# AntimicrobialResistanceRogue Klebsi: (*Klebsiella pneumoniae*): An Armored Bacterium that Defies Antibiotics

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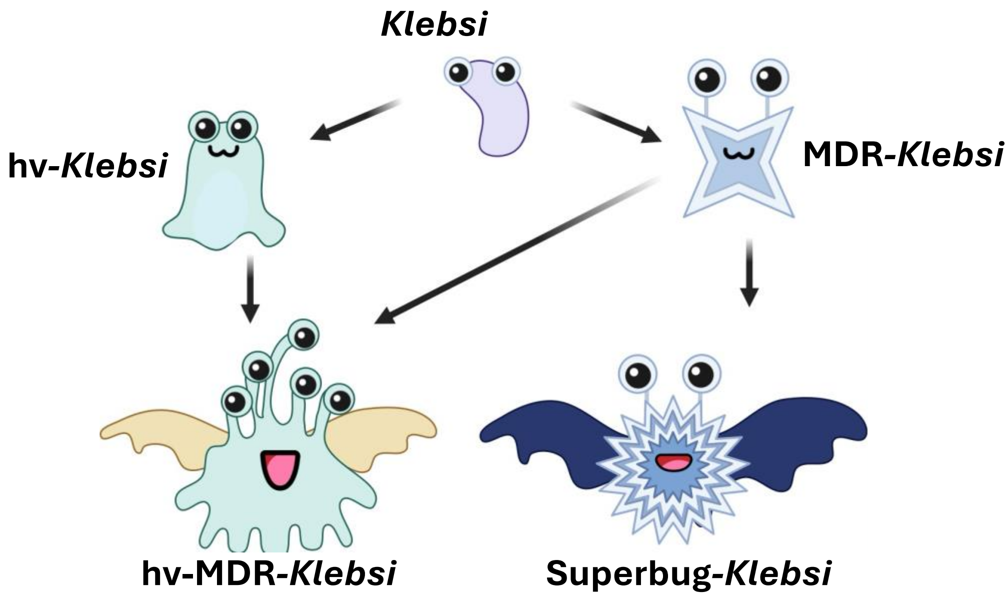



The figure illustrates the evolutionary process of *Klebsiella* using a monster-inspired analogy. It starts with a "base form, Klebsi," representing a non-virulent and antibiotic-susceptible strain. This base form can evolve into distinct variants, each reflecting specific adaptations. On one side, Klebsi can acquire different antibiotic resistance genes through mechanisms such as conjugation or transduction (detailed below), evolving into MDR-Klebsi (Multidrug resistant *Klebsiella*). If Klebsi acquires and accumulates resistance to all available antibiotics, then it advances further into a "superbug" Klebsi form. Alternatively, Klebsi can evolve into a hypervirulent form, referred to as hv-Klebsi. This form is characterized by the acquisition of different virulence powers, such as enhanced capsule production and specialized iron acquisition systems. The convergence of both forms can lead to the most concerning form: hv-MDR-Klebsi, a highly antibiotic-resistant and virulent strain capable of causing severe infections. This figure was created using BioRender.com

**Klebsi: a ubiquitous environmental bacterium with potential to cause disease**

Klebsi (*Klebsiella pneumoniae,* a member of the Enterobacteriaceae family) is a common inhabitant of the gut. Beyond the intestinal environment, Klebsi can be found all around us: in soil, water, and even on the roots of plants. While it can exist as a free-living organism, it's also capable of colonizing a host, whether it be a human, animal, or insect.

In the host, Klebsi can behave as an opportunistic pathogen, a microbe that ordinarily does not cause disease but can in immunocompromised people, that is, individuals who are already sick, or the elderly. It can cause different types of infections, including pneumonia, urinary tract, and blood infections. Though rare, Klebsi can also infect healthy individuals, and produce meningitis or liver abscesses.

**The invisible health threat: the antibiotic resistance sharing party**

In addition to the infections that Klebsi can cause, this bacterium has become a major public health concern because most of the available antibiotics are no longer effective against it. It is common for Klebsi to be resistant to more than three different antibiotics; such microbes are known as multidrug-resistant strains (MDR-Klebsi). On rare occasions, Klebsi can resist all antibiotics used in medicine, and then is referred to as a 'superbug' or pan-resistant strain.

Indeed, Klebsi has a large arsenal of strategies for fighting antibiotics. For example, it can modify the chemical structure of antibiotics, rendering them ineffective, or it can build specialized structures known as efflux pumps that actively expel antibiotics from the cell, thereby preventing them from reaching a lethal concentration inside.

**Klebsi transmits resistance to sensitive bacteria**

Klebsi is also quite a generous bacterium! It lends a helping hand to its neighbors, empowering them to resist antibiotics through the sharing of its strategies. Consequently, within the host, where different Klebsis coexist, we might find some regular Klebsi without any 'tricks' alongside those with antibiotic resistance abilities. Moreover, Klebsi can share these tricks with a bunch of other different bacteria!

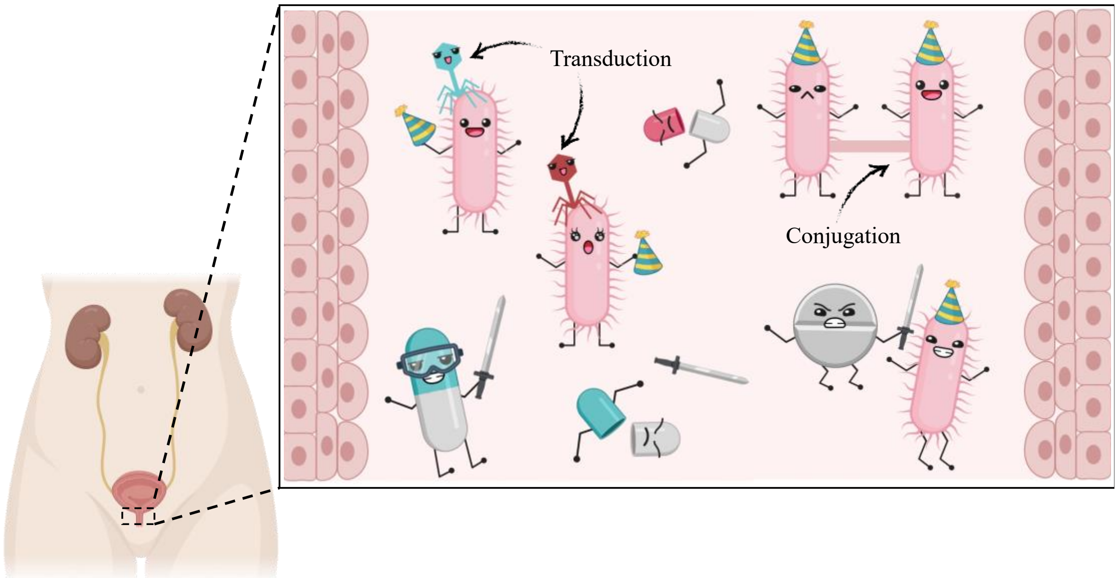
Klebsi facilitates the transfer of antibiotic resistance through multiple mechanisms. In conjugation, Klebsi builds a little 'bridge' to share, allowing the passage of genes to other bacteria, which in turn will also share with other bacteria, propagating resistance throughout the population. Klebsi can also use transduction, a process where tiny helpers called viruses pick up resistance genes from one bacterium and deliver them to another. As a result of this continuous sharing, the Klebsi army becomes increasingly resilient, making it a tough opponent for antibiotic treatments.

**A squishy enemy with a protective shield and ingenious survival strategies**

One remarkable characteristic of Klebsi is its large protective shield called the capsule, which acts like a squishy raincoat made of sugar (polysaccharides). This shield helps Klebsi stay hidden from our body's immune system during infections. Interestingly, different Klebsi strains have capsules made up of different sugars. There are over 140 different types: a whole candy store!

Sometimes, these capsules are very thin, but they hide another enemy! Other virulence weapons! Fimbriae are hair-like structures that act like small hooks that enable Klebsi to stick to surfaces or tissues in our bodies. Once fimbriae have helped bacteria attach, Klebsi begins to produce a protective matrix of gooey material known as extracellular polymeric substances (EPS); this material is essential for building a biofilm, which acts as a bunker protecting the bacteria from harsh environmental conditions. It also promotes communication and facilitates the exchange of various virulence tools between Klebsi.

At other times, Klebsi can evolve a very thick, slimy, and squishy raincoat. This results in extreme "mucoidy" (resembling mucous) that increases their capacity to infect. These are known as hypervirulent Klebsi (hvKlebsi), and can infect healthy individuals. This mucous raincoat allows the bacteria to repel immune cells and stick better together in our tissues, intensifying inflammation and worsening infections.




The figure illustrates the primary mechanisms by which Klebsi shares antibiotic resistance genes with its neighbours. Two major processes are illustrated: i) conjugation, the transfer of antibiotic resistance genes between bacterial cells through direct cell-cell contact by creating 'bridges', and ii) transduction, the transfer of antibiotic resistance genes mediated by viruses, which can pick up and package resistance genes from one bacterium and inject them into another during infection. This figure was created using BioRender.com; it is not drawn to scale and serves as a conceptual representation.

**An iron thief**

One hvKlebsi strategy is to become iron thieves. Bacteria, just like us, need iron to survive and grow, because some of our/their enzymes responsible for metabolic processes contain iron. Therefore, hvKlebsi has acquired additional iron-catchers called siderophores, to thrive in the host environment where iron is limited.

**Use of molecular syringes to inject toxins into host cells**

Lastly, certain strains of hvKlebsi*i* possess an impressive arsenal of protein-based tools known as the Type VI Secretion System (T6SS). This clever system allows them to inject toxins into human cells.

**The evolution of increasingly powerful Klebsi variants**

Typically, hvKlebsi strains are not multidrug resistant (MDR); however, there have been increasing reports of resistant Klebsi also becoming hypervirulent, resulting in hybrid strains (hvKlebsi-MDR) that are both highly antimicrobial resistant and exceptionally virulent, exacerbating the wider public health threat.

***Klebsi is a mightly awful rogue that is a major challenge for human health***

**Conclusions and Future Perspectives**

Klebsi is one of the nasty ESKAPE+ pathogens: Entoco (*Enterococcus faecium*; VRE), Staphi (*Staphylococcus aureus;* MRSA), Klebsi (*Klebsiella pneumoniae*), Aciba (*Acinetobacter baumannii*), Pseuda (*Pseudomonas aeruginosa*), Entoba (*Enterobacter sp.*), plus Myco (*Mycobacterium tuberculosis;* MDR-TB) and Ecoli (*Escherichia coli*), bacteria which the World Health Organisation considers to be among the greatest threats to human health. A complex evolutionary process shapes Klebsi's global presence as a significant healthcare-associated pathogen. This process involves the acquisition and integration of antibiotic resistance abilities, bolstered by the gain of several virulence factors, like increased capsule production. Continuous antibiotic usage selects for resistant Klebsi; for this reason, using antibiotics prudently is essential, as is the thorough monitoring of Klebsi to spot potential new virulence factors and prevent their spread.