Peut-on se passer des antibiotiques en 2024 ?

La phagothérapie est-elle une alternative aux antibiotiques ?

tristan.ferry@univ-lyon1.fr

@FerryLyon

Infectious and Tropical Diseases Unit, Croix-Rousse Hospital , Hospices Civils de Lyon, Claude Bernard Lyon1 University, Lyon
Centre International de Recherche en Infectiologie, CIRI, Inserm U1111, CNRS UMR5308, ENS de Lyon, UCBL1, Lyon, France
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Centre de Référence des IOA complexes de Lyon (CRIOAc Lyon)

Conflict of interest

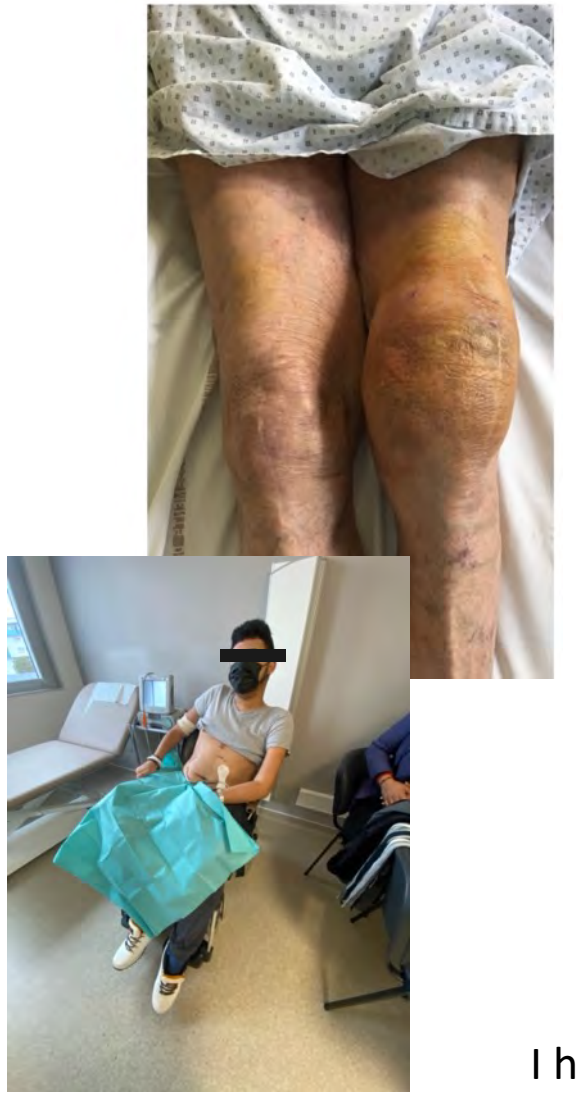
- **Phaxiam (ex-Pherecydes) :** Expert (Board), research grant, investigator coordinator of clinical trials (contract with hospital, no direct funding)
- **Armata :** Punctual expert (contract with university, no direct funding)
- **Contrafect :** Expert investigator coordinator of clinical trial (contract with hospital, no direct funding)

All photos and videos are my property

I am infectious disease physician (with a PhD)

HCL
HOSPICES CIVILS DE LYON

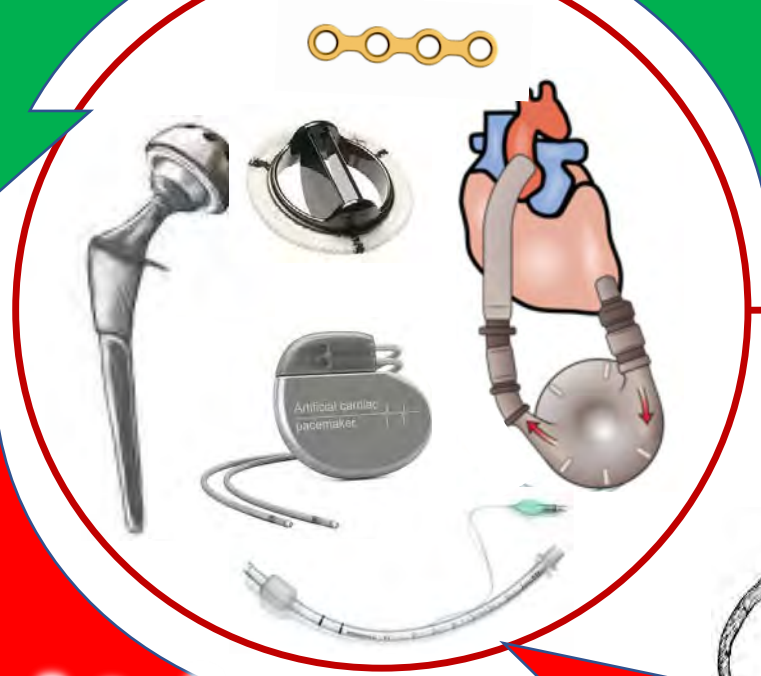
RIOAc
LYON



I have conflict of interest with the patients!

Two major problems

Implantable medical device (connected)



Implant-associated infections

Antimicrobial resistance

Severe bacterial infections

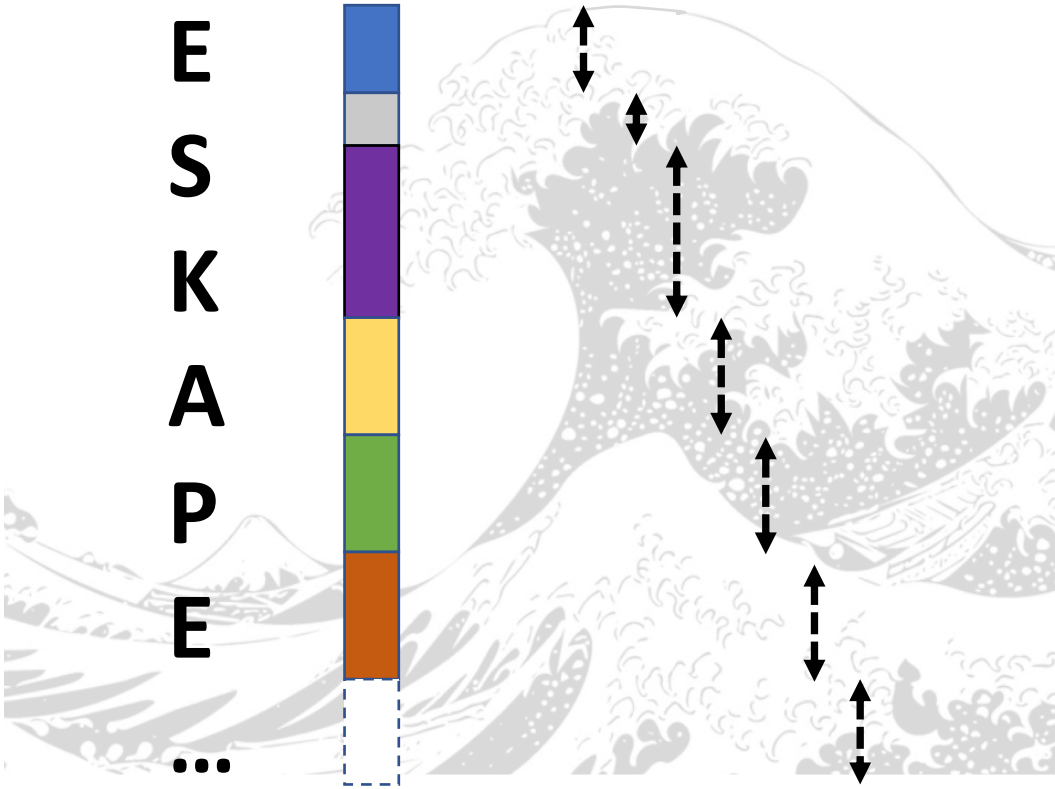
(bone and joint, pneumonia, endocarditis, sepsis)

T. Ferry

World Health Organization

"Slow motion tsunami"

Katsushika Hokusai (葛飾 北斎)

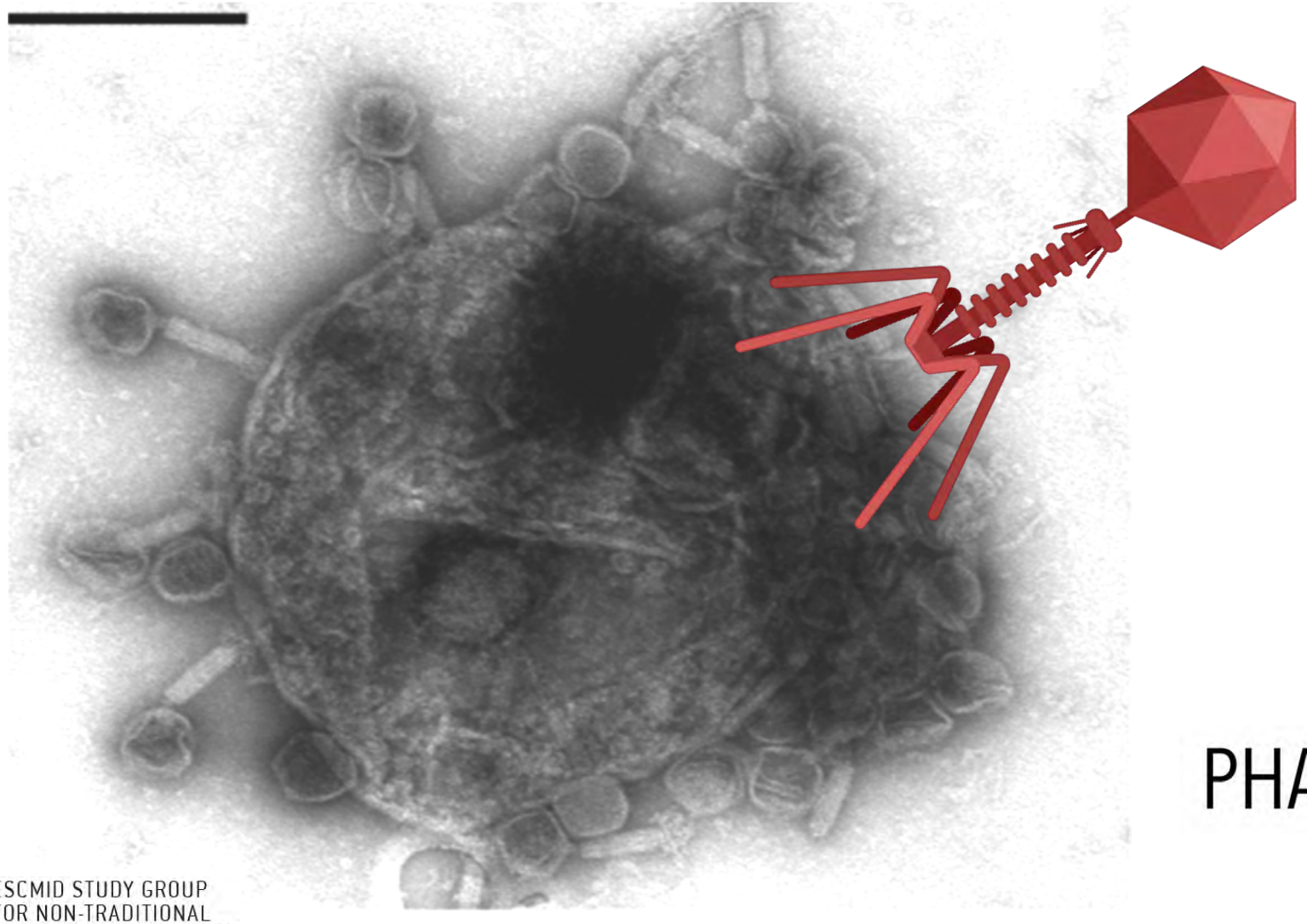


T. Ferry: "Plural silent pandemia"

Bacteria have also their pandemia!

World Health Organization

Non-**T**raditional
Antibacterial
therapy



ESGNTA
ESCMID STUDY GROUP FOR NON-TRADITIONAL ANTIBACTERIAL THERAPY
European Society of Clinical Microbiology and Infectious Diseases

Merabishvili et al. *PloS ONE* 2009

FONDATION HCL HOSPICES CIVILS DE LYON

PHAGE*in*LYON
Clinic

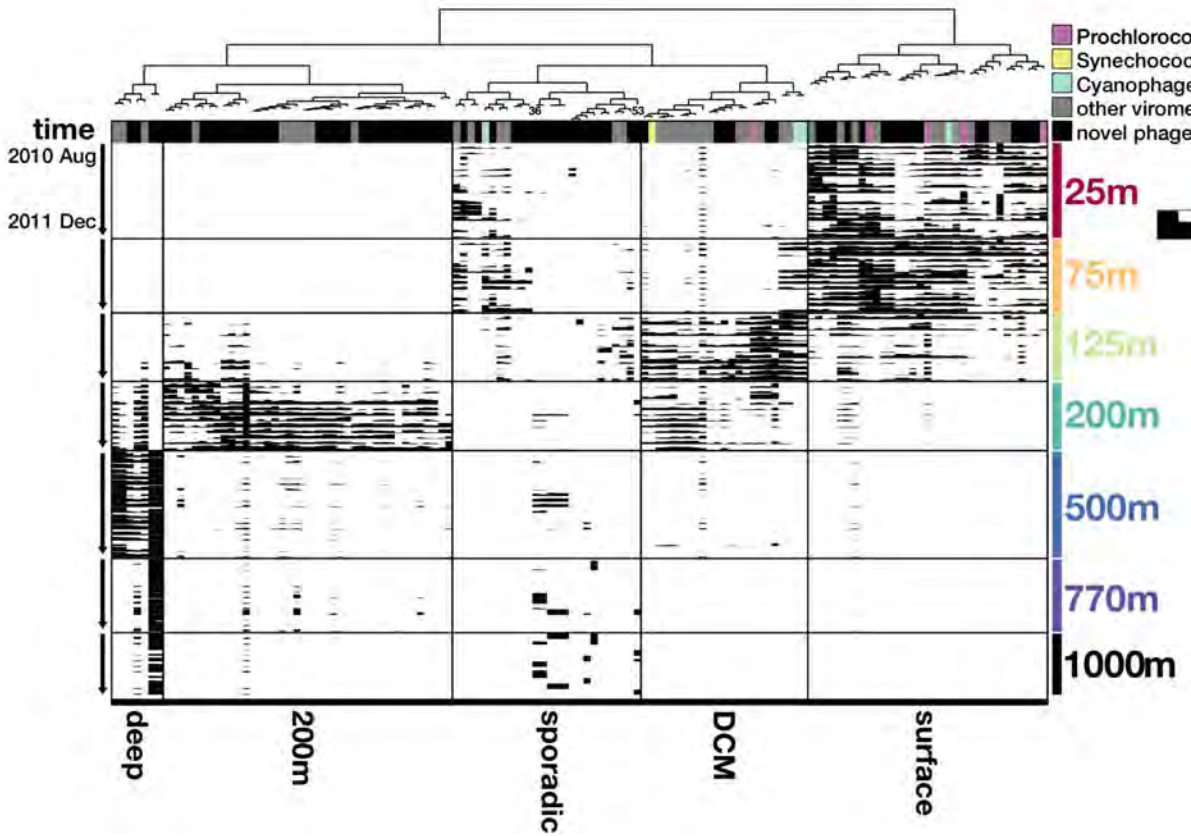
Bacteriophage Distributions and Temporal Variability in the Ocean's Interior

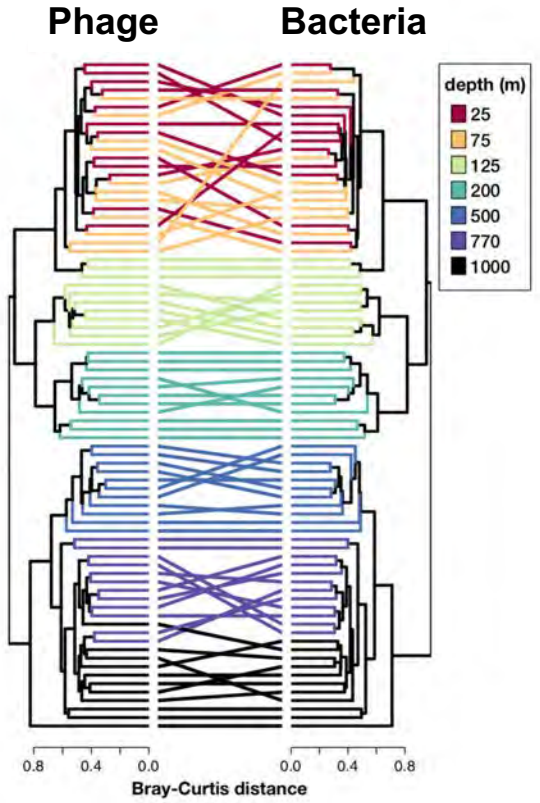
AMERICAN SOCIETY FOR MICROBIOLOGY | mBio®

2017

Elaine Luo, Frank O. Aylward,* Daniel R. Mende, Edward F. DeLong

Daniel K. Inouye Center for Microbial Oceanography: Research and Education, University of Hawaii, Honolulu, Hawaii, USA

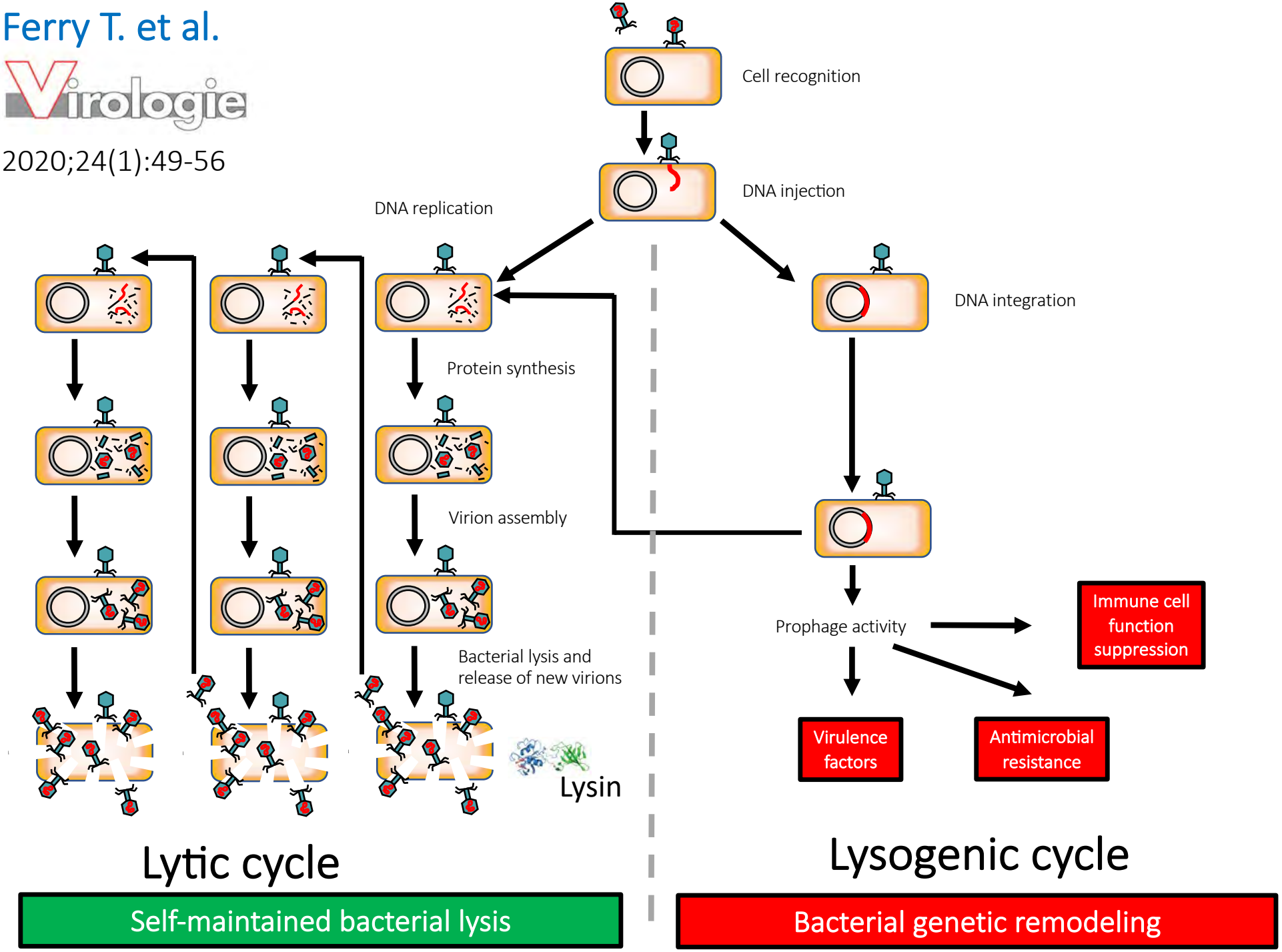




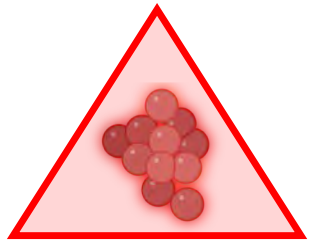
Ferry T. et al.

Virologie

2020;24(1):49-56



A large panel of **severe** bacterial infections



Central nervous system infections

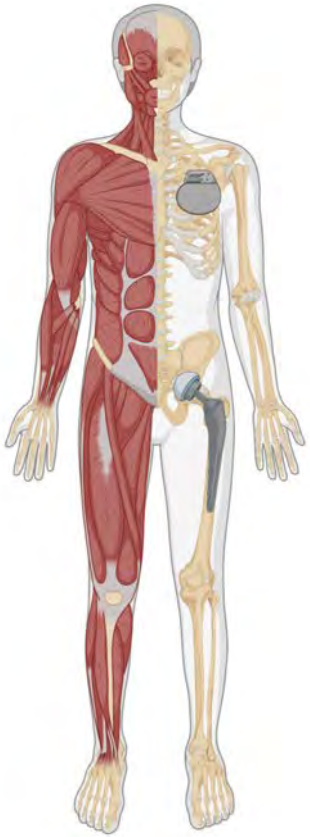
Implant-associated meningitis

Lung infections

Ventilator-associated pneumonia
Exacerbation in cystic fibrosis
Exacerbations in bronchiectasis

Urinary tract infections

Pyelonephritis
Ureteral stent-associated infection



Cardiovascular infections

Endocarditis
Cardiac electronic device infection
Prosthetic-valve endocarditis
Vascular graft infection

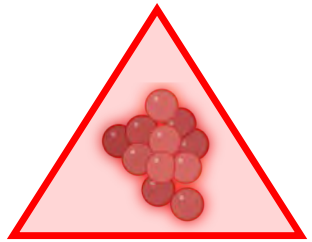
Muskuloskeletal infections

Wound infection
Osteomyelitis, fracture-related infection
Implant-associated bone and joint infection
Prosthetic joint infection

Digestive-tract infections

Typhoid fever, shigellosis
Cholera

A large panel of **severe** bacterial infections



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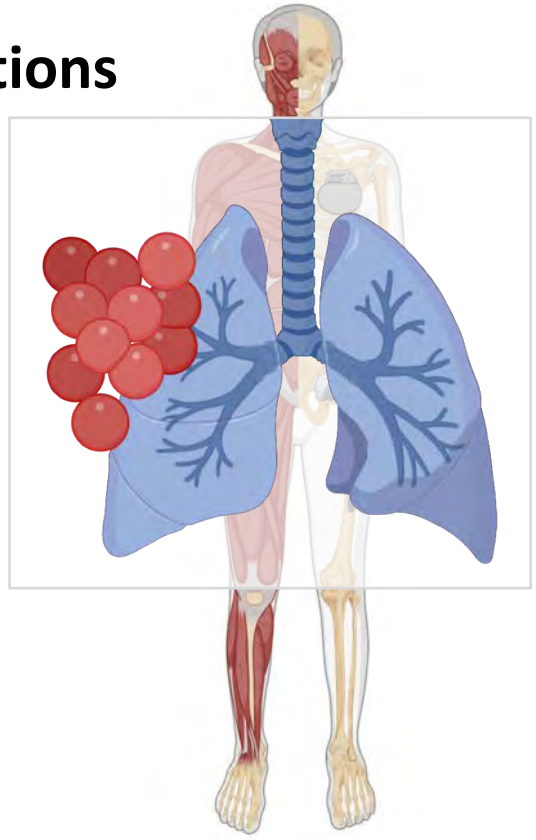

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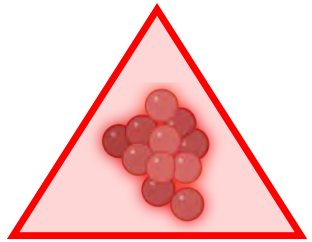

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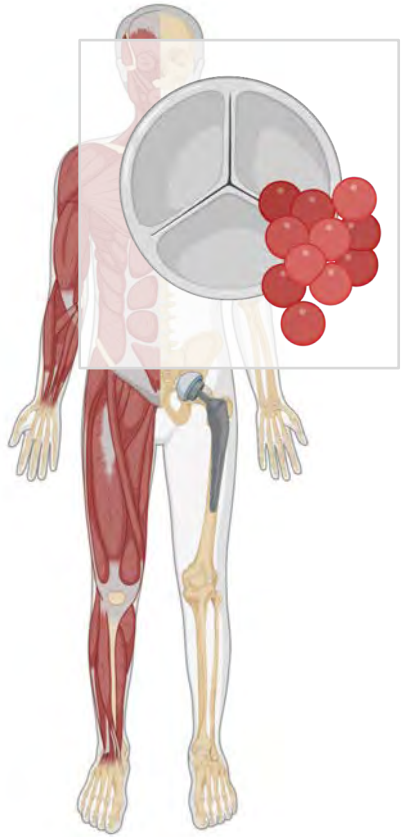

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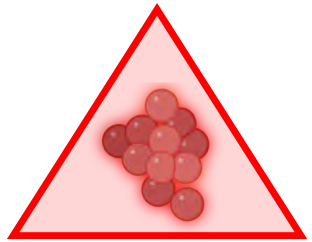

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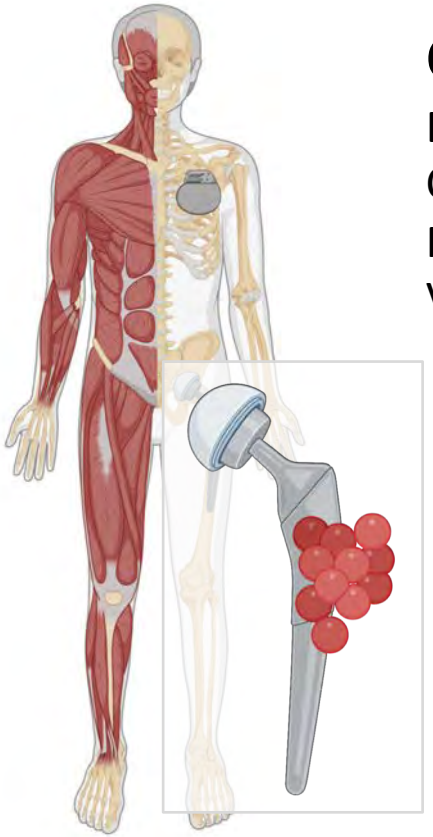

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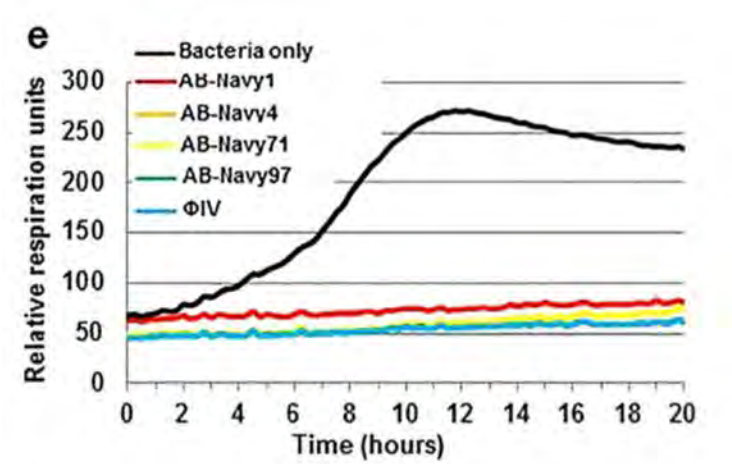
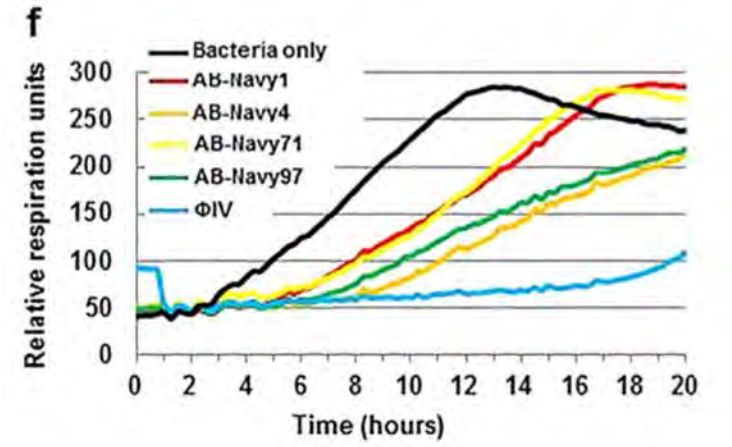
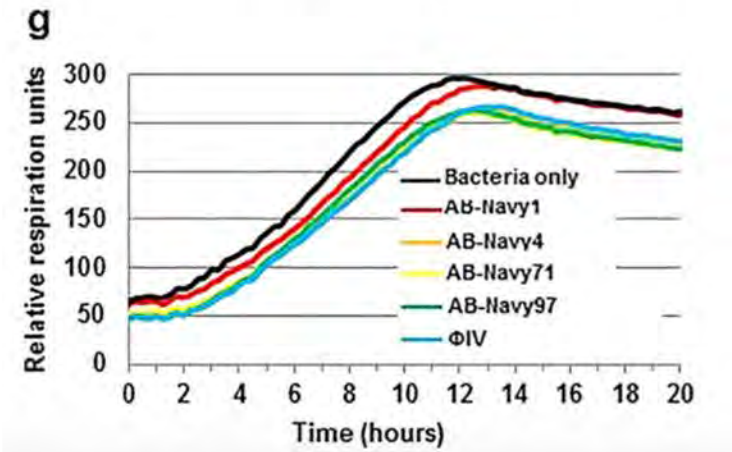
AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

Development and Use of Personalized Bacteriophage-Based Therapeutic Cocktails To Treat a Patient with a Disseminated Resistant *Acinetobacter baumannii* Infection

Robert T. Schooley,[a] Biswajit Biswas,[b,c] Jason J. Gill,[d,e] Adriana Hernandez-Morales,[f] Jacob Lancaster,[e] Lauren Lessor,[e] Jeremy J. Barr,[g,o] Sharon L. Reed,[a,h] Forest Rohwer,[g] Sean Benler,[g] Anca M. Segall,[g] Randy Taplitz,[a] Davey M. Smith,[a] Kim Kerr,[a] Monika Kumaraswamy,[a] Victor Nizet,[i,j] Leo Lin,[i] Melanie D. McCauley,[a] Steffanie A. Strathdee,[a] Constance A. Benson,[a] Robert K. Pope,[k] Brian M. Leroux,[k] Andrew C. Picel,[l] Alfred J. Mateczun,[b] Katherine E. Cilwa,[n] James M. Regeimbal,[b] Luis A. Estrella,[b] David M. Wolfe,[b] Matthew S. Henry,[b,c] Javier Quinones,[b,c] Scott Salka,[m] Kimberly A. Bishop-Lilly,[b,c] Ry Young,[e,f] Theron Hamilton[b]



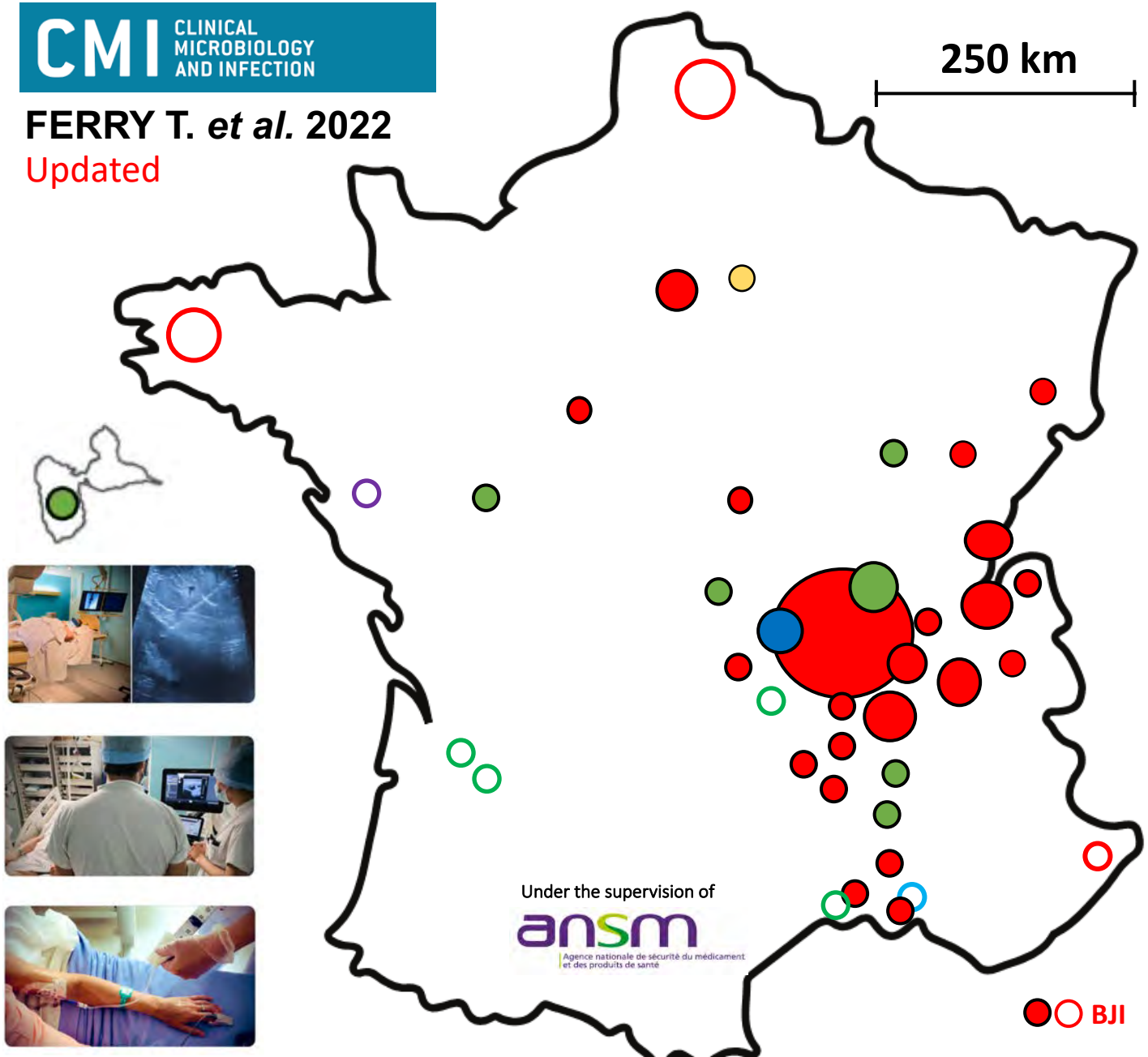




Implementation of a **Phage Therapy Center** in a CRIOAc

CMI CLINICAL MICROBIOLOGY AND INFECTION

FERRY T. *et al.* 2022
Updated



HCL HOSPICES CIVILS DE LYON — PHAGE*in*LYON *Clinic* — FONDATION HCL HOSPICES CIVILS DE LYON

Lyon 1 — CIRI Centre International de Recherche en Infectiologie — CRIOAc LYON

59 patients in Lyon since 2017
~75% of the whole patients treated in France

- 55 with phages from PHERECYDES PHARMA / PHAXIAM
- 4 with phages from MHKA / HMRA

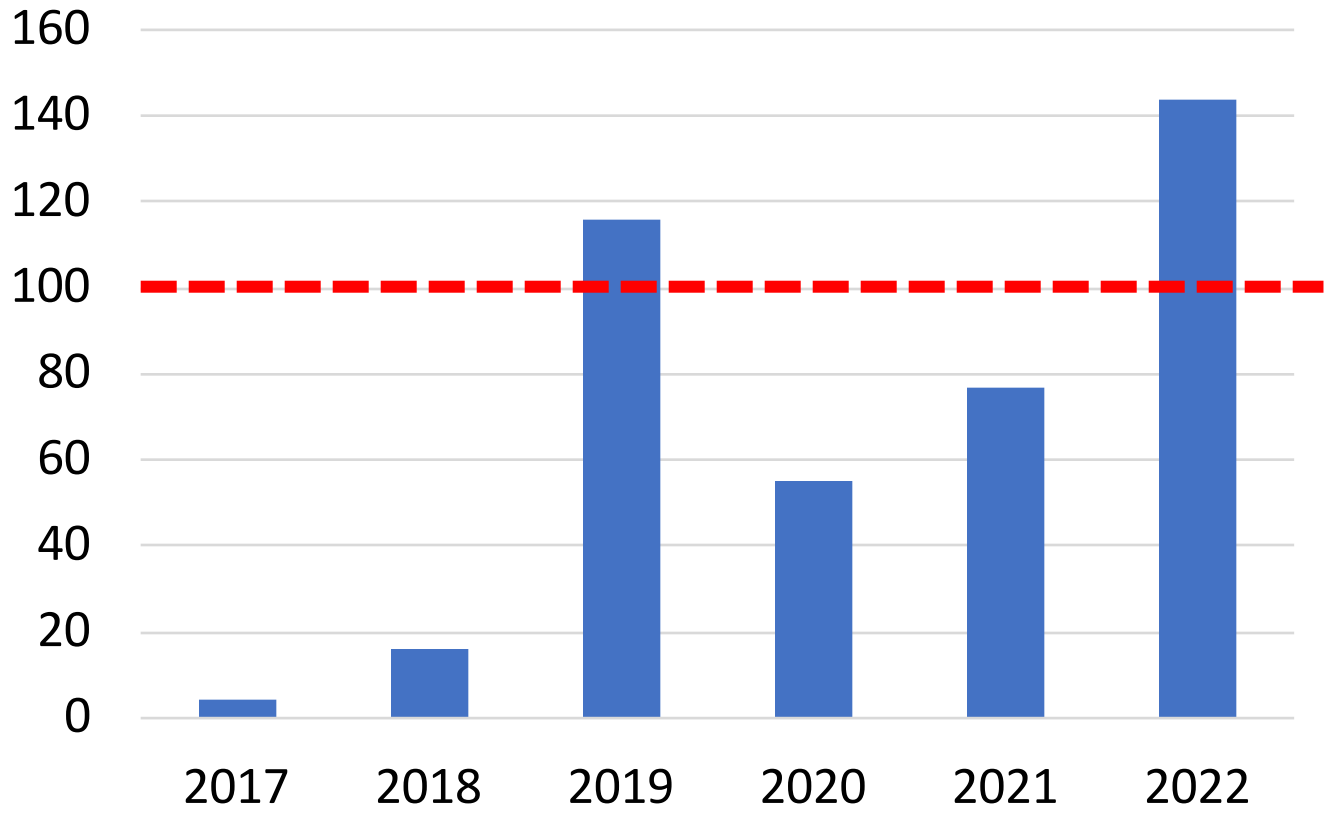
- 46 **BJI** (including **38 PJI**)
- 10 **endocarditis/vascular graft**
- 3 **lung infections** (VAP + bacteremia, pneumonia in lung graft bronchectasia, cystic fibrosis exacerbation)

+ 14 patients managed outside Lyon
including 1 in **and 1 in**

BJI Endocarditis Pneumonia Burn Abscess

Phage requests

PHAGE*in*LYON *Clinic*



Involved bacteria

32 % *Staphylococcus aureus*

16 % *Pseudomonas aeruginosa*

6 % *Staphylococcus epidermidis*

Type of infction

37% Prosthetic-joint infection

27% Other bone and joint infection

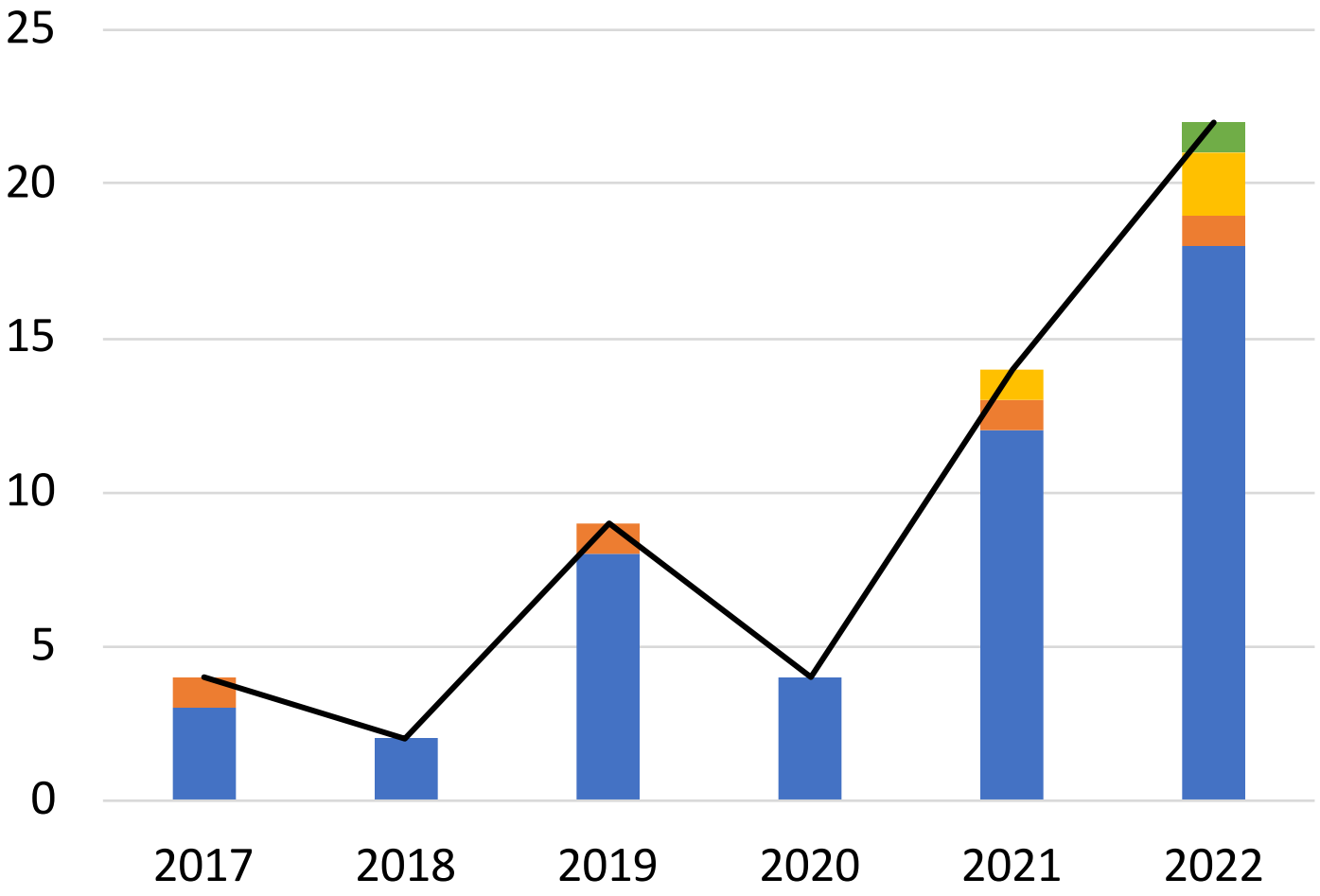
8% Lung infection

Source : T. Ferry

Lyon 1 RIOAc LYON ciri Centre International de Recherche en Infectiologie FONDATION HCL HOSPICES CIVILS DE LYON HCL HOSPICES CIVILS DE LYON

Treated patients

PHAGE*in*LYON *Clinic*



- Bone and joint
- Endocarditis
- Lung
- Other
- Vascular graft infection

Source : T. Ferry

Bone and joint infections: Lyon becomes the national expert center for phage therapy

The reference center for complex bone and joint infections, based at the Hospices Civils de Lyon, will centralize all requests concerning this last resort treatment, using viruses against resistant bacteria.

Le Progrès - 23 Feb. 2023 at 17:51 | updated 23 Feb. 2023 at 18:08 - Reading time: 2 min

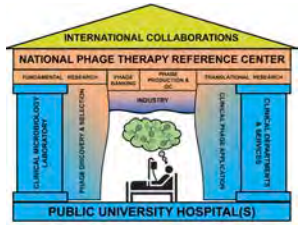
National online multidisciplinar meetings

MINISTÈRE DE LA SANTÉ ET DE LA PRÉVENTION
Liberté Égalité Fraternité

Dedicated to innovative anti-infective therapies

Conclusion

- Phage therapy has a **high potential** in patients with bacterial infections due to multidrug-resistant pathogen, as **adjuvant to antibiotics**
- **Complex personalized therapy** (specific to the infecting strain, various scheme of administrations, etc.)
- **Few pharmaceutical grade phages are available at this time**
- **Need to develop phages that aim to target the ESKAPE pathogens**
- **Growing clinical evidence and clinical trials are coming**
- Phages as adjuvant **could be an option to prevent** a relapse with acquisition of resistance to antibiotics (*P. aeruginosa*)
- **CRIOAc Lyon, PHAGE*in*LYON *Clinic* program and creation Lyon Phage HUB under the supervision of the French healthcare authority to select active phages is a rupture**
- **Access and evaluation of phage therapy**



ESGNTA ESCMID STUDY GROUP FOR NON-TRADITIONAL ANTIBACTERIAL THERAPY
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Unités d'Enseignements Libres d'Histoire de la Médecine – Faculté de médecine Lyon Est

La fabuleuse histoire de la phagothérapie

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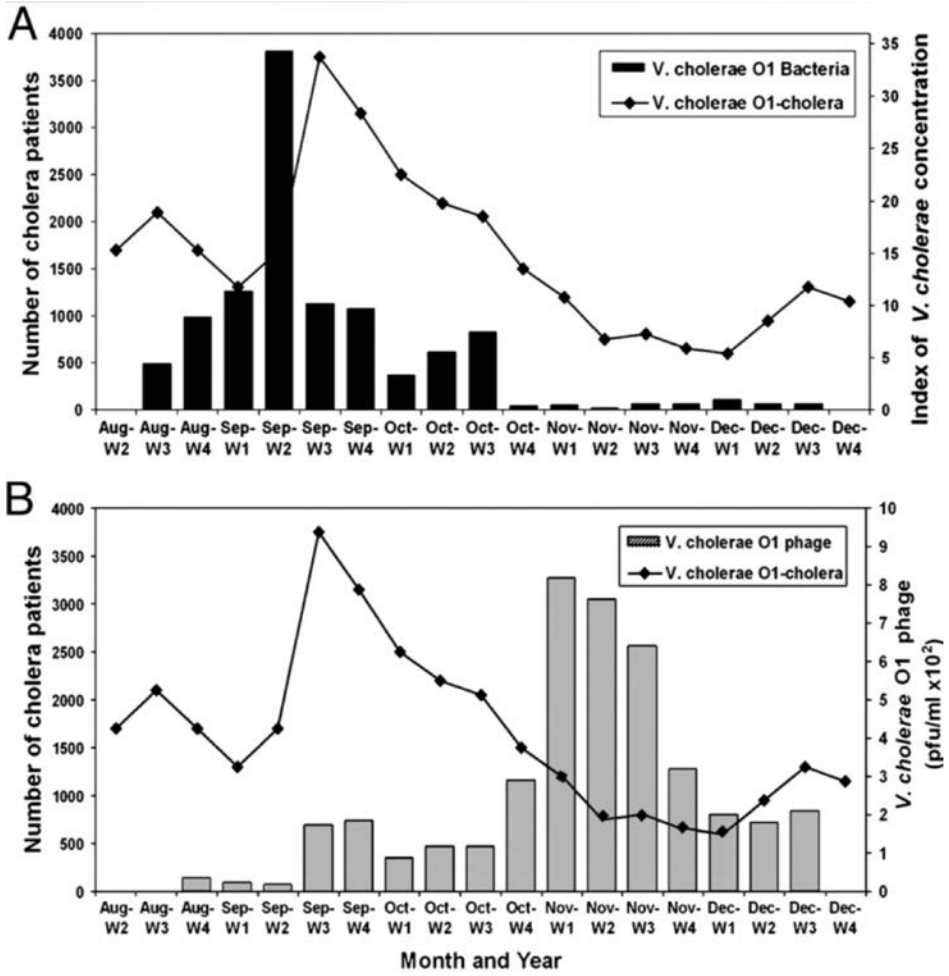
Self-limiting nature of seasonal cholera epidemics: Role of host-mediated amplification of phage

Shah M. Faruque*†, M. Johirul Islam*, Qazi Shafi Ahmad*, A. S. G. Faruque*, David A. Sack*, G. Balakrish Nair*, and John J. Mekalanos‡

Proc Natl Acad Sci U S A. 2005



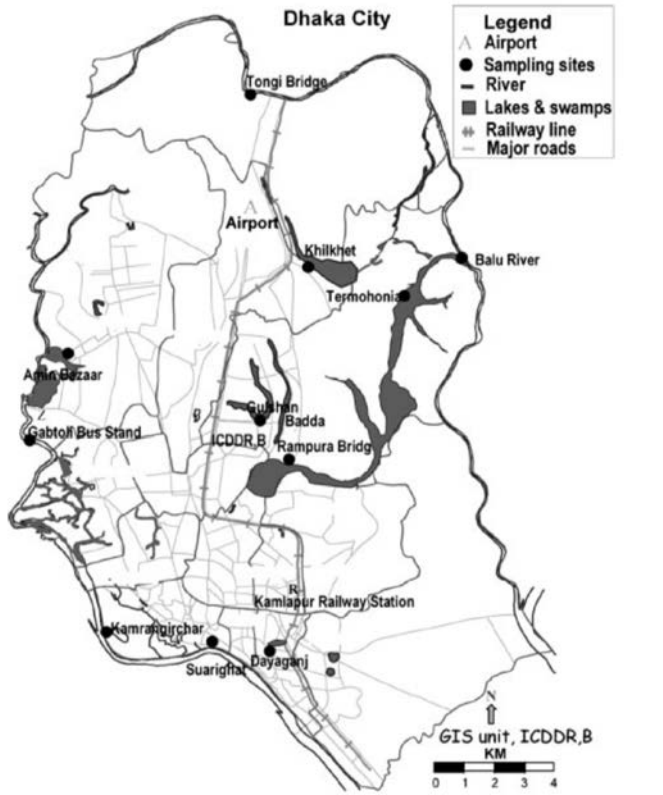
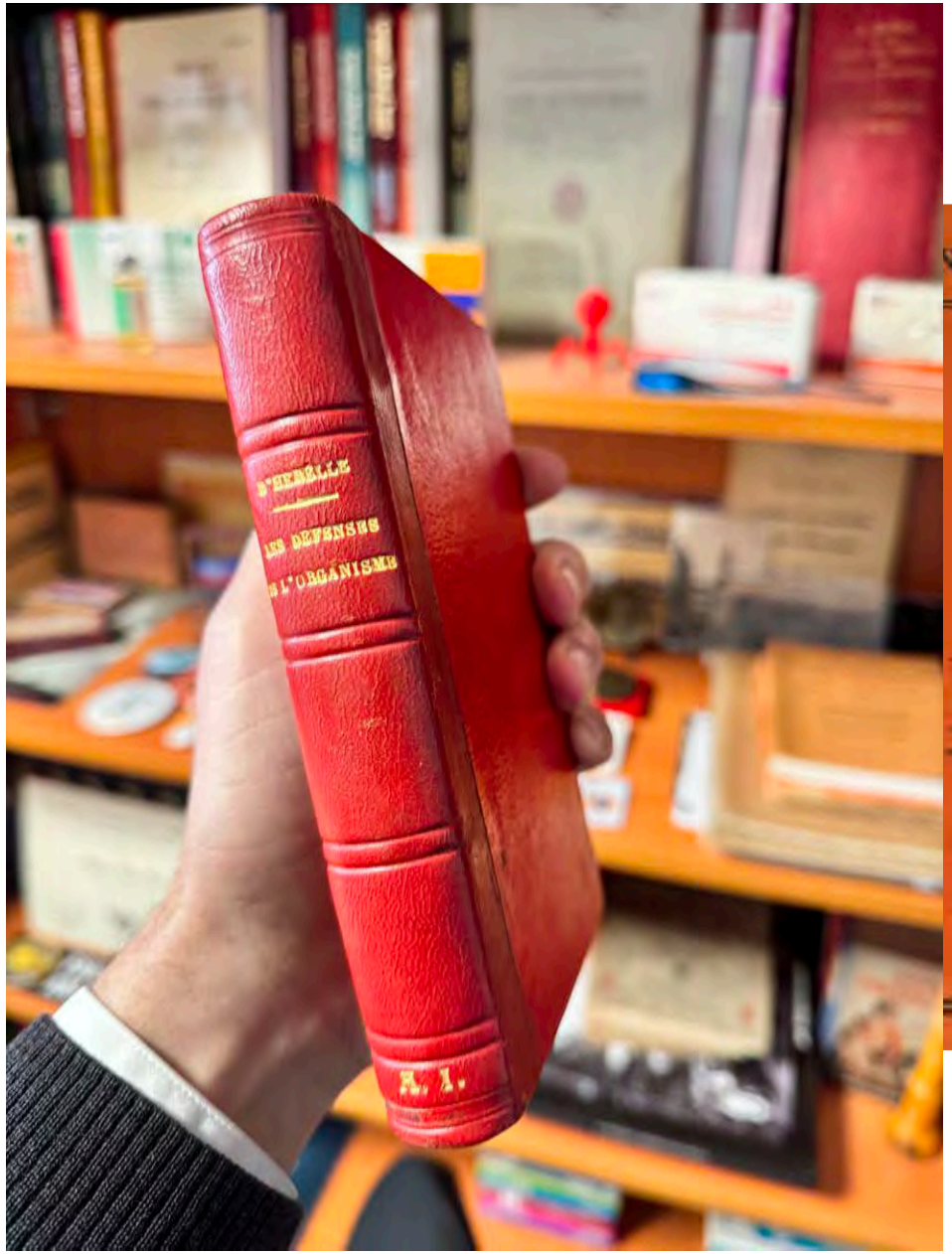
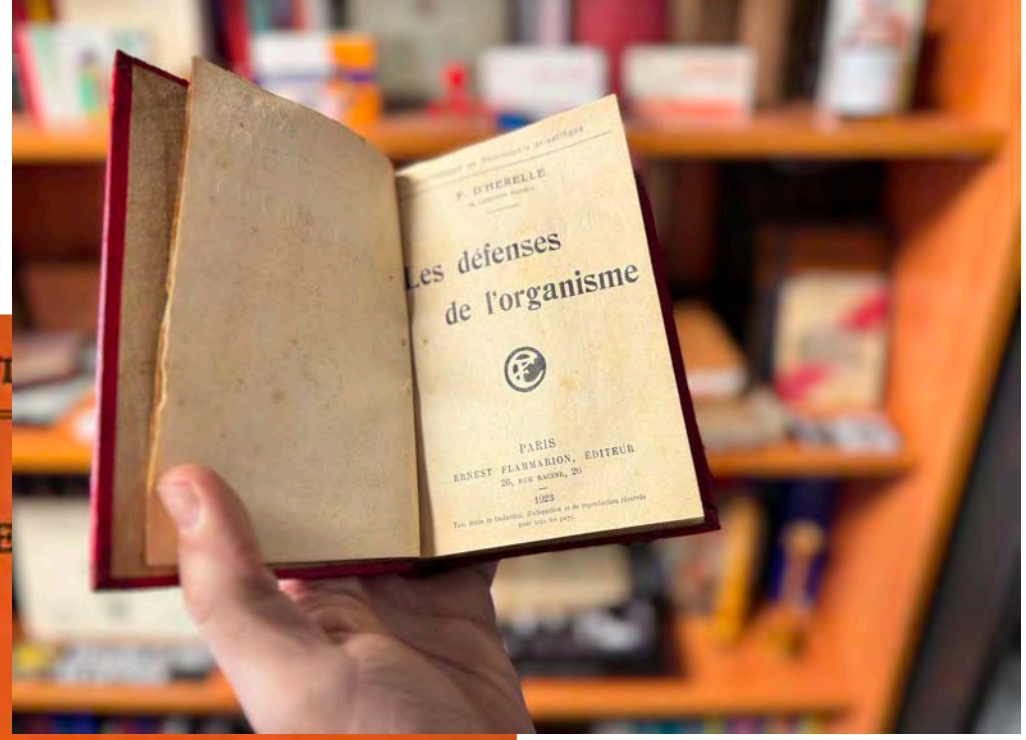
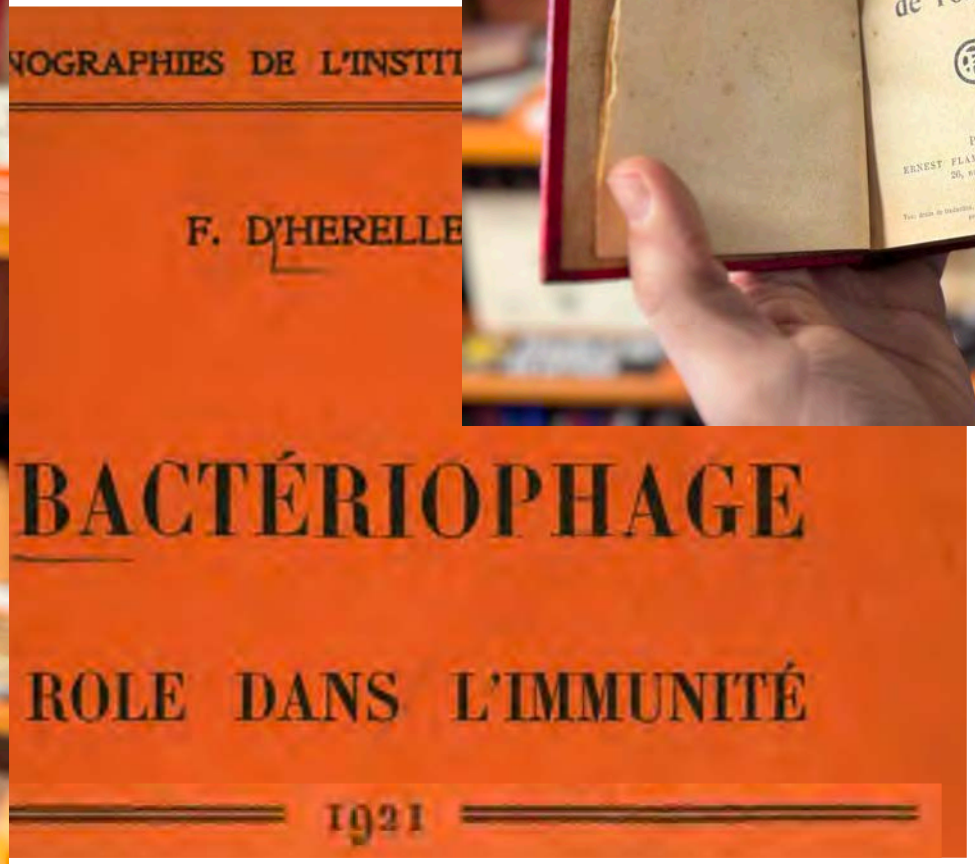


Fig. 1. Map of Dhaka showing the environmental sampling sites (●) and the location of the ICDDRB cholera hospital at the center of the city.

Bangladesh







Félix d'Herelle

1873-1949

Victor Henri Hutinel

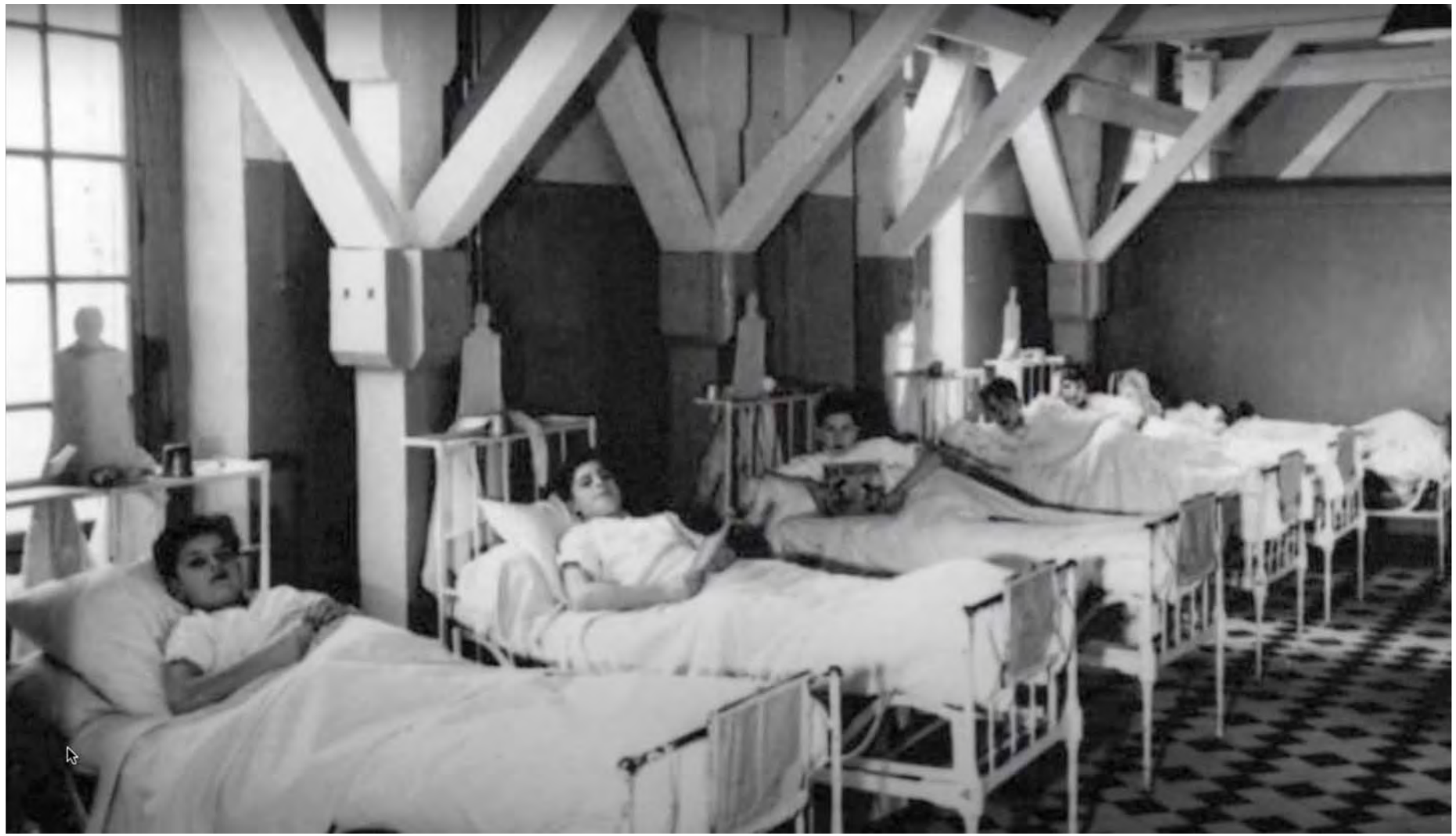
- 1849-1933
- Faculté de médecine de Nancy
- 1907 : Direction Hôpital Enfants Malades, Paris

Victor Henri Hutinel

- 1849-1933
- Faculté de médecine de Nancy
- 1907 : Direction Hôpital Enfants Malades, Paris
- 1912 : Fondation et 1er congrès de la « *International Pediatric Association* » à Paris
- **1919 : Contacté par Félix d'Hérelle pour traiter des premiers patients**

Félix d'Hérelle

- **« Victor Henri Hutinel était d’accord pour me laisser traiter des jeunes patients à condition que je démontre que l’ingestion d’une culture de bactériophage est inoffensive »**
  - Préparations contenant des phages concentrés
  - Démonstration de l’innocuité par ingestion (d’Herelle et les internes du service)
  - « Pas mauvais goût… », pas d’effet indésirable

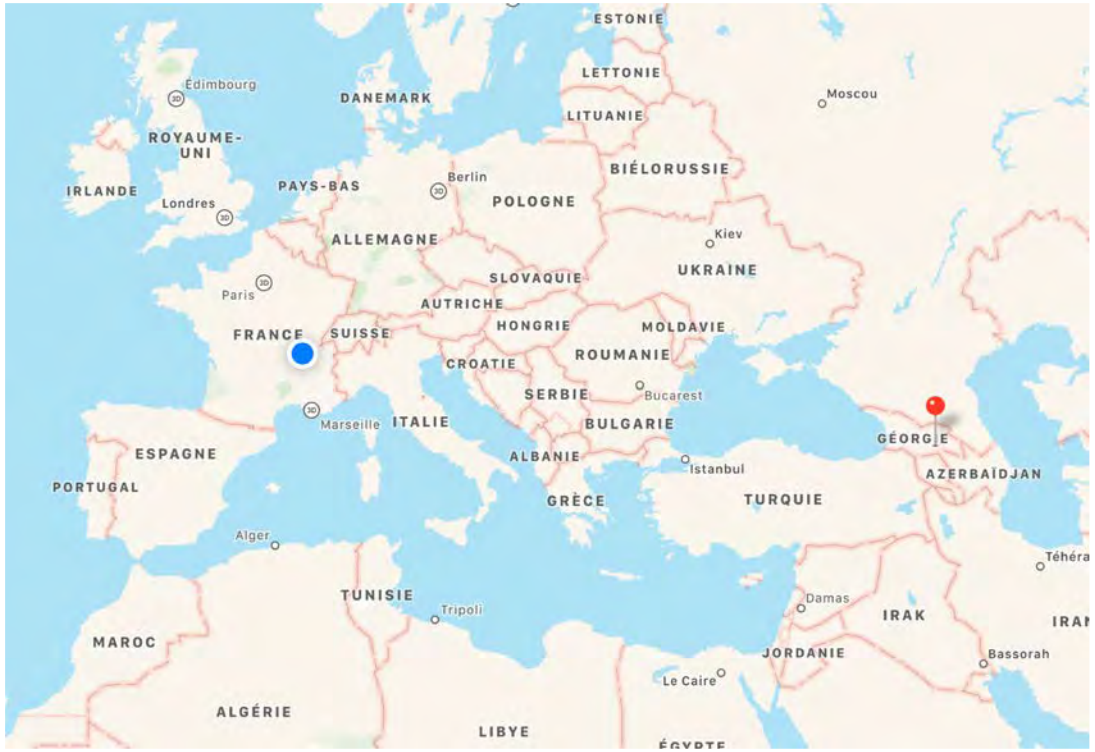


Félix d'Hérelle et Institut Pasteur

- **Encadrement d'élèves**
  - Georges Eliava
  - André Raiga-Clémenceau

- Une controverse scientifique éclate entre d'Hérelle et **Jules Bordet** de l'Institut Pasteur de Bruxelles, récent prix Nobel de médecine-physiologie, et il est « congédié » en 1925.

Félix d'Hérelle et Georges Eliava

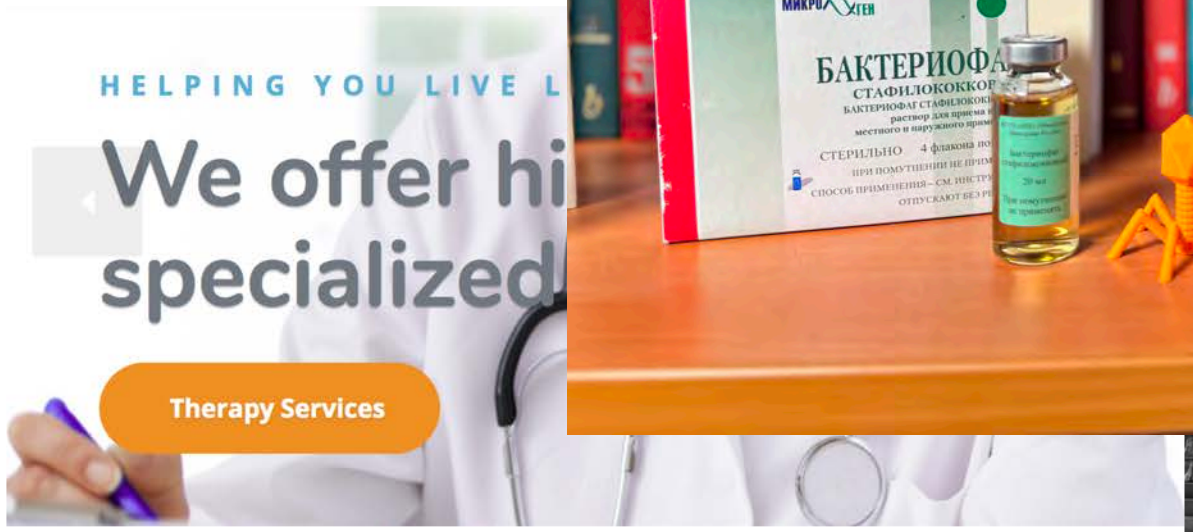


1937: Eliava est considéré comme un « ennemi du peuple » : **arrestation** (avec son épouse) et **exécution** par Lavrenti Beria, chef de la police secrète de Joseph Staline (cause politique ? sentimentale ?)

Eliava Institute (Georgia)

ELIAVA
Phage Therapy Center

100th anniversary

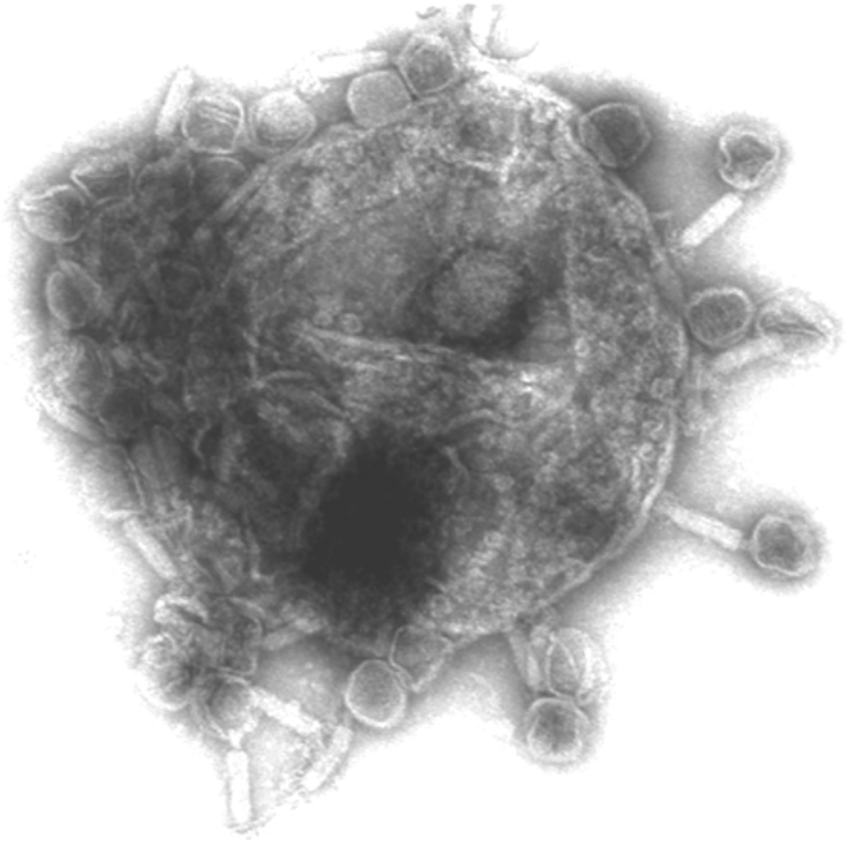


Eliava Institute (Georgia)

- PYO Bacteriophage
- FERSIS Bacteriophage
- STAPHYLOCOCCAL Bacteriophage
- SES Bacteriophage
- INTESTI Bacteriophage
- ENKO Bacteriophage

Ferry T.

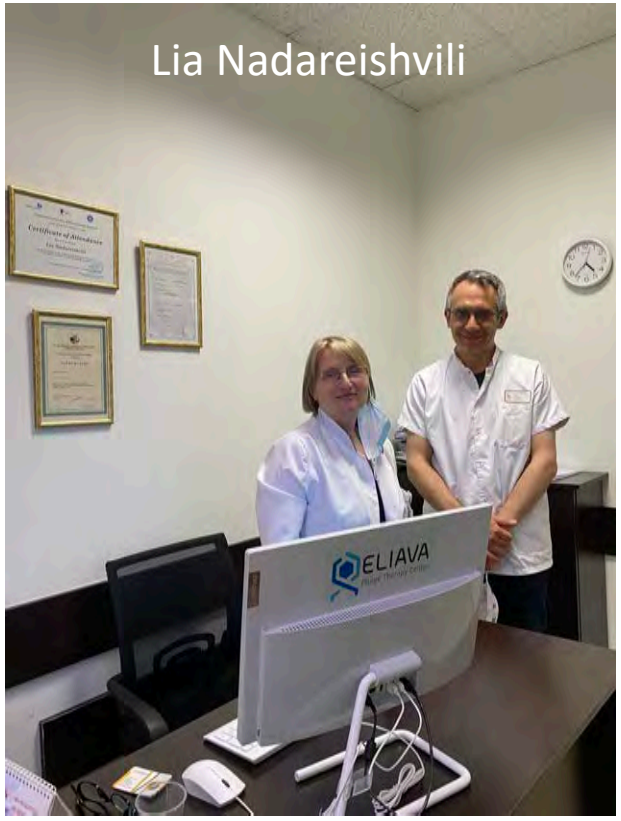
Bacteriophage (*Myoviridae*) targeting *S. aureus*

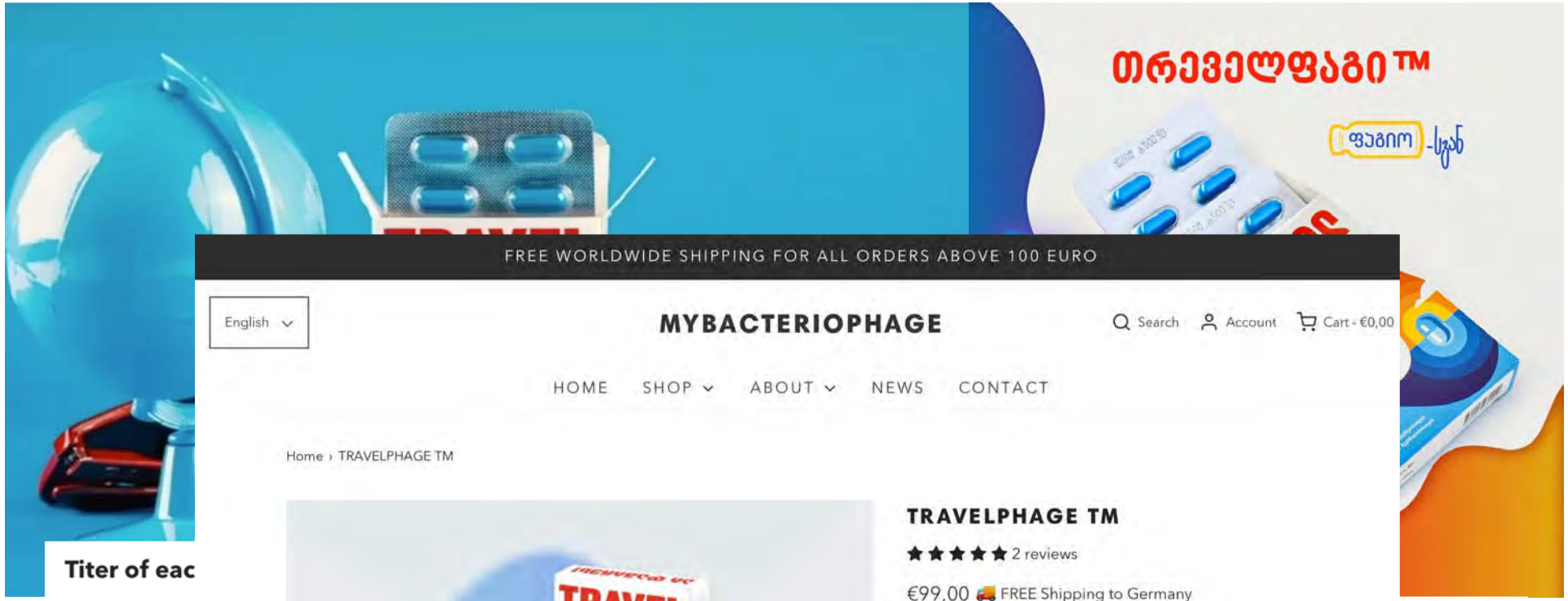


Merabishvili et al. PloS ONE 2009

Eliava Institute (Georgia)

ELIAVA
Phage Therapy Center





Titer of eac

Bacteriopha

Bacteriopha

Bacteriopha

Bacteriopha

Bacteriopha

Bacteriophagum Pseudomonas;

Bacteriophagum Enterococcus

Is not less than – 10^5.

Félix d'Hérelle

- **Missions contre la peste** en Égypte (injection de phage en intra-ganglionnaire) **et le choléra** (IV et per os) en Indochine et en Inde (traitement de masse; essai comparatif)
- Prof. à l'université de Yale, **Etats-Unis** (1928-1934)

BULLETIN OF
THE NEW YORK
ACADEMY OF MEDICINE

VOL. VII MAY, 1931 No. 5

ANNUAL GRADUATE FORTNIGHT

BACTERIOPHAGE AS A TREATMENT IN ACUTE MEDICAL AND SURGICAL INFECTIONS*

F. d'HERELLE

Professor of Bacteriology,
Yale University School of Medicine

Bacteriophage therapy is still in its infancy and many studies are still necessary before we will learn all the results that we may anticipate, but that which has already been done in many diseases justifies the belief that this is the specific treatment *par excellence* and that it will attain a wider and wider application.

CHOLERA

In the year 1927 while in India, as the result of the experiments of which I have spoken, I attempted the treatment of Asiatic cholera. These attempts at therapy were made in the Punjab, on the natives cared for in their homes and to whom no other medication was given. Each patient received an initial dose of two cubic centimeters of a virulent bacteriophage, and with the family a second dose of four cubic centimeters diluted in one hundred cubic centimeters of water was left with instructions to give it to the patient by spoonfuls during the three or four hours following. I should state that I merely furnished the cultures of bacteriophage, treatment was carried out by Major Malone of the Indian Medical Service, assisted by the other officers of the Service. As it was impossible to enforce any one mode of treatment, the family of the patient was free to accept or refuse it, in the latter case usually resorting to the prescriptions of the Hindoo medicine man. The majority of the patients for whom authorization was granted were found in a critical state; indeed, it was only because of this that parents, despairing of saving them, accepted the new treatment. As a control series we have taken those cases in which the bacteriophage treatment was refused. In spite of these extremely unfavorable conditions the mortality in the controls was 62.9 per cent, and among those treated with bacteriophage 8.1 per cent.

EDITION DE 5 HEURES

5H

Le Matin

5H

PARIS VARIABLE

LE NUMÉRO 25 Centimes

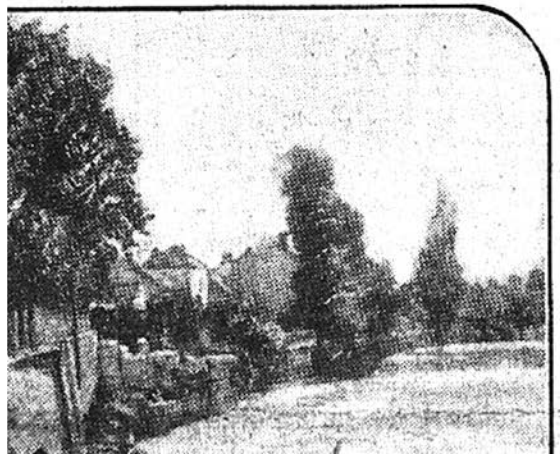
BOUL[d] & FAUB[g] POISSONNIÈRE, PARIS (IX[e]). ADRESSE TÉLÉGR. : MATIN-PARIS TÉL. : PROVENCE 15-01, 15-02, 15-03, 15-08

CRIME DE LA HAUTE-VIENNE

SERAIT BIEN L'ASSASSIN FEUR DE TAXI FAURE

épit des dénégations de l'inculpé nts encore obscurs, les conclusions s sur un faisceau de présomptions

AVRE DE LA VICTIME T PAS RETROUVÉ



Un palliatif à la crise de la marine marchande : le crédit maritime

UN PROJET DE LOI VA ÊTRE DÉPOSÉ

Notre marine marchande stagne. Nous avons ici même poussé le cri d'alarme lorsque, il y a quelques mois, l'Italie nous eut dépassés.

Nous indiquions alors qu'une aide à l'armement était nécessaire, notamment pour lui assurer le crédit nécessaire aux constructions neuves, presque totalement interrompues.

M. Tardieu, ministre de la marine marchande, déposera incessamment, et sans doute aujourd'hui même, sur le bureau de la Chambre, un projet de crédit maritime répondant à ce vœu.

Il a pour but une convention passée avec le Crédit foncier afin de faire bénéficier l'industrie maritime de prêts hypothécaires jusqu'à concurrence de 200 millions par an pendant cinq ans. Les emprunts seront remboursables en 20 ans.

En principe, ils devront être destinés uniquement à des constructions de navires dans les chantiers français. Cependant, une part, n'excédant pas 40 millions par an, pourra être utilisée à des commandes à l'étranger, notamment en application du plan Dawes, ou à des achats, à l'extérieur, de navires âgés de moins

LA SUPPRESSION DES ÉPIDÉMIES DE CHOLÉRA

Les expériences aux Indes du docteur d'Hérelle ont permis d'abaisser la mortalité de 62 % à 8 %

GRACE AU BACTÉRIOPHAGE QU'IL A DÉCOUVERT

L'allure épidémique foudroyante du choléra est bien connue. Ses ravages sont particulièrement sévères dans les pays où les règles de l'hygiène sont ignorées ou mal appliquées.

Phot. H. Manuel.
Dr D'HERELLE

Le gouvernement britannique, désirant diminuer l'intensité des épidémies de choléra aux Indes, avait chargé le docteur d'Hérelle d'en rechercher les moyens.

Le *Matin* a signalé à plusieurs reprises les tra-

L'AI DU SER AU 1er N

Le gouverne de l'ar se sont mis

Ainsi que hier un ac entre le gou sion de l'ar la date de l service d'ur

La commi midi M. conseil, et la guerre, a général Gir exact de la fois les div communs d sence et af d'arriver à

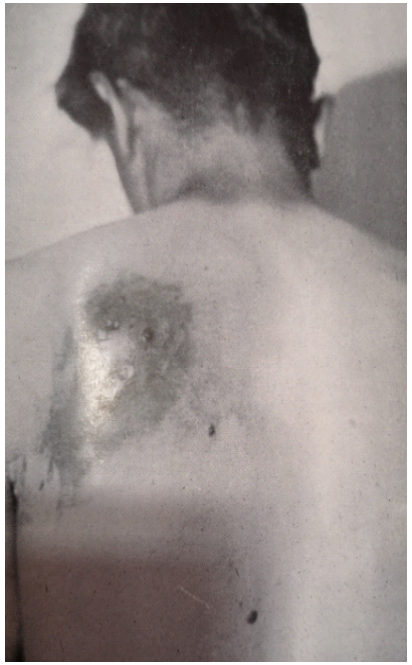
M. Poinc Girod d'avo même la ba puis il sou texte transa

Après un sion l'adopt

Le nouve conditions p sables à la

PESTE

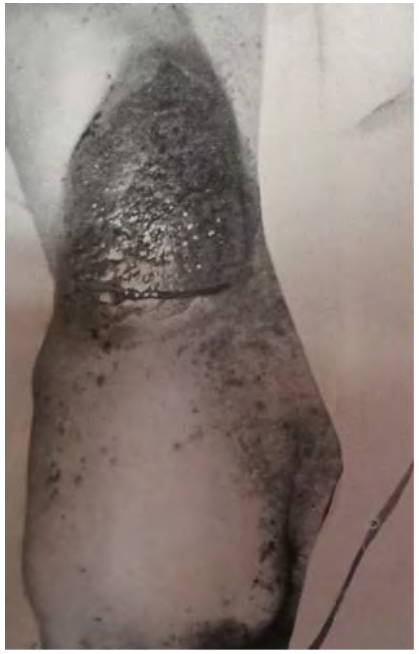
In the course of an epidemic which occurred in Senegal, Dr. Couvy, Director of the School of Medicine at Dakar, faced with the non-effectiveness of antiplague serum in severe cases of the disease, attempted the treatment by bacteriophage, utilizing a strain isolated from a convalescent. In order to ascertain in a definite manner the value of this treatment he applied it solely to cases of extreme severity in whom death seemed to be certain within a short time. "Either they appeared moribund after failure of the serum treatment, or it was given at once to patients whose condition appeared desperate" as he states in his paper. Among such patients the mortality is practically one hundred per cent, but with bacteriophage treatment he obtained 15 recoveries among the 21 cases treated. In the course of this epidemic 8 cases of septicemic plague were treated by serum before the trial of bacteriophage. All of these died. Two cases treated by bacteriophage recovered in spite of the fact that the bacilli were so abundant in the blood that they could be disclosed by direct microscopic examination. Of nine cases of pneumonic plague treated by serum all died (as is well known, pneumonic plague is without exception fatal) while one case treated with bacteriophage recovered.

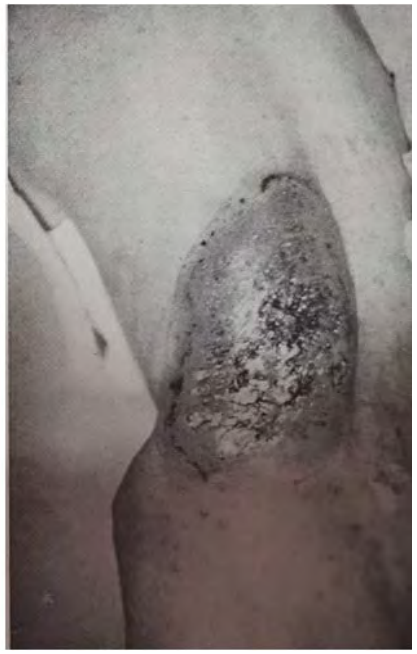


Story of phage Therapy in Lyon

Dr. Emile PESCE

- Medical thesis "Contribution to the study of the treatment of furuncles and anthrax by bacteriophage", 1931





"Need for a microbiological analysis to select the phage, based on its activity on the patient's strain"

"If microbiological analysis could not be done, use fixed cocktail"

Archives from Ferry T.

Professeur Paul Sédallian (1894-1960)

Médecin des hôpitaux
Deuxième titulaire de la **chaire des maladies infectieuses** de la faculté de médecine

Directeur du service des contagieux de l'hôpital de la Croix Rousse 1942-1960

Directeur de l'institut Pasteur de Lyon

Sédallian (Paul). — Né à Lussan (Gard) le 5 septembre 1894. — Elu correspondant national pour la division d'hygiène le 15 novembre 1955. — Mort à Lyon (Rhône) le 5 février 1960. — *Notice par P. Lépine le 8 mars 1960.*

Méningite purulente à colibacilles traitée par un bactériophage adapté intrarachidien

Par MM. P. SEDALLIAN, A. BERTOYE, J. GAUTHIER.
J.-M. MULLER et A.-L. COURTIEU.

Clinique des Maladies Infectieuses et Institut Pasteur de Lyon

Une injection intrarachidienne d'1/10 de centimètre cube n'ayant été suivie d'aucun accident, on commence, dès le lendemain 30 septembre, le traitement aux doses thérapeutiques : 1 centimètre cube de bactériophage intraventriculaire et 1 centimètre cube intrarachidien par vingt-quatre heures. Rapidement, le nombre des éléments du liquide céphalo-rachidien s'effondre à 356 contre 1.800 deux jours auparavant. Dès lors, la situation va s'améliorer très vite et on peut espérer la partie gagnée, malgré la persistance dans le liquide céphalo-rachidien d'un taux d'albumine aux alentours d'un gramme et de 50 à 200 éléments.

A une demande de **M. Roche, M. Bertoye** précise que nombre de germes peuvent être dotés d'un bactériophage. Il faut quatre à cinq jours pour l'adaptation du bactériophage : ce ne peut donc pas être une médication d'urgence.

Lyon Med. 1958 Mar 30;90(13):509-12

Le Journal de Médecine de Lyon

After d'Herelle, The story continued in Lyon

Traitement des infections à bacilles pyocyaniques par des bactériophages adaptés par sélection.

Par MM. André Bertoye et A.-L. Courtieu.

Les bacilles pyocyaniques sont fréquemment résistants aux antibiotiques usuels ... otitiq... attribuées semble être en augmentation. Leur caractère rebelle est une de leurs caractéristiqu... ...peutique différente de ...naissait l'existence de ... l'emploi de stock-bact... ... l'adaptation par sélection à une variété de bactériophage à la souche isolée du malade permet ... nutritif ... indispen... pouvoir ... intravei... Un ... cette publication.

Antimicrobial resistance

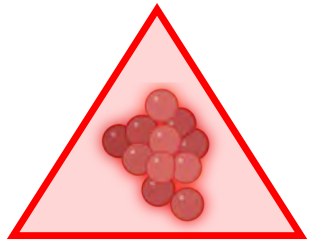
Phage banking
Phage training

Meningitis
Skin and soft tissue
Bone and joint infection

Clinique des Maladies Infectieuses, Hôpital de la Croix-Rousse
Hospices Civils de Lyon

1958-1960

A large panel of **severe** bacterial infections



Central nervous system infections

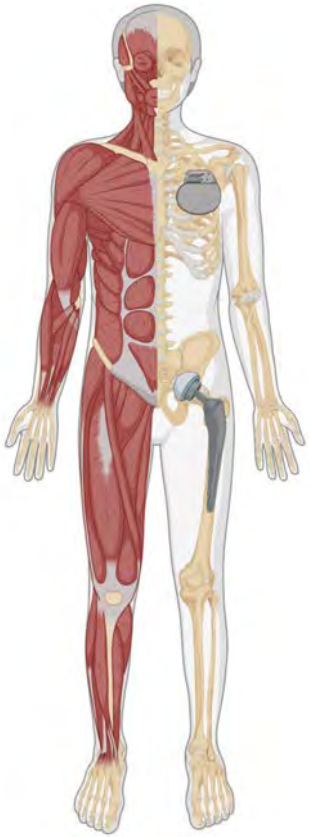
Implant-associated meningitis

Lung infections

Ventilator-associated pneumonia
Exacerbation in cystic fibrosis
Exacerbations in bronchiectasis

Urinary tract infections

Pyelonephritis
Ureteral stent-associated infection



Cardiovascular infections

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Vascular graft infection

Muskuloskeletal infections

Wound infection
Osteomyelitis, fracture-related infection
Implant-associated bone and joint infection
Prosthetic joint infection

Digestive-tract infections

Typhoid fever, shigellosis
Cholera

A large panel of **sever**

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Lung

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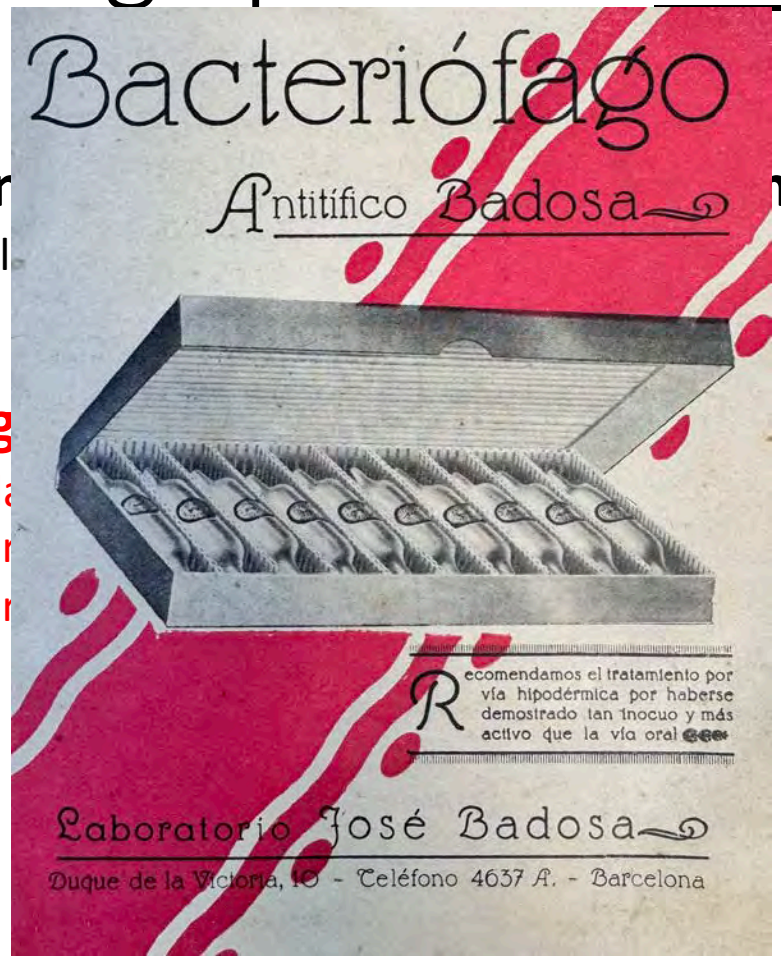

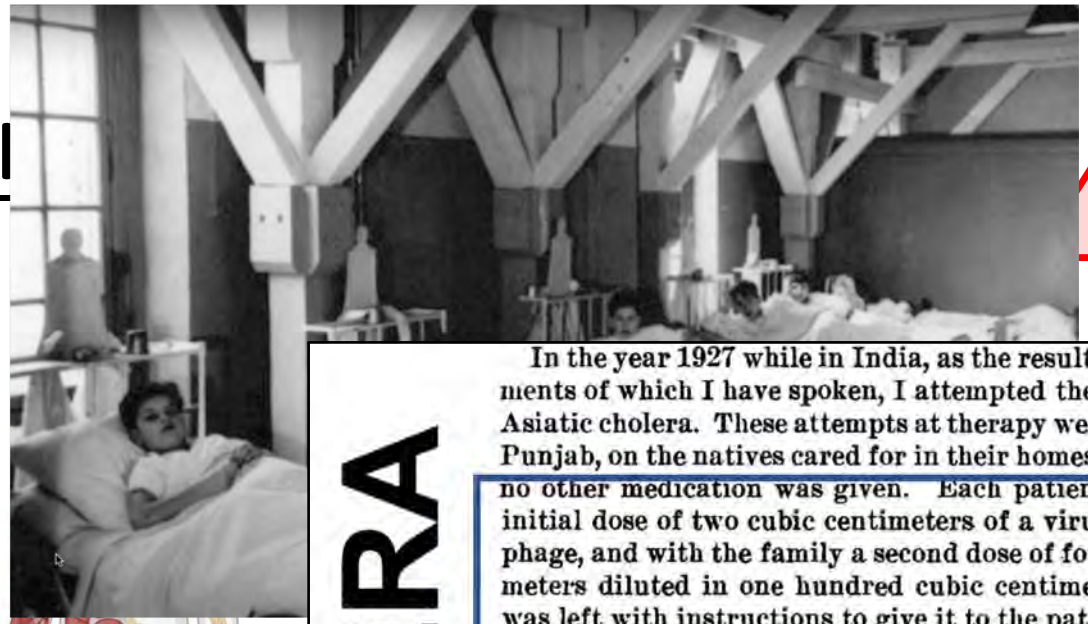

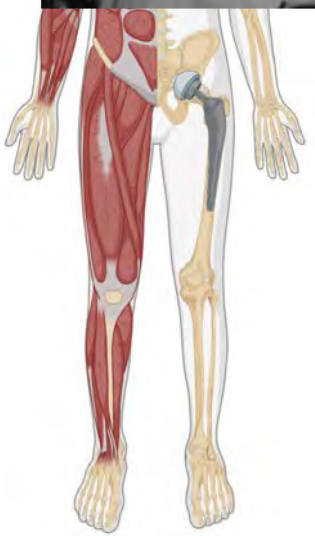

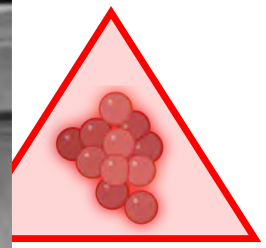

CHOLERA

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Digestive-tract infections

Typhoid fever, shigellosis

Cholera

FEMS Microbiology Reviews, fuab040, 46, 2022, 1–17

https://doi.org/10.1093/femsre/fuab040
Advance Access Publication Date: 21 July 2021
Review Article

REVIEW ARTICLE

Recent progress toward the implementation of phage therapy in Western medicine

Jean-Paul Pirnay[1,†], Tristan Ferry[2,3,†] and Grégory Resch[4,*,†]

Table 1. Published clinical trials registered on clinicaltrials.org, EudraCT or other clinical trials registry evaluating oral intake of phages, from the most recent to the oldest publication date.

Reference (PMID), year	Country	Clinical condition, number of patients treated with phages	Targeted bacteria	Type of phages, health authority (or Ethics committee) approval	Phage cocktail (Yes/No, number of phages)	Number of administration, duration	Type of clinical trial	Comparison	Results	Limits
30157383, 2019 and 30897686, 2019	United States	Healthy adults with mild to moderate gastrointestinal distress ($n = 43$)	*E. coli*	Commercial cocktail PreforPro from Deerland Enzymes, USA No dedicated FDA approval	Yes, $n = 4$	1 capsule Once a day 28 days	Phase I randomized blinded cross-over clinical trial Single center	Yes, vs placebo (1:1)	No safety signal No improvement of gastrointestinal symptoms or blood parameters between the two groups Potential positive effect on gut microbiota	No information about phage stability in the cocktail
26981577, 2016	Bangladesh	6–24-month-old boys with dehydrating acute diarrhea ($n = 79$)	*E. coli Proteus*	Commercial T4-phage cocktail (targeting *E. coli*) Commercial ColiProteus phage cocktail from Microgen, Russia (targeting *E. coli* and *proteus*) Neither FDA nor EMA approval	Yes, $n = 12$ or 18, respectively	Administration (mix of phage with mineral water and oral rehydration solution) 3 times per day for 4 days	Phase II randomized blinded clinical trial Single center	Yes, vs SOC (oral rehydration solution used in both groups) (1:1:1)	No safety signal. Failure to improve diarrhea outcome	The study was initially planned to enroll 225 patients

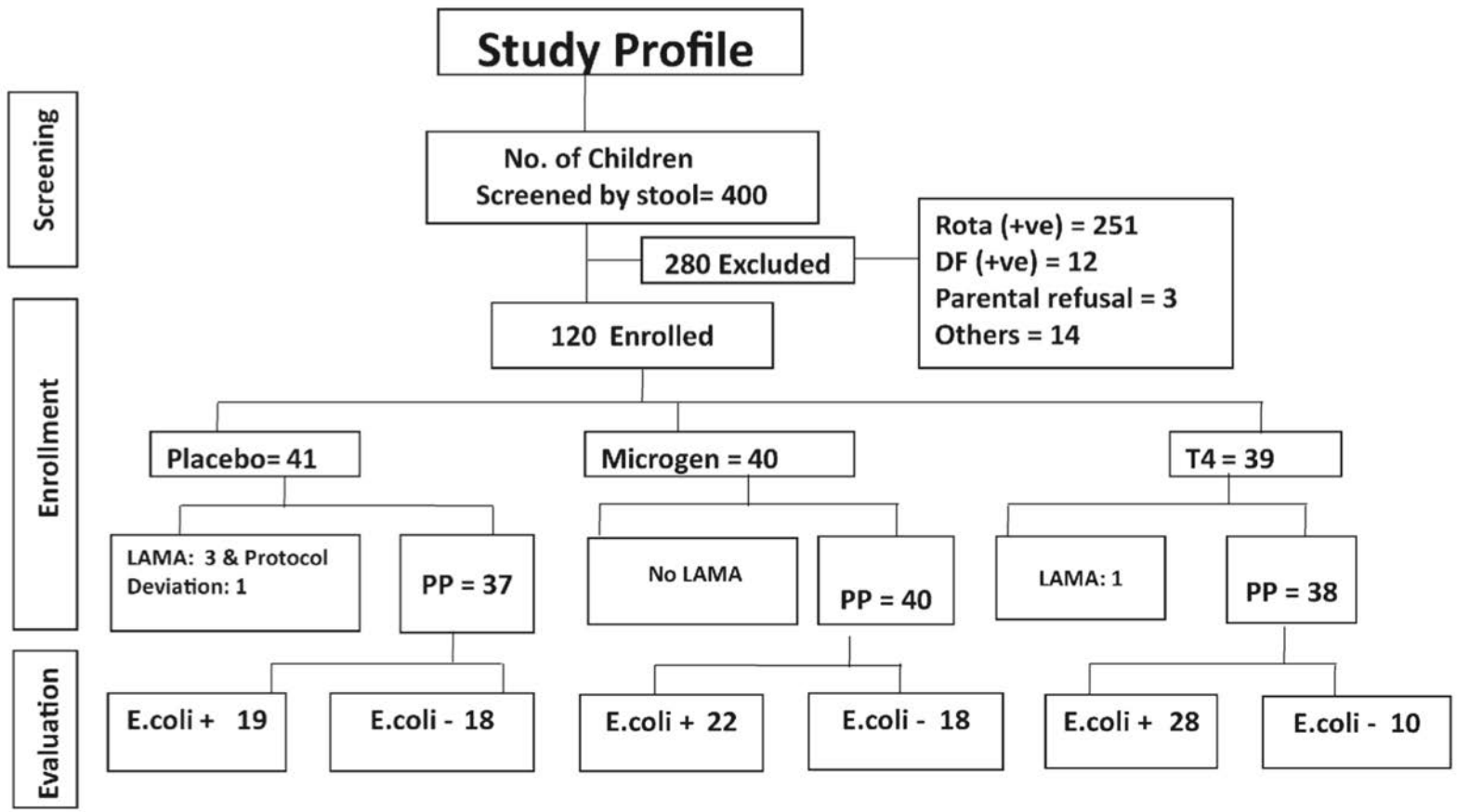
Note: EudraCT, European Union Drug Regulating Authorities Clinical Trials Database; GMP, good manufacturing practice; FDA, Food and Drug Administration; EMA, European Medicines Agency; SOC, standard of care.

Research Paper

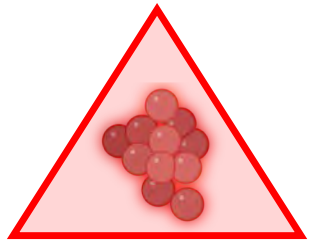
Oral Phage Therapy of Acute Bacterial Diarrhea With Two Coliphage Preparations: A Randomized Trial in Children From Bangladesh

Shafiqul Alam Sarker [a], Shamima Sultana [a], Gloria Reuteler [b], Deborah Moine [c], Patrick Descombes [c], 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], Kaisar Talukdar [a], Mohamed Kassam [c], Michèle Delley [b], Chloe Loiseau [b], Ying Deng [b], Sahar El Aidy [b], Bernard Berger [b], Harald Brüssow [b,*]

[a] *International Centre for Diarrheal Diseases Research, Bangladesh (icddr,b), 68 Shaheed Tajuddin Ahmed Sharani, Mohakhali, Dhaka 1212, Bangladesh,*
[b] *Nestlé Research Centre, Nestec Ltd., Vers-chez-les-Blanc, CH-1000 Lausanne 26, Switzerland*
[c] *Nestlé Institute of Health Science, EPFL Innovation Park, CH-1015 Lausanne, Switzerland*



A large panel of **severe** bacterial infections



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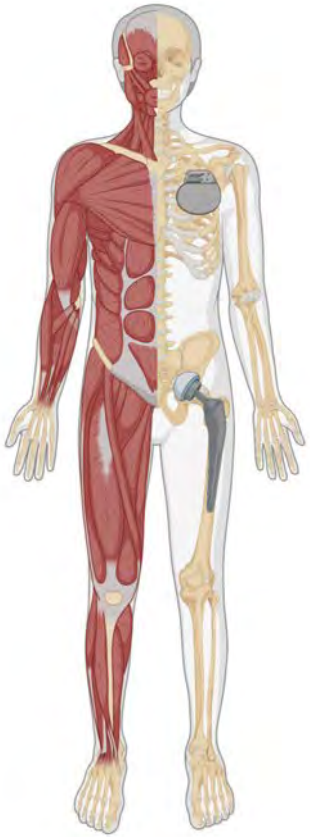

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Implant-associated bone and joint infection
Prosthetic joint infection

Angines ?

Digestive-tract infections

Typhoid fever, shigellosis
Cholera

Infection peau et tissus mous

Infection chez le brulé ?

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

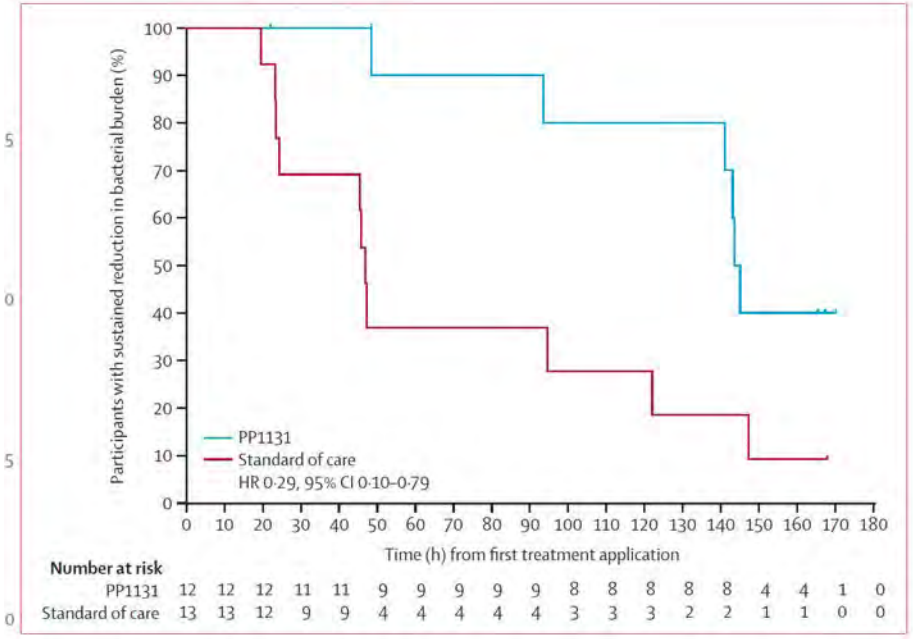


Figure 2: **Time to observe reduction in bacterial burden in the most infected wound**
Kaplan-Meier analysis of median time to sustained semi-quantitative reduction of two or more quadrants of highest daily bacterial burden compared with day 0. HR=hazard ratio. PP1131=cocktail of 12 natural lytic anti-*Pseudomonas aeruginosa* bacteriophages.

Lancet Infect Dis 2018

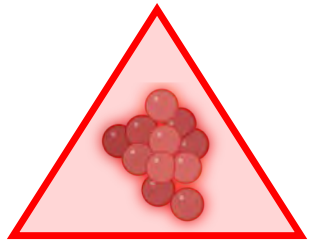
A

	Number of colonies	Resistant	Intermediatly susceptible	Susceptible
Participants who reached primary endpoint by day 7				
1	5	0	0	5
2	5	0	0	5
3	6	0	2	4
4	6	0	0	6
5	6	0	1	5
Total	28	0	3	25
Participants who did not reach primary endpoint by day 7				
1	13	1	12	0
2	5	5	0	0
3	11	0	11	0
4	11	1	4	6
5	5	0	0	5
Total	45	7	27	11

B

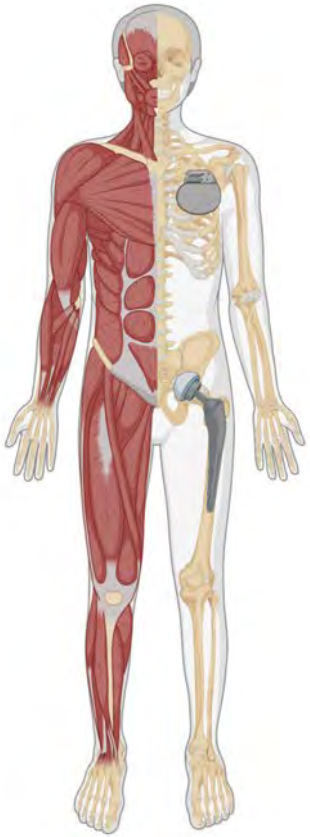
Figure 4: **PP1131 susceptibility of *Pseudomonas aeruginosa* strains recovered from the day 0 swabs of participants in the per-protocol population**
(A) Susceptibility of the different recovered clones. The five participants did and five participants did not reach the primary endpoint by day 7. (B) Three different patterns observed in spot tests. Three different susceptibility patterns to PP1131 are shown: resistance, intermediate susceptibility, and susceptibility. PP1131=cocktail of 12 natural lytic anti-*Pseudomonas aeruginosa* bacteriophages.

A large panel of **severe** bacterial infections



Central nervous system infections

Implant-associated meningitis



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Typhoid fever, shigellosis
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Infection peau et tissus mous

Infection chez le brulé ?

Intravesi
infection
of the pr
double-b

Lorenz Leitner, Aleks
Giorgi Changashvili,
Thomas M Kessler

Interpretatio
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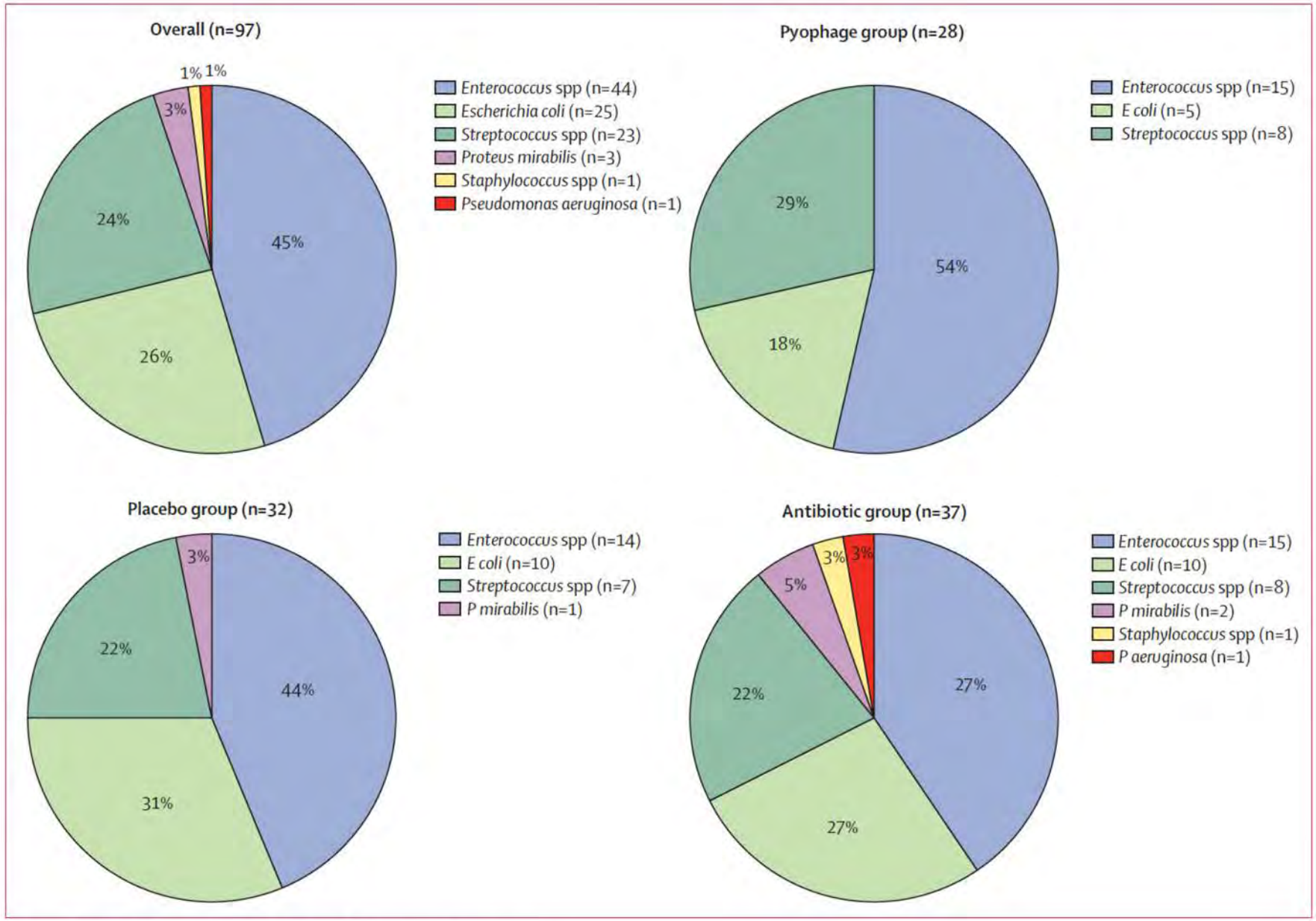

Figure 2: Distribution of bacterial species by treatment group

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Dimension co-évolutive et autres problématiques

- Traitement spécifique
- Diagnostic microbiologique
- « Phagogramme »
- Accès au site infecté

- Essais thérapeutiques en médecine de ville

Peut-on se passer des antibiotiques en 2024 ?

La phagothérapie est-elle une alternative aux antibiotiques ?

tristan.ferry@univ-lyon1.fr

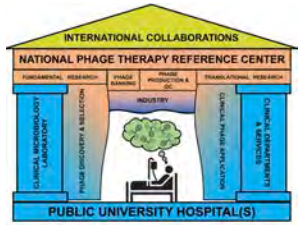
@FerryLyon

Infectious and Tropical Disea[illegible]Unit, Croix[illegible]ousse Ho[illegible]s Civils [illegible]on, Claud[illegible]ernard Lyon1 University, Lyon
Centre International de Rec[illegible]en Infec[illegible]logie, [illegible], Inserm U[illegible]1, CNR[illegible]5308, E[illegible]de Lyon, UCBL1, Lyon, France
Clinical of[illegible]er [illegible]CMID S[illegible]dy gro[illegible]for Non-Tradi[illegible]nal An[illegible]ac[illegible]al ther[illegible]y (ESGNTA)
Member o[illegible]xecu[illegible]Con[illegible]ittee [illegible]the European E[illegible]e and[illegible]oint I[illegible]ction[illegible]ociety (EBJIS)
Centre[illegible]Re[illegible]rence[illegible]s IOA complex[illegible]de Ly[illegible](CRIO[illegible]Lyo

NON

Conclusion

- Phage therapy has a **high potential** in patients with bacterial infections due to multidrug-resistant pathogen, as **adjuvant to antibiotics**
- **Complex personalized therapy** (specific to the infecting strain, various scheme of administrations, etc.)
- **Few pharmaceutical grade phages are available at this time**
- **Need to develop phages that aim to target the ESKAPE pathogens**
- **Growing clinical evidence and clinical trials are coming**
- Phages as adjuvant **could be an option to prevent** a relapse with acquisition of resistance to antibiotics (*P. aeruginosa*)
- **CRIOAc Lyon, PHAGE*in*LYON *Clinic* program and creation Lyon Phage HUB under the supervision of the French healthcare authority to select active phages is a rupture**
- **Access and evaluation of phage therapy**



ESGNTA ESCMID STUDY GROUP FOR NON-TRADITIONAL ANTIBACTERIAL THERAPY
European Society of Clinical Microbiology and Infectious Diseases

THE MYTHOLOGY
OF PHAGE THERAPY

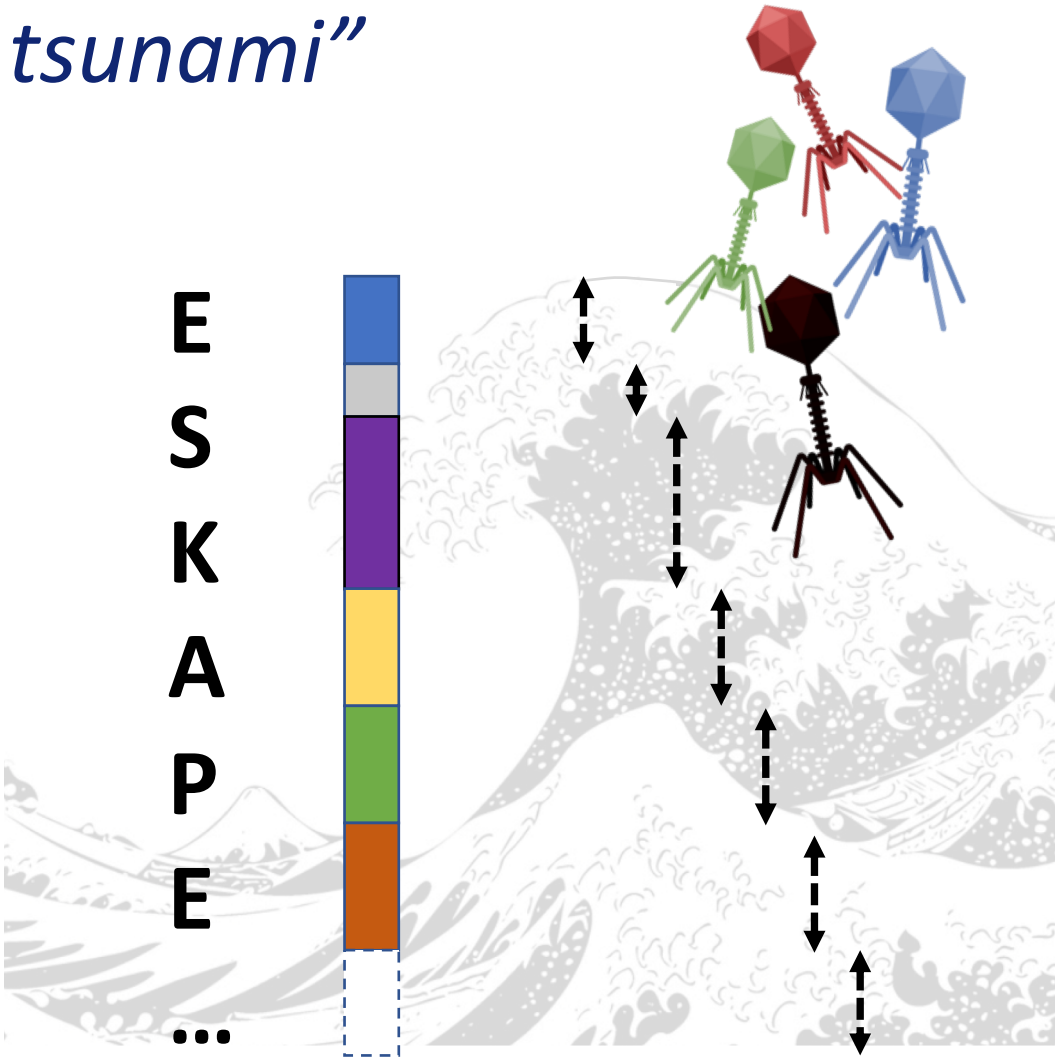
T. FERRY

T. FERRY

World Health Organization

"Slow motion tsunami"

Katsushika Hokusai (葛飾 北斎)



T. Ferry: "Plural silent pandemia"

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European Society of Clinical Microbiology and Infectious Diseases

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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;

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Microbiologists – Laetitia Beraud, Tiphaine Roussel-Gaillard, Céline Dupieux, Camille Kolenda, Jérôme Josse;

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

Clinical research assistant and database manager– Eugénie Mabrut

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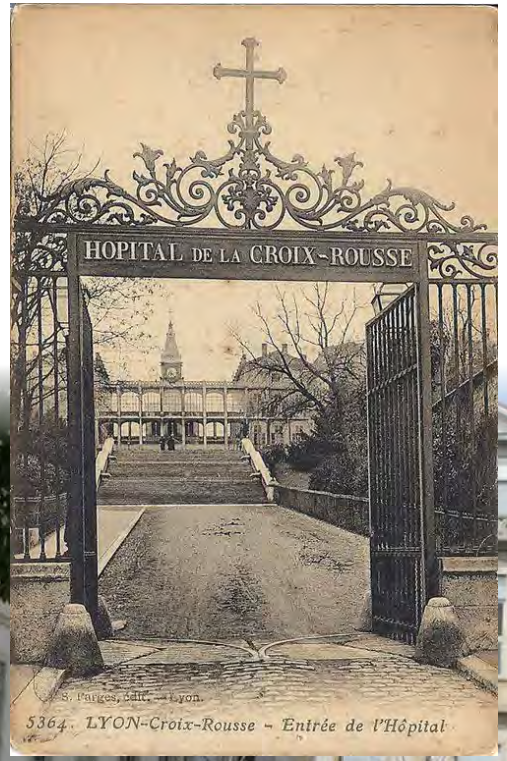
Acknowledgments to ANSM, Phaxiam, and QAMH!

Coordinator: Tristan Ferry

Tristan Ferry, Myrtille Le Bouar, Gilles Leboucher, Thomas Briot, Camille Kolenda, Tiphaine Roussel-Gaillard, Karine Dallosto

Croix-Rousse Hospital



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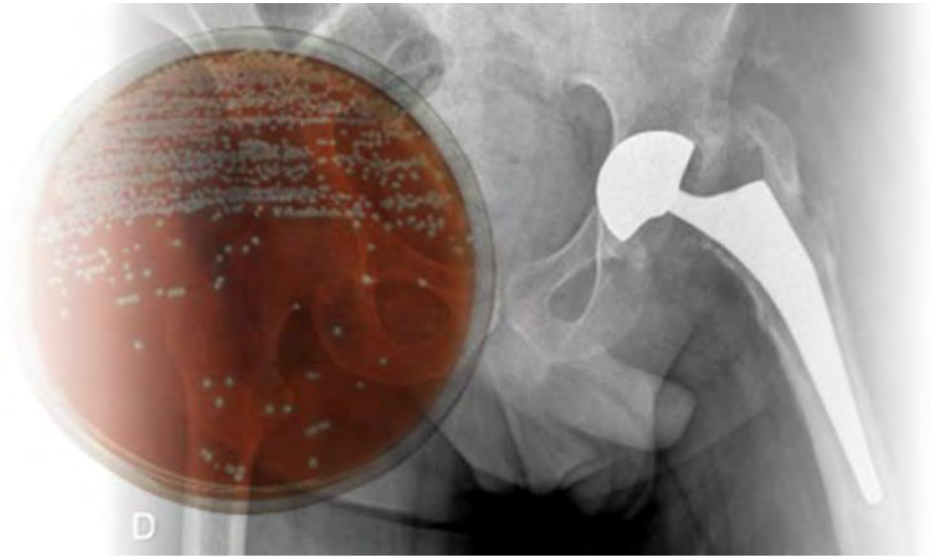

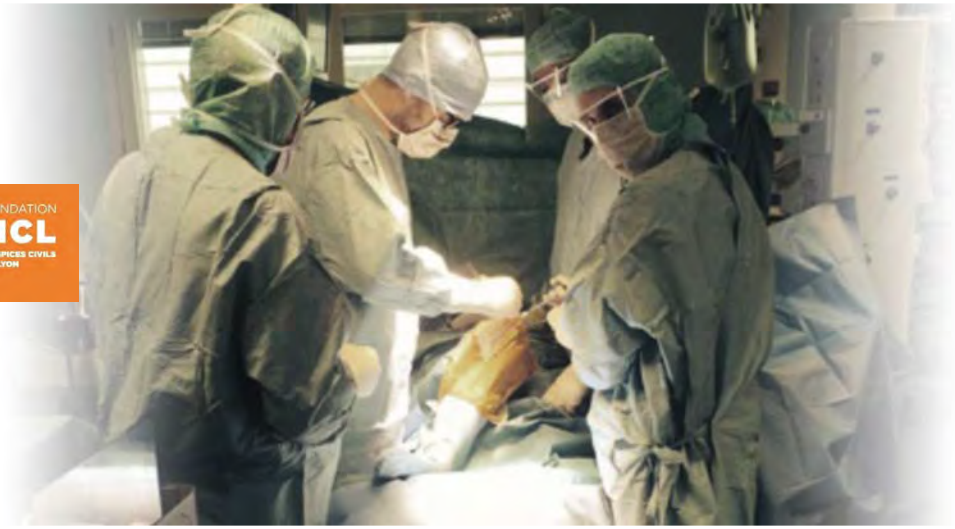

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