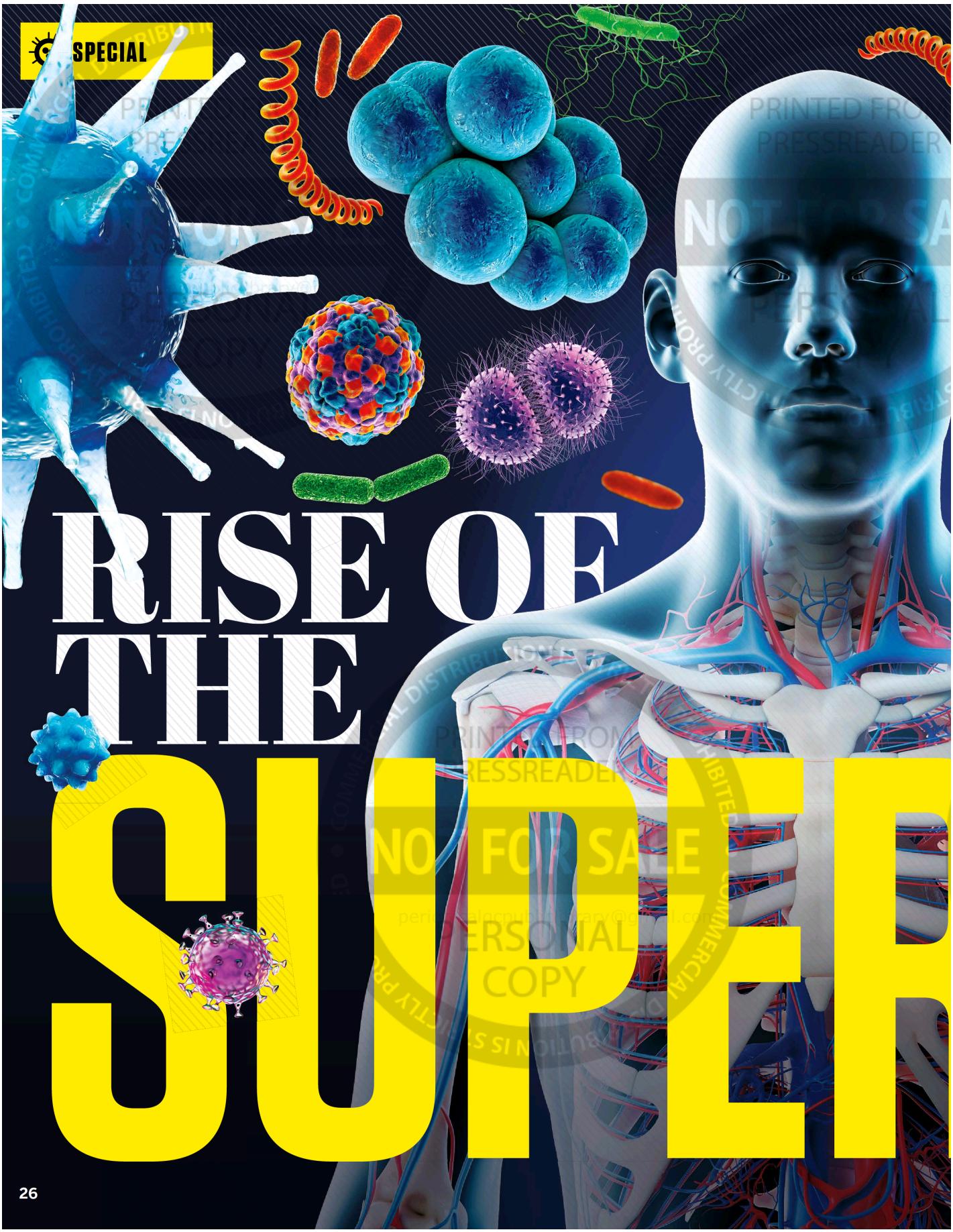
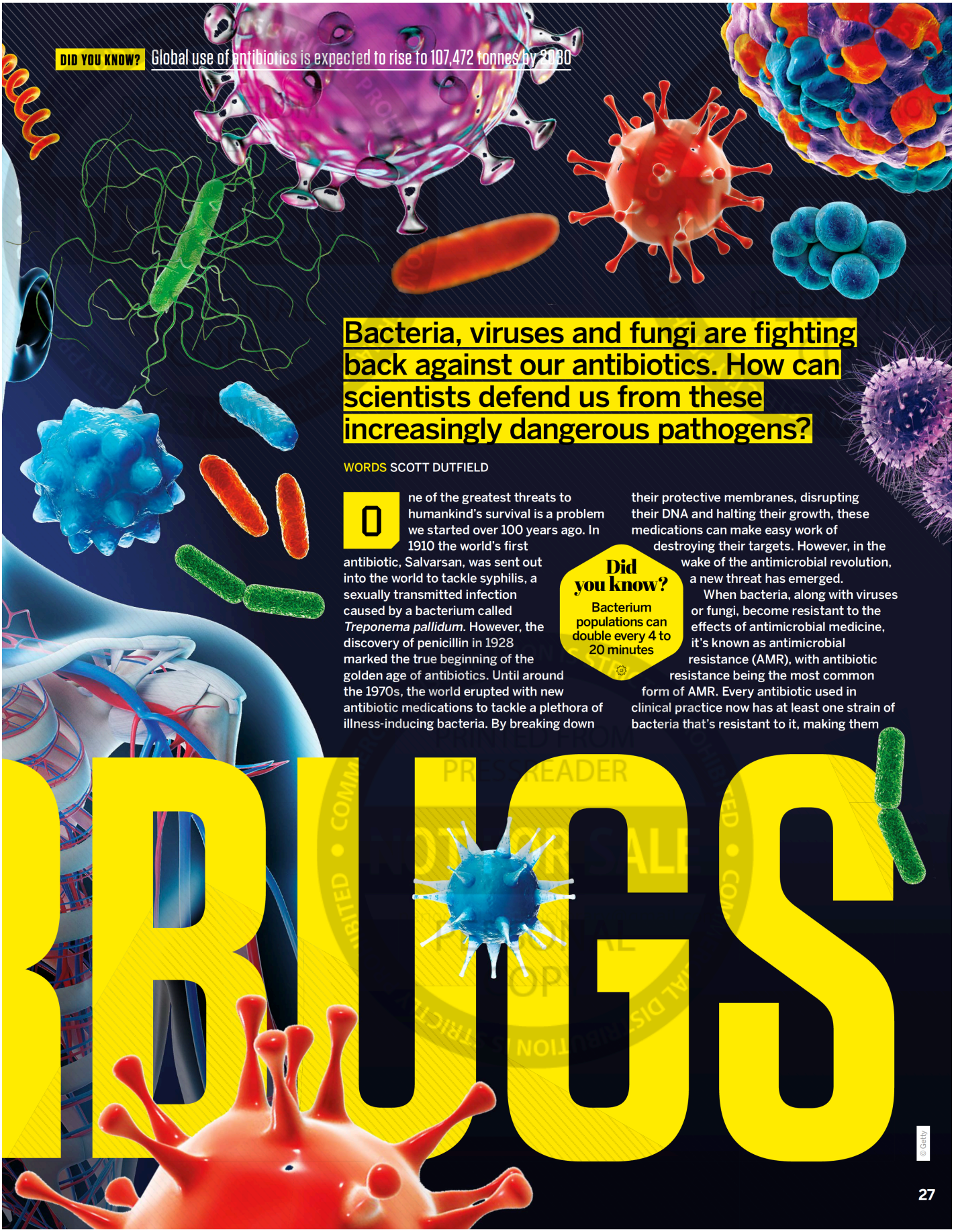
- Bacteria





DID YOU KNOW? Global use of antibiotics is expected to rise to 107,472 tonnes by 2030

BUGS

Bacteria, viruses and fungi are fighting back against our antibiotics. How can scientists defend us from these increasingly dangerous pathogens?

WORDS SCOTT DUTFIELD

One of the greatest threats to humankind's survival is a problem we started over 100 years ago. In 1910 the world's first antibiotic, Salvarsan, was sent out into the world to tackle syphilis, a sexually transmitted infection caused by a bacterium called *Treponema pallidum*. However, the discovery of penicillin in 1928 marked the true beginning of the golden age of antibiotics. Until around the 1970s, the world erupted with new antibiotic medications to tackle a plethora of illness-inducing bacteria. By breaking down their protective membranes, disrupting their DNA and halting their growth, these medications can make easy work of destroying their targets. However, in the wake of the antimicrobial revolution, a new threat has emerged.

Did you know?

Bacterium populations can double every 4 to 20 minutes

When bacteria, along with viruses or fungi, become resistant to the effects of antimicrobial medicine, it's known as antimicrobial resistance (AMR), with antibiotic resistance being the most common form of AMR. Every antibiotic used in clinical practice now has at least one strain of bacteria that's resistant to it, making them

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SPECIAL

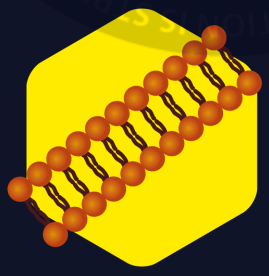
OBLITERATING BACTERIA

How antibiotics take down their microscopic foes



1 HALTING PROTEIN PRODUCTION

Some antibiotics inhibit the production of proteins in bacteria, preventing them from growing, which leads to their death.



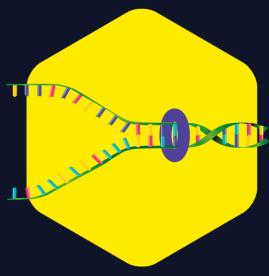
2 DNA DISRUPTION

By binding with the enzyme that transcribes bacterial DNA, some antibiotics stop DNA replication, causing bacteria to die.



3 BREAKING DOWN WALLS

The production of a cell wall-building polymer called peptidoglycan can be inhibited by some antibiotics. This causes the wall to open up, leading to osmotic lysis, where water fills the cell and pops it like a water balloon.



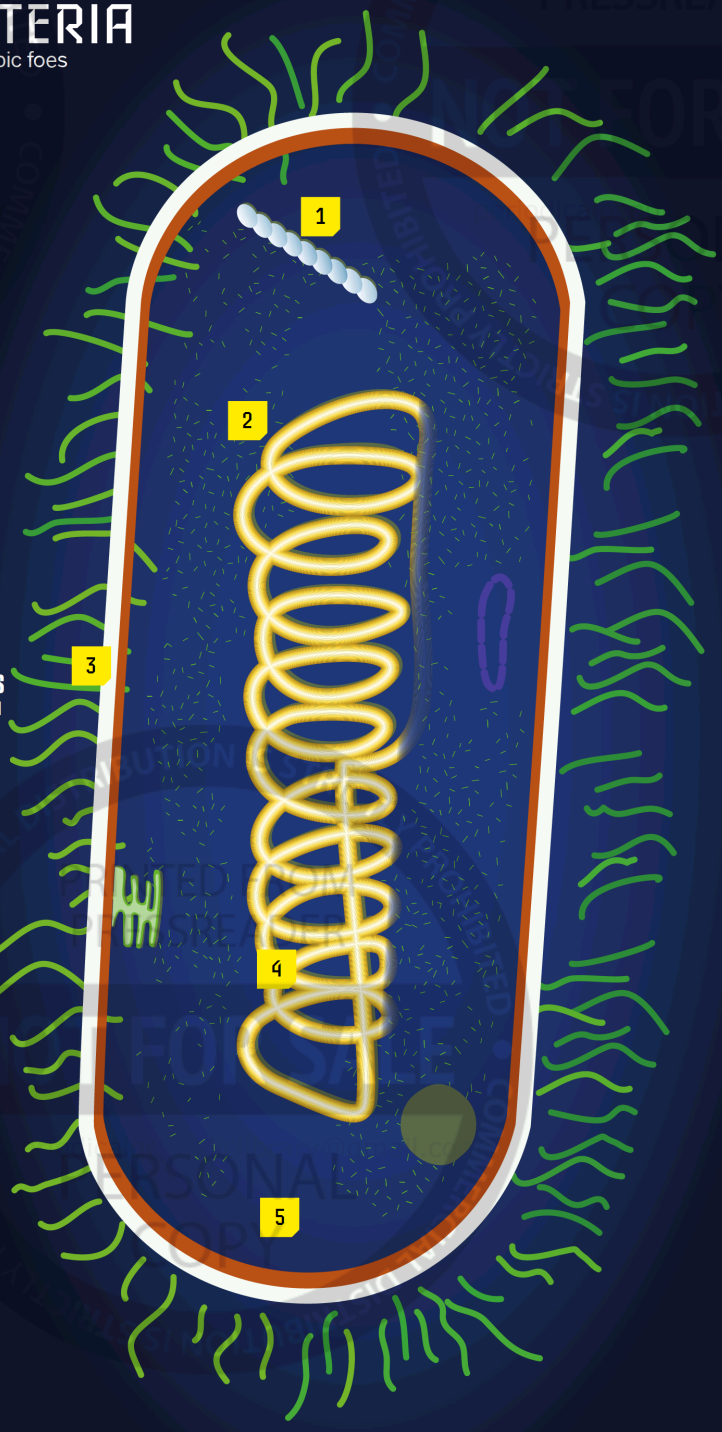
4 MEMBRANE MELTDOWN

Antibiotics can bind to the membranes of bacteria, reducing their functionality and causing them to redirect protein production to the membrane for growth and replication.



5 MESSING WITH METABOLISM

By inhibiting enzymes involved in bacteria's production of metabolites for DNA production, some antibiotics prevent them from growing.



DID YOU KNOW? China is the largest user of antimicrobials in food-producing animals in the world

increasingly difficult to treat. Commonly known as 'superbugs', these defiant microbes get their powers of antimicrobial resistance from mutations in their DNA that lead to changes in the structure of the enzymes, proteins and membranes that antimicrobials target. Some bacteria have even developed 'biochemical pumps' to evict antibiotics that enter their cells.

These genetic mutations, which are often referred to as 'spontaneous resistance', can occur randomly and at any time. Much like the changes that lead to the evolution of any other living organism, Darwin's evolutionary concept of the 'survival of the fittest' is at play here. For example, bacteria that aren't killed by antibiotics because of a mutation go on to multiply and become the remaining dominant strain of bacteria. To make matters worse, bacteria can also share these mutated genes with other bacteria. In a process called 'horizontal gene transfer', circular pieces of DNA called plasmids cross the membranes of bacteria when they come into direct contact with one another.

The other main causes of AMR include the misuse and overuse of antimicrobials. Not completing a course of antibiotics or misusing them can allow bacteria to multiply and form new DNA mutations that lead to resistance. Similarly, antibiotics can be misused to treat symptoms that are caused by another pathogen, like a virus. In a 2017 report released by the World Health Organization (WHO), researchers estimated that just 50 million of the 150 million prescriptions for antibiotics written by doctors in the US were necessary.

One of the most formidable bacteria that has kept scientists on their toes for decades is *Staphylococcus aureus*. As a widely found bacteria in our everyday environments, *S. aureus* doesn't typically cause infection when it comes into contact with healthy skin. However, when this persistent pathogen finds its way into the body's bloodstream or internal tissue it can cause serious infection and can lead to the development of serious complications, such as sepsis and respiratory failure, if left untreated.

Similarly, viruses have found ways to dodge the effects of antivirals by changing their genetic make-up. For example, changes in the DNA of human immunodeficiency virus (HIV) have led to instances of antiviral resistance, stopping this vital medication's ability to block



An illustration of the superbug fungus *Candida auris*



The WHO placed carbapenem-resistant *Klebsiella pneumoniae* at the top of its 2024 AMR priority list

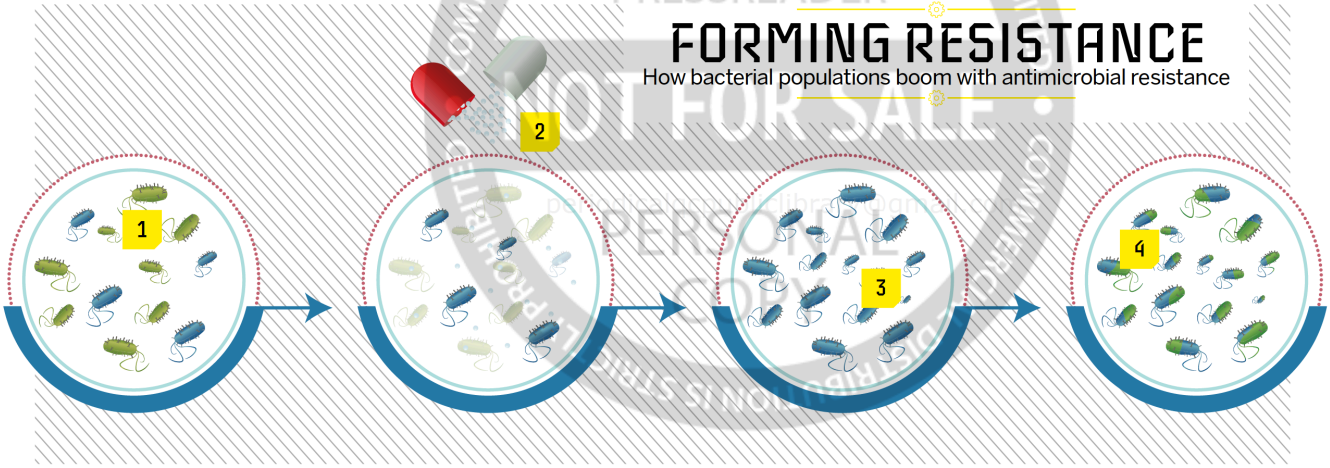
Did you know?

***S. aureus* can grow in temperatures between 18 and 40 degrees Celsius**

"Viruses have found ways to dodge the effects of antivirals"

FORMING RESISTANCE

How bacterial populations boom with antimicrobial resistance



1 MICROBE POPULATIONS
Microorganisms such as bacteria and fungi grow and spread, causing infection.

2 ANTIMICROBIAL MEDICINE
Medicines destroy the majority of harmful microbes but leave behind any that have mutated a resistance to the medicine.

3 REPOPULATE
The population of resistant microbes grows and spreads, unaffected by medicine.

4 SHARING RESISTANCE
Microbes can share their DNA with other microbes and essentially pass on their resistance.

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SPECIAL

We'll need to develop new ways to treat infections if current medicine no longer works

virus replication. Among the world's fungi species, *Candida auris* has emerged as a multidrug-resistant yeast that can lead to severe illness, particularly in sick people and those with invasive medical devices. Infections have been on the rise, especially in the US, which between January and December 2022 had 2,377 cases of this variety of superbug infection – a huge increase from the 476 cases in 2019.

At present, the world is facing its greatest superbug threat, especially in the war against antibiotic resistance. It's estimated that bacterial AMR caused 1.27 million deaths worldwide in 2019 and contributed to the deaths of 4.95 million others. Across the European Union, Iceland and Norway, more than 35,000 die from antibiotic-resistant infections each year.

Superbugs pose an enormous threat, not only to healthy individuals, but for those with existing conditions, especially those who are undergoing surgeries and run the risk of contracting infections that doctors may struggle to treat with antimicrobials. Superbugs can have an effect on global economies, too. Without mass-produced medicines to take down infections, other more expensive and intensive measures are required to treat infected patients. The World Bank estimates that AMR could lead to $1 trillion (£800 billion) of additional health costs in the US alone by 2050.

So how do you treat an infection that's become immune to the medicine designed to destroy it? In place of finding a new class of antibiotics – which hasn't happened since the 1980s – scientists have to rely on several other ways to subdue superbugs. From repurposing existing medicines to genetically altering bacteria to fight themselves, scientists have come up with a myriad of ways to ease the threat of AMR. However, one of the most effective ways to stop new superbugs from emerging is by protecting yourself from infection. Maintaining good food preparation hygiene and personal hygiene, especially regular hand washing, can help prevent the transmission of bugs that can cause an infection. Keeping yourself up to date with vaccinations can also help prevent the overuse of antibiotics.

Did you know?

Over 200 viruses are known to cause disease in humans



SMALL BUT DEADLY

The annual predicted deaths attributed to AMR by 2050

1 North America
317,000

2 Europe
390,000

3 Asia
4,730,000

4 South America
392,000

5 Africa
4,150,000

6 Oceania
22,000

THE PERSISTENT RESISTANCE OF MRSA

1944 Penicillin was used to treat *Staphylococcus aureus* for the first time.

1946 Just two years after being treated with penicillin, the first cases of resistance were recorded.

1954 Vancomycin, a new class of antibiotic, was introduced to tackle bacterial resistance.

1959 A new antibiotic called methicillin was first used to combat penicillin-resistant *S. aureus*.

1960 In just a year, strains of methicillin-resistant *S. aureus* (MRSA) were detected.

1997 The first cases of an MRSA strain with reduced susceptibility to vancomycin were reported.

2002 Five years after MRSA showed resistance to vancomycin, the first cases of full vancomycin-resistance occurred.

2003 Daptomycin was introduced to treat skin infections caused by MRSA.

2005 Reports of resistance to daptomycin for MRSA strains emerged.

DID YOU KNOW? Each year the US records more than 2.8 million antimicrobial-resistant infections

TOP-TEN SUPERBUGS

In 2024 the WHO released an update to its 2017 'Bacterial Priority Pathogen List'. The WHO ranks bacterium as a priority on its hit list based on several factors, such as mortality, incidence and treatability, and places them into three groups: critical, high and medium. Here are the top-ten priority bacteria species in 2024



KLEBSIELLA PNEUMONIAE

Ranking in 2024	Ranking in 2017
1	5

DRUG RESISTANCE
Carbapenem-resistant

GROUP
Critical



ESCHERICHIA COLI

Ranking in 2024	Ranking in 2017
2	4

DRUG RESISTANCE
Third-generation cephalosporin-resistant

GROUP
Critical



ACINETOBACTER BAUMANNII

Ranking in 2024	Ranking in 2017
3	1

DRUG RESISTANCE
Carbapenem-resistant

GROUP
Critical



MYCOBACTERIUM TUBERCULOSIS

Ranking in 2024	Ranking in 2017
4	N/A

DRUG RESISTANCE
Rifampicin-resistant

GROUP
Critical



ESCHERICHIA COLI

Ranking in 2024	Ranking in 2017
5	10

DRUG RESISTANCE
Carbapenem-resistant

GROUP
Critical



KLEBSIELLA PNEUMONIAE

Ranking in 2024	Ranking in 2017
6	3

DRUG RESISTANCE
Third-generation cephalosporin-resistant

GROUP
Critical



SALMONELLA TYPHI

Ranking in 2024	Ranking in 2017
7	18

DRUG RESISTANCE
Fluoroquinolone-resistant

GROUP
High



SHIGELLA SPECIES

Ranking in 2024	Ranking in 2017
8	25

DRUG RESISTANCE
Fluoroquinolone-resistant

GROUP
High



ENTEROCOCCUS FAECIUM

Ranking in 2024	Ranking in 2017
9	11

DRUG RESISTANCE
Vancomycin-resistant

GROUP
High



PSEUDOMONAS AERUGINOSA

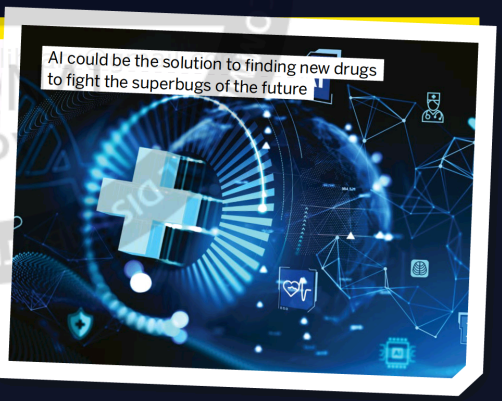
Ranking in 2024	Ranking in 2017
10	2

DRUG RESISTANCE
Carbapenem-resistant

GROUP
High

AI TO THE RESCUE

Artificial intelligence (AI) has proven to be an invaluable tool in finding the antibiotic answers doctors need to tackle superbugs. In 2023, researchers in Canada and the US released the results of a study that used AI to comb through thousands of compounds. These compounds had the potential to be a new antibiotic for a 'critical-threat' bacteria called *Acinetobacter baumannii*. In just an hour and a half, the AI program had sieved through 6,680 compounds and produced a shortlist – nine of which scientists discovered could be potential antibiotics. Due to the rigorous clinical testing potential new antibiotics have to undergo before general use, it's expected that the first 'AI antibiotics' will emerge around 2030.



AI could be the solution to finding new drugs to fight the superbugs of the future

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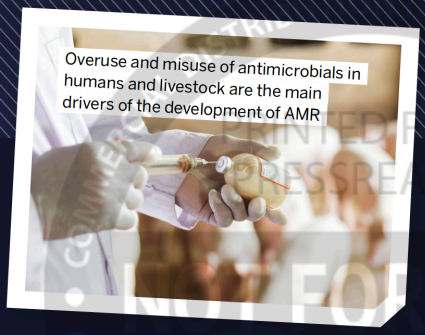
SPECIAL



THE SUPERBUG SPREAD

How antibiotic resistance finds its way around the world

1

1 ANIMAL ANTIBIOTICS
Farm animals, such as pigs and cows, are fed antibiotics, and resistant bacteria remain in the gut.

2 IN THE GUT
A person gets ill and takes antibiotics and resistance develops in their gut.

2

3

3 MEAT-FLAVOURED AMR
Resistant bacteria can be trapped in meat. When humans improperly cook or handle meat, they can become infected with resistant bacteria.

8 COMMUNITY SPREAD
Someone who doesn't realise they have resistant bacteria passes them on to others in their community.

8

4 FERTILISING WITH AMR
Crops fertilised with manure packed with resistant bacteria become contaminated.

"At present, the world is facing its greatest superbug threat"

4

HOSPITAL

7 DOCTOR SPREAD
Medical professionals treating a patient with resistant bacteria can unknowingly transfer them to another patient if the correct safety precautions aren't met.

6

5

5 VEGGIE AMR
Crops can pass on resistant bacteria when they're eaten by humans.

7

6 PATIENT SPREAD
Someone seeking medical attention who's harbouring resistant bacteria can introduce the bacteria to other patients.

Did you know?
There are currently 27 new antibiotics in clinical development

DID YOU KNOW? By 2029, the UK government has pledged to reduce total antibiotic use by five per cent from 2019 levels

PREVAILING OVER PATHOGENS

This is the medical arsenal doctors can deploy to combat the growing threat of resistance



VACCINES

A helpful tool in fighting the spread of superbugs by blocking their transmission between an infected and healthy person. Curbing the spread of pathogens decreases the chance that one may mutate a resistance to antimicrobial drugs.



BIOTHERAPEUTICS

Doctors can use live probiotics as a way to outcompete AMR bacteria in the gut. Researchers have found that when treating a resilient bacteria called *Helicobacter pylori*, the use of probiotics improved eradication by ten per cent.



PHAGE THERAPY

Using a virus to treat an AMR pathogen might seem like a conflicting idea, but bacteriophage virus theory, or 'phage theory', is a promising path to tackling superbugs. Like sending troops to battle, viruses can be used to find bacteria that might harbour AMR genes, inject them with harmful DNA and ultimately destroy them.



GENETIC ENGINEERING

An emerging tool for tackling bacterial resistance is CRISPR-Cas9, which uses a bacterium's natural gene-sharing habit against it. CRISPR-Cas9 is a technology that allows scientists to 'edit' the genetic information of bacteria, especially the plasmids that they pass between each other.



ANTIMICROBIAL PEPTIDES

By disturbing the membranes of some pathogens, charged peptides, which are short chains of amino acids, can be used as an alternative to other antimicrobials. These are naturally occurring and are derived from many different organisms, such as amphibians, mammals and even insects.



DRUG REPURPOSING

Developing new drugs to tackle AMR is a costly endeavour and can take more than a decade to complete. However, repurposing or modifying existing medicines can deal a fatal punch to AMR infections. This approach comes with mixed success and has been found in some cases to increase AMR in pathogens.

BATTLING THE BUGS

We speak with the European Centre for Disease Prevention and Control (ECDC), who shed some light on how doctors fight superbug infections and how we can help ourselves

How is AMR monitored with so many pathogens in the world?

Data on antimicrobial resistance comes from laboratories that test for infections in humans and animals, and even from laboratories that test bacteria in the environment. This data tells us if the bacteria and fungi from humans, animals and the environment are resistant to treatment to the medicines used for infections with these pathogens. National public health agencies collect data on AMR that originate from laboratories to evaluate what AMR threats – sometimes known as superbugs – are looming.

What are the most effective methods that doctors are using to combat AMR?

Doctors know that taking the wrong antibiotic or taking unnecessary antibiotics can contribute to bacteria becoming resistant. Bacteria evolve to survive their environment, and when they're exposed to antibiotics, they can become resistant. Doctors restrict prescribing antibiotics for infections caused by viruses, as antibiotics don't work against viruses. They also test, when possible, to confirm that an infection is due to bacteria and use information from the laboratory that tells them which antibiotics could be effective for the infection.

What advice would you give people to help in the fight against superbugs?

Everyone has a role in fighting AMR. Antibiotics should be treated with respect: do not self-medicate with antibiotics. If you are prescribed antibiotics by your doctor, take them only in the amount, frequency and duration as prescribed by your doctor. Encourage others to treat antibiotics with respect as well. Controlling the spread of infections can also reduce AMR. Getting vaccinated, washing our hands appropriately and covering our coughs and sneezes all help reduce infections. When we reduce infections, we also reduce the need for antibiotics and the potential spread of resistant pathogens.

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

"Bacteria evolve to survive their environment, and when they're exposed to antibiotics, they can become resistant"

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