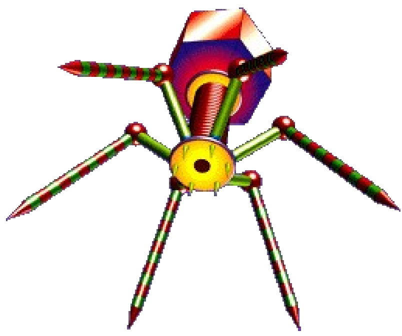

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Bacteriophage Ecology Group (BEG) News

Dedicated to the ecology and evolutionary biology of the parasites of unicellular organisms (UOPs)

© Stephen T. Abedon (editor)

July 1, 2000 issue (volume 5)

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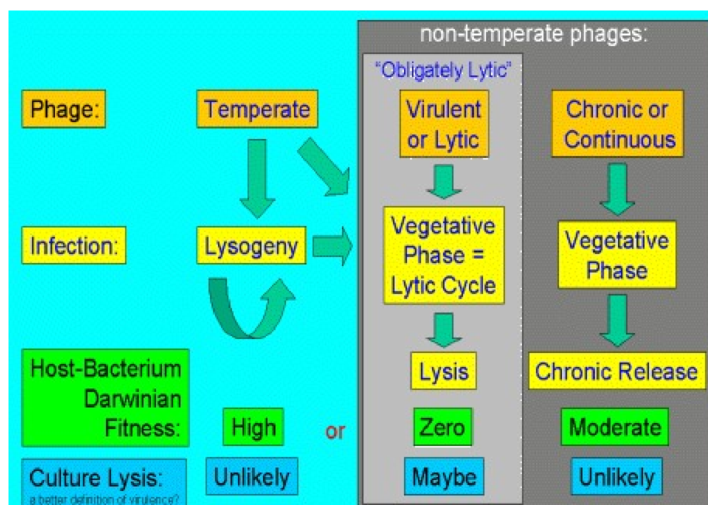
Editorial

Editorials should be written on subjects relevant to The Bacteriophage Ecology Group as an organization, to *BEG News* (either the concept or a given issue of *BEG News*), or the science of Bacteriophage Ecology. While my assumption is that I will be writing the bulk of these editorials, I wish to encourage as many people as possible to seek to relieve me of this duty, as often as possible. Additionally, I welcome suggestions of topics that may be addressed. Please address all correspondences to abedon.1@osu.edu or to "Editorials," *Bacteriophage Ecology Group News*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906. Please send all submissions as Microsoft Word documents, if possible (I'll let you know if I have trouble converting other document formats), and in English.

Lytic, Lysogenic, Temperate, Chronic, Virulent, Quoi?



"The power to lysogenize is the property of temperate phages, as opposed to virulent ones."

- André Lwoff, 1953 -

Welcome to the wonderful world of bacteriophage classification based on phage-host interaction. It turns out that there is some confusion as to how one classifies these interactions. Here, then, are a few definitions, which I follow with a proposition that we stop describing lytic, non-temperate phages as "virulent." I find all of these terms useful (except virulence as typically defined), but only when properly employed. Thus, there is no such thing as a "lysogenic phage" and temperate phages typically are perfectly capable of lysing their bacteria hosts.

Lytic:	In order to release progeny into the extracellular environment, a lytic phage must terminate its infection and breach its host's cell envelope. "Lytic phage" and "Virulent phage" are used synonymously (Lwoff, 1953. Lysogeny. *Bacteriological Reviews* 17:269-337).
Chronic (Continuous):	A lytic infection contrasts with a chronic (or continuous) infection. A chronically infecting phage (or virus) can release progeny into the extracellular environment without terminating its infection. That is, phages are extruded across the host cell envelope continuously (a.k.a., chronically).
Lysogenic:	Also contrasting lytic (as well as chronic) is lysogenic. "A lysogenic bacterium is a bacterium possessing and transmitting the power to produce bacteriophage" (p. 271, Lwoff, 1953). During the lysogenic cyle an infected bacterium does not produce phage progeny nor release phage progeny into the extracellular environment.
Temperate:	A temperate phage is one that is capable of displaying a lysogenic infection. Note that temperate phages typically display a lytic cycle as their vegetative (i.e., non-lysogenic) phase. Nevertheless, one does not refer to temperate phages as lytic phages.
Virulent:	Unfortunately, the standard term used to describe a lytic but not temperate phage is virulent. A virulent phage is one that does not display a lysogenic cycle.

Common practice has been to differentiate phages into at least two types, temperate versus virulent or lytic, to which a third type, chronic or continuous, should be habitually included. Temperate phages can produce reductive (lysogenic), productive, or abortive infections while non-temperate phages can give rise only to productive or abortive infections. Chronically infecting phages extrude their progeny from infected cells without lysing their hosts, while both temperate and lytic (or virulent) phages lyse their hosts to release progeny phages. Unfortunately, this contrast between chronic release and lytic release gives rise to an ambiguity: Temperate phages, in practice, are lytic, but, strictly speaking, are not "Lytic phages." Less ambiguous, temperate phages are not virulent phages, but as I will consider, this latter term, too, is problematic.

The term "Virulence" dates from early phage characterization in which it was noted that some phages more readily lyse cultures of bacteria than others. For instance:

> The question of virulence has been mentioned and emphasis placed upon the necessity of utilizing a race of maximum virulence. By this is meant a race of bacteriophage which will cause a complete and permanent dissolution of the organisms actually present in the infectious process. (p. 178, F. d'Herelle as translated by G. H. Smith, 1930. The *Bacteriophage and its Clinical Applications.* Charles C. Thomas, Publisher. Springfield, Illinois)

Only subsequently did the term "Virulent" come to designate those phages that fail to display lysogeny in the modern sense of that term:

> Phages have been classified in two categories, temperate and virulent according to the presence of [sic] absence of the power to lysogenize. (p. 319, Lwoff, 1953)

Regardless, I am of the opinion that it is time to stop employing the term virulent as a synonym for not temperate. Why? First, it is very likely that by doing so we do not use the term in its original sense. Second, especially as we ponder the use of phages as antibacterial agents, it is probably useful (taking d'Herelle's lead) to have a term that distinguishes those phages that more readily lyse bacterial cultures from those that less readily lyse bacterial cultures. Virulent is the obvious and perhaps original term used for this purpose. Third, without extensive molecular characterization there is always significant uncertainty surrounding our declarations of phage virulence in the Lwoff sense:

> Unfortunately, the definition of the character virulent is purely negative. If, after the action of a temperate phage, most survivors are nonlysogenic, the rare lysogenic survivors, because of their low proportion, may be practically impossible to find. Thus, as a result of the study of a system with a low lysogenization quotient, a temperate phage could be considered as virulent... and one may conceive of a phage behaving as a strong virulent in one bacterium and able to be reduced to a prophage into another. (p. 319, Lwoff, 1953)

Lastly, as pointed out by Michael DuBow during this past June's Montreal phage meeting, the term **VIRULENT** has some serious PR baggage as phage therapists ponder injecting what we hope are harmless little viruses into people's arms.

What's the alternative? Except for the various *vir* derivatives of temperate phages (the description of which is sufficiently ingrained that there is no going back), I propose using "Obligately lytic" to describe those phages that obligately initiate their lytic cycle upon successful adsorption, especially if one has demonstrated to some reasonable degree that a "Lytic phage" truly is not capable of inducing lysogeny on any host. I reject "Non-temperate" as a synonym because chronically infecting phages are also non-temperate but are not obligately lytic.

We should reserve virulent as a description of the ability of a phage to kill some (large) proportion of the cells found within a bacteria culture.

MicroDude, a.k.a., **Stephen T. Abedon**

Developer and Editor

Editorial Archive

- BEG: What we are, Where we are, Where we're going
- When Grown *In Vitro*, do Parasites of Multicellular Organisms (MOPs) become Unicellular Organism Parasites (UOPs)?
- Bacteriophages as Model Systems
- 2000 and Sun: A Phage Odyssey
- Lytic, Lysogenic, Temperate, Chronic, Virulent, Quoi?

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New BEG Members

The BEG members list can be found at www.phage.org/beg_members.htm as well as on the BEG home page. As we add new members, these individuals will be introduced in this section. Note that, in fact, there are two ways of "joining" BEG. One, the "traditional" way, is to have your name listed on the web page and on the list server. The second, the "non-traditional" way, is to have your name only listed on the list server. The latter I refer to as "non-members" on that list. Members, e.g., individuals listed on the BEG home page, should be limited to individuals who are actively involved in science and who can serve as a phage ecology resource to interested individuals. If you have an interest in phage ecology but no real expertise in the area, then you should join as a non-member. To join as a member, please contact BEG using the following link: abedon.1@osu.edu. Include:

- your name
- your e-mail address
- your snail-mail address
- the URL of your home page (if you have one)
- a statement of whether or not you are the principal investigator
- a statement of your research interests (or phage ecology interests)
- a list of your phage ecology references, if any

Note that it is preferable that you include the full reference, including the abstract, if the reference is not already present in the BEG bibliography. Responsibility of members includes keeping the information listed on the BEG members list up to date including supplying on a reasonably timely basis the full references of your new phage ecology publications. Reprints can also be sent to *The Bacteriophage Ecology Group*, care of Stephen Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906. To join BEG as a non-member, please contact BEG using the following link: abedon.1@osu.edu and minimally include your name and e-mail address.

Please welcome our newest members

name (home page links)	status	e-mail	address
Richard M. Carlton	PI	carltonebi @erols.com	Exponential Biotherapies, Inc., 150 Main Street, Port Washington, NY 11050
	interests:	Exponential Biotherapies, Inc. ("EBI") is a development-stage biotechnology company with phages about to enter into clinical trials. The company's major targets at this time are the highly drug-resistant hospital strains of *Enterococcus faecium*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Additional pathogens are on the "back burner", and the company is interested in hearing from scientists as well as clinicians who have interests in the pathogens both in the human sector and the agricultural sector. Press here for more.	
Aidan Coffey	PI	acoffey @moorepark.teagasc.ie	Department of Dairy Quality, TEAGASC-Moorepark, Fermoy Co., Cork, Ireland
	interests:	Impact of bacteriophages on dairy fermentations; Bacteriophage therapy in dairy husbandry.	
Allan L. Delisle	PI	ald001 @dental.umaryland.edu	Associate Professor of Microbiology, Dept. of O.C.B.S., School of Dentistry, Univ. of Maryland, Baltimore, Baltimore, MD 21201
	interests:	I've had a long-standing interest in, and have worked with many, phages of oral bacteria, both gram-negatives and gram-positives.	
Michael S. DuBow	PI	msdubow @microimm.mcgill.ca	Department of Microbiology and Immunology, McGill University, 3775 University Street, Montreal, Quebec, Canada H3A 2B4
	interests:	Genome conformational and sequence rearrangement; *Pseudomonas aeruginosa* temperate transposable bacteriophages (Mu and D108). Our ultimate goal is to understand, at the molecular level, the organization and regulation of a cell's genome, and the protein-DNA interactions that govern its dynamic structure and expression.	
Jason Gill	---	jasongil @uoguelph.ca	Department of Food Science, University of Guelph, Guelph, Ontario N1G 2W1
	interests:	Phage therapy against plant and animal pathogenic bacteria. Current work is focusing on prophylaxis and/or treatment of *Staphylococcus aureus* infections. This work includes collection and characterization of phages from the environment.	

David Kairys	---	kairysod @key-net.net	Pennsylvania State University, Du Bois, 269 Treasure Lake, DuBois, Pennsylvania 15801
	interests:	Streptococcal phage.	
Andrew M. Kropinski	PI	kropinsk @post.queensu.ca	Dept. of Microbiology, Queen's University, Kingston, Ontario K7L 3N6, Canada
	interests:	Bacteriophage genomics and evolution. We have recently sequenced the genome of the serotype- converting *Pseudomonas aeruginosa* bacteriophage D3. In addition, we have completed the sequence of *Salmonella typhimurium* bacteriophage P22 and I have authored an online analysis tool of step-by-step sequence analysis using available online methods.	
Victor Krylov	PI	krylov@genetika.ru, kry38vik@yahoo.com, krylov @vniigenetika.msk.su	The State Institute for Genetics and Selection of Industrial microorganisms, 1-st Dorozhnii proezd, 1, Moscow 113545, RUSSIA
	interests:	Looking for and studyiing phages active on different pseudomonads, mainly belonging to fluorescent group, including soil pseudomonads.	
Maria I. Pajunen	---	maria.pajunen @utu.fi	Department of Medical Biochemistry, University of Turku, Kiinamyllynkatu 10, FIN-20520 Turku FINLAND
	interests:	Genomes, interrelationships, evolution and host ranges of T7 group phages.	
Markus Weinbauer	PI	wein @nioz.nl	Netherlands Institute of Sea Research, Dept Biological Oceanography, POB 59, 1790 AB Den Burg, Texel, The Netherlands
	interests:	Distribution of lytic and lysogenic life cycles in natural marine-virus communities; effect of viral lysis on bacterial mortality and element cycling; viral diversity and effect of phages on marine bacterial diversity; phage-host interactions; evolution of viruses and their subcellular relatives, the transposable elements.	

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New Links

Links relevant to The Bacteriophage Ecology Group fall into a number of categories (e.g., see Bacteriophage Ecology Links at www.phage.org/beg_links.htm). Listed below are new links found on that page. If you know of a link that should be included on this page, or the whereabouts of a now-dead link, please let me know.

New Bacteriophage Ecology (Etc.) Links

- **The Bacteriophage Ecology Group Phage-Ecology Synopsis**
- Cyanophage Project
- Isolation of Cyanophages from Environmental Sources
- Microbial Predation in Planktonic Communities
- Comparison of viruses that lyse the marine photosynthetic flagellate *Micromonas pusilla* using quantitative DNA-DNA hybridization
- Design and use of PCR primers for B-family DNA polymerase genes to detect and identify viruses and microbes
- Development of a PCR-based technique for detecting and quantifying algal viruses in aquatic environments
- DNA polymerase genes as probes of the diversity and phylogeny of marine microbial populations
- The effect of cyanophages on *Synechococcus* spp. during a bloom in the western Gulf of Mexico
- The effect of viruses on the mortality of natural communities of phytoplankton
- Genetic diversity in marine viral communities
- Hopanoids as molecular tracers for cyanobacteria in modern and ancient marine environments (this abstract is not at the top of this page)
- In situ light mediated destruction and repair of marine virus communities and isolates
- Infective cyanophages persist in anoxic sediments on the continental shelf of the Gulf of Mexico
- Induction of a temperate marine cyanophage by heavy metal
- Isolation and characterization of a species specific bacterial pathogen which lyses the marine diatom *Navicula pulchripora*
- Isolation and initial characterization of a lytic mycoplasmalike organism which infects a marine diatom (*Navicula pulchripora*)
- Isolation of lytic viruses which infect a marine heterotrophic nanoflagellate
- Occurrence and isolation of viruses which infect marine *Chrysochromulina* spp
- Persistence and infectivity of cyanophage from polar environments: Implications for planetary protection (this abstract is not at the top of this page)
- A persistent bloom-forming alga that cannot use nitrate-nitrogen
- Photorepair restores UV-radiation-induced damage in marine bacteriophages and maintains high bacterial mortality
- Phylogeny of *Aureococcus anophagefferens* and a morphologically similar bloom-forming alga from Texas, as determined by 18S rDNA sequence analysis
- Phylogeny of large double-stranded DNA viruses which infect microalgae, as inferred from DNA polymerase gene sequences
- Seasonal light effects on cyanophage communities
- Sequence analysis indicates high genetic diversity in marine algal virus communities
- Significance of photoreactivation for maintaining high concentrations of infectious viruses in the sea
- Sunlight-induced DNA damage and in marine viral communities
- The use of cyanine dyes for quantifying free viruses in natural water samples by epifluorescent microscopy
- Viruses as regulators of nutrient cycles in aquatic environments
- What is the impact of viruses on marine *Synechococcus*?
- **The Bacteriophage Ecology Group Phage-Therapy Providers**
- Bacteriophages in Biotechnology (July 13 London meeting that includes coverage of phage therapy)

- Bacteriophage Therapy (AP Biology site)
- Biotech (review of Intralytix) (WashTech.com-*The Sun*)
- Defeat of a Superbug (abc News.com)
- Fight Fire with Fire
- Fighting Superbugs With Phages (radio web rebroadcast)
- Hospital Horror
- The Hunt is On: For New Ways to Overcome Bacterial Resistance
- More Phages (eGroups transcript of Phage Medicine April 10, 2000, radio interview)
- PhageTherapy.Com (5/14/00 note to phagetherapy.com webmaster: your e-mail form is not working)
- PhageTherapy.Com Links Page
- Phage/Phage Medicine (transcript of a phage-therapy themed radio show)
- Revealed: our best hope to beat the killer 'superbugs' (Millennium Debate)
- Sewage saves Lives!
- Viruses may help fight bacteria that resist antibiotics (*The Guardian*)
- Window Of Superbug Vulnerability Begins (www.sightings.com)
- Bacteriophage (Encyclopedia Britannica)
- Lysogeny
- Werner Arbor (1929-present)
- Sir (Frank) Macfarlane Burnet (1899-1985): Encyclopedia Britanica
- Deoxyribonucleic acid
- Max Delbrück (1906-1981): Encyclopedia Britanica
- Felix D'Herelle (1873-1949)
- Alfred Day Hershey (1908-1997): Encyclopedia Britanica
- Joshua Lederberg (1925-present): Encyclopedia Britanica
- The Joshua Lederberg Papers
- Joshua Lederberg (1925-present): Nobel Prize
- Salvador Luria (1912-1991): Encyclopedia Britanica
- Phage Group
- Norton David Zinder (1928-present): Encyclopedia Britanica
- Laboratory of Genetics (Zinder's lab homepage)
- Intralytix, Inc.

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New Features

In this section I highlight new or updated features of the BEG site. If you have any ideas of how either the BEG site or *BEG News* might be improved, please let me know.

Bacteriophage Ecology Synopsis:

The Bacteriophage Ecology Synopsis summarizes the various sub-fields encompassed by bacteriophage ecology. This page is a work in progress and I am very much open to suggestions on such things as content, order, addition/removal of headings/subheadings, addition/removal of associated researchers, etc. Please contact me with any suggestions.

Bacteriophage Ecology Group Meetings page:

The Bacteriophage Ecology Group Meetings page has been updated to include: a calendar with meeting days highlighted and linked to meetings descriptions, and with additional meetings included. Please contact me with suggestions and corrections. Note that not all listed meetings have phage ecology as their primary emphasis. Instead, I've listed as many meetings as I have become aware of that might be of interest to phage workers so that phage ecology-emphasizing meetings could be scheduled during non-conflicting times. I am particularly lacking on this page meetings that are appealing to ecological/evolutionary types so please, if you are interested in phage ecology plus attend meetings with this latter emphasis, please contact me with meeting names and dates.

Phage-Therapy Providers:

This new page is very meager with its listings, but has the potential to lead people to providers that employ phage therapy in their practice. The list is intended to be worldwide inclusive rather than limited to North American providers. If there is sufficient interest, the list can always be subdivided by region. Please see the page for an indication of what information is needed for you to be listed, and please make sure you send a brief description of what you do.

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Upcoming Meetings

The BEG Meetings link will continue. Reminders of upcoming meetings will be placed in this section of *BEG News*. If you know of any meetings that might be of interest to BEG members, or would like to recap a meeting that you've attended, then please send this information for posting to abedon.1@osu.edu or to "BEG Meetings," *Bacteriophage Ecology Group News*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906.

International Phage Meeting:

This meeting, held June 7-11, 2000, in Montreal was a blast and very good to boot. Montreal is great (though the cafeteria food left much room for improvement). Thank you to Michael Dubow and Betty Kutter for their efforts organizing and hosting the meeting. A copy of the meeting's program can be found at the web site. BEG members in attendance included:

- Stephen Abedon
- Hans Ackermann
- Richard Carlton
- Michael DuBow
- Jason Gill
- Larry Goodridge
- Cameron Haase-Pettingell
- Sidney Hayes
- Andrew Kropinski
- Betty Kutter
- Michael McShan
- Maria Pajunen

A number of additional individuals with phage ecology interests, but who are not-yet BEG members, also attended. All together an impressive phage ecology presence and one we will, with your help, improve upon next time.

International Phage Meeting:

So when is next time? Reasonably confident word has it that the next International Phage Meeting (no web site yet) will be held August 8-13, 2001, on the campus of The Evergreen State College in Olympia, Washington, with Betty Kutter back in her familiar role as host. Yes, that was not a typo, the next meeting will be next year, not just in 2002. Be there, or be square!

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Jobs

The BEG Employment / Job Listings page is no longer be maintained. Instead, any job listings will be found in this section of *BEG News*. If you are looking to *fill* a bacteriophage-ecology related position or are in *search of* a bacteriophage-ecology related position, please feel free to advertise as s uch here (there will be no charge, of course). Legitimate information only, please, and *BEG News* cannot be held responsible for any incorrect information supplied by posters. Send any information for posting to abedon.1@osu.edu or to "BEG Jobs," *Bacteriophage Ecology Group News*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906.

POSITION ANNOUNCEMENT: POSTING DATE: 1-31-2000; AVAILABILITY: IMMEDIATE

Post-doctoral position in *Salmonella* and enterohemorragic *E.coli* (EHEC) phage ecology and phage therapy: Position available to investigate the natural history, field ecology and diagnostic and/or therapeutic potential of bacteriophages specific for *Salmonella typhimurium* and EHEC O157, O111, and O26 in the livestock production environment. Will involve both lab and field based research. Ideal candidate will be a PhD microbiologist with experience in isolating and characterizing bacteriophages from the field. Previous work experience with Salmonella and EHEC is not necessary. Two year position with annual extensions possible. Annual salary of approx. $38,000 + benefits. Starting date: negotiable, but prefer between prior to Sept 2000. Interested candidates should contact Jim Keen, Animal Health Research Unit, USMARC, Clay Center, NE 68933; Ph: 402-762-4343 Email: keen@email.marc.usda.gov for additional information.

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Submissions

Submissions are non-editorial items describing or highlighting some aspect of bacteriophage ecology including news pieces, historical pieces, reviews, and write- ups of research. Peer review of submissions is possible and a desire for peer review should be indicated. Send all submissions to abedon.1@osu.edu or to "Submissions", Bacteriophage Ecology Group News, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906. Please send all submissions as Microsoft Word documents, if possible (I'll let you know if I have trouble converting any other doc ument formats), and in English.

No entry.

Submission Archive

- On an Invisible Microbe Antagonistic to the Dysentery Bacillus by Felix d'Herelle
- Obituary: Hansjürgen Raettig - Collector of Bacteriophage References (October 12, 1911 - December 1, 1997)
- Some Quotations

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Letters

Letters should consist of comments, short statements, or personal editorials. Send all letters to abedon.1@osu.edu or to "Letters", Bacteriophage Ecology Group News, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906. Please send all letters in English and all mailed or attached letters as Microsoft Word documents, if possible (I'll let you know if I have trouble converting any other document formats). In addition, to standard letters, BEG receives questions on a regular basis that may be addressed by BEG members. These questions are listed below. Anybody interested in answering these questions through *BEG News*, e-mail me at the following address: abedon.1@osu.edu. Alternatively, answer by clicking the authors name. Please note that these questions have not been edited for grammar, spelling, or clarity.

Questions

Question:

My name is Deepa Alagesan, and I am a ninth grader at Manhasset High School. I have been visiting your site regularly online. I am in the science research program at my school, and came across your site while searching for a new topic for my sophomore year. This year I did a study on The Effects of Subinhibitory Concentrations of Ampicillin and Tetracycline on the Development of Antibiotic Resistance, which I won 3rd place overall in general biology at the Shipley Ronal Invitational Science Fair in two weeks. I became really interested in the use of bacteriophage therapy as an alternative to antibiotic treatment.

When I read your paper, I was fascinated by the possibility of being able to use a virus to combat bacterial infections. I have started to look into the area of bacteriophage therapy and the work that is being done is amazing! I also think that it is a great area for research. Unfortunately, I am currently stuck in trying to come up with a significant problem and purpose. I have been unable to establish a controversy. My research advisor, Peter Guastella, suggested that I look in the area of urinary tract infections, and bacteriophages as a novel treatment in that area.

Being totally new to this subject, I was wondering what challenges you faced during your work. I would really like to be able to develop this new interest into a project for next year. Do you have any ideas of directions that I could head in? Any suggestions or help that you can offer would be greatly appreciated!

Sincerely,

Deepa Alagesan

Reply:

Dear forward-looking highschooler: get a copy of the 1994 issue of *Molecular Biology of Bacteriophage T4*, THEN try to read just a few pages (my favorite is the one RE mutagenesis)... Next, look yourself in the mirror and sincerely ask yourself if you are really barking up the right tree, or not! I am, from my own personal experience, psyched out by this stuff... the relatively simple concept of a virus doing to bacteria what we do here in the Pennsylvania forests (spraying gypsie moth populations with a bacterium toxic to the insects) is of course quite nice and attractive, but lets face it, that one cute idea won't build you an experimental program! There is a huge amount of "heavy lifting" to do before one can play with these coliform bacteriophages... I'm on my 2nd night of 30 minute reading and I'm not a happy camper... Perhaps, just perhaps, we can steal some TECHNIK from the brains of another colleague, and proceed to do a study whereby we apply some of the pretty mathematical calculations to our findings... I envision manipulating a radiation parameter, and determining what effect that has on one of the dependent variables of phage population growth dynamics... BUT, I've just GOT to get some more of this jargon straight first... Why not get a copy of that book, and then get back to me... They say all the truly powerful science is done by people under 30 (that's you buddy), so I'm really in this just for fun, and I doubt my ability to do much beyond just that! Its no fun looking at words when you've got no idea about (rII for example) but I'll muddle just a bit more...

David Kairys

Question:

I read the informations on phage.org and I have some special questions to you:

1. Are phages avaliable for treatment of *Brucella* species (*abortus*, *suis*, *melitensis*) ?
2. If yes, are these phages able to penetrate in different kinds of human cells to infect and kill intracellular located *Brucella* bacteria (because *Brucella* is an intracellular phatogen)?
3. How are the chances in chronic and long-term infections to reach and destroy all bacteria?

Thanks in advice for your efforts.

Sincerely,

Markus Bollmann

Question:

I am trying to track down a viable culture of the small *P. aeruginosa* RNA phage PP7. The lab that published the complete sequence no longer has viable stock and I have tried a variety of other sources. If you could suggest possible routes to track this down I would be most grateful.

Regards,

Paul Rainey

Question:

I am a high school biology teacher and I just recently watched a BBC video on the Georgian's work in the field of Phage medicine. This is extremely interesting to me. If I can get any information on the most recent attempts to make Phage medicine a main stream practice in the US please e-mail me back and tell me where I could get this information.

Thank You,

S Sralla

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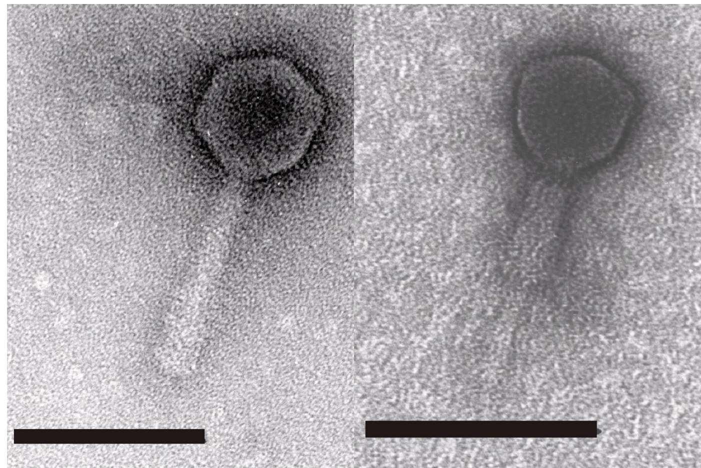
Phage Images

Please send any phage images that you would like to present in this section to "Phage Images," *The Bacteriophage Ecology Group*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906. Alternatively, you may scan the images yourself and send them as an attachment to abedon.1@osu.edu. Please save all scans in gif or jpg formats and preferably with an image size (in terms of width, height, and kbytes) that will readily fit on a standard web page.



Phage Image Archive

- The Face of the Phage
- Bacteriophage T2 by H.-W. Ackermann
- SSV1-Type Phage
- Saline Lake Bacteriophage - David Bird
- Coliphage LG1 - Larry Goodridge

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New Publications

New bacteriophage publications are listed below. Each quarter not-yet-listed publications from the previous two years will be presented along with their abstracts. The indicator "???" denotes, of course, that specific information is not yet in the BEG Bibliography. Please help in the compilation of the BEG Bibliography by supplying any updated information, correcting any mistakes, and, of course, sending the references to your bacteriophage ecology publications, as well as the references to any bacteriophage ecology publications that you know of but which are not yet in the bibliography (send to abedon.1@osu.edu or to "BEG Bibliography," *Bacteriophage Ecology Group News*, care of Stephen T. Abedon, Department of Microbiology, The Ohio State University, 1680 University Dr., Mansfield, Ohio 44906). Also, be sure to indicate any listed publications that you feel should not be presented in the BEG Bibliography. This list is also present with available abstracts at the end of *BEG News*.

1. Serotype-converting bacteriophages and O-antigen modification in *Shigella flexneri*. Allison, G. E., Verma, N. K. (2000). *Trends in Microbiology* 8:17-23. [PRESS FOR ABSTRACT]

2. Inactivation of MS-2 phage and poliovirus in groundwater. Alvarez, M. E., Aguilar, M., Fountain, A., Gonzalez, N., Rascon, O., Saenz, D. (2000). *Canadian Journal of Microbiology* 46:159-165. [PRESS FOR ABSTRACT]

3. Application of bacteriophages as surrogates for mammalian viruses: a case for use in filter validation based on precedents and current practices in medical and environmental virology. Aranha-Creado, H., Brandwein, H. (1999). *PDA Journal of Pharamaceutical Science and Technology* 53:75-82. [PRESS FOR ABSTRACT]

4. A shared strategy for virulence. Barinaga, M. (2000). *Science* 272:1261-1263. [no abstract]

5. 'Deja vu all over again': the similar structures of bacteriophage PRD1 and adenovirus. Belnap, D. M., Steven, A. C. (2000). *Trends in Microbiology* 8:91-93. [no abstract]

6. Biological UV dosimeters in the assessment of the biological hazard from environmental radiation. Berces, A., Fekete, A., Gaspar, S., Grof, P., Rettberg, P.,

Horneck, G., Ronto, G. (1999). *Journal of Photochemistry and Photobiology B, Biology* 53:36-43. [PRESS FOR ABSTRACT]

7. Reconsidering the relationship between virally induced bacterial mortality and frequency of infected cells. Binder, B. (1999). *Aquatic Microbial Ecology* 18:207-215. [no abstract]

8. *Helicobacter pylori*-antigen-binding fragments expressed on the filamentous M13 phage prevent bacterial growth. Cao, J., Sun, Y., Berglindh, T., Mellgard, B., Li, Z., Mardh, B., Mardh, S. (2000). *Biochimica et Biophysica Acta* 1474:107-113. [PRESS FOR ABSTRACT]

9. Increasing the phage resistance of cheese starter *Lactococcus lactis* DPC4268 in response to the emergence of a novel highly virulent phage in industry. Coffey, A., Coakley, M., McGarry, A., Fitzgerald, G. F., Ross, R. P. (1998). pp. 460-481 in ??? (ed.) *Actes du Colloque LACTIC-97 Lactic Acid Bacteria: Which strains? For which products?*. Villers Bocage, Cedex, France. [no abstract]

10. Determination of enteroviruses, hepatitis A virus, bacteriophages and *Escherichia coli* in Adriatic Sea mussels. Croci, L., De, Medici D., Scalfaro, C., Fiore, A., Divizia, M., Donia, D., Cosentino, A. M., Moretti, P., Costantini, G. (2000). *Journal of Applied Microbiology* 88:293-298. [PRESS FOR ABSTRACT]

11. Convergence of the secretory pathways for cholera toxin and the filamentous phage, CTXphi. Davis, B. M., Lawson, E. H., Sandkvist, M., Ali, A., Sozhamannan, S., Waldor, M. K. (2000). *Science* 288:333-335. [PRESS FOR ABSTRACT]

12. [Water quality control of 2 swimming pools in Rome. Evaluation of the bacteriophage parameter]. Donia, D., Divizia, M., della, Sallette Mattiacci, Pana, A. (2000). *Annali di Igiene* 12:35-39. [no abstract]

13. Evaluation of F-specific RNA bacteriophage as a candidate human enteric virus indicator for bivalve molluscan shellfish. Dore, W. J., Henshilwood, K., Lees, D. N. (2000). *Applied and Environmental Microbiology* 66:1280-1285. [PRESS FOR ABSTRACT]

14. Genetic analysis of chromosomal regions of *Lactococcus lactis* acquired by recombinant lytic phages. Durmaz, E., Klaenhammer, T. R. (2000). *Applied and Environmental Microbiology* 66:895-903. [PRESS FOR ABSTRACT]

15. Toward antiviral strategies that resist viral escape. Endy, D., Yin, J. (2000). *Antimicrobial Agents and Chemotherapy* 44:1097-1099. [PRESS FOR ABSTRACT]

16. Widespread distribution of a group I intron and its three deletion derivatives in the lysin gene of *Streptococcus thermophilus* bacteriophages. Foley, S., Bruttin, A., Brussow, H. (2000). *Journal of Virology* 74:611-618. [PRESS FOR ABSTRACT]

17. The effect of cyanophages on the morality of *Synechococcus* spp. and selection for UV resistant viral communities. Garza, D. R., Suttle, C. A. (1998). *Microbial Ecology* 36:281-??? [no abstract]

18. Evolution: the long evolutionary reach of viruses. Hendrix, R. W. (1999). *Current Biology* 9:R914-R917. [PRESS FOR ABSTRACT]

19. The microbial genetics of antibiotic cycling. John, J. F. Jr, Rice, L. B. (2000). *INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY* 21:S22-S31. [PRESS FOR ABSTRACT]

20. Shiga toxins even when different are encoded at identical positions in the genomes of related temperate bacteriophages. Karch, H., Schmidt, H., Janetzki-Mittmann, C., Scheef, J., Kroger, M. (1999). *Molecular and General Genetics* 262:600-607. [PRESS FOR ABSTRACT]

21. Target genes for virulence assessment of *Escherichia coli* isolates from water, food and the environment. Kuhnert, P., Boerlin, P., Frey, J. (2000). *FEMS Microbiology Reviews* 24:107-117. [PRESS FOR ABSTRACT]

22. Multiplex PCR for detection and identification of lactococcal bacteriophages. Labrie, S., Moineau, S. (2000). *Applied and Environmental Microbiology* 66:987-994. [PRESS FOR ABSTRACT]

23. Genetic analysis of a bacterial genetic exchange element: the gene transfer agent of *Rhodobacter capsulatus*. Lang, A. S., Beatty, J. T. (2000). *Proceedings of the National Academy of Sciences, USA* 97:859-864. [PRESS FOR ABSTRACT]

24. Bacteriophages as indicators of enteric viruses and public health risk in groundwaters. Leclerc, H., Edberg, S., Pierzo, V, Delattre, J. M. (2000). *Journal of Applied Microbiology* 88:5-21. [PRESS FOR ABSTRACT]

25. Isolation and characterization of a generalized transducing phage for the marine luminous bacterium *Vibrio fischeri* MJ-1. Levisohn, R., Moreland, J., Nealson, K. H. (2000). *Journal of General Microbiology* 133:1577-1582. [no abstract]

26. Complete nucleotide sequence, molecular analysis and genome structure of bacteriophage A118 of *Listeria monocytogenes*: implications for phage evolution. Loessner, M. J., Inman, R. B., Lauer, P., Calendar, R. (2000). *Molecular Microbiology* 35:324-340. [PRESS FOR ABSTRACT]

27. Rapid in vivo evolution of a beta-lactamase using phagemids. Long-McGie, J., Liu, A. D., Schellenberger, V (2000). *Biotechnology and Bioengineering* 68:121-125. [PRESS FOR ABSTRACT]

28. [Natural interspecific hybrids of transposable phages of *Pseudomonas aeruginosa*]. Mit'kina, L. N., Krylov, V. N. (1999). *Genetika* 35:1182-1190. [PRESS FOR ABSTRACT]

29. *Escherichia coli* O157 strains which caused Japanese outbreaks have residues of bacteriophage sequences. Miyahara, M., Konuma, H. (1999). *Biological and Pharmaceutical Bulletin* 22:1372-1375. [PRESS FOR ABSTRACT]

30. The role of the spectral sensitivity curve in the selection of relevant biological dosimeters for solar UV monitoring. Modos, K., Gaspar, S., Kerekgyarto, T., Vink, A. A., Roza, L., Fekete, A. (1999). *Journal of Photochemistry and Photobiology B Biology* 53:20-25. [PRESS FOR ABSTRACT]

31. Multiple independent horizontal transfers of informational genes from bacteria to plasmids and phages: implications for the origin of bacterial replication machinery. Moreira, D. (2000). *Molecular Microbiology* 35:1-5. [PRESS FOR ABSTRACT]

32. Occurrence and numbers of bacteriophages and bacterial indicators in faeces of yellow-legged seagull (*Larus cachinnans*). Muniesa, M., Jofre, J., Lucena, F. (1999). *Letters in Applied Microbiology* 29:421-423. [PRESS FOR ABSTRACT]

33. Occurrence of phages infecting *Escherichia coli* O157:H7 carrying the Stx 2 gene in sewage from different countries. Muniesa, M., Jofre, J. (2000). *FEMS Microbiology Letters* 183:197-200. [PRESS FOR ABSTRACT]

34. Investigation of the relationship between lysogeny and lysis of *Lactococcus lactis* in cheese using prophage-targeted PCR. O'Sullivan, D., Ross, R. P., Fitzgerald, G. F., Coffey, A. (2000). *Applied and Environmental Microbiology* 66:2192-2198. [no abstract]

35. Isolation of bacteriophages specific to a fish pathogen, *Pseudomonas plecoglossicida*, as a candidate for disease control. Park, S. C., Shimamura, I, Fukunaga, M., Mori, K. I., Nakai, T. (2000). *Applied and Environmental Microbiology* 66:1416-1422. [PRESS FOR ABSTRACT]

36. Induction of vaginal *Lactobacillus* phages by the cigarette smoke chemical benzo[a]pyrene diol epoxide. Pavlova, S. I., Tao, L. (2000). *Mutation Research* 466:57-62. [PRESS FOR ABSTRACT]

37. First report of a putative cyanophage, MC-1 of *Microcoleus* sp. Rosowski, J. R., Shaffer, J. J., Martin, E. L. (1999). *Microsc. Microanalysis* 5:1142-1143. [no abstract]

38. Hospital Horror. Sardar, Z. (1999). *New Statesman* ???-??? [PRESS FOR ABSTRACT]

39. Phenoptosis: programmed death of an organism. Skulachev, V. P. (1999). *Biochemistry* 64:1418-1426. [PRESS FOR ABSTRACT]

40. Identification of four loci isolated from two *Streptococcus thermophilus* phage genomes responsible for mediating bacteriophage resistance. Stanley, E., Walsh, L., van, der Zwet, Fitzgerald, G. F., van, Sinderen D. (2000). *FEMS Microbiology Letters* 182:271-277. [PRESS FOR ABSTRACT]

41. [The effect of low-frequency electromagnetic fields on living organisms]. Strasak, L., Vetterl, V, Smarda, J. (1998). *Sbornik Lekarsky* 99:455-464. [PRESS FOR ABSTRACT]

42. The future of bacterial vaginosis-related research. Taylor-Robinson, D. (1999). *International Journal of Gynaecology and Ostetrics* 67 Suppl 1:S35-S38. [PRESS FOR ABSTRACT]

43. A new *Mesorhizobium loti* HAMBI 1129 phage isolated from Polish soil. Turska-Szewczuk, A., Russa, R. (2000). *Current Microbiology* 40:341-343. [PRESS FOR ABSTRACT]

44. Construction of mini-Tn10luxABcam/Ptac-ATS and its use for developing a bacteriophage that transduces bioluminescence to *Escherichia coli* O157:H7. Waddell, T. E., Poppe, C. (2000). *FEMS Microbiology Letters* 182:285-289. [PRESS FOR ABSTRACT]

45. Effective phage therapy is associated with normalization of cytokine production by blood cell cultures. Weber-Dabrowska, B., Zimecki, M., Mulczyk, M. (2000). *Archivum Immunologiae et Therapiae Experimentalis* 48:31-37. [PRESS FOR ABSTRACT]

46. Cell size-specific lysis of lake bacterioplankton by natural virus communities. Weinbauer, M. G., Höfle, M. G. (1998). *Aquatic Microbial Ecology* 156:103-113. [no abstract]

47. Family values in the age of genomics: comparative analyses of temperate bacteriophage HK022. Weisberg, R. A., Gottesmann, M. E., Hendrix, R. W., Little, J. W. (1999). *Annual Review of Genetics* 33:565-602. [PRESS FOR ABSTRACT]

48. Estimating the infectivity of marine viral communities from measurements of DNA damage and photoreactivation. Wilhelm, S. W., Weinbauer, M. G., Jeffrey, W. H., Suttle, C. A. (1998). *Aquatic Microbial Ecology* 14:215-222. [no abstract]

49. Viruses and nutrient cycles in the sea. Wilhelm, S. W., Suttle, C. A. (1999). *Bioscience* 49:781-788. [no abstract]

50. Virioplankton: viruses in aquatic ecosystems. Wommack, K. E., Colwell, R. R. (2000). *Microbiology and Molecular Biology Reviews* 64:69-114. [no abstract]

51. Quinolone antibiotics induce Shiga toxin-encoding bacteriophages, toxin production, and death in mice. Zhang, X, McDaniel, A. D., Wolf, L. E., Keusch, G. T., Waldor, M. K., Acheson, D. W. (2000). *Journal of Infectious Diseases* 181:664-670. [PRESS FOR ABSTRACT]

52. [Examining interaction of phages with microorganisms by fluorometry and electro-orientation spectroscopy]. Zhilenkov, E. L., Fomchenkov, V. M., Novikov, I. A., Sadomov, V. E., Oborotov, M. V., Gremiakova, T. A. (1999). *Vestnik Rossiiskoi Akademii Medisinskiky Nauk* 24-29. [PRESS FOR ABSTRACT]

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New Publications with Abstracts

For your convenience, a list of new publications without associated abstracts (but with links to abstracts) is found above. The list presented below is identical to the above list except that abstracts are included.

1. **Serotype-converting bacteriophages and O-antigen modification in *Shigella flexneri*. Allison, G. E., Verma, N. K. (2000). *Trends in Microbiology* 8:17-23.** O-antigen modification (serotype conversion) in *Shigella flexneri*, which is an important virulence determinant, is conferred by temperate bacteriophages. Several serotype-converting phages have been isolated and preliminary characterization has identified the genes involved in O-antigen modification, and has also provided insight into the molecular biology of these phages

2. **Inactivation of MS-2 phage and poliovirus in groundwater. Alvarez, M. E., Aguilar, M., Fountain, A., Gonzalez, N., Rascon, O., Saenz, D. (2000).**

***Canadian Journal of Microbiology* 46:159-165.** Since temperature affects the inactivation rate of viruses in natural water systems, the aim of this study was to determine if a temperature shift could influence the structural integrity of model viruses. When crude lysates of MS-2 phage were seeded into groundwater microcosms and incubated at 27 degrees C, complete virus inactivation took place in eight days. The temperature was then shifted to 4 degrees C. Three days after the temperature shift, a two-log increase in virus titer (reactivation) occurred. However, when purified MS-2 lysates were added to groundwater microcosms, no reactivation was obtained. No reactivation of poliovirus took place when similar microcosm experiments were done. The sedimentation coefficients of MS-2 shifted from 80S to 58S, 48S, 37S, 32S, and 18S as inactivation proceeded in groundwater and distilled water controls. Similarly, the sedimentation coefficients of polioviruses changed from 156S to 142S, 135S, 117S, 105S, 95S, and 80 S as inactivation took place. There was no correlation between % virus inactivation and % decrease in virions with intact sedimentation coefficients, as reported earlier for poliovirus inactivated by chlorine. The results presented support our hypothesis that virus inactivation proceeds gradually, involving the rearrangement and (or) loss of capsomere components that may eventually lead to the ejection of nucleic acids. The intermediate particles generated as inactivation proceeds may be in a reversibly inactivated state, and may revert back to a fully infectious state when chemical components stabilize the virus particle

3. **Application of bacteriophages as surrogates for mammalian viruses: a case for use in filter validation based on precedents and current practices in medical and environmental virology. Aranha-Creado, H., Brandwein, H. (1999). *PDA Journal of Pharamaceutical Science and Technology* 53:75-82.** Infectivity-based assays are the assays of choice for the detection of pathogenic mammalian viruses. While it is intuitively appropriate to conduct testing and validation studies with the known viral burden or a closely related mammalian species, logistic considerations often dictate otherwise. Consequently, bacteriophages have served as suitable surrogates for mammalian viruses in both medical and environmental virology applications. The wide range of bacteriophages available offers a powerful analytical tool amenable to several different applications: filter validation studies (where removal is based on size exclusion), investigations into virus contamination control issues, evaluation of barrier materials, etc. There is a considerable body of evidence to suggest and support the use of bacteriophages as surrogates for mammalian viruses. Use of appropriately sized bacteriophages provides an innocuous, efficacious and expeditious method for economical testing and validation of viral clearance capabilities of virus removal filters, thus facilitating performance of filter validation studies in biopharmaceuticals under product- and process-specific conditions in an overall effort towards ensuring the virological safety of biologicals. This paper discusses the limitations associated with mammalian virus assays and provides a rationale for the use of bacteriophages as surrogates for mammalian viruses. Data from published literature documenting applicability of bacteriophages in filter validation studies, especially when removal is based on size exclusion, is reviewed along with examples of studies from the fields of medical and environmental virology

4. **A shared strategy for virulence. Barinaga, M. (2000). *Science* 272:1261-1263.**

5. **'Deja vu all over again': the similar structures of bacteriophage PRD1 and adenovirus. Belnap, D. M., Steven, A. C. (2000). *Trends in Microbiology* 8:91-93.**

6. **Biological UV dosimeters in the assessment of the biological hazard from environmental radiation. Berces, A., Fekete, A., Gaspar, S., Grof, P., Rettberg, P., Horneck, G., Ronto, G. (1999). *Journal of Photochemistry and Photobiology B, Biology* 53:36-43.** To determine the impact of environmental UV radiation, biological dosimeters that weight directly the incident UV components of sunlight have been developed, improved and evaluated in the frame of the BIODOS project. Four DNA-based biological dosimeters ((i) phage T7, (ii) uracil thin layer, (iii) spore dosimeter and (iv) DLR-biofilm) have been assessed from the viewpoint of their biological relevance, spectral response and quantification of their biological effectiveness. The biological dosimeters have been validated by comparing their readings with weighted spectroradiometer data, by comparison with other biological doses, as well as with the determined amounts of DNA UV photoproducts. The data presented here demonstrate that the biological dosimeters are potentially reliable field dosimeters for measuring the integrated biologically effective irradiance for DNA damage

7. **Reconsidering the relationship between virally induced bacterial mortality and frequency of infected cells. Binder, B. (1999). *Aquatic Microbial Ecology* 18:207-215.**

8. ***Helicobacter pylori*-antigen-binding fragments expressed on the filamentous M13 phage prevent bacterial growth. Cao, J., Sun, Y., Berglindh, T., Mellgard, B., Li, Z., Mardh, B., Mardh, S. (2000). *Biochimica et Biophysica Acta* 1474:107-113.** Colonization of the human stomach by *Helicobacter pylori* is associated with the development of gastritis, duodenal ulcer, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer. *H. pylori*-antigen-binding single-chain variable fragments (ScFv) were derived from murine hybridomas producing monoclonal antibodies and expressed as a g3p-fusion protein on a filamentous M13 phage. The recombinant ScFv-phage reacted specifically with a 30-kDa monomeric protein of a *H. pylori* surface antigen preparation and by means of immunofluorescence microscopy the phage was shown to bind to both the spiral and coccoid forms of the bacterium. In vitro, the recombinant phage exhibited a bacteriocidal effect and inhibited specifically the growth of all the six strains of *H. pylori* tested. When H. pylori was pretreated with the phage 10 min before oral inoculation of mice, the colonization of the mouse stomachs by the bacterium was significantly reduced ($P<0.01$). The results suggest that genetic engineering may be used to generate therapy-effective phages

9. **Increasing the phage resistance of cheese starter *Lactococcus lactis* DPC4268 in response to the emergence of a novel highly virulent phage in industry. Coffey, A., Coakley, M., McGarry, A., Fitzgerald, G. F., Ross, R. P. (1998). pp. 460-481 in ??? (ed.) *Actes du Colloque LACTIC-97 Lactic Acid Bacteria: Which strains? For which products?*. Villers Bocage, Cedex, France.**

10. **Determination of enteroviruses, hepatitis A virus, bacteriophages and *Escherichia coli* in Adriatic Sea mussels. Croci, L., De, Medici D., Scalfaro, C., Fiore, A., Divizia, M., Donia, D., Cosentino, A. M., Moretti, P., Costantini, G. (2000). *Journal of Applied Microbiology* 88:293-298.** The aim of the present study was to evaluate the incidence of enteric viruses in mussels and to verify the possibility of using phages as indirect indicators of mussel viral contamination. Mussels (36 samples) collected from three different areas of the Adriatic Sea were analysed to determine the following parameters: *Escherichia coli*, somatic coliphage (T6 phage), F-Plus (MS2 phage), B40-8 (phage of *Bacteroides fragilis*), enteroviruses and hepatitis A virus. Most of the results of the bacteriological analysis (most probable number (MPN) ml-1) were in accordance with the bacteriological limits established by European law, with the exception of seven samples. The bacteriophage analyses were always negative for F-Plus and B40-8, with the exception of a few samples, whereas the somatic coliphages were generally between 0 and 20 MPN g-1, with the exception of two samples (110 MPN g-1). The virological analysis showed five samples positive for the presence of enteroviruses and 13 for the presence of hepatitis A virus (in three samples both viruses were present). Most of these samples presented acceptable bacteriological parameters and the bacteriophages were absent or their value was generally very low. The results show that the detection of *E. coli* and phages does not seem to be a good indicator of viral contamination

11. **Convergence of the secretory pathways for cholera toxin and the filamentous phage, CTXphi. Davis, B. M., Lawson, E. H., Sandkvist, M., Ali, A., Sozhamannan, S., Waldor, M. K. (2000). *Science* 288:333-335.** Virulence of *Vibrio cholerae* depends on secretion of cholera toxin (CT), which is encoded within the genome of a filamentous phage, CTXphi. Release of CT is mediated by the extracellular protein secretion (eps) type II secretion system. Here, the outer membrane component of this system, EpsD, was shown to be required for secretion of the phage as well. Thus, EpsD plays a role both in pathogenicity and in horizontal transfer of a key virulence gene. Genomic analysis suggests that additional filamentous phages also exploit chromosome-encoded outer membrane channels

12. **[Water quality control of 2 swimming pools in Rome. Evaluation of the bacteriophage parameter]. Donia, D., Divizia, M., della, Sallette Mattiacci, Pana, A. (2000).** ***Annali di Igiene*** **12:35-39.**

13. **Evaluation of F-specific RNA bacteriophage as a candidate human enteric virus indicator for bivalve molluscan shellfish. Dore, W. J., Henshilwood, K., Lees, D. N. (2000).** ***Applied and Environmental Microbiology*** **66:1280-1285.** *Escherichia coli* is a widely utilized indicator of the sanitary quality of bivalve molluscan shellfish sold for human consumption. However, it is now well documented that shellfish that meet the *E. coli* standards for human consumption may contain human enteric viruses that cause gastroenteritis and hepatitis. In this study we investigated using F-specific RNA bacteriophage (FRNA bacteriophage) to indicate the likely presence of such viruses in shellfish sold for consumption. FRNA bacteriophage and *E. coli* levels were determined over a 2-year period for oysters (*Crassostrea gigas*) harvested from four commercial sites chosen to represent various degrees of sewage pollution. Three sites were classified as category B sites under the relevant European Community (EC) Directive (91/492), which required purification (depuration) of oysters from these sites before sale. One site was classified as a category A site, and oysters from this site could be sold directly without further processing. Samples were tested at the point of sale following commercial processing and packaging. All of the shellfish complied with the mandatory EC E. coli standard (less than 230 per 100 g of shellfish flesh), and the levels of contamination for more than 90% of the shellfish were at or below the level of sensitivity of the assay (20 *E. coli* MPN per 100 g), which indicated good quality based on this criterion. In contrast, FRNA bacteriophage were frequently detected at levels that exceeded 1,000 PFU per 100 g. High levels of FRNA bacteriophage contamination were strongly associated with harvest area fecal pollution and with shellfish-associated disease outbreaks. Interestingly, FRNA bacteriophage contamination exhibited a marked seasonal trend that was consistent with the trend of oyster-associated gastroenteritis in the United Kingdom. The correlation between FRNA bacteriophage contamination and health risk was investigated further by using a reverse transcription-PCR assay for Norwalk-like virus (NLV). NLV contamination of oysters was detected only at the most polluted site and also exhibited a seasonal trend that was consistent with the trend of FRNA bacteriophage contamination and with the incidence of disease. The results of this study suggest that FRNA bacteriophage could be used as viral indicators for market-ready oysters

14. **Genetic analysis of chromosomal regions of** ***Lactococcus lactis*** **acquired by recombinant lytic phages. Durmaz, E., Klaenhammer, T. R. (2000).** ***Applied and Environmental Microbiology*** **66:895-903.** Recombinant phages are generated when *Lactococcus lactis* subsp. lactis harboring plasmids encoding the abortive type (Abi) of phage resistance mechanisms is infected with small isometric phages belonging to the P335 species. These phage variants are likely to be an important source of virulent new phages that appear in dairy fermentations. They are distinguished from their progenitors by resistance to Abi defenses and by altered genome organization, including regions of L. lactis chromosomal DNA. The objective of this study was to characterize four recombinant variants that arose from infection of *L. lactis* NCK203 (Abi(+)) with phage phi31. HindIII restriction maps of the variants (phi31.1, phi31.2, phi31.7, and phi31.8) were generated, and these maps revealed the regions containing recombinant DNA. The recombinant region of phage phi31.1, the variant that occurred most frequently, was sequenced and revealed 7.8 kb of new DNA compared with the parent phage, phi31. This region contained numerous instances of homology with various lactococcal temperate phages, as well as homologues of the lambda recombination protein BET and *Escherichia coli* Holliday junction resolvase Rus, factors which may contribute to efficient recombination processes. A sequence analysis and phenotypic tests revealed a new origin of replication in the phi31.1 DNA, which replaced the phi31 origin. Three separate HindIII fragments, accounting for most of the recombinant region of phi31.1, were separately cloned into gram-positive suicide vector pTRK333 and transformed into NCK203. Chromosomal insertions of each plasmid prevented the appearance of different combinations of recombinant phages. The chromosomal insertions did not affect an inducible prophage present in NCK203. Our results demonstrated that recombinant phages can acquire DNA cassettes from different regions of the chromosome in order to overcome Abi defenses. Disruption of these regions by insertion can alter the types and diversity of new phages that appear during phage-host interactions

15. **Toward antiviral strategies that resist viral escape. Endy, D., Yin, J. (2000).** ***Antimicrobial Agents and Chemotherapy*** **44:1097-1099.** We studied the effect on viral growth of drugs targeting different virus functions using a computer simulation for the intracellular growth of bacteriophage T7. We found that drugs targeting components of negative-feedback loops gain effectiveness against mutant viruses that attenuate the drug-target interaction. The greater inhibition of such mutants than of the wild type suggests a drug design strategy that would hinder the development of drug resistance

16. **Widespread distribution of a group I intron and its three deletion derivatives in the lysin gene of** ***Streptococcus thermophilus*** **bacteriophages. Foley, S., Bruttin, A., Brussow, H. (2000).** ***Journal of Virology*** **74:611-618.** Of 62 *Streptococcus thermophilus* bacteriophages isolated from various ecological settings, half contain a lysin gene interrupted by a group IA2 intron. Phage mRNA splicing was demonstrated. Five phages possess a variant form of the intron resulting from three distinct deletion events located in the intron-harbored open reading frame (orf 253). The predicted orf 253 gene sequence showed a significantly lower GC content than the surrounding intron and lysin gene sequences, and the predicted protein shared a motif with endonucleases found in phages from both gram-positive and gram-negative bacteria. A comparison of the phage lysin genes revealed a clear division between intron-containing and intron-free alleles, leading to the establishment of a 14-bp consensus sequence associated with intron possession. The conserved intron was not found elsewhere in the phage or S. thermophilus bacterial genomes. Folding of the intron RNA revealed secondary structure elements shared with other phage introns: first, a 38-bp insertion between regions P3 and P4 that can be folded into two stem-loop structures (shared with introns from Bacillus phage SPO1 and relatives); second, a conserved P7.2 region (shared with all phage introns); third, the location of the stop codon from orf 253 in the P8 stem (shared with coliphage T4 and *Bacillus* phage SPO1 introns); fourth, orf 253, which has sequence similarity with the H-N-H motif of putative endonuclease genes found in introns from *Lactococcus*, *Lactobacillus*, and *Bacillus* phages

17. **The effect of cyanophages on the morality of** ***Synechococcus*** **spp. and selection for UV resistant viral communities. Garza, D. R., Suttle, C. A. (1998).** ***Microbial Ecology*** **36:281-???**

18. **Evolution: the long evolutionary reach of viruses. Hendrix, R. W. (1999).** ***Current Biology*** **9:R914-R917.** The structure of a phage capsid protein provides good evidence this phage shares ancestry with an animal virus. In this and similar cases, either the viral lineages predate the emergence of the three contemporary domains of life, or viruses have been leaping the phylogenetic chasms that separate the domains

19. **The microbial genetics of antibiotic cycling. John, J. F. Jr, Rice, L. B. (2000).** ***INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY*** **21:S22-S31.** Cycling of currently available antibiotics to reduce resistance is an attractive concept. For cycling strategies to be successful, their implementation must have a demonstrable impact on the prevalence of resistance determinants already dispersed throughout the hospital and associated healthcare facilities. While antibiotic use in hospitals clearly constitutes a stimulus for the emergence of resistance, it is by no means the only important factor. The incorporation of resistance determinants into potentially stable genetic structures, including bacteriophages, plasmids, transposons, and the more newly discovered movable elements termed integrons and gene cassettes, forces some degree of skepticism about the potential for such strategies in institutions where resistance determinants are already prevalent. In particular, the expanding role of integrons may pose an ultimate threat to formulary manipulations such as cycling. Despite these concerns, the crisis posed by antimicrobial resistance warrants investigation of any strategy with the potential for reducing the prevalence of resistance. Over the next decade, new studies with carefully designed outcomes should determine the utility of antibiotic cycling as one control measure for nosocomial resistance

20. **Shiga toxins even when different are encoded at identical positions in the genomes of related temperate bacteriophages. Karch, H., Schmidt, H., Janetzki-Mittmann, C., Scheef, J., Kroger, M. (1999).** ***Molecular and General Genetics*** **262:600-607.** The nucleotide sequence of an 11,142-bp region including the stx2 operon in the genome of the temperate bacteriophage 933W in the EDL933 strain of *Escherichia coli* 0157 was determined and

compared to the respective regions derived from other lambdoid bacteriophages. In phage 933W, a region of ORFs interlinked by overlapping start-stop codons (ATGA) was detected preceding the toxin gene. These ORFs show a high degree of sequence identity to genes of the nin region of phage lambda. Immediately downstream of these nin genes we identified an ORF that may code for an anti-terminator similar to the lambda Q protein. It is concluded that toxin expression is directly associated with the initiation of cell lysis. Downstream of the stx2 operon we identified an ORF that is homologous to the holin gene S of bacteriophage PA-2. PCR primers were designed, which, based on a comparison of the phage sequences, appeared to be common to both stx1- and stx2-harbouring phages. However, only seven of the 22 STEC strains investigated from serogroups 0157, 026, 0103 and 0111 yielded the expected PCR amplification product. The data reported here may be useful in developing new strategies for inhibiting the expression of Stx and for developing universal diagnostic primers for use in tracking the origin and evolution of Shiga toxins and the phages that carry them

21. **Target genes for virulence assessment of *Escherichia coli* isolates from water, food and the environment. Kuhnert, P., Boerlin, P., Frey, J. (2000). *FEMS Microbiology Reviews* 24:107-117.** The widespread species *Escherichia coli* includes a broad variety of different types, ranging from highly pathogenic strains causing worldwide outbreaks of severe disease to avirulent isolates which are part of the normal intestinal flora or which are well characterized and safe laboratory strains. The pathogenicity of a given *E. coli* strain is mainly determined by specific virulence factors which include adhesins, invasins, toxins and capsule. They are often organized in large genetic blocks either on the chromosome ('pathogenicity islands'), on large plasmids or on phages and can be transmitted horizontally between strains. In this review we summarize the current knowledge of the virulence attributes which determine the pathogenic potential of *E. coli* strains and the methodology available to assess the virulence of *E. coli* isolates. We also focus on a recently developed procedure based on a broad-range detection system for *E. coli*-specific virulence genes that makes it possible to determine the potential pathogenicity and its nature in *E. coli* strains from various sources. This makes it possible to determine the pathotype of *E. coli* strains in medical diagnostics, to assess the virulence and health risks of *E. coli* contaminating water, food and the environment and to study potential reservoirs of virulence genes which might contribute to the emergence of new forms of pathogenic *E. coli*

22. **Multiplex PCR for detection and identification of lactococcal bacteriophages. Labrie, S., Moineau, S. (2000). *Applied and Environmental Microbiology* 66:987-994.** Three genetically distinct groups of *Lactococcus lactis* phages are encountered in dairy plants worldwide, namely, the 936, c2, and P335 species. The multiplex PCR method was adapted to detect, in a single reaction, the presence of these species in whey samples or in phage lysates. Three sets of primers, one for each species, were designed based on conserved regions of their genomes. The c2-specific primers were constructed using the major capsid protein gene (mcp) as the target. The mcp sequences for three phages (eb1, Q38, and Q44) were determined and compared with the two available in the databases, those for phages c2 and bIL67. An 86.4% identity was found over the five mcp genes. The gene of the only major structural protein (msp) was selected as a target for the detection of 936-related phages. The msp sequences for three phages (p2, Q7, and Q11) were also established and matched with the available data on phages sk1, bIL170, and F4-1. The comparison of the six msp genes revealed an 82. 2% identity. A high genomic diversity was observed among structural proteins of the P335-like phages suggesting that the classification of lactococcal phages within this species should be revised. Nevertheless, we have identified a common genomic region in 10 P335-like phages isolated from six countries. This region corresponded to orfF17-orf18 of phage r1t and orf20-orf21 of Tuc2009 and was sequenced for three additional P335 phages (Q30, P270, and ul40). An identity of 93.4% within a 739-bp region of the five phages was found. The detection limit of the multiplex PCR method in whey was 10(4) to 10(7) PFU/ml and was 10(3) to 10(5) PFU/ml with an additional phage concentration step. The method can also be used to detect phage DNA in whey powders and may also detect prophage or defective phage in the bacterial genome

23. **Genetic analysis of a bacterial genetic exchange element: the gene transfer agent of *Rhodobacter capsulatus*. Lang, A. S., Beatty, J. T. (2000). *Proceedings of the National Academy of Sciences, USA* 97:859-864.** An unusual system of genetic exchange exists in the purple nonsulfur bacterium *Rhodobacter capsulatus*. DNA transmission is mediated by a small bacteriophage-like particle called the gene transfer agent (GTA) that transfers random 4.5-kb segments of the producing cell's genome to recipient cells, where allelic replacement occurs. This paper presents the results of gene cloning, analysis, and mutagenesis experiments that show that GTA resembles a defective prophage related to bacteriophages from diverse genera of bacteria, which has been adopted by *R. capsulatus* for genetic exchange. A pair of cellular proteins, CckA and CtrA, appear to constitute part of a sensor kinase/response regulator signaling pathway that is required for expression of GTA structural genes. This signaling pathway controls growth-phase-dependent regulation of GTA gene messages, yielding maximal gene expression in the stationary phase. We suggest that GTA is an ancient prophage remnant that has evolved in concert with the bacterial genome, resulting in a genetic exchange process controlled by the bacterial cell

24. **Bacteriophages as indicators of enteric viruses and public health risk in groundwaters. Leclerc, H., Edberg, S., Pierzo, V, Delattre, J. M. (2000). *Journal of Applied Microbiology* 88:5-21.** Low concentrations of all types of bacteriophages in groundwater limit their power to predict the presence of enteric viruses. There is little concordance in the literature regarding phage detection methods, thus making comparisons extremely difficult. Different authors have used different hosts, phage concentration methods, and end-point determinations. Also, markedly different volumes of sample have been employed, varying from 1 litre to 400 l. Bacteriophage concentration methods are not reproducible. There has been marked variability among groups in the natural substrates used (for example, beef extract), the type of adsorbing filter used, centrifugation instruments and conditions, and the delivery of the concentrate to the host cells. There is no consensus on the best bacterial host strain. Currently, several are employed with each showing differential sensitivities and specificities. In particular, host stability must be considered. Host stability has two components: the ability of the host to continue to be receptive to the bacteriophage after continued sub-culture, and the lack of lysogenic or temperate bacteriophage in the host cell line which may be randomly and unpredictably activated. There is a lack of consistent recovery of bacteriophages from individual faecal specimens. In particular, only approximately 3% of individual humans carry the FRNA phages. While there is some evidence to indicate that the phages multiply in sewage, it is not clear how they do so since the host pili should not be produced at lower temperatures. These ecological factors need to be understood. Of all the phages thus far studied, Bacteroides fragilis HSP40 has the highest recovery rate from individual people. However, Bacteroides, being an anaerobe, is a difficult host for routine laboratory analysis. Methods for the enumeration of F(+)-specific phages and Bacteroides phages are complex, time-consuming, costly and not reproducible. Conversely, somatic coliphage methods are simpler and results can be available in 4-6 h. The occurrence of phages and viruses in groundwater depends on physicochemical characteristics that control their fate and transport in the groundwater/aquifer environment. There are very little actual data taken from the field that allow an understanding of the ecology and life span of phages in their natural environment. Moreover, the ability of phages to serve as a source of food for other microbes needs to be understood. There has been a lack of association of bacteriophage recovery with gastroenteritis outbreaks due to enteric viruses. There is only a small epidemiological database concerning the occurrence of enteric viruses in groundwater

25. **Isolation and characterization of a generalized transducing phage for the marine luminous bacterium *Vibrio fischeri* MJ-1. Levisohn, R., Moreland, J., Nealson, K. H. (2000). *Journal of General Microbiology* 133:1577-1582.**

26. **Complete nucleotide sequence, molecular analysis and genome structure of bacteriophage A118 of *Listeria monocytogenes*: implications for phage evolution. Loessner, M. J., Inman, R. B., Lauer, P., Calendar, R. (2000). *Molecular Microbiology* 35:324-340.** A118 is a temperate phage isolated from *Listeria monocytogenes*. In this study, we report the entire nucleotide sequence and structural analysis of its 40 834 bp DNA. Electron microscopic and enzymatic analyses revealed that the A118 genome is a linear, circularly permuted, terminally redundant collection of double-stranded DNA molecules. No evidence for cohesive ends or for a terminase recognition (pac) site could be obtained, suggesting that A118 viral DNA is packaged via a headful mechanism. Partial denaturation mapping of DNA cross-linked to the tail shaft indicated that DNA packaging proceeds from left to right with respect to the arbitrary genomic map and the direction of genes necessary for lytic development. Seventy-two open reading frames (ORFs) were identified on the A118

genome, which are apparently organized in a life cycle-specific manner into at least three major transcriptional units. N-terminal amino acid sequencing, bioinformatic analyses and functional characterizations enabled the assignment of possible functions to 26 ORFs, which included DNA packaging proteins, morphopoetic proteins, lysis components, lysogeny control-associated functions and proteins necessary for DNA recombination, modification and replication. Comparative analysis of the A118 genome structure with other bacteriophages revealed local, but sometimes extensive, similarities to a number of phages spanning a broader phylogenetic range of various low G+C host bacteria, which implies relatively recent exchange of genes or genetic modules. We have also identified the A118 attachment site attP and the corresponding attB in *Listeria monocytogenes*, and show that site-specific integration of the A118 prophage by the A118 integrase occurs into a host gene homologous to comK of *Bacillus subtilis*, an autoregulatory gene specifying the major competence transcription factor

27. **Rapid in vivo evolution of a beta-lactamase using phagemids. Long-McGie, J., Liu, A. D., Schellenberger, V (2000). *Biotechnology and Bioengineering* 68:121-125.** RNA viruses are capable of undergoing extremely rapid evolution due to their high rates of reproduction, small genome size, and a high frequency of spontaneous mutagenesis. Here we demonstrate that a virus-like, evolutionary state can be created by propagating a phagemid population in a hypermutator strain of *Escherichia coli* in the presence of a helper phage. This enables one to subject individual phagemid-encoded genes to rapid in vivo evolution. We applied this approach to TEM-1 beta-lactamase which confers resistance to 0.05 mg/L of the antibiotic cefotaxime. After 3 weeks of in vivo evolution we were able to isolate a double mutant, E104K/G238S, of the enzyme which confers a 500-fold increased level of resistance to cefotaxime compared to the starting enzyme. In two independent experiments we obtained a triple mutant, E104K/G238S/T263M, which confers a 1000-fold increase in resistance compared to the wild type enzyme. The same three mutations have been previously observed in TEM-4 beta-lactamase which was discovered in a highly cefotaxime-resistant clinical isolate. The probability of randomly obtaining a beta-lactamase carrying three identical point mutations is less than 10(-10). This indicates that phagemid evolution can rapidly reproduce evolution occurring in nature.

28. **[Natural interspecific hybrids of transposable phages of *Pseudomonas aeruginosa*]. Mit'kina, L. N., Krylov, V. N. (1999). *Genetika* 35:1182-1190.** Bacterial viruses of *Pseudomonas aeruginosa* assigned to two groups, D3112 and B3, recombine with very low frequencies. Previous study of the genome structure of intergroup hybrids suggested the incompatibility of some genetic modules of these bacteriophages. In this work, several natural hybrid transposable phages that had the genomes largely consisting of modules of phages from group D3112 and B3, were described. The discovery of these phages suggests the continuous genetic exchange in nature of these viruses belonging to different species. This model is considered as promising from the viewpoint of monitoring virus evolution

29. ***Escherichia coli* O157 strains which caused Japanese outbreaks have residues of bacteriophage sequences. Miyahara, M., Konuma, H. (1999). *Biological and Pharmaceutical Bulletin* 22:1372-1375.** Twelve strains of *Escherichia coli* O157 which caused outbreaks in Japan were used as DNA sources. The sequences of the gene encoding the Shiga toxin 2 in all 12 strains were almost identical and the sequences downstream of this gene were similar to that of bacteriophage 933W

30. **The role of the spectral sensitivity curve in the selection of relevant biological dosimeters for solar UV monitoring. Modos, K., Gaspar, S., Kerekgyarto, T., Vink, A. A., Roza, L., Fekete, A. (1999). *Journal of Photochemistry and Photobiology B Biology* 53:20-25.** To estimate the risk of enhanced UV-B radiation due to stratospheric ozone depletion, phage T7 and uracil thin-layer biological dosimeters have been developed, which weight the UV irradiance according to induced DNA damage. To study the molecular basis of the biological effects observed after UV irradiation, the spectral sensitivity curves of the two dosimeters and induction of the two major DNA photoproducts, cyclobutane pyrimidine dimers (CPDs) and 6-4 photoproducts ((6-4)PDs), in phage T7 have been determined for polychromatic UV sources. CPDs and (6-4)PDs are determined by lesion-specific monoclonal antibodies in an immunodotblot assay. Phage T7 and uracil biological dosimeters together with a Robertson-Berger (RB) meter have been used for monitoring environmental radiation from the polar region to the equator. The biologically effective dose (BED) established with the three different dosimeters increases according to the changes in the solar angle and ozone column, but the degree of the change differs significantly. The results can be explained based on the different spectral sensitivities of the dosimeters. A possible method for determining the trend of the increase in the biological risk due to ozone depletion is suggested

31. **Multiple independent horizontal transfers of informational genes from bacteria to plasmids and phages: implications for the origin of bacterial replication machinery. Moreira, D. (2000). *Molecular Microbiology* 35:1-5.** In contrast to the universality of other central genetic mechanisms, the replication machinery of Bacteria is clearly different from those of Archaea and Eukaryotes. A large number of bacterial genes involved in DNA replication can also be found in plasmids and phages. Based on this, it has been recently proposed that the ancestral bacterial genes were displaced by non-orthologous replication genes from plasmids and phages, which would explain the profound difference between Bacteria and the other domains of life. The alternative hypothesis is that these DNA replication genes have been frequently transferred from bacterial hosts to the genomes of their plasmids and phages. The phylogenetic analysis of the bacterial DNA replication proteins most abundant in databases (replicative helicase DnaB, single-strand binding protein Ssb and topoisomerase TopB) presented here supports the latter hypothesis. Each protein tree shows that sequences from plasmids and phages branch close to their bacterial-specific hosts, suggesting multiple independent horizontal transfers. Therefore, there is no evidence so far for non-orthologous gene displacement of these genes

32. **Occurrence and numbers of bacteriophages and bacterial indicators in faeces of yellow-legged seagull (*Larus cachinnans*). Muniesa, M., Jofre, J., Lucena, F. (1999). *Letters in Applied Microbiology* 29:421-423.** Faeces from feral populations of yellow-legged seagulls from the northern coastal area of Catalonia (North-eastern Spain) contained variable amounts of faecal coliforms, faecal streptococci, somatic coliphages, F-specific bacteriophages and Bacteroides fragilis bacteriophages. Occurrence and numbers of bacterial indicators and bacteriophages in the faeces of yellow-legged seagulls are in the ranges described in the faeces of different animals. The ratios between numbers of bacterial indicators and numbers of bacteriophages are much higher in faeces of seagulls than in treated or raw sewage contributed by out-falls of the same area

33. **Occurrence of phages infecting *Escherichia coli* O157:H7 carrying the Stx 2 gene in sewage from different countries. Muniesa, M., Jofre, J. (2000). *FEMS Microbiology Letters* 183:197-200.** Shiga toxin-converting bacteriophages are involved in the pathogenicity of some enteric bacteria, such as *Escherichia coli* O157:H7. Recent studies have demonstrated a relatively high presence of Shiga toxin 2 phages in sewage from Spain, but no data on sewage from other areas were available. In order to evaluate the presence of such phages in sewage from diverse geographical origins, 33 sewage samples, including samples from eight different European countries as well as from New Zealand and South Africa were analysed. Using an experimental approach based on the detection of Stx 2 gene by a phage enrichment culture followed by PCR, bacteriophages infecting *E. coli* O157:H7 carrying the Shiga toxin 2 gene were detected in 15 of the samples studied. Results presented here show that the presence of phages carrying the Stx 2 gene is common in sewage from developed countries

34. **Investigation of the relationship between lysogeny and lysis of *Lactococcus lactis* in cheese using prophage-targeted PCR. O'Sullivan, D., Ross, R. P., Fitzgerald, G. F., Coffey, A. (2000). *Applied and Environmental Microbiology* 66:2192-2198.**

35. **Isolation of bacteriophages specific to a fish pathogen, *Pseudomonas plecoglossicida*, as a candidate for disease control. Park, S. C., Shimamura, I, Fukunaga, M., Mori, K. I., Nakai, T. (2000). *Applied and Environmental Microbiology* 66:1416-1422.** Two types of bacteriophage specific to *Pseudomonas plecoglossicida*, the causative agent of bacterial hemorrhagic ascites disease in cultured ayu fish (*Plecoglossus altivelis*), were isolated from

diseased ayu and the rearing pond water. One type of phage, which formed small plaques, was tentatively classified as a member of the family Myoviridae, and the other type, which formed large plaques, was classified as a member of the family Podoviridae. All 27 strains of *P. plecoglossicida* examined, which were isolated from diseased ayu from geographically different areas in 1991 to 1999, exhibited quite similar sensitivities to either type of phage. One strain of *P. plecoglossicida* was highly virulent for ayu, and the 50% lethal dose (LD(50)) when intramuscular injection was used was 10(1.2) CFU fish(-1); in contrast, phage-resistant variants of this organism were less virulent (LD(50), >10(4) CFU fish(-1)). Oral administration of phage-impregnated feed to ayu resulted in protection against experimental infection with *P. plecoglossicida*. After oral administration of *P. plecoglossicida* cells of this bacterium were always detected in the kidneys of control fish that did not receive the phage treatment, while the cells quickly disappeared from the phage-treated fish. Bacterial growth in freshwater was lower in the presence of phage, and the number of phage PFU increased rapidly. These results suggest that it may be possible to use phage to control the disease caused by *P. plecoglossicida*

36. **Induction of vaginal *Lactobacillus* phages by the cigarette smoke chemical benzo[a]pyrene diol epoxide. Pavlova, S. I., Tao, L. (2000).** ***Mutation Research*** **466:57-62.** Because smoking increases a woman's risk of contracting bacterial vaginosis (BV), which is manifested by a reduction of vaginal lactobacilli and an overgrowth of anaerobic bacteria, chemicals contained in cigarette smoke were analyzed in vitro to determine their role in reducing lactobacilli. The result showed that trace amounts of benzo[a]pyrene diol epoxide (BPDE), which can be found in vaginal secretion of women who smoke, significantly increased phage induction in lactobacilli. This finding implies that smoking may reduce vaginal lactobacilli by promoting phage induction

37. **First report of a putative cyanophage, MC-1 of *Microcoleus* sp. Rosowski, J. R., Shaffer, J. J., Martin, E. L. (1999).** ***Microsc. Microanalysis*** **5:1142-1143.**

38. **Hospital Horror. Sardar, Z. (1999).** ***New Statesman*** **???-???** Our hospitals are becoming hazardous places. One can go in with a curable illness and come out with an incurable one. The risk of being infected by a "superbug", bacterial infection that is resistant to antibiotic, is very real. It has always been possible to die from surgical infection, but the arrival of superbugs has increased this risk enormously. Within ten years most of these infections will not be treatable with antibiotics. ¶
This crisis is solely due to overuse of antibiotics. We use antibiotics as a panacea for all illnesses, and doctors have become accustomed to prescribing them as blanket coverage for all complaints. Patients, too, think antibiotics are magic bullets and demand them for every flu of every season. Worse, we use antibacterial agents in household products such as washing-up liquid, bin liners and kitchen utensils. A recent essay in Nature shows how this domestic overuse is leading to resistant bacteria. For example, E coli, one of the most common causes of food poisoning, is developing resistance to triclosan, a common antibacterial agent. ¶
That is the bad news. The good news is that there is a relatively safe and easy cure for drug-resistant strains of infectious bacteria. It's called phage therapy. Bacteriophage, or "bacteria eaters", are viruses extracted from , raw sewage. They thrive wherever bacteria thrive -- in our bodies, waste products, rivers. Phage therapy has been freely available in the former communist world for decades. Even now, a dilapidated factory in Tblisi, Georgia, is producing supplies of bacteriophage under the most difficult conditions. And we in the west, having spent astronomical sums in a vain attempt to contain killer bugs, are beginning to think about learning from them.

39. **Phenoptosis: programmed death of an organism. Skulachev, V. P. (1999).** ***Biochemistry*** **64:1418-1426.** Programmed cell death (apoptosis) is well-established in many multicellular organisms. Apoptosis purifies a tissue from cells that became useless or even harmful for the organism. Similar phenomena are already described also at subcellular level (suicide of mitochondria, i.e., mitoptosis) as well as at supracellular level (degradation of some organs temporarily appearing in the course of ontogenesis and then disappearing by means of apoptosis of the organ-composing cells). Following the same logic, one may put a question about programmed death of an organism as a mechanism of purification of a kin, community of organisms, or population from individuals who became unwanted for this kin, etc. A putative mechanism of such kind is proposed to be coined "phenoptosis" by analogy with apoptosis and mitoptosis. In a unicellular organism (the bacterium *Escherichia coli*), three different biochemical mechanisms of programmed death are identified. All of them are actuated by the appearance of phages inside the bacterial cell. This may be regarded as a precedent of phenoptosis which prevents expansion of the phage infection among *E. coli* cells. Purification of a population from infected individuals looks like an evolutionary invention useful for a species. Such an invention has high chances to be also employed by multicellular organisms. Most probably, septic shock in animals and humans serves as an analog of the phage-induced bacterial phenoptosis. It is hypothesized that the stress-induced ischemic diseases of brain and heart as well as carcinogenesis if they are induced by repeated stresses also represent phenoptoses that, in contrast to sepsis, are age-dependent. There are interrelations of programmed death phenomena at various levels of complexity of the living systems. Thus, extensive mitoptosis in a cell leads to apoptotic death of this cell and extensive apoptosis in an organ of vital importance results in phenoptotic death of an individual. In line with this logic, some cases are already described when inhibition of apoptosis strongly improves the postischemic state of the organism

40. **Identification of four loci isolated from two *Streptococcus thermophilus* phage genomes responsible for mediating bacteriophage resistance. Stanley, E., Walsh, L., van, der Zwet, Fitzgerald, G. F., van, Sinderen D. (2000).** ***FEMS Microbiology Letters*** **182:271-277.** Sequence data derived from the *Streptococcus thermophilus* phages phiO1205 and phi7201 indicated that each of these phages contains a distinct DNA region dedicated to replication. Southern blotting experiments showed that phages infecting *S. thermophilus* may be divided into at least two groups, each containing the presumptive replication functions of either fO1205 (group I) or f7201 (group II). Specific regions from the putative replication module of each of the two phages were examined for their ability to provide phage resistance

41. **[The effect of low-frequency electromagnetic fields on living organisms]. Strasak, L., Vetterl, V, Smarda, J. (1998).** ***Sbornik Lekarsky*** **99:455-464.** This report studies effect of alternating low-frequency electromagnetic fields (Bm = 5-21.5 mT, f = 50 Hz, duration of exposure t = 0-24 min) on viability of bacteria *Escherichia coli*. We have shown that the growth of bacteria is impaired the electromagnetic field. Their ability to form colonies on a solid medium decreases in dependence on magnitude of magnetic field and on duration of exposure. The growth curve is influenced by the electromagnetic field as well. Effects of electromagnetic fields are independent of biological age in first four hours of their growth. We have found no morphological changes in bacterial systems in electromagnetic field by optical microscope. Viability of bacteria is bigger in a liquid medium and less in a solid medium. Bacteriophage BF 23 attach less to bacteria influenced by electromagnetic field. And finally, magnetic field did not make induction of production of bacteriophage. This effect indicates, that magnetic field did not damage DNA of exposed bacteria

42. **The future of bacterial vaginosis-related research. Taylor-Robinson, D. (1999).** ***International Journal of Gynaecology and Ostetrics*** **67 Suppl 1:S35-S38.** Various ways and criteria are used to diagnose BV. Guidelines should be redrawn and they should embody greater uniformity. The etiology of BV remains enigmatic. However, various observations suggest that host factors, possibly hormonal, cause an imbalance in the vaginal microflora. Exogenous factors, such as semen and antibiotics, may then help to bring about a more prolonged change. This forms a working hypothesis for further exploration. The role of the lactobacillus phage in the development of BV also needs to be determined. Various conditions may occur as a consequence of BV in non-pregnant and pregnant women and BV may also affect men. A subjective assessment of the extent to which these associations occur or are likely to be shown to occur by further investigations is presented in Table 1. The ability to cure acute BV needs to be improved as does the treatment of chronic BV, for which vaginal recolonization with exogenous lactobacilli is an approach to be evaluated further

43. **A new *Mesorhizobium loti* HAMBI 1129 phage isolated from Polish soil. Turska-Szewczuk, A., Russa, R. (2000).** ***Current Microbiology*** **40:341-343.** Phage A1 isolated from the rhizosphere of *Lotus corniculatus* was studied. It had a very narrow host range, as it was active only against *Mesorhizobium*

loti HAMBI 1129. Phage A1 was classified as belonging to C Bradley's group bacteriophages. The latent period of A1 was 120-130 min and a burst size 13-17 particles per cell. The nature of the phage receptor was examined. Lipopolysaccharide from the phage-sensitive strain inactivated phage A1 in contrast to LPS from the phage-resistant bacteria. Purified LPS obtained from *M. loti* HAMBI 1129 had a high receptor activity with PhI(50) value of 0. 025 microgram/ml

44. **Construction of mini-Tn10luxABcam/Ptac-ATS and its use for developing a bacteriophage that transduces bioluminescence to *Escherichia coli* O157:H7. Waddell, T. E., Poppe, C. (2000). *FEMS Microbiology Letters* 182:285-289.** Mini-Tn10luxABcam/Ptac-ATS was constructed in order to develop a luciferase-transducing bacteriophage for detecting *Escherichia coli* O157:H7. The transposon was designed to deliver a 3.6-kb insertion that confers n-decanal-dependent bioluminescence and resistance to chloramphenicol and was constructed using mini-Tn10cam/Ptac-ATS in the plasmid pNK2884 and luxAB from Vibrio harveyi. PhiV10, a temperate bacteriophage infecting common phage types of *Escherichia coli* O157:H7, was mutagenized as a prophage in *E. coli* O157:H7 strain R508. PhiV10::luxABcamA1-23 was rescued from the strain by propagating it on a strain lacking the bacteriophage and the vector containing the transposon. The bacteriophage transduced n-decanal-dependent bioluminescence to *E. coli* O157:H7 strain R508 that was measurable approximately 1 h post infection

45. **Effective phage therapy is associated with normalization of cytokine production by blood cell cultures. Weber-Dabrowska, B., Zimecki, M., Mulczyk, M. (2000). *Archivum Immunologiae et Therapiae Experimentalis* 48:31-37.** The aim of this study was to investigate the effect of phagotherapy on tumor necrosis factor alpha (TNF-alpha) and interleukin 6 (IL-6) serum levels and the ability of blood cells to produce these cytokines in culture. Fifty one patients with long-term, suppurative infections of various tissues and organs were enrolled. The ability of cells to secrete cytokines was tested using whole blood cell cultures, unstimulated or stimulated with lipopolysaccharide (LPS) from E. coli. In addition, cytokine serum levels were determined. Measurement of cytokine activity was performed using bioassays. We showed that TNF-alpha, but not IL-6 serum levels, were regulated upon division of patients into categories exhibiting initial: low, moderate and high cytokine levels. The low spontaneous production of IL-6 by blood cell cultures was elevated significantly on day 21 of phage therapy, whereas high release of this cytokine was inhibited. No such correlation was observed with LPS-induced IL-6 production in cell cultures when cells from low-, moderately- or highly-reactive patients were studied. Phage therapy modified TNF release according to the initial ability to produce that cytokine: it reduced TNF production in high responders and increased it in low responders. Patients infected only with Gram-positive bacteria demonstrated analogous changes in the spontaneous and LPS-induced TNF-alpha production as in the whole studied group. A similar kind of regulation was observed in TNF-alpha and LPS-induced production, i.e. low production was significantly elevated, high strongly inhibited, and moderate only slightly affected. In summary, we demonstrated for the first time that effective phage therapy can normalize TNF-alpha serum levels and the production of TNF-alpha and IL-6 by blood cell cultures

46. **Cell size-specific lysis of lake bacterioplankton by natural virus communities. Weinbauer, M. G., Höfle, M. G. (1998). *Aquatic Microbial Ecology* 156:103-113.**

47. **Family values in the age of genomics: comparative analyses of temperate bacteriophage HK022. Weisberg, R. A., Gottesmann, M. E., Hendrix, R. W., Little, J. W. (1999). *Annual Review of Genetics* 33:565-602.** HK022 is a temperate coliphage related to phage lambda. Its chromosome has been completely sequenced, and several aspects of its life cycle have been intensively studied. In the overall arrangement, expression, and function of most of its genes, HK022 broadly resembles lambda and other members of the lambda family. Upon closer view, significant differences emerge. The differences reveal alternative strategies used by related phages to cope with similar problems and illuminate previously unknown regulatory and structural motifs. HK022 prophages protect lysogens from superinfection by producing a sequence-specific RNA binding protein that prematurely terminates nascent transcripts of infecting phage. It uses a novel RNA-based mechanism to antiterminate its own early transcription. The HK022 protein shell is strengthened by a complex pattern of covalent subunit interlinking to form a unitary structure that resembles chain-mail armour. Its integrase and repressor proteins are similar to those of lambda, but the differences provide insights into the evolution of biological specificity and the elements needed for construction of a stable genetic switch

48. **Estimating the infectivity of marine viral communities from measurements of DNA damage and photoreactivation. Wilhelm, S. W., Weinbauer, M. G., Jeffrey, W. H., Suttle, C. A. (1998). *Aquatic Microbial Ecology* 14:215-222.**

49. **Viruses and nutrient cycles in the sea. Wilhelm, S. W., Suttle, C. A. (1999). *Bioscience* 49:781-788.**

50. **Virioplankton: viruses in aquatic ecosystems. Wommack, K. E., Colwell, R. R. (2000). *Microbiology and Molecular Biology Reviews* 64:69-114.** [no abstract]

51. **Quinolone antibiotics induce Shiga toxin-encoding bacteriophages, toxin production, and death in mice. Zhang, X, McDaniel, A. D., Wolf, L. E., Keusch, G. T., Waldor, M. K., Acheson, D. W. (2000). *Journal of Infectious Diseases* 181:664-670.** Shiga toxin-producing *Escherichia coli* (STEC) cause significant disease; treatment is supportive and antibiotic use is controversial. Ciprofloxacin but not fosfomycin causes Shiga toxin-encoding bacteriophage induction and enhanced Shiga toxin (Stx) production from *E. coli* O157:H7 in vitro. The potential clinical relevance of this was examined in mice colonized with *E. coli* O157:H7 and given either ciprofloxacin or fosfomycin. Both antibiotics caused a reduction in fecal STEC. However, animals treated with ciprofloxacin had a marked increase in free fecal Stx, associated with death in two-thirds of the mice, whereas fosfomycin did not. Experiments that used a kanamycin-marked Stx2 prophage demonstrated that ciprofloxacin, but not fosfomycin, caused enhanced intraintestinal transfer of Stx2 prophage from one *E. coli* to another. These observations suggest that treatment of human STEC infection with bacteriophage-inducing antibiotics, such as fluoroquinolones, may have significant adverse clinical consequences and that fluoroquinolone antibiotics may enhance the movement of virulence factors in vivo

52. **[Examining interaction of phages with microorganisms by fluorometry and electro-orientation spectroscopy]. Zhilenkov, E. L., Fomchenkov, V. M., Novikov, I. A., Sadomov, V. E., Oborotov, M. V., Gremiakova, T. A. (1999). *Vestnik Rossiiskoi Akademii Medisinskiky Nauk* 24-29.** Bacterial sensitivity to different various phages was examined by electro-orientation spectroscopy, fluorometry, and electron microscopy. The strains of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Yersinia pestis*, *Mycobacterium smegmatis*, and *Xanthomonas campestris* were used. The fluorescence intensity of a membranotropic agent in the ANS-cell-phage system was shown to depend on the interaction of a bacterial virus and a microorganism. Fluorometric data correlated with electro-orientation spectroscopic findings. An analysis of the low-frequency site makes it possible to determine phage adsorption on the bacterial surface. The changes in electro-orientation effects at high frequencies suggest that there are barrier dysfunctions in the external membranes and that there is cellular phage reproductions. Whether fluorometry and electro-orientation spectroscopy can be further used for rapid identification of microorganisms by using phages is discussed

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Acknowledgements

Thank you to Larry Goodridge for this volume's phage images.

Contact Steve Abedon (microdude+@osu.edu) with suggestions, criticisms, comments, or anything else that might help make this a better site.