Preparing for Emerging and Unknown Threats in Crops

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Diseases of plants have had significant impact on the course of human history. Almost every schoolchild learns of the devastating famine that occurred in Ireland in the mid-1800s, when unusually cold, damp conditions caused an oomycete pathogen, *Phytophthora infestans,* to wreak far more damage than usual on the potato crop on which millions of subsistence farmers and their families relied. The stories of a million starving Irish who perished as a result, and of the 1.5 million who emigrated—many to the United States—are familiar to us (Large, 1940). But countless other stories of plant diseases have helped to shape social, political, military, and financial decisions and actions around the globe. Why do the British drink tea? It wasn't always that way. At about the same time that the Irish potato famine was causing such misery in the British Isles, the rust fungus *Hemileia vastatrix* was devastating what was then the greatest coffee-growing region of the world, the island of Ceylon (now Sri Lanka), then a British colony. Despite extensive efforts to manage the disease, the coffee industry was unable to survive the severe economic losses, and British farmers on Ceylon began to transform their acreages into tea plantations. Soon, British consumers were drinking tea, and the habit stuck. On a more serious note, severe food shortages during the most critical period of World War I resulted after cool and humid conditions on both sides of the Atlantic Ocean favored pathogens of potatoes and wheat, forcing military leaders of both sides to alter their troops' movements and strategies.

Plant diseases still affect human health and society (Stack and Fletcher, 2007). Although they are unlikely to cause significant food shortages or malnutrition in the United States and other developed nations (in the event that a particular crop—even a major staple—were to be eliminated by disease we, in the United States, would just eat something else), it is a different story in developing nations. Imagine, for example, the loss of the rice crop in southeast Asia, or of cassava in eastern and central Africa. Such events are not merely speculation; the International Institute for Tropical Agriculture in Nigeria reports that cassava brown streak virus has been spreading in central and eastern Africa, seriously threatening food security in already-unstable regions such as Rwanda and Tanzania (Ferguson *et al.,* 2010).

That a clear relationship exists between food security and the stability of social and political systems has been demonstrated repeatedly (Chakraborty and Newton, 2011), and a number of recent and even current examples are available. Low-income economies are more sensitive to food inflation as the poor spend a higher percentage of their incomes on food. In the aftermath of the 2010 earthquake in Haiti, slow distribution of aid and supplies to hard-hit areas and refuges established for newly homeless citizens led to squalid conditions of hunger and disease. Sporadic violence, rioting and looting resulted as food prices skyrocketed; the price of rice more than doubled in the post-quake period. Limited resources and desperation triggered by deplorable conditions pushed tempers and patience past the breaking point and vigilante groups took matters into their own hands. Soaring food prices of staple commodities such as sugar, rice and milk have forced people in many Arab states to allocate larger portions of their income to the basic necessities of life, pushing them deeper into poverty and sparking a revolutionary wave of demonstrations and protests known as Arab Spring (Javid, 2011). A similar food-price crisis in 2008 led to protests and riots in more than thirty countries.

Crop Vulnerability to Disease

The United States' agricultural enterprise includes myriad crop species grown in many systems from extensive field acreages (corn, wheat, barley, *etc*.) to small plots of exotic, organic and specialty crops (artichokes, microgreens, jicama, herbs, *etc*.). Every plant species is vulnerable to a variety of diseases caused by microbial agents, including fungi, bacteria, viruses and viroids, nematodes, protozoa, and even parasitic plants. Increasing the complexity of the plant-pathogen relationships, many plant pathogens are transmitted by plant-feeding insects such as leafhoppers and sharpshooters, aphids, whiteflies, and beetles.

The vulnerability of US agriculture to emerging pathogens and pests derives from a number of factors (NRC, 2002a; Whitby, 2002; Gullino *et al.* 2008; Fletcher *et al*., 2010). First is the monetary value of these crops, considering that they generate a sixth of our gross domestic product and represent between 15% and 20% of our employment. Features of our agricultural practices also contribute to vulnerability. Most of our crops are planted as monocultures, the genetic identity of which ensures that a pathogen sickening one plant has the potential to sicken them all. Vast acreages planted to field crops go unmonitored for extended periods, usually from planting until harvest. Naturally occurring plant resources, such as forests and rangelands, are similarly un-watched. These factors can result in very long lag periods between the introduction of a pathogen and its detection and identification, and the initiation of a response. Vulnerability results also from the ease and frequency with which exotic new pathogens traverse our borders, whether on the winds of hurricanes, in the bilge water of ships, on the shoes of tourists who visited farms outside the United States, on the imported fresh fruits and vegetables that we now expect as year-round supplements to our menus, or by a thousand other pathways that occur daily, naturally, and predictably.

Additional vulnerability comes from the cost of plant diseases and crop losses (NRC, 2002a; Whitby, 2002; Madden, 2003; Gullino *et al.*, 2008; Fletcher *et al.*, 2010). These include reductions in yield and quality of the commodities (blemished fruit, toxins in grain), as well as the costs of growing less-desirable crops. These factors often lead to higher food prices and to shortages of certain types of foods. Costs of disease prevention and management also add up, including the cost of short-term control strategies such as pesticide application, biocontrol adoption, or crop replacement, as well as long-term strategies such as the incorporation of disease-resistance genes into high-value crops. Even more critical, however, are the national and international trade disruptions brought about by quarantines and embargoes against the presence of specific pathogens or toxins in particular crops or commodities. Subsequent downstream impacts are often felt in rural communities where the economy is often tied to the success of their agricultural ventures.

Challenges for Assuring Food Stability Nationally and Globally

Vulnerabilities from New Crops and Pathogens

New crops and new pathogens bring new vulnerabilities. The USDA Animal and Plant Health Inspection Service (APHIS) maintains, and regularly updates, a list of plant pathogens of unusually threatening nature, called select agents (USDA APHIS, undated). This list helps in the prioritization of resource allocations and defines the boundaries of the stringent regulatory policy deemed essential for US crop security. All of the plant pathogen select infectious agents are exotic to the United States. Since the creation of the list, two plant pathogen select agents have arrived and become established within US borders (*Phakopsora pachyrhizi,* causal agent of soybean rust, in 2004 and *Liberibacter asiaticus*, causal agent of citrus greening, in 2006). Once clearly established, the causal pathogens were removed from the select agent list to facilitate research to manage these diseases. However, plant pathogens other than those on the select agent list also pose significant threats to US agriculture. Most notably, a relatively new race of the wheat stem rust pathogen, *Puccinia graminis* f. sp. *tritici* race TTKS ("Ug99")—which emerged in Uganda in 1998 and has since spread well beyond the area initially affected—is of significant concern because of the lack of resistance in most of the wheat varieties currently grown in the world, including in the United States (Njau *et al.*, 2010). The FAO (2010) has described the potential impact on the human condition in certain wheat-dependent regions as "disastrous." A high priority for US wheat breeders is to identify and incorporate resistance to this fungal race into key US wheat varieties.

Climate Change

The predicted transitions of global climate zones will affect the optimal distributions and possible ranges of plants, insects and pathogens (Coakley *et al.*, 1999; Eastburn *et al.*, 2011; Garrett *et al.*, 2011; Shaw and Osborne, 2011) It is likely that members of all of these groups will become prevalent in areas not now occupied, and will cease to thrive in others. In some cases, the outlines of new geographical ranges for a plant species may not precisely coincide with those of certain pathogens or insect vectors, creating the possibility for new host-pathogen-vector associations. The range changes constitute a new vulnerability for food security as well as for emerging pathogens and pests.

Nefarious Use of Plant Pathogens

Plant pathogens offer attractive features to those with harmful intent, whether their motives are terrorism, economic gain, revenge, or social/political expression (NRC, 2002a; Fletcher and Stack, 2007; Fletcher *et al.*, 2010). They are easily available at little or no cost and offer little or no threat to the health of the handlers. Although a plant disease may not be perceived as catastrophic, its impacts on food insecurity and social instability may be quite serious, as noted above. Plant pathogens were included as components of consideration in the biowarfare programs of a number of nations prior to the Biological Weapons Convention in 1975, which commits the 163 state signers to prohibit the development, production, and stockpiling of biological agents and toxins.

Human Pathogens on Plants

Foodborne illnesses are on the rise worldwide, and, although they once were considered to be associated primarily with meat contamination, an ever-increasing percentage of outbreaks is associated with fresh produce such as tomatoes, spinach and sprouts (Brandl, 2006; Teplitski *et al.*, 2009). Although most disease outbreaks result from accidental contamination, some have been linked to cases of criminal negligence (in which distributors failed to maintain sanitary conditions, or knowingly released contaminated products). However, remarkably, to our knowledge, only one significant case of intentional contamination, resulting in hundreds of illnesses, has emerged. This incident was the 1984 deliberate contamination by a religious cult of restaurant salad bars in Oregon, as part of a plan to sway a local election. However, the recent outbreak of a particularly aggressive and virulent strain of *Escherichia coli* in Germany, in which forty-six died and nearly 4,000 were taken ill (Kupferschmidt, 2011), demonstrates our lack of preparedness to prevent, quickly detect and diagnose, and minimize damage from such events—whether naturally occurring or intentionally caused.

Elements of a Strong National Security Plan

A report produced by the National Research Council (2002b) suggested that a strong national biosecurity plan should consist of:

- early detection and diagnostic systems;
- epidemiological models for predicting pathogen spread;

- reasonable but effective strategies and policies for crop biosecurity;
- distributed physical and administrative infrastructure;
- a national response-coordination plan and infrastructure, and
- strategies for forensic investigation and attribution in cases of intentional or criminal activity.

Homeland Security Presidential Directive 9, issued by President Bush in 2004, mandated a National Plant Disease Recovery System (NPDRS). The task was assigned to the Secretary of Agriculture, then Anne Veneman, who made it the responsibility of the USDA Office of Pest Management Policy. The initiative consists of the preparation of response plans for each of the APHIS plant pathogen select agents as well as a number of other threatening plant pathogens; completed plans can be viewed at http://www.ars.usda.gov/Research/docs.htm?docid=14271. The NPDRS's purpose is to ensure that the tools, infrastructure, communication networks, and capacity required to mitigate the impacts of high-consequence plant-disease outbreaks are such that a reasonable level of crop production is maintained in the United States. The recovery plans represent a cooperative effort of university, industry, and government scientists managed by the American Phytopathological Society (APS) in partnership with the USDA.

A second initiative emerging after the 2001 attacks was the establishment of the National Plant Diagnostic Network (NPDN) (Stack *et al.*, 2006). This nationwide system of plant diagnostic laboratories—an initiative led by the USDA's CSREES[1] (now NIFA[2])—was a achieved through strong cooperation among USDA agencies, land-grant universities, state Departments of Agriculture (SDAs), and private laboratories. Prior to this time, plant diagnostic laboratories, of which there was generally one per state, were in some cases associated with a land-grant university and in other cases part of the SDAs. They often were under-funded and their diagnosticians operated in isolation and without coordination. The NPDN structure and funding brought, for the first time, all of the laboratories into a single framework. Organized into five regional units, but coordinated as a whole, the network assured a minimum level of capability through training and equipment resources. By adopting common assay protocols, positive and negative controls, and reagents, data and records could be shared and compared among the labs. Expertise from each lab was available to the other state laboratories. Plant disease diagnosticians, now recognized for their important contributions to the US agricultural enterprise, took new pride in their accomplishments. The NPDN is a true success story in which preparation for potential threats against our agricultural systems generated substantial benefit for managing everyday agricultural problems. As this paper is being written, the future of the NPDN is threatened by severe federal budget cuts. Its loss due to lack of funding would erase a decade of progress, value and capability, and turn the business of plant-disease diagnosis back to an inefficient and minimally supported enterprise lacking optimal capability to anticipate, detect, respond to and mitigate the effects of the ever-increasing emerging pathogens and pests that continue to threaten our crops.

[1]Cooperative State Research, Education, and Extension Service.
[2]National Institute for Food and Agriculture.

In addition to the NPDRS and the NPDN, many other initiatives that emerged following September 11, 2001, addressed agricultural vulnerability and preparedness. The USDA established an Office of Homeland Security within the office of the secretary, APHIS developed new response and regulatory policies (including the select agent list), the USDA Agricultural Research Service (ARS) initiated research programs related to pathogens of concern, and CSREES developed and supported new initiatives in education, outreach and research (now under the auspices of NIFA). The newly formed Department of Homeland Security (DHS) established the National Biodefense Analysis and Countermeasures Center (NBACC[3]), within which the National Bioforensic Analysis Center (NBFAC) was charged with developing and providing forensic capabilities for attribution and prosecution of those involved in criminal actions related to homeland security (both NBACC and NBFAC are now managed by a non-governmental organization).

The Need for New Capability in Microbial Forensics

A study commissioned by the US defense community in 2002, following the mailing of letters containing anthrax spores to a number of targets, called for the development of greater capability in microbial forensics (Budowle *et al.*, 2005a, 2005b). Although most of the effort that followed was focused, logically, on solving the anthrax case, the report included specific language indicating the need for plant-pathogen forensics. A panel of plant pathologists was charged to review existing capabilities that could be brought to bear in the investigation of a criminal case involving plant pathogens, as well as to identify needs and gaps and recommend priorities for near-term funding, research and applications. In their report (Fletcher *et al.*, 2006), the authors noted a difference between plant-disease diagnostic activities carried out following "normal" disease outbreaks, when the goal is to identify the pathogen to species or strain as needed to formulate effective management strategies, and those needed for a crime-scene investigation, which must be conducted at a high level of stringency with validated tests having high confidence levels so as to stand up to aggressive counter-arguments in court. Furthermore, challenges particular to the development and application of microbial forensic science to plant pathology were explored. For example, forensic scientists dealing with human victims need concern themselves with only one host species and the pathogens and toxins to which that host is susceptible, whereas plant pathologists deal with hundreds of host-plant species, each having a different set of pathogens. Because so many plant species are important to us, the basic biology of both host and pathogen is well understood for only a fraction of them. For many lesser-known plant pathogens, diagnostic technologies often are still rudimentary, and, even when molecular approaches are developed for them, the databases (public genome libraries, databases of substrate utilization and fatty acid profiles) lack information for these plant pathogens and their relatives. And, despite a growing recognition on the part of federal policymakers of the importance of our nation's agricultural enterprise, funding for work on plants remains comparatively very low and even some post-2011 funds targeted to this area have since been eliminated.

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[3]http://www.bnbi.org/.

The National Institute for Microbial Forensics & Food and Agricultural Biosecurity

While the work of the NPDN, the NPDRS, APHIS, and ARS and others is relevant to plant-pathogen forensics, the mission and focus of each of these entities are directed to different goals. At Oklahoma State University the concept of a new program to focus specifically on plant-pathogen forensics and its role in agricultural biosecurity grew as the needs and gaps in this emerging discipline were clarified in the assessment study. OSU administrative leaders at all levels were supportive and provided encouragement and preliminary resources for the program's initiation. In 2007, the National Institute for Microbial Forensics & Food and Agricultural Biosecurity was established as a cross-disciplinary and cross-departmental unit at OSU. Its goal is to identify, assess, prioritize, facilitate and conduct research, education and outreach (the three activities fundamental to any land-grant university) related to national needs in microbial forensic science with respect to pathogens of crops, forests, rangelands and other plant resources, with an additional component related to human pathogens on fresh produce. Its mission statement is:

> *NIMFFAB will build on, connect and enhance existing programs that support and address issues of crop and food security.*

The Institute's core staff of five faculty members, enhanced by a growing group of partners and collaborators, has strong expertise in plant pathology, forensic sciences, microbiology, vector-plant pathogen interactions, diagnostics and detection design and development, microbial population biology, molecular biology, metagenomics and next-generation sequencing, bioinformatics, produce safety, and human pathogens on plants.

The NIMFFAB uses targeted strategies and approaches to accomplish its mission. A key role is to serve as a link between the plant-pathology community and law enforcement and security communities, policymakers, and funding agencies. Critical to its effectiveness is maintaining strong and open ties with end-users and other stakeholders within the Department of Homeland Security's affiliated National Bioforensic Analysis Center (of which NIMFFAB is a Spoke Laboratory), the Federal Bureau of Investigation (FBI), the USDA's Office of Homeland Security, APHIS, ARS, NIFA, NPDRS, and NPDN, the Defense Threat Reduction Agency, the Food and Drug Administration (FDA), and other government agencies, industry, and scientific societies.

Education

NIMFFAB directs and mentors graduate students in novel MS and PhD programs that blend multidisciplinary programs in new ways. For example, funding from an innovative USDA program designed to address emerging national needs has allowed NIMFFAB graduate students to be the first in the United States to take coursework and perform research that incorporates both plant pathology and forensic sciences. An invaluable opportunity afforded our graduate students is the summer internship that they complete at a homeland security-related federal agency or industry. For example, two PhD students spent 3 months doing research at the FBI laboratory in Quantico, VA. Because young scientists rarely have a realistic understanding of careers in law enforcement or homeland security, these internships provide a unique opportunity to experience these environments.

Research

Almost all plant-pathology research is relevant in some way to agricultural applications of microbial forensics and homeland security. However, NIMFFAB faculty and their postdocs and students focus their research on initiatives targeted to support the forensic investigator's capabilities in evaluating a criminal case involving plant pathogens or human pathogens on fresh produce. Most projects involve collaboration and partnerships with the agencies concerned. Examples of research areas include adaptation of current or novel plant-disease diagnostic methods for forensic investigation, adapting existing human forensic technologies to plant pathogens, and developing new investigative tools that facilitate the work of forensic investigators at the scene of a crop-focused crime. Plant pathologists have a unique advantage as developers of field-targeted tools and technologies, in that model systems involving locally common plant pathogens can be readily field-tested. Furthermore, data from naturally occurring plant-disease outbreaks can be compared directly to those from outbreaks of the same disease generated in field plots (following all regulatory requirements) by the investigators.

Outreach

Outstanding training courses and exercises related to crops and plant pathogens are offered frequently by the NPDN and APHIS. Such activities are generally targeted toward NPDN plant-disease diagnosticians, APHIS personnel, and local and regional responder communities. The training niche that NIMFFAB addresses is designed specifically to bring federal forensic and security investigators into the picture, to provide information and practice for law enforcement in agricultural crime-scene settings, and to create opportunities for security and law-enforcement personnel to interact with the agricultural community, including Cooperative Extension educators, crop advisors and farmers. Furthermore, NIMFFAB facilitates interaction between the plant-pathology and law-enforcement/security agencies by organizing members of the APS—the primary professional association for plant pathologists—interested in these disciplines into interactive groups. The APS Microbial Forensics Interest Group and the APS Food Safety Interest Group meet yearly during the APS annual meeting, as a forum for prioritizing needs, providing community input, and developing collaborative initiatives in forensic plant pathology and fresh-produce safety.

Final Thoughts

US preparedness for maintaining the most secure and abundant food supply in the world has been improving, but gaps remain. Justifiable concerns about new and emerging pathogens and pests that threaten agricultural resources demonstrate the need for greater exploration of new and more effective ways of addressing these issues. Greater blending of disciplines will facilitate the creation of new knowledge, support the development of new technologies and capabilities, and allow the broad, cross-disciplinary training that young scientists will need to address these global challenges.

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She served on the APS Council for ten years, including the four-year presidential sequence. In the months following September 11, 2001, she led APS responses and input to new national biosecurity initiatives. Her research focuses on mechanisms of virulence and insect transmission of plant-pathogenic bacteria, the relationships between human pathogens and plants, and on the emerging disciplines of microbial forensics and agricultural biosecurity.