



Review in Advance first posted online
on June 8, 2016. (Changes may
still occur before final publication
online and in print.)

Disease Impact on Wheat Yield Potential and Prospects of Genetic Control

Ravi P. Singh,¹ Pawan K. Singh,¹ Jessica Rutkoski,^{1,2}
David P. Hodson,³ Xinyao He,¹ Lise N. Jørgensen,⁴
Mogens S. Hovmøller,⁴ and Julio Huerta-Espino⁵

¹International Maize and Wheat Improvement Center (CIMMYT), 06600, Mexico, DF, Mexico; email: r.singh@cgiar.org

²Department of Plant Science, Cornell University, Ithaca, NY 14853

³CIMMYT-Ethiopia, Addis Ababa, Ethiopia

⁴Department of Agroecology, Aarhus University, DK-4200, Slagelse, Denmark

⁵INIFAP-CEVAMEX, 56230, Chapingo, México

Annu. Rev. Phytopathol. 2016. 54:13.1–13.20

The *Annual Review of Phytopathology* is online at
phyto.annualreviews.org

This article's doi:
10.1146/annurev-phyto-080615-095835

Copyright © 2016 by Annual Reviews.
All rights reserved

Keywords

Triticum, pathogen, epidemiology, resistance, breeding, genetics

Abstract

Wheat is grown worldwide in diverse geographical regions, environments, and production systems. Although many diseases and pests are known to reduce grain yield potential and quality, the three rusts and powdery mildew fungi have historically caused major crop losses and continue to remain economically important despite the widespread use of host resistance and fungicides. The evolution and fast spread of virulent and more aggressive race lineages of rust fungi have only worsened the situation. Fusarium head blight, leaf spotting diseases, and, more recently, wheat blast (in South America) have become diseases of major importance in recent years largely because of intensive production systems, the expansion of conservation agriculture, undesirable crop rotations, or increased dependency on fungicides. High genetic diversity for race-specific and quantitative resistance is known for most diseases; their selection through phenotyping reinforced with molecular strategies offers great promise in achieving more durable resistance and enhancing global wheat productivity.

INTRODUCTION

Wheat (*Triticum* spp.) is the second most important staple food crop after rice and is cultivated worldwide on approximately 220 million ha at diverse latitudes and altitudes under irrigated, severe drought, and wet conditions. Demand for wheat is projected to rise at a rate of 1.6% annually until 2050 because of increased population and prosperity. As a result, average global wheat yields on a per hectare basis will need to increase to approximately 5 tons per ha from the current 3 tons (112). Nearly 200 diseases and pests have been documented, and approximately 50 are considered economically important because of their potential to damage crops and hurt farmer incomes (109). Overall, potential grain yield losses due to disease have been estimated at 18%, and actual losses under current disease control have been estimated at 13% (73). Although the scale of disease impact can vary from year to year, diseases are always active and can pose a significant challenge even if they attack only certain plant parts. Furthermore, all plant parts are prone to diseases, and multiple diseases can occur on the same plant. They can occur in any field, depending on environmental conditions and the susceptibility of host cultivars. All disease symptoms draw attention and generate concern because of their effects on grain or straw yield and quality.

Strategies for managing wheat diseases and pests include host resistance, chemicals, cultural practices, biological control, and integrated disease management. Most globally important diseases are caused by either biotrophic or necrotrophic fungi. Some seedborne diseases, such as smuts and bunts, have been efficiently controlled through seed sanitation strategies, including seed treatment with chemicals. In contrast, management of some other diseases has required multiple strategies and global efforts to reduce major crop losses. Some fungal diseases of global importance in reducing yields are discussed below as examples.

DISEASES CAUSED BY BIOTROPHIC FUNGI

Biotrophic fungi are obligate parasites that attack only living plants and cause such globally important diseases of wide distribution as leaf rust (LR; or brown rust, caused by *Puccinia triticina*), stripe rust [or yellow rust (YR) caused by *Puccinia striiformis* f. sp. *tritici*], stem rust (SR; or black rust, caused by *Puccinia graminis* f. sp. *tritici*) and powdery mildew (PM caused by *Blumeria graminis* f. sp. *tritici*). The causal pathogens also have many distinct strains or physiologic races determined by testing host response to infection on a set of tester lines carrying different resistance genes or their combinations. Rusts and mildew have been a major focus of research and breeding because of their ability to overcome deployed race-specific resistance genes in a short time, leading to the phenomenon commonly known as “Boom and Bust” and causing major yield losses.

Leaf Rust

LR is the most widely adapted disease of wheat on a global basis, and its main epidemic regions are spread throughout the Americas, Europe, South, Central, and North Asia, South and North Africa, and Australia, causing various levels of damage (62). In the United States, economic losses of \$350 million were attributed to LR between 2000 and 2004. In China, annual yield losses due to LR are estimated at 3 million tons. In the past, it was also a devastating disease in Mexico and South Asia but has become negligible in recent decades because of cultivars protected by slow rusting resistance genes (41).

Stem Rust

SR is the most devastating rust disease and has wide distribution globally, especially in Africa, the Americas, Europe, and Australia (97). Historically, it caused yield losses of 19.3–28.4% in

13.2

Singh et al.



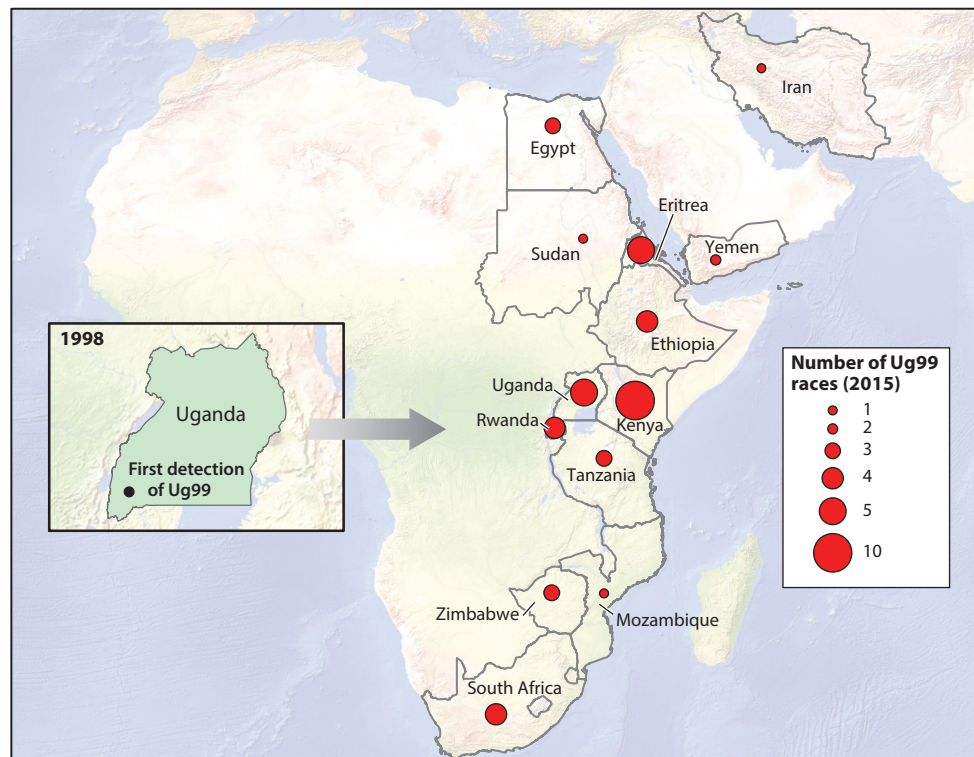


Figure 1

Change in number and spread of detected Ug99 races of stem rust between 1998 and 2015 (92, 93).

the United States from the 1910s to the 1950s; however, SR has been under satisfactory control since 1954 because of the wide adoption of resistant cultivars and the removal of barberry, the alternate host of the SR fungus (93). Epidemics also remained low globally for three decades in the past century except for major epidemics in Ethiopia in 1993 and 1994 on Enkoy, which carries resistance gene *Sr36*. SR reemerged in the form of the Ug99 race, causing great economic losses (92). First detected in Uganda in 1998, Ug99 and its related races are now known in several eastern and southern African countries, Yemen, Iran, and Egypt, threatening these and other wheat growing regions (**Figure 1**) (93).

Yellow Rust

YR has traditionally occurred on wheat in cooler and wetter regions, including Asia and Europe. However, since 2000, new aggressive races that are adapted to warmer climates have spread to other continents and caused severe losses in many countries (**Figure 2**) (111). YR generally causes yield reductions of 5% to 50%, depending on the year, the region, and the developmental stage of wheat plants. According to a recent estimation, annual yield reductions of 5.47 million tons of wheat are attributable to this disease, which is equivalent to annual losses of \$979 million (7). In Australia, YR is the most damaging rust disease, causing average annual economic losses of AUD\$127 million (71).

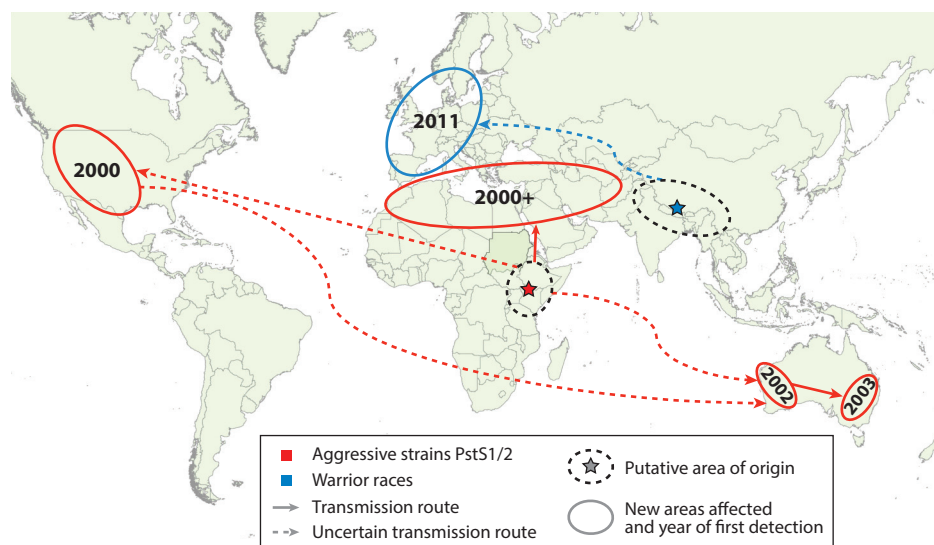


Figure 2

Schematic overview of the recent emergence and spread of important new races of stripe rust fungus (2, 37, 38, 39). The spread of PstS1 to the United States and Australia represents the introduction of a single lineage. The appearance of the Warrior race group across large areas in Europe within the first year of detection represents the incursion(s) of genetically diverse strains.

Powdery Mildew

PM has a global distribution but is especially important in regions with dry and cool climates, including China, Europe, and the Southern Cone of South America (21). In recent decades, this disease has become important even in some warmer and drier regions because of intensive production with higher plant densities, nitrogen fertilizers, and irrigation (16). Although commercial yield losses in Western Europe are generally below 10%, a record high of 20% was reported in the United Kingdom, 5–17% in North Carolina, 10–15% but sometimes reaching 30–35% in Russia, up to 62% in Brazil, and 30–40% in China under heavy epidemics (65). Generally speaking, yield reductions of higher than 40% are rare, but early infections may lead to the death of seedlings or tillers that eventually fail to produce seeds (19).

DISEASES CAUSED BY NECROTROPHIC FUNGI

Necrotrophic fungi are facultative parasites surviving on dead tissues and do not necessarily need living plants. The most important diseases caused by necrotrophs are *Fusarium* head blight (FHB), the leaf spotting diseases (LSDs) involving *Septoria tritici* blotch (STB), tan spot (TS), spot blotch (SB), and *Stagonospora nodorum* blotch (SNB), and, more recently, wheat blast (WB) in South America.

Fusarium Head Blight

Worldwide reemergence of FHB with severe epidemics in the 1990s threatened several major wheat producers, including China, the United States, Canada, Argentina, and some European countries (12). The various *Fusarium* species are capable of infecting all plant parts and have

a very broad host spectrum. In wheat, they cause crown rot and root rot, but FHB is the far more important disease. More than 17 species of *Fusarium* cause FHB; but *Fusarium graminearum* is the most important globally. The disease is promoted by warm and humid environments at anthesis, resulting in yield reductions, quality deterioration, and, more significantly, mycotoxin contamination. Deoxynivalenol (DON; or vomitoxin) produced by *F. graminearum* and *Fusarium culmorum* is the most frequently encountered mycotoxin and is a virulence factor on wheat and is toxic to humans and animals (12). The disease is expanding rapidly in many regions. A good example is China, where the epidemic area has expanded to major wheat production regions, including the Yellow and Huai River valley wheat zones and the northern winter wheat zone, because of the lack of resistant cultivars and an increase in acreage with no-tillage cultivation and maize-wheat rotation (116).

Early FHB infections around anthesis often cause floret sterility or poor grain filling, leading to higher yield losses, whereas later infections could have low yield impacts but may lead to high DON content (12). The thresholds of DON content in wheat and its products are now regulated in many countries; the market price of wheat grain is sharply reduced if DON concentration exceeds the thresholds, and grain may completely lose its market value under heavy DON contamination (64). In the United States, economic losses attributable to FHB in wheat and barley between 1993 and 2001 were \$7.67 billion, but annual losses varied greatly, e.g., \$2.59 billion (29.9%) was lost from 1998 to 2001 (64). Approximately 18% of the wheat area in northwestern Minnesota was not harvested in 1994 due to heavy FHB (64). In China, 12 severe and 17 moderate FHB epidemics were recorded between 1950 and 2012, with an occurrence frequency of 46%. FHB usually causes 5–10% of yield losses in China, but the damage can increase to 20–40% under severe epidemics and can even reach 100% (12, 13). Yield reductions in Europe and South America can reach up to 50–60% and 70%, respectively (12, 47, 65).

Leaf Spotting Diseases

The LSD complex comprises STB, TS, SB, and SNB. Wheat is often infected simultaneously by multiple LSDs, but the components differ from region to region despite similar symptoms. LSD-induced yield losses under favorable conditions can be higher than 50% (24, 35, 90). Susceptible germplasm usually exhibits poor grain filling, lower test weight, and fewer kernels per spike, leading to serious quantity losses in addition to quality deterioration represented by shriveled kernels, red smudge, salmon-pink or red discoloration, and black point (61, 90). Increases in the occurrence of LSD epidemics were attributed to the expansion of conservation agriculture (CA), with stubble retention on soil surface. In addition, intensified wheat production, including shorter crop rotations, monoculture, and susceptible cultivars, also contributed significantly to the expansion of LSDs in epidemic proportions worldwide. Increasing temperatures and drought due to climate change may further result in a higher degree of leaf senescence that will favor LSD diseases.

STB, also known as speckled leaf blotch, is caused by the *Zymoseptoria tritici* (syn. anamorph *Septoria tritici*; teleomorph *Mycosphaerella graminicola*), and the pathogen is seed transmitted, heterothallic (two mating types), has high genetic variation, can be seed-transmitted, and survives on dead or dying host tissues in its nonparasitic phase, producing many windborne ascospores, which play a major role in distribution. Losses can range from 30–50% during severe epidemics but typically are lower (27). Epidemics are most severe in areas with extended periods of cool, wet weather, particularly North America (United States, Canada, and Mexico), East Africa (Ethiopia and Kenya), and South America (Brazil, Chile, Uruguay, and Argentina), and the most damage occurs in Europe and in the Central and West Asia and North Africa (CWANA) region (35).



TS, also known as yellow spot or yellow leaf blotch, and caused by *Pyrenophora tritici-repentis* (anamorph *Drechslera tritici-repentis*) has two distinct symptoms, necrosis and chlorosis, on susceptible cultivars. TS occurs in North America (United States, Canada, and Mexico), South America (Brazil, Argentina, and Uruguay), the CWANA region, South Asia, and Australia, where it is considered the most important disease causing average annual losses of AUD\$212 million (71). The TS fungus is a homothallic and hemibiotroph pathogen but is considered to be a necrotroph, as it causes extensive tissue damage to the host in its parasitic phase, but also survives on dead or dying host tissues in its nonparasitic phase. Eight races of TS fungus are known worldwide, as determined by their ability to induce necrosis and chlorosis symptoms on a set of differential cultivars (90).

SB, also called Helminthosporium leaf blight or foliar blight, is caused by *Cochliobolus sativus* (anamorph *Bipolaris sorokiniana*) and affects approximately 25 million ha of wheat in the warmer regions of Bangladesh, Nepal, Bolivia, eastern India, Brazil, southeast China, southeast Australia, northeast Argentina, Paraguay, Zambia, northern Kazakhstan, and the Great Plains of the United States and Canada (23). Heat and drought stresses and the low inputs of nutrient and water increase disease severity. Yield losses from 40–85% were reported in the Philippines and Zambia (50, 77). The fungus is a hemibiotroph, exerting a biotrophic phase during initial infection followed by a necrotrophic growth phase, and is heterothallic, requiring opposite mating types for sexual reproduction.

SNB, also called Septoria glume blotch, is caused by *Parastagonospora nodorum* (anamorph *Stagonospora nodorum*) and is a necrotrophic fungus that infects both glumes and leaves causing glume and leaf blotch, respectively. SNB causes substantial yield losses in Europe, North America, and Australia. However, since the 1980s, importance of SNB has been reduced in Western Europe and it was largely replaced by STB. According to Murray & Brennan (71), SNB causes annual yield losses of AUD\$108 million in Australia. SNB, a seedborne disease, is more prevalent in areas with a rainy, moist spring and more damaging when those conditions persist until the heading stage. The pathogen produces several proteinaceous necrotrophic effectors, or host-selective toxins (HSTs), that increase disease severity. The HSTs interact with the host genes in an inverse gene-for-gene manner (toxin model) wherein products of sensitivity genes in the host recognize the effectors produced by the fungus and trigger a hypersensitive response, leading to increased susceptibility in the field. Although seven HSTs have been identified (32), indicating pathogen diversity, race specialization remains inconclusive.

Wheat Blast

WB, or brusone, caused by *Magnaporthe oryzae* (anamorph *Pyricularia oryzae*) has emerged as a highly significant disease in the tropical parts of the Southern Cone of South America. First reported in the state of Paraná in Brazil in 1985, the pathogen has spread to Bolivia, Paraguay, and Argentina (48). The highest losses occur when fungus attacks the rachis at the base of the spike, affecting total or partial spike death or grain filling, depending upon the time of infection (22). Most severe blast years were characterized by continuous rainfall with average temperatures of 18–25°C during the flowering stage, followed by sunny, hot, and humid days, with yield losses of 10–100%, depending on the year, cultivar, and planting date (22, 48, 65). Early records from 1988–1992 indicate 11–55% yield reductions in Brazil on the highly susceptible cultivar Anahuac. In the mid-1990s, Anahuac was withdrawn; however, the situation did not change much with cultivars that improved resistance (104). More strikingly, even under two applications of fungicide, yield reductions of 14–32% were observed for two widely grown cultivars under the 2005 blast epidemics in Brazil (104).



SIGNIFICANT CHANGES IN PATHOGEN POPULATIONS

The evolution and spread of new virulent race lineages of both SR and YR fungi had significant impacts during the past two decades and resulted in global efforts to mitigate epidemic threats (38, 93). The Ug99, or TTKSK, race of SR fungus, first detected in Uganda in 1998, possesses a unique combination of virulence involving *Sr31* and numerous other resistance genes deployed worldwide (76, 93). The speed of its spread to 13 countries in Africa and the Middle East and a rapid increase in the number of variants to 13 within the Ug99 lineage both contribute to it being a major threat to wheat yields (**Figure 1**). The global threat to food security is high because the majority of cultivars grown worldwide lack adequate resistance.

In 2014, five new Ug99 variants were identified in Kenya. The two most significant variants, TTKTK (Ug99+*SrTmp* vir) and TTKTT (Ug99+*Sr24*+*SrTmp* vir), added virulence to resistance gene *SrTmp* and caused susceptibility of the widely grown cultivar Robin in Kenya. Race TTKTK was also detected in Uganda, Rwanda, Eritrea, and Egypt in 2014. The Ug99 race group is not the only cause of the current stem rust problem in East Africa. In Ethiopia, another *SrTmp* virulent non-Ug99 race TKTTF was detected at trace levels in 2012 on the popular cultivar Digalu and has caused continuing epidemics since 2013 (74). The rapid spread of race TKTTF in Ethiopia and *SrTmp* variants of Ug99 in neighboring countries has increased rust populations in East Africa, with serious consequences for farmers in the region and enhanced vulnerability globally.

Since 2000, two new, closely related strains, PstS1 and PstS2, of the YR fungus were identified and spread to North America, Australia, and Europe in fewer than 3 years (**Figure 2**) (2, 39). PstS1 shows adaptation to warmer temperatures and exhibits increased aggressiveness, causing epidemics in the south-central United States from 2000 onward (68). The same strain PstS1 was detected in Mexico and Western Australia in 2002, with subsequent spread to eastern Australia the following year (110). PstS2 was reported in Europe (Austria and Germany in 2000, then Scandinavia in 2001), the Mediterranean, the Middle East, and East Africa (39). Subsequent genetic population studies have indicated that East Africa is the putative origin of these highly aggressive races (107). Since 2010, virulence to the important resistance gene *Yr27* within the PstS1/2 backgrounds resulted in major YR epidemics across the CWANA, South Asia, and East Africa regions. In Ethiopia, the most severe YR epidemic in decades occurred in 2010 on the popular cultivars Kubsa and Galema and resulted in dramatic shifts in cultivars and control strategies. Several variants of the PstS1/S2 lineages adding new virulences to deployed resistance genes have since emerged, further threatening wheat yields worldwide even in several areas where YR was considered insignificant.

In 2011, a new exotic incursion of YR fungus, the Warrior race group causing susceptibility of the UK cultivar Warrior, was detected in several European countries (37). This race group was found throughout Central and Western Europe in the first year of detection, with many previously resistant cultivars becoming susceptible, and, conversely, some previously susceptible cultivars becoming more resistant (100). The Warrior race group is genetically diverse and highly divergent from previous western European populations, with a likely origin in the near Himalayan region (2, 37), and is now spreading into Africa and the Middle East, with confirmed presence in Morocco in 2013 and Algeria and Turkey in 2014 (66, 79). The Warrior race group serves as another example of the recent, rapid emergence, spread, and colonization of new rust lineages with increased aggressiveness and complex virulence profiles of potential global significance.

Gain-of-virulence in necrotrophic pathogens is less common. A well-known example is the breakdown of the STB resistance gene *Stb4* in the highly resistant cultivar Gene released in 1992 in the United States. Its resistance was reduced substantially by 1995 and was completely defeated in 1997 (15). This demonstrated that the resistance of Gene was race-specific, allowing selection



of virulent isolates in the local population of the pathogen. The *Stb1* resistance gene, however, maintained its effectiveness for more than 25 years (15). Nevertheless, as stated by Goodwin (35), the gene-for-gene interactions in STB are generally weak, but the virulent races can cause infections as severe as those of rusts and PM.

EVOLUTION OF RESISTANCE TO FUNGICIDES IN PATHOGEN POPULATIONS

Most foliar fungicides used widely in wheat are demethylation inhibitors (DMIs), quinone outside inhibitors (QOIs), or methyl benzimidazole carbamates (MBCs), and the newly developed succinate dehydrogenase inhibitors (SDHIs). Fungal isolates resistant to MBC and QOI fungicides were found after only 2–3 years of use (6, 8, 42). In the United Kingdom, MBC resistance in the eyespot pathogen was observed in 1981 (46), only seven years after the increasing use of MBC fungicides for eyespot control. When a pathogen isolate develops resistance, it is also typically resistant to other fungicides of the same group.

STB pathogen isolates with resistance to QOIs developed quickly, following a few years of intensive use, and existed before these fungicides were deployed. Once deployed, the resistant isolates dramatically increased in frequency in Europe, Tunisia, Morocco, and the United States (25). STB fungal insensitivity to DMIs has gradually been observed during the past 10–15 years, and the first isolates have already been reported in recently introduced SDHIs from regions with high disease pressure and intensive use of fungicides (87).

Fungicide resistance is also reported in PM and rusts (20), but the situation is not as grave as in STB. QOIs were used for controlling PM and rusts in northern Germany but rapidly lost effectiveness to PM because of intensive application. DMIs were used in the United Kingdom for YR, and 54% isolates were found to be less sensitive. Felsenstein et al. (29) tested 2,509 isolates of *B. graminis* for sensitivity toward metrafenone and found that the proportion of insensitive strains increased after the fungicide exposure; but only 3.4% were classified as moderately insensitive and merely 0.3% as resistant. Similarly, Reimann & Deising (78) demonstrated the induced strobilurin fungicide insensitivity in the TS pathogen and attributed this to the activation of fungal efflux transporters.

For FHB, reduced fungicide effectiveness is also reported. In China, benzimidazole fungicides represented by carbendazim have been used extensively to control FHB since the 1970s. The resistance to benzimidazole in *F. graminearum* populations has been detected since 1992 (113). The use of DMI fungicides in China has also led to increased insensitivity in the FHB pathogen population, although this has not yet caused a problem in the field (113). DMI insensitive isolates were also reported in Europe and the United States (101); however, DMI fungicides are still considered effective.

DISEASE CONTROL STRATEGIES

Intensive Agriculture in Western Europe

Wheat in Western Europe is grown under high rainfall conditions and high fertilizer inputs, which permit ideal conditions for YR, PM, LR, STB, FHB, and eyespot. The use of disease-resistant cultivars represents a significant potential for reducing disease severity and the need for fungicide treatment (14, 45, 57). Intensive resistance breeding during the 1960s successfully led to cultivars with high disease resistance, thereby reducing disease prevalence and severity. However, the use of systemic fungicides has become a common practice since their introduction in the 1980s and, to some extent, reduced the importance of genetic resistance in disease control. Today, the common



European agricultural policy questions the increasing dependency on pesticides and states that from 2014 all European Union members should have implemented integrated pest management (IPM) with the aim of reducing the impact and use of pesticides (26).

For YR, LR, PM, and eyespot, race-specific resistance genes can provide highly effective disease control, despite their vulnerability to the emergence and selection of new virulent races. Susceptible cultivars can be easily replaced with those that are resistant because of the presence of various private seed companies continuously releasing new varieties and their ability to produce and disseminate large seed quantities in a relatively short time. Although resistance to STB and PM was less predominant in European wheat cultivars, no high-yield penalties were observed for multiple disease-resistant cultivars in France and the yield gap between multiple disease-resistant and susceptible cultivars has decreased (57). This contrasts with past experiences in the United Kingdom, where resistant cultivars often produced a lower yield than did susceptible cultivars in the absence of disease (9). Grain yield is generally ranked as the most important factor for farmers' choice of cultivars, followed by quality parameters and then disease resistance. The most resistant cultivars often give profitable yield responses to fungicide treatment, indicating that disease resistance rarely covered all diseases and that fungicide treatment may have positive physiological effects on the crop (6). Despite this, resistant cultivars clearly reduce potential yield losses and costs spent on fungicides (14, 45). The cost of disease control can be halved if resistant cultivars are chosen, and low input strategies in France with resistant cultivars have led to yields similar to those of high input systems with susceptible cultivars (57).

Small-Scale Farmers of Ethiopia

Wheat is produced primarily under rainfed conditions, but with varying levels of rainfall, by 5 million households on 1.7 million ha in Ethiopia, with SR, YR, and STB considered the most important diseases. The East African highlands are a hot spot for rusts because of diverse agroecologies that allow continuous wheat cropping, favorable climatic conditions, and reliance on a few cultivars with single race-specific resistance genes. Recurring rust epidemics have challenged food security and farmer livelihoods. Small-holder wheat farmers in Ethiopia and neighboring East African countries rely mainly on resistant cultivars for disease control.

The recent, rapid changes in races of rust fungi have had a severe impact on farmers through a series of epidemics. Cultivars, possessing single race-specific genes, quickly gained large area shares only to be rapidly overcome by new races of either YR or SR fungi. The 2010 YR epidemic was the most severe in recent history, resulting in major production losses on an estimated 0.6 million ha equivalent to 30% of the total area. Despite spraying \$3.2 million worth of fungicides, individual on-farm losses of 70–100% in the worst affected areas and national production losses of 15–20% (approximately 0.5 million tons) occurred (1). Widespread cultivation of susceptible cultivars Kubsa and Galema, the presence of an aggressive *Yr27*-virulent race, an extremely favorable climate, and a lack of timely access to and/or ineffective use of registered fungicides in many areas contributed to the losses.

Although increasing, the overall use of fungicides remains low in Ethiopia compared with use in the United Kingdom (roughly equivalent wheat acreage) based on 1995–2010 trends (**Figure 3**). The 2010 YR epidemic was a turning point in promoting the more widespread use of fungicides in Ethiopia, especially in high potential areas. Increases in on-farm wheat yields and the availability of more affordable fungicides are contributing factors to the fungicide-use trend. However, the challenges of obtaining effective rust control through fungicides in a diverse, small-holder farming system like Ethiopia are numerous. Limitations include cost, availability at critical times, distribution to remote areas, training in effective and safe use, appropriate application methods, and



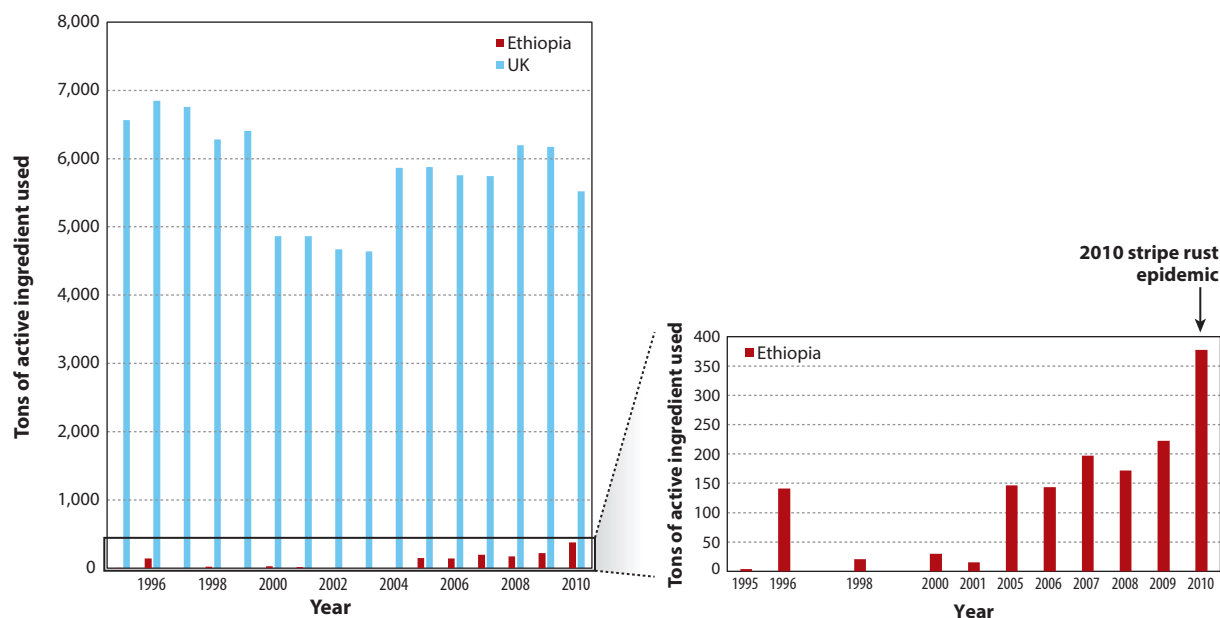


Figure 3

Contrasting fungicide use in the United Kingdom and Ethiopia between 1995 and 2010 and the trend in fungicide use in Ethiopia (31).

optimal timing of application for different diseases (e.g., SR versus YR). Genetic control remains the best option for the majority of wheat farmers in the foreseeable future.

Heavy losses to YR in 2010 provided a strong impetus for Ethiopian wheat farmers to adopt new YR- and SR-resistant cultivars such as Digaalu, released in 2005. Despite predicted vulnerability to SR due to protection by a single resistance gene, *SrTm*p (105), Digaalu became popular with farmers and covered approximately 0.5 million ha by 2013. Cultivars Danda'a and Kakaba, released in 2010 and with moderate SR resistance, were also spread on 10% of the growing area. The *SrTm*p virulent race TKTTF, within a matter of weeks from detection in 2013, caused severe epidemics on an estimated 20,000–40,000 ha, and yields were reduced to 0.3 t/ha in the worst affected areas, representing >90% losses. Average yield losses on Digaalu in three districts at the core of the 2013/14 epidemic were estimated at 51% (74). Continued extensive cultivation of Digaalu in 2014/15 due to the lack of seeds of replacement varieties, ineffective fungicide use, and/or the lack of fungicide availability resulted in repeat epidemics on 30,000–50,000 ha, with near complete losses on individual farms and devastating impacts on households.

Ethiopia represents perhaps one of the most challenging situations for disease control encountered by smallholder farmers. Implementing a holistic approach includes the development and promotion of genetically diverse rust-resistant cultivars, fast-track releases in 2015, seed multiplication of cultivars such as Kingbird with high levels of adult plant resistance (APR), extensive awareness, and training campaigns around effective fungicide use, and the development of a rust early warning system.

BREEDING RESISTANT CULTIVARS TO REDUCE DISEASE IMPACTS

Wheat germplasm has high genetic diversity for its resistance to a number of diseases, and numerous race-specific and some durable resistance genes have been characterized (63). This diversity

has been further enriched by systematically transferring a number of resistance genes from various species and genera related to wheat through cytogenetic interventions. The race-specific, or major, genes usually confer resistance from the seedling growth stage to physiological maturity, but in some cases resistance expression initiates at later growth stages. Moreover, the magnitude of resistance conferred by these genes varies to a great extent, ranging from immunity to only small reductions in disease symptoms. Although several known race-specific rust and PM resistance genes were overcome by matching virulences in the pathogen population, opportunities to enhance their longevity exist by pyramiding multiple, undefeated genes through marker-assisted selection (MAS).

Durable resistance is often conferred by quantitative trait loci (QTLs), which have small to intermediate but additive effects, and the accumulation of multiple QTLs can lead to a high level of APR approaching near immunity (95). Although many QTLs are known to confer resistance to rusts and PM (52, 80, 114), three pleiotropic multipathogen resistance genes are known, of which *Lr34/Yr18/Sr57/Pm38* and *Lr67/Yr46/Sr55/Pm46* are cloned and found to confer resistance through novel mechanisms (49, 70). Breeding at CIMMYT, targeted for small-holder farmers in Asia, Africa, and Latin America, strongly emphasizes selecting high-yielding wheat germplasm that possesses high levels of rust resistance based on diverse combinations of multiple pleiotropic resistance genes and other QTLs with significant progress made for all three rusts (92, 93). Deployment of CIMMYT-derived wheat cultivars with APR in Mexico, Asia, and Africa has stabilized LR fungal populations for more than two decades in contrast to other regions such as South America where race-specific resistance genes were used (33). We believe that success in achieving high levels of complex APR to rusts in the CIMMYT high-yielding germplasm pool will enhance resistance durability, provide excellent yield protection, and free up resources to focus on much needed, accelerated yield enhancement and make progress toward resistance in other diseases that are gaining importance.

FHB resistance is highly quantitative and conditioned by numerous moderate-to-minor effect genes. Different resistance mechanisms, e.g., invasion (Type I), fungal spread (Type II), toxin accumulation (Type III), kernel infection (Type IV), and yield reduction (Type V), further enhance the complexity (67). Heading, plant height, and anther extrusion also show significant correlations with FHB resistance (12). Although resistance QTLs were identified on all 21 chromosomes (53), only seven are designated as FHB resistance genes, of which only *Fhb1*, *Fhb2*, *Fhb4*, and *Fhb5* are from wheat and *Fhb3*, *Fhb6*, and *Fhb7* from wild relatives (36). Progress in breeding has been relatively slow and the development of high-yielding cultivars with resistance similar to the old Chinese cultivar Sumai 3 remains a breeding challenge.

Diversity for STB resistance is high, and both major and minor genes are known. The major genes tend to follow the gene-for-gene interaction and thus are race-specific. To date, 21 resistance genes are identified and tagged by molecular markers (10). Although these race-specific genes are unlikely to be durable, changes in the pathogen population are relatively slow and often resistance remains effective for decades. A combination of several minor genes of moderate-to-small effects leads to resistance durability. To date, 89 meta-QTLs have been identified; however, some QTLs are mapped at or near known genes, especially *Stb6*, which is present in several sources of resistance (10). New broad-spectrum resistance to STB derived from synthetic hexaploid wheat was also recently identified (34, 88). Breeding semidwarf, high-yielding wheat germplasm initiated at CIMMYT in the early 1970s and the accumulation of both major and minor genes in current germplasm trace to diverse origins, including synthetic wheats. It is also common to find high-yielding lines that combine high levels of resistance to rusts and STB under high disease pressures in Mexico, Ethiopia, and other target environments worldwide, indicating that STB can be effectively controlled through genetic resistance.



Both major and minor genes confer resistance to TS; the fungus produces at least three HSTs, known as Ptr ToxA, Ptr ToxB, and Ptr ToxC, which interact directly or indirectly with the products of the dominant host genes *Tsn1*, *Tsc2*, and *Tsc1*, respectively. Host resistance is therefore highly correlated to toxin insensitivity, and eight race-specific genes are known. Wheat-*P. tritici-repentis* interaction largely follows the toxin model of the gene-for-gene hypothesis, although other mechanisms of host-pathogen interaction, including several broad-spectrum QTLs and recessively inherited resistance genes are also known. Incorporating all types of resistance can possibly be achieved through MAS of HST insensitivity genes and race-nonspecific resistance simultaneously (28, 90). Resistance to TS appears to be durable, and adequate resistance for multiple LSDs can be readily found in improved CIMMYT wheat germplasm.

Resistance to SB is mostly quantitative but highly heritable. With major emphasis on breeding SB resistance, CIMMYT has successfully developed moderately resistant germplasm with the desired phenology, i.e., early and semidwarf along with high yield potential (91). Several studies on the association of SB resistance with agronomic and morphological traits, e.g., plant height, leaf angle, maturity, and stay green, have been conducted in association with leaf tip necrosis studied in detail. The pleiotropic rusts and mildew resistance gene *Lr34/Yr18/Sr57/Pm38/Ltn1* was shown to confer partial resistance to SB and designated as *Sb1* (91). Recently, Kumar et al. (51) and Lu et al. (58) mapped the *Sb2* and *Sb3* genes on chromosomes 5B and 3B, respectively. Developing highly resistant germplasm by combining different resistance genes is expected to provide better yield protection, especially under high disease pressures in warm and humid conditions.

Resistance to SNB is generally controlled by several independently inherited loci, conferring leaf and spike resistance. These genes are subject to environmental and pleiotropic effects, including plant height and heading time (103). Monogenic resistance has been reported only in some studies under controlled conditions, whereas quantitative resistance is observed in field studies (30, 89).

Knowledge on resistance to WB has also progressed despite being a relatively new disease and confined to South America and, as of 2016, to Bangladesh. Cultivars such as BH1146, BR18, IPR85, CD113, and CNT8 were found to possess moderate resistance levels, and derivatives of CIMMYT line Milan displayed much better resistance across years and locations (48). Both qualitative and quantitative resistance are thought to be present, but the former has been validated only at the seedling stage (60). So far, five resistance genes, designated *Rmg1*–*Rmg5*, have been identified in common wheat (4, 72). A recent finding indicated that the 2NS/2AS translocation from *Aegilops ventricosa* confers WB resistance with 50.4–80.5% reduction in disease (18). However, unpublished reports from Paraguay show the presence of new isolates that have overcome this resistance. Breeding for resistance is expected to remain challenging, as some of the identified resistance genes are race-specific and relatively few resistance sources are known to date.

COST OF DISEASE RESISTANCE ON YIELD IMPROVEMENT

Some wheat studies have investigated the cost of disease resistance genes on yield in the absence of disease, often by developing near isolines through repeated backcrossing in a susceptible cultivar. The et al. (102) backcrossed the SR resistance gene *Sr26*, located on a wheat-*Thinopyrum* translocation, in a set of Australian varieties and found that, although some lines with yields similar to recurrent parents were recovered, on the average the presence of this gene caused grain yield reductions. The et al.'s (102) study is often cited despite the fact that the resistance gene *Sr26* was present in some widely grown cultivars within Australia. Another interesting case is the widely deployed wheat-rye translocation 1BL.1RS, which carries resistance genes *Sr31*, *Lr26*, *Yr9*, and *Pm8* for which various studies comparing the yield effects are published and positive, null, and



13.12 Singh et al.

negative effects are reported depending on the background (96). In the absence of disease, *Lr41* had no effect on yield, but quality was affected (17). The presence of another wheat-*Thinopyrum* translocation carrying *Lr19* and *Sr25* enhanced grain yield under irrigated conditions but reduced yield under drought stress (96). Comparing resistance and susceptibility alleles at the *Lr34* locus in wheat selections from the heterogeneous cultivar Jupateco 73, Singh & Huerta-Espino (94) found that the resistant reselection was slightly lower yielding. However, comparing mutants with small deletions in the gene sequence failed to show any grain yield penalty in our recent studies. Various defeated resistance genes are commonly found in high-yielding wheat germplasm, indicating a lack of selection disadvantage. Studies of the impact of the FHB resistance allele at the *Fhb1* locus on yield and other agronomic traits have failed to show a yield penalty in the absence of disease (5, 84, 106).

The observed negative effects on yields are likely due to linkage rather than pleiotropy, and the negative effects of resistance genes in the absence of disease in terms of grain yield or fitness vary on a case-by-case basis and genetic background. Despite the yield penalties of resistance observed in some cases, breeding programs have been able to successfully improve both resistance and yield, although the rate of progress for both traits is likely to be adversely affected simply on probabilities. Selection for both disease resistance and yield is common in many breeding programs and at CIMMYT. Based on quantitative genetic theory, also relevant for complex disease resistance, selecting for more than one gene/trait should lead to lower genetic gain relative to the gain that could be achieved if only one trait/gene was targeted. However, selecting for all traits of interest is required to most effectively improve net merit, which is the overall value to farmers. The CIMMYT breeding program has employed strong simultaneous selection pressures for both grain yield and disease resistance, which has required expanding the population sizes in various segregating generations and the testing of a larger set of advanced breeding lines. This strategy has maintained the rate of genetic progress for grain yield similar to breeding programs that have focused largely on grain yield (55, 86).

IMPROVING DISEASE RESISTANCE THROUGH MARKER-ASSISTED SELECTION, GENOMIC SELECTION, AND GENETIC MODIFICATIONS

MAS has been used for selecting resistance to some diseases in wheat; however, the majority of breeding programs continue to rely on phenotypic selection because of high cost of genotyping, lack of reliable markers, and high phenotypic selection accuracy. By using a marker closely linked to resistance gene *Fhb1*, Anderson et al. (3) were able to screen and cull a large number of F₄ lines to effectively increase the level of FHB resistance. However, field phenotyping was still necessary to capture other resistance QTLs. Jefferies et al. (43) successfully applied backcross selection for incorporating the *Barley yellow dwarf virus* resistance gene *Yd2*. Somers et al. (99) incorporated multiple resistance genes into Canadian wheat breeding lines in 25 months, using foreground and background selection.

Marker-assisted gene pyramiding of multiple race-specific resistance genes to increase durability is widely proposed; however, closely linked markers are needed, and this approach can be time consuming, allowing the pathogen to defeat one or more resistance genes in case cultivars carrying them singly are already grown. Resistance gene pyramids must also be reconstructed every time a new cross is made because of the segregation of these loci. Overall, MAS for major effect resistance genes can be effective when closely linked markers are available, but rapid introgression strategies, or forward selection, are needed to ensure that lines developed remain competitive and cultivars with single genes are not deployed.



For disease resistance conferred by multiple small effect loci, genomic selection (GS) is a better approach than MAS. With GS, reviewed by Lorenz et al. (56), a model training population that is both phenotyped and genotyped is used to calibrate a prediction model that is used to predict breeding values, enabling selection of candidates prior to phenotyping. In wheat, cross-validation studies have been conducted to evaluate the potential of GS for FHB (69, 81) and STB (69), and APR to SR (75, 82). Some studies have concluded that GS would lead to greater rates of genetic gain compared with MAS (81, 82) and phenotypic selection (69). However, implementing both genomic and phenotypic selection in parallel for quantitative SR resistance (83) found that with equal selection intensities, genetic gains per unit time from genomic and phenotypic selection were equal. For quantitative disease resistance, greater selection intensities under GS may be needed to outperform phenotypic selection. Although GS is more effective than MAS for polygenic traits, GS prediction models must be continually updated to maintain prediction accuracy.

Transgenic and genome editing are other technologies available for genetic control of disease in wheat. Transformation of genes involved in defense can improve resistance against FHB (12). Transgenesis also improved resistance to take all (54), *Wheat streak mosaic virus* (98), *Barley stripe mosaic virus* (115), LR (59), YR (40), and PM (11). Successful cloning of some wheat rust resistance genes offers opportunities to utilize multiple genes on the same construct as *cis*-gene cassettes for enhancing resistance durability (93). The *cis*-gene cassettes with pyramided genes would inherit as a single locus, making it easier to maintain multiple genes in a breeding program. Because *cis*-genes are genes that have originated in species of the same genus or related species and are already utilized in wheat varieties, this concept is possibly a more attractive strategy for consumer acceptance and for simplifying the selection for resistance in breeding programs. Although promising, the feasibility of *trans*- or *cis*-genics is limited by regulatory and consumer acceptance issues. Transgenic wheat cultivars are not grown anywhere in the world at present, and acceptance of *cis*-genic approach is required.

Recently, genome editing, or the targeted modification of a native DNA sequence, was found effective for improving PM resistance in wheat (108) and is considered to have great potential for a range of traits. From a regulatory perspective, genome editing is promising because it is not a transgenic approach and thus may face fewer barriers. The U.S. Department of Agriculture deemed that genome-edited products are not genetically modified organisms, but the European Commission has yet to decide its stand (44).

CONCLUSION

Significant progress has been made since the Green Revolution of the mid-twentieth century in reducing yield losses in wheat caused by diseases, either by growing resistant cultivars or through fungicides. However, evolution and fast spread of more virulent/aggressive pathogen races, selection for fungicide resistance due to excessive use, and the increasing importance of some diseases due to changes in cropping systems and crop intensification require reinforcing breeding strategies to develop adequate and durable resistance to multiple diseases for enhancing wheat productivity and farmers' income worldwide by reducing crop losses. Molecular breeding in conjunction with phenotypic selection provides great promise for harnessing the ample genetic diversity for resistance that exists in wheat for a number of important diseases. Fungicides are crucial in disease management strategies, at least in some hot-spot areas or under emergency situations, but their use should be more rational.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

Singh et al.

13:14



ACKNOWLEDGMENTS

The authors appreciate the technical editing by Julie Mollins.

LITERATURE CITED

1. Abeyo B, Hodson D, Hundie B, Woldeab G, Girma B, et al. 2014. Cultivating success in Ethiopia: the contrasting stripe rust situations in 2010 and 2013. In *Abstracts of BGRI 2014 Technical Workshop*, ed. R McIntosh, Z Pretorius, pp. 22–25. Ithaca, NY: BGRI. <http://www.globalrust.org/sites/default/files/2014%20BGRI%20Plenary%20Abstracts-ALL.pdf>
2. Ali S, Gladieux P, Leconte M, Gautier A, Justesen AF, et al. 2014. Origin, migration routes and worldwide population genetic structure of the wheat yellow rust pathogen *Puccinia striiformis* f. sp. *tritici*. *PLOS Pathog.* 10(1):e1003903
3. Anderson JA, Chao S, Liu S. 2007. Molecular breeding using a major QTL for Fusarium head blight resistance in wheat. *Crop Sci.* 47:S112–19
4. Anh VL, Anh NT, Tagle AG, Vy TTP, Inoue Y, et al. 2015. *Rmg8*, a new gene for resistance to *Triticum* isolates of *Pyricularia oryzae* in hexaploid wheat. *Phytopathology* 105:1568–72
5. Bakhsh A, Mengistu N, Baenziger PS, Dweikat I, Wegulo SN, et al. 2013. Effect of Fusarium head blight resistance gene *Fhb1* on agronomic and end-use quality traits of hard red winter wheat. *Crop Sci.* 53:793–801
6. Bartlett DW, Clough JM, Godwin JR, Hall AA, Hamer M, Parr-Dobrzanski B. 2002. The strobilurin fungicides. *Pest Manag. Sci.* 58:649–62
7. Beddow JM, Pardey PG, Chai Y, Hurley TM, Kriticos DJ, et al. 2015. Research investment implications of shifts in the global geography of wheat stripe rust. *Nat. Plants* 1:15132
8. Bollen GJ, Scholten G. 1971. Acquired resistance to benomyl and some other systemic fungicides in a strain of *Botrytis cinerea* in cyclamen. *Neth. J. Plant Pathol.* 77:83–90
9. Brown JKM. 2002. Yield penalties of disease resistance in crops. *Curr. Opin. Plant Biol.* 5:339–44
10. Brown JKM, Chartrain L, Lasserre-Zuber P, Saintenac C. 2015. Genetics of resistance to *Zymoseptoria tritici* and applications to wheat breeding. *Fungal Genet. Biol.* 79:33–41
11. Brunner S, Hurni S, Herren G, Kalinina O, von Burg S, et al. 2011. Transgenic *Pm3b* wheat lines show resistance to powdery mildew in the field. *Plant Biotechnol. J.* 9:897–910
12. Buerstmayr H, Adam G, Lemmens M. 2012. Resistance to head blight caused by *Fusarium* spp. in wheat. See Ref. 85, pp. 236–76
13. Cheng S, Zhang Y, Bie T, Gao D, Zhang B. 2012. Strategy of wheat breeding for scab resistance in China. *Proc. Int. Symp. Fusarium Head Blight, 4th, Nanjing, China*, Aug. 23–26, p. 5. Nanjing, China: Nanjing Agric. Univ.
14. Couleaud G. 2004. Des programmes à repenser en 2004. *Perspect. Agricoles* 298:62
15. Cowger C, Hoffer ME, Mundt CC. 2000. Specific adaptation by *Mycosphaerella graminicola* to a resistant wheat cultivar. *Plant Pathol.* 49:445–51
16. Cowger C, Miranda L, Griffey C, Hall M, Murphy JP, Maxwell J. 2012. Wheat powdery mildew. See Ref. 85, pp. 84–119
17. Cox TS, Bequette RK, Bowden RL, Sears RG. 1997. Grain yield and breadmaking quality of wheat lines with the leaf rust resistance gene *Lr41*. *Crop Sci.* 37:154–61
18. Cruz CD, Peterson GL, Bockus WW, Kankanala P, Dubcovsky J, et al. 2016. The 2NS translocation from *Aegilops ventricosa* confers resistance to the *Triticum* pathotype of *Magnaporthe oryzae*. *Crop Sci.* 5:1–11
19. Cunfer BM. 2002. Powdery mildew. In *Bread Wheat: Improvement and Production*, ed. BC Curtis, S Rajaram, MH Gomez, pp. 301–8. Rome: FAO
20. Deising HB, Reimann S, Peil A, Weber WE. 2002. Disease management of rusts and powdery mildews. In *Agricultural Applications*, ed. F Kempken, pp. 243–69. New York: Springer
21. Dubin HJ, Duveiller E. 2011. Fungal, bacterial and nematode diseases of wheat: breeding for resistance and other control measures. In *The World Wheat Book: A History of Wheat Breeding*, Vol. 2, ed. AP Bonjean, WJ Angus, M Van Ginkel, pp. 1131–81. Paris: Lavoisier



22. Duveiller E, Hodson D, Sonder K, von Tiedermann A. 2011. An international perspective on wheat blast. *Phytopathology* 101:S220
23. Duveiller E, Kandel YR, Sharma RC, Shrestha SM. 2005. Epidemiology of foliar blights (spot blotch and tan spot) of wheat in the plains bordering the Himalayas. *Phytopathology* 95:248–56
24. Duveiller E, Sharma RC. 2012. Wheat resistance to spot blotch or foliar blight. See Ref. 85, pp. 120–35
25. Estep LK, Torriani SFF, Zala M, Anderson NP, Flowers MD, et al. 2015. Emergence and early evolution of fungicide resistance in North American populations of *Zymoseptoria tritici*. *Plant Pathol.* 64:961–71
26. Eur. Union. 2009. Directive 2009/128/ec of the European parliament and of the council of 21 October 2009: establishing a framework for community action to achieve the sustainable use of pesticides. *Off. J. Eur. Union* <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:309:0071:0086:en:PDF>
27. Eyal Z, Scharen AL, Prescott JM, van Ginkel M. 1987. *The Septoria Diseases of Wheat: Concepts and Methods of Disease Management*. Mexico, D.F.: CIMMYT
28. Faris J, Liu Z, Xu S. 2013. Genetics of tan spot resistance in wheat. *Theor. Appl. Genet.* 126:2197–217
29. Felsenstein F, Semar M, Stammler G. 2010. Sensitivity of wheat powdery mildew (*Blumeria graminis* f. sp. *tritici*) towards metrafenone. *Gesunde Pflanz.* 62:29–33
30. Feng J, Ma H, Hughes GR. 2004. Genetics of resistance to *Stagonospora nodorum* blotch of hexaploid wheat. *Crop Sci.* 44:2043–48
31. Food Agric. U. N. 2015. FAOSTAT database. Rome: FAO. <http://faostat.fao.org/site/291/default.aspx>
32. Gao Y, Faris JD, Liu Z, Kim YM, Syme RA, et al. 2015. Identification and characterization of the Sntox6-Snn6 interaction in the *Parastagonospora nodorum*–wheat pathosystem. *Mol. Plant-Microbe Interact.* 28:615–25
33. Germán S, Barcellos A, Chaves M, Kohli M, Campos P, et al. 2007. The situation of common wheat rusts in the Southern Cone of America and perspectives for control. *Aust. J. Agric. Res.* 58:620–30
34. Ghaffary SMT, Faris JD, Friesen TL, Visser RGF, van der Lee TAJ, et al. 2012. New broad-spectrum resistance to *Septoria tritici* blotch derived from synthetic hexaploid wheat. *Theor. Appl. Genet.* 124:125–42
35. Goodwin SB. 2012. Resistance in wheat to *Septoria* diseases caused by *Mycosphaerella graminicola* (*Septoria tritici*) and *Phaeosphaeria* (*Stagonospora*) *nodorum*. See Ref. 85, pp. 151–59
36. Guo J, Zhang X, Hou Y, Cai J, Shen X, et al. 2015. High-density mapping of the major FHB resistance gene *Fhb7* derived from *Thinopyrum ponticum* and its pyramiding with *Fhb1* by marker-assisted selection. *Theor. Appl. Genet.* 128:2301–16
37. Hovmøller MS, Walter S, Bayles RA, Hubbard A, Flath K, et al. 2015. Replacement of the European wheat yellow rust population by new races from the centre of diversity in the near-Himalayan region. *Plant Pathol.* 65:402–11
38. Hovmøller MS, Walter S, Justesen AF. 2010. Escalating threat of wheat rusts. *Science* 329:369
39. Hovmøller MS, Yahyaoui AH, Milus EA, Justesen AF. 2008. Rapid global spread of two aggressive strains of a wheat rust fungus. *Mol. Ecol.* 17:3818–26
40. Huang X, Wang J, Du Z, Zhang C, Li L, Xu Z. 2013. Enhanced resistance to stripe rust disease in transgenic wheat expressing the rice chitinase gene *Rc24*. *Transgenic Res.* 22:939–47
41. Huerta-Espino J, Singh RP, Germán S, McCallum BD, Park RF, et al. 2011. Global status of wheat leaf rust caused by *Puccinia triticina*. *Euphytica* 179:143–60
42. Ishii H, Fraaije BA, Sugiyama T, Noguchi K, Nishimura K, et al. 2001. Occurrence and molecular characterization of strobilurin resistance in cucumber powdery mildew and downy mildew. *Phytopathology* 91:1166–71
43. Jefferies SP, King BJ, Barr AR, Warner P, Logue SJ, Langridge P. 2003. Marker-assisted backcross introgression of the *Yd2* gene conferring resistance to barley yellow dwarf virus in barley. *Plant Breed.* 122:52–56
44. Jones HD. 2015. Regulatory uncertainty over genome editing. *Nat. Plants*. doi: 10.1038/NPLANTS.2014.11

45. Jørgensen LN, Hovmøller MS, Hansen JG, Lassen P, Clark B, et al. 2014. IPM strategies and their dilemmas including an introduction to www.Eurowheat.org. *J. Integr. Agric.* 13:265–81
46. King JE, Griffin MJ. 1985. Survey of benomyl resistance in *Pseudocercospora berpotricoides* on winter wheat and barley in England and Wales in 1983. *Plant Pathol.* 34:272–83
47. Kohli MM, de Ackermann MD. 2013. Resistance to Fusarium head blight in South American wheat germplasm. In *Fusarium Head Blight in Latin America*, ed. TM Alconanda Magliano, SN Chulze, pp. 263–97. New York: Springer
48. Kohli MM, Mehta YR, Guzman E, De Viedma L, Cubilla LE. 2011. *Pyricularia* blast: a threat to wheat cultivation. *Czech J. Genet. Plant Breed.* 47:S130–34
49. Krattinger SG, Lagudah ES, Spielmeier W, Singh RP, Huerta-Espino J, et al. 2009. A putative ABC transporter confers durable resistance to multiple fungal pathogens in wheat. *Science* 323:1360–63
50. Kumar J, Schäfer P, Hükelhoven R, Langen G, Baltruschat H, et al. 2002. *Bipolaris sorokiniana*, a cereal pathogen of global concern: cytological and molecular approaches towards better control. *Mol. Plant Pathol.* 3:185–95
51. Kumar S, Röder MS, Tripathi SB, Kumar S, Chand R, et al. 2015. Mendelization and fine mapping of a bread wheat spot blotch disease resistance QTL. *Mol. Breed.* 35:218
52. Li Z, Lan C, He Z, Singh RP, Rosewarne GM, et al. 2014. Overview and application of QTL for adult plant resistance to leaf rust and powdery mildew in wheat. *Crop Sci.* 54:1907–25
53. Liu S, Hall MD, Griffey CA, McKendry AL. 2009. Meta-analysis of QTL associated with Fusarium head blight resistance in wheat. *Crop Sci.* 49:1955–68
54. Liu X, Yang L, Zhou X, Zhou M, Lu Y, et al. 2013. Transgenic wheat expressing *Thinopyrum intermedium* MYB transcription factor TiMYB2R-1 shows enhanced resistance to the take-all disease. *J. Exp. Bot.* 64:2243–53
55. Lopes MS, Reynolds MP, Manes Y, Singh RP, Crossa J, Braun HJ. 2012. Genetic yield gains and changes in associated traits of CIMMYT spring bread wheat in a “historic” set representing 30 years of breeding. *Crop Sci.* 52:1123–31
56. Lorenz AJ, Chao S, Asoro FG, Heffner EL, Hayashi T, et al. 2011. Genomic selection in plant breeding: knowledge and prospects. *Adv. Agron.* 110:77–123
57. Loyce C, Meynard JM, Bouchard C, Rolland B, Lonnet P, et al. 2008. Interaction between cultivar and crop management effects on winter wheat diseases, lodging, and yield. *Crop Prot.* 27:1131–42
58. Lu P, Liang Y, Li D, Wang Z, Li W, et al. 2015. Fine genetic mapping of spot blotch resistance gene *Sb3* in wheat (*Triticum aestivum*). *Theor. Appl. Genet.* 129:577–89
59. Luo L, Zhang J, Yang G, Li Y, Li K, He G. 2008. Expression of puroindoline A enhances leaf rust resistance in transgenic tetraploid wheat. *Mol. Biol. Rep.* 35:195–200
60. Maciel JLN, Ceresini PC, Castroagudin VL, Zala M, Kema GHJ, McDonald BA. 2014. Population structure and pathotype diversity of the wheat blast pathogen *Magnaporthe oryzae* 25 years after its emergence in Brazil. *Phytopathology* 104:95–107
61. May WE, Fernandez MR, Selles F, Lafond GP. 2014. Agronomic practices to reduce leaf spotting and Fusarium kernel infections in durum wheat on the Canadian prairies. *Can. J. Plant Sci.* 94:141–52
62. McCallum B, Hiebert C, Huerta-Espino J, Cloutier S. 2012. Wheat leaf rust. See Ref. 85, pp. 33–62
63. McIntosh RA, Yamazaki Y, Dubcovsky J, Rogers J, Morris C, et al. 2012. Catalogue of gene symbols for wheat. <http://www.shigen.nig.ac.jp/wheat/komugi/genes/macgene/2012/GeneSymbol.pdf>
64. McMullen M, Bergstrom G, De Wolf E, Dill-Macky R, Hershman D, et al. 2012. A unified effort to fight an enemy of wheat and barley: Fusarium head blight. *Plant Dis.* 96:1712–28
65. Mehta YR. 2014. *Wheat Diseases and their Management*. New York: Springer. 256 pp.
66. Mert Z, Nazari K, Karagöz E, Akan K, Öztürk İ, Tülek A. 2015. First incursion of the warrior race of wheat stripe rust (*Puccinia striiformis* f. sp. *tritici*) to Turkey in 2014. *Plant Dis.* 100:528
67. Mesterhazy A, Bartok T, Kaszonyi G, Varga M, Toth B, Varga J. 2005. Common resistance to different *Fusarium* spp. causing Fusarium head blight in wheat. *Eur. J. Plant Pathol.* 112:267–81
68. Milus EA, Kristensen K, Hovmøller MS. 2009. Evidence for increased aggressiveness in a recent widespread strain of *Puccinia striiformis* f. sp. *tritici* causing stripe rust of wheat. *Phytopathology* 99:89–94



69. Mirdita V, He S, Zhao Y, Korzun V, Bothe R, et al. 2015. Potential and limits of whole genome prediction of resistance to Fusarium head blight and Septoria tritici blotch in a vast Central European elite winter wheat population. *Theor. Appl. Genet.* 128:2471–81
70. Moore JW, Herrera-Foessel S, Lan C, Schnippenkoetter W, Ayliffe M, et al. 2015. A recently evolved hexose transporter variant confers resistance to multiple pathogens in wheat. *Nat. Genet.* 47:1494–98
71. Murray GM, Brennan JP. 2009. Estimating disease losses to the Australian wheat industry. *Australas. Plant Pathol.* 38:558–70
72. Nga NTT, Hau VTB, Tosa Y. 2009. Identification of genes for resistance to a *Digitaria* isolate of *Magnaporthe grisea* in common wheat cultivars. *Genome* 52:801–9
73. Oerke E-C. 2006. Crop losses to pests. *J. Agric. Sci.* 144:31–43
74. Olivera P, Newcomb M, Szabo LJ, Rouse M, Johnson J, et al. 2015. Phenotypic and genotypic characterization of race TKTTF of *Puccinia graminis* f. sp. *tritici* that caused a wheat stem rust epidemic in southern Ethiopia in 2013–14. *Phytopathology* 105:917–28
75. Ornella L, Singh S, Perez P, Burgueño J, Singh R, et al. 2012. Genomic prediction of genetic values for resistance to wheat rusts. *Plant Genome J.* 5:136–48
76. Pretorius ZA, Singh RP, Wagoire WW, Payne TS. 2000. Detection of virulence to wheat stem rust resistance gene *Sr31* in *Puccinia graminis* f. sp. *tritici* in Uganda. *Plant Dis.* 84:203
77. Raemaekers RH. 1988. *Helminthosporium sativum*: disease complex on wheat and sources of resistance in Zambia. In *Wheat Production Constraints in Tropical Environments*, ed. AR Klatt, pp. 175–86. Mexico DF: CIMMYT
78. Reimann S, Deising HB. 2005. Inhibition of efflux transporter-mediated fungicide resistance in *Pyrenophora tritici-repentis* by a derivative of 4'-hydroxyflavone and enhancement of fungicide activity. *Appl. Environ. Microbiol.* 71:3269–75
79. Rodriguez-Algaba J, Walter S, Sørensen CK, Hovmöller MS, Justesen AF. 2014. Sexual structures and recombination of the wheat rust fungus *Puccinia striiformis* on *Berberis vulgaris*. *Fungal Genet. Biol.* 70:77–85
80. Rosewarne GM, Herrera-Foessel SA, Singh RP, Huerta-Espino J, Lan CX, He ZH. 2013. Quantitative trait loci of stripe rust resistance in wheat. *Theor. Appl. Genet.* 126:2427–49
81. Rutkoski J, Benson J, Jia Y, Brown-Guedira G, Jannink J-L, Sorrells M. 2012. Evaluation of genomic prediction methods for Fusarium head blight resistance in wheat. *Plant Genome* 5:51–61
82. Rutkoski J, Poland JA, Singh RP, Huerta-Espino J, Bhavani S, et al. 2014. Genomic selection for quantitative adult plant stem rust resistance in wheat. *Plant Genome* doi: 10.3835/plantgenome2014.02.0006
83. Rutkoski J, Singh RP, Huerta-Espino J, Bhavani S, Poland J, et al. 2015. Genetic gain from phenotypic and genomic selection for quantitative resistance to stem rust of wheat. *Plant Genome* doi: 10.3835/plantgenome2014.10.0074
84. Salameh A, Buerstmayr M, Steiner B, Neumayer A, Lemmens M, Buerstmayr H. 2011. Effects of introgression of two QTL for Fusarium head blight resistance from Asian spring wheat by marker-assisted backcrossing into European winter wheat on Fusarium head blight resistance, yield and quality traits. *Mol. Breed.* 28:485–94
85. Sharma I, ed. 2012. *Disease Resistance in Wheat*. Wallingford, UK: CABI
86. Sharma RC, Crossa J, Velu G, Huerta-Espino J, Vargas M, et al. 2012. Genetic gains for grain yield in CIMMYT spring bread wheat across international environments. *Crop Sci.* 52:1522–33
87. Sierotzki H, Scalliet G. 2013. A review of current knowledge of resistance aspects for the next-generation succinate dehydrogenase inhibitor fungicides. *Phytopathology* 103:880–87
88. Simón MR, Cordo CA, Castillo NS, Struik PC, Börner A. 2012. Population structure of *Mycosphaerella graminicola* and location of genes for resistance to the pathogen: recent advances in Argentina. *Int. J. Agron.* 2012:680275
89. Singh PK, Feng J, Mergoum M, McCartney CA, Hughes GR. 2009. Genetic analysis of seedling resistance to Stagonospora nodorum blotch in selected tetraploid and hexaploid wheat genotypes. *Plant Breed.* 128:118–23

90. Singh PK, Singh RP, Duveiller E, Mergoum M, Adhikari TB, Elias EM. 2010. Genetics of wheat–*Pyrenophora tritici-repentis* interactions. *Euphytica* 171:1–13
91. Singh PK, Zhang Y, He X, Singh RP, Chand R, et al. 2015. Development and characterization of the 4th CSISA-spot blotch nursery of bread wheat. *Eur. J. Plant Pathol.* 143:595–605
92. Singh RP, Hodson DP, Huerta-Espino J, Jin Y, Bhavani S, et al. 2011. The emergence of Ug99 races of the stem rust fungus is a threat to world wheat production. *Annu. Rev. Phytopathol.* 49:465–81
93. Singh RP, Hodson DP, Jin Y, Lagudah ES, Ayliffe MA, et al. 2015. Emergence and spread of new races of wheat stem rust fungus: continued threat to food security and prospects of genetic control. *Phytopathology* 105:872–84
94. Singh RP, Huerta-Espino J. 1997. Effect of leaf rust gene *Lr34* on grain yield and agronomic traits of spring wheat. *Crop Sci.* 37:390–95
95. Singh RP, Huerta-Espino J, Rajaram S. 2000. Achieving near-immunity to leaf and stripe rusts in wheat by combining slow rusting resistance genes. *Acta Phytopathol. Entomol. Hung.* 35:133–39
96. Singh RP, Rajaram S, Crossa J. 1998. Agronomic effects from chromosome translocations 7DL.7Ag and 1BL.1RS in spring wheat. *Crop Sci.* 38:27–33
97. Singh S, Singh RP, Huerta-Espino J. 2012. Stem rust. See Ref. 85, pp. 18–32
98. Sivamani E, Brey CW, Talbert LE, Young M, Dyer WE, et al. 2002. Resistance to wheat streak mosaic virus in transgenic wheat engineered with the viral coat protein gene. *Transgenic Res.* 11:31–41
99. Somers DJ, Thomas J, DePauw R, Fox S, Humphreys G, Fedak G. 2005. Assembling complex genotypes to resist *Fusarium* in wheat (*Triticum aestivum* L.). *Theor. Appl. Genet.* 111:1623–31
100. Sørensen CK, Hovmöller MS, Leconte M, Dedryver F, de Vallavieille-Pope C. 2014. New races of *Puccinia striiformis* found in Europe reveal race specificity of long-term effective adult plant resistance in wheat. *Phytopathology* 104:1042–51
101. Spolti P, Del Ponte EM, Dong Y, Cummings JA, Bergstrom GC. 2014. Triazole sensitivity in a contemporary population of *Fusarium graminearum* from New York wheat and competitiveness of a tebuconazole-resistant isolate. *Plant Dis.* 98:607–13
102. The TT, Latter BDH, McIntosh RA, Ellison FW, Brennan PS, et al. 1988. Grain yield of near isogenic lines with added genes for stem rust resistance. In *Proceedings of the 7th International Wheat Genetics Symposium*, ed. TS Miller, RMD Koebner, pp. 901–6. Cambridge, UK: Inst. Plant Sci. Res.
103. Tommasini L, Schnurbusch T, Fossati D, Mascher F, Keller B. 2007. Association mapping of *Stagonospora nodorum* blotch resistance in modern European winter wheat varieties. *Theor. Appl. Genet.* 115:697–708
104. Urashima AS, Grosso CRF, Stabili A, Freitas EG, Silva CP, et al. 2009. Effect of *Magnaporthe grisea* on seed germination, yield and quality of wheat. In *Advances in Genetics, Genomics and Control of Rice Blast Disease*, ed. W Xiaofan, B Valent, pp. 267–77. New York: Springer
105. Vaidyanathan G. 2011. Science in Africa: the wheat stalker. *Nat. News.* 474:563–65
106. Von der Ohe C, Ebmeyer E, Korzun V, Miedaner T. 2010. Agronomic and quality performance of winter wheat backcross populations carrying non-adapted *Fusarium* head blight resistance QTL. *Crop Sci.* 50:2283–90
107. Walter S, Ali S, Kemen E, Nazari K, Bahri BA, et al. 2016. Molecular markers for tracking the origin and worldwide distribution of invasive strains of *Puccinia striiformis*. *Ecol. Evol.* <http://onlinelibrary.wiley.com/doi/10.1002/ece3.2069/full>
108. Wang Y, Cheng X, Shan Q, Zhang Y, Liu J, et al. 2014. Simultaneous editing of three homoeoalleles in hexaploid bread wheat confers heritable resistance to powdery mildew. *Nat. Biotechnol.* 32:947–51
109. Weiss M V. 1987. *Compendium of Wheat Diseases*. St. Paul, MN: APS Press. 2nd ed.
110. Wellings CR. 2007. *Puccinia striiformis* in Australia: a review of the incursion, evolution, and adaptation of stripe rust in the period 1979–2006. *Aust. J. Agric. Res.* 58:567–75
111. Wellings CR, Boyd LA, Chen XM. 2012. Resistance to stripe rust in wheat: pathogen biology driving resistance breeding. See Ref. 85, pp. 63–83
112. WHEAT. 2013. *Wheat: vital grain of civilization and food security*. CGIAR Res. Program Wheat 2013 Annu. Rep., CGIAR, Mexico, D.F.
113. Yin Y, Liu X, Li B, Ma Z. 2009. Characterization of sterol demethylation inhibitor-resistant isolates of *Fusarium asiaticum* and *F. graminearum* collected from wheat in China. *Phytopathology* 99:487–97



114. Yu L-X, Barbier H, Rouse MN, Singh S, Singh RP, et al. 2014. A consensus map for Ug99 stem rust resistance loci in wheat. *Theor. Appl. Genet.* 127:1561–81
115. Zhang L, French R, Langenberg WG, Mitra A. 2001. Accumulation of barley stripe mosaic virus is significantly reduced in transgenic wheat plants expressing a bacterial ribonuclease. *Transgenic Res.* 10:13–19
116. Zhang X, Halder J, White RP, Hughes DJ, Ye Z, et al. 2014. Climate change increases risk of Fusarium ear blight on wheat in central China. *Ann. Appl. Biol.* 164:384–95

