

The Resistance

Cattle treatments that work today might not tomorrow.

by Miranda Reiman, Certified Angus Beef LLC

Your veterinarian has treated thousands of calves with the same symptoms. She knows the tools that work. Just choose the right antibiotic at a prescribed dosage for so many days, and they'll be good as new. Works almost every time.

Until it almost never works.

"We hear about antibiotic resistance as it relates to people and to animals, and a lot of concerns about the relevance to agriculture," says Amelia Woolums, Mississippi State University veterinarian.

But it also has importance in animal health.

"If a cow has an antibiotic-resistant bacteria that's causing an infection, the cow may not get better if we treat it with antibiotics," she says.

New decade, old dilemma

Antibiotic resistance may sound like a modern-era quandary, but early examples pepper our past.

"In some ways it's a big problem, but it's not really a new problem,"

Woolums says. Penicillin was used widely during World War II and by 1948 resistant staphylococcus had become a global problem. Methicillin was developed as an answer, and a year later the first methicillin-resistant staph, commonly known today as MRSA, emerged.

"I think we thought, in the arms race against bacteria, that we could win it," she says. But bacteria replicate quickly, and disclose their tricks to other bacteria by sharing DNA. "It's really not a race we are winning."

In the cattle community, studies show it is on the rise, especially in the last decade.

The growing resistance

"There are diseases cattle get where in the past we might have said, 'Well, let's just give an antibiotic, just in case,'" Woolums says. "That's the attitude we've got to get away from."

The time to make that shift is now.

Bovine respiratory disease (BRD) provides one complex case study, she

says. There are four main bacteria that cause BRD, and 11 antimicrobials on the market are labeled to treat the most common one: *Mannheimia haemolytica*.

That's where much of the research rests. Studies from

1994, 2004 and 2011 showed an increase from virtually no resistance.

"Basically we had 20 years of not much antimicrobial resistance. We thought, 'We don't have to worry about this,'" she says. "That's foreshadowing."

Then work from Kansas State University's diagnostic lab caught the attention of the animal science and veterinary community.

Nearly 400 samples across a three-year period, from 266 unique locations, gave insight into possible trends. In 2009, only 5% of the bacteria were resistant to five or more antimicrobials; by 2011 that jumped to 35%.

Treatment history of the animals was unknown, "but these data still worried a lot of people," Woolums says.

At the University of Georgia, 169 high-risk stocker cattle were measured at arrival, given metaphylaxis — or preventative antibiotic treatment — and swabbed again two weeks later.

Three-quarters of the cattle came in with bacteria that would respond to any antibiotic they were given. Two weeks later, that 75% number was 1%.

"Ninety-seven percent were resistant to the antibiotics we use all the time," Woolums says. "They'd only been given one antibiotic."

Although concerning, she says, "It's important to note that this was not related to an unusually high rate of morbidity and mortality."

More research is needed to



An evolving target

determine the level that would cause a treatment failure.

Woolums and her colleagues completed an additional study that took those same swabs at four points from day one to day 21. It showed that the number of cattle shedding the bacteria went from 10% on the first day to 88%.

"That's textbook," she says. "But what we didn't really expect was that the pattern of multi-drug resistance would completely follow it."

By day seven, 80% of the bacteria were resistant to multiple drugs, and they were genetically diverse, meaning they didn't just proliferate from one carrier calf.

This isn't meant to be a dire warning, Woolums says, but more of a caution sign. More research is needed, and best practices need to follow suit.

Prevention, protocols and precautions

Sick cattle still need to be treated, and there are no new antibiotics on the horizon — in fact, there hasn't been a new class added since 1978.

So what's a producer to do?

"The No. 1 goal is efficient use of antibiotics, that we're really heading off problems before they start," says Brandi Karisch, Mississippi State University Extension beef cattle specialist. "Good animal husbandry and hygiene practices, routine health exams and vaccination are key strategies."

To lessen the chances of needing treatment, limit stress, improve nutrition and identify disease earlier, she says. "So, doing a good job of monitoring those cattle is vital."

Then use antibiotics sparingly — only for the sick or highest-risk cattle — and use them right: follow labels, work closely with a veterinarian and observe proper withdrawals.

It's easy to take antibiotics for granted. They're there to treat strep throat or a sinus infection, and in cattle they solve common ailments like bovine respiratory disease (BRD).

But they may not always be the answer to routine herd health challenges. As research addresses the best ways to keep them working, it's a good time to review how they work in the first place, says Amelia Woolums, Mississippi State University veterinarian.

Different classes of antibiotics work to defeat bacteria in different ways, such as:

- Disrupt the cell wall
- Disrupt the cell membrane
- Inhibit protein synthesis
- Alter the metabolism
- Inhibit DNA replication

"Antibiotics basically block or prevent different things the bacteria have to do to live, or destroy structures of the bacteria," she says. "If the bacteria change those things so the antibiotic no longer works, that's how they become resistant. The sensitive ones are killed and that just leaves the resistant ones, and they get together and say, 'Let's have a family.'"

They use several different tactics for building resistance, Woolums says, such as:

Genetic mutation. That's the spontaneous change in a portion of the DNA of the bacteria. "If the protein changes, and that's the target of the antibiotic, it no longer works," Woolums says. That change is coded into the bacteria's progeny, too, so it passes on the resistance.

Efflux. "That basically pumps the antibiotic right out," she says. The drugs aren't in the cells long enough to work.

Destruction by enzymes. Many bacteria possess genes that then produce enzymes that chemically degrade or inactivate the antibiotics.

"Research shows bacteria are very generous with their DNA," Woolums says, noting they can share them across different kinds of organisms. A *Pastuerella* or *Mannheimia* can pass along resistant chunks of DNA — called integrative and conjugative elements, or ICE — to *E. coli* or salmonella, for example.

"Bacteria replicate at crazy rates," she says. So when one of these mutations sticks, very quickly there are millions of cells with the same tactics. "It's survival of the fittest."

"Treat for the recommended time period," Karisch says. "How many of you know someone who starts feeling better and stops taking the antibiotic?"

For the greater good

When cattle are sick, cattlemen need medicine that works. When humans are sick, doctors need the same. The Centers for Disease Control (CDC) has already flagged this as growing area of concern.

"Antibiotic resistance is one of the biggest public health challenges of our time," Karisch says, citing the CDC. More than 2.9 million people get an antibiotic-resistant infection each year. "So this is a very serious threat, not just on the livestock side of things."

Growing consumer concerns add

another level of urgency.

"We've probably all seen the news headlines," she says.

There's a chance every tool your veterinarian has today will work for years, and there's a chance it won't work next week.

"We don't really know yet. The negative impact on morbidity or mortality has not been clearly evident," Karisch says. "But there's that 'yet' that goes along with that."

"In the meantime, it's really important that we're doing a good job taking care of those cows," she says. **AJ**

Editor's note: Woolums and Karisch spoke as part of the 2020 Cattlemen's College at the Cattle Industry Convention in San Antonio in February.