Churchill Fellowship Report 2007

The health value of bacteriophages

Phage scientists come to the rescue for the treatment of antibiotic-resistant bacteria and for other health challenges

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Would you like to read a scientific adventure story with a political twist? My journey took me to the USA, Canada, Georgia and Poland – and back to England.

Here are the main characters: **bacteria** and **bacteriophages** (**phages**, for short).



Dr. Beata Weber-Dabrowska shows a glass plate, with bacteria destroyed naturally by phages.

It is a simple view of thriving bacteria growing on a glass plate – a 'petri dish', and covered with a lid for safety. Do you see the cloudy germs? Do you notice a big clear area where a drop of carefully chosen invisible phages was placed? Now those infective bacteria are destroyed - gone!

Phages are actually viruses that infect and kill solely bacteria. Yes, by their very nature, they are anti-bacterial agents. We have only known about this science for about 100 years. What is so interesting is that harmful bacteria can be targeted exactly, without harming the bio-friendly ones.

Over the last 50 years, many bacteria have acquired 'superbug' relatives, such as MRSA - so called because they are resistant to many antibiotics. The worry is that humans may catch superbug infections in hospitals and other places in the community such as sports clubs and gyms, prisons and schools, especially when they are already unwell or their immune systems are weakened. There are similar risks with animals. Note that we all breathe the same air and basic hygiene is often ignored.

So, this story investigates the health value of bacteriophages - especially the ones that keep these particularly difficult species of bacteria under control. No longer can we always rely on new man-made antibiotics to do the job, and anyway some people have allergic reactions to them. We also need to avoid the adverse effects of antibiotics that can cause liver damage and diarrhoea. Can phages assist us?

What is the health value of phages? Is it true that they help to heal very serious flesh wound infections, including life-threatening diabetic foot infections and MRSA skin infections? Are there any new possibilities to look at?

A scientific discovery

It just so happened that, while I was visiting a pioneering Wound Care Center and the university in Lubbock, Texas, an exciting science investigation was taking place with bacteria growing in a few petri dishes in the lab. The scientists discovered a long-lasting germicidal effect when they added natural phages <u>plus</u> an enzyme called Dispersin B. A catalyst perhaps. I was the first person they told!

In the following graph (Figure 1), down at the bottom, just look at that green line. Then compare it with the red, blue and black lines much higher up. This shows us that the *E.coli* bacterial slime (biofilm) suddenly became much less active, and stayed that way.

Even the tiny photographs of the dishes are much paler and smaller.

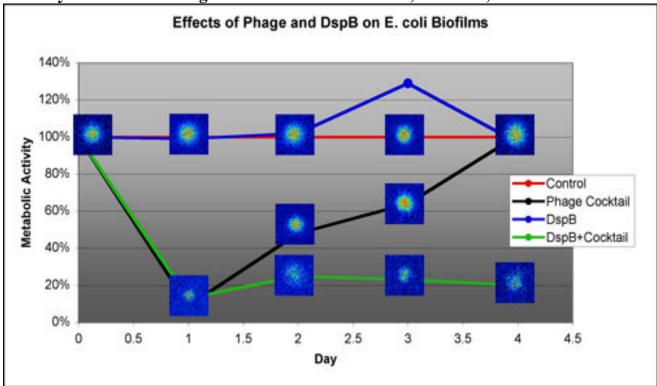
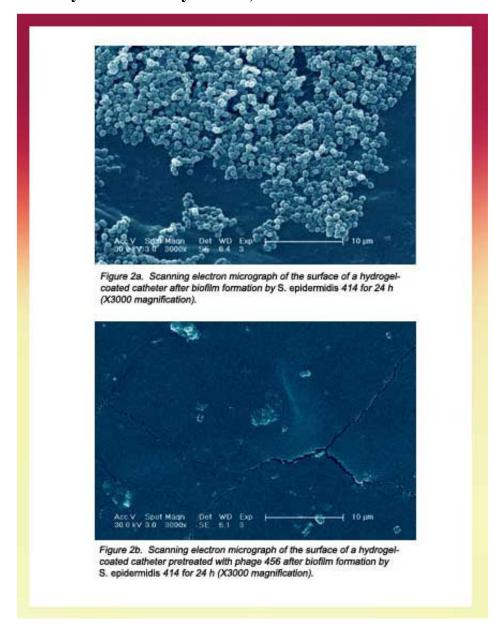


Figure 1: Effects of phage and an enzyme on E.coli biofilms courtesy of Drs. Lasha Gogokhia and Randall Wolcott, Lubbock, TX

Another scientific discovery

Here's some more good news from the United States, based on CDC research with British phages. When hospital hydrogel-coated catheters are actually pre-treated with phages, the growth of bacterial slime (biofilm) is prevented. Figure 2a shows a hydrogel catheter after a heavy layer of biofilm has formed after 24 hours. But in Figure 2b we see the difference if the catheter is pre-treated with phages. The biofilm doesn't grow. Now there's an idea. That problem could be solved, and lives could be saved, couldn't they? Patients become miserable if they develop infections with the use of hospital catheters and all manner of artificial pipes or tubes. The pre-treatment of catheters with phages would help to keep them clean and working properly, by reducing the formation of a biofilm.

Figures 2a and 2b: Biofilm on catheters courtesy of Dr. Rodney Donlan, USA – BiofilmsOnline



Yet more discoveries

The next picture is of nurses and the Matron at the Military Hospital in Gori, Georgia. Phages are applied routinely for helping to prevent and treat infections in military and civilian patients.



At the new Military Hospital in Gori, Georgia. Photo courtesy of Robin Rotherham

I had visited to learn about the use of phages in medicine from the Chief Surgeon, Dr. Guram Gvasalia. This was at the invitation of key personnel from supporting institutes - Dr. Zemphira Alavidze, Head of the Laboratory in Phage Morphology and Biology at the Eliava Institute, Georgian Academy of Sciences with Dr. Teona Danelia, the Co-ordinator of the Phage Therapy and Surgical Infection Training Program for the PhageBiotics Foundation. I was informed of some extraordinary phage pioneering work from years ago that needs to be re-investigated.

It is about a very serious risk in surgery that needs to be avoided at all costs peritonitis. The message is that phages could be applied therapeutically as prevention or rescue work, directly through the lymphatic system – without even having to go through the blood system. Indeed, the experiments with animals and case reports of human patients indicate that it works very quickly and efficiently. Additional scientific clinical trials in this phage research are needed.

It is therefore my honour and privilege as a Winston Churchill Fellow, to bring this to your attention. These are the notes:

http://www.amazingphage.info/page6.htm#12415 http://www.amazingphage.info/page6.htm#12514 http://www.amazingphage.info/page6.htm#12534 http://www.amazingphage.info/page6.htm#12606 http://www.amazingphage.info/page6.htm#12604

How are phages being used therapeutically?

Carefully selected phages are being used routinely in Georgia for gunshot wounds, road injuries and trauma. I was shown photographic evidence (in full colour and anatomical detail) in conjunction with the scientific research documents by well-qualified and experienced medical people and scientists. Phages are being used therapeutically with babies, infants, children, adults and the elderly, if they have acute or chronic bacterial infections, and across the whole spectrum of different bacterial infections such as bacterial conjunctivitis, gangrene, gingivitis, diphtheria and dysentery. In Georgia, phages are used in small clinics and in entire hospitals. New special dressings made of novel bio-composites (phages + enzymes + painkillers) are also being used and patented.

Phage products are at very low cost over the counter in pharmacies in Georgia. Three women from Tbilisi said that about a third or even a half the city's population are well aware of the health value of bacteriophages.

Success rates with phage for the treatment of bacterial infections vary.

Individual cases

In March and in July 2007, I personally used a bacteriophage preparation with interdental brushes for my periodontitis symptoms (bleeding gums). The results were excellent within just a few days. My dentist has confirmed the results. In March 2007, one UK patient from my home town of Reigate, who went to Georgia for the treatment of his chronic sinusitis had no improvement with the bacteriophages, but the question is, was the cause of his sinusitis really just bacterial, or poly-microbial. Additional follow-up is still needed. The costs of phage therapy may be excessive if patients have to travel to foreign countries.

In March 2007, an American patient told me that she had travelled to the Phage Therapy Center in Georgia during 2005 for phage therapy for a severe MRSAsinusitis infection; it cleared and saved her life. In May, another American patient who is a paraplegic had significant improvement with bacteriophage therapy for severe MRSA in his multiple chronic wounds. Both patients were very thankful for bacteriophage therapy and they wish to let people know through this report. Another American patient who travelled to Georgia in March for the treatment of his chronic sinusitis states that he is feeling better; in June, an Australian patient who had travelled to Georgia for treatment that included phages for an abdominal medical condition also said that she was feeling better.

In September 2007, at the L.Hirszfeld Institute of Immunology and Experimental Therapy in Wroclaw, Poland, I was introduced to two patients that had previously acquired bacterial infections during routine surgery in local hospitals. Whereas even strong antibiotics had been ineffective, phage therapy provided a cure. Treatment is provided on a not-for-profit basis and the institute is accredited as a 'Center of Excellence' for its work. Their clinicians and scientists pointed out that bacteriophage therapy is not guaranteed 100% effective, but they fully confirm that the treatment is harmless, and approved by the Polish Bioethics Committee. As we know, antibiotics are not 100% effective. A Wroclaw hospital pediatrics department has approved phage therapy research trials for children's allergies.

"In no patient so far have we had any evidence of liver dysfunction that could be caused by phages."

Prof. A.Gorski, Vice-President, Polish Academy of Sciences

The Polish phage therapy doctors explained that their intentions are quality and the highest standards of medical research, with all necessary insurances and the decisions of national and European committees. Any doubts can be clarified with data to prove results.

It was also interesting to meet a Polish patient who had contracted MRSA via some metal wires in his chest bone after open heart surgery. The hospital doctors acknowledged responsibility and therefore decided to refer him to the phage clinic in Wroclaw at their own expense, honouring a moral obligation.

It must be noted that there is a lack of fully randomized, double-blinded clinical trials. The patients that I met are just a few of many hundreds and thousands of individual cases and observational studies. Many people would consider that the successes are nevertheless a testament to the health value of bacteriophages in the treatment of bacterial infections.

There is a fascinating little story of a senior scientist that I was introduced to in Poland. She had been cured of a chronic streptococcal throat infection when aged 7-8 during the 1950s. Her mother, who was a pharmacist working in Warsaw at the time, had personally extracted and purified the phages from the river sewage water to ease her daughter's pain and suffering; the treatment was successful in just a couple of days!

In the 1970s-80s at the institute in Wroclaw, Poland, phage therapy was started on humans and animals. Many patients were referred by their family doctors and the Military Hospital. Their scientific papers documented more than 2000 case reports of patients being treated with bacteriophages, although without placebos. This was because at that time, phage therapy was simple and there were no regulatory limits. When the Polish BioEthics Committee was introduced, there were other ethical and financial pressures placed on physicians. These were because not only would military doctors have wanted the medication free of charge, but they chose to do clinical trials with other methods e.g. antibiotics because they would be paid for the work if they used antibiotics. There was no financial incentive for them to use phages. This is clearly one of the main reasons why there is a lack of fully randomized, double-blinded clinical trials currently in Poland for phage therapy. Future quality clinical trials are needed to verify bacteriophage therapy.

It is necessary to record that some evidence has previously not been published accurately because of "contractions" and "counter attacks" by people with a "conflict of interest". It can even be a very subtle effect taking place at the editing stages of a publication. I do believe I have found evidence of this process, comparing an author's original article submitted to a major scientific journal with the published text. There is another specific example reported to me of pioneering phage research results that were "hushed up" when a scientist's widow was attempting to publish them after his death. They never were published.

The clinicians in Georgia, Poland and the USA are continuing with their phage research and therapeutics in the public interest - at a time when there is an acute health crisis with resistant bacterial infections. Latest scientific data published by the Polish team points out that phage therapy offers an alternative treatment for *Staphylococcus aureus* infections at 10% of the cost of antibiotic therapy. Major benefits are that the phage treatment does not have adverse effects like antibiotics, and are essentially much less expensive.

The production of phages is very economical but there are bureaucratic obstacles still in place in the West which restrain phage research and therapy. As a result, Dr Randall Wolcott, the medical director at the clinic in Lubbock, Texas made the bold decision to provide phages free of charge to some patients with infected diabetic ulcers and similar wound infections. Now after a few questions and long delays, an FDA-approved Phase 1 clinical trial study for bacteriophage has been started and is privately funded. Generally the Texas physicians use multiple concurrent strategies working in synergy and they collaborate with phage scientists internationally through meetings, visits and emails. Examples would be visitations to the Eliava Institute in Georgia and the Evergreen Phage Meetings near Olympia, Washington USA.

Phages are just one of their "tools" pertaining to wounds and biofilm. They are being used compassionately and in a benevolent outreach manner.

"The ideal antibacterial therapy would need to have both anti-biofilm and antibiotic features in order to effectively reduce infection."

Dr. L. Gogokhia – poster at the 17th Evergreen International Phage Meeting, WA

It is now apparent from having personally benefited from dental phages and from having attended three conferences as a guest, that the role of this Winston Churchill researcher and educator is to collaborate with the phage scientists, doctors and molecular biologists, and help them communicate with the media, the politicians, the policy advisers and the general public about the importance of phage therapy in healthcare.

There is consensus that high quality phage research is urgently needed across the whole range of bacterial infections to satisfy medical and scientific scrutiny around the world. Yet the recurring message, I hear, is that funding is rarely forthcoming. Scientists sometimes have to postpone or abandon worthwhile projects, simply to make a living. During the course of my research, an international collaborative dental bio-composite project application was rejected, even though, this time, there was a letter of support from a UK dentist. She had seen the far-ranging health value of such a project from her experience and her pioneering charitable dentistry work in Tanzania. Dental decay is the world's most common disease. Perhaps phage for dental care could be a fast-acting, cheap and effective treatment for dental decay, when it is fully tested and proven. This would be greatly welcomed around the world. In April, a British dentist was sent phage information for review by experts in periodontal disease.

Perhaps the delays and oversights may come as no surprise. There is an excellent article online, originally from the UK's Guardian newspaper dated 5th April 1984 entitled "On the brink of a fresh phage". Over 23 years later, the situation has hardly changed at all, because the health potential has been largely ignored and funding has been minimal. Having investigated phage research over the past several years, I would sum it up by stating that the bureaucratic machine is the root of the problem.

"The bureaucratic machine is the root of the problem."

Grace Filby, Churchill Fellow of 2007

Polish molecular biologist Dr. Malgorzata Lobocka is recommending a very practical strategy. Her advice is that phage researchers need to work together internationally with all scientific disciplines. She advocates national centres. Looking ahead, she can see that what is needed urgently is a structured and coordinated plan, not just 'more research'. It would accelerate progress rather than simply repeat work that unnecessarily wastes financial resources.

"The overarching principle must be integrity."

Dr. M. Lobocka, molecular biologist, Poland

Novel applications of bacteriophages

Bacteriophages were originally identified and are perhaps best known for their antibacterial effect. However, thanks to the latest molecular science and extremely hitech developments, there are now some even less-recognized potential medical applications.

Overall, the breaking news phage research on various new applications is definitely being reported to major scientific meetings. In May 2007 in Toronto at the General Meeting of the American Society of Microbiology, researcher Prof. Beka Solomon from Israel informed us of how some special types of phages, filamentous in shape, could soon help with restoring the cognitive abilities of Alzheimers' patients. Administered through the nose, the phages can reach the brain directly and rapidly. Her team's research with mice demonstrates that phages can reduce the extracellular plaque and also brain inflammation without adverse effects. This may open the way for various new treatments of other neurological diseases including Parkinson's Disease and Huntingdon's Disease. This breakthrough research goes way beyond the application of phages just as an anti-infective agent. What an opportunity!

In September 2007 in Wroclaw, the Polish Pharmacological Society heard from Prof. Andrzej Gorski about research investigating the oncological and immunological interactions of phages with higher organisms. This science is uniquely based on some inspiring observations that pieces of lung tissue bathed in HAP1 phages (lovely name!) had significantly less melanoma. The effect is clearly visible in photographs. The scientists state that the effect of phages is immunological. The research publications prove that, under well-defined circumstances, phages can have antimetastatic activity (anti-cancer/anti-tumour). The conference delegates were also shown slides of data proving that phages can be immuno-suppressive both in-vivo (in living cells) and in-vitro (in the lab).

Professor Gorski pointed out that phages can prevent inflammatory diseases of the bowel, and they can improve renal function when administered in transplant patients. Furthermore, there is very strong evidence of phage safety.

His triumphal point to note, is that because phages are viruses, some have common receptors, in fact they may neatly block harmful viruses (such as adenoviruses, the flu-like infections common in children, and the Herpes virus). New therapeutic treatments or preventatives for a range of viral infections would be a novel application of bacteriophages!

They are certainly versatile little organisms, whose value has been vastly underrated so far. The antiviral activity is detailed in the book entitled "Bacteriophage Genetics and Molecular Biology" by Stephen McGrath and Douwe Van Sinderen (editors), ISBN: 978-1-904455-14-1, in Chapter 5, published July 2007. An additional reference book on bacteriophages is "Bacteriophages: Biology and Applications" by Elizabeth Kutter and Alexander Sulakvelidze (editors), ISBN: 978-0849313363 published 2005.

Another key point that is being explained in conferences and lectures internationally is the concept that biofilms are not just bacterial - they can also incorporate fungal cells and other microbes. This is not simply a medical matter – it affects industry, waste disposal, agriculture etc.. The theory is that there are multi-organism 'gangs' of germs that get established very quickly in a wound (or on a surface) and become almost impenetrable because of the polysaccharide slime they make. When removed physically, they regenerate new layers just as in the movie 'Terminator 2'. That sounds a good analogy from having observed a traumatic wound being treated numerous times, even with maggots to help remove the biofilm. This is why there is such an urgency to protect sensitive skin and new wounds immediately from contact microbes or airborne transmission on dust particles. In May 2007, some UK Dept of Health personnel were asked if they knew of biofilm and they did not, even though biofilm research has been going on for over 20 years. Dentists who teach us about brushing, flossing and rinsing, are actually teaching us to treat biofilm in the mouth. Research indicates that phages could help in treating oral bacterial infection and biofilms too.

It is a very natural process to consider using bacteriophages because ordinary tap water contains millions of phages anyway, as do our bodily fluids. We are drinking phages and washing with them every day, without demanding clinical trials! Application is the key.

Public awareness

Microbiologists are an integral part in phage research. It has come to my attention that the number of UK microbiologists was low even six years ago. In June 2007, this official finding was confirmed by the Department of Health's Chief Microbiologist and the UK Clinical Research Collaboration, and in July 2007, pointed out at their public meeting in London. Evidently, in the whole academic discipline of medical microbiology in the UK, there is weak capacity. If there are simply not enough microbiologists, why was nothing done about it during the last six years? If this situation is to be put right, perhaps the professional development syllabus also needs an overhaul regarding biofilm – as well as the health value of phages in general.

Many significant breakthroughs in phage science and technology go unreported by the news media to the general public. In April 2007, a consulting editor of the Telegraph Media Group exhibited a lack of understanding of phages generally. He wrote to me that any discussion about efficacy would be too specialized for their Health and Beauty readers, and that a simple suggestion of a DVD about the health value of phages would 'no doubt... be of more interest to a scientific journal'. I disagree. In my opinion, we need to inform and educate the general public about the advances in healthcare with bacteriophages and how they can be used by our scientists and physicians. I only hope the national press will consider their ethics and responsibilities of educating the public about bacteriophages. In July 2007 the BBC Radio 4 reported on UK phage developments. In August 2007, the Times and the Daily Express also reported on phage developments. In September 2007 a scientific journal has shown interest in helping me to develop an educational DVD on phages for the general public, based on my travelling research. In October 2007, the Daily Mail even reported the news about Prof. Beka Solomon's phage research on Alzheimer's. Better late than never!

This summer at the British Association for the Advancement of Science, the Chief Executive stated that their focus is on generic activities of engaging and inspiring people with science, and promoting open discussion about the place of science in society. Does this really mean that they have no interest in phage research for therapy in the United Kingdom?

I wrote to the new Prime Minister Gordon Brown to ask him whether he has heard of bacteriophages. My faxed letter was deferred to the Foreign and Commonwealth Office for comment. No reply was ever received even though I wrote to remind them.

Next steps?

It is timely to note that if it weren't for phages, we would have no knowledge of DNA or genomes, let alone modern genetic engineering, forensics etc.. Phages are regarded as model organisms for scientific research. There is a great deal of work to be done.

Looking far ahead, we are advised by Dr Lobocka that if we were to start to consider the industrial value of bacteriophages first, even before the health value, we would find sound business reasons for massive investment in phage research and genetic sequencing. The main point here is that there is a huge incentive in molecular scientists finding new genes in phages for industry that they cannot find in the organisms they have studied so far. Genetic sequencing of the vast number of phages could be of great value, but it would need international collaboration. Teamwork could avoid unnecessary repetition or wastage of scarce funding. In short, scientists need to find new genes that encode proteins that will be useful for industry. The science involves the proteases that chop up genomes. It is necessary to compare the genomes of different phages because they are far more diverse than the range of mammalian genomes. The money which governments and industry invest into 'hunting for new genes' would indirectly benefit medical and therapeutic research.

Educationally, there are tasks to be done by publishers, editors and teachers, in order to help sort out the facts from the fiction. For example, one objection to using phages therapeutically is that they are viruses. Yes, bacteriophages are viruses, but they are not pathogenic to humans, or animals or plants, because lytic bacteriophages can only specifically destroy <u>bacteria</u>. Dictionary editors could check that they are defining viruses correctly. Bacteriophages are explained in a cartoon for children at <u>http://www.relax-well.co.uk/a_little_story.html</u>.

Again, in terms of education and awareness-raising, Dr. Revaz Adamia, Director of the Eliava Institute of Bacteriophages, Microbiology and Virology in Georgia (former Georgian Ambassador to the United Nations) told me that if he had one message for the UK, it would simply be that bacteriophage therapy is harmless. There are some who suspect that they might be harmful, but there is no scientific evidence that lytic bacteriophages can transfer genetic material. He believes it would be a significant step forward if that psychological difficulty – a psychological block, could be overcome.

A visitor to my **amazingphage.info** website comments:

"The sad part is that while most pharma companies want to be innovative, a lot of the regulatory agencies within the individual countries are so far behind the times...The thought of actively introducing a virus into an organism scares most to death."

Jamie Critelli, Novartis Animal Health

Instead of governments or pharmaceutical companies offering incentives to encourage development of new antibiotics (as proposed in March 2007 by the USbased RRF report, I suggest they could offer unrestricted research funding to encourage the development of research for phage therapy.

A spotlight on the health value of bacteriophages could help allay their fearful concerns such as "Approach is largely speculative. Bacteriophages may themselves cause toxicity.", neither of which are necessarily true. It seems from this Churchill Fellow's research that negative claims may be (1) unfounded and (2) without scientific evidence or proof of being harmful. They are just assumptions from lack of trust, or lack of access to modern data. Such a step could illuminate the harmless nature of therapeutic bacteriophages used correctly. Doctors, rather than pharmaceutical companies, could use bacteriophages as a biological control agent for

the very reasons that they can attack and destroy antibiotic-resistant bacteria.

There is another project that could be a step towards world peace. It is likely to make a difference in military situations such as the Iraqi war zone. Pioneering work in the 1990s with therapeutic phages on Georgian battlefields was left unattended to for years by researchers and governments, even though it was reported in the Lancet in 2005 by a journalist. Some of his findings would now need updating. However he included a well-written account of a clinical trial. Soldiers who were given spray canisters of various phages for the prevention of bacterial wound infections fared much better than the others who got wounded but did not receive phage therapy. Today, a team of American and Georgian scientists supported by the PhageBiotics Foundation and Prof. Elizabeth Kutter would be willing to provide training for Iraqi doctors, as they do already for volunteers. British colleagues and I could immediately see the medical and humanitarian value of this. We also feel that British people would like to offer some gesture of support, financially or perhaps just logistically. In May 2007 I sent a PowerPoint presentation to the British Embassy in Washington DC. I, a Winston Churchill travelling researcher, specifically visited and discussed this proposed project at length, with staff. To cut a long story short, we have yet to have any feedback - even from my local British Member of Parliament. There is a slideshow about it here: http://www.amazingphage.info/page17.htm.

In August 2007, I read a published letter in the Times newspaper that the Government

"fully recognises the importance of international collaboration on scientific research"

John Denham, Secretary of State for Innovation, Universities and Skills, 27.8.07

This does not fit with the British Embassy staff remits which are strictly bilateral rather than enabling them to embrace the spirit of wider international collaboration. Is this hampering scientific progress - including phage science?

Medical personnel should consider phage therapy when antibiotic therapy has failed. Phage therapy could work synergistically with other therapies for maximum patient benefit. Immune system boosting treatment and probiotics can be recommended. Nutritional supplements along with antibiotics (to help prevent some antibiotic adverse effects) are referred to very briefly in the British Health Care Commission's official Investigation Report 2006 into the *C.difficile* outbreaks at Stoke Mandeville. An interview with a dietician revealed that the nursing staff were too busy to administer the recommended nutritional supplements. Yet those nutritional supplements were not mentioned at all in the hospital trust's subsequent Action Plan, and the crucial point was lost - perhaps because it wasn't grasped at the time or emphasized boldly enough. Perhaps there were other reasons that the advice was not acted upon. Even from the start of the investigation, the HCC did have detailed information about phages though - and copper. In my interview visit, I supplied them with multiple scientific references as advised by a Canadian microbiologist. Months later, the studies were returned by post - unread because they had decided that the subject of phages was outside their terms of reference.

Environment and Rural Affairs civil servants could also pay more attention rather than ignoring messages about phages. There are public health dilemmas with *Campylobacter*-infected poultry and *Salmonella*-infected chocolate, and *E.coli*-infected beef, resulting in court cases and huge financial penalties in addition to illness, animal culling and loss of jobs - even an imprisonment. The list goes on.

Meanwhile in the Education sector, day nurseries are declared unhealthy and uncaring places for young children. This needs to be improved before children are under age 5 become acutely or chronically ill. Such stressful conditions weaken their immune systems. They sleep poorly and then may catch infections very easily.

In the Health sector generally, there appears to have been a powerless lack of resolve, action or concerted effort – with the result that they would stick with what they knew, 'pass the buck' with any correspondence about bacteriophages and wait to see if any daring individuals would take the initiative with clinical trials. Some have had to use their own private funding. There is minimal official backing, or even incentive, given the potential value of such medical research.

Perhaps the time has come for a change of direction and a fresh approach. Please could the government regulations be updated to make room for this special science?

"I think there is a lot of work to do in phage therapy so that it is well described. It is very promising and wonderful - a special alternative to antibiotics."

Dr.K.Dabrowska, phage biologist, Poland

UK News in brief

UK clinical trial

Phages are not generally available in the UK, but there is demand, and fortunately the first phage clinical trial is nearing completion at the Royal National Throat, Nose and Ear Hospital in London. At phase 2, their experiments are leading the way, designed scientifically and rigorously to give proof of safety, dosage and efficacy. Participants

in this trial had persistent ear ache caused by a specific bacterium, *Pseudomonas aeruginosa* and already some have had dramatic improvements after only one dose. They are helping to provide robust, impartial scientific evidence. The researchers hope to have initial products on the market within 4 years.

"Phase 2 results are the necessary proof of principle to bring this technology into the mainstream."

Dr. David Harper, UK virologist and phage researcher

Medical tourism from the UK

From 2006-7, several UK patients have travelled for phage therapy in Georgia and Poland at their own expense, for antibiotic-resistant bacterial infections. Perhaps it is now time for phage therapy to become available in the UK.

Research funding

Sizeable amounts of funding are now being made available in the UK to enable bold infection research initiatives for the foreseeable future - ± 16.5 million at present.

In Europe there is new funding to encourage scientific networking generally. Internationally there is strong scientific interest in the health value of bacteriophages, and a great wealth of knowledge. There is ongoing research with 'bits of phage' and genetic modification in the UK, USA and worldwide beyond the scope of this project.

The Science and Technology Center in Ukraine have financed five bacteriophage projects to a total amount of 900,000USD.

In August 2007, the Bill Gates Foundation was showing interest in the Georgian work on bacteriophage therapy for acute intestinal/diarrhoeal disease.

In September 2007, the European Union was considering a large application for funding from the Polish Academy of Sciences for funding bacteriophage research and clinical trials. However, note that in general, only 8-10% of funding applications are accepted in Poland.

In August 2007, informal discussions with UK scientists at the 17th Evergreen International Phage Conference in Olympia, WA indicated that financial support for phage research and education in the UK is minimal. Many researchers and students are having to be self-funded. Media interest and consequently public, political and educational awareness in the UK are still considered very poor. However, with the latest news announcements, the conference host Prof. Betty Kutter commented that media interest in the UK has gathered momentum over the summer, so perhaps this will result in more successful UK funding applications soon.

Phage products available

The US government in recent months has approved that phages can be added to some food products that have previously carried the risk of bacterial contamination. This decision is based on evidence and professional consensus that bacteriophages are safe and of value to public health. There is no indication that the UK government is planning to follow suit. It is hot news that there are five phage products available in the marketplace. The first product using bacteriophage was approved in November 2005 for the treatment of bacterial infections in tomatoes and peppers. In 2006 there were two products permitted to prevent *Listeria* in cold meat products. In 2007, there were two new phage products approved, to be used to treat E.coli and Salmonella on live animals and their environment prior to the animals' slaughter.

UK Government phage projects

US and UK government Defence agencies take an interest in phage developments for bio-defence. Scientists have come up with a phage-based 'biological disinfectant' against a serious bio-terrorism agent, *Anthrax*.

The Ministry of Defence is also in charge of a priority G8 Global Partnership-funded retrospective research project trawling through documentary evidence at the Eliava Institute, Georgia of the use of phages. They will report the findings to other UK government departments, in the hope that they would become interested parties (e.g. Dept of Health) for exploitation of phages at some stage in the future. I pointed out to Dr. David Harper, a British virologist, that there were several inaccuracies and omissions in the Ministry of Defence's 2006 official reply to me about the G8-funded research project. The feedback and other key points have also been brought to the attention of the MoD and the Health Protection Agency.

Official environmental agencies would have the responsibility of furthering developments to benefit the health of our livestock and crops, including the many potential applications in veterinary science and food science. Government emphasis is on patenting aspects, rigorous testing and the commercial business potential.

Public servants in UK government departments have tended to be slow and even unhelpful in their responses to this research. Some have shown very little interest, background knowledge or willingness to consider using phage therapy to help improve health and wellbeing. This pattern of inertia in bureaucracy is reported very clearly by others internationally. Some senior scientists and consultants have also been unable to find the time to reply to pertinent queries. As a result, opportunities have been delayed or even lost.

Bacteriophage-related news

Jeanine Thomas, founder of the MRSA Survivors Network contributed to this travelling research in Chicago by describing in detail her traumatic experiences with an MRSA infection. In August 2007, she and her team achieved legal history regarding MRSA reporting and surveillance in the USA. Her bill was enacted in the State of Illinois. Knowing the true incidence of MRSA infections will encourage the development of other treatments such as bacteriophage therapy. Bacteriophage therapy may be of great value for patients with MRSA infections.

The 'DispersinB + phage' phenomenon is arousing strong scientific interest amongst those 'in the know'. Kane Biotech is offering to provide DspB to interested researchers. There is a strong likelihood of an international collaborative project with patients who have chronic antibiotic-resistant infections associated with biofilms.

In July 2008 an international phage conference will be held in Edinburgh, Scotland, UK. For further information see <u>http://www.amazingphage.info/page24.htm</u>.



Bacteriophages everywhere

Bacteriophages are everywhere, including rivers in Georgia. Photo courtesy of Dr. Amy Filby

Bacteriophages!

'made by nature'

'do no harm to the body'

'do no harm to nature'

'no side effects'

'present in the atmosphere, soil, water, living things etc.'

viral agents whose function is to destroy bacteria'

"Billions of phages occur naturally; their weight in the oceans alone is though to be equal to the weight of human beings on Earth. The first inkling that phages existed came in 1896 when British chemist Ernest Hanbury Hankin discovered that the murky waters of the River Ganges could destroy cholera bacteria." [sic]

Tom Parfitt, The Lancet Volume 365, June 2005

"From a clinical standpoint, phages appear to be innocuous."

Harald Brüssow, Phage Therapy: The Western Perspective, 2007

"This is about half the cost of 10-day therapy with vancomycin and several times less compared with the other drugs ... "

Miedzybrodzki R et al, 2007. This article is online at **http://www.relax-well.co.uk/less expensive than antibiotics.pdf**

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This 'once in a lifetime' experience is opening many doors and possibilities for the future regarding the health value of bacteriophages. For me, it is presenting exciting adventures and special joys. There are invitations to international phage conferences and medical research centers, along with informal opportunities to let people know about the health value of phages. It is my privilege and honour to meet scientists and clinicians who are devoting their life's work to this most important subject - bacteriophages. It is also my privilege and honour to witness and share the stories of the lives of the people whose health has benefited hugely from these miniscule and relatively unknown microbes – the bacteriophages.

The Winston Churchill Travelling Fellowships are awarded for originality, enterprise, character and a sense of responsibility. While those selected travel to all corners of the world as individuals in their own right, they do so as representatives of the United Kingdom and in the memory of Sir Winston Churchill. I highly encourage others to consider applying for a Winston Churchill Travelling Fellowship award.

In summary

"Hope that the phages become as "phamous" as Sir Winston."

Dr.Revaz Adamia, Georgia

"J'ai toujours admiré Sir Winston. Je le répète ici."

Prof. Hans-W. Ackermann, Canada

"This is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning."

Winston S.Churchill, United Kingdom

A guestbook, further acknowledgements and references can be accessed via **www.amazingphage.info**.

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