The Perfect Predator: A Scientist's Race to Save Her Husband from A Deadly Superbug

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UC San Diego
SCHOOL OF MEDICINE

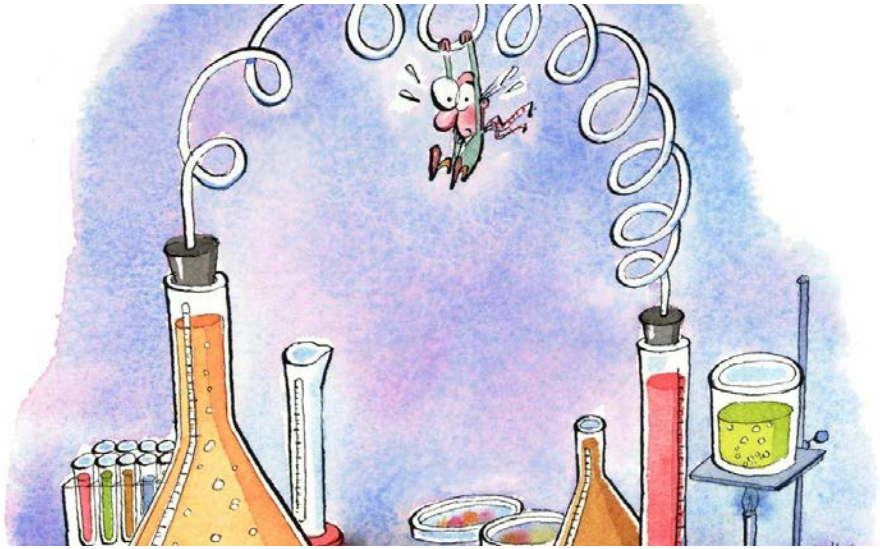
Disclosures

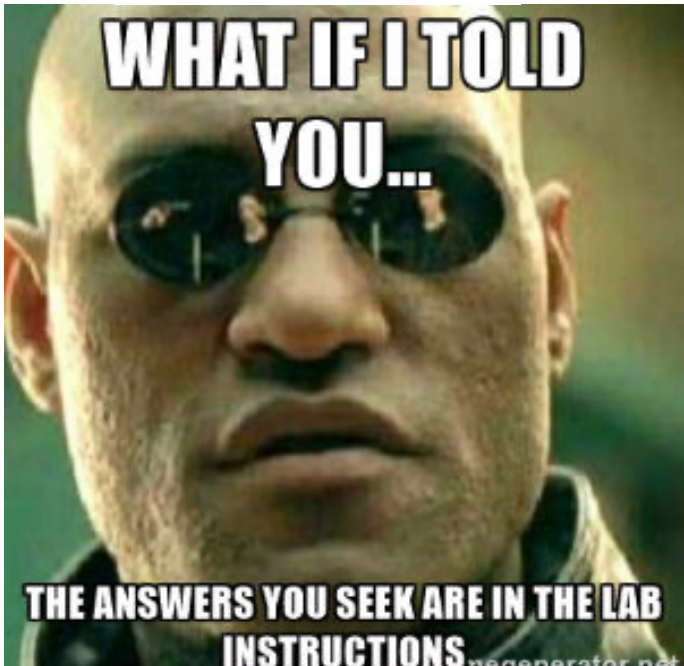
- My husband and I hold stock in Adaptive Phage Therapeutics.

- All patient photos shown are used with permission.

Career Aspirations

Early Challenges





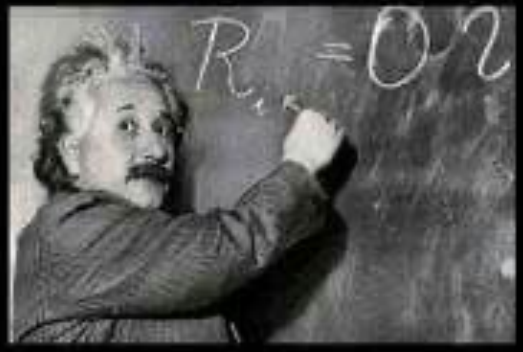
SCIENTISTS

what my mom thinks I do

what my friends think I do

what society thinks I do

what my boss thinks I do



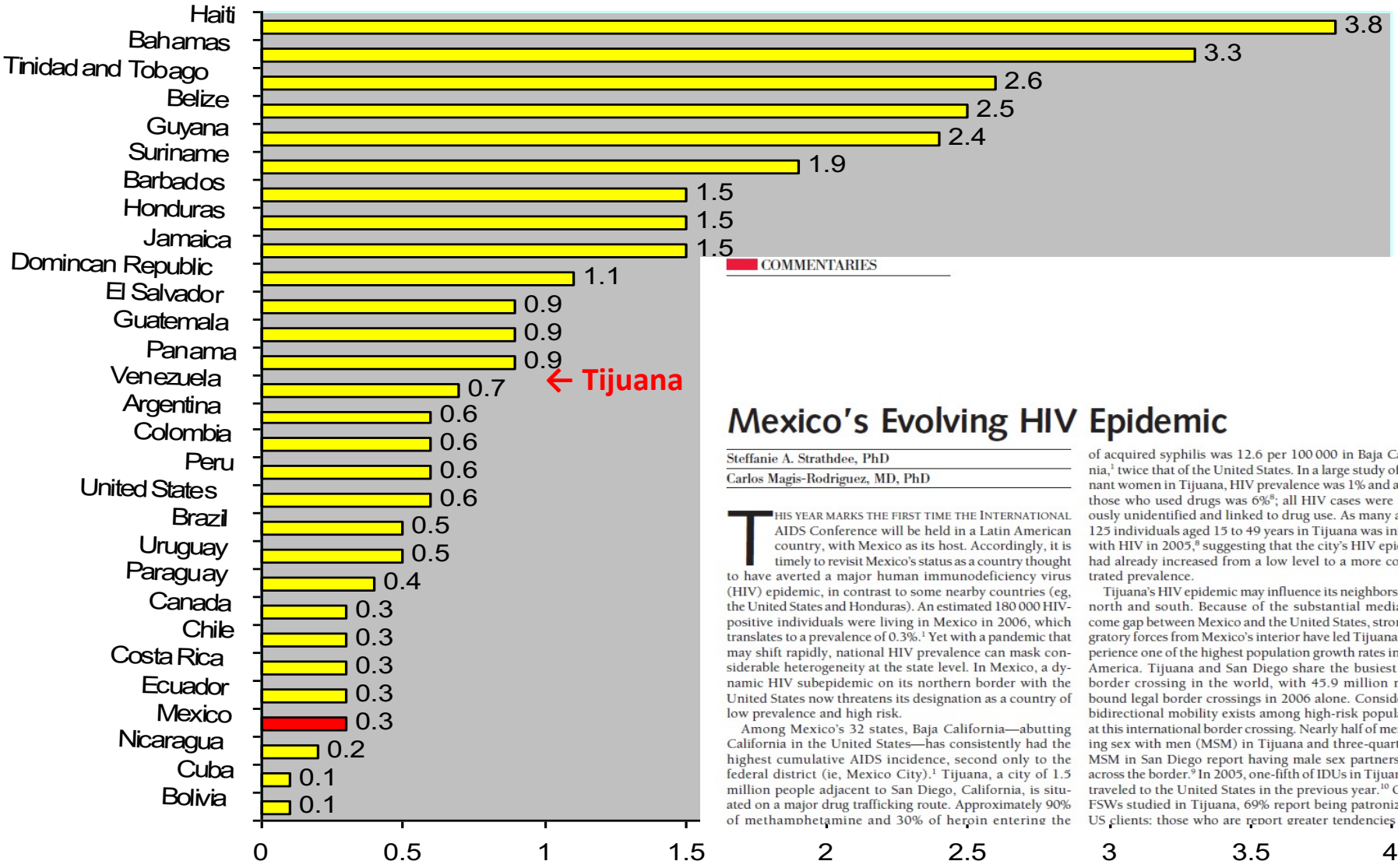
what I think I do

What I really do

“Go West Young Woman”!

… but following the Road Less Travelled

HIV prevalence in the Americas



COMMENTARIES

Mexico's Evolving HIV Epidemic

Steffanie A. Strathdee, PhD
Carlos Magis-Rodriguez, MD, PhD

THIS YEAR MARKS THE FIRST TIME THE INTERNATIONAL AIDS Conference will be held in a Latin American country, with Mexico as its host. Accordingly, it is timely to revisit Mexico's status as a country thought to have averted a major human immunodeficiency virus (HIV) epidemic, in contrast to some nearby countries (eg, the United States and Honduras). An estimated 180 000 HIV-positive individuals were living in Mexico in 2006, which translates to a prevalence of 0.3%.[1] Yet with a pandemic that may shift rapidly, national HIV prevalence can mask considerable heterogeneity at the state level. In Mexico, a dynamic HIV subepidemic on its northern border with the United States now threatens its designation as a country of low prevalence and high risk.

Among Mexico's 32 states, Baja California—abutting California in the United States—has consistently had the highest cumulative AIDS incidence, second only to the federal district (ie, Mexico City).[1] Tijuana, a city of 1.5 million people adjacent to San Diego, California, is situated on a major drug trafficking route. Approximately 90% of methamphetamine and 30% of heroin entering the

of acquired syphilis was 12.6 per 100 000 in Baja California,[1] twice that of the United States. In a large study of pregnant women in Tijuana, HIV prevalence was 1% and among those who used drugs was 6%[8]; all HIV cases were previously unidentified and linked to drug use. As many as 1 in 125 individuals aged 15 to 49 years in Tijuana was infected with HIV in 2005,[8] suggesting that the city's HIV epidemic had already increased from a low level to a more concentrated prevalence.

Tijuana's HIV epidemic may influence its neighbors to the north and south. Because of the substantial median income gap between Mexico and the United States, strong migratory forces from Mexico's interior have led Tijuana to experience one of the highest population growth rates in Latin America. Tijuana and San Diego share the busiest land-border crossing in the world, with 45.9 million northbound legal border crossings in 2006 alone. Considerable bidirectional mobility exists among high-risk populations at this international border crossing. Nearly half of men having sex with men (MSM) in Tijuana and three-quarters of MSM in San Diego report having male sex partners from across the border.[9] In 2005, one-fifth of IDUs in Tijuana had traveled to the United States in the previous year.[10] Of 924 FSWs studied in Tijuana, 69% report being patronized by US clients; those who are report greater tendencies to in-

ADAPTED FROM: Report on the Global AIDS Epidemic, UNAIDS, 2006

HIV and STDs increasingly common along U.S./Mexico border

The 'quasi-legal' nature of the sex trade in 'sex tourism' cities gives a false sense of safety.

Tijuana may be facing AIDS crisis

Cross-border report urges quick action

By Cheryl Clark
STAFF WRITER

Tijuana, long thought to have a relatively small prevalence of HIV infection, is on the cusp of an alarming AIDS outbreak rivaling those experienced by many major U.S. cities, including San Diego, with as many as one in 125 people ages 15 to 49 now infected.

That's the conclusion of a new report from the University of California San Diego and Mexican researchers, who predict a public health crisis in Tijuana if steps aren't taken quickly.

The researchers looked at current infection rates in groups engaging in low- to high-risk behaviors and compared them with similar statistics from the 1990s. The findings were then extrapolated to the 686,000 people in Tijuana ages 15 to 49. It was concluded that 1,803 to 5,472 in that age bracket are infected, or up to one in 125 people.

"This suggests we may be on the verge of a major HIV-AIDS outbreak in Tijuana," said Steffanie Strathdee, chief of UCSD's division of international health and cross-cultural medicine and the principal author of the report.

"HIV prevention efforts and treatment should be a priority in the border region, but no one has been paying attention to this problem," she said. "Interventions to reduce ongoing spread of HIV are urgently needed."

The rate of one in 125 mirrors the rate for the same age group in San Diego County, according to statistics from the county Office of AIDS Coordination and the San Diego Association of Governments.

The UCSD and Mexican study was co-written by Kimberly Brouwer, a UCSD assistant professor, and several researchers with Mexico's AIDS prevention agency in Mexico City. It was published in the February *Journal of Urban Health*.

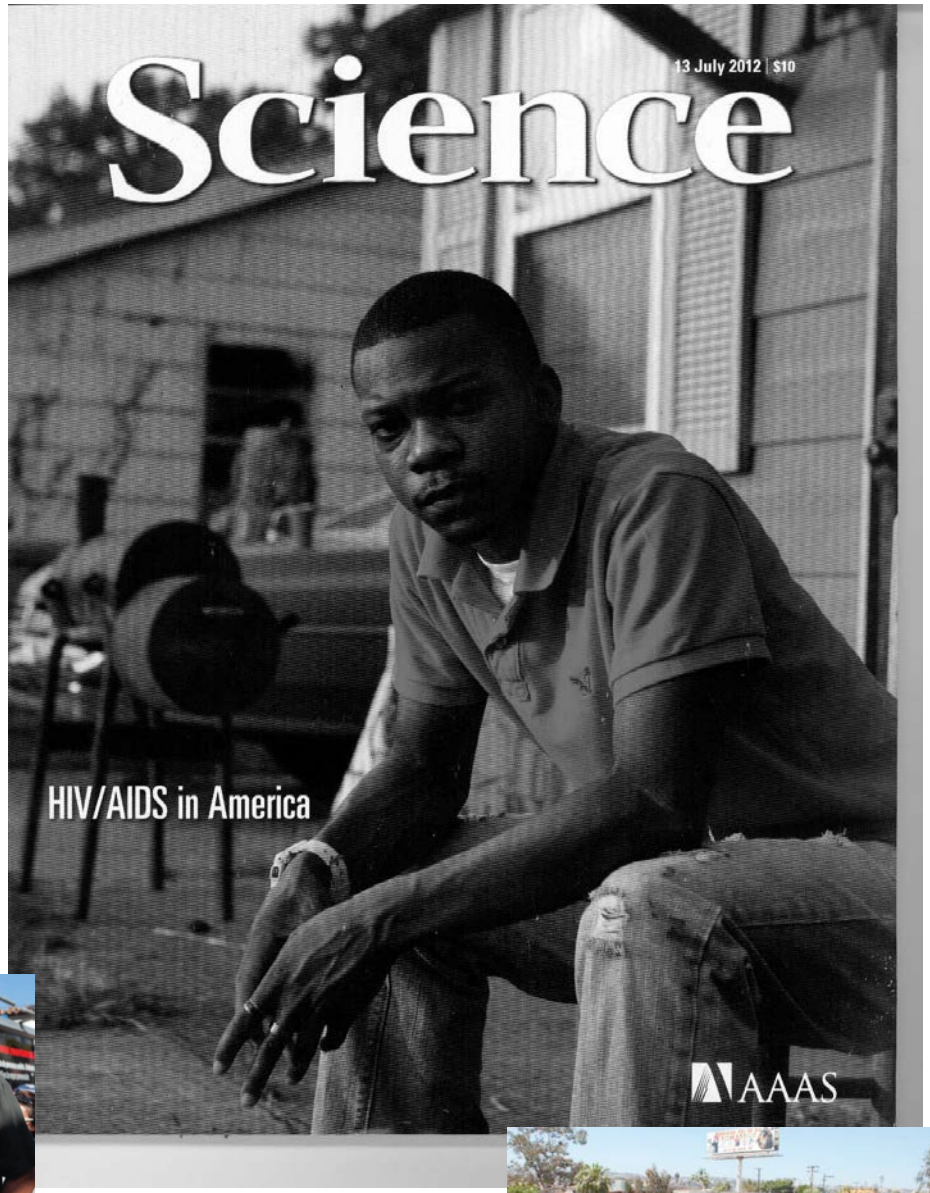
The study found the following increases in infection since the 1990s:

- Among female sex workers, infection went from five per 1,000 to 48 per 1,000, or 4.8 percent of sex workers.
- Among injection drug users, the rate went from 20 per 1,000 to as many as 65 per 1,000, or 6.5 percent of drug users.

SEE **Tijuana, B8**

San Diego Tribune, Reuters, CNN

2010: Data informed Mexico's successful bid for Global Fund ($76 M for HIV Prevention)



Special Issue ,
IAS 2012

Breaching borders. Steffanie Strathdee and Thomas Patterson track regional spread of HIV.

Painful reality. Many deported heroin users who live in the Tijuana

THE LANCET

Profile

Steffanie Strathdee: "called" to HIV prevention

For Steffanie Strathdee, Associate Dean of Global Health Sciences at the University of California San Diego (UCSD) and one of the leaders of a *Lancet* Series on HIV prevention in sex workers, being drawn into the world of HIV/AIDS was no accident. "When I was an undergraduate in microbiology at the University of Toronto, one of my teachers didn't show up one week. He had died of AIDS", she recalls. "Later I lost my PhD supervisor and my best friend to the disease as well, so for me, coming to work in the HIV/AIDS field was a calling, something I just had to do."

Much of Strathdee's work over the past decade has focused on HIV research and prevention programmes in Tijuana, a frontier city on the USA–Mexico border. A magnet for migrants on a drug-trafficking route, sex work and injecting by recruiting sex workers and drug users to a WHO research programme. "I was struck by how many sex workers and people who injected drugs confided to me that they had experienced sexual abuse in childhood and adolescence, even though it wasn't included in the survey", she says. "This was an under-researched area of HIV epidemiology at that time, which I found compelling, not least because I had experienced sexual abuse myself in adolescence." This became a focus of postdoctoral research for her after a move to the University of British Columbia in Vancouver.

Vancouver was also the host of the 1996 International AIDS Society conference, a milestone in Strathdee's career. She was selected to present her work on the independent association between sexual abuse and increased HIV risk, winning a

Photography © 2014Pablo Mason/"Notes to our Sons and Daughters" project, © 2014 Alexis Dixon

Published Online
July 22, 2014


Optima


ULANCE
PHOENIX
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2445

Centers for Disease Control and Prevention

Bacteria (WHO category)	WHO (2017)	CDC (2013)	ESKAPE (2008-9)
Acinetobacter baumannii, carbapenem-R	Critical	Serious (MDR)	Yes
Pseudomonas aeruginosa, carbapenem-R	Critical	Serious (MDR)	Yes
Enterobacteriaceae, carbapenem-R, 3rd-gen ceph-R (ESBL+)	Critical	Urgent (carbapenem-R) Serious (ESBL+)	Yes
Enterococcus faecium, vancomycin-R	High	Serious (VRE)	Yes
Staphylococcus aureus, methicillin-R, vancomycin-I/R	High	Serious (MRSA) Concerning (VRSA)	Yes
Helicobacter pylori, clarithromycin-R	High		
Campylobacter spp., fluoroquinolone-R	High	Serious (drug-R)	
Salmonellae spp., fluoroquinolone-R	High	Serious (drug-R)	
Neisseria gonorrhoeae, 3rd-gen ceph-R, fluoroquinolone-R	High	Urgent (drug-R)	
Streptococcus pneumoniae, penicillin-NS	Medium	Serious (drug-R)	
Haemophilus influenzae, ampicillin-R	Medium		
Shigella spp., fluoroquinolone-R	Medium	Serious	
Clostridium difficile		Urgent	
Candida spp. fluconazole-R		Serious (Flu-R)	
M. tuberculosis		Serious (drug-R)	
Group A *Streptococcus*		Concerning (erythro-R)	
Group B *Streptococcus*		Concerning (clinda-R)	

Uniklinick Antibiogram

Name: **Patterson**
Vorname: **Thomas Leroy (M)**
Geb. Datum: *** 18.02.1947**

Untersuchungsmaterial: **Abszesspunktat**
Abnahmeort: **transgastrales Punktat**

Anforderung:
Mikrobiologische Untersuchung

Befund:

1: Acinetobacter baumannii (4MRGN) ***vereinzelt***
*Keine Spezies-spezifischen Grenzwerte vorhanden.

2: Candida albicans ***reichlich***

3: Candida glabrata ***reichlich***
Das Antimykogramm siehe Befund 51569953.

Bemerkung/Bewertung
Die anaeroben Kulturen werden weiterbebrütet. Nur im positiven Falle erhalten Sie einen erneuten Befund.
Telefonische Befunddurchsage erfolgte am 10.12.2015 um 10:03 Uhr
Faxmitteilung erfolgte am 10.12.2015 um 10:17 Uhr
4MRGN: Multiresistentes gramnegatives Stäbchenbakterium mit Resistenz in 4 Antibiotikagruppen (KRINKO-Definition).
Aufgrund der Meldepflicht nach Hessischer Verordnung für besondere Antibiotikaresistenz ist dieser Befund an das Amt für Gesundheit gemeldet worden.

Antibiogramm

Keim	1	*MHK*				
Piperacillin	R					
Cefotaxim	R					
Ceftazidim	R					
Meropenem	R	>=32				
Gentamicin	R					
Tobramycin	R					
Amikacin	R	>=256				
Co-Trimoxazol	R	4				
Fosfomycin i.v.	R					
Levofloxacin	R					
Ciprofloxacin	R					
Minocyclin	S	4				
Rifampicin	*	8				
Colistin	S	1				
Ampicillin/Sulbactam	R	>=256				

Erläuterung: S = sensibel, I = intermediär, R = resistent

Antimykogramm

Keim	3	*MHK*				
Caspofungin	S	0.125				

Erläuterung: S = sensibel, I = intermediär, R = resistent
Nummerische Angaben sind MHK in µg/ml


By 2050,
Superbugs Could Kill
10 Million
People a Year
Source: Review On Antimicrobial Resistance

Credit: Scott Brundage, Scientific American

Review

Emerging therapies for multidrug resistant *Acinetobacter baumannii*

Meritxell García-Quintanilla*, Marina R. Pulido*, Rafael López-Rojas, Jerónimo Pachón, and Michael J. McConnell

Unit of Infectious Disease, Microbiology, and Preventive Medicine, Institute of Biomedicine of Sevilla (IBiS), University Hospital Virgen del Rocío/CSIC/University of Sevilla, 41013, Sevilla, Spain

The global emergence of multidrug resistant *Acinetobacter baumannii* has reduced the number of clinically available antibiotics that retain activity against this pathogen. For this reason, the development of novel prevention and treatment strategies for infections caused by *A. baumannii* is necessary. Several studies have begun to characterize nonantibiotic approaches that utilize novel mechanisms of action to achieve antibacterial activity. Recent advances in phage therapy, iron chelation therapy, antimicrobial peptides, prophylactic vaccination, photodynamic therapy, and nitric oxide (NO)-based therapies have all been shown to have activity against *A. baumannii*. However, before these approaches can be used clinically there are still limitations and remaining questions that must be addressed.

these infections. In this review, recent advances in nonantibiotic approaches that are currently being explored for prevention and treatment of *A. baumannii* infections are described.

Phage therapy

Bacteriophages, or phages, are viruses that infect, and in some cases lyse, bacterial cells. The potential use of bacteriophages as antibacterial agents was recognized at almost the same time as their discovery nearly a century ago [9]. However, the dawn of the antibiotic era slowed interest in this area in western countries. In the present context of infections caused by multidrug-resistant bacteria for which there are a decreasing number of active antimicrobials, research exploring the use of phage therapy as an alternative treatment has been renewed. In 2010

Trends in Microbiology, 2013

Early Pioneers

Charles Hankin

Nicolai Gamaleya

Bronislaw Fejgen

Frederick Twort

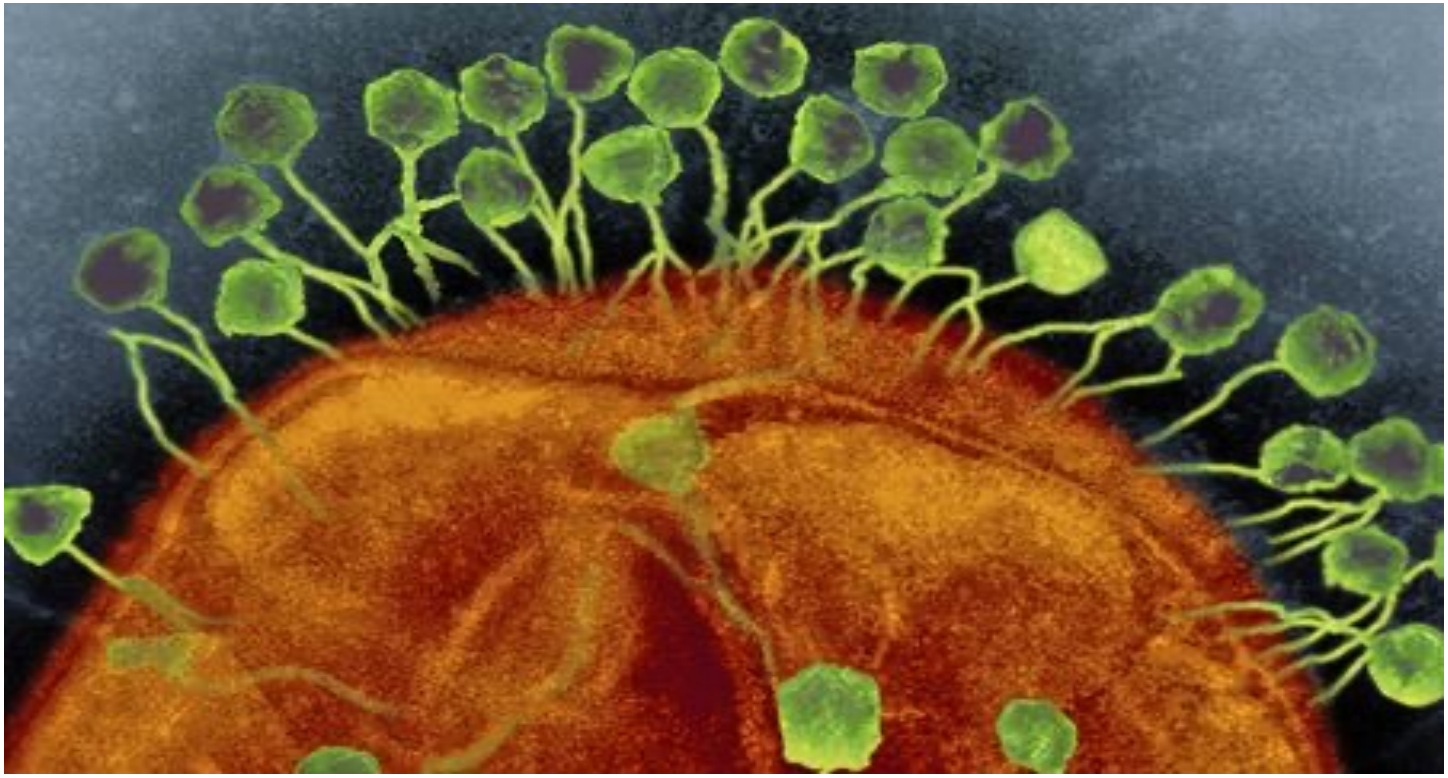
Felix d'Herelle

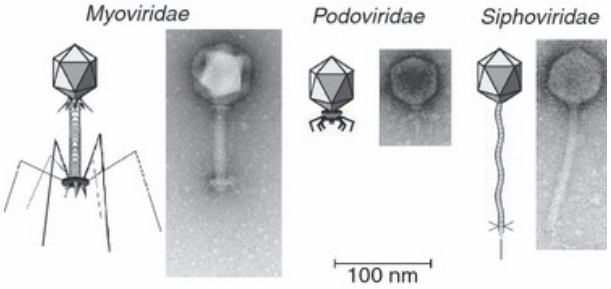
Giorgi Eliava

Phage Therapy Unit
Wrocław, Poland

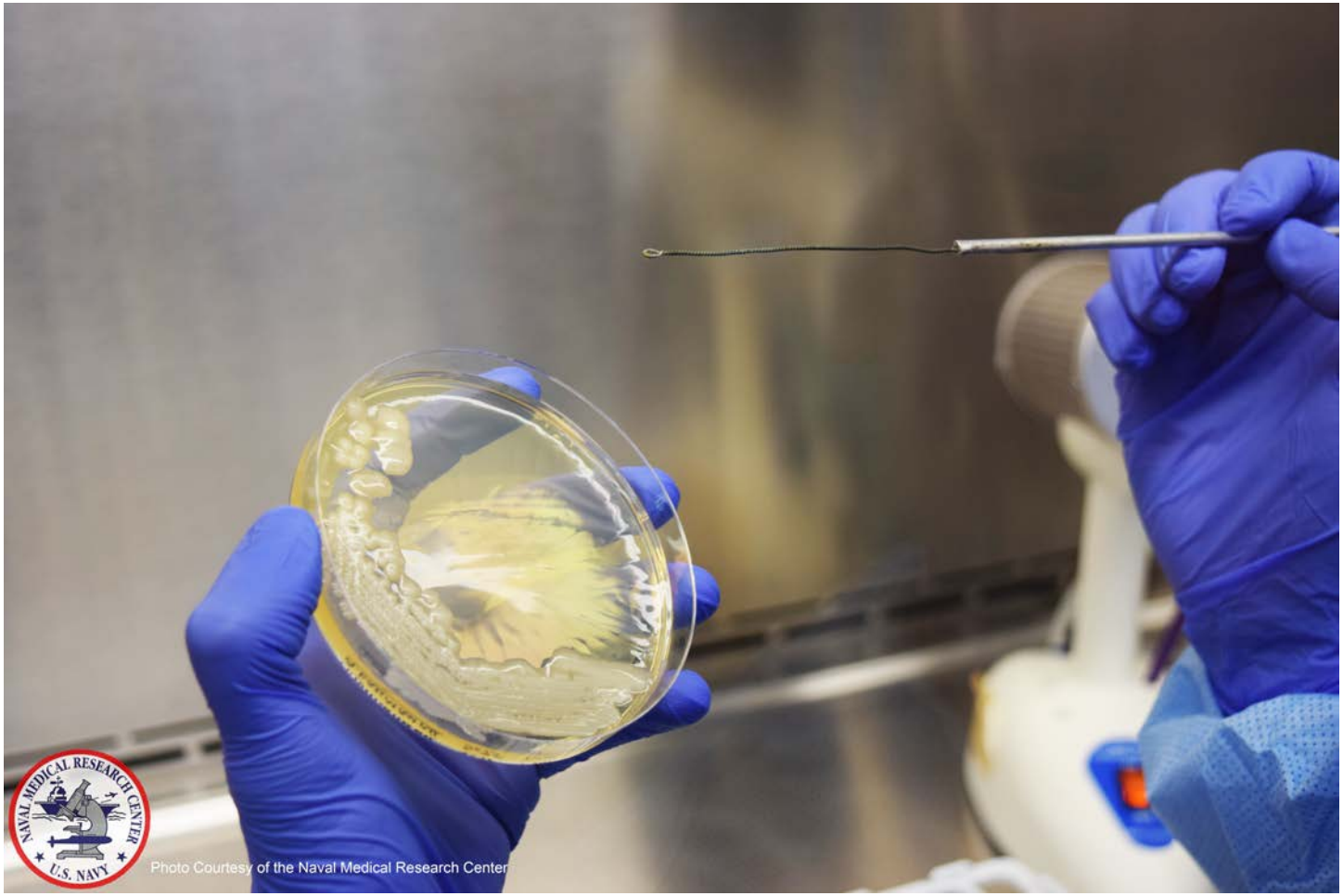
Foundation ELIAVA

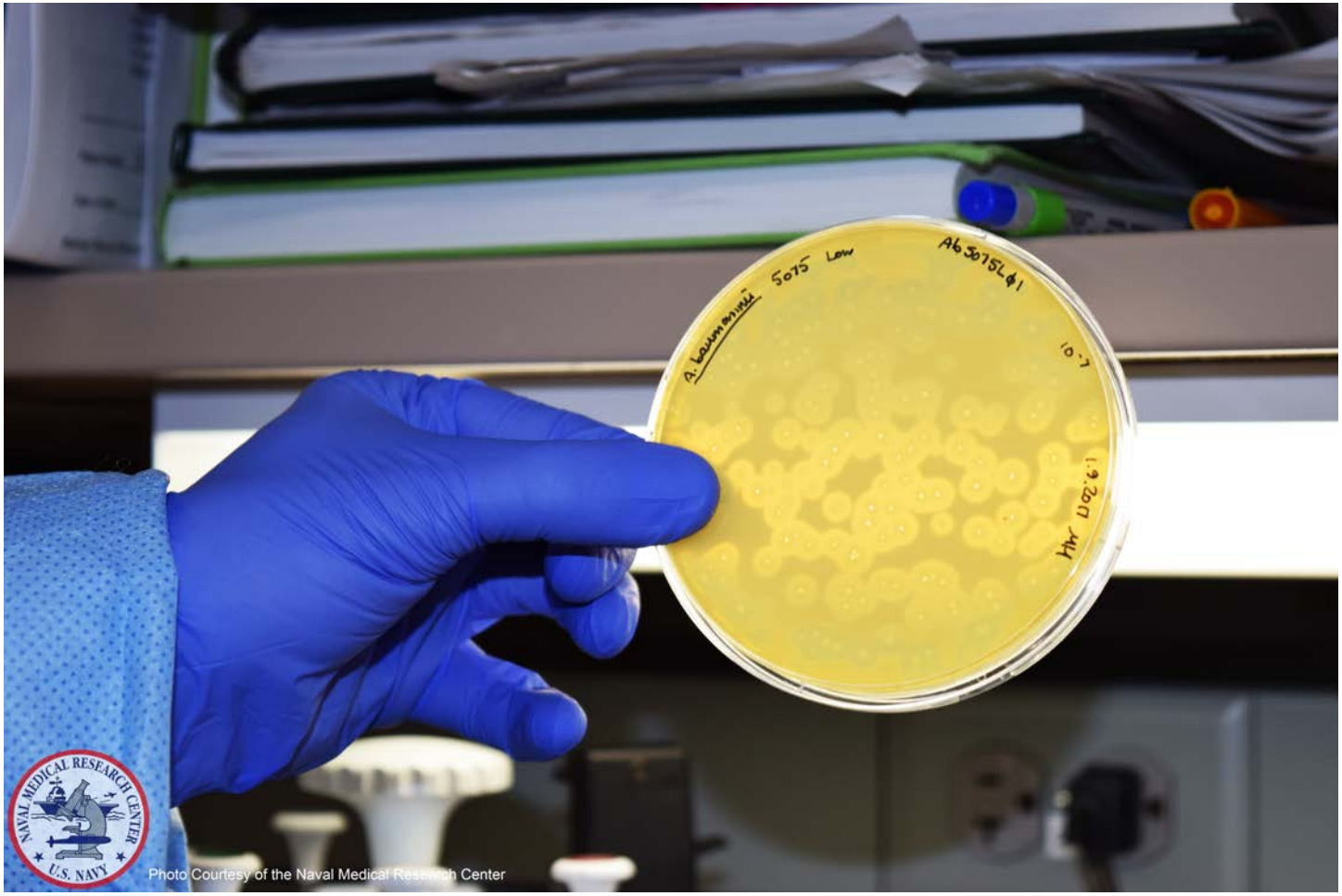

Thanks to PENICILLIN
...He Will Come Home!




Myoviridae
Podoviridae
Siphoviridae
100 nm


NEW BRUNSWICK SCI
4000 ml
PYREX
Photo Courtesy of the Naval Medical Research Center


NAVAL MEDICAL RESEARCH CENTER
U.S. NAVY
Photo Courtesy of the Naval Medical Research Center


A. baumannii 5075 Low
A6307SL01
10-7
1:2001 MH
NAVAL MEDICAL RESEARCH CENTER
U.S. NAVY
Photo Courtesy of the Naval Medical Research Center

The Phage Hunt Begins…

Dr Ry Young

Texas A&M- Center for Phage Technology

Contacting the FDA….

Dr Robert (Chip) Schooley, UCSD

Dr Cara Fiore, FDA

US Navy Biological Defense Research Directorate

Photo Courtesy of the Naval Medical Research Center

The Dosing Dilemma

Maia Merabishvilli, PhD

Carl Merril, MD

Phage Therapy ELIAVA

How much phage to administer?

What routes?

How often?

How long?


PROTECT FROM LIGHT
Investigational Study Medication
Patterson Thomas Leroy
Age:69 yrs [2/18/1947]
MRN#1580^264
Unit:2-TICU-IC11
Ord#118683420
Bacteriophage cocktail (AB1, AB4, AB71, AB97 phages) 5 x 10^9 in 5 mL lactated ringers, IV solution
Dose:
Frequency: Q12H
Route: IntraVENOUS
Due Time:3/18/16 0900
Investigational Drug eIND# 16907 Bacteriophage cocktail (AB1, AB4, AB71, AB97 phages) 5 x 10^9 in 5 mL lactated ringers, IV solution for bolus per MD discretion. Handle as biohazardous agent - dispose of properly. Investigational drug cosignature required. Protect from light. Discard 24 hours after preparation time.
Pharmacy instruction: Obtain 0.5 mL of 1x 10^11 PFU/mL stock and add to 4.5 mL LR to make working solution #1 (5mL, 1x 10^10 PFU/mL). Obtain 0.5 mL of working solution #1 and add to 4.5 mL LR to make final solution of 5 mL, 1x 10^9 PFU/mL, total dose= 5x 10^9 PFU.
Printed: 3/17/16 1856 (FD)
Tech:_____
RPh:
REFRIGERATE


WARNING


HAPPY BIRTHDAY!

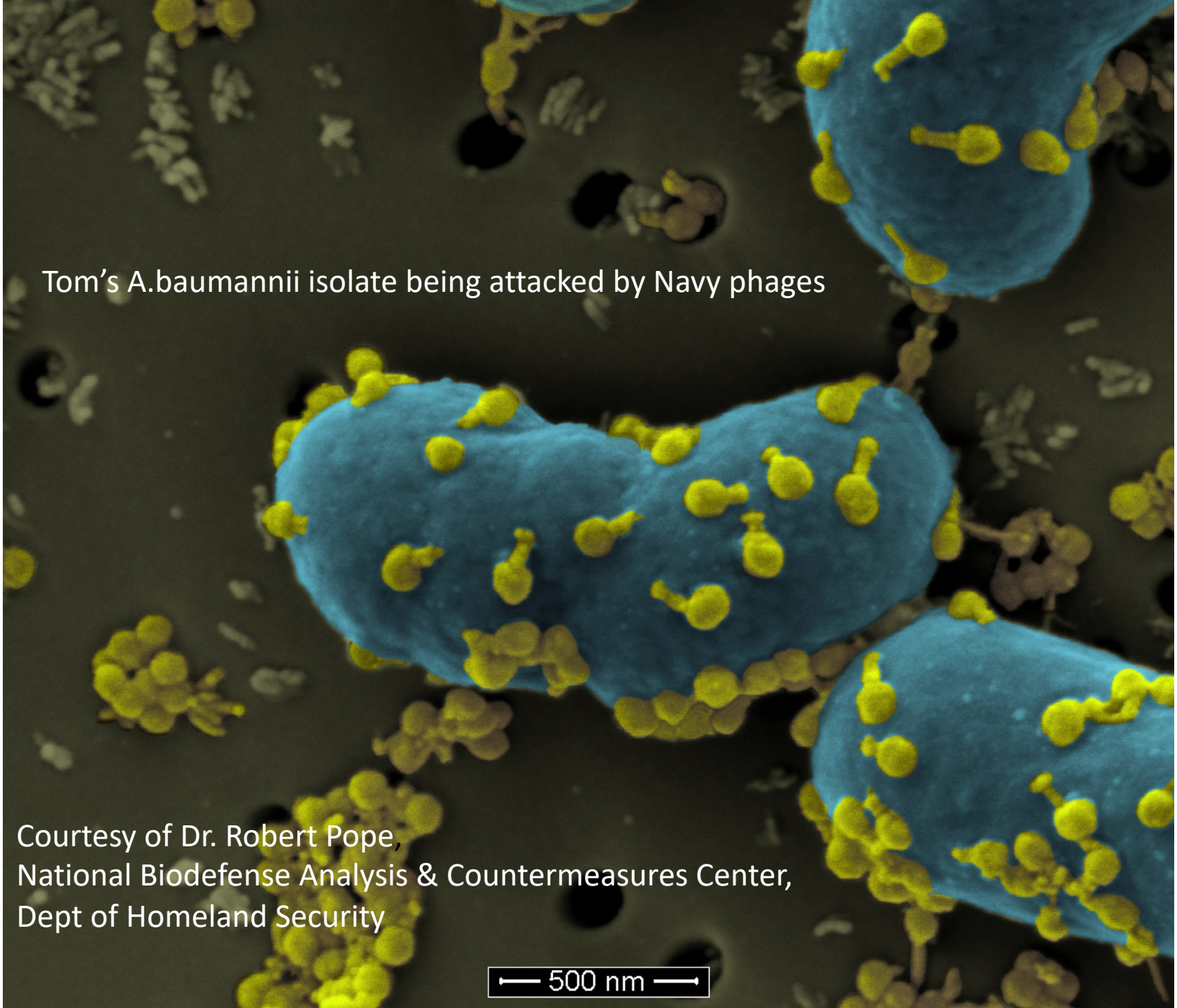

220

Thomas Patterson and Lt Commander Theron Hamilton

Antimicrobial Agents and Chemotherapy®

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

Schooley et al, AAC, 2017


Tom’s A.baumannii isolate being attacked by Navy phages
Courtesy of Dr. Robert Pope,
National Biodefense Analysis & Countermeasures Center,
Dept of Homeland Security
500 nm

BuzzFeed NEWS / REPORTING TO YOU

Her Husband Was Dying From A Superbug. She Turned To Sewer Viruses Collected By The Navy.

Scientists have long dismissed "phage therapy" as a fringe idea pushed by eccentrics who enjoy fishing in sewage. But now the Navy is betting on it.

WELLNESS

Sewage Saved This Man's Life. Someday It Could Save Yours.

Bacteriophages — viruses found in soil, water and human waste — may be the cure in a post-antibiotic world.

By Lauren Weber

Daily Mail .com

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Could gargling a virus that eats bacteria solve the SUPERBUG CRISIS? As overused antibiotics become less and less effective, a tantalising discovery may revolutionise healthcare

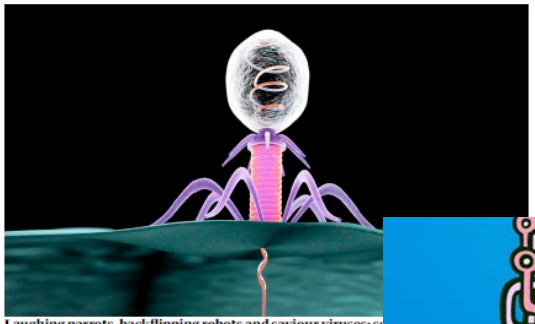
- Steffanie Strathdee feared the worst when husband Tom Patterson comatosed
- Husband of 13 years lay in a deep coma, the victim of an aggressive superbug
- His heart, lungs and major organs were all shutting down with little hope left
- Apparently miraculous recovery is result of natural phenomenon that could combat growth of antibiotic-resistant infections and also treat sore throats

HUFFPOST

JAMA®

The Journal of the American Medical Association

theguardian



Laughing parrots, backflipping robots and saviour viruses: s

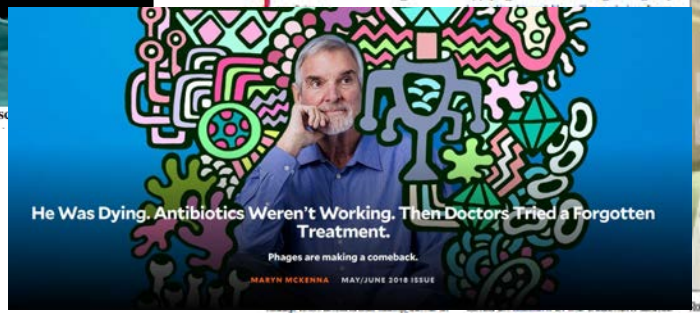
Medical News & Perspectives

Phage Therapy's Role in Combating Antibiotic-Resistant Pathogens

Jeff Lyon

Sometimes, what's old is new again—even in the ever-advancing world of

tered under Schooley's direction after applying for and receiving Emergency



obert T. Schooley, MD

THE LANCET

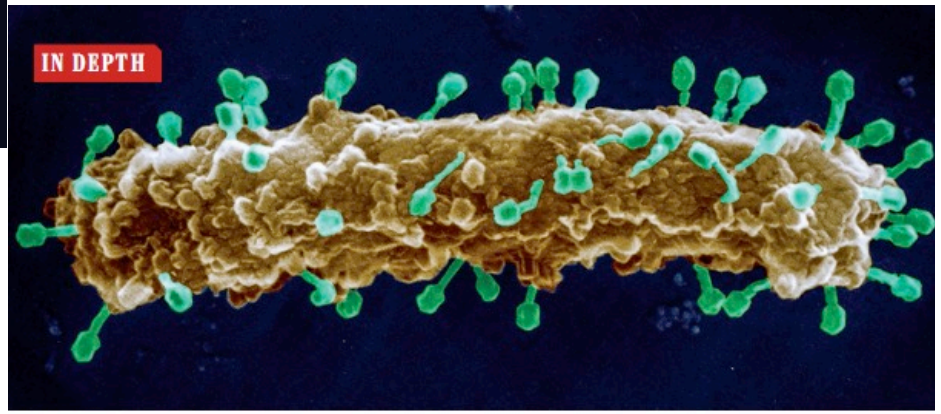
Phage therapy: revival of the bygone antimicrobial

The idea of using bacteriophages as vectors for antimicrobial therapy has existed for decades, but development towards clinical application still lags behind. Geoff Watts reports.

Phage Therapy Patients treated at IPATH

Patient	Age	Underlying Condition	Organism	Start Date	Outcome
1	67	Disseminated infection	A. Baumannii	May 2016	Treatment success
2	67	Bilateral lung transplant	P. Aeruginosa	May 2017	Treatment success
3	74	Open head trauma	A. Baumannii	June 2017	Treatment success
4	23	CF; pre lung transplant	P. Aeruginosa	September 2017	Treatment success
5	65	Infected LVAD	P. aeruginosa +	December 2017	Failure
6	63	Infected LVAD	S. Aureus	April 2018	Treatment success
7	61	Infected left knee prosthesis	S. Aureus	March 2019 September 2019	First treatment failed, second treatment success
8	83	Infected LVAD	P. aeruginosa	August 2019	Treatment failure, patient passed away
9	56	Recurrent UTI	ESBL E. coli	February 2020	Partial success
10	64	Recurrent bacteremia, aortic graft infection	P. Aeruginosa	March 2020	Treatment success
11	65	Bacteremia	ESBL E. Coli	July 2020	Outcome pending
12	77	Lung infection	P. aeruginosa	September 2020	Outcome pending

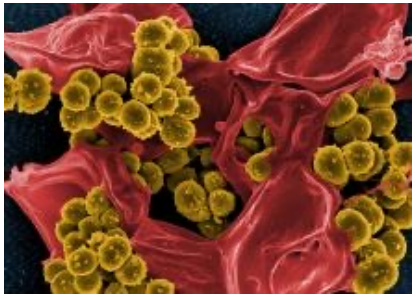
Science
AAAS



BIOMEDICINE

U.S. center will fight infections with viruses

Proving ground for phage therapy will organize full clinical trials of the approach



NIH Funds First Phase Therapy Trial ($12 M) through the Antibacterial Resistance Leadership Group

December 13th, 2019

Design: Adaptive Phase 2 Trial

Enrollment to start in 2022

PI: Robert T. Schooley

nature medicine

BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-019-0437-z

May 2019

Engineered bacteriophages for treatment of a patient with a disseminated drug-resistant *Mycobacterium abscessus*

Rebekah M. Dedrick[1,4], Carlos A. Guerrero-Bustamante[1,4], Rebecca A. Garlena[1], Daniel A. Russell[1], Katrina Ford[2], Kathryn Harris[2], Kimberly C. Gilmour[2], James Soothill[2], Deborah Jacobs-Sera[1], Robert T. Schooley[3], Graham F. Hatfull[1*] and Helen Spencer[2*]

Before treatment Post treatment

Conclusions

- A “D” in Calculus is not the end of the world.
- What first appears as the worst ordeal of your life may have a silver lining.
- Importance of the role of privilege in global health.

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ThePerfectPredator.com

Acknowledgements

Rob Knight
Doug Conrad
Constance Benson

UC San Diego

TEXAS A&M UNIVERSITY

Ryland Young
Jason Gill
Mei Liu
Carlos Gonzalez

Stuart Tyner
Brett Swierczewski
Mikeljon Nikolich
Nelson Michael

Walter Reed Army Institute of Research

NAVAL MEDICAL RESEARCH CENTER
U.S. NAVY

Theron Hamilton
Biswajit Biswas
Kim Bishop-Lilly

NIH National Institute of Allergy and Infectious Diseases

John Beigel Joseph Campbell
Jane Knisely

ARLG
Antibacterial Resistance Leadership Group

Chip Chambers Vance Fowler
Pranita Tamma