

BACTERIOPHAGES : COULD EARTH'S MOST ANCIENT VIRUSES SAVE US FROM SUPERBUGS?



An old ally that could shift treatment strategies as an alternative to standard therapies.

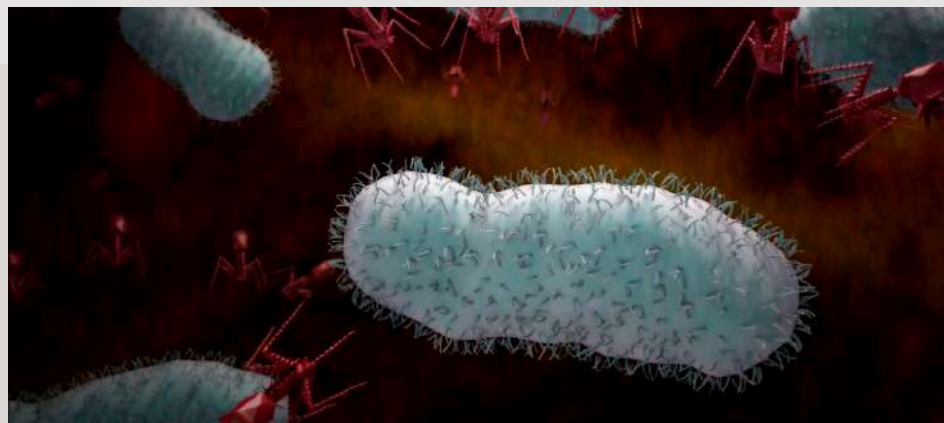
A feature article by

Dalene Lesen

THE SILENT PANDEMIC

Antimicrobial resistance (AMR) is no longer a distant theoretical threat; it is a silent pandemic gathering pace in our hospitals and communities. In Malaysia, we are standing on the precipice of a public health crisis. Recent projections by the World Health Organisation (WHO) and the Western Pacific Regional Office suggest that without immediate intervention, drug-resistant infections could claim 87,000 Malaysian lives between 2020 and 2030. This represents roughly 0.26% of our population, a staggering figure for a crisis that remains largely invisible to the public eye.¹

Globally, the outlook is even more sombre. By 2050, AMR is projected to cause 10 million deaths annually, surpassing cancer as a leading cause of mortality.² As the "superbug" phenomenon renders our standard antibiotics ineffective, which complicates once-routine surgeries and common infections, we must look beyond traditional medicine. Paradoxically, the solution may lie in Earth's most ancient predator: the bacteriophage.



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THE "BACTERIA-EATER": A FORGOTTEN HISTORY

Bacteriophages, or "phages," are naturally occurring viruses that exist for a single purpose: to hunt and kill bacteria. Discovered independently by Frederick Twort in 1915 and Félix d'Hérelle in 1917, these "bacteria-eaters" were used to treat dysentery and cholera decades before the mass production of penicillin.³

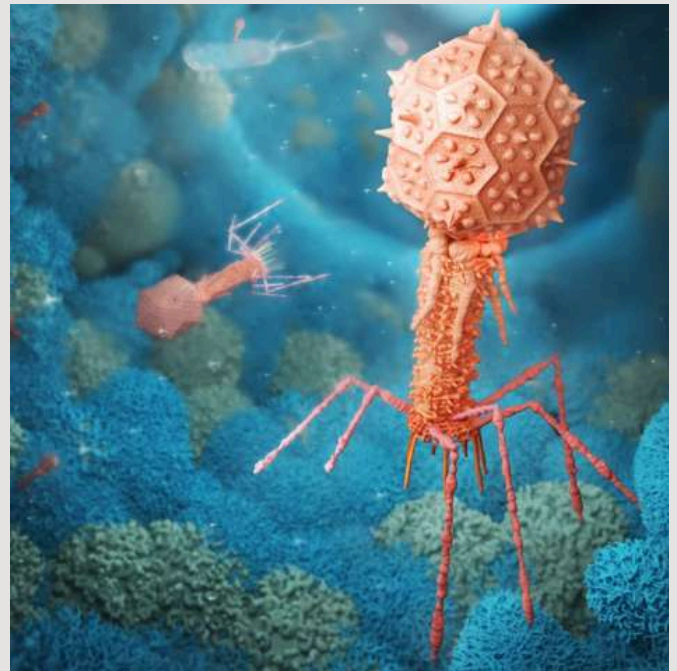
However, when antibiotics arrived in the 1940s, they were hailed as "miracle drugs" due to their broad-spectrum ability to kill many types of bacteria at once. In the West, phage therapy was largely abandoned in favour of these easy-to-use pills. Meanwhile, in Eastern Europe, specifically at the Eliava Institute in Georgia, phage research continued, serving as a primary medical tool for over a century.⁴ Today, as our miracle drugs are slowly becoming ineffective, the global medical community is turning back to this "biological precision" that we once sidelined.

PHAGES ARE EVERYWHERE

Phages are the invisible giants of our planet. From the depths of our oceans and the soil beneath our feet to the sewage and hot springs, phages are everywhere. Scientists estimate there are ten times more phages on Earth than there are bacteria, making them a vast biological army found in every corner of the globe.⁵ They act as nature's ultimate balancing force, quietly driving bacterial evolution and recycling vital nutrients within every ecosystem they touch.⁶



*Artist impression of phages (red) attacking a bacterium (green).
(Source: nobeastsofierce/Shutterstock.com)*



Artist impression of a Bacteriophage. (Source: Winpharma)

PRECISION MEDICINE:

HOW PHAGES DIFFER FROM ANTIBIOTICS

To understand why phages are effective, view them as "precision-guided missiles" rather than "carpet bombs." Standard antibiotics are chemical agents that often kill both harmful and beneficial bacteria, disrupting our internal microbiome. In contrast, a phage is highly specific; it targets only a particular strain or species of bacteria.⁷

Once a phage identifies its target, it attaches to the surface and injects its genetic material, hijacking the bacterial cell and turning it into a factory to produce more phages. Eventually, the bacterium bursts in a process called lysis, to release a new army of phages to continue the cycle. Crucially, because phages recognise only receptors on the surface of bacterial cells, they ignore eukaryotic cells entirely.⁸ This allows them to eradicate deep-seated infections without the "collateral damage" to the body often caused by harsh chemical treatments.



*Bacteriophages attaching to the bacterial cell.
(Source: science.org)*

Beyond their specificity, phages possess a unique ability to dismantle biofilms, the slimy, protective shields that bacteria build around themselves to repel antibiotics. This makes phages particularly effective against chronic, recalcitrant infections on medical implants or heart valves where traditional drugs often fail to penetrate.⁹

From the depths of our oceans and the soil beneath our feet to the sewage and hot springs, phages are everywhere.



*Artist impression of a video rendering of bacteriophages floating in media.
(Source: Canva)*

PHAGES VS. ANTIBIOTICS: DAYS VS. DECADES

The timeline of modern medicine is often measured in years, but the “superbug” crisis moves in days. When it comes to speed and cost, isolating phages from nature far outpaces the development of new antibiotics. Developing a single new antibiotic is a monumental undertaking, requiring decades of chemical synthesis and billions in investment, often with very few successes to show for it.^{10,11}

In contrast, phages can be “harvested” rather than manufactured. By taking a sample from a phage-rich environment, such as treated sewage, and introducing it to a specific pathogen, scientists can identify and purify a targeted “bacteria-eater” in a matter of days using basic laboratory equipment.^{12,13}

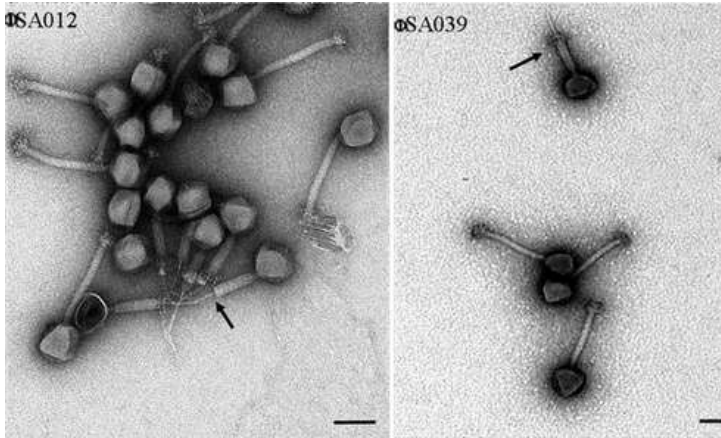
Because phages self-replicate at the site of infection, target only the “bad” bacteria without harming the body’s microbiome, and penetrate through biofilms that antibiotics cannot touch, they represent a revolutionary bypass of the traditional pharmaceutical pipeline. Today, laboratories worldwide are proving that we can find custom, natural solutions to multidrug-resistant “superbugs” in the time it takes to ship a package.

One of the most remarkable features of phage therapy is its self-terminating nature. Because phages are biological “specialists” that require a specific bacterial host to replicate, they cannot linger indefinitely. Once the target bacteria are eradicated, the phages lose their only means of survival and reproduction.

The remaining viral particles are then naturally and safely cleared from the body by the immune system, much like any other inert biological debris. This ensures a clean exit, leaving the patient’s healthy microbiome intact and the “predators” gone once their mission is complete.¹⁴

A REGIONAL BREAKTHROUGH IN SINGAPORE

The potential of phage therapy was recently demonstrated on our doorstep. In September 2024, Singapore General Hospital (SGH) successfully treated a woman in her 30s with a life-threatening *Pseudomonas aeruginosa* infection.



TEM images of bacteriophages. Bar, 100 nm. The arrow indicate contracted sheaths. (Source: Synnott et al, 2009)

The patient, who had a congenital heart condition, faced a grim choice: a high-risk surgery to remove her infected heart valve implant or lifelong, ineffective intravenous antibiotics. Instead, clinicians at SGH used a "cocktail" of three phages specifically matched to her infection.

Over a two-week course, the phages eradicated the biofilm and the infection, allowing her to transition to simple oral antibiotics.¹⁴ This success story illustrates the power of phages as adjuvants, where they can work alongside antibiotics, often "re-sensitising" the bacteria and making them vulnerable to drugs they previously resisted.

THE PATH FORWARD FOR MALAYSIA

While phage therapy is currently reserved primarily for "compassionate use" (a last-resort option for patients who have exhausted all other treatments), the global momentum is shifting toward making it a frontline reality. Leading the charge is Belgium, which established a pioneering legal pathway in 2018 that allows pharmacists to "compound" personalised phage cocktails much like a tailor-made prescription.¹⁵

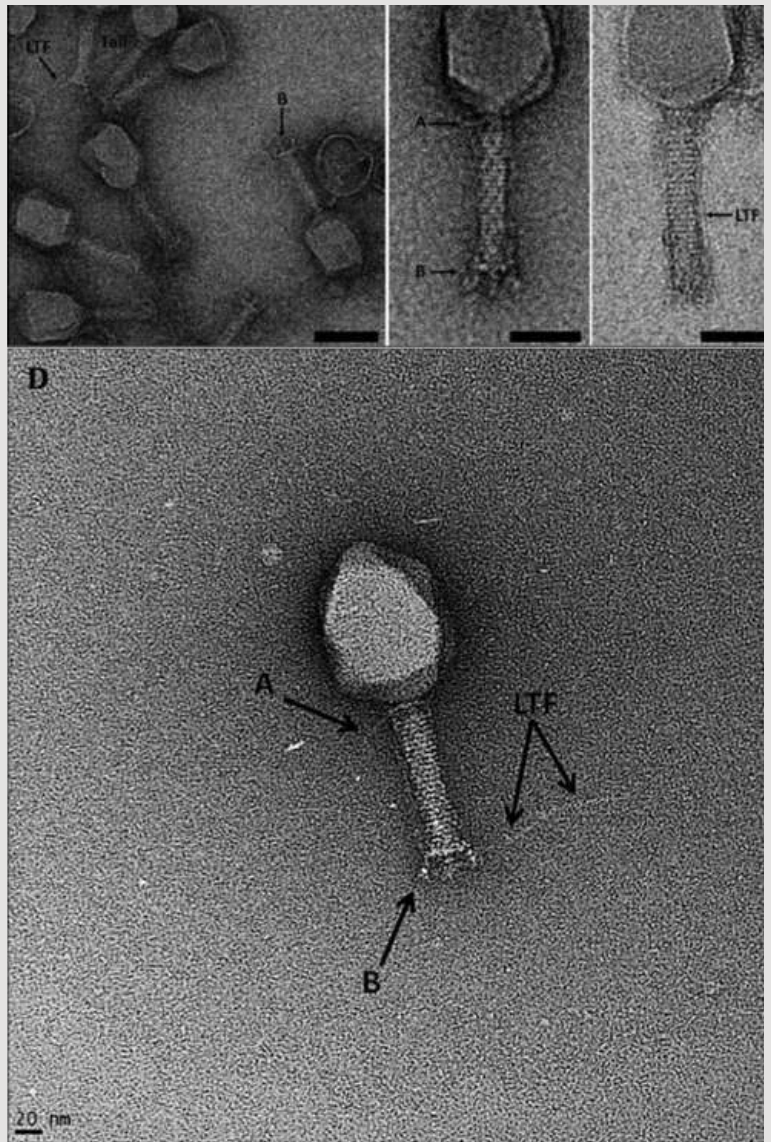
Other nations are following suit with their own frameworks: Germany utilises specific provisions in its Medicinal Products Act to permit tailor-made treatments for individual patients, while France manages access through rigorous national authorised programs. In the United States, the Food and Drug Administration (FDA) is increasingly clearing the way through "Expanded Access" pathways, allowing clinicians to bypass traditional red tape to save lives.⁵ These countries are proving that with the right rules in place, we can move from mass-produced "one-size-fits-all" medicine to a future of precision healing.

For Malaysia, the integration of phage therapy could be a cornerstone of our National Action Plan on AMR. By leveraging our local biodiversity to build phage libraries and collaborating with regional partners like hospitals and research institutes, we can move toward a future where a "superbug" diagnosis is no longer a death sentence.

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(D) Bacteriophage TG1 virion shown at $\times 150,000$ magnification. A neck and collar with neck fibres (labelled A), a baseplate with protruding tail pins (labelled B), and an extended LTF can be observed.

The scale bar indicates size in nanometers.
(Source: Carlos G Leon-Velarde et al, 2016)



CONCLUSION

The lesson from the Singapore miracle and the century of success in Georgia is clear: nature has already provided the predator for our greatest microscopic enemy. Malaysia, with its immense tropical biodiversity, is sitting on a goldmine of untapped phage potential. From our diverse soil ecosystems to our urban water systems, the "predators" we need to fight local superbugs are already here. It is time we put them to work.

By establishing our own phage biobank, researchers and physicians could eventually pre-identify and match effective phages to dangerous bacteria long before a patient reaches a crisis point. This proactive infrastructure represents a significant leap in AMR pandemic preparedness, ensuring that when the next resistant infection emerges, we have the precision tools ready to fight back.

In doing so, SIDC aspires to nurture bacteriophage research and development within Sarawak, tapping into our region's vast biodiversity to find a sustainable, nature-led approach to this growing global threat.

As we look toward the future of medicine in Sarawak, the priority is clear: we must stay one step ahead of the 'superbugs' currently circulating in our healthcare systems. To meet this challenge, the Sarawak Infectious Disease Centre (SIDC) is envisioning the establishment of a centralised biobank dedicated to locally sourced phages. The goal of such a facility would be to catalogue these natural predators of clinically relevant bacteria found right here in our environment.

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