



A NEW WAY TO LOOK AT ANIMAL HEALTH BASED ON QUORUM SENSING SCIENCE

Much has changed around animal health over the past decades. Animal husbandry systems have gone through major changes. These include size (number of farms, number of animals), increased production levels, technological developments, animal welfare requirements, environmental measures and tightened antibiotic policies. Livestock farming is in an interesting time where developments are happening in rapid succession. However, when we talk about animal health, we often still work with tools devised decades ago. The problem behind this is that more and more animal health issues are chronic. With our own developed AHV QSA (Quorum Sensing Antagonist) Technology, we want to influence this. In the article below, you can read how we approach this, among other things, in our own lab.

How to deal with antibiotic resistance?

The overuse and misuse of antibiotics has contributed to the rise and spread of multidrug-resistant bacteria. To address this global public health threat, many countries have restricted the use of antibiotics as growth promoters and promoted the development of alternatives to antibiotics in human and veterinary medicine and animal farming (Rahman et al, 2022). CDC's 2019 estimates are still the strongest data to show the U.S. burden of antimicrobial resistance—at least 2.8 million antimicrobial-resistant infections continue to occur in the U.S. each year and more than 35,000 people die as a result (CDC 2019). According to the World Bank, antimicrobial-resistance may cost the world economy US\$1 trillion annually after 2030 (Tang et al, 2017).

The increase of antibiotic resistance has also been observed in poultry and livestock farming worldwide (Van Boeckel et al 2019) and contributes directly as well as indirectly to the rise of infections caused by antibiotic-resistant bacteria in human (Chang Q et al, 2015 and Reddy et al, 2020).

Future for the agricultural sector

As more resistant germs emerge, the harder it is going to be to start treating animals that are really sick. The spread of resistant bacteria may mean that eventually no antibiotic will be effective. Our vision is to create a high-quality and

healthy dairy and food supply chain. Where, together with the agricultural sector, we can start changing the future when it comes to animal health. Proactive animal health optimization always pays off, for both farmer and animal!

Biofilm formation as a survival strategy

The use of antibiotics has another limitation. This is because the mode of action of antibiotics targets planktonic (free-living) bacteria, but are less effective against bacteria hiding in a biofilm. This is because antibiotics have little or no ability to penetrate the biofilm. A very large number of bacteria, especially virulent strains, are able to form a so-called biofilm (Figure 1). This is a layer of mucus that they produce themselves and which attaches to a surface inside or outside the animal. Recognizable examples of biofilm are dental plaque or a slimy layer in water pipes.

Biofilm formation is a highly effective microbial defense mechanism to ensure bacterial survival. Biofilm-associated bacteria have natural resistance to antibiotics, disinfectants and the animal immune system. Bacteria in a biofilm are 100-1,000 times less sensitive to antibiotics and are also found to be 10^{-1,000} times more antibiotic resistant compared to free-living bacteria of the same strain (Donlan, 2000; Abranches J., 2011).

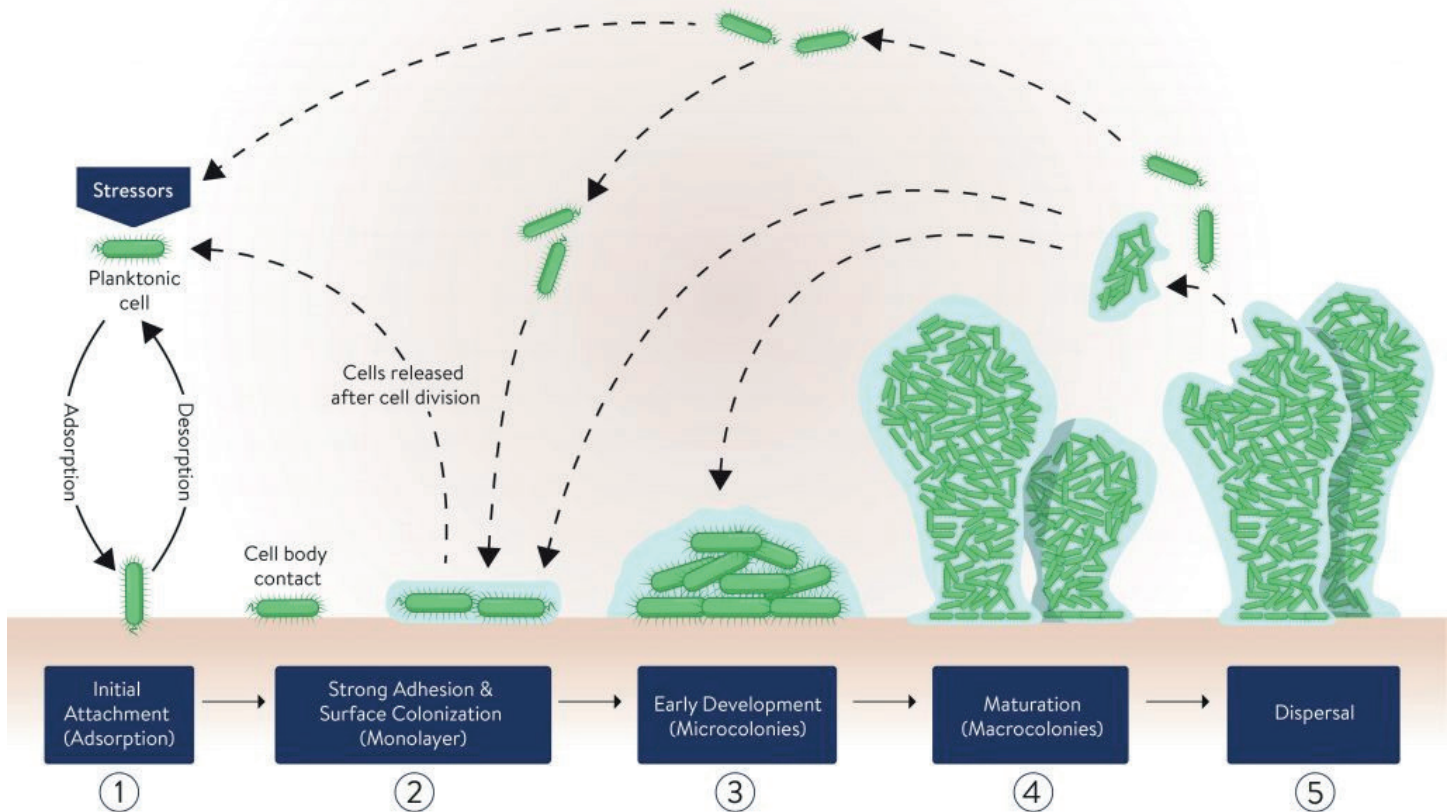


Figure 1: Schematic representation for biofilm formation of a bacterium on a solid surface (AHV International, based on Guzmán-Soto et al., 2021).

Recurrent nature

In the case of recurrent inflammation, as well as chronic inflammation, we often have to deal with biofilms (M.B. Melchior et al., 2006). Bacteria can hide in the body for short or long periods of time because, in a biofilm, they are invulnerable to immune cells and antibiotics. In addition, the animal does not have to show signs of illness at that time at all, as the bacteria are inactive and waiting for the right moment to emerge en masse. These are often times around stress periods of the animal (calving, ration changes, weaning, moving, heat stress, etc.).

The animal's resistance goes down and the bacteria see an opportunity to attack. If this succeeds, the animal is visibly ill and is often treated with antibiotics. This is symptom control, without removing the cause: the biofilm. A frustrating, expensive and time-consuming activity because of its recurrent nature (Figure 2).

Investing proactively in animal health

An emerging animal health strategy is to invest in proactive measures. The starting point at the moment is: healthy livestock farming reduces the need for deployment of reactive agents. Health is characterized by optimising the balance between animal resistance and external infection pressure. Optimal nutrition, optimal barn climate and avoiding stress moments as much as possible are important issues for higher animal resistance (Griebel et al. 2014).

Effect of AHV products

AHV's solutions match this perfectly and take into account the needs of each animal species at each life stage. AHV products are ideally suited to maintaining the health of your

animals, especially around stressful times. AHV products are based on dual mode of action:

1. Prevent biofilm formation and break open pre-existing biofilm;
2. Stimulate and activate the immune system to remove the released bacteria.

This reduces the number of cases of illness on a farm and animals that do fall ill will recover faster, as they are in better condition and may recover under their own steam. Incidentally, the use of antibiotics will decrease which will have a positive impact on your Defined Daily Dose (DDD).

AHV Quorum Sensing Antagonist (QSA) Technology

AHV is the market leader in innovative solutions that prevent biofilm formation and effectively tackle existing biofilm with plant-derived extracts. New plant extracts are continuously screened at AHV for their effectiveness against biofilm, based on the above mode of action. One component of this new mechanism can be found in the role QS (Quorum Sensing) plays in biofilm formation.'

QS is one of the main signalling mechanisms of bacteria that directly contributes to biofilm formation. AHV's patented QSA Technology consisting of plant extracts influence this process and can also easily penetrate the protective layer. Our plant extracts disrupt the QS process. This prevents and disrupts biofilm formation, allowing the immune system to remove the bacteria.

No resistance development by nature

Biofilm-associated bacteria have a natural resistance to antibiotics, disinfectants and the animal immune system

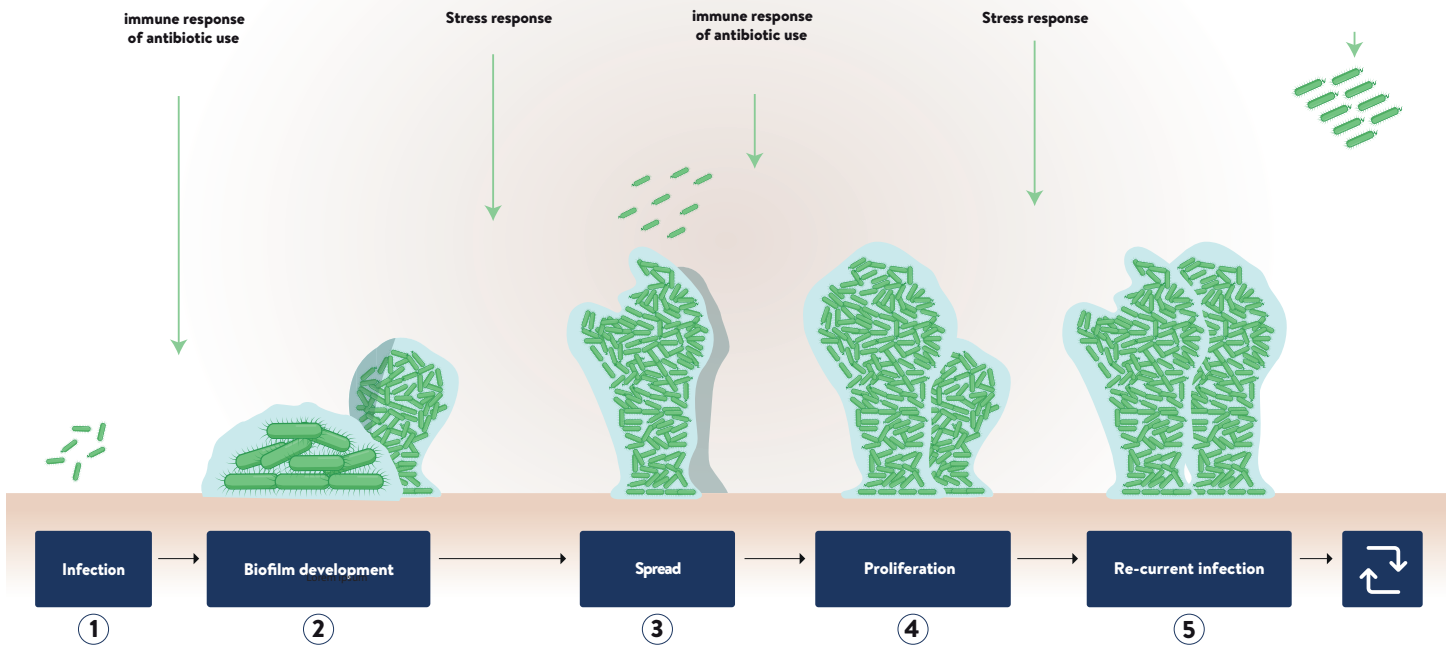


Figure. 2 Biofilm-related infections can lead to chronic infections

due to billions of years of evolutionary adaptations. Bacteria in a biofilm are 100-1000 times less sensitive to antibiotics compared to planktonic bacteria of the same strain (Donlan, 2000). This bacterial persistence, through biofilm formation, is responsible for resistance and often the cause of recurrent problems.

AHV's patented QSA Technology manages to address this by penetrating deep into a biofilm and influencing the communication between bacteria. The extract interferes with molecules emitted by the bacteria, and not with the bacteria themselves. This is in contrast to antibiotics. Because of this mode of action, resistance cannot naturally develop against the extract. In addition, the extract is as active against antibiotic-resistant bacteria as it is against non-resistant bacteria. By using their own communication, AHV is, so to speak, hitching a ride on the evolutionary success that bacteria have achieved with biofilm formation.

A new strategy for animal health

AHV's mission is to empower farmers through unique innovations, tool and solutions in animal health. With our products and the accompanying service and advice, we give livestock farmers control over their animal health and business results. After all, only healthy animals produce optimally. An additional advantage is that in a healthy herd, there is less need to administer regular means such as antibiotics. This benefits the intended decrease in antibiotic use in livestock farming and reduces the risk of further resistance.

In addition, our plant extracts are effective in preventing biofilm formation of antibiotic-resistant bacteria which offers a solution when no longer workable antibiotics are available due to resistance formation. With a sustainable and quorum sensing-based approach, we can make a real impact on the future of the agricultural sector in terms of

environment and nature, economy, health, information, innovation and resources. With the ultimate goal of a high-quality and healthy dairy and food supply.

Disclaimer: The above statements are based on internal and external research. More background information can be requested through AHV.

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