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DON'T WORRY, BE HAPPY

MEET THE SCIENTISTS WHOSE RESEARCH MIGHT JUST SAVE THE WORLD

WORDS: HAYLEY BENNETT, DUNCAN GEERE, HELEN PILCHER AND ANDY RIDGWAY

THE NEW HERBALIST

*Superbugs are becoming more resistant to **antibiotics** by the day.*
***Cassandra Quave** is searching for a solution in forgotten herbal remedies*

Roaming around southern Italy, picking up interesting plants and having a chat with the locals might sound like a holiday, but ethnobotanist Dr Cassandra Quave assures us it's not. "You know, it's not a vacation," she says. "It's really hard work." It's also vital work – Quave and her team from Emory University in Atlanta, Georgia, are scouring the Mediterranean for medicines that could help tackle the mounting crisis of antibiotic resistance. In the US and Europe alone, 50,000 people die each year from infections caused by resistant bacteria they picked up during a hospital stay. Without new treatments, global deaths will soon soar into the millions. Quave believes that those treatments can be found in plants.

A self-described history of medicine geek, Quave talks to local people about plants that have been used, often for centuries, in their traditional medicines. In this way, she hopes to track down those with the greatest potential for fighting infection. She admits other researchers looking for new antibiotics are dismissive about her approach because they think plants have already been found lacking. "But no one has looked at the scope of plants that we're looking at, and some of these are [already] being used in traditional medicines for fighting infection," says Quave. "Also, no one has looked at the other potential ways that these might be acting beyond just killing bugs." What's curious about some of the plant extracts that Quave has tested is that they work in a different way to the antibiotics used in clinics today. As they stop short of killing their targets – working instead against microbial communication systems – the bugs shouldn't evolve resistance to these extracts, making them an exciting prospect for future antibiotics.

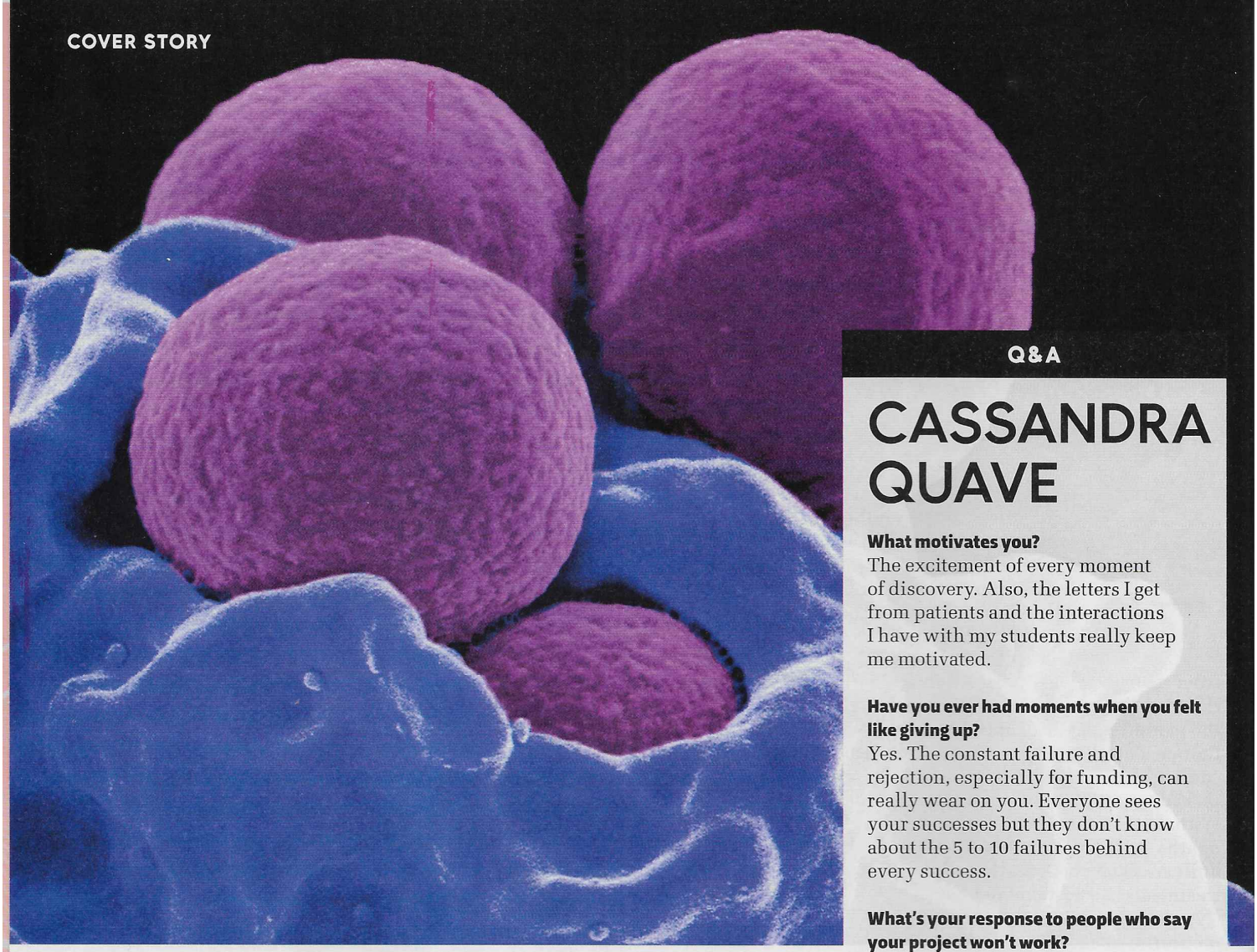
The approach could work against different species of bacteria, but top of Quave's hit list is methicillin-resistant *Staphylococcus aureus*, more commonly known as MRSA. Quave has something of a personal vendetta against the 'staph' bug: at the age of three, she was hospitalised for months with an MRSA infection after having part of her right leg amputated. Later, she got involved with science fair projects and became completely absorbed in the idea of bacterial resistance via news stories about *E. coli*-infested burgers. "I was an odd kid!" she jokes. MRSA is notorious as the hospital 'superbug' that causes dangerous skin infections by using wounds, burns, drips and catheters to gain access to deeper layers of the skin. Quave regularly receives letters and emails from patients' frightened relatives, who are desperate to try any new treatment for the disease. It's a constant reminder that her ultimate goal is helping people, not making the next blockbuster drug.

> **"Over time and within these cultures, they've become attuned to these plant compounds and to the resolution of disease, and I think that's exciting"**

So has Quave found anything on her Italian field trips that could help those individuals suffering from life-threatening skin infections? "In Italy, we asked people 'what plants do you put on the skin to treat infections, rashes... all of these kinds of things'," she says. "And sweet chestnut came up." Yes, the exact same plant that gives us roasted chestnuts at Christmas. In a recent paper, Quave's team showed that sweet chestnut leaf extract can block some of the toxic effects of MRSA and, in a mouse infected with the bug, decrease the area of skin affected, all without killing the bacteria. They've now narrowed it down to five compounds that seem to be responsible for most of the benefit.

Quave, who practises what she preaches, making medicinal teas from plants she grows in her own garden, also hopes to validate some age-old remedies. "This is giving cultural value to people who have been using these remedies for centuries. Perhaps a healer doesn't understand the intricacies of bacterial signalling, but over time and within these cultures, they've become attuned to these plant compounds and to the resolution of disease, and I think that's exciting."

PHOTO: DAMON CASAREZ/REDUX PICTURES. ILLUSTRATION: MARIO WAGNER



Q&A

CASSANDRA QUAVE

What motivates you?
The excitement of every moment of discovery. Also, the letters I get from patients and the interactions I have with my students really keep me motivated.

Have you ever had moments when you felt like giving up?
Yes. The constant failure and rejection, especially for funding, can really wear on you. Everyone sees your successes but they don't know about the 5 to 10 failures behind every success.

What's your response to people who say your project won't work?
Well, first and foremost I try to listen to them – I'm always open to ideas and feedback – but I don't let unnecessarily dismissive comments stop my work.

If you were able to rent out a billboard in Times Square, what would you write on it?
'Stop habitat destruction, and support preservation of biodiversity and cultural diversity.' That doesn't make a very sexy headline, but that would be my main message to the public.

What will your field of research look like in 2050?
I envision a new era of medicine in which we approach drug-resistant infections in a whole new way. Advances in our understanding of how synergistic therapies work will enable us to design better medicines that quickly reduce the severity of disease and achieve cures even for difficult-to-treat, antibiotic-resistant infections.

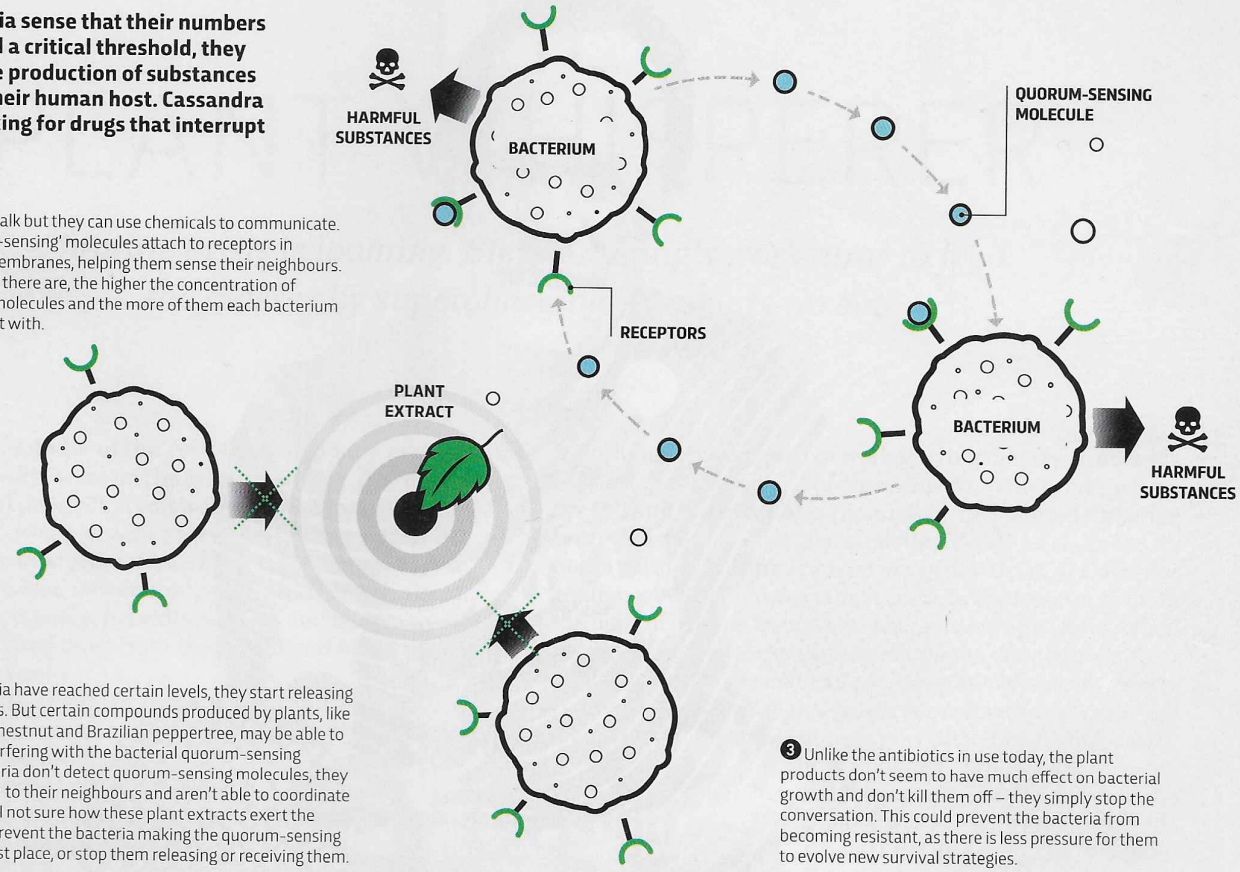
ABOVE: **MRSA bacteria (pink spheres) are resistant to many common antibiotics, making an infection hard to treat**

LEFT: **Extracts from sweet chestnut can block the effects of MRSA**

HOW IT WORKS

QUORUM SENSING

When bacteria sense that their numbers have reached a critical threshold, they switch on the production of substances that attack their human host. Cassandra Quave is looking for drugs that interrupt this process.

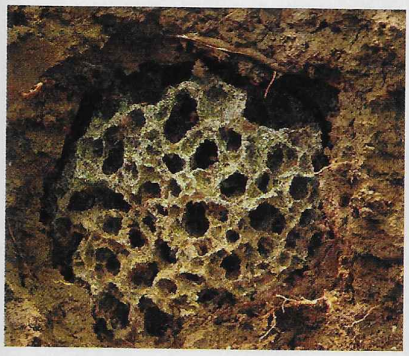


❶ Bacteria can't talk but they can use chemicals to communicate. Bacterial 'quorum-sensing' molecules attach to receptors in bacteria's outer membranes, helping them sense their neighbours. The more bacteria there are, the higher the concentration of quorum-sensing molecules and the more of them each bacterium comes into contact with.

❷ Once the bacteria have reached certain levels, they start releasing harmful substances. But certain compounds produced by plants, like extracts of sweet chestnut and Brazilian peppertree, may be able to prevent this by interfering with the bacterial quorum-sensing system. If the bacteria don't detect quorum-sensing molecules, they are essentially deaf to their neighbours and aren't able to coordinate an attack. We're still not sure how these plant extracts exert the effect – they may prevent the bacteria making the quorum-sensing molecules in the first place, or stop them releasing or receiving them.

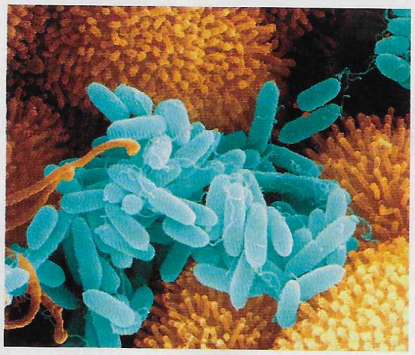
❸ Unlike the antibiotics in use today, the plant products don't seem to have much effect on bacterial growth and don't kill them off – they simply stop the conversation. This could prevent the bacteria from becoming resistant, as there is less pressure for them to evolve new survival strategies.

ALTERNATIVE MEDICINES



❶ FUNGUS-FARMING ANTS

Leafcutter ants keep fungi gardens. They cut leaves to feed to the fungi, which will in turn feed the ants' larvae. This fungi 'farming' attracts lots of unwanted microbes, but the ants combat the bugs with antimicrobials produced by *Actinomycete* bacteria that grow on their own bodies – a potential source of new drugs being studied at the University of East Anglia. Most antibiotics used today come from the same group of bacteria.



❷ CATFISH MUCUS

The striped dwarf catfish, found in Asian estuaries, may look unremarkable, but it secretes an antibiotic-filled mucus from its skin. Actually, many fish produce mucus that's rich in antimicrobials, because it helps protect them from disease. However, Indian researchers found that slime from the catfish was particularly potent against bugs that infect humans, including *Pseudomonas aeruginosa*, which causes pneumonia.

❸ THE ENDS OF THE EARTH

Scientists from the University of Illinois, Chicago, are searching in places that until recently remained unexplored for antibiotics. They plunge their test tubes into Iceland's hot springs and the muck at the bottom of freshwater lakes, to look for bacteria that produce novel compounds. They've already found bacteria in Lake Michigan that produce antibiotics capable of killing the tuberculosis bug.