

Scientific approaches to the development of new chemotherapeutic drugs

Chemotherapeutic Agents

Classification and Basic Mechanisms of Action

Resistance Issues

Part 2

World health organization recommended



Access

This indicates the antibiotic of choice for each of the 25 most common infections. These antibiotics should be available at all times, affordable and quality-assured.



Watch

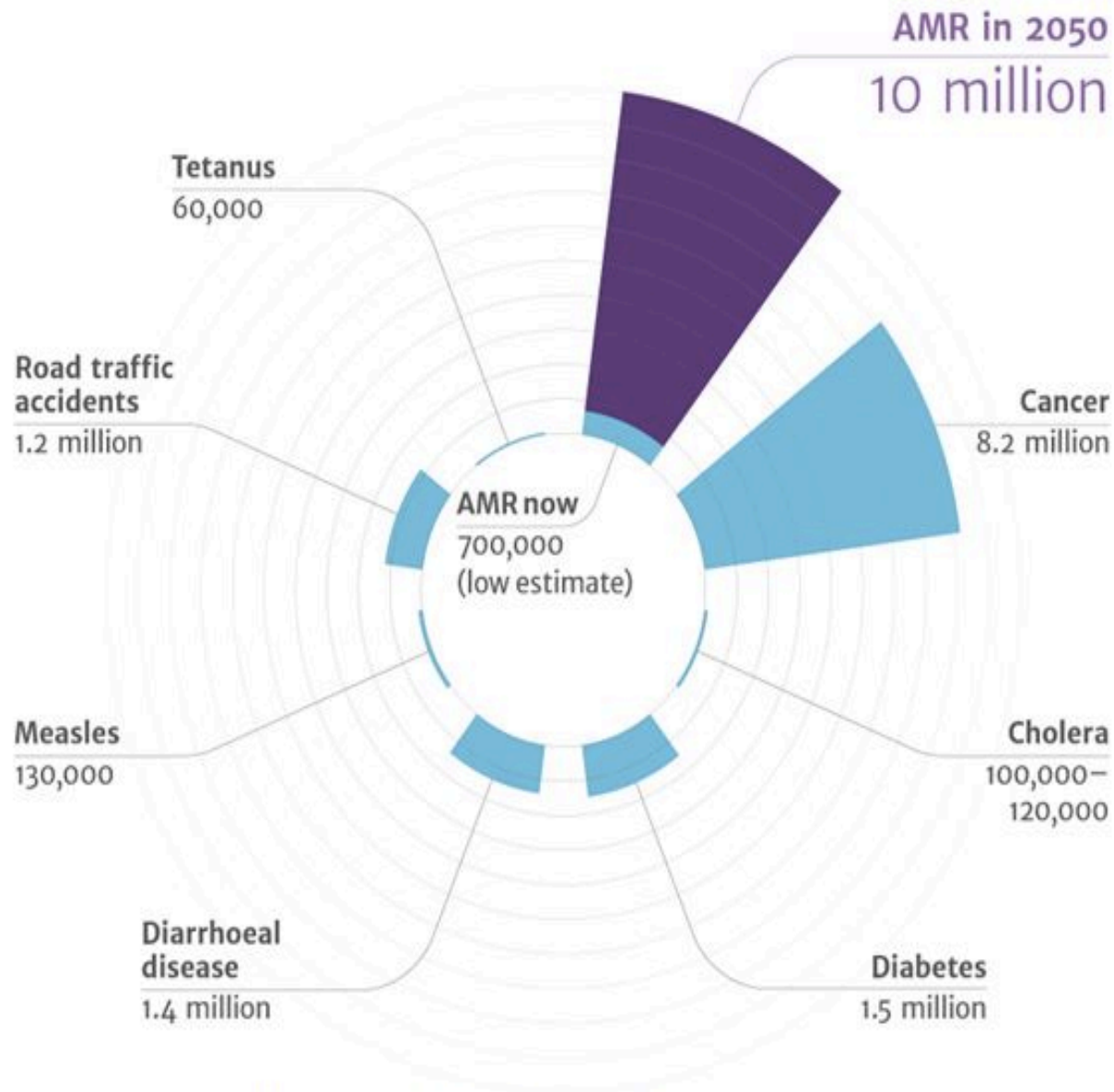
This includes most of the 'highest priority critically important antimicrobials' for human medicine and veterinary use. These antibiotics are recommended only for specific, limited indications.



Reserve

These antibiotics should only be used as a last resort when all other antibiotics have failed.

DEATHS PER YEAR WORLDWIDE



IF NOT TACKLED, RISING AMR COULD HAVE A DEVASTATING IMPACT



By 2050, the death toll could be a staggering
one person every three seconds
if AMR is not tackled now.



What is antibiotic resistance?



THE PROBLEM

Antibiotics treat infections by killing bacteria, but now the bacteria are fighting back. Our medicines are becoming less effective which means more deaths and more complications for people receiving treatment in hospital. We have to tackle this problem before it gets worse.



HOW THIS HAPPENED

There are many reasons why antibiotics lose their effectiveness, but here are two key ones:

Firstly, we take medicines that we don't need. Antibiotics don't help most colds or coughs get better but we still request antibiotics for them.

Secondly, we make things worse when we don't take antibiotics exactly as prescribed for instance, missing doses. Never save antibiotics for future use or give them to someone else.



WHAT CAN WE DO?

Antibiotic resistance is one of the biggest threats facing us today but you can help. Please visit www.antibioticguardian.com and find out about simple steps you can take to save our antibiotics.



A world without antibiotics



PRE-ANTIBIOTIC AGE

In a world before antibiotics, as recently as the 1930s, people often died from infections like pneumonia or meningitis. Simple medical procedures/operations were risky due to the chance of infection. Antibiotics changed that.



ANTIBIOTIC AGE

Since the 1940s our antibiotics have allowed us to fight infections and save millions of lives. But they are becoming ineffective against many infections because we aren't using them properly.



POST-ANTIBIOTIC AGE

If bacteria become 'resistant' to our antibiotics many routine treatments will again become increasingly dangerous. Setting broken bones, basic operations, even chemotherapy all rely on access to antibiotics that work. Antibiotic resistance is one of the biggest threats facing us today but we have a chance to fight back. Find out how at: www.antibioticguardian.com



Antibiotic resistance

What can I do?



BE AN ANTIBIOTIC GUARDIAN

Antibiotics are some of our most precious medicines, used to treat both humans and animals.

The Antibiotic Guardian campaign was launched to kick-start collective action from both healthcare professionals and members of the public to work together to slow the spread of antibiotic resistance.

By pledging to become an Antibiotic Guardian you choose to perform a simple action which protects antibiotics against the threat of antibiotic resistance.



TAKE THESE SIMPLE ACTIONS

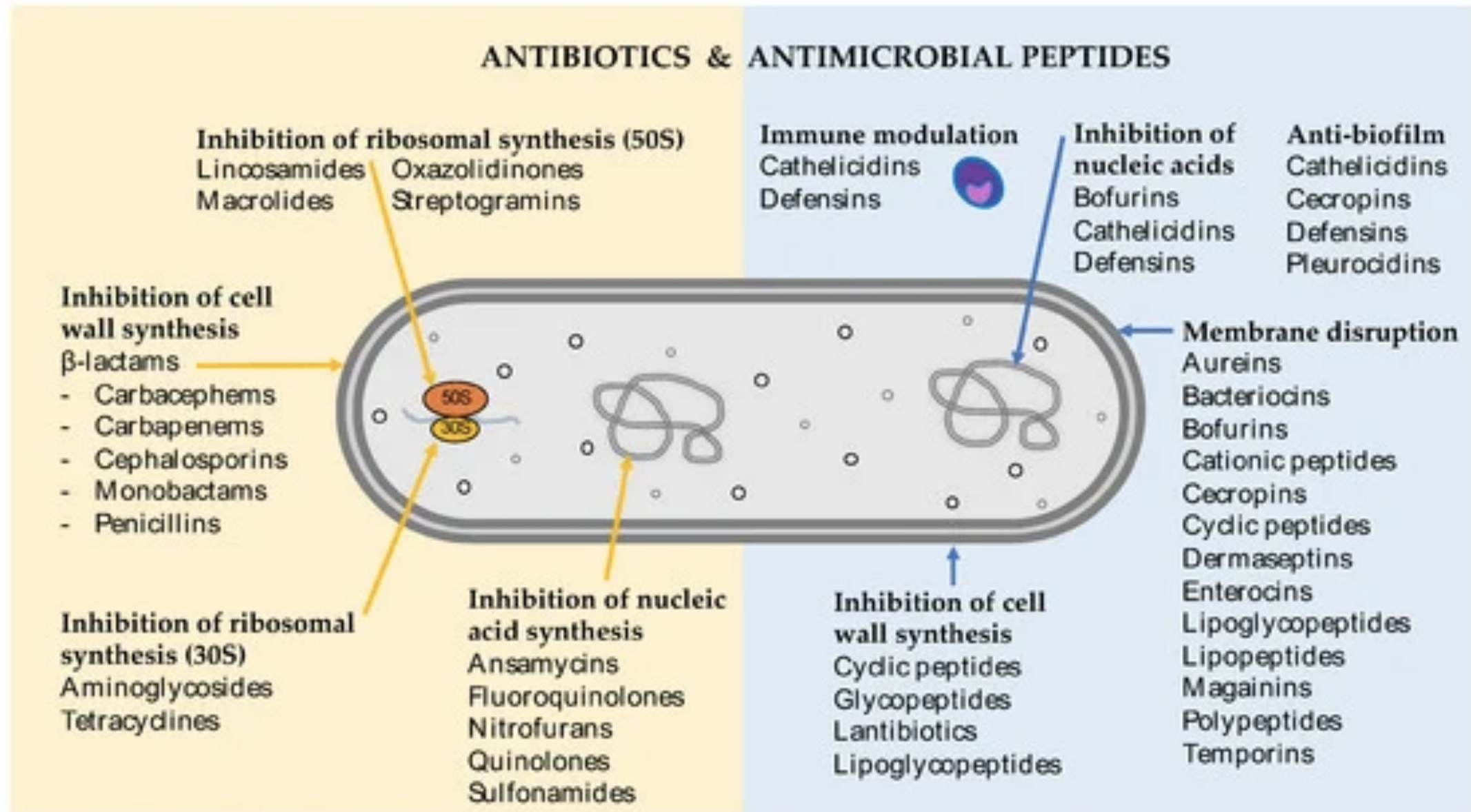
- Don't ask for antibiotics, treat your cold and flu symptoms with pharmacist advice and over the counter medicines
- Take antibiotics exactly as prescribed, never save them for later, never share them with others
- Spread the word, tell your friends and family about antibiotic resistance



SIGN UP AND LEARN MORE

Rally together at antibioticguardian.com and choose a pledge that feels right for you. Remember that your actions protect antibiotics.

Mechanistic targets of antibiotics and antimicrobial peptides.



New directions in the search for antimicrobial agents

Bacterial cell components as a target for the search for new antibacterial agents

Teixobactin

binds lipid II, lipid III, the precursor of WTA, wall teichoic acid. The toxicity of teixobactin for eukaryotes was low, and the development of bacterial resistance to it was not detected.

Nisin-like lipopeptides

belong to the lantibiotic family of antimicrobial peptides. It binds the pyrophosphate moiety of lipid-II and forms pores in the bacterial membrane, leading to cell lysis and death, is not suitable for systemic administration.

Microbisporicin -

blocks the biosynthesis of peptidoglycan, accumulation of its precursor in the cell. Microbisporicin is called one of the most powerful lantibiotics

Oritovanine

antibiotic for the treatment of skin infections, structurally similar to vancomycin and binding to lipid-II. Has a long half-life in vivo (once per week).

New directions in the search for antimicrobial agents

Antimicrobial peptides are “natural antibiotics” because they are produced in animals.

- ✓ **The new peptide antibiotic klebsazolicin (KLB)** inhibits protein synthesis by binding to the bacterial ribosome (*in vitro*).
- ✓ **A combination of peptides from four families:** defensins, cecropins, dipterocins and proline-rich peptides.

New directions in the search for antimicrobial agents

- ✓ **Synthetic antibiotics** - oxazolidinones (linezolid, tedizolid, cadazolid) bind the 23S rRNA molecule of the bacterial ribosome, prevent normal protein synthesis
- ✓ **Molecules of the alkylresorcinol class** - destroyed on membranes, various proteins and the bacterial genome. As a result, the microorganism develops stress, and the antibiotic gains easier access to its target. The best results from the use of alkylresorcinols can be achieved in combination with antimicrobial agents - “superbullet”. The most promising of them is under the laboratory *code M13*.
- ✓ **Cobaltocene-containing polymers**
- ✓ **Antimicrobial peptides** are “natural antibiotics” because they are produced in animal bodies.

New directions in the search for antimicrobial agents

Antimicrobial peptides are “natural antibiotics” because they are produced in animals.

FLIP7 complex - it is a combination of peptides from four families: defensins, cecropins, dipterocins and proline-rich peptides.

- ✓ **Defensins** - target predominantly the membranes of gram-positive bacteria
- ✓ **Cecropins and dipterocins** - target predominantly membranes of Gram-negative bacteria
- ✓ **Proline-rich peptides** are directed to intracellular targets. Bacteria that are sensitive to such a “cocktail” and do not develop resistance to it.

WHEN ANTIBIOTICS ARE NEEDED

Antibiotics are needed for serious bacterial infections including:

- Sepsis
- Pneumonia
- Urinary tract infections
- Sexually transmitted infections like gonorrhoea
- Meningococcal meningitis

If you're worried, speak to a doctor who will be able to advise you on the best treatment for your symptoms.

Remember never share antibiotics or keep for later use. Your pharmacist can safely dispose of any unwanted or out-of-date medicines. For more information on antibiotics visit www.nhs.uk/keepantibioticsworking



Become an Antibiotic Guardian and protect yourself, your family and friends against the spread of antibiotic resistance. Join us at antibioticguardian.com

Taking ANTIBIOTICS when you don't need them puts you and your family at risk



Taking antibiotics encourages harmful bacteria that live inside you to become resistant. That means that antibiotics may not work when you really need them. This puts you and your family at risk of a more severe or longer illness.

Take your doctor or pharmacist's advice.