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The War Against Blue Mold

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Summary. An epidemic of blue mold of tobacco unexpectedly attacked crops in the United States and Canada in 1979, causing an estimated loss of almost a quarter billion dollars. The disease, caused by a fungus, apparently started in Cuba where half the crop was destroyed in 1979 and 90 percent in 1980. Control of blue mold is difficult and expensive. Resistant cultivars become susceptible within a few years. A therapeutic fungicide, metalaxyl, gives efficient control, but resistant strains of the fungus may soon appear. Blue mold is an international problem that will require the collaboration of scientists, governments, and industries for an adequate solution.

When an aggressive plant pathogen attacks an intensively cultivated crop in a suitable environment, great devastation often results. Such an event occurred in the tobacco-growing regions of the eastern United States and Canada in the summer of 1979 when a tobacco blue-mold epidemic struck simultaneously in several states where the weather had been unseasonably cool and wet. Conditions were ideal for extensive destruction of tobacco leaf tissue, systemic infection, and stunting of plants. In the 14 tobacco-producing states, only the plants in Wisconsin did not became infected by the end of the growing season.

Some farmers plowed their crops under. Combined losses in the United States and Canada were estimated to be in excess of $240 million (*1*). Severe losses also occurred in Cuba where yields of the cigar crop were reduced by about a third (*2*).

Early in 1980, blue mold struck Cuba again and destroyed 90 percent of the cigar crop, dealing Cuba's already ailing economy a major blow. The government had to lay off 26,000 workers and temporarily close the country's cigar factories (*2*). These losses place the blue-mold epidemics of 1979 and 1980 in the category of a catastrophic plant disease.

The Cuban tobacco crop failures of 1979 and 1980 may be one of the reasons Castro permitted the exodus of more than 100,000 Cuban refugees to the United States in 1980. This sequence of events brings to mind the devastation of the potato crops in Ireland by another fungus disease between 1845 and 1860. One million people died as a direct result of famine and 1.5 million Irish peasants fled their land (*3*). More recently, in the United States, the 1970 epidemic of southern corn leaf blight caused losses, estimated at $1 billion, that cut deeply into the agricultural economy of the South and the nation's corn belt (*4*).

Occurrence of Blue Mold

Blue-mold epidemics are not new. The causal agent is apparently endemic wherever native *Nicotiana* occurs, namely, in North and South America and Australia (*5*).

A downy mildew of cultivated tobacco was first reported from Australia in 1891 (*5*), although it probably had been there for 40 years or more. In succeeding years, it was reported from all tobacco-growing provinces of that country and became the most destructive of all tobacco diseases. Before 1962 and the use of fungicidal sprays, crop losses of up to 80 percent commonly occurred in some areas.

The first report of blue mold on cultivated tobacco in the United States came from Georgia in 1921. The disease did little damage and, oddly enough, disappeared until 1931 when it recurred in tobacco-producing states from Florida to Maryland. For the next three decades the disease posed an annual threat to tobacco transplant production in the United States.

In 1949, a blue-mold epidemic caused a serious shortage of transplants in North Carolina. In desperation, farmers purchased transplants wherever they could find them. Many unknowingly bought plants infected with another disease, black shank, caused by a destructive pathogen that lives in the soil and infected their fields. This is an example of how the spread of one disease accelerated the spread of another. Blue mold, however, was of minor importance in tobacco production in the United States and Canada from 1955 to 1970.

The appearance of blue mold in Georgia in 1921 as a disease of cultivated tobacco raises questions such as: Where did the disease come from? Why was it not seen for 10 years? Wolf (*6*) proposed that the original outbreaks of this downy mildew on tobacco in the Southeast were due to: (i) the opening through irrigation of the lower Rio Grande region of Texas after World War I for citrus and truck crops, which favored the spread of a wild tobacco, *Nicotiana repanda*, and, coincidentally, the growth of its blue-mold parasite and (ii) the increase in tobacco acreage after World War I, which enabled the fungus to blow from native tobacco in Texas to cultivated tobacco in Louisiana and then eastward to the principal tobacco-growing states along the East Coast.

Blue mold appeared in Cuba in 1957, probably carried by spores blown across the Caribbean from infected areas such as Florida, approximately 200 kilometers away. Considerable crop losses occurred in 1958, but then the disease disappeared from Cuba until its unexpected appearance in 1979.

Blue mold broke out across large areas

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of Europe in 1960 with disastrous results. The origin of this epidemic is unknown, but there is suspicion that it was started by blue-mold infected plants introduced from Australia in 1958 (*5*). The fungus spread across Europe in waves, moving from focal points in Holland and West Germany at the rate of 22 to 25 km a week. In West Germany, some fields were totally destroyed, and severe losses occurred in other countries (*7*). The disease has caused losses there every year since; the severity of the outbreak depends on the weather.

When blue mold appeared in tobacco seedbeds in Greece in 1961, the village priests urged the farmers to apply fungicides, and army flamethrowers were used to destroy the plants in badly infected beds. This is the only instance I know of where the clergy and the military joined forces to combat a plant disease.

From Europe the fungus spread across the Mediterranean to Sardinia, Algeria, and Tunisia, and then to Israel and Iran. In 1969, blue mold appeared in Iraq. Every year it is a threat to tobacco production in these countries.

In 1964 blue mold appeared in Mexico, apparently for the first time. Spores blowing south from the Rio Grande valley appear to be implicated. The disease caused considerable losses in some fields at that time, but it had not reappeared as of 1979. In nearby countries, however, it was a different story. Blue mold appeared in Jamaica in December 1979, and by March 1980, it showed up in Nicaragua, Honduras, and Guatemala, causing considerable damage and alarm.

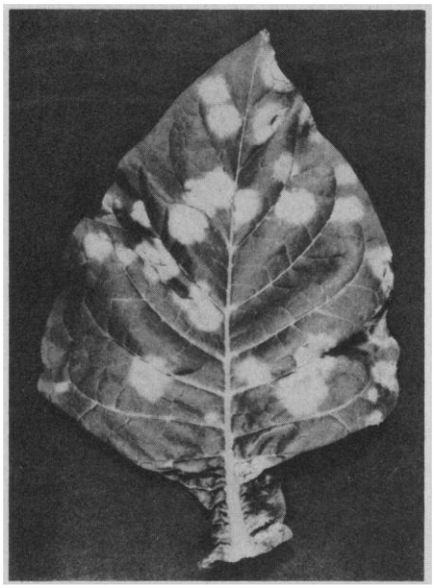


Fig. 1. Mature tobacco leaf, about 60 centimeters long, with blue-mold lesions. [Courtesy of North Carolina State University, Raleigh]

Host Range and Symptomatology

The main hosts of the blue-mold fungus are restricted to the genus *Nicotiana*, of which there are about 65 recognized species. Most species, including *Nicotiana tabacum*, cultivated tobacco, are highly susceptible. Other species range from susceptible to highly resistant to immune. Occasionally the fungus occurs on peppers, tomatoes, eggplants, and certain weeds, but these are not preferred hosts (*5*).

The fungus grows in the living tissues of the leaves and produces a gray or bluish downy mold on the lower surface, hence the name blue mold. Usually diseased plants appear first in only a few scattered areas of the seedbed. Then in a week or so, after sufficient inoculum has been produced, a general outbreak occurs and the entire seedbed becomes diseased almost overnight. Tobacco seedlings less than a month old may be killed outright. The dead plants become dry and shriveled and lie flat on the ground. In damp weather, a characteristic foul odor associated with rapidly decaying vegetable matter develops.

On older plants in the field, groups of yellow spots appear on the leaves (Fig. 1) and often coalesce to form light brown, dead areas. Large portions of the leaves disintegrate and entire leaves become unusable. The fungus can destroy all leaves at any growth stage. Systemic infection, with overall stunting of the plant, frequently occurs (Fig. 2). Lesions may occur on buds, flowers, and developing seedpods. Plants commonly exhibit wilt symptoms with narrow, stunted, mottled leaves; and vascular discoloration occurs in the stems. If the bark is scraped away, the lesions are visible as brown streaks. If these occur near the base of weakened stems, the plants break and serious losses result.

Sometimes blue mold may damage the crop in the curing barn. Leaves that appeared healthy and free of blue mold when harvested apparently become infected shortly before harvest, and the fungus continues to grow and infect more tissues before the leaf dries out and dies.

Causal Agent

The most commonly used name for the blue-mold fungus is *Peronospora tabacina* Adam, but the fungus is extremely variable and quickly forms new strains. Therefore, it is appropriate to include all strains under the name *Peronospora hyoscyami* de Bary, which has priority (*5*).

Blue mold is caused by a fungus belonging to the Phycomycetes, the class of fungi that includes the downy mildews. The fungus is an obligate parasite, that is, it must have a living host (tobacco) on which to grow and complete its life cycle.

The blue-mold fungus produces myriads of tiny, colorless, lemon-shaped spores (conidia), which are about 25 by 15 micrometers. They grow on tree-like stalks (conidiophores) (Fig. 3) that emerge from the stomata (breathing pores) on the underside of the leaves. The conidia are fragile and short-lived. They are sensitive to ultraviolet light, and direct exposure to sunlight kills most conidia within an hour. The fungus produces as many as 1 million conidia per square centimeter of infected leaf surface. These conidia float like fragile balloons and are easily spread long distances by the wind.

In addition to the airborne conidia, the blue-mold fungus also produces sexual spores or oospores in the mesophyll of dead parts of infected leaves (Fig. 4) and other parts of the plants. Mature oospores are thick-walled, spherical, reddish-brown to gold, and range from 20 to 60 μm in diameter. Little is known concerning the methods of and conditions necessary for oospore germination. Whether the fungus is heterothallic (cross-fertile) or homothallic (self-fertile) is unknown. However, new strains of the fungus constantly appear. They may arise from crossbreeding, mutations, or otherwise unexplained methods.

Host-Parasite Relations

Conidia of the blue-mold fungus form at night and are mature at dawn. If the spores, blown by the wind, alight on a wet tobacco leaf, they may germinate within 2 hours, penetrate, and begin their silent ravage of the leaf. The spores will germinate at temperatures between 2° and 30°C, but the optimum range is 15° to 25°C. Mature spores that are less than a day old have a higher rate of germination than older spores. However, some conidia remain viable for weeks.

The conidia germinate by forming an infection peg, which penetrates the leaf. From this peg, threadlike hyphae grow between the cells until they come in contact with mesophyll tissue where they form special feeding branches (haustoria) inside the cells. From these cells the fungus absorbs the food necessary for its own growth. Often the fungus

grows from the leaf into the stem, particularly in small plants. When the pathogen becomes established in the cambium region of the stem at an early stage of plant growth, xylem development is inhibited. Such infected plants, when full grown, are brittle and snap off easily.

An outstanding feature of stem infection is its destructiveness over a wide temperature range and its spread under conditions usually considered unfavorable for disease development. Pathogen development in the stem, however, is also favored by high humidities. It is arrested by subjecting the plants to a daily temperature between 24° and 40°C when humidity is not higher than 70 percent (desert conditions).

High temperature combined with high humidity permit growth of the pathogen and help explain how the fungus can maintain itself in living plants during prolonged periods of hot, humid weather.

A few days after infection—the length of time depends on temperature, moisture, fungus strain, and host physiology—masses of conidiophores appear on the under surface of the leaves. In general the first symptoms (yellow spots) appear 4 to 8 days after the infection peg penetrates the leaves. Conidiophores and conidia appear within 6 to 10 days after infection. Leaf growth almost stops in diseased plants by the third day after infection, whereas growth in healthy plants increases about 10 percent per day.

Spread of the Pathogen

Wind. Wind is the principal agent that spreads conidia of the blue-mold fungus. On windy days, especially after nights of abundant spore production, conidia are blown locally from one infected plant to another and over long distances.

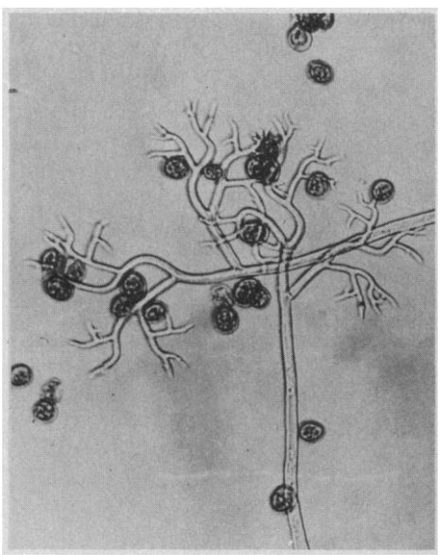
Spore-trapping studies (*8*) with fungi indicate that spores may be wafted up 2 km or more and blown hundreds of kilometers before they descend with the rain. Evidence of these "spore showers" appears when the disease occurs in several adjacent counties or states at about the same time. The 1960 epidemic in Europe illustrates the rapidity and efficiency by which wind-blown conidia spread the fungus over large land masses.

The 1979 epidemic in the eastern United States and Canada may have originated in Cuba. Typically the Cuban crop is harvested between January and March, and it may be June before all the old plants are plowed under or otherwise destroyed—if, indeed, they are destroyed. By June U.S. farmers are growing seedlings, transplanting, and starting the new crop in the fields. A massive supply of inoculum carried north by prevailing winds from Cuba or other Caribbean areas on successive weather fronts, when other weather conditions are suitable, helps explain the almost simultaneous outbreaks in Florida, Georgia, and South Carolina in 1979. Figure 5 shows the wind direction near the top of the planetary boundary layer at 1800 Greenwich mean time on 30 May 1979. Synoptic weather conditions during the last few days of May and the first few days of June were ideal for transporting conidia to the north.

Wind dissemination may also explain the 1980 outbreaks in various countries in Central America. Considering the swirling winds and weather fronts that periodically occur in the Caribbean area, it appears likely that blue mold, spread by the invisible dust of spores carried on the wind, will appear in more tobacco-producing countries of Central and South America that border on the Caribbean Sea.

Transplants and other agents. Anoth-

Fig. 2. Burley tobacco plants in western North Carolina severely stunted by blue mold in 1979. This crop was a complete loss. [Courtesy of North Carolina State University]



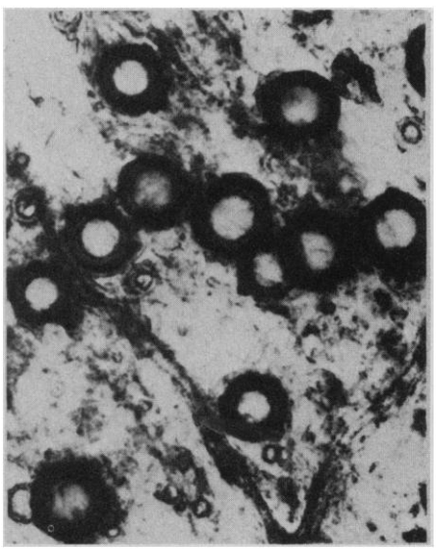
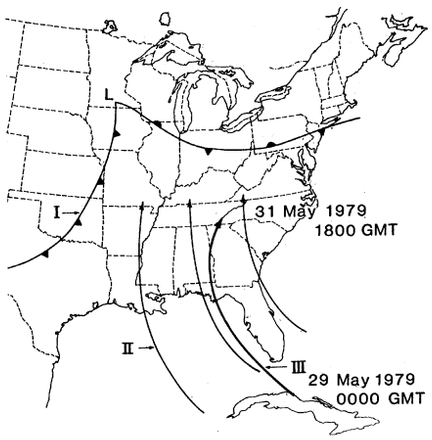


Fig. 3 (left). Fragile asexual spores (about 20 μm in diameter) of *Peronospora hyoscyami* de Bary are produced on tree-like stalks (conidiophores) that emerge from the underside of the tobacco leaf. [Courtesy of North Carolina State University] Fig. 4 (right). Mature oospores (about 40 μm in diameter) of *Peronospora hyoscyami* de Bary in dead leaf tissue. [Courtesy of Biologische Bundesanstalt für Land-und Forstwirtschaft, Berlin]



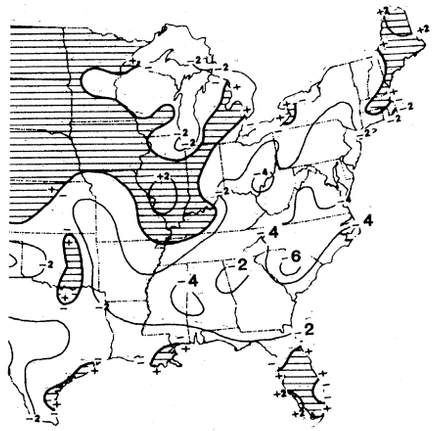


Fig. 5 (left). Weather map of eastern United States. (I) Position of surface front at 1800 Greenwich mean time (GMT) on 30 May 1979. (II) Wind direction (thin arrows) at the top of the planetary layer (about 1 km) at 1800 GMT, 30 May 1979. (III) A trajectory for spore movement at the top of the planetary boundary layer. Clouds of spores leaving the vicinity of Cuba on 29 May 1979 would reach North Carolina about 3 days later. [Courtesy of North Carolina State University.] Fig. 6 (right). Departures from normal temperatures (30-year mean) of average surface air temperature (degrees F) for June 1979 (*23*). [Courtesy of National Oceanic and Atmospheric Administration]

er common way to spread the blue-mold fungus is by infected transplants. Apparently healthy transplants may already be infected, and farmers who periodically buy transplants, sometimes from distant growers, run the risk of buying diseased plants. Conidia may also be disseminated by workers, animals, cars, and airplanes. Ordinarily these agents would be of minor importance, but considering the vast amount of inoculum produced and the rapidity of modern transportation, such minor methods could easily be responsible for outbreaks hundreds of kilometers from where the inoculum was produced.

Overwintering plants. In many of the warmer regions of the world, tobacco plants sometimes remain alive over the winter and produce a new crop of axillary shoots (suckers) in the spring. *Peronospora hyoscyami* is often maintained as systemic mycelium in such volunteer plants. Under suitable conditions, the fungus grows from the infected stems into the new shoots with subsequent sporulation on the leaves and thus starts another blue-mold outbreak. The fungus overwinters in the southern United States and Cuba in this way. Freezing temperatures that kill only the portion of the plant above ground will not eliminate the fungus since it can remain alive in the roots and underground dormant buds. In regions where entire tobacco plants are killed by freezing, there is little possibility of the mycelium serving as an inoculum source because the fungus cannot remain alive in a dead plant.

Infected tobacco debris and seed. Oospores probably constitute another principal method of fungus dissemination, although this has not been confirmed. Any agent that moves infected plant tissue from one spot to another can spread the fungus. Oospores are probably responsible for localized, small areas of primary infection on a few plants in seedbeds planted the previous year. Presumably oospores must remain on or near the soil surface to infect young seedlings. Seed transmission has been demonstrated once in Australia but not elsewhere.

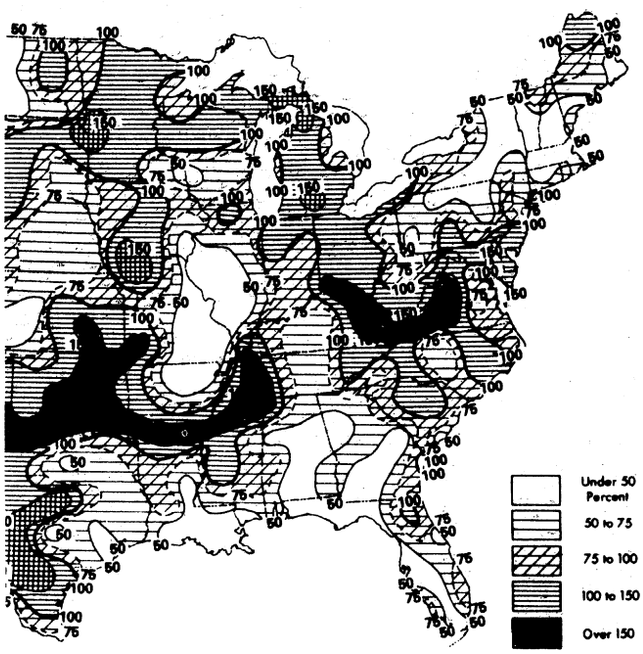


Fig. 7. Percentages of normal precipitation for June 1979 in the eastern United States (*24*). [Courtesy of National Oceanic and Atmospheric Administration]

Epidemiology

Amount of inoculum. The quantity of primary inoculum is important in blue-mold epidemics. When conditions are favorable for conidial production and release, and a large number of plants become infected at the same time, disease buildup and spread increases rapidly.

Temperature. As was mentioned above, optimum temperatures for the development of blue mold range from 15° to 25°C, but spores will germinate between 1° to 2°C and 30°C. The conidia are produced in successive crops each day for 4 to 17 days with a maximum spore production at 7 to 8 days. If temperatures the previous day were in excess of 30°C or below 8°C for more than 6 hours, sporulation will be greatly reduced. The longer such temperatures prevail, the less sporulation occurs.

Since conidial germination occurs over a wide range of temperatures, blue mold remains active during the coldest periods tolerated by tobacco plants. Blue mold can cause extensive damage in the seedbed during long periods in which night temperatures approach freezing and there are wide fluctuations between day and night temperatures.

Fungus activity is greatly restricted by warm temperature. High temperatures accompanied by low humidities also inhibit spore germination. Blue mold rarely does much damage to field tobacco in the southeastern United States, probably because the mean maximum temperatures during the summer months are uniformly high for extended periods. The 1954, 1963, and 1979 outbreaks in the Southeast occurred in May and June

when temperatures were 3° to 6° below normal and rains were frequent (Fig. 6). Prevailing temperatures during the growing season throughout most of Europe and in the mountains of North Carolina are optimum for blue-mold infection and development.

Before the 1979 epidemic, oospores were considered to constitute the principal source of primary infection in the seedbeds. McGrath and Miller (*9*) showed a correlation between above normal January temperatures in the Southeast and the severity of blue-mold infection the following spring. They postulated that the warmer temperatures stimulated oospore germination at an early date with a consequent buildup of inoculum. However, if vast numbers of conidia blow north from Caribbean areas each spring, oospore inoculum may be of little importance in the United States.

Humidity and light. Cruickshank and co-workers (*10*) showed that night humidities must exceed 95 percent for a minimum continuous period of 3 hours for conidial production to begin, and, this must occur on a night after a day when temperatures did not exceed 30°C for more than 6 hours. The delicate conidiophores are hygroscopic and the slightest change in humidity, such as that caused by the breath of an observer, at once produces changes in their turgidity and distortion. Hill (*11*) believes that the daily cycle of conidial dissemination results from the collapse of the conidiophores as a consequence of the withdrawal of water into the mycelium in the leaf. Many conidia are dislodged by the violent twisting and springlike action of the branches as the conidiophores collapse or disengage. Wind, rain, and mechanical shock cause sudden leaf movements and, in combination with changes in relative humidity, are also important contributing factors in conidial discharge.

Humidity is not an important factor in limiting the spread of viable conidia, and dry, hot conditions cannot be expected to eliminate them. Dry conidia resist exposure to sunlight more than those in water (*11*). Although observations of survival under extremely adverse conditions are in conflict with the concept that conidia are fragile and short-lived, it appears that some conidia can withstand wide ranges of temperature and humidity.

Moisture levels are critical factors in spore germination. Water droplets must be present on the tobacco leaf for at least an hour or until the germ tube has penetrated the epidermis. Dews and light rains usually supply adequate moisture for several hours each day, especially if the plants are crowded. Drying of plants is delayed in the shade tents in which cigar tobacco is grown, thus favoring disease development. Taylor and Aylor (*12*) showed that raising the tent wall does not significantly speed the drying of wet leaves, and ventilating the tent by raising the side walls may actually encourage the spread of blue mold. Furthermore, when light is reduced either naturally or by the shade tents, tobacco plants have more succulent and tender growth than they do during periods of bright sunshine, making them more susceptible to fungus attack.

Fig. 8. Control of blue mold in the seedbed. (A) The tobacco plants in this bed were protected by regular applications of a fungicide. (B) Most of the plants in this unprotected bed were killed by blue mold. [Courtesy of U.S. Department of Agriculture]

Intermittent rainy weather favors blue-mold development (Fig. 7). In addition to providing the high humidities necessary for sporulation and conidial germination, rain may also wash inhibitory substances from the leaf surface, thereby increasing leaf susceptibility.

Sporulation of *Peronospora hyoscyami* is a phenomenon induced by darkness, which appears to play a dominant and irreversible role in spore production. Hormonal changes are probably inhibited by a photosensitive mechanism (*5*).

Host physiology. Young, rapidly growing, succulent leaves produce more conidia than older, slow-growing, riper leaves. Any combination of environmental factors that delays leaf maturity contributes to increased spore production and host susceptibility.

Interaction with Other Diseases

When developing cultivars resistant to a major disease, plant breeders sometimes unknowingly perpetuate genes for susceptibility to hitherto minor diseases. Before the blue-mold outbreak of 1960, veinbanding caused by potato virus Y (PVY) was a minor disease of tobacco in Europe. Soon after blue-mold resistant cultivars began to be planted extensively, various workers reported that many blue-mold resistant lines were susceptible to veinbanding. It may be that widescale use of blue-mold resistant cultivars will be limited unless resistance to PVY can be bred into them.

Oddly enough, tobacco plants already infected with PVY are resistant to blue mold. The same is true of plants infected with tobacco mosaic virus. Apparently infection of a plant by one pathogen induces the plant to produce chemicals that make it resistant to other pathogens.

Control of Blue Mold

Blue mold is difficult and expensive to control. For the most efficient control, all known measures should be included in an integrated pest management program that begins with the selection of a seedbed site and continues through the growing and harvest season to the destruction of tobacco debris after the crop is harvested. Although the disease may not be equally severe every year, farmers should take steps to control each outbreak.

Fungicides. Before World War II, there were no fungicides that gave efficient blue-mold control. The discovery of the dithiocarbamates in 1942 opened a new era of plant disease control in the United States (Fig. 8). These compounds offered dependable, practical control when applied properly, that is, applied to prevent the disease with weekly or biweekly applications. If the chemicals are washed off by rain another application should be made as soon as possible.

The antibiotic streptomycin is curative and can be applied after blue mold appears and need not be used as frequently as the dithiocarbamates. During severe attacks, however, it sometimes fails to hold the disease in check. It is more expensive than the dithiocarbamates and is not effective against other fungus diseases, such as anthracnose and damping-off, which occur on young seedlings.

Application of preventative fungicides has obvious disadvantages. It is expensive and bothersome. During rainy weather proper application is difficult

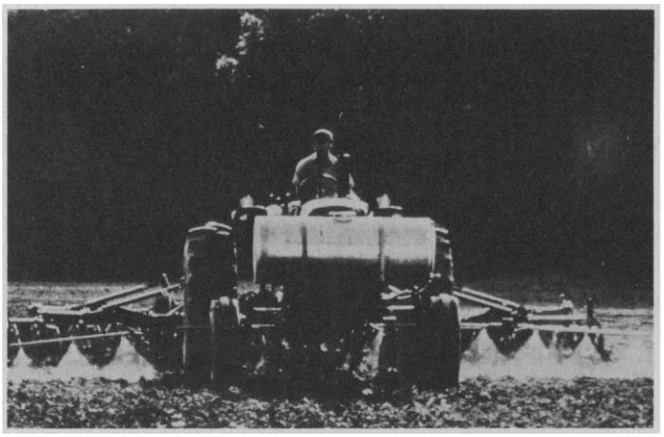


Fig. 9. This tractor rig can spray a nematocide-insecticide, a weedicide, and a blue-mold fungicide simultaneously and then uniformly turn them into 6 to 10 cm of topsoil with a disk harrow before the tobacco is transplanted. [Courtesy of Elanco Corporation]

with resulting poor control. Camilli (*13*) estimated that the costs of fungicides and equipment to control blue mold were 6 to 10 percent of the annual crop value in Italy. In certain European countries, as many as 20 to 25 applications must be made from seedbed to harvest. Hitier (*14*) reported that blue-mold fungicides are applied 10 to 25 times to the crop in some countries during the growing season, amounting to as much as 40 kilograms of active ingredients per hectare. Furthermore, large amounts of residue may remain when the tobacco is processed, and some fungicides may change the tobacco flavor, or could harm the smoker. Extensive tests must be conducted, therefore, to make sure that fungicides or their residues do not injure the smoker.

A big step forward in blue-mold control occurred when Ciba-Geigy in the mid-1970's developed the new systemic fungicide metalaxyl [*N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl) alanine methyl ester] under the name Ridomil. This unusual compound appears to be specifically effective against Phycomycetes (*15*). It is apparently not phytotoxic, is transported rapidly in plant tissues, and is effective at low doses. It can be applied to the soil immediately before transplanting (Fig. 9) as it is absorbed quickly by the tobacco roots and may protect the plants for 6 weeks or longer. The chemical is curative and, when applied as a spray on blue-mold infected plants, effectively suppresses disease development.

In North Carolina during the 1979 blue-mold epidemic, tobacco plants growing in plots treated with Ridomil for black shank control remained free of blue mold, whereas plants growing in adjacent, untreated plots suffered considerable blue-mold damage.

Ridomil is credited with saving the 1979–1980 Jamaica tobacco crop. Although blue mold had never been reported on the island before, the disease exploded in the seedbeds late in December 1979. Agronomists convinced the minister of agriculture to grant immediate permission to import Ridomil from Switzerland. In late February 1980, the disease had been effectively controlled by spray applications of Ridomil at 2-week intervals. In fields where the chemical may have been applied improperly at the wrong rates, however, the disease was still active.

Chemicals are valuable weapons in the war against plant diseases, but they are not the ultimate weapon. As Van der Plank (*16*) noted, Ridomil is a "vertical" fungicide, that is, it interferes chemically in a limited number of ways in the host-parasite physiology of a limited number of strains of the blue-mold pathogen. Sublethal doses of Ridomil or other improper methods of application exert selection pressures on populations of *Peronospora hyoscyami* and increase the chances that new strains of the fungus resistant to Ridomil will appear. As documented by Dekker (*17*), these new strains could arise within a few years.

As of 1980, Ridomil was registered for control of blue mold on tobacco in six countries. Based on results of toxicological studies, the Environmental Protection Agency (EPA) granted conditional registration to Ridomil in the United States on 28 February 1980 for use in the control of blue mold and black shank of tobacco. Results of additional toxicology and environmental studies currently in progress will have to be evaluated before EPA will grant Ridomil an unrestricted label for use on tobacco (*18*).

Resistant cultivars. No commercially acceptable cultivars resistant to blue mold were in use before the 1960 European epidemic. Fortunately, breeding lines that derived their resistance from *Nicotiana debneyi* were available. These were pressed into use and several thousand hectares of blue-mold resistant cultivars were grown in 1962. A new approach in the use of resistant germ plasm was tried in 1963. Blue-mold resistant F_1 hybrids, developed from male-sterile (pollenless) parents crossed with others of high quality, were grown extensively in several countries.

Since 1965, additional resistant cultivars have been used both in Europe and Australia. Most of these have proved to be susceptible to new pathogenic races of the fungus that developed within 3 years. In addition, the blue-mold resistant cultivars are more susceptible to root rots and virus diseases than cultivars formerly grown. To be useful in the United States, especially in areas where tobacco is flue-cured, a blue-mold resistant cultivar must also be resistant to root knot and black shank since these two diseases occur widely in the Southeast. Breeders are trying to incorporate resistance to other diseases into blue-mold resistant cultivars, but this may take a long time.

Cultural practices. Good cultural practices alone will not control blue mold, but they help prevent early infection, reduce severity of outbreaks, and aid in control. Growers should (i) locate seedbeds where they receive a maximum amount of sunshine; (ii) avoid damp, shaded, poorly drained sites; (iii) avoid using tobacco trash as fertilizer on seedbeds; and (iv) as soon as transplanting is completed, disk under the remaining plants and sow a cover crop. To prevent the fungus from overwintering in infected plants, farmers should cut the stalks after the harvest, plow under all the crop remains, prevent all sucker growth, and destroy volunteer plants.

Warning service. In the United States a blue-mold warning service was established in 1945 and operated by the U.S. Department of Agriculture and cooperating states (*19*). As soon as blue mold appeared, it was reported by telephone to the nearest state experiment station, which relayed the information to the central office of the Plant Disease Survey in Beltsville, Maryland. Reports were sent out to the various tobacco-producing states, and growers were advised by radio, television, or newspaper releases about where blue mold was a threat and when to begin fungicide treatments. The warning service was not needed from 1965 to 1979 because blue mold was inactive.

A similar warning service was created in 1961 by the Centre de Cooperation pour les Recherches Scientifiques Relatives au Tabac (CORESTA) with correspondents in most European and Medi-

terranean countries (*20*). Any occurrence of blue mold is reported to CORESTA headquarters in Paris, which informs the countries most threatened and warns correspondents in all countries.

After the 1979 epidemic, the U.S. Tobacco Disease Council established the National Blue Mold Warning System, which also covers Canada. This system has state coordinators who collect information on occurrences of blue mold and advise a central office at North Carolina State University about them. The information is analyzed at the central office and warning statements, describing the status of the disease, relevant weather forecasts, and control actions needed, are released weekly. In North Carolina, where tobacco is grown in 80 counties, the tobacco extension agent in each county serves as county coordinator.

Forecasting systems. With the advent of systems analysis and mathematical modeling, and the rapid development of computers during and after World War II, the procedures and tools needed to examine, integrate, and predict significant features of an epidemic became available. Forecasting provides a systematic way to assess the influence of environmental factors on disease progress and tells growers the probabilities of when and where a disease may appear. It thus provides a means for determining how to apply various management practices.

The development of forecasting systems is a rapidly growing aspect of plant pathology (*21*), and several blue-mold forecasting systems have been tested in Australia and Europe (*22*). Forecasting systems are also in use for other plant diseases, such as late blight of potato and apple scab.

Projection

More epidemics of blue mold are certainly possible. Plant pathogens are slippery enemies that change all the time. They constantly challenge our judgment, skill, and resources. Although the war against plant diseases may never end, we can learn to live with them.

Blue mold is a continental as well as a local problem, and its control will require the cooperation of scientists and government officials from many countries. Blue-mold epidemics have already caused enormous financial losses, upset a specialized field of agricultural production, and induced social consequences that are difficult to evaluate. Nonetheless, the very threat of recurrent epidemics may strengthen the concept of collective responsibility and the need for international collaboration that will be required to control not only blue mold but the many other diseases whose causal agents are spread principally by the wind.

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Elimination of Synapses in the Developing Nervous System

Dale Purves and Jeff W. Lichtman

The formation of neural circuitry during development is a complex and poorly understood process. In general, the nervous system must solve two problems. One problem is essentially qualitative: how are synapses established between appropriate partners? The solution presumably depends on mechanisms of differentiation, cell migration, guidance of growing axons, and ultimately the selective formation of synapses. A second problem is quantitative: how does the system regulate the number of cells in the pre- and postsynaptic populations and the number of synaptic contacts between them? In particular, how does the nervous system guarantee that every cell in the target population is promptly innervated and that, in the long run, synapses are correctly distributed among the target cells?

There is little consensus about the way the developing nervous system solves the problem of qualitative accuracy. Somewhat more is known about the strategies used to achieve quantitative accuracy. There is, for example, some agreement about the way in which the size of the innervating population is matched to the capacity of the target. Neurons in many (perhaps all) regions of the developing vertebrate nervous system are overproduced initially and appear to compete for survival in early embryonic life (*1*). Various experiments indicate that presynaptic neurons are dependent on some aspect of their target; for example, artificially increasing target size enhances the survival of innervating neurons, while decreasing target size in-

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