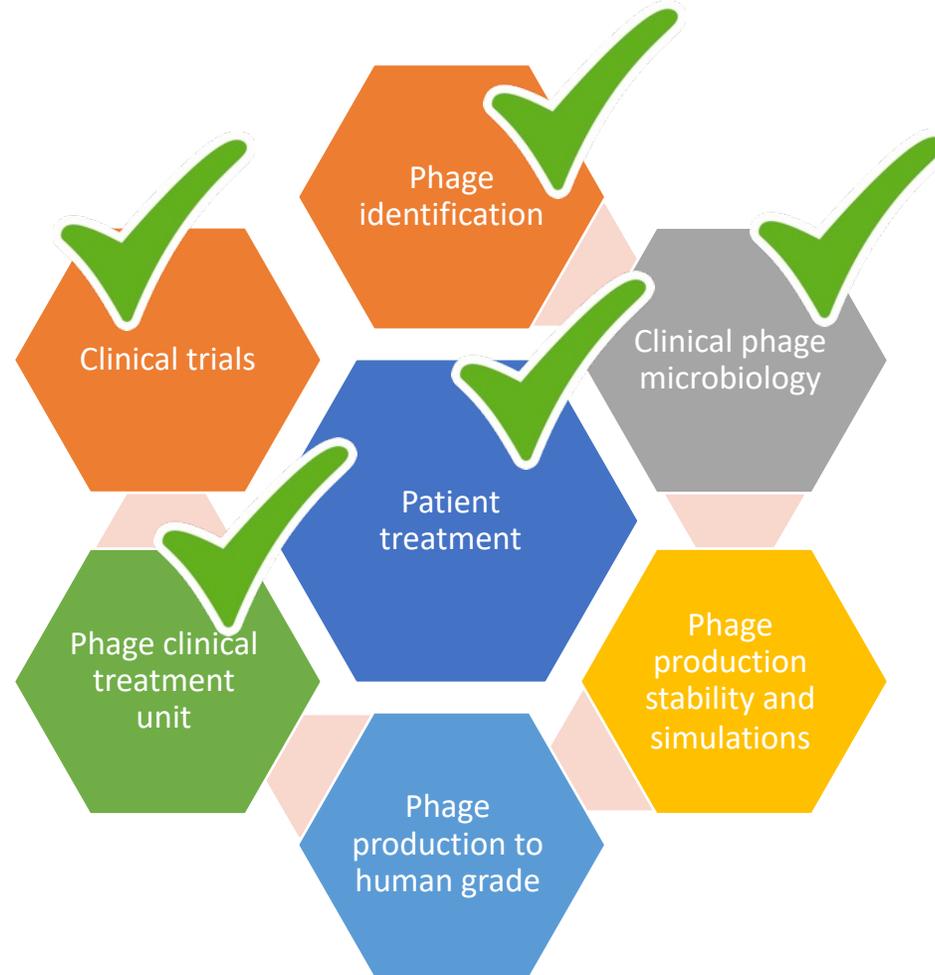
Spot assay		Plaque assay		Phage kinetic		Phage + antibiotic combination	
Clear plaque	C	Sensitive	S	Sensitive	S	Synergistic/ Additive	SEY/ ADD
Turbid plaque	U	Intermediate	I	Sensitive regrow	+ S-RG	Antagonistic	ANT
No plaque	NP	Unknown	U	Intermediate	I	No effect	NE
		Resistance	R	R	R		

Table 5: Susceptibility key.

Complex problem

- Different type of infections
 - Different type of disease kinetics (Pathogenesis)
 - Different type of bacteria and phage kinetics in bacteria
 - Presence of multiple pathogens
 - Pharmacokinetics of phages in host and target organ
 - Lytic VS Lysogeny
-
- Phase I studies may not be enough to give a direction....

Hadassah Hebrew university phage therapy center



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Ronen Hazan

Current and past students (Ronen Hazan Lab and Nir-Paz Lab)



- MD
 - Daniel Gelman
 - Ben Porat Shira
 - Roi Marom
- Highschool students ("The Phage Hunters Project")
 - Students of the gifted project Alpha
 - Biology and biotechnology high school students

- MSc
 - Mohaned AbdElRahman
 - Ron Brownstein

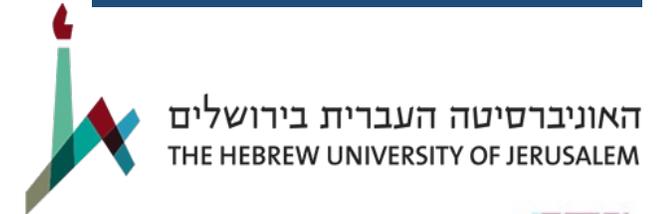
- PhD
 - Sivan Alkaly-Oren
 - Amit Rimon
 - Musa Mujahed
 - Liron Khalifa
 - Ortal Yerushalmy

Our Patients in Israel

- Over 20 treated
- 11 eIND
- Over 120 tested for potential treatment

Funding

- PostDoc
 - Daniel Gelman
 - Hadil Onalla



האוניברסיטה העברית בירושלים
THE HEBREW UNIVERSITY OF JERUSALEM



Collaborations

Collaborations in Israel

- Orthopedic, Pediatric pulmonary, Dentistry, Cardiology, Urology, Dermatology and ENT departments in HMC
- BiomX LTD
- Infectious diseases departments of Tel Aviv medical center, Infectious diseases at Belinson Schneiders medical center in Petach tickva

Collaborations around the world:

- Establishing a European study group under ESCMID - **ESGNTA**
- **Adaptive Phage Therapeutics** (APT, <http://www.aphage.com>) Located in Maryland USA. We are on the verge of establishing a strategic cooperation under discussion. They supported us with the predication of PASA16 phage for human use, and planned to be part of a clinical trial.
- **Center for phage therapy UCSD (iPATH)**. On both PA phages, and grant of *Burkholderia* patients from all of North America. Collaborating with Prof Schooley, Prof Strathdee, Prod Aslam and Prof. Pride. 2 Grants (BSF and CF foundation). 4 manuscripts. This also leads to other collaborations around the USA.
- Hatfull lab @ **Univ of Pittsburg** (mycobacteria phages for Israeli patients) Currently treating a lung transplant @ Belinson.
- Queen Astrid military center in Belgium. Jean-Paul Pirney. Our enterococcal phages were produced here and were used to treat 3 patients.
- Phage Australia / Irdell group **Westmed Institute and Hospital**, Sydney Australia
- Greg Rechs Lausanne, Switzerland.
- Phage Directory – A worldwide network of phage therapy labs (<https://phage.directory>).
- Technophage (clinical trial)

ESGNTA – ESCMID study group for Non-Traditional Antibacterial therapy

Ran Nir-Paz MD on behalf of the executive committee

https://www.escmid.org/research_projects/study_groups/study_groups_g_n/non_traditional_antibacterial_therapy/

To join:

https://www.escmid.org/research_projects/study_groups/study_groups_g_n/non_traditional_antibacterial_therapy/esgnta_membership_application/

Activity

- Online course **Personalized phage therapy: basic principles of monitoring and treatment (PPT2022)** 7th and 8th of June 2022. Organized by Alex Petrovic Fabijan and Jon Iredell for ESGNTA <https://events.escmid.org/event/34>

To join:

https://www.escmid.org/research_projects/study_groups/study_groups_group/non_traditional_antibacterial_therapy/esgnta_membership_application/



ESCMID Online
Education Course

**Personalised phage
therapy: basic principles
of monitoring and
treatment**

Online
7 – 10 June, 2022

