



Controversial antibiotic use for crops approved in Florida

Experts warn that extensive spraying of medical antibiotics could encourage the development of antimicrobial resistance. Roxanne Nelson reports.

The US Environmental Protection Agency (EPA) has permitted mass spraying of medically useful antibiotics across citrus groves in Florida, USA, to combat citrus greening, a bacterial infection that is harming trees. The decision has been criticised by academics and experts at the US Centers for Disease Control and Prevention (CDC) who say that the approach could harm human health through promoting antimicrobial resistance and that the efficacy of the strategy is unproven.

The citrus industry in Florida is big business. It generates more than US\$8.6 billion in economic activity per year, with 4000 citrus growers cultivating almost half a million acres of land. It is a source of employment for 45 000 people who work either directly or indirectly in the industry, and Florida produces more oranges than anywhere else in the world except for Brazil.

But citrus farmers are contending with a formidable threat and are taking desperate measures to combat it. For the past 10 years, citrus greening has spread across the state, affecting groves in dozens of counties. Citrus greening, caused by *Candidatus Liberibacter* spp, is a disease that decimates citrus trees. Once a tree is infected, there is no cure or even an economically viable option for management and most will die off within a few years. While citrus greening poses no threat to human or animal health, it causes fruit to become green, bitter, and misshapen, rendering it unfit for sale as either fresh fruit or juice.

The economic effect on citrus growers has been extensive, including steep declines in production and forcing some growers into bankruptcy. Estimates vary as to how many trees

are affected, but in a survey by the University of Florida (Gainesville, FL), respondents said that 80% of their trees had citrus greening.

As a result of the threat to industry, the EPA gave approval in November, 2018, to spray 480 000 acres of citrus trees with 388 000 lbs of oxytetracycline, and it has now proposed the additional use of 650 000 lbs of streptomycin per year. Both antibiotics are medically important: oxytetracycline is a broad-spectrum antibiotic used to treat infections such as chlamydia and mycoplasma; and streptomycin is also used for several diseases.

“All selection pressure anywhere creates resistance”

The overuse of antibiotics in any setting, whether it is overprescribing or inappropriate use in agriculture, can fuel the spread of drug-resistant bacteria. It has been speculated that intensive spraying of antibiotics across large areas of cultivated plants could increase the frequency of antibiotic resistance genes in bacteria that live on plant surfaces. Then in turn, the genes conferring resistance could subsequently be transferred into clinically important bacteria that may affect human health.

“The idea of using these large quantities on fruit trees makes little sense when we are dealing with a serious public health problem with resistant pathogens”, says Ramanan Laxminarayan (Center for Disease Dynamics, Economics & Policy, Washington, DC, USA). “Although streptomycin is not used for tuberculosis treatment any longer, there is cross resistance with amikacin and kanamycin which are important antibiotics.”

Dawn Sievert, CDC, also warned against the decision. “Antibiotics are valuable tools for treating infections, but using antibiotics anywhere, including in people, in animals, and on crops can lead to antibiotic resistance that may impact human health”, she said.

“Our mental model of resistance is that it is selected in both humans and in the environment—whether in crops or in animals—and then resistance spreads to humans in a number of ways including on farm workers, food, and water, mostly in developing countries”, says Laxminarayan. “All selection pressure anywhere creates resistance”.

A spokesperson for the EPA told *The Lancet Infectious Diseases* that “compared to the potential exposure associated with FDA-approved allowable residue levels from the use of antibiotics on animals for agriculture, potential human and environmental exposure from the use of oxytetracycline and streptomycin on treated agricultural commodities is considered negligible”, noting that the EPA works with experts from the Food and Drug Administration (FDA), CDC, and the US Department of Agriculture. “Both CDC and FDA evaluated the



A grapefruit tree affected by citrus greening

For more on the evidence around the use of antibiotics in plant agriculture see *Rev Sci Tech* 2012; 31: 199–210

process, and EPA incorporated their suggestions into the analyses.”

Antibiotic use in plant agriculture is not new but has received far less attention than the more common use of antimicrobials in livestock. In the USA, most conventional apple and pear producers use antibiotics to treat fire blight and in 2015 roughly 50 000 acres were treated, yet fruit production accounts for only 0.2% of total domestic traditional antibiotic use. By contrast, almost 80% of all antibiotics in the USA are used in animal agriculture. Despite decreases in use due to tighter regulations, in 2017, 4.3 million kg of medically important antibiotics were used in the beef and pork industries, and 268 000 kg in poultry. Antibiotics have legitimate uses in farming, such as for treating sick animals.

Efforts to curb excess antibiotic use in agriculture to prevent the development of drug resistance have largely focused on the widespread use of antibiotics as growth promoters in healthy animals. As a result, the EU banned use of the drugs as growth promoters in food animals in 2006, with the USA doing the same in 2017. China and Brazil have banned the use of colistin—an antibiotic of last resort in human infections—for growth promotion in animals. “We know that oversight by health-care providers and veterinarians has helped reduce the amount of antibiotics used in humans and animals, and has improved how these drugs are used; for example, veterinarians only use medically important antibiotics to treat, control, or prevent infections in food animals and not as growth promoters” said Sievert.

The use of medically important antibiotics for crops is also closely regulated in many parts of the world. The EU has banned the agricultural use of both streptomycin and oxytetracycline. So too has Brazil, which is dealing with widespread citrus greening. Brazil has implemented an integrated pest management

programme aimed at reducing sources of citrus greening and its insect vectors (two species of psyllid: *Diaphorina citri* and *Trioza erytreae*) around its groves. This includes spraying with pesticides and insecticides, using sticky traps along the borders of groves to detect where psyllids are coming from, removing infected trees, and releasing wasps, which prey on psyllids, in areas with infrequent spraying.

Since 2016, antibiotics have been deployed as emergency applications in citrus groves in Florida, and streptomycin and oxytetracycline have been sprayed on pear and apple orchards in the USA for over 50 years to control fire blight, but never on the scale that has recently been approved in Florida for citrus growers.

“There is little evidence that a massive campaign of tree spraying will halt the spread of citrus greening in any significant way”

There is little evidence that a massive campaign of tree spraying will halt the spread of citrus greening in any significant way. It will not cure the disease, but the hope is that it will boost the survival of infected trees. Data are limited as to the effect of spraying on resistance, as only a few small-scale tests have been done, says Nathan Donley, Center for Biological Diversity (Portland, OR). “Antibiotics are used very differently in animals compared to plants”, he says. “In animals they are used in very high doses and the animals are in very unsanitary conditions, while in plants they are used at lower doses but over large areas of land.”

Spraying fields exposes many types of bacteria to suboptimal doses of antibiotics and resistance has developed. “But what we don’t know is how it will affect human pathogens”, says Donley. “We don’t have the data, and it has not come under the same scrutiny in plants. There have not been any studies done so far, at least none

that were submitted to the EPA, that looked at whether this use could lead to greater resistance.”

A 2012 paper published in *Revue Scientifique et Technique* showed that in pear and apple trees, antibiotics have efficacy only when used as a prophylactic, and are not curative when sprayed on trees. It also reported that “antibiotics are non-persistent on plant surfaces and lose activity rapidly”, and that a direct link between spraying plants and antibiotic resistance in clinical bacteria has not been observed. But this study primarily looked at fire blight, and at usage far below the levels that have been approved for citrus trees.

“Opinions about effectiveness vary by grower”, says Rick Dantzler, chief operating officer of Florida’s Citrus Research and Development Foundation. “Some believe they are helped, while others do not.”

He notes that soil conditions, maturity of trees, and other factors have much to do with farming practices, so it is important that growers have a wide variety of tools available to them. “Tree removal, optimal watering, enhanced nutrition, pest management...growers use many options and are trying new things constantly”, says Dantzler.

As for the risk that mass spraying could help to generate antimicrobial resistance, “the EPA, in partnership with the Florida Department of Agriculture and Consumer Services, imposes science-based requirements upon growers to ensure safe levels are adhered to and resistance is mitigated”, he says.

Florida is not the only region affected by citrus greening. It has been reported in a number of other parts of the USA, including California, Georgia, Louisiana, Puerto Rico, South Carolina, Texas, and the US Virgin Islands. Globally, the disease has been reported in Asia, Africa, the Arabian peninsula, Latin America, and Europe.

Roxanne Nelson