Fungal Pathogen Pathology Timeline

300–286 BCE — Theophrastus, "Father of Botany," wrote and studied diseases of plants.

1665 CE — Robert Hooke, developed early microscopes and coined the biological term "cell;" illustrates rose rust disease, caused by the fungus *Phragmidium tuberculatum*.

1675 — Antonie van Leeuwenhoek invents compound microscope.

1729 — Pier Antonio Micheli observes fungal spores and conducts germination experiments.

1755 — Mathieu Tillet successfully treats wheat seeds infected with wheat bunt, caused by the fungus *Tilletia caries*.

1845–1849 — Potato late blight epidemic in Europe caused by the fungus-like organism, *Phytophthora infestans*; mass starvation results. Disease remains a very serious problem today.

1853 — Heinrich Anton de Bary, "Father of Plant Pathology," establishes that fungi are the cause, not the result, of plant diseases.

1868–1882 — Coffee rust epidemic (caused by the fungus *Hemileia vastatrix*) in Sri Lanka, destroys coffee industry there. Epidemic rages on to this day.

1878–1885 — Downy mildew of grape (caused by *Plasmopara viticola*) epidemic in Europe. Wine industry in France especially hard hit with losses of 50-80%.

1879 — Robert Koch establishes germ theory: diseases are caused by microorganisms.

1885 — Bordeaux mixture (copper sulfate and slaked lime) introduced by Pierre Marie Alexis Millardet to control downy mildew on grape in France, saving wine industry.

Did you know?

Wheat stem rust caused severe destruction to the wheat crop in North America in the early 1900s. But it's likely been a bane to humanity for millennia. Historians have determined that the Romans, as far back as the first century BCE, held a feast day on April 25 annually. The feast honored the god of wheat, Robigus. These "robigalias" were held to ensure a successful crop—and to ward off destruction that periodically befell the crop in the form of a red, "burning" of the plants' stems and leaves—the rust fungus. Indeed, an infected field when disturbed by wind will send billowing clouds of red rust spores into the air. Sacrifices of anything red in color were made to Robigus; red wine was spilled on altars, dogs and other animals with red coats were sacrificed.

Witches' broom of cacao … good fungus, bad fungus.

After the conquest of Mexico, the Spanish introduced cacao (*Theobroma cacao*) into Europe and, by the 17th century, fashionable chocolate houses were springing up everywhere. To meet the rapidly-growing demand for chocolate products, commercial cultivation took off for the first time in the native range of cacao in South America. Numerous fungal pests lay in wait.

The most important disease of cacao is witches' broom, so-called because of the grossly distorted shoots that manifest on infected plants. Cultivated plants are completely destroyed by this fungus; plantations wiped out. Twenty five years after the first scientific identification of the disease, the Swiss mycologist G. Stahel, working in Suriname, identified and named the pathogen as *Marasmius perniciosus*: a novel basidiomycete species producing small, crimson mushrooms on necrotic brooms. Almost three decades later, Rolf Singer transferred it to *Crinipellis* (today it is *Moniliophthora perniciosa*). This fungus is very unusual as few agarics (mushroom-producing fungi having a cap, gills, and stem) are serious economic pests of plants.

And cacao is one of the most economically-important crops of the world. Until the 1990s, Brazil produced the vast majority of the world's cacao. That came to a swift end in the 1990s with witches' broom. Since then, production has moved to Africa, primarily Ivory Coast and Ghana. But it's only a matter of time before

1904 Chestnut blight (caused by the fungus *Cryphonectria parasitica*) first noted at Bronx Zoo in New York. Ensuing epidemic wiped out all mature American chestnut trees in eastern North America and continues to be a big problem today.

1904 Wheat stem rust epidemic (caused by the fungus *Puccinia graminis*) wipes out hundreds of millions of bushels of wheat in North America. And returns again in 1916. Discovery of barberry plant as alternate host and eradication programs lead to control of the fungus.

1906 White pine blister rust (caused by the fungus *Cronartium ribicola*) first discovered in New York. Ensuing epidemic caused widespread damage to forests of five-needle pine across North America and continues to be a big problem today in some regions. Discovery of currant plant as alternate host and eradication programs lead to control of the fungus in some areas.

1910 Panama disease (caused by *Fusarium oxysporum* f. sp. *cubense*), reaches Western Hemisphere; by 1925 the epidemic affects every banana-growing country.

1930 Dutch elm disease (caused by the fungus *Ophiostoma ulmi*) first identified in Ohio. Ensuing epidemic wiped out nearly all mature American elm trees in eastern North America and continues to be a big problem today.

1989 Witches' broom of cacao (caused by the fungus *Crinipellis perniciosa*) first identified on farms in Brazil. By the end of the 1990s, more than 80% of the cacao industry of Brazil was destroyed.

1993 Chytridiomycosis of amphibians (caused by the chytrid fungi *Batrachochytrium dendrobatidis* and *B. salamandrivorans*) first identified in Australia. Ensuing pandemic has greatly diminished amphibian populations in much of the world and led to the extinction of many species. The pandemic remains a threat to amphibians.

1995 Sudden oak death (caused by the fungus-like organism *Phytophthora ramorum*) first identified; ongoing epidemic has been very destructive to oak trees in California and Oregon.

2007 White-nose syndrome of bats (caused by the fungus *Pseudogymnoascus destructans*) first detected in a cave near Albany, New York. Ensuing epidemic has caused widespread declines of bats across North America, and especially in the East. Some species have declined more than 90% in some regions.

2012–2013 Coffee rust epidemic in Americas, state of emergency declared in Central America. Coffee industry and entire economies of several countries imperiled.

witches' broom find its way there.

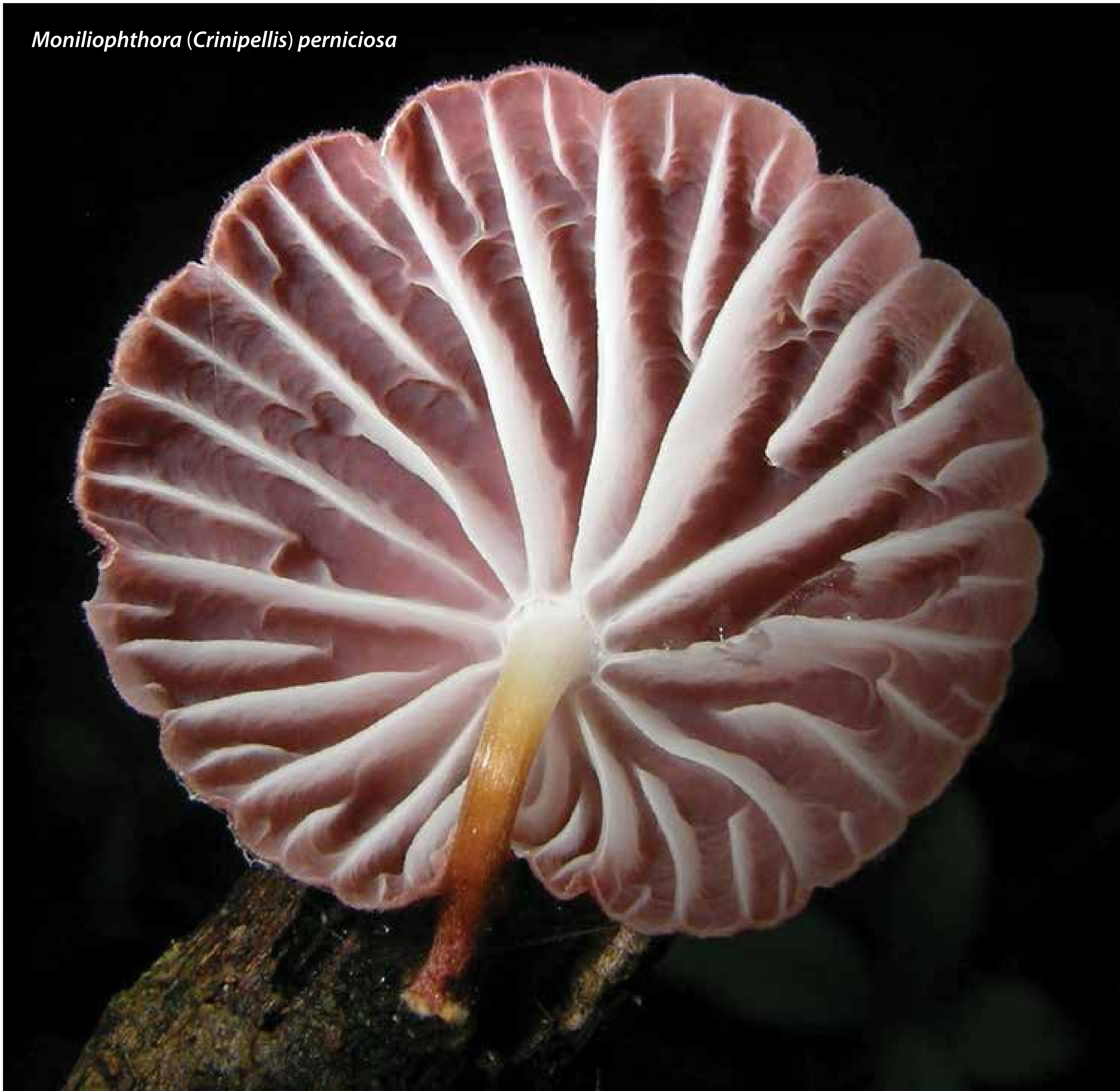
But a cure to witches' broom may be on the horizon … in the form of another fungus. Researchers have found that some endophytic and epiphytic fungi (that naturally are found in and on, respectively, cacao plants) may exclude the plant's fungal pests like witches' broom, keeping the host plant free from infestation. Another fungus, *Trichoderma stromaticum*, is being looked at. This *Trichoderma* is a mycoparasite, specializing in infecting and killing colonies of *Moniliophthora*. (Photos of *Moniliophthora* (*Crinipellis*) *perniciosa* courtesy Harry C. Evans, CAB International, Egham, Surrey, UK.)

Did you know?

Although not toxic, the teliospores of the common bunt fungus, also called stinking smut (*Tilletia tritici* and *T. laevis*), give wheat flour an unappealing gray color and foul odor of rotting fish. From the late 1800s to the 1930s this fungus was particularly devastating to the wheat crop—in Kansas alone 25–50% of the crop was lost—and supplies of flour were at times scarce. Similar losses were occurring in Europe. Even tainted flour could not be wasted. Historians have determined that this was the impetus for the invention of gingerbread. Adding molasses to the dough sweetened and masked the color and smell of the flour—along with this new spicy ingredient from India (ginger)—and resulted in a sensational new treat that is popular to this day.

Chytridiomycosis of amphibians … a mysterious pandemic unveiled.

For many years, herpetologists around the world had noticed amphibian populations were in decline but the evidence remained largely anecdotal. It was not until the end of the last century that a quantitative assessment confirmed the negative population trends. This pretty much coincided with the identification of the disease—chytridiomycosis—causing widespread amphibian mortality in Australia and Central America. Thus a fungal pathogen, a member of the phylum Chytridiomycota (primitive,



zoosporic fungi informally called chytrids), came to occupy center stage in the studies of amphibian demise. The causative agent of amphibian chytridiomycosis is *Batrachochytrium dendrobatidis* (*Bd*).

The lifecycle of *Bd* involves a motile, swimming spore that finds a host animal and sticks to its skin; hyphae called rhizoids then grow into the host's skin. In a matter of days, a zoosporangium forms and therein new zoospores develop that are eventually released. Zoospores swim about and further infect the same host; if they find another amphibian, a new infection begins. As with all infectious agents, infection can have varied outcomes depending on a number of genetic and environmental factors, doubtless including age and any underlying chronic disease of each frog involved. Comparative genomics between the parasite *Bd* and saprotrophic chytrid species has revealed some differences suggesting that certain secreted proteins might be virulence factors. Specifically, *Bd* encodes and produces a greater amounts of metalloproteases of the fungalysin family. The end result is that *Bd* has evolved into an effective pathogen.

This pathogen is responsible for what is perhaps the largest panzootic (the word for a pandemic involving an animal disease) in history. *Bd* has an extremely broad host range, infecting 50% of tested frog species (order Anura), 55% of salamander and newt species (clade Caudata), and 29% of caecilian species (Gymnophiona). And *Bd* is broadly distributed, having been found in 3,705 of 9,503 field sites tested (39%)

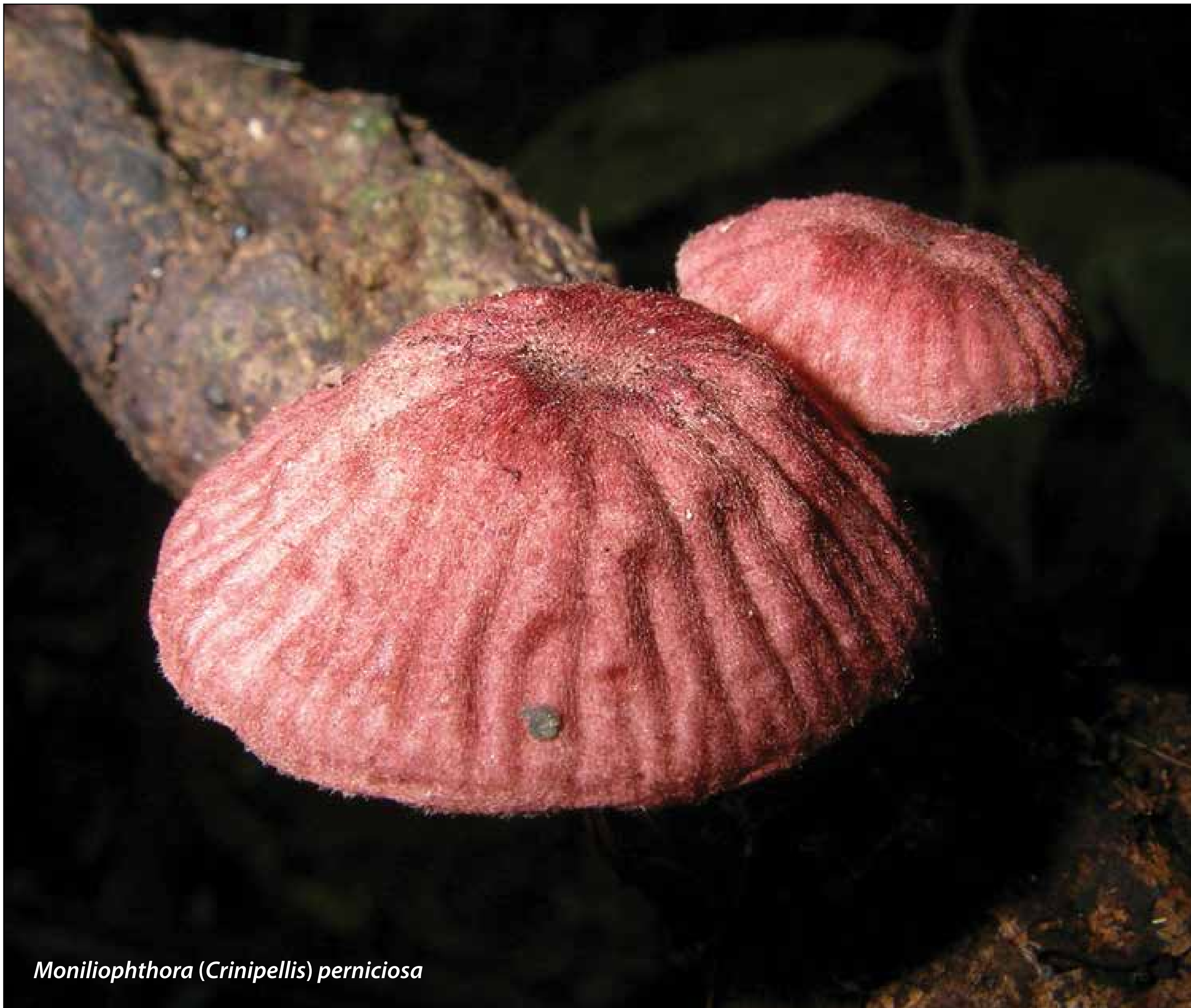
by scientists. The effects have been devastating: *Bd* has contributed to the decline of at least 501 species (6.5% of all amphibian species), leading to 90 presumed extinctions, and decreases in abundance exceeding 90% in another 124 species. This represents the greatest documented loss of biodiversity attributable to a pathogen and places *Bd* among the most destructive invasive species, globally.

Where did this pathogen come from? Initially, investigators proposed two competing arguments. On the one side was the "novel pathogen hypothesis" (NPH) which stated that chytridiomycosis emerged at various locations after it had been seeded by intercontinental trade routes into naive ecosystems. On the other side was the argument known as the "endemic pathogen hypothesis" (EPH), stating that *Bd* was a widespread endemic commensal of amphibians that became more virulent as a result of global environmental change. Through comparative genomics and other analyses, it now seems that *Bd* emerged in Asia. There, it appears to have been infecting amphibians for millions of years. As such there has been ample time for the evolution of stable host-pathogen dynamics. How did the pathogen become so widespread? All of the evidence points at the international amphibian trade that was greatly accelerated throughout the 20th century. Lending additional support to these conclusions, in 2010 a second chytrid species, *Batrachochytrium salamandrivorans* (*Bsal*) of Asian origin, caused the local extinction of fire salamanders in the Netherlands.

What does the future hold for amphibians? Research in multiple disciplines suggests there might be ways to mitigate the global effects of chytridiomycosis. A promising avenue is the recognition that interactions between commensal fungi and bacteria of the amphibian skin microbiota may limit the disease. There are some other signs of hope. First off, die-offs peaked in the 1980s, and of the 292 surviving species for which population trends are known, 60 (20%) have shown initial signs of recovery. However, recoveries generally represent small increases in abundance of individual populations, not complete recovery at the species level. Some recoveries may be underpinned by selection for increased host resistance, whereas management of concurrent threats may have facilitated other recoveries (a promising avenue for conservation interventions). As yet, the remaining 232 species have shown no signs of recovery. (Much of this article courtesy of Roberto Kolter, Professor Emeritus, Harvard Medical School, and the wonderful blog Small Things Considered, created and edited by Moselio Schaechter.)

Did you know?

The British are known for their love of tea. But before the late 1800s, the British were devout coffee drinkers. Historians attribute the switch from coffee to tea as a result of the coffee rust epidemic which wiped out the British Empire's source of java in Southeast Asia, which was then planted in tea plantations.



Moniliophthora (*Crinipellis*) *perniciosa*

Chestnut trees . . . back from the brink?

American chestnuts (*Castanea dentata*) once dominated forests throughout eastern North America. That all changed with the introduction of a fungal pathogen in the early 1900s. Chestnut blight caused by *Cryphonectria parasitica* —an accidental import from Asia—wiped out nearly all mature eastern chestnut trees by midcentury. But optimism is growing that the American chestnut tree may make a comeback. There has been success in breeding varieties of chestnut with resistance to the pathogen (more on this below). But research as well as keen observations have led to some very interesting ways to save trees infected with this destructive pathogen.

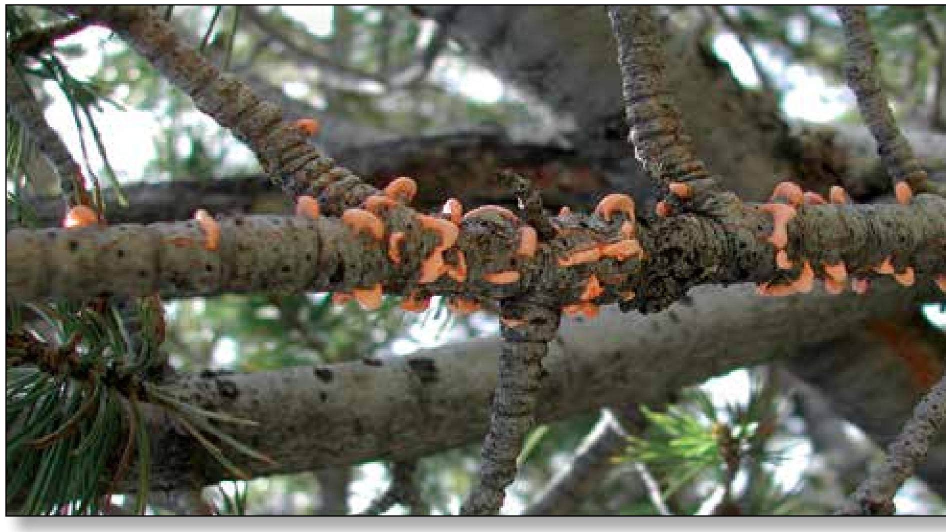
Cryphonectria parasitica kills through the release of a toxin that girdles trees and kills everything above the infection site, although roots sometimes survive and send up new shoots. Some years ago Wayne Weidlich, a scientist at Michigan State University and Director of the American Chestnut Foundation, noted that while the chestnut blight fungus normally does not cause cankers to form on roots, it will grow on chestnut roots if they are exposed to air. He suspected something in the soil was inhibiting the pathogen and wondered if packing soil over trunk cankers might have some curative effect. Amazingly, the soil compress worked! Something in soil effectively eliminates the blight fungus and allows the tree to heal, and for the past several decades this has been a widely used remedy. (Simply covering a canker with airtight wrapping or covering with tar etc., does not work.) Research later has shown the inhibitory substance in soil around the infected chestnut trees is another fungus, *Trichoderma viride*, which is a mycoparasite of the chestnut blight fungus.

This soil compress method is inconvenient to use on very large trees. It will not protect your tree from new infections, nor save a tree that is already girdled, but it can cure individual cankers which might otherwise kill a tree in the early stages of the disease. The basics of the soil compress method are simple: you must keep the blight canker (and the entire trunk all around it at least a foot above and below any signs of blight) covered with moist soil for at least a couple of months. This is usually accomplished by making a black plastic sleeve to fit around the trunk, securing it with weatherproof tape, and filling it at least 2 inches thick with moist soil. You can add water at the top occasionally if it dries out.

Another form of biocontrol of chestnut blight has been discovered: hypovirulence. Hypovirulence is a condition in which the blight fungus itself gets sick. A virus has been found to be the cause of hypovirulence; once infected, the virulent fungus becomes very slow growing and causes far less harm to infected trees. And the virus can be spread from one fungus to another. At the time of discovery, hypovirulence was touted as an easy method to use for saving chestnut trees, and although it has led to some success, it isn't a magic bullet. Firstly, virulent chestnut blight fungal strains spread very quickly in the environment. Weakened hypovirulent strains (infected with the virus) spread much more slowly. And it has been shown that many strains of the chestnut blight fungus have evolved resistance to the hypovirulence virus.

If you have infected chestnut trees at home, chemical fungicides can help. Chemicals would be useless in a forest situation, but they can be used if there are one or two prized trees around your home that you would like to save. You may have seen elm trees being injected with chemicals to keep them from dying of Dutch elm disease—the same method can work on American chestnuts. Treating chestnut blight is pretty serious business and requires injections of systemic fungicides; it is recommended that a professional tree service be hired to handle the job. The systemic fungicides are powerful chemicals and a license may be required to use them in your area. Trees protected chemically have to be re-treated every year, the treatments are expensive, and sometimes don't work longer than one or a few seasons.

And lastly, the preservation of American chestnut trees may be on the horizon thanks to better genes. After decades of searching, no natural resistance has been seen in native trees. There has been success in crossing resistant species of chestnut from other parts of the world, but of course those resistant trees can no longer be considered true American chestnuts (and there are other detractors such as inferior fruits, etc.). But now there is hope for a truly resistant American chestnut tree, thanks to geneticists. In 1990, tree geneticists William Powell and Charles Maynard working at the State University of New York have genetically engineered resistant trees. The scientists inserted into the tree's genome a wheat gene that codes for an enzyme called oxalate oxidase, or OxO. It breaks down the oxalic acid the pathogenic fungus releases, which is what kills the trees—basically taking the weapon away from the fungus. After many years of effort they finally had success and reported in 2014 that a variety of American chestnut called "Darling 58" both resisted blight infection and transmitted resistance to its offspring. Subsequent tests showed that it produces nuts indistinguishable from those of native trees, according to researchers. And other tests of pollen, flowers, and decaying leaves have shown no harm to bees, beneficial soil fungi, or tadpoles that hatch in pools on the forest floor. If the genetically-modified tree is approved by the USDA and FDA, the trees could become available for widespread planting by 2021.



White pine blister rust, courtesy A. Biggs.

Did you know?

Gray mold is caused by one of the first genera of fungi to be described (way back in 1729). The pathogen is *Botrytis cinerea*, and it's one of the most economically important pathogens of all sorts of fruits and vegetables. It is pernicious anywhere there is high humidity, like greenhouses. And your refrigerator (it's that gray fur coat you've seen on strawberries and other fruit). But when the conditions are just right and it attacks vineyards … magic can happen. "Noble rot." This is the source of Sauternes, which are some of the most highly prized—and priced—wines on the planet.