Science AMA Series: I'm Heather Hendrickson, Senior Lecturer in Molecular Biosciences at Massey University in Aukland, New Zealand. I'm here to answer questions about bacterial resistance and the future of health. AMA!

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Whats your opinion of antibiotics being primarily used for agriculture? Do you think this is the prime reason why bacteria are becoming immune to our antibiotics? How concerned are you about an outbreak from a mega farm ie mega dairy within the next 10 - 20 years.

Also I think your one of the most important people in the world, because I take these dangers very seriously & no one i ever speak to has ever heard or thought of anything like this. So please don't stop or give up!

Thank you for helping us!

bigorse88

Hi, Thanks for your question and your support! We all need to reconsider our use of antibiotics and be sure that we are only using them when they are medically relevant and required (not for flu, viral infections etc.) That being said, I think antibiotic use in agriculture is a massive issue and one that will require both public will (you and me) and political intervention to address. Every use of antibiotics goes a small way in reducing how long these drugs will be necessary. To my mind, antibiotics should be preserved for therapeutic use in humans and for life saving situations in animals. In the USA it is estimated that as much as 80% of antibiotics are used in agriculture. In New Zealand the estimates are closer to the around 50% but that is largely because we have low levels of antibiotic use in our grass grazing livestock (cattle and sheep). This is a lot of our production here. The NZ veterinarian society has vowed to cut unnecessary antibiotic use by 2030. This is good news but I don't think it is far reaching enough.

We need a combination of monitoring and serious consequences for farmers and growers who use antibiotics to compensate for over crowded conditions. Without these measures, I don't think that we will see the decreases in non-necessary use that we need to see in order to preserve these precious drugs. The US has implemented CARB (https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf_) with a goal of cutting non-necessary antibiotic use by 2020.

As for the "big outbreak" idea … I think that we are currently experiencing the gradual trickle of

antibiotic resistant superbugs from agriculture, aquiculture and animal production into human infections. I don't think that bacterial superbugs generally evolve like a tidal wave (the way viruses do). The genes that allow bacteria to be resistant to the antibiotics that we use today are already present in the soil and the environment because they are defenses that bacteria use against one another. The selection that we impose by using antibiotics means that ANY bacterium that inherits one of these genes will benefit if they encounter antibiotics and we are flooding groundwater and soil with low levels of these drugs.

OK I know how ridiculous this question might seem but I am serious. Do you know of any serious study of men or women "who have never been ill in their lives..."? Obviously I would limit the scope of this question to those who display significantly enhanced immunities to bacteriologically based illness.

Has there ever even been a significant search for natural immunes across this species? Obviously the idea leans towards apochryal, but how do we know the perfect anti-ill state doesn't exist at least in some forms at some stages in some rare people without such a deliberate search?

They'd never present at the doctors/clinics/specialists etc because, they never get sick, so the health services/scientists never get to hear of them.

I only ask, as it would seem if they did exist, that they themselves might have something to contribute to your field of study.

SoFarceSoGod

Hey SoFarceSoGod,

I love the idea that you are proposing here. What would their microbiomes (the trillions of bacteria that support their gut health) look like, for example? Speaking of that, it does remind me of the comparisons that are being made in the microbial world between the microbiomes of people in non-westernised societies and modern western societies... We have seen a doubling of asthma rates every 20 years for the past 60 years in Western Societies. This, along with a lot of other data, have suggested to us that we have perhaps gone too far with our hygiene and we have eliminated certain "old friends" from our systems: bacteria and possibly parasites that we evolved with and have served to both develop and regulate our immune systems. I really like these ideas... you can learn more by looking up the "hygiene hypothesis" or the "Biodiversity hypothesis". It's a fascinating field!

You say you are working on using viruses to kill bacteria but isn't that going to result in the same problem when all the virus-resistant bacteria survive?

Thank you for your work.

auCoffeebreak

This is a great question as well! What a fun forum! Thanks :) YES! Bacteria and viruses have been battling it out for billions of years and bacteria are very good at evolving ways of combatting viruses (CRISPR-cas is a great example of this). However, there are actually 10 times more bacteriophages on the planet than there are bacteria and we have barely scratched the surface of their diversity today! So, with about 200 antibiotics that have come to market but 10 ^ 31 (that is over a Nonillion) bacteriophages in the soil, I would say that we have huge, untapped, pharmacy potential in the soil beneath our feet!

do bacteria loose their resistance over time? i mean if a bacteria grows inmune to antibiotic A, then we

switch ot antibiotic b, c, d... by the time we hit antibiotic z, does it still have the same resistance to antibiotic A?

mejillonius

Hey there,

This is an interesting question. It really depends on the mechanism of resistance that the bacterium has acquired. There are many types of antibiotic resistance. For example, Pumps or anti-porters are protein machines that are able to recognise and selectively pump specific antimicrobial drugs back out of the cell.

These can pump out multiple chemicals and antibiotics.

There have been some papers published that suggest that some antibiotic resistance genes make life a little bit harder for the bacteria so when we switch antibiotics we might expect these do be eliminated from the population. Unfortunately, not all resistance genes appear to be costly, so some bacteria can just keep acquiring new resistance genes.

How serious a problem is bacterial resistance? I know it's serious, but I can't get a handle on how serious. How will it effect how medical treatments are delivered in the next decade or two?

tgoesh

A recent report suggested that if our use of antibiotics doesn't significantly change then by 2050 we should expect to see 10 million people dying of antibiotic resistant infections each year. That is more than the 8 million people who die of cancer each year today. I would say this is very serious. This is part of the reason that I think considering new types of therapies and bringing back those we have abandoned is crucial.

Hi there!

Sorry for the maybe silly question, but I don't know the first thing about bacteria.

I remember hearing that the problem with the HIV was the it mutated too fast and therefore kept becoming resistant to every single cure. The extremely successful cure was to use a mix of drugs, so that we could be sure that it couldn't be mutating against the second one at the same time.

Why aren't we doing the same thing with antibiotics? I.e.: mixing a bunch of different antibiotics together, so that bacteria can't evolve randomly to become resistant to two different ones at the same time?

lucaxx85

One of the things that makes bacteria different is the way that they evolve. The property of a single cells having resistance against antibiotics emerges in bacteria in two primary ways: random mutations in pre-existing genetic material (Mutation frequencies and Antibiotic resistance) or the gain of new genetic material from other bacteria that are resistant, Horizontal Gene Transfer (HGT) (Origins and evolution of ABR). Though the absolute levels of HGT in nature are not trivial to measure, we can observe that recent HGT explains the presence of an estimated 20% of genetic material in many genomes. This can be as high as 60% in some lineages. Some groups of proteins appear more recalcitrant to successful HGT (eg. those that have a large number of proteins they must work with), but essentially, any gene can be transferred. The more antibiotics we put into an environment, the more individuals are likely to have genes for resistance and they can trade these around like playing

cards that self-replicate.

Where in the world is the issue of bacterial resistance most pressing? I would think it's for more developed countries where antibiotics are over-prescribed but will it eventually hit everyone equally?

zedlam97

Hey! I think this is a pretty insightful statement. Antibiotic resistance is certainly higher in places that have not regulated their use. However, the WHO divided the world into 6 big regions and every one of these had at least one nation with 50% resistance observed in clinical settings for one of the big concern bugs: *Streptococcus pneumoniae* or *Klebsiella pneumoniae*. There aren't borders to antibiotic resistance and this **IS** a global issue.

What are steps each person can take on their own to help reduce this problem? How much does being vegetarian help?

Thank you very much for your time!

NotABMWDriver

I think we can make our values clear by speaking with our wallets. By personally avoiding foods that are made with antibiotics. Unfortunately, there are still growers of fruits and vegetables who are ALSO using antibiotics in production to cut down on costs and avoid losses so being a vegetarian is a great step but there are more questions that we need to ask as consumers about where our food is coming from.

Thanks for this Heather!

Can you please tell me how to reduce usage of antibiotics?

birgirm

Great question! I have posted this elsewhere in the forum: Next week is officially the WHO “Antibiotic Resistance Week and they have this advice for the public: ● Only use antibiotics when prescribed by a certified health professional ● Never demand antibiotics if your health worker says you don’t need them ● Always follow your health worker’s advice when using antibiotics ● Never share or use leftover antibiotics ● Prevent infections by regularly washing your hands, handling food in a safe/clean manner, avoiding close contact with sick people, practising safer sex & keeping vaccinations up to date

I would add that by choosing foods for which you are certain that antibiotics have NOT been used during production. This isn’t easy but we can let producers know what our values are with our wallets!

Check out more information from the WHO on antibiotic resistance here: http://www.who.int/campaigns/world-antibiotic-awareness-week/en/

I've tried to reassure my "doom" mongering father that the "Antibiotic Apocalypse" won't happen due to research such as yours or research into nano technology. What else could I say to reassure him that we as a species will survive?

Wackyal123

Hey there,

You are right, "Antibiotic Apocalypse" is too strong. Going back to a pre-antibiotic era... when we did not have the advantage of antibiotics to clear infections, will mean a few things for us if we don't find new tools. In general, I would say a shortening of the human expected life span. Some people will get infections that they can not clear and they will die early. I wouldn't expect humanity to end. I think there is a lot of hope in the technologies that science is pursuing at present but in order to take advantage of these we need better systems in place for sharing what we are learning and for funding basic research.

How long does it take to characterize a new virus? I'm assuming that you already have a pretty detailed protocol for separating them, but do you just sequence them first and then look for sequence homologies against known viral proteins to determine if you have a 'hit'?

aristotelianrob

Hi there!

In terms of finding and describing new bacteriophages this can be extremely quick. I had a group of teenagers (20) who discovered 6 new bacteriophages in two weeks this year. We haven't sequenced these yet but with the new sequencer technologies available (like the MINion sequencers), we could sequence these in 24 hours. WE just got one of these at my uni ... so cool.

So, sequencing the DNA tells you everything (essentially) you need to know about a new bacteriophage. Discovery and sequencing can be rapid.

Thanks for this.

What are the ramifications of a rouge private lab creating a bunch of bacteria that are all resistant and a few also resistant to viruses you speak of? What are some private companies doing this research or commercializing it?

Unrelated question is plan B for the apocalypse?

kadan5

Hey there, This is a very sci-fi question! I will go on a limb here and say the following: there are an estimated 10 bacteriophages per bacterial cell on this planet. To me, that says that there are not bacteria that can not be infected by some bacteriophage. That gives me a lot of hope, even in the face of nefarious unnamed "labs" creating things!

Thanks for this.

What are the ramifications of a rouge private lab creating a bunch of bacteria that are all resistant and a few also resistant to viruses you speak of? What are some private companies doing this research or commercializing it?

Unrelated question is plan B for the apocalypse?

kadan5

Also! There are a few companies like Ampliphi and Intralytix who are developing phage applications for various uses. Check them out!

Whatever happened with Shu Lam's tiny star shaped molecule that supposedly killed super bugs? Does that have potential? Is it even real?

Nyxtia

I have seen the paper describing this. It has great potential! That said, it appears to be another example of a "broad spectrum" destroyer: kills all the bacteria, rather than being as specific as bacteriophages can be.

Hey! I'm an undergraduate studying Microbiology at the University of Sheffield in the UK, and the work you're doing now is more or less my dream job.

I've been considering phage therapy as a potential solution to the 'antibiotic apocalypse' for some time, but I was always curious as to why there's not much focus on phage therapy or other alternative solutions so much as just producing more antibiotics. I'm assuming that the lucrative nature of the antibiotic industry is to blame for it, but I imagine that there must be inherent problems with phage therapy for it to not have been considered a viable option until recently (unless I'm mistaken and just haven't heard of enough researchers looking into phage therapy and other alternative solutions).

What are the problems or shortcomings with phage therapy as opposed to antibiotic treatment? It seems to me like it'd be a once-and-for-all solution, owing to the ability of bacteriophages to mutate and evolve at the rate of their hosts. Is there a possible issue with bacteria already being too well-equipped to handle viral infection (restriction modification, CRISPR, etc.) due to their constant exposure to bacteriophages in their natural environment?

Thanks in advance!

bluntCube

Hi there! Great question :) We need to do a lot of work in order to get bacteriophage therapy to a state where it could be approved in the rest of the world (outside Georgia and Russia). This includes the sorts of exciting clinical trials that are going on today in France: phagoburn.

Known possible problems with phage therapy: Phage therapies curse and blessing is specificity. A phage therapy treatment must be tailored to the precise bacteria in an infection. This means, pre testing, comparing to a library of known phages and the construction of the perfect "cocktail" for treatment.

Phages are not as durable as antibiotics so they can loose efficacy over time more easily.

Phages are made out of protein they can cause allergic responses in some patients.

Phages are quickly cycled out of the body by our kidneys. This means additional doses are required to reach some areas. It does appear possible to select for resistant bacteriophages however that will survive this process.

There are issues but they can be overcome with more research so there is also a lot of promise!

On a scale of 1 - 10, how are you feeling about the world wide effort currently being put into addressing these kind bacterial problems?

The_Brad

We have a LONG way to go to address the issue of antibiotic resistance! I think we are at 5. We need to stop the needless use of antibiotics in agriculture and put more funding in alternatives!

Can we use our conventional gene editing techniques to design viruses with specific abilities useful for attacking bacteria or are we still figuring out how to modify their RNA? Does a catalog of useful RNA snippets even exist / are you building one?

Awesome to hear this is going on at Massey.

bostwickenator

:) Go Massey! Gene editing of bacteriophages is one way of thinking about using them in the future. They are also so diverse that there are more different bacteriophages in 1 gram of soil than there are people on the planet ... SO, editing may not be necessary. Discovery is key. The bacteriophages that infect bacteria are primarily DNA based. There is an incredible resource being built around the diversity of bacteriophages that are able to kill mycobacteria. This is being fuelled by the work of the incredible people at the HHMI SEA PHAGES program. You can learn more at phagesdb.org.

Essentially, they have over 1000 Mycobacteriophages sequenced and preserved in Pittsburgh PA as part of an educational program. SEA = Science Education Alliance.

I was a PhD student at Pittsburgh and got to know about phages there. Today, Massey University is the only University outside of the USA that has officially joined this incredible phage hunting program.

Where do you get the patients willing to try this - your first guinea pigs? Has this been tried yet anywhere or in any similar capacity? Thank you!

HolySmokeyPants

Bacteriophage therapy has been practiced for about 80 years in Georgia and Russia so there are many people who have tried this form of therapy successfully. If you want to read a great story about phage therapy saving a man from never walking again, check out Alfred's story and Betty Kutter's Evergreen phage blog: http://blogs.evergreen.edu/phage/about/alfreds-story/

How are you going to solve the problem of the patient reacting to the phage itself. Surely an IV of phage would cause a devastating immune response, secondly how does one maintain copy number without inducing lysis in the bacteria which is going to spill its contents and cause sepsis?

jarh1000

These are great questions. Some patients may experience allergic reactions and this must be taken into account before phages are administered system wide.

In terms of your second question, the sort of sepsis that you are talking about is when the bacterial pathogens have endotoxins in their membranes. This is not the case with all pathogens but lysis in these cases can make a patient more sick. There are ways of engineering bacteriophages (for these infections) such that they are killed but not lysed. However, there may be pathogens that would not be advisable to treat with bacteriophages. Another thought is that using bacteriophage proteins, rather than whole bacteriophages, we may be able to poke holes in the pathogen, killing or disabling it, without lysis. Great question!

Would you use some kind of gene editing like CRISPR to edit out resistance genes and then use bacteriophages to insert the dna into resistant bacteria? Or just use phages to kill the bacteria? How would you mass produce the right ones or would a cocktail be used, as some kind of broad antibiotic? And what kind of delivery system would be used to get the phages to the bacteria, I understand so far they are only used topical for infected wounds in some countries.

jenzett

I generally think that simply using the bacteriophages to kill most of the pathogens and then allowing our immune system to finish the job is the best strategy. I have heard of various ways of administering bacteriophages directly to blood or even surgically. You are right though, my understanding is that topical administration is most simple. There is currently a clinical trial going on in France for burn patients called : Phagoburn that should be very interesting when it is complete.

I think most practitioners recommend a cocktail approach. This allows for the subset of the population of pathogens that might be resistant or evolve resistance to the phage during treatment.

How well funded are you, considering you're in New Zealand?

(Asking as a fellow Kiwi)

Przedrzag

I get some funding from the university. I haven't tried the major sources of funding for bacteriophage funding yet. I'd like to publish a few papers first. I got through the first round of Marsden this year with another project (bacterial evolution) but didn't get funded. So... maybe next year? :) Funding is hard everywhere!

Dr. Hendrickson, Bacteriophage resistance in these bacteria can become a real problem. Two questions: How do you intend on protecting the phage from CRISPR-like systems. What protocols would you instigate (akin to antibiotic stewardship) to prevent misuse of phage treatments.

Downsideupside

Hi there!

The abundance of alternative bacteriophages to discover, try out and use makes this sort of concern largely irrelevant. There have been about 200 types of antibiotics. There are more bacteriophages in a gram of soil than there are people on the planet. I think the numbers are on our side if we get out there, discover them, sequence them and find out what their host ranges are. We have what we need...

What's to stop a virus that's been implanted from mutating such that it's no longer beneficial, or perhaps even now harmful to the host?

kehbleh

Bacteriophages have had 2 billion years to start infecting humans and they haven't yet. To be honest, this isn't a big surprise ... there are WAY more bacterial cells on the planet to attack than there are human cells! Also, taking over a bacterial cell is relatively easy, the DNA and all of the working machinery is just sitting in the cell. Eukaryotic cells (like ours) have the DNA wrapped up and hidden in an extra organelle. Too complicated! Infecting bacteria is a pretty great job (if you can get it). At least , that is what the bacteriophages tell me.

What do you think the bacterial, viral, drug, health landscape will look like in 50 years?

Will people still be getting colds and flus? How will they be treating them? Will nurses and doctors in hospitals be wearing more and bigger masks and more gloves, or will that have changed thanks to advances in antibiotics, targeted viruses, antivirals, etc.?

immerc

I hope that we will working WITH our natural micobiota rather than against them. This could me a deeper understanding of our microbiomes and how these bacteria affect our health. For viral infections (like the flu) I would like to see us modifying our internal environments to make their replication less likely. I liked the idea that Magnesium can do this in the case of viruses but some of the products that provided this magnesium gel seem to be harder to find today than they were 5 years ago.

Are there different virus types for hunting different bacteria types or infection sites, or are most of the viruses you're looking at a systemic solution?

Do you understand the process by which a virus will select and attack specific bacteria and not others, or more trial and error to find viruses that limit themselves to undesirable bacteria?

alcimedes

Bacteriophages are very specific to their host strain but we see clear evidence that this relationship can change as evolution takes place over time on the bacterial and viral sides. In order to find a reasonable solution to a bacterial infection, you would generally want a huge collection of bacteriophages that infect that stain of bacteria and you would want to combine these as a cocktail.

Came here to ask your opinion on bacteriophage therapy, but it looks like that's what you guys are pursuing. The idea of using phages fascinated me when I was in high school and I wondered why we weren't using them in place of antibiotics.

How specific are phages to the bacteria they attack? Do we have to wait until a culture identifies the organism responsible for the infection or can we give patients a "cocktail" of various phages as a shotgun approach if they need immediate treatment?

How long of a shelf life would they have? Are only lytic phages effective for treatment or can temperate phages also be used? How quickly can phages adapt to bacterial resistance?

Neighsus

Great questions! Phages are generally highly specific to the bacteria that they infect but there have been some reports of "broad specificity" bacteriophages in the literature. The phages that we have found are generally very specific to the strain... A cocktail approach is therefore generally recommended so that evolution inside the organism doesn't evade the bacteriophages that are used. Phages can be long lived or short lived. They vary a lot. Lytic phages (those that do not take up residence in the bacterial genome) are preferred for therapeutic use as lysogens (bacteriophage that are hanging out in the host genome) generally confer immunity against that phage. I sometimes like to imagine finding phages that are temperate in a plant friendly bacterium (mostly hanging out) and lytic against a plant pathogen. That would be a neat way of sustainably treating a crop.

In the far future, evolutionarily speaking, would it ever be possible for humans to be completely immune to bacteria and viruses? Could the human body evolve over time to completely protect itself from infectious diseases? Or will bacteria and viruses always adapt along with human body and the antibiotics/drugs used to fight them? If the human body could evolve this way, in your opinion, what would the future look like? Thanks so much for this AMA!

ieatbugsandstuff

Future talk! I actually think we don't want to think about getting away from bacteria and viruses in the future. These are an important part of the ecosystem inside of us, the microbiome. Rather, in the future I would love to see us seeing our microbial component as companions that we work with... The human body, like all other bodies, has evolved with a suite of helpful passengers and our health suffers when we try to separate ourselves from these "old friends". Check out the Hygiene hypothesis!

How would you even begin to hypothesize what sort of viruses might kill bacteria? What do you look for?

gsbadj

You can find bacteriophages that kill a particular bacterial strain by putting a soil sample through a filter to isolate only the smallest particles (virus sized) and then add this to the bacterial population on a plate and look for places where the bacteria are killed by the bacteriophages.

How do you disable our immune system from attacking the virus?

bofasonsofa

I don't think that you can (or should) the immune system and the bacteriophages need to work in concert. Not all bacteriophages cause allergic reactions or immune responses.

A lot of our antibiotics come from fungi, which is not surprising, as they often live in the same ecological niche. The fungi have evolved the antibiotics against those bacteria.

Bacteria evolve resistance in the presence of the antibiotics. Is anybody trying to evolve the fungi in the presence of antibiotic resistant bacteria to get new antibiotics?

jbsinger

I am not aware of any research projects like that. However, I believe that the fungal world is also a very diverse place that we have not fully explored, perhaps evolution experiments aren't needed as much as fungal discovery!

I always thought Massey University was in Palmerston North...

TheLuckyBlackbird

We have three campuses. I have a laboratory and teach at the Auckland campus in the Institute of Natural and Mathematical Sciences. We do a lot of fundamental research. The agricultural aspects of the university (and others) are in Palmerston North and the Artistic side of the University is in Wellington.

How do you spell Auckland in New Zealand....?

malan4reddit

Ha ha, Good point! I can't edit that line for some reason! My BBC friends put it up! HH