



Some Principles of Fungicide Resistance¹

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SECTION 1

THE BASICS OF RESISTANCE DEVELOPMENT

Fungicides are important tools in modern crop production. Unfortunately, one of the risks of using these products is that fungi sometimes develop resistance to them. Resistance development is a concern because the products may become less effective—or even useless—for controlling resistant pathogens and pests. This is a concern for all pesticides, including fungicides, insecticides, and herbicides. This fact sheet is intended to help pesticide applicators better understand this process.

The basic process of resistance development is illustrated in FIGURES 1 to 3, as follows (ref. 2)²:

- **FIGURE 1:** Resistance can only develop in spore populations where there is the genetic potential to resist the disease (represented by the filled circles in the figures). Normally, resistant spores occur at extremely low numbers: one in a million to one in a billion. But that is all it takes to start the process.
- **FIGURE 2:** When a fungicide spray is applied,

many of the fungal spores are killed. This is the reason for using a fungicide, of course. However, resistant spores can survive the treatment. Note that some of the sensitive spores also survived, because they “escaped” the fungicide treatment. This means that they were lucky enough to be in a microsite that was not treated with fungicide. (This can result from incomplete spray coverage, for example.)

- **FIGURE 3:** If environmental conditions favor continued disease activity, the surviving spores grow and produce a new crop of spores. Note that this new crop of spores has a higher percentage of resistant spores, because the resistant spores preferentially survived the fungicide treatment (FIGURES 1 to 2).

The development of resistance is a form of evolution, and it happens if two conditions are in place:

1. **Genetic variability:** The fungus has spores with the genes necessary to resist the toxin.
2. **Selection:** The toxin is used repeatedly.

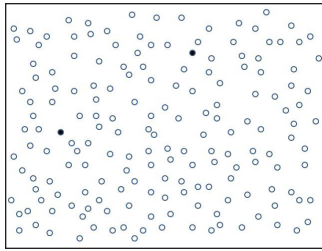


FIGURE 1. POPULATION OF SPORES BEFORE FUNGICIDE USE. MOST SPORES ARE SENSITIVE (OPEN CIRCLES), BUT SOMETIMES A VERY LOW NUMBER ARE GENETICALLY RESISTANT TO THE FUNGICIDE (FILLED CIRCLES).

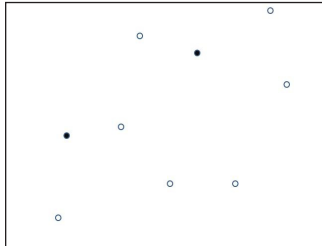


FIGURE 2. AFTER A FUNGICIDE APPLICATION, THE NUMBER OF SURVIVING SPORES IS GREATLY REDUCED. NOTE THAT THE RESISTANT SPORES SURVIVED THE TREATMENT. ALSO, SOME SENSITIVE SPORES (OPEN CIRCLES) ESCAPED THE TREATMENT.

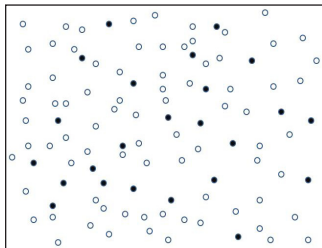


FIGURE 3. IF ENVIRONMENTAL CONDITIONS FAVOR A NEW CYCLE OF DISEASE ACTIVITY, THE NEXT GENERATION OF SPORES WILL HAVE A HIGHER PERCENTAGE OF RESISTANT SPORES. CONTINUED USE OF THE FUNGICIDE SELECTS FOR THESE RESISTANT SPORES.

The first of these conditions—the genetic potential—is out of human control (for the most part). The mutant either exists in the field or does not. The second condition—selection—is what happens when we apply the at-risk fungicide.³ Our use of the fungicide selects for those spores that can survive the presence of the toxin. That condition is clearly under human control. It is a natural outcome of the use of at-risk fungicides.

SECTION 2 INCREASED CROP DISEASE PRESSURE INCREASES RISK OF RESISTANCE

The subtitle summarizes the present section perfectly: higher disease pressure means higher risk of fungicide resistance (ref. 2). FIGURES 4 to 5 help in understanding why this is so. Field 1 (represented by FIGURE 4) has approximately twice the number of spores as Field 2 (FIGURE 5). Clearly, Field 1 has higher disease pressure than Field 2. You can also see that Field 1 has two resistant spores, rather than one.

If you count them up, you will find that the percentage of spores with resistance is slightly over 1% in both fields. That is to say, the mutation rate⁴

is the same in both fields, which is what we expect to find in nature. However, because of the higher disease pressure, Field 1 has approximately twice the overall spore population as Field 2. Thus, no matter what the mutation rate is, twice as many resistant spores will show up in Field 1 than in Field 2, because the overall spore population is twice as high.

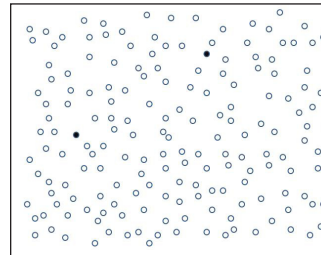


FIGURE 4. THE INITIAL STEP IN FUNGICIDE RESISTANCE DEVELOPMENT: OCCURRENCE OF MUTANT SPORES WITH RESISTANCE TO THE FUNGICIDE (FILLED CIRCLES). NOTE THAT THERE ARE TWO RESISTANT SPORES IN THIS IMAGINARY CROP FIELD.

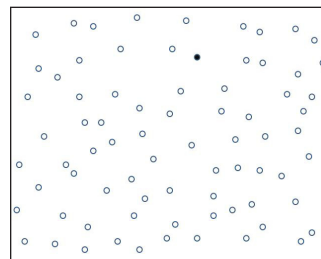


FIGURE 5. IMAGINE THAT THIS A SECOND CROP FIELD, WHERE THE POPULATION OF INFECTIOUS SPORES IS ABOUT HALF THAT OF FIGURE 1. ONLY ONE MUTANT SPORE WITH RESISTANCE HAS OCCURRED, INSTEAD OF THE TWO MUTANTS THAT EMERGED IN FIELD 1. SEE TEXT FOR EXPLANATION.

So does this really matter? After all, resistant spores emerged in both fields. The answer is, “Yes, it matters,” because resistance development is a matter of risk. Not all mutant spores that show up in a field will go on to cause disease. Some fall to the ground and never have a chance to infect a plant. Others may land on a plant but not be exposed to enough wetness to infect. Still others may infect but fall victim to plant biochemical defenses. So the higher number of resistant spores in Field 1 does definitely represent a higher risk for the producer, especially when one considers that billions of fungal spores can easily present in an acre of crop.

So, what does this mean for a producer? It means that, the more we depend on at-risk fungicides for disease control, the more pressure we are putting on the fungus to develop fungicide resistance (ref. 2). If it is possible to use others practices to reduce disease pressure, we reduce the overall risk of resistance. Anything that reduces disease pressure reduces the size of the spore population. And as FIGURES 4 to 5 show, reducing the spore population reduces the chance that a resistant mutant will occur in our fields.

This guideline applies to **all** practices that contribute to disease control: sanitation, crop rotation, varieties with partial resistance, proper fertility, and irrigation practices, etc. Anything we do to reduce disease pressure, reduces the risk. Thus, the best way to protect the utility of fungicides is by not over-relying on them.

SECTION 3

FACTORS THAT ENHANCE RISK

In the previous sections, I covered how higher disease pressure can result in higher risk of fungicide resistance. Higher disease pressure can come at you from several directions, including (ref. 2):

- Disease-favorable weather conditions
- Agronomic management and
- Characteristics of fungal pathogens themselves.

Disease-Favorable Weather

Many fungal diseases are favored by moisture. In contrast, some diseases are more aggressive under drier conditions. Whatever the weather conditions that favor a particular disease, those conditions also increase the risk of fungicide resistance. See FIGURES 4 to 5 for a reminder of how increased fungal activity results in increased risk of fungicide resistance.

Agronomic Management

Virtually every agronomic practice potentially can have an impact on development of one disease or another. Common agronomic factors that affect disease development include: site selection, previous crop, variety selection, planting date, tillage program, fertility, irrigation practices, proper field drainage, and plant spacing. Other factors can include seeding depth, harvest practices, seed treatment, compaction management, etc. So, anything that increases disease pressure increases the risk of fungicide resistance.

Characteristics of the Fungus

Some fungi pose a greater risk than others for the development of resistance. Here are some examples of pathogen characteristics that can influence resistance buildup:

- Some fungi, such as rusts, powdery mildews, downy mildews, and leaf spots and blights, produce spores in multiple cycles during the growing season. These are called polycyclic

(“many cycles”). Others, like *Fusarium* head blight of wheat and the many smut diseases, only have one infection cycle per season (monocyclic). Polycyclic pathogens are more likely to develop resistance to a particular fungicide because they build up (reproduce) more rapidly than monocyclic pathogens. This is because it may produce a new generation of spores as quickly as every week or two.

- Fungicide resistance in airborne fungi poses a greater threat than in soilborne fungi. The reason is that fungal spores that disperse with air movement (FIGURE 6) can sometimes move very long distances: from field to field, across the county, or even among states. A fungicide-resistant fungal colony that develops in a soilborne fungus tends to move around much more slowly. It may only move a few feet per year, as it is commonly moved around by implements that work the soil. Of course, soilborne spores may move further, maybe from one farm to the next on tractors and on fertilizer spreaders. However, spores in the soil only move as far as the soil itself is moved. In contrast, airborne fungi can travel very long distances.

- Some fungi seem to have a strong genetic tendency to adapt quickly to fungicides. *Botrytis cinerea*, the cause of gray mold in many different plants, is a notorious example. In this fungus, resistance to several fungicide groups⁵ (=FRAC Codes) is common in many locations throughout the US. Controlling gray mold with fungicides is a perennial challenge for many producers because of resistance problems. Some species of *Cercospora* fungi are also highly adaptable genetically. For example, resistance to QoI fungicides in the frogeye leaf spot pathogen of soybean occurs in numerous locations in Kentucky and the region. However, not all fungi are so genetically adaptable. For example, there is preliminary evidence that the *Cercospora* that causes gray leaf spot of corn may not adapt so easily to QoI fungicides. Plus, mutation rates may vary from one fungus to the next. Thus, each fungus has its own unique genetic capability to generate fungicide-resistant strains. Some are better at it than others.

In summary, numerous factors increase the risk of fungicide resistance. Some of these, like agronomic factors, are under our control. Others—like the weather and the genetic characteristics of the fungus—are outside the range of human

control. As was emphasized in Section 2, Avoiding over-dependence on fungicides continues to be a cornerstone for reducing the risk of fungicide resistance.

SECTION 4 FRAC CODES

The previous three sections showed how fungicide resistance develops, and why over-reliance on fungicides is risky. This section “switches gears” by considering the submicroscopic world of fungicide resistance.

Although they are too small to see with the naked eye, cells of fungi are amazingly complex. Fungicide manufacturers take advantage of this complexity by creating chemicals that poison the biochemical activity of one or more of molecules in fungal cells.

In order to understand how fungicides poison fungi, it is important to understand the normal metabolism of a healthy fungal cell. See FIGURE 6 for an example. In a healthy cell, enzymes turn a certain molecule (called “substrate”) into another molecule (called “product”). Without the simultaneous, furious activity of many thousands of enzymes, the cell would be unhealthy or dead.

A fungicide is simply a material that interferes with the normal function illustrated in FIGURE 6. One way it might interfere is illustrated in FIGURE 7: by binding the active site of the enzymes. Other fungicides interfere in other ways, but in all cases, they interfere with some molecule normally present in healthy fungal cells.

Thus, each fungicide has a particular biochemical way of poisoning the cell. Why is this important for users of fungicides? This is the key point: **if two fungicides poison the cell in precisely the same way, they are the same fungicide, from the point of view of the fungus.** It does not matter:

- Whether the active ingredients have different chemical structures
- Whether the active ingredients have different names
- Whether they are sold under different trade names
- Whether they are made by different manufacturers
- Whether they are formulated differently.

From the point of view of the fungus, if they poison the cell in the same way, they are the same fungicide.

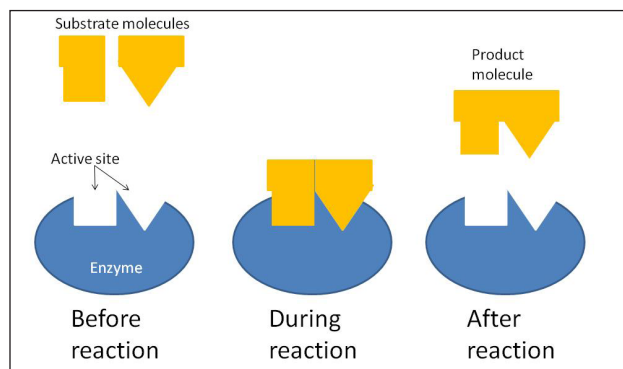


FIGURE 6. NORMAL MOLECULAR FUNCTION OF ENZYMES WITHIN A LIVING CELL.

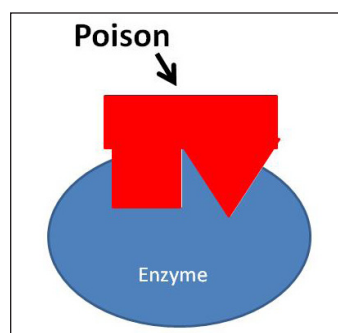


FIGURE 7. THE RED CHEMICAL IS A TOXIN THAT INTERFERES WITH THE NORMAL FUNCTIONING OF THE ENZYME PICTURED IN FIGURE 8. IT BINDS TO THE ACTIVE SITE OF THE ENZYME, PREVENTING ENZYMATIC ACTIVITY.

Here is a classic example. Benomyl was the first systemic fungicide. It was sold under various trade names, including Agrocit®, Benex®, Benlate®, Tersan 1991®, and others. Another fungicide that continues to be important today is thiophanate-methyl, which has been sold under a wide variety of trade names, including Cleary’s 3336®, Fungo®, Topsin M®, and many others.

Benomyl and thiophanate-methyl have different chemical structures.⁶ However, they both poison the fungal cell in exactly the same way. Therefore they are both considered to be benzimidazole fungicides, a name which communicates this shared mode of action (ref. 14 to 15). This means that, even if you alternate between fungicides within a fungicide group, the fungus “sees” them as the same fungicide. It also means that if resistance develops to one member of the group, usually resistance is present for all members of that group.

So which group a fungicide belongs to is really important for crop producers who want to steward fungicides wisely. Our producers have a lot “on

their plate,” so fortunately, you don’t have to learn any biochemistry, or even learn the names of fungicide groups. Several years ago, members of the global Fungicide Resistance Action Committee (FRAC) decided to represent fungicide groups using numbers. So the benzimidazole group (which includes benomyl and thiophanate-methyl) is represented as FRAC Code 1. Any fungicide with FRAC Code 1 poisons fungi in the same way. This also means that any product with any other FRAC Code poisons a different biochemical target, so any fungicides with a FRAC Code other than #1 truly are different from the members of FRAC Code 1.

FRAC Codes are well-publicized in *FRAC List of Fungicide Common Names-2012* (<http://www.frac.info/publication/anhang/2012%20FRAC%20List%20Fungicide%20Common%20Names.pdf>). FRAC Codes are present on the labels of most fungicidal products sold in the USA. See FIGURE 10 for an example. This makes it easy to alternate products having different biochemical modes of action—just look for products having a different FRAC Code.

More information on FRAC Codes is available at <http://www.frac.info/index.htm>.

SECTION 5 ECOLOGICAL FITNESS

Previous sections have presented basic concepts about how fungicide resistance develops in populations of infectious fungi. This section presents a more advanced concept, but one that is key to understanding fungicide resistance.

Ecologists use the term “fitness” to describe the overall ability of an organism to thrive and reproduce in a given environment. Many qualities contribute to ecological fitness. An obvious example is fungicide resistance. In a crop field where a fungicide is being used, if a spore has genetic resistance to that fungicide, it is more “fit” than a spore that doesn’t. Think of fungicide resistance like a coat of armor, protecting the fungus from the fungicide.

Let’s take the “armor” metaphor a little further. On the battlefield, having a coat of armor is beneficial. However, in daily life, having to wear a coat of armor would get tiresome very fast. Sometimes, this is how it is with fungicide resistance (ref. 17).

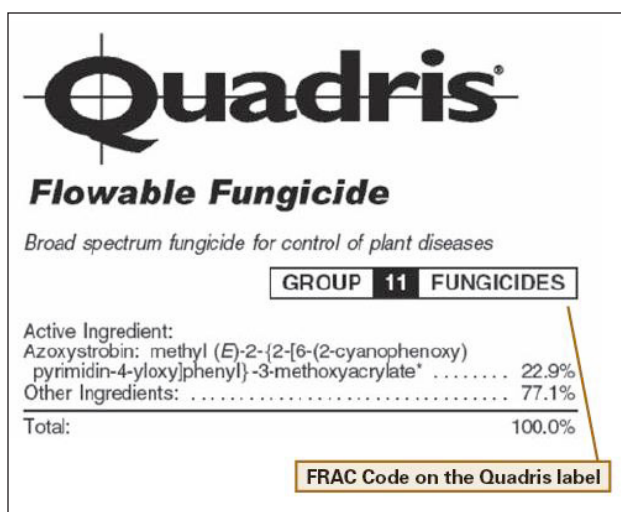


FIGURE 8. EXAMPLE OF A FRAC CODE ON A PRODUCT LABEL. IMAGE FROM: [HTTP://WWW.IPM.IASTATE.EDU/IPM/ICM/2006/6-12/FUNGICIDES.HTML](http://www.ipm.iastate.edu/ipm/icm/2006/6-12/FUNGICIDES.HTML)

The genetic resistance to fungicides helps protect the fungus for as long as the fungicide is being used. However, if the producer stops using the fungicide—or switches to a fungicide in another FRAC group—the genetic resistance to fungicides actually may be a burden, like an unnecessary coat of armor.

Here are some real-world examples:

- When resistance develops to strobilurin fungicides (azoxystrobin, trifloxystrobin, pyraclostrobin, and other FRAC Code 11 fungicides), it commonly confers very little to no “fitness cost” (ref. 1 and 8). It is as if the armor were weightless.
- Resistance to the many triazoles and related fungicides (FRAC Code 3) often results in a modest fitness cost, like wearing light-weight armor (ref. 7).
- Resistance to dicarboximides (FRAC Code 2) sometimes comes at a significant fitness cost to the fungus, as if the armor it was carrying was very heavy (ref. 6).

Although you may have never heard of ecological fitness, it really can work to a producer’s advantage, or disadvantage. Imagine that a fungicide-resistant spore occurs on your farm. Here is the range of possibilities:

- If you are lucky, that genetic resistance to fungicides may have a substantial fitness cost, (=heavy armor). If so, that fungal strain may “limp along” and cause disease on your farm as long as you continue to use fungicides in that FRAC group. However, if you stop using those

fungicides, the resistant strain can commonly begin to die out, and it may eventually return to very low levels on your farm. If there is a substantial fitness cost to fungicide resistance, you can commonly go back to using the fungicide, at least for awhile, until resistant strains build up again.

- If you are unlucky, the resistant strain will have absolutely no fitness cost, as if the coat of armor weighed nothing at all. What this usually means is, you are stuck with resistance indefinitely. Even if you stop using fungicides in that particular FRAC group, the resistant strain will persist for a long time.

So here are some practical questions that follow from this concept of ecological fitness:

1. **When fungicide resistance occurs, how fit are the resistant strains?** It is a key question, but it takes quite a bit of research to answer it for any given case of resistance. It is complicated by the fact that each new fungal strain, like people, is a unique individual and we will only know how well-adapted a strain is by watching how it does in nature. However, one thing is for sure: the occurrence of resistance does not necessarily pose a threat to a farming operation, depending on how fit the resistant strain is.
2. **How can we manipulate the ecological fitness of pesticide-resistant microbes?** Great question. But we can't. We have no influence on whether or not the fungal spores in a particular field carry a heavy coat of armor or a weightless one. We can only reduce the risk that the coat of armor will arise on its own (through mutation). You can only hope that, once it arises, the coat of armor is heavy. In ecological terms, we can only reduce the chance that a fit mutant will occur in our fields, but we cannot influence whether there is a fitness cost to that resistance.
3. **How can we reduce the chance of a fit mutant occurring in our fields?** The only way to reduce the risk of the fit mutant is by reducing disease activity on the farm. See Section 3 for more on this topic, but basically, it means using resistance varieties and cultural practices to reduce disease pressure. The lower the disease pressure, the lower the chance that a fit mutant will spontaneously occur.

In summary, fungicide resistance is like a coat of armor, protecting the fungus from the fungicide. In

some cases, the coat of armor is heavy, becoming a burden to the fungus in the absence of fungicide. This is referred to as a “fitness cost” to the fungicide resistance. If resistant strains in your field carry a fitness cost, sometimes it is possible to still use that fungicide selectively, because the resistant strain may die out during periods when that fungicide is not applied. In contrast, if there is no fitness cost to resistance, resistant strains will likely stick around for a long time.

SECTION 6

APPLICATION RATE & FUNGICIDE RESISTANCE

This section addresses several practical questions about application rate and the buildup of fungicide resistance. First, it is important to understand the two broad ways that fungicide resistance shows up in fields (ref. 4).

- In **quantitative resistance**,⁷ resistant spores are less sensitive than the wild-type⁸ spores, much like an undersized, partially effective shield (compare FIGURES 9 & 10). If quantitative resistance is present, you may notice you aren't getting the level of control you once did, but that you can still achieve decent control at high rates and short spray intervals. Common examples of this would be cases of resistance to DMI fungicides (=FRAC Code 3).
- In **qualitative resistance**, resistant spores are completely insensitive to normal field rates of the fungicide. It is as if a large shield prevented all fungicide from contacting the spores (FIGURE 10). To the producer, qualitative resistance looks like a complete loss of disease control. In fact, sometimes these resistant spores can actually cause more disease when the fungicide is applied, a phenomenon called “hormesis” (ref. 3). (See TABLE 1 for a real-world example of hormesis on a Kentucky golf course.)

TABLE 1. DISEASE ENHANCEMENT FOLLOWING APPLICATION OF A FRAC GROUP 11 FUNGICIDE ON PERENNIAL RYEGRASS INFECTED WITH A FUNGUS RESISTANT TO GROUP 11 FUNGICIDES.

Treatment (formulation & amt product/1000 sq ft)	% of plot affected ^a
Water	53 b
Thiophanate-methyl + chlorothalonil 90WDG, 8 oz	2 c
Azoxystrobin 50WG, 0.2 oz	66 a

^aWaller-Duncan statistical test, k=100, P<0.05

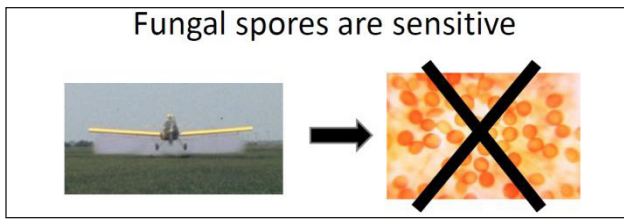


FIGURE 9. IN A POPULATION OF FUNGAL SPORES (ORANGE OBJECTS AT RIGHT), SENSITIVE SPORES ARE KILLED BY FUNGICIDE. (IMAGE OF SHIELD FROM OFFICE.MICROSPORT.COM)

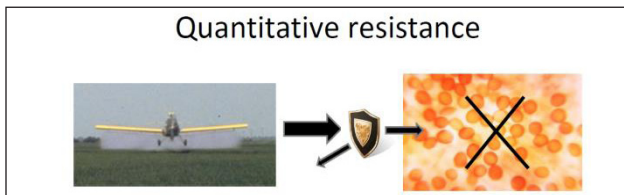


FIGURE 10. QUANTITATIVE RESISTANCE: SOME SPORES ARE PARTIALLY RESISTANT. IT IS AS IF A SMALL, PARTIALLY EFFECTIVE SHIELD PROTECTED SOME OF THE SPORES. SOME OF THEM WILL SURVIVE THE APPLICATION, THOUGH MANY WILL ALSO DIE. (IMAGE OF SHIELD FROM OFFICE.MICROSPORT.COM)

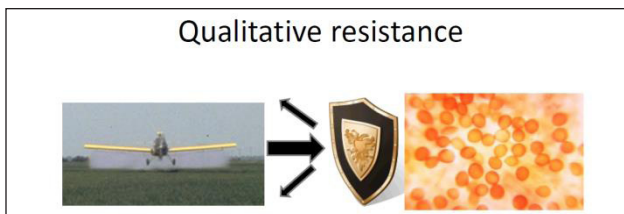


FIGURE 11. QUALITATIVE RESISTANCE: THE LARGE MAJORITY OF SURVIVING SPORES ARE COMPLETELY RESISTANT TO FUNGICIDE. IT IS AS IF A LARGE SHIELD PREVENTED FUNGICIDE FROM CONTACTING THE SPORES.

With that background, here are two common questions relating to application rate and fungicide resistance.

1. If disease pressure is very low, doesn't it make sense to apply a fungicide at a half-rate?

Yes, in a sense, it does. Reducing the application rate of a pesticide benefits one's pocketbook, the environment, field workers, and consumers. However, applying a fungicide at rates below those listed on the label may sometimes increase the risk of fungicide resistance (ref. 2, 9, 12). This is of special concern for cases of quantitative resistance, such as resistance to FRAC Code 3 fungicides.

Let's consider a fictional example, called "Blight-Be-Gone." Suppose Blight-Be-Gone is labeled to control a disease at 3-6 oz/acre. However, disease pressure is really low, so we may

logically decide that we probably don't need the fungicide. Nevertheless, suppose I decide to include it with a post-emergence herbicide spray, because I am already in the field, and it gives me peace of mind. Since disease pressure is so low, I might spray it at 1.5 oz/acre (which is half the minimum labeled rate). It seems like sensible plan. However, the risk in using the half-rate is that I am allowing the spores with partial resistance to build up over time. And the more opportunity they have to multiply, the greater the risk that even more resistant spores will emerge.

In cases of qualitative resistance,⁹ half-rates probably have little influence on the buildup of resistance. This is because spores that exhibit qualitative resistance thrive even at the highest labeled rate of the fungicide.

2. Can't I prevent fungicide resistance by using the high, labeled rate of a fungicide?

No, definitely not. If a fungus has the genetic potential to develop resistance to the product we are using, there is no way to **prevent** fungicide resistance, short of never using the at-risk fungicide. We can **only slow down** the buildup of resistance. See Section 1 for more on this.

So, can we slow down the development of resistance using a high, labeled rate? Yes and no. Generally, the answer is "yes" if the resistance is quantitative, "no" if it is qualitative.

If resistance in your field is **quantitative** (FIGURE 10), high doses can suppress many of the spores, even many of those that have partial resistance. In these cases, higher doses may indeed slow down the buildup of resistant populations.

If resistance in your field is **qualitative** (FIGURE 11), high doses essentially have no effect on the fungus. The mutant spores survive even the highest doses, so typically no disease control occurs following the application of even the highest labeled rate.

Thus, fungicide resistance can appear as a partial loss of disease control (quantitative resistance) or as a complete loss of disease control (qualitative resistance). In cases of quantitative resistance, using less than labeled rates is inadvisable, because it may accelerate the buildup of resistance. Use of labeled rates may slow down (though not prevent)

the development of quantitative resistance. In cases of qualitative resistance, even high rates don't suppress resistance buildup.

SECTION 7

ADAPTABILITY OF PLANT PATHOGENS

I have learned never to underestimate plant pathogens. One of the most important principles of fungicide resistance is that microorganisms, such as plant pathogens, are remarkably adaptable. From a practical standpoint, what this means is that we cannot assume that resistance will never develop to the fungicides we use for disease control. This is especially the case for the many new products with very specific modes of action.

Here is an example. In Section 5, I wrote about how fungicide resistance can be like a coat of armor, protecting the fungus when fungicide is sprayed, but weighing it down in the absence of fungicide. In such a case, we say that there is a "fitness cost" for resistance to that fungicide.

So if there is a heavy cost to resistance to a pesticide, what might microorganisms do? Sometimes they genetically fix that problem, in two steps:

- First, they develop the resistance to the toxin (the heavy armor);
- Then, over several generations, they evolve a progressively lighter and lighter armor, to the point where they still carry the protective armor, but it is no longer a burden.

This process, called "compensatory mutation", has been documented in bacteria (ref. 16), though to my knowledge, not in fungi. But honestly, I know of no reason why it shouldn't happen in fungi. After all, if the armor is heavy, basic evolutionary biology suggests that strains carrying lighter armor will provide a competitive advantage.

Another example: As discussed in Section 1, mutation (FIGURE 12) is a driving force behind the development of fungicide resistance. It turns out that mutation rates vary, depending on the environment. It is especially interesting that environmental stress can actually trigger higher mutation rates in some microorganisms. In other words, under a stressful environment, the genetic machinery of microorganisms may generate more variants than normal. This is highly adaptive, since some of the new variants might be "just right"

for the new environmental conditions. In fact, in bacteria, researchers have shown that antibiotics can substantially increase the rate of mutation (ref. 5). It is interesting to wonder whether this may happen in response to pesticide application in crops fields.

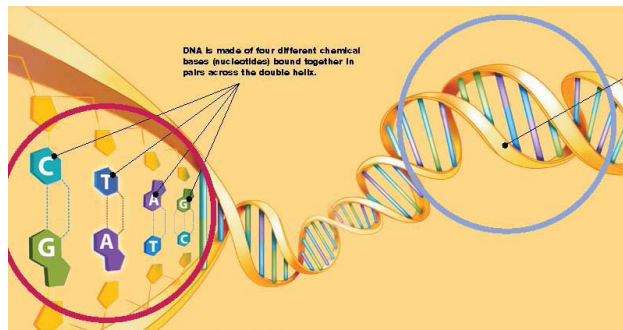


FIGURE 12. THE DOUBLE HELIX OF DNA, SHOWING A FEW LETTERS OF THE GENETIC CODE. A "MUTATION" CAN SIMPLY BE SOME CHANGE IN ONE OR MORE LETTERS OF THE GENETIC CODE OF AN ORGANISM, USUALLY RESULTING IN A CHANGE IN THE ORGANISM. SOURCE OF IMAGE IS THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE. (IMAGE IS IN THE PUBLIC DOMAIN).

Commercial fungicides are recent inventions, so how is it that fungi even have genes for resistance to these chemicals? The fact is that microorganisms typically use genes that have evolved for other purposes. For example, fungi sometimes resist a fungicide by simply pumping it out of the cell using a molecular "efflux pump." This means that the fungus has a molecular mechanism for pumping the fungicide out as it penetrates the cell. Efflux pumps have existed for millions of years, so they didn't evolve specifically to resist modern fungicides. They evolved to pump out naturally occurring toxins. However, they often work well against our modern pesticides. In fact, they usually work against a variety of unrelated toxins, so they are said to give the microorganism "multi-drug resistance." Thus, fungi may sometimes be "pre-adapted" to resist our modern fungicides because they possess an efflux pump. We simply select these resistant strains by applying fungicides.

Fungi and other microorganisms are remarkably adaptable. They have many biochemical ways to adapt to fungicides (ref. 11). Based on this principle, a conservative assumption is that fungi will find ways to adapt to the fungicides we use for disease control, especially against the many new products with very specific biochemical modes of action.

SECTION 8

FUNGICIDE DEPENDENCE PROMOTES RESISTANCE RISK

An important—and very logical—question is, “How can I prevent fungicide resistance?” It is an easy question to answer: Never use fungicides. That’s right—never using a fungicide is the only way to prevent resistance. If a fungal population has genes or mutations for resistance to the fungicide you are about to use, applying it creates selection pressure towards resistance. See Section 1 for a more detailed explanation of this.

While prevention of fungicide resistance is impractical, you can reduce the risk. The best way to do so is to avoid over-relying on fungicides. A metaphor for over-reliance on fungicides is depicted by a “fungicide umbrella.”

An alternative to over-reliance on fungicides is to use a variety of disease-control measures, appropriate to your particular production system (ref. 2, 13). Appropriate disease-control practices may include:

- Crop rotation
- Resistant varieties
- Management of irrigation and leaf surface moisture
- Fertility practices that impact disease
- Planting dates that reduce disease risk
- Sanitation in all its many forms
- Plant spacing and sowing practices that reduce disease
- Management of vectors and other pests
- Improved surface and subsurface drainage
- Raised beds
- Cover crops that reduce disease pressure
- Addition of organic matter to soil
- Mulching
- Pathogen-free seed

A diversified plant disease management program will slow down the development of fungicide resistance. Furthermore, even if resistance develops, it will not be as damaging, as compared to a farm where only fungicides are used for disease control. A diversified plant disease management program is buffered against severe damage from fungicide-resistant strains, since there are other tactics that are contributing to disease management.

Thus, the best way to protect the utility of fungicides is by not over-relying on them. Many crop-management practices can help reduce the reliance on fungicides.

SECTION 9

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ENDNOTES

¹ This publication is based on a series of articles written by the same author and first published in the Kentucky Pest News newsletter in 2013 (<http://www2.ca.uky.edu/agcollege/plantpathology/extension/kpnindex.htm>). The original content has been revised for this publication.

² References to scientific literature listed at the end of this article are provided for those who wish to know more about the scientific basis of key statements.

³ The phrase “at-risk fungicide” means that the fungicide has a moderate to high risk of resistance development.

⁴ For the record, a 1% mutation rate, like that illustrated here, is thousands of times higher than normal mutation rates. This high mutation rate is used here only for illustrative purposes.

⁵ Fungicide groups are identified by FRAC Codes; see Section 4.

⁶ For the “geeks” like me, you can see these chemical structures at <http://webbook.nist.gov/cgi/cbook.cgi?ID=C17804352&Mask=200> and at <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+6937>

⁷ “Quantitative resistance” is sometimes referred to as “reduced sensitivity.”

⁸ “Wild-type spores” refers to the spore population that predominates before the widespread use of a fungicide. These spores would be predominantly sensitive to the fungicide.

⁹ Examples of qualitative resistance would include many cases of resistance to fungicides with FRAC Codes 1 and 11.

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