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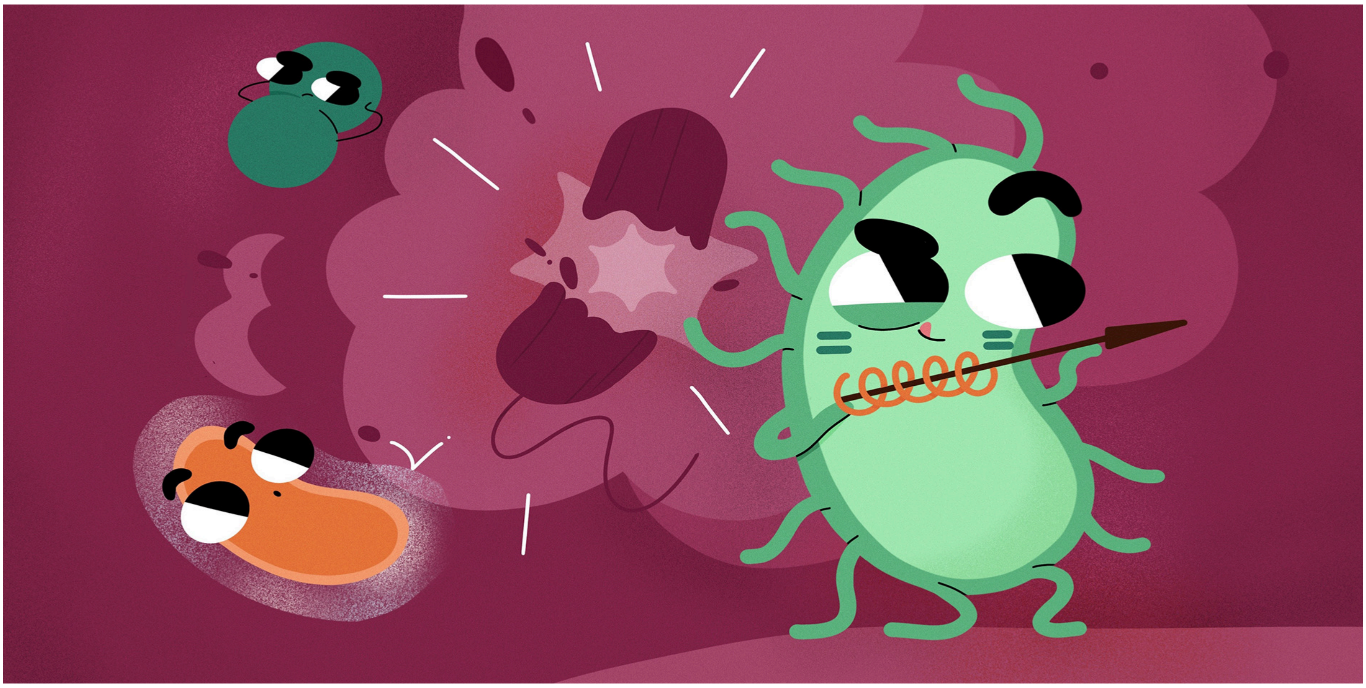

CROSSBOW, MURDER HOLE, POISON, AND GRENADE: THE DEADLY ARSENAL OF BACTERIA

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Like humans, bacteria live in communities where they can help each other and collaborate. However, when conditions become harsh, such as when there is a lack of food, bacteria turn aggressive—they kill each other to access limited resources. To do this, bacteria have developed some fascinating weapons, including a microscopic crossbow! This crossbow is made of an arrow wrapped in a spring. The arrow is capped with a spike, to which poison, sometimes in a grenade-like container, is attached. Once in contact with a competitor, the spring propels the arrow through a hole in the bacterium's membrane—like a murder hole used in castle defense—toward the enemy. Bacteria have also developed strategies to protect themselves against these weapons: antidotes to poisons, shields to block arrows, or the ability to join together in protective groups. Mines, crossbows, murder holes, grenades, poisons, antidotes, and shields: these make up the military arsenal of bacteria!

BACTERIA LIVE IN COMMUNITIES

Bacteria are microscopic organisms that live everywhere, all around us! They have an extraordinary ability to adapt to their environments and have therefore colonized all ecosystems on the planet. Bacteria are found in the soil, in the sea, in lakes and other freshwater, on polar ice caps, in geysers and hot springs, and on plants and animals. They are also found in our food, on door handles, on cell phones, and even on human skin and in some of our organs (Figure 1)!

BACTERIA

One-celled microorganisms that can either be helpful to other organisms or cause diseases.

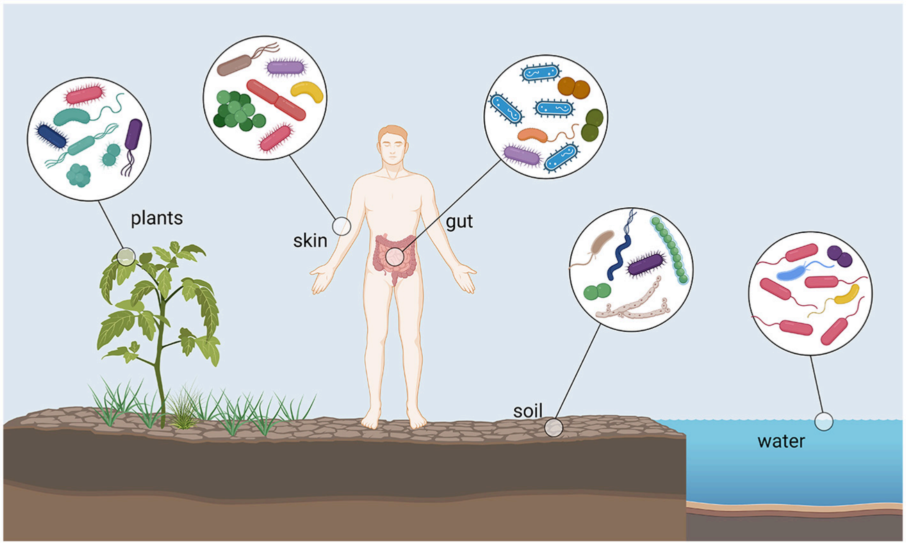

Figure 1

Figure 1

Bacteria are found in very different environments such as in the soil, in water, on plants, on our skin or our gut.

Our bodies contain billions of bacteria. Most of these bacteria are harmless, and many even help us with important functions like obtaining nutrients from food. But some bacteria try to attack us and can cause diseases that can make us very sick. Like humans, bacteria do not live alone—they often live in communities. Communities of bacteria that live on or in organisms are called the **microbiota** [1]. These communities are highly organized and keep the bacteria safe: bacterial communities can protect themselves against toxic compounds, **antibiotics**, or even against the human body's defenses. Within these communities, bacteria exchange information, materials, and foods such as amino acids, sugars, or small molecules. Overall, they help each other, cooperate, and collaborate. But when conditions become difficult, for example when there is stress on the community or when there is not enough food, the situation can be less friendly! Bacteria can become nasty and aggressive toward each other, and they even try to kill each other to get the limited resources or to have more space. You cannot imagine the intense war that is going on around you, and even inside you, as you read this!

MICROBIOTA

All the microorganisms that live in the same place, like in or on another organism (including humans).

ANTIBIOTICS

Small molecules that kill living cells, often used as medicines to treat
bacterial infections.

THE WEAPONS OF BACTERIA

To wage war on each other, bacteria have developed very sophisticated weapons (Figure 2a) [2]. Surprisingly, these weapons are very similar to weapons invented by humans, except that bacteria have been inventing and perfecting them for millions of years. These are weapons of mass destruction! First, bacteria make chemical weapons: they produce antibiotics that kill other bacteria around them. You may know antibiotics as medicines the doctor prescribes when you have certain kinds of infections, but bacteria make antibiotics to fight each other, too. Bacteria can also construct "devices" that act like mines. These are called **bacteriocins**, and they are released into the environment, causing other bacteria that pass over them to explode. Antibiotics and bacteriocins can spread out in the environment and therefore can act at long distances.

BACTERIOCINS

Poisons released by bacteria that diffuse in the environment.

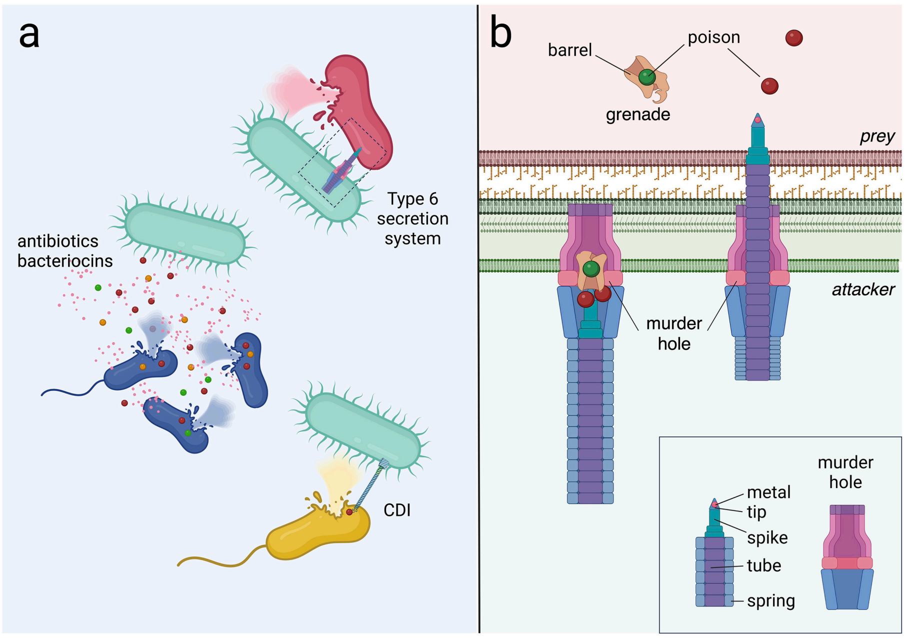

Figure 2

Figure 2

Bacterial weapons. **(a)** The different weapons used by bacteria: antibiotics and colicins which act at distance, and CDI and type 6 secretion system, which need a contact between the attacker and the prey. **(b)** Zoom-in of the type 6 secretion system highlighting the weapon in its extended (left) and contracted (right) states, assembled in the attacker. The grenade and poison delivered into the target are shown. The inset (bottom right) shows the components of the type 6 secretion system: the murder hole and the needle (purple) with its spike tip (green) wrapped by the spring (blue).

Bacteria have also evolved weapons that are activated when another bacterium gets too close. One of them is called **contact-dependent growth inhibition** (CDI): this is kind of like a stick with poison on the tip. When this poison stick touches enemy bacteria that get too close, it kills them.

CONTACT-DEPENDENT GROWTH INHIBITION

A bacterial weapon disposed at the surface of the bacterium that poisons enemy bacteria by touching them.

A SOPHISTICATED WEAPON: THE CROSSBOW

The most impressive weapon is like a tiny crossbow that bacteria make inside themselves (Figure 2b), called the **type 6 secretion system** [3]. This crossbow is only about 0.8 micrometers long, or about a million times smaller than a meter! How does this crossbow work?

TYPE 6 SECRETION SYSTEM

A bacterial weapon that can inject poisons into enemy bacteria.

First, the bacterium makes an arrow that ends with a spike, and then it adds an extra sharp metallic point, which makes the arrow stronger. To propel the arrow, the bacterium builds a spring around it, in a stretched-out form. When the spring contracts, it propels the arrow toward the enemy.

But since the arrow is made *inside* the bacterium, how does it launch outside? To do this, the bacterium constructs a tunnel in its cell membrane, which works like a murder hole. A murder hole is a hole found in middle-age castle fortifications allowing to throw various objects against the attackers. The arrow can be propelled through this tunnel to kill the enemy! The hole created when the arrow penetrates the enemy is not enough to kill it, because the targeted bacterium will repair its damaged membrane very quickly—like when you put a bandage on a small wound. So, the attacking bacterium often adds poison to the end of the arrow, or sometimes within the arrow itself. You may have heard that the Amazon Indians used to put a poison called curare on the heads of their arrow for the same purpose. Bacteria have a very important collection of poisons—some of them can break down the membrane of the target bacterium, others can destroy its skeleton or its DNA, and others can prevent it from growing or dividing.

Recently, researchers have discovered a new weapon associated with this crossbow: a poison grenade! In this case, the poison that a bacterium attaches to the arrow is enclosed in a small barrel (Figure 2b) [4]. Once inside the enemy bacterium, the two lids of the barrel are removed, and the poison comes out of the barrel and kills the enemy bacterium.

BACTERIA PROTECT THEMSELVES

Bacteria are not defenseless against these weapons—many have ways to protect themselves (Figure 3) [5]. Bacteria that produce poisons often also make the **antidotes** to those poisons (Figure 3a). By doing so, they protect themselves from their own poison, but also from the poisons that could be directed against them by their sisters. Some bacteria have developed different tactics to protect themselves. For example, some will jealously guard all the recipes for antidotes that they find, allowing them to resist many poisons. Others surround themselves with a shield called a **capsule** (Figure 3b). The capsule is made of a slightly sticky material, in which the enemy's arrows can become entangled. Another strategy used by bacteria is to organize themselves to form a cluster resembling a Roman testudo formation—a packed formation covered with shields on front and top that the Roman legions used during battles (Figure 3c). The bacteria on the outside take hits, but they protect the ones on the inside.

ANTIDOTE

A substance that neutralizes a poison.

CAPSULE

A protective layer outside the bacterial cell membrane that protects against attacks, toxic compounds, and drying out.

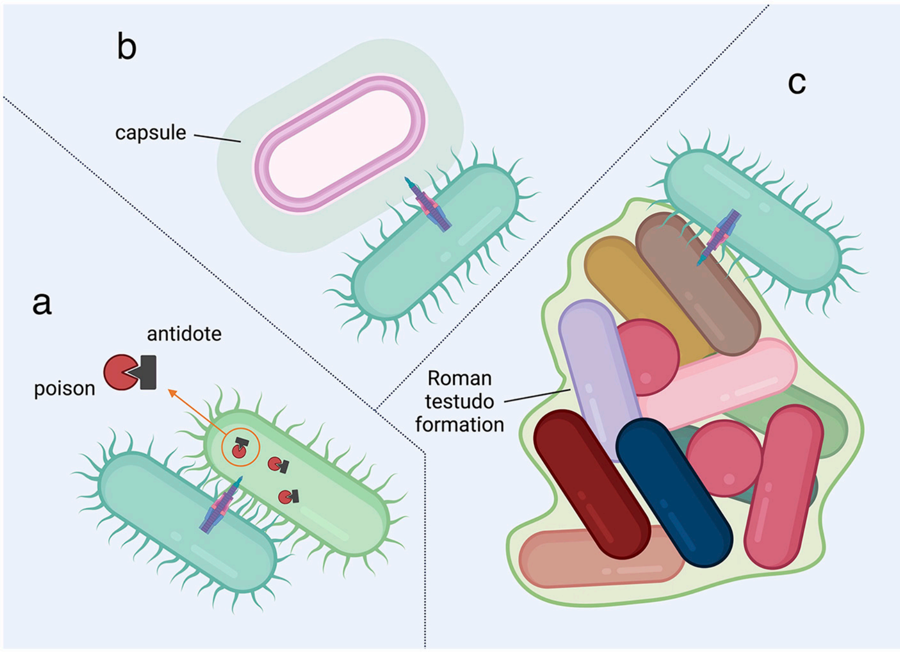

Figure 3

Figure 3

Bacterial defenses. **(a)** Antidotes. The prey bacterium (green) protects itself against the attacker bacterium (blue) by producing antidotes (black) against the poisons (red). **(b)** Capsule. The prey bacterium (pink) is protected against the attacker (blue) by making a shield around itself (capsule). **(c)** Roman testudo formation. Bacteria form a packed structure that protects the ones in the inside.

So, you can clearly see that bacteria are fearless warriors! They have developed an impressive military arsenal to fight each other: mines, crossbows, murder holes, shields, grenades, poisons, and antidotes! All of these weapons and defenses help bacteria to survive when conditions get tough. They have also invented weapons to fight against *us* and make us sick... but that is a story for another article!

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CONFLICT OF INTEREST: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

YOUNG REVIEWERS

JOCELYN, AGE: 15
I like animals and plants and go out to discover new traditions and cultures. My favorite subjects at school are chemistry and mathematics.

TANISHKA, AGE: 14
Possessing a strong affinity for science/health, Tanishka enjoys participating in numerous science competitions. She persistently receives 1st fair in STEM Fair and has gotten the Best of Fair award. She has also published two scientific articles in high-impact-factor journals. She is a part of numerous health-science-related clubs such as Hosa and has gotten 1st place at the international level in the Hosa International Conference. Tanishka can be found playing her violin or reading whenever not studying or part-taking in competitions.

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Eric Cascales is a researcher at the CNRS (the French National Centre for Scientific Research) in a department associated to the Aix-Marseille University (France). He earned his Ph.D. from the Aix-Marseille University working on bacteriocins and pursued his formation at the Houston Medical School (University of Texas), working on a bacterium responsible for crown gall disease in plants. He currently heads a team whose interests are centered on bacterial competition and on bacterial gliding motility. Outside of the lab, he spends as much time as he can rowing, studying wild orchids, practicing violin, and listening to barocco music and opera. *cascales@imm.cnrs.fr