forests

Opinion

Two Infectious Diseases: "COVID-19" and "Pine Wilt Disease"

Kazuyoshi Futai

Kyoto University, Kyoto 606-8501, Japan; kazun4696060@gmail.com

Abstract: Two epidemics, a new coronavirus disease (hereafter COVID-19) and pine wilt disease (hereafter PWD) whose causal agent is the pine wood nematode *Bursaphelenchus xylophilus*, are similar in terms of disease spread, particularly in an important role of the latent carrier in the spread of the disease. In Japan, damage caused by PWD has gradually decreased over the past 40 years, not because of successful control of PWD, but because pine forests susceptible to pine wilt have been drastically reduced by the disease. Meanwhile, COVID-19, which was first identified in China in 2019, became a pandemic in 2020 and caused long-term disruptions to people's lives worldwide. Even after the declaration of the end of the emergency by the WHO in May 2023, the coronavirus continues to produce new variants and maintains the potential for new waves of infection. In this paper, I would like to discuss the issues of control measures for the forest disease PWD, especially for the measures against asymptomatic carrier trees, with reference to the efforts implemented for COVID-19, which is more closely related to human society. This is because an asymptomatic carrier has been a blind spot in conventional PWD control measures, and I believe that a fundamental review of control measures considering this aspect is essential, and understanding the similarities between COVID-19 management and PWD control can provide guidance on how to effectively deal with both human and plant epidemics.

Keywords: pine wilt disease (PWD); COVID-19; asymptomatic carrier; control measures; epidemic spread

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1. Introduction

In Japan, there are three species of two-needled pines (*Pinus densiflora*, *P. thunbergii*, and *P. luchuensisi*), and five species of five-needled pines (*P. koraiensis*, *P. parviflora*, *P. parviflora var. pentaphylla*, *P. pumila*, and *P. amamiana*). Among these, the pine forests familiar to the Japanese people, such as Japanese red pine (*P. densiflora)*, Japanese black pine (*P. thunbergia*), and Ryukyu pine (*P. luchuensisi)* forests, which are distributed in lowland areas, have been devastated by a forest epidemic, PWD, that typically kills affected pine trees within a few weeks to a few months. The causal pathogen is the pine wood nematode *Bursaphelenchus xylophilus*, which is transmitted by vector pine sawyer beetles in the genus *Monochamus* [1]. In Japan, the damage caused by PWD has been decreasing over the past 40 years (Figure 1). As a result, public interest in PWD seems to have completely faded. However, this decrease in damage is not because pine wilt disease has been suppressed, but because the pine forests susceptible to the disease have drastically decreased due to PWD.

On the other hand, the novel coronavirus disease (COVID-19), which was first confirmed in Wuhan City, China, in 2019, became a pandemic in 2020 and caused long-term disruptions to people's lives worldwide. By the time the World Health Organization (WHO) declared the end of the Public Health Emergency of International Concern (PHEIC) in May 2023, approximately 7 million people had fallen victim to the disease globally. Even after the declaration of the end of the emergency, the coronavirus continues to produce new variants and maintains the potential for new waves of infection, becoming endemic in human society.

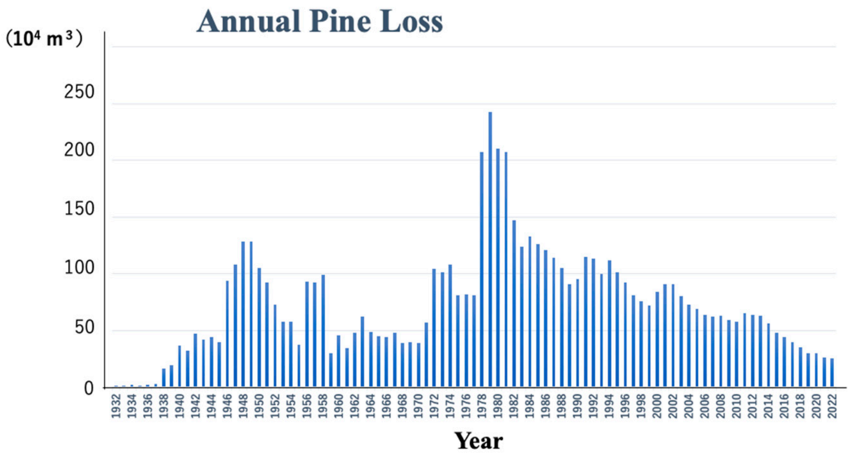

Figure 1. Annual pine loss caused by pine wilt disease in Japan [2].

In this paper, I will examine the issues related to the control measures for the forest disease PWD, especially the measures against asymptomatic infection, by referencing the efforts implemented for COVID-19, which is more closely related to human society. This is because asymptomatic infection has been a blind spot in previous PWD control measures, and we believe that a fundamental review of control measures considering this aspect is necessary.

The author has been researching pine wilt disease as his primary subject for many years but is an outsider regarding COVID-19. To ensure the accuracy of the discussion, a wealth of information has been referenced, particularly the "Guidelines for the Medical Treatment of Novel Coronavirus (COVID-19) Infection" published by the Ministry of Health, Labour and Welfare of Japan. The 5.2 edition published in 2021, the 7.2 edition published in 2022, and the 10.0 edition published in 2023 [3] were especially referenced. The COVID-19 policy briefs [4] presented by the WHO were also referred to in order to know the measures taken on a global scale to stop the spread of COVID-19. It recommends eight specific actions that countries and institutions should take to protect human life and livelihoods.

2. The Definition of Asymptomatic Infection

Before beginning the discussion, let me share the definition of asymptomatic infection. Asymptomatic infection, also known as latent infection, refers to a state where an individual is infected with a pathogen but does not exhibit any symptoms. This can include those in the pre-symptomatic incubation period and those who remain healthy without developing symptoms (latent infection). In the case of PWD, the distinction between these two is not clear, as some trees may develop symptoms after a long incubation period [5]. However, for the purpose of devising control measures, it is not necessary to differentiate between these two conditions. Therefore, both will be collectively referred to as asymptomatic infection as an obstacle to countermeasures. It should be noted that there are significant differences between the processes leading to symptom onset in COVID-19 and PWD. In the case of COVID-19 infection, even if the individual appears healthy, symptoms like fever or taste disorders make it relatively easy to confirm the onset of the disease. On the other hand, in the case of PWD, infected trees can maintain a healthy appearance (asymptomatic) for a long time after infection and disease onset, and the typical symptom of the disease, wilting, appears only in the late stages of disease progression. In other words, when color abnormalities in the needles (such as fading or yellowing) are detected, the tree is already dead, making it unsuitable for determining infection and disease onset. A well-known early symptom that appears before needle color abnormalities is the reduction or cessation of resin exudation [6], which is currently the only symptom that can be used to determine the presence of infection early [7,8].

3. Assessing the Infection Trends in a Certain Area

To understand the infection status of a particular disease in a certain area, it is necessary to regularly screen a significant number of individuals (humans or pine trees) living in that area, preferably all individuals. In the case of COVID-19 infection measures targeting humans, samples such as saliva or nasal mucus are collected, and the presence of the virus is tested using nucleic acid detection tests that amplify and detect the viral RNA via real-time PCR methods, or antigen tests that detect specific proteins of the coronavirus using antibodies.

In contrast, for PWD, regular infection screening of numerous pine trees within a forest stand is necessary to grasp the infection trends. In such cases, resin exudation levels are used as an indicator (Figure 2).

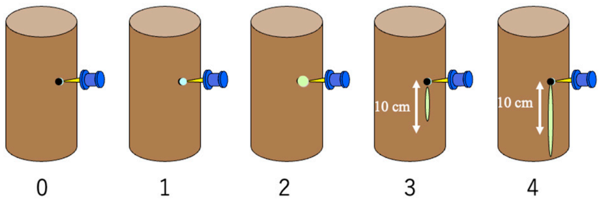

Figure 2. The monitoring method of pine trees for health. To check the pine trees for health, the modified Oda method [6] was used as follows. The amount of the oleoresin exuded from a needle hole of a thumbtack was examined. The degrees of the exuded oleoresin were classified into five levels and were rated according to an index from 0 to 4, as follows—0: no resin exuded; 1: the pin hole of the thumbtack was filled with the resin, or the needle of the thumbtack became sticky due to the resin; 2: a small amount of resin exuded from the thumbtack-pierced point to make a drop, but never flowed down; 3: the resin flowed down from the point shorter than 10 cm; 4: the resin vigorously flowed down 10 cm or more from the point. To monitor the physiological condition of each test tree, all resin indices evaluated until then were summed up at each measurement, and thereby a cumulative curve was drawn for each tree [9].

However, such investigations are limited in number (e.g., [9,10]). A spatiotemporal study conducted over four years on Korean pine forests revealed the role of asymptomatic infected trees in the spread of pine wilt disease [9].

The study found that resin exudation used as an infection indicator decreases or stops during the cold period (November to February), and that the resin exudation, once stopped or decreased due to infection, can resume and then stop again, showing physiological fluctuations during the disease progression. This highlights important facts to be aware of when using resin exudation as an infection indicator. In the case of PWD, there may be a significantly long period after infection when external symptoms do not appear (latent infection period, incubation period). Particularly troublesome is that asymptomatic infected pine trees, although appearing normal externally, release volatile gasses such as ethanol and terpenes. These volatile gasses attract sexually mature male and female *Monochamus* pine sawyers (vectors of the pathogenic nematode, hereafter referred to as the *Monochamus* beetle) [11,12], providing them with a place to lay eggs. *Monochamus* beetles then fly to nearby healthy trees and infect them with the pathogenic nematodes they carry. After emerging, *Monochamus* beetles remain sexually immature, for about a week in males and two weeks in females. It has been thought that during sexual immaturity time, they feed on the bark of young branches of healthy trees and transfer the majority of the pathogenic nematodes into the healthy host pines through the wounds they marked. Therefore, it was believed that sexually mature *Monochamus* beetles visiting for mating and oviposition carried few nematodes. Actually, however, many *Monochamus* beetles visiting for mating and oviposition still carry a significant number of nematodes [13,14], and they visit surrounding healthy trees for their feeding activities, infecting these healthy trees with a considerable number of nematodes (Futai, K., and Ishiguro, H., personal communication). When sexually mature *Monochamus* beetles fly to weakened trees for reproductive activity late in the pine wilt season (August to September) and visit surrounding healthy trees to keep feeding, the current- to second-year shoots of feeding target changes in their tissue structure and chemical composition [15], making nematodes less likely to invade and move into host tissues compared to earlier in the season (June to early July). This may inhibit the disease progression even if the nematodes infect the tree. Thus, healthy trees infected with pathogenic nematodes by sexually mature beetles late in the season are more likely to become asymptomatic infected trees (latent carrier) rather than developing symptoms and dying within that year. This is one possible mechanism by which asymptomatic carrier trees persist within a forest (Futai, K., and Ishiguro, H., personal communication). These asymptomatic infected trees are not removed and are left in the forest, where, with rising temperatures and dryness in subsequent years weakening the host's resistance, the pathogenic nematodes proliferate, and the disease progresses [16]. Consequently, these trees release ethanol and terpenes, attracting beetles, causing "pine wilt" to reappear around the trees that died and were removed the previous year by attracting sexually mature beetles from distant locations.

4. Basic Measures to Prevent Infections

For both COVID-19 and pine wilt disease, several fundamental measures should be strictly followed to prevent the spread of infection. These include

1. Rapid and thorough measures at a border;
2. Accurate understanding of infection trends;
3. Comprehensive and proactive measures to prevent widespread infection.

Let me compare these basic infection prevention measures for both diseases.

5. Border Screening and Quarantine

Quarantine measures at ports and airports to prevent the entry of infectious diseases are referred to as "border measures".

In the case of COVID-19, the virus spreads through infected individuals (carriers) themselves. Therefore, PCR testing was conducted on entrants and returnees at ports and airports. If they tested positive, they were isolated in designated accommodations to restrict their movement. If the entry of infected individuals at the border could be completely prevented, it would theoretically stop the entry of the disease from abroad. However, in practice, many countries repeatedly experienced the unnoticed entry of new variants, leading to further outbreaks. This was due to delays in establishing testing and quarantine systems, which failed to block the entry of infected individuals. Even after these systems were established, asymptomatic or low-viral-load carriers might have slipped through quarantine.

5.1. In the Case of the First PWD Discovery in Japan

In the case of plant diseases like PWD, the movement of people and goods between continents or countries facilitates the entry of pathogens into other countries. For PWD, it was first discovered in the Japanese port city of Nagasaki in 1905. The North American *Monochamus* beetles, which had been hiding in large quantities of imported lumber from North America, likely flew to nearby healthy Japanese pine trees, and infected them with the pathogenic nematode. The native Japanese *Monochamus* beetles, which came to the weakened pines for breeding, then carried the foreign pathogenic nematodes, establishing a new transmission relationship [17]. Unlike human cases, the quarantine of lumber at ports was likely to be extremely weak at that time [18]. Several subsequent records of PWD outbreaks in Japan are also near ports.

5.2. 1984: Finland Incident and Subsequent Measures

In 1984, the pine wood nematode (*Bursaphelenchus xylophilus*) was detected in the wood chips of pines imported from North America at a Finnish port. The Finnish government immediately banned the import of coniferous wood from countries where the nematode was present, including North America and Japan. The following year, Sweden and Norway implemented similar import bans, and in 1986, the European and Mediterranean Plant Protection Organization (EPPO) designated the nematode as a significant quarantine pest. These swift border measures seemed to have successfully prevented the entry of pine wilt disease into Europe. However, in 1999, an outbreak occurred in a *Pinus pinaster* forest in the port area of Lisbon, Portugal. This was believed to be due to packing materials used for large imported goods, which contained pine wood infested with *Monochamus* beetles carrying the pathogenic nematode. Despite stringent quarantine measures, pathogens can sometimes evade detection and enter through unexpected routes.

6. Infection Trend Monitoring

To prevent the spread of infection, it is essential to accurately understand how far the infection has spread and how fast it is.

For COVID-19, at the early stage of an outbreak, it was necessary to test all residents in the affected area to identify the presence of the pathogen. Infected individuals were isolated from healthy people, the movements of close contacts were restricted, and the spread of the disease was tracked. The tests used for this purpose included PCR tests and antigen tests. These methods are highly sensitive but require significant time (1–5 h), specialized equipment, and skilled operators, and are costly, which appeared to deter widespread implementation in Japan. The decision not to expand PCR testing may have been influenced by early findings. PCR tests conducted in the early stages of the pandemic revealed many asymptomatic carriers (latent infections*) in the community, leading authorities to conclude that further widespread testing was not feasible due to manpower and cost constraints. However, if this was the reason for limiting large-scale PCR testing, it was a flawed decision. Early in an outbreak, it is crucial to understand the infection status as accurately as possible and isolate all infected individuals, including asymptomatic ones, from healthy people. Delays in initial response, or non-response to asymptomatic carriers, can significantly hinder efforts to prevent the spread of infection (Figure 3(b1,b2)).

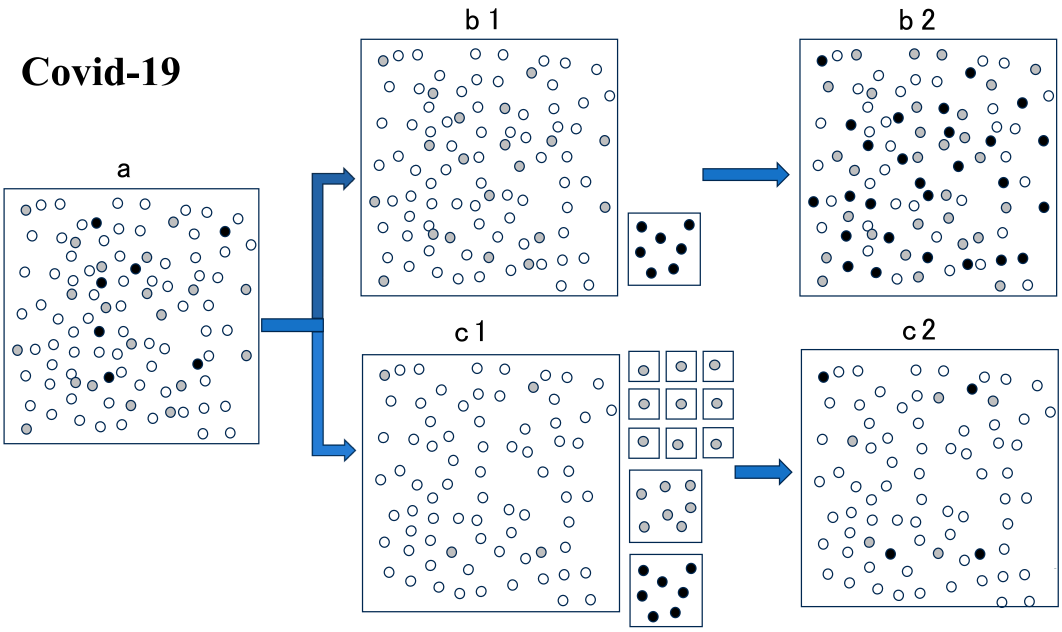

Figure 3. (**a**) If two different measures are implemented—(**b1**): the isolation of only symptomatic individuals (●) from healthy ones (○), and (**c1**): the isolation of both symptomatic individuals (●) and asymptomatic carriers (●) from healthy ones (○). The large squares represent the study area and the medium and small squares represent the facilities for isolation. (**b2**,**c2**): expected spread of the disease after the respective isolation has been implemented.

* For COVID-19, the incubation period averages 5–6 days, with a maximum of 2 weeks [3].

6.1. Proactive Use of PCR Testing for Surveillance: The Case of South Korea

South Korea was proactive in using PCR testing for surveillance to understand the extent of damage and prevent the spread of infection. The first COVID-19 case in South Korea was detected on 20 January 2020, around the same time as in Japan. In February, a large cluster outbreak occurred in Daegu, a city in southeastern South Korea. This incident prompted the South Korean government to strengthen its control measures, prioritizing the early detection of infected individuals and their contacts, and preventing the spread of the virus. They built a system with the support and cooperation of the public, successfully controlling the first and second waves of infection (Figure 3(c1,c2)). The policies implemented by the South Korean government to prevent the spread of COVID-19 were termed the "K-Quarantine System" and were highly praised internationally. Among the measures, the large-scale PCR testing carried out in the early stages of the outbreak to detect infected individuals early and suppress the spread of infection was particularly effective. Numerous screening clinics were set up, and thorough PCR testing was conducted [19].

However, following the vaccine dissemination, South Korea used a vaccine with somewhat lower efficacy, and as the vaccination rate exceeded 70%, they shifted their focus to prioritizing economic activities. This led to a significant relaxation of the strict movement restrictions that had been in place, resulting in a sharp increase in infections. By 2022, the number of daily infections exceeded 600,000, an explosive number of infections [20]. Nonetheless, this outcome does not negate the initial success of large-scale PCR testing in the early detection and isolation of infected individuals, which had a remarkable effect on inhibiting the spread of infection.

6.2. Lessons for PWD Control from COVID-19 Measures in Japan and South Korea

The differences in measures taken by Japan and South Korea to prevent the spread of COVID-19 and the subsequent progression of damage provide valuable lessons for controlling the spread of PWD. One key lesson is the importance of identifying infected hosts (pine trees in the case of pine wilt) as early as possible and isolating them from healthy hosts. However, for PWD, even if the first pine tree in a forest in a given area dies, it is likely that neither the local government nor the community would notice such a tree. Dead trees left in the forest would inevitably become sources of infection for the following year's outbreak, causing patches of dead trees to emerge in the surrounding area. The population of *Monochamus* beetles would rapidly increase, accumulating latent carrier trees around the dead ones. When a cluster of dead pines appears in a forest, the authorities finally take action and begin felling and removing the dead trees. However, by that time, latent infected trees have spread widely within the forest, and when conditions are right, they become symptomatic and attract beetles from outside the forest, leading to persistent damage even with annual removal efforts.

6.3. Comparison of Cluster Infection Control of COVID-19 and PWD Management

In the early stages of the COVID-19 outbreak, the Japanese government implemented measures to trace patients from cluster infections (large groups of infections in one place) and monitor the activities of close contacts, requesting them to refrain from going out. Although somewhat inefficient, these measures achieved certain success in the initial phase. Applying this approach to PWD can be insightful. In the early stages of an outbreak, when dead or abnormal trees appear, the surrounding healthy pines should be regarded as "close contacts" (asymptomatic carrier trees) and monitored for subsequent symptoms. If symptoms become evident, these trees should be targeted for removal, isolating them from healthy trees, even if they appear healthy. However, this method requires a basis for selecting asymptomatic infected trees, and although there are molecular biological diagnostic methods based on nematode DNA [21,22], they are not widely available and currently rely on resin exudation [7]. During winter, even healthy trees reduce or stop resin exudation, and some trees may repeatedly stop and resume resin exudation in spring and beyond. Therefore, using resin exudation as a criterion for asymptomatic infection requires repeating this method at least once a month, three times in total, from spring onwards. The survey should focus on "close contacts", i.e., trees around the dead ones. Ideally, all trees in the forest should be surveyed, but practically, focusing on surrounding trees can still be effective. However, like COVID-19, this approach is only effective in the early stages of an outbreak and when applied to all asymptomatic carriers around the trees killed in the previous year (Figure 4(b1–b3)). If not, many trees in the forest become asymptomatic carrier trees (latent carrier trees) over time, making it impossible to stop the spreading of pine wilt (Figure 4(c1–c3)). Unfortunately, there is no equivalent to the PCR method used to detect COVID-19 infections for PWD.

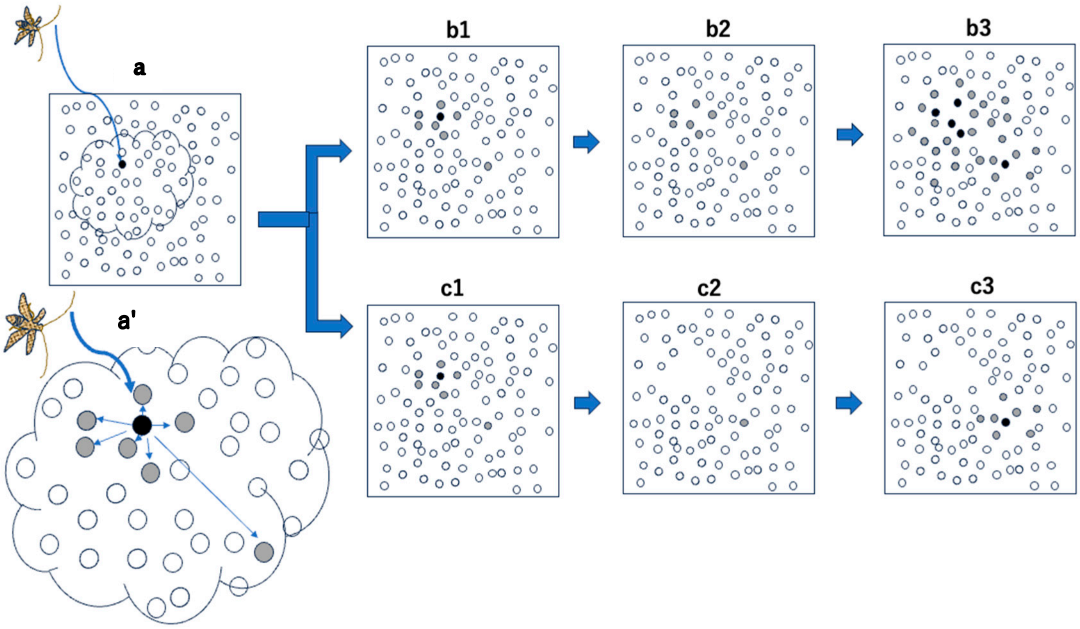

Figure 4. Predicted spread of PWD if two different measures are implemented—(**b1**,**c1**): spread of infection from a weakened tree (breeding target) to surrounding healthy trees. (**b2**): only symptomatic trees (●) are removed, and (**c2**): both symptomatic trees (●) and asymptomatic carriers (●) are removed from the forest, and (**b3**,**c3**): extent of damage in the year following the respective removal. Square (**a**) shows an original forest before the invasion of PWD, composed of only healthy pines, where *Monochamus* beetles fly into for feeding. (**a'**) is a partial enlargement of (**a**), illustrating the way sexually mature beetles enter into surrounding healthy trees and spread new infections.

7. Monitoring Infection Trends in Widespread Epidemics

For COVID-19, the infection trends were monitored by each local government, which tracked the number of patients and deaths reported by medical institutions. The national government then compiled and published these data. Additionally, the World Health Organization (WHO) collected data on the progression of the disease from various countries, comparing outbreaks internationally.

Similarly, in Japan, annual numbers of dead pine trees and volumes of dead wood are compiled on a prefectural basis and then aggregated by a national institution (the Forestry Agency) to track infection trends over the years (Figure 1).

8. Use of Mathematical Models to Predict Future Trends

Both COVID-19 and PWD have utilized mathematical models to predict future trends. However, the extent to which these predictions influenced policy differs significantly. For COVID-19, countermeasures based on model predictions were recommended following discussions among researchers (e.g., [23]), though it is unclear how faithfully the administration implemented them. In the case of PWD, several models predicting the spread of damage were published [24–26], but these predictions were rarely discussed among researchers and officers in charge of or applied in control measures.

9. Comprehensive and Proactive Measures for Preventing Spread: Isolation of Asymptomatic Infected Individuals from Healthy Ones

A familiar approach to preventing the spread of COVID-19 includes wearing masks, sanitizing hands with alcohol, and measuring body temperature—practices enforced at various entry points of stores, offices, and hospitals. These measures assume the presence of asymptomatic carriers or those in the incubation period among seemingly healthy people, posing a risk of community transmission. Avoiding the "three Cs" (closed spaces, crowded places, and close-contact settings), ventilating transportation, and restricting loud conversations are all strategies based on the assumption that asymptomatic carriers are mingling in the community.

In contrast, for PWD, "asymptomatic" (latent) infection strictly means that there are no visible symptoms to the naked eye, although the infection may be established, and symptoms (in this case, the cessation of resin exudation) may be progressing. Trees that continually cease resin exudation will eventually show wilting symptoms and die. Unlike COVID-19, the concept of "asymptomatic infection" is not well understood in the field of PWD by either administrative officers or foresters, hindering the prevention of its spread. For example, such asymptomatic infected trees are typically not targeted for removal (the elimination of the infection source) and are left in the forest. This is analogous to leaving highly contagious symptomatic COVID-19 patients in the community, which is highly inappropriate from a preventive standpoint.

Recent research has been vigorously advancing methods to detect and diagnose PWD-infected trees. This mainly involves aerial detection techniques that integrate various wavelengths of remote sensing and UAV (unmanned aerial vehicle) technology [27–29], as well as methods employing diverse technologies to identify infected trees [8]. The former approach, combined with satellite imagery [30] and ground surveys, allows for the detection of infected individuals within forests and tracking the spread of damaged trees to examine damage trends on a large scale [31]. However, it has the drawback of it being difficult to distinguish infected trees from other backgrounds of similar color and requires visible abnormalities in the needles for detection, leaving systems for identifying asymptomatic infected trees incomplete [32]. I totally agree with Lee et al.'s view that while it is important to diagnose and treat symptomatic trees promptly, asymptomatic trees also need prompt diagnoses and removal [32].

On the other hand, attempts to identify infected trees through detecting pathogenic nematodes or volatiles specific to infected trees [33] involve traditional methods such as isolating nematodes from wood samples for microscopic identification, or amplifying small amounts of DNA from the samples to identify *Bx* nematode-specific DNA sequences [34]. While traditional methods are fundamental, they require highly skilled techniques and knowledge for identifying *Bx* and distinguishing it from related cohabiting species. Molecular identification methods for *Bx* can be performed by anyone with the necessary equipment and expertise, but they are costly and not suitable for repeated field surveys involving many pine trees. Additionally, although these methods are sensitive, the density of nematodes in asymptomatic infected trees is extremely low, making detection in small samples often unsuccessful.

Insecticide sprays targeting *Monochamus* beetles (vector), which have been implemented to protect important pine forests in Japan, have no effect on latently infected trees that have been infected by pathogenic nematodes by the time of application. If the tree was infected late in the previous season, or if only a few nematodes infested the tree at the time of infection, it is highly likely that the tree will not become diseased during the season and will become a "latently infected tree". And no matter how many insecticide sprays are applied to such trees to prevent the new infestation of pathogenic nematodes by

Monochamus beetles, if the dryness and high temperatures continue, the nematodes that have previously infested the trees will multiply and become active, thereby causing the pine trees to become diseased and die [16].

The administration must be fully aware of the existence of asymptomatic latently infected trees and had better explain this to forestry workers engaged in pest control so as not to damage their morale. This is because the reappearance of damaged trees after a complete eradication of dead trees could frustrate their morale.

10. Protection of Healthy Individuals

The ultimate measure for preventing the spread of COVID-19 is vaccination. With the global spread of COVID-19, many pharmaceutical companies have ventured into vaccine production, successfully creating several types. The most reliable in terms of efficacy to date is the mRNA vaccine, which prevents infection by activating the body's immune system. Widespread and rapid vaccination can prevent infection and mitigate severe illnesses even if infection occurs.

In PWD, host pines possess various levels of resistance to the pathogen, but the nematodes overcome these defenses by moving and proliferating within the host tissue, exhibiting pathogenicity. The delicate balance between host resistance and nematode pathogenicity is maintained under normal conditions, but environmental stresses such as prolonged drought or high temperatures can weaken host resistance, leading to disease progression and death. On the other hand, trunk injection agents available on the market target the nematodes, inhibiting their activity and proliferation within the host tree, thus compensating the host's resistance and protecting the tree from death. Several types of trunk injection agents are commercially available, but their high cost is a major barrier to forest application. Efforts to reduce the price by pharmaceutical companies are needed, along with appropriate government subsidies, similar to COVID-19 vaccines, to make widespread use of trunk injection agents feasible.

In any case, the most crucial aspect of infectious disease control is the decision to implement appropriate measures intensively as soon as the disease is detected. Administrative officials should pay more attention to researchers' insights.

11. Conclusions

This paper focuses on the importance of asymptomatic carriers as a critical factor influencing the spread of infectious diseases by comparing PWD (pine wilt disease), a forest disease caused by nematodes, and COVID-19, a human disease caused by a virus. Much of the knowledge gained from the well-studied COVID-19, where experience has been accumulated in controlling its spread, will be highly useful in developing further measures for controlling pine wilt disease, a forest epidemic.

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