Division of Marketing
Agricultural Development and Diversification (ADD) Program

1997 Grant Final Report

Grant Number 12008

Grant Title Streptomycin Resistance in the Fire Blight Pathogen: Orchard Survey and Grower Education

Amount Awarded $9,652.00

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Department of Agriculture, Trade and Consumer Protection
Division of Marketing, Wisconsin Farm Center

Agricultural Development and Diversification Program (ADD)
1998 Grant Project Final Report
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Project Beginning Date: January 1, 1998
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Submitted by: Patricia McManus **Date:** September 29, 1998

Department of Agriculture, Trade and Consumer Protection
Division of Marketing, Wisconsin Farm Center

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In many important apple-growing regions worldwide, streptomycin-resistant strains of *Erwinia amylovora*, the fire blight pathogen, have been identified, and fire blight has been increasingly difficult to manage. In recent years apple growers in Michigan have cited fire blight as their most serious production problem. Since the discovery of streptomycin-resistant *E. amylovora* in Michigan in 1990, fire blight has been so severe in that state that some apple growers have gone out of business largely because of economic losses due to fire blight. Wisconsin growers have also suffered fire blight epidemics in recent years. Thus, the **intent of this project** was to i) survey apple orchards in Wisconsin to determine whether strains of *E. amylovora* are resistant to the antibiotic streptomycin; and ii) educate apple growers on the economic losses that result if *E. amylovora* becomes streptomycin resistant and how growers can reduce the risk of resistance developing in their orchards. These objectives were **projected to benefit Wisconsin growers** by i) identifying sites with streptomycin-resistant *E. amylovora* before strains became widespread; ii) informing growers of the streptomycin-resistance status of their orchards so that appropriate fire blight management programs could be implemented; and iii) ensuring that growers are fully aware of practices that might delay or prevent the emergence of streptomycin-resistant *E. amylovora*.

Grant funds supplied by WDATCP-ADD program were critical in meeting the objectives of this project. Because of the difficulty in dealing with receipts for travels, supplies, and other expenses incurred, funds were directly used to pay Steve Wraith, a part-time employee with a Master's degree in Plant Pathology from UW-Madison. Matching funds were used to cover other expenses.

Successes and challenges. We **succeeded** in surveying 19 different apple orchard blocks in Wisconsin that were afflicted with fire blight despite streptomycin use. In almost all cases we recovered at least five isolates per site. Previous experience indicates that if streptomycin-resistant *E. amylovora* can be detected in 50 samples from a site, it is usually detected in the first five samples tested (McManus and Jones, 1994; Phytopathology 84:627-634). In other words, when detected, streptomycin-resistant *E. amylovora* usually occurs at an incidence of at least 10%. The fact that streptomycin-resistant *E. amylovora* was not found in the current study indicates that when fire blight is severe despite streptomycin use, it is probably not because of a resistant pathogen. The greatest **challenge** encountered during the course of this work was a low incidence of fire blight in central and northern Wisconsin in 1998 which prevented sampling from those sites. However, the risk of low pest pressure is inherent in any field survey and was understood at the outset.

The **education and outreach** objective of this project was the focus of three oral presentations during January and February and two articles in The Apple Press, the newsletter of the Wisconsin Apple Growers Association (see Appendix). A third article will report the final results. Total attendance at the presentations was approximately 300. An estimated 16 telephone calls from growers wanting further information resulted directly from the presentations and articles.

The **results** of the survey are summarized in the attached table. During 1997 and 1998, 19 orchard blocks in eight counties were sampled for streptomycin-resistant strains of *E. amylovora*. No resistant strains of *E. amylovora* were detected, but other species of streptomycin-resistant bacteria were found in all samples from two sites in Crawford county and in at least a few samples from all the other sites. These results are essentially what was expected.

Technology development, benefits, and impact. During the course of the project, we refined our methods of isolating *E. amylovora* so that by the end of the work we were using approximately 50% fewer agar plates than when we started. We also discovered that samples continued to consistently yield *E. amylovora* even after 8 days in cold storage. These findings indicate that in future years, should the need arise, we will be able to test isolates from suspicious orchards at a modest price, especially if we have the assistance of growers in collecting samples and the Plant Pathogen Detection Clinic in isolating the pathogen. In other words, we don't intend to survey the state on an annual basis, but we are prepared to do limited sample on an as-needed basis. For example, if a severe fire blight outbreak occurs on newly planted stock from a nursery in a region where streptomycin-resistant *E. amylovora* is common (e.g., Michigan or Washington), then the site should definitely be tested. Finally, if an orchard tested negative in our 1997-1998 study, but tests positive in the near future after infected nursery stock is planted, our data would lend support for the Wisconsin grower to claim damages against the nursery.

This project has heightened growers' awareness not only of streptomycin resistance but of resistance to other pesticides as well. Understanding how resistance comes about and persists, and steps that might delay resistance, will be critical as fewer chemicals are available to manage pests. Thus, the educational objective of this project is ongoing and should have a lasting impact on growers in Wisconsin.

Future research. In addition to the direct results and benefits described above, this project will likely lead to future research and outreach in the area of sources and acquisition of antibiotic resistance genes in orchard bacteria. For example, the funds from WDATCP-ADD were beneficial in securing $20,000 from the UW College of Agriculture and Life Sciences Institute for Pest and Pathogen Management for research. Likewise, the Principal Investigator, Patricia McManus has or will pursue funding from US-EPA and USDA. McManus is also co-authoring a chapter tentatively titled, "Antibiotic Use Outside of Human Medicine." The primary audience for the chapter will be medical professionals—a group that is in dire need of education on antibiotic use in crop protection.

The economic impact survey can be found in the appendix.

Survey Streptomycin-resistant *Erwinia amylovora*, 1997-1998

Orchard Block	County	Cultivar	Collection date, collector	No. streptomycin-resistant isolates/ total isolates
A	Crawford	Talman Sweet Pioneer Mac/M.9	7/17/97 Aue 7/28/97 McManus	0/6 0/9
B	Crawford	Golden Russet Talman Sweet Fortune	7/17/97 Aue 7/28/97 McManus 7/28/97 McManus	0/5 0/5 0/4
C	Richland	Ozark Gold	7/20/97 Aue	0/12
D	Richland	Paulared Paulared (by shop) Paulared (same as 7/19) Jonathan	7/19/97 Aue 7/28/97 McManus 7/28/97 McManus 7/28/97 McManus	0/5 0/18 0/17 0/12
E	Richland	Jersey Mac Cortland	??? Aue 7/28/97 McManus	0/5 0/8
F	Columbia	various	7/12/97 McManus	0/15
G	Fond du Lac	Paulared	7/23/97 McManus	0/16
H	Crawford	Haralson	6/9/98 McManus	0/7
I	Crawford	Gala	6/9/98 McManus	0/10
J	Crawford	Jersey Mac	6/9/98 McManus	0/8
K	Crawford	???	6/9/98 McManus	0/32
L	Crawford	???	6/9/98 McManus	0/17
M	Green	Jonathan	6/20/98 McManus	0/56
F	Columbia	Golden Delicious	6/26/98 McManus	0/21
N	Columbia	Gala, others	6/26/98 McManus	0/23
O	Columbia	Various	6/26/98 McManus	0/29
P	Walworth	Various	7/14/98 McManus	0/3
Q	Juneau	McCoun, Idared, Honeycrisp, Jonagored	7/27/98 McManus	031
R	Sauk	Various	7/27/98 McManus	0/7
S	Sauk	Jonagold	7/27/98 McManus	0/4

No streptomycin-resistant *E. amylovora* found in Wisconsin in 1997 or 1998. Only Orchard Block F was sampled in both 1997 and 1998.

APPENDIX

THE APPLE PRESS
Vol. 11 No. 15 Sept 1997

ORCHARD SURVEY FOR STREPTOMYCIN-RESISTANT *ERWINIA AMYLOVORA*

Patricia McManus,
UW-Madison Plant Pathologist

Of the major diseases affecting popular apple cultivars, fire blight is the most difficult to manage. Unfortunately, some current cultural practices, such as vigorous, high density plantings of susceptible cultivars on susceptible rootstocks, exacerbate the problem. Thus, many growers apply streptomycin (Agrimycin, Agristrep) to keep the bacterial pathogen Erwinia amylovora in check. In some of the world's major apple-growing regions (Michigan, California, Oregon, Washington, and New Zealand) strains of E. amylovora that are resistant to streptomycin are prevalent, and streptomycin use is obsolete.

What about Wisconsin? We've had some bad fire blight from time to time, including 1997, but can it be attributed to streptomycin-resistant E. amylovora? The best way to address this question is to survey orchards for resistant strains, and I have received support from WDATCP (the state ag. dept.) to do just that in 1998. As a prelude, I tested samples from seven orchards this year and found no E. amylovora that were resistant to streptomycin. But two facts prompt concern: First, we are planting trees from nurseries in regions where resistant E. amylovora is prevalent. Second, streptomycin-resistance genes are present in other bacteria in the orchard, and the genes can probably be transferred to E. amylovora during bacterial mating.

I am most interested in sampling:

1) Trees that have fire blight the first year of planting despite having few flowers and no obvious source of inoculum (e.g., adjacent mature block with blight), especially if the trees were from Michigan or the western U.S.

2) Plantings that have severe BLOSSOM blight even though streptomycin was used during bloom; this would imply a failure of streptomycin at the time when it usually works.

Most growers get by bloom just fine but then have problems with shoot blight in late June and July. This is probably not because the pathogen is resistant to streptomycin, but I will test samples from such plantings anyway, especially if I cannot locate sites like 1 and 2 described above. I will provide more details about how this survey will be conducted as the 1998 season approaches. For now, good luck with harvest. And read my other article in this newsletter about scab on the undersides of leaves.

SPECIAL NOTE

WAGA has made arrangements with American Fruit Grower magazine so that each of WAGA's members will receive a one-year complimentary subscription.

ORCHARD SURVEY FOR STREPTOMYCIN-RESISTANT ERWINIA AMYLOVORA

Patty McManus, UW-Madison Extension
Department of Plant Pathology

Last fall I told you about a survey for streptomycin- resistant strains of the fire blight bacterium, *Erwinia amylovora*, that I would be conducting in 1998 with support from the Wisconsin Department of Agriculture, Trade, and Consumer Protection (see Apple Press, Sept. 1997). As you may have surmised from all my rambling on fire blight and antibiotic resistance, I find the topic fascinating. Moreover, judicious use of streptomycin is relevant to the health of your orchard, you, and your families. Streptomycin resistance has seriously hindered fire blight control in the western U.S. and parts of Michigan. Although streptomycin isn't used much anymore to treat humans, excessive exposure to the drug may favor the build up of resistance to other antibiotics that still are used in treating humans. More on safety to humans in a later newsletter; for now I'll focus on the survey.

In Wisconsin we've had some bad fire blight from time to time, including in 1997, but can it be attributed to streptomycin-resistant *E. amylovora*? That is what I want to learn. Last year I tested samples from seven orchards and found no *E. amylovora* that were resistant to streptomycin. But two facts prompt concern: First, we are planting trees from nurseries in regions where resistant *E. amylovora* is prevalent. Second, streptomycin-resistance genes are present in other bacteria in the orchard, and the genes can probably be transferred to *E. amylovora* during bacterial mating.

I am most interested in sampling:

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- Plantings that have severe BLOSSOM blight even though streptomycin was used during bloom; this would imply a failure of streptomycin at the time when it usually works.

- Orchards with a long history of streptomycin use, including sprays applied past bloom.

Most growers get by bloom just fine but then have problems with shoot blight in late June and July. This is probably not because the pathogen is resistant to streptomycin, but I will test samples from such plantings anyway, especially if I cannot locate sites like 1-3 described above. As the season progresses, contact me at (608-265-2047; psm@plantpath.wisc.edu) if you think your orchard is a candidate. Other research and extension commitments will limit the time I can devote to the survey. Therefore, I cannot promise to sample every orchard. But with some hired help, we'll do our best to hit the hot spots. The way research goes, my planning this survey will squelch blight this year. For your sake, I hope so!

TRADE SHOW COORDINATOR NEEDED

continued from back page

sites, bookkeeping and coordinating events with commodity associations and UW-Extension. Qualified applicants will have experience managing trade shows, sales and or vendor relations. Computer skills are essential. Compensation is based on per space commission. An independent contractor is preferred. Interested parties should contact Corine Hill at the WI Berry Growers Association office, 608-592-7970.

Outreach Programs for WDATCP-ADD Grant 12008
Streptomycin Resistance in the Fire Blight Pathogen: Orchard Survey and Grower Education

Conference	Presentation	Location, date	Participants
Apple Management: Biology of the Crop and its Pests	Fungicide and Bactericide Resistance	Madison, WI Jan 6, 1998	30
Stateline Fruit and Vegetable Conference	Fire Blight: A New Face for an Old Foe	Harvard, IL Feb 6, 1998	70
Wisconsin Fresh Fruit and Vegetable Conference	Fire Blight: A New Face for an Old Foe	Stevens Point Feb 24, 1998	200

Fire Blight—A New Face for an Old Foe
Fresh Fruit and Vegetable Conference, February 23-24, 1998
Stevens Point, WI

By:
Patricia McManus
University of Wisconsin-Madison
University of Wisconsin-Extension

The Old Face *vs.* the New Face
Although fire blight was discovered in the Hudson Valley of New York State, and has been recognized as a bacterial plant disease since the late 1800s, there are many gaps in our understanding of the biology and control of this disease.

- **The Old Face:** apple trees were grown on seedling rootstocks or rootstocks that were not very susceptible to fire blight. The trees were large, so even if *Erwinia amylovora*, the fire blight bacterium, infected a succulent shoot tip and traveled through the tree, most of the tree was left unharmed and the infections could be pruned out without losing too much fruiting wood. Trees were left in the orchard for several decades, so the grower didn't replant as often and therefore decreased his risk of introducing new strains of *E. amylovora* on nursery stock.
- **The New Face:** fire blight-susceptible cultivars and rootstocks, in high-density, nitrogen-enriched plantings have changed the genetic, physical, and biochemical traits of apple trees in a manner that has been very conducive to fire blight. Moreover, streptomycin-resistant strains of *E. amylovora*, have emerged in several regions of the U.S. (Michigan, Washington, Oregon, California, Missouri) and New Zealand, making fire blight control especially difficult.

What about the pathogen? Has *E. amylovora* itself become more aggressive? Most of the evidence suggests that this is not the case. Time and again research has shown that *E. amylovora* isolated from pome fruits from different times and locations appear to be genetically, biochemically, and physiologically similar. There are some differences in aggressiveness, but there has been no recent trend to increased virulence reported. Also, remember that the pathogen is only one component of the "disease triangle"—the state of the plant and the environment are the other two big influences on whether a plant becomes diseased or remains healthy.

THE BOTTOM LINE: Changes in cultural practices (cultivar/rootstock choice, planting density, changes in tree architecture, and in some cases streptomycin-resistance) are largely responsible for the fire blight that has reared its ugly new face over the past 8-10 years.

How did we get into this mess? I'm not sure where it all started, but somehow consumers became enamored of some highly susceptible cultivars (*e.g.*, Gala, Braeburn, Fuji, Jonagold, Paulared, Idared, and the list goes on and on). To meet the demand, growers started planting more of the favorites, and to keep the trees more manageable, used dwarfing rootstocks such as M.9 and M.26 more frequently. The recent trend to promote early bearing has involved specialized training systems, abundant nitrogen and much physical manipulation of young trees. In turn, nurseries have responded to meet the demands of orchardists, and they too have gone the way of susceptible cultivars on susceptible rootstocks, heavy nitrogen rates to make a bigger tree to sell to the orchardists. So, no matter how we got on this treadmill, the orchardist appears to be stuck in the middle.

Consumers: love those susceptible cultivars!

Orchardists
- plant susceptible cultivars, rootstocks
- intensive cultivation (high density, nitrogen, manipulations)
- more frequent planting, especially dwarf trees

Nurseries:
- plant susceptible cultivars, rootstocks
- intensive cultivation (high density, nitrogen, manipulations)

Relevant Features of the New Face. The traits that we'll focus on today are:

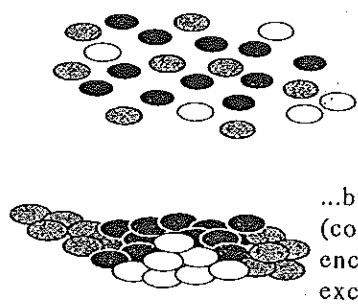
1. **Colonization of flowers by *E. amylovora***—relevant to the old face but with some important implications for the new face.
2. **Internal colonization and movement of *E. amylovora***—this has been known since early in this century, but never before has it been so critical to the health of your orchard.
3. **Rootstock blight**—the sometimes deadly outcome of internal movement of *E. amylovora* that can result in 10-20%, or even entire losses of high-density plantings.

1. Importance of Flower Colonization

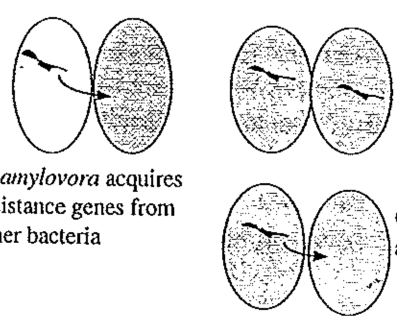
- **Disease development**—*E. amylovora* grows exponentially (numbers of cells double every 30 minutes under ideal conditions) to about one million cells on the floral stigma; then rain or dew carry the bacteria *en masse* to the floral nectaries whereupon infection occurs (blossom blight). But why do you some times get terrible cases of shoot blight in late June or early July despite having seen no blossom blight earlier? Perhaps the bacteria overwintered in inconspicuous cankers and then moved internally to the shoots. Or, can relatively small populations of *E. amylovora* enter nectaries without causing blossom blight, but then move internally to the shoots? We don't know the answer. This is one of many major gaps in our knowledge of fire blight.
- **Other bacterial species occupy the same niches on flowers as does *E. amylovora*.** This provides an opportunity for biological control of fire blight which is a good thing for apple trees and growers. However, the flower and its parts may be a suitable site for gene exchange among bacterial species including *E. amylovora*. In general, gene exchange benefits the pathogen. In the case of acquiring streptomycin-resistance genes, this would be a major plus for the pathogen.
- **Biological control:** Blight Ban A506 is a commercially available biological control produced by Plant Health Technologies (Boise, ID 208-3454-1021). It is a formulation of the non-pathogenic bacterium *Pseudomonas fluorescens* strain A506. The premise is that A506 competes with nutrients on the floral stigma. In order to work, however, A506 must reach the flowers before *E. amylovora* does. In other

words, it needs to establish "squatter's rights" (the technical term for this is "preemptive colonization"). A506 must persist and spread within the orchard, and repeated applications are usually needed. A506 has suppressed fire blight most successfully in the western U.S. on pears and when integrated with streptomycin. In most studies, it has not successfully controlled fire blight of apple in the midwestern or eastern U.S.

- **Gene exchange.** Although it has not been experimentally proven that *E. amylovora* acquires streptomycin-resistance genes from other bacteria on the flower surface, this is certainly not an unreasonable idea. Many different bacterial species inhabit apple and apple flowers, and their colonies are not distinct. In fact, they may exist as "biofilms" which would be analogous to bacterial plaque that causes tooth decay.



Different species probably intermingle and exchange genes on mobile pieces of DNA by a process known as "conjugation". In fact, in the laboratory we know that *Erwinia herbicola* (a relative of *E. amylovora* that is not pathogenic on apple) can transfer its streptomycin-resistance genes to *E. amylovora*.



Once *E. amylovora* has acquired resistance genes it passes them on to daughter cells during regular cell division and also to other *E. amylovora* that haven't yet acquired the genes. Then, if an application of streptomycin is made, these lucky cells that carry streptomycin-resistance genes will flourish.

2. **Importance of Internal Colonization and Movement of *E. amylovora*.**

- Once bacteria are inside the plant, they are out of reach of known chemical and biological controls.
- Internal colonization leads to the devastating loss of major scaffolds and rootstock blight. As seen in the table below, *E. amylovora* moves quickly in either the upward or downward direction in an apple tree. Sometimes the pathogen is found in tissues well beyond the visible symptoms of disease, and even in rootstocks.
- *E. amylovora* overwinters and survives quite nicely internally in apple trees; it will not survive in dead leaves or soil.
- Long-distance dispersal of *E. amylovora* (*e.g.*, from a nursery to your orchard or between continents) is possible on asymptomatic nursery stock and budwood.

Internal Colonization: How fast? How far?

Cultivar	*Direction*	*Distance/Time*
Jonathan	down	28 in./14 days*
Jonathan	up	6 in./7 hours 14 in./4 days
Empire/M.26	down	>18 in./11 days
Golden Delcious/M.26	down	>18 in./11 days

*visible symptoms only 6 inches from inoculation point

3. **Rootstock Blight**

- Preliminary tests by Aldwinckle and Momol at the Cornell Geneva station in NeW York have shown that young trees can succumb to rootstock blight in a matter of one season, and they believe this is because of the internal movement of *E. amylovora* through apparently healthy scion wood down to the rootstock. They inoculated the tips of several young trees of Golden Delicious/M.26 and Empire/M.26 and found that after 21-41 days, *E. amylovora* was in the rootstock. Also, they noted that if the scion was infected later in the season (early July) there was a greater risk for rootstock infection than if the scion were inoculated earlier (mid May or early June).

Alternatives for Controlling Fire Blight—What's in the Pipeline?

With the demise of streptomycin in some regions, the inconsistency of Blight Ban A506, nd a growing problem with shoot blight and rootstock blight as opposed to blossom ight, what does the future hold?

- **More bacterial biocontrols.** Some newly discovered strains show more promise than A506. It will be several years, however, before these are marketed. Also, these are primarily aimed at controlling blossom blight rather than shoot blight.
- **Fire blight resistant rootstocks.** The CG series (see other handouts) has some promising candidates, and scientists at Cornell have inserted an antibacterial gene from the silkworm larva into Gala and M.26 to help apple fight off *E. amylovora* These need more testing and also need to overcome regulatory hurdles.
- **Growth regulation.** An experimental growth regulator acts by inhibiting production of the plant hormone gibberellin. In doing so, shoots tend to be less lush and succulent and therefore more resistant to fire blight. Again, the product is not yet registered, and you must consider how this growth regulator would fit into the overall scheme of orchard management.
- **Systemic acquired resistance (SAR).** This is a plant's idea of an immune system. Although plants do not have true immune systems, they often do respond to attack by a pathogen or even some chemicals by putting up an arsenal of defenses so that they're somewhat resistant to subsequent attacks. Novartis Corp. is developing a chemical inducer of SAR which has been highly successful in controlling powdery mildew diseases of cereal crops. There is precedent, however, for SAR in controlling fire blight and apple scab, and this is an area of interest for researchers.

Presented at Short Course
Apple Management, Biology of the Crop and Its Pests
Jun 5-7, 1998

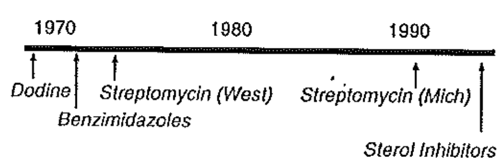
Pesticide Resistance in Apple Pathogens

- How it happens
- High-risk situations
- SI resistance in *Venturia inaequalis*
- Streptomycin resistance in *Erwinia amylovora*
- Delaying the onset of resistance

What is Resistance?

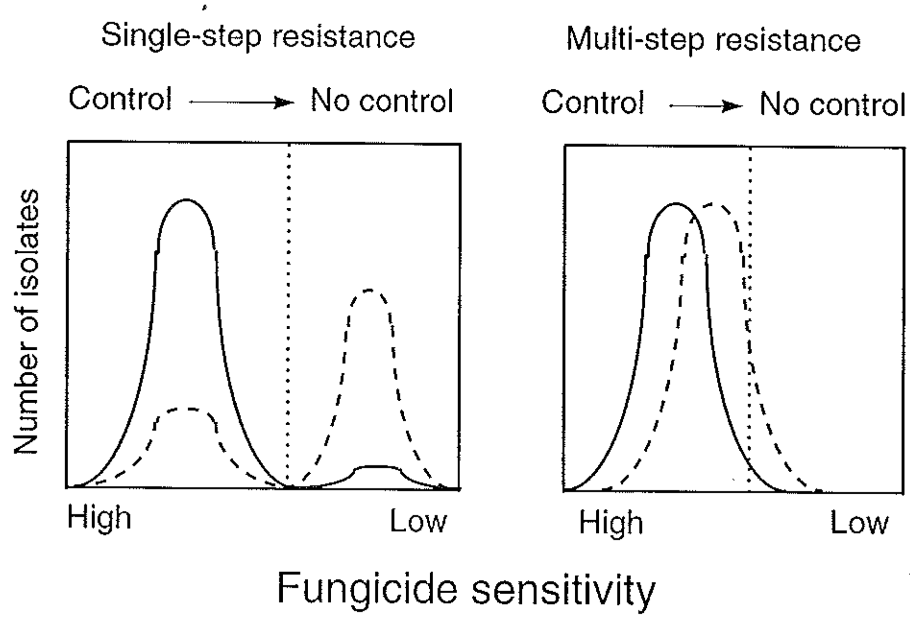
- Laboratory resistance
  - resistant strains grow on medium containing fungicide or bactericide
- Field resistance
  - resistant strains present in the orchard
- Practical resistance
  - resistant strains so prevalent that fungicide/bactericide no longer controls disease

Resistance to Apple Fungicides/Bactericides



After repeated exposure to a fungicide, practical resistance arises in two ways:

- Multi-step: proportion of the population that is resistant increases with each fungicide application
  - likely when fungicide acts on many targets or when many genes involved in resistance
- Single-step: pathogen mutates to a resistant form which is selected for by additional sprays
  - likely when fungicide acts on a single target or when a single gene mutation confers resistance



Scab severity (lesions/leaf) on inoculated trees in the greenhouse

Treatment	*Sensitive isolate*	*Resistant isolate*
Fenarimol	0	26
Myclobutanil	0	14
Untreated	59	53

Koller et al., 1997 Phytopathology

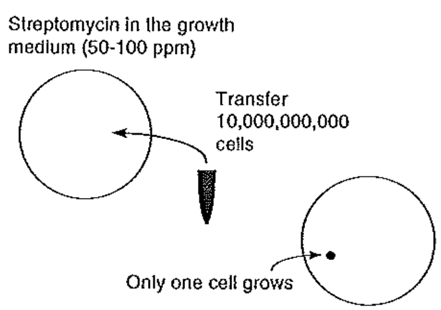
Apple Fungicide Resistance Risk

High risk	Moderate risk	Low risk
benomyl (Benlate) thiophanate-methyl (Topsin-M)	Fosetyl-Al (Alliete)	mancozeb, maneb (Manzate, Dithane, Penncozeb)
metalaxyl (Ridomil)	fenarimol (Rubigan)	Sulfur
dodine (Syllit, Cyprex)	myclobutanil (Nova)	captan
streptomycin (Agristrep, Agrimycin)	triflumazole (Procure)	ferbam, thiram, ziram
		copper compounds

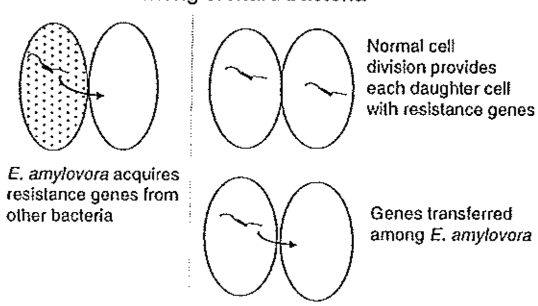
Streptomycin

- How it works
  - binds to ribosomes in *E. amylovora* thereby disrupting protein synthesis
- How it's overcome (resistance mechanisms)
  - *E. amylovora* produces enzymes that alter streptomycin
  - ribosomal proteins in *E. amylovora* are altered (mutated) and not bound by streptomycin

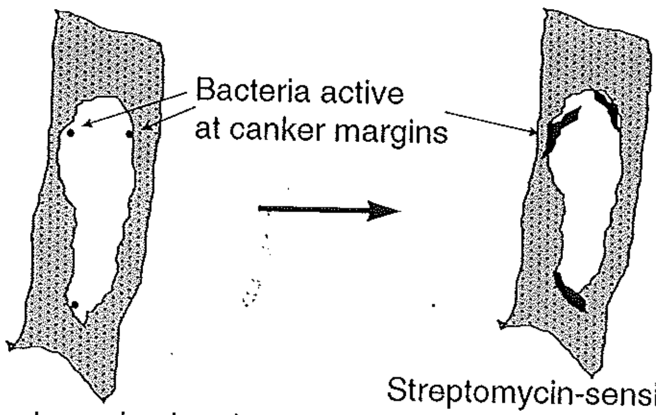
Gene for critical ribosomal protein mutates at a frequency of about 1 in 10 billion cells



E. amylovora produces enzymes that alter streptomycin; genes for the enzymes are transferred among orchard bacteria



Selection for streptomycin resistant *E. amylovora*



Streptomycin aimed at blossoms lands on oozing cankers

Streptomycin-sensitive strains killed; streptomycin-resistant strains flourish

Exposure to Streptomycin: Human Health Risks

- Antibiotic resistance a *huge* problem in hospitals and vet clinics
- Exposure to streptomycin will increase streptomycin resistance among your resident bacteria
- Streptomycin use minimal in medicine, but related compounds still used
- Antibiotic resistance genes tend to accumulate on mobile DNA
- Selection for streptomycin-resistant bacteria will likely select for resistance to other antibiotics
- Resistance genes readily transferred from your resident bacteria to pathogenic bacteria

Who uses antibiotics in the U.S.?

- Major animals (poultry, cattle, pigs, horses, dogs, cats)
  - > 30 million lbs/year
- Minor animals (lamb, sheep, goats, fish, mink, misc. pets)
  - < 0.5 million lbs/year
- Plant protection (tree fruit, vegetables, tobacco)
  - < 0.1 million lbs/year

Factors that increase the risk of development of practical resistance

Pathogen

- population dynamics--pathogens with shorter generation times and secondary infection cycles (*e.g.*, scab and fire blight pathogens at greater risk than rust fungi)
- gene exchange--sexual reproduction allows more mixing of genes, variation; most important apple fungal pathogens have sexual reproduction; bacteria capable of gene exchange
- worst case scenario is a sexually-reproducing pathogen with several secondary cycles

Factors that increase the risk of development of practical resistance

Pesticide

- mode of action--single-site, single gene targeted; a single mutation could lead to a resistant strain
- high efficacy--selection for resistant strains is rapid if product is highly effective
- frequent use and persistence--selection occurs over a longer period
- application to sporulating tissues--high populations undergo selection

Delaying the Onset of Resistance*

- minimize number of applications
- alternate fungicides with different modes of action
- mix high-risk fungicides (*e.g.*, SIs) with broad-spectrum fungicide (*e.g.*, captan or EBDCs)
- avoid applying fungicide/bactericide to high populations of pathogens (*e.g.*, sporulating scab lesions, oozing fire blight infections)

*General recommendations; specifics vary from case to case; experimental data for only a few cases!

Failure to control disease does not always mean fungicide resistance!

- Poor spray coverage
- Too low a rate used
- Poorly timed application
- Deteriorated or inappropriate product
- Cultural and edaphic factors
- Extremely high disease pressure
- Misidentified pathogen/problem