CONVENED BY GEORGE P. SHULTZ

GOVERNANCE IN AN EMERGING NEW WORLD

HEALTH AND THE CHANGING ENVIRONMENT

Milana Boukhman Trounce, Kari Nadeau,
Lucy Shapiro, Harley McAdams,
Stephen R. Quake

A PUBLICATION OF THE HOOVER INSTITUTION

HOOVER
INSTITUTION

GOVERNANCE IN AN EMERGING NEW WORLD

Convened by George P. Shultz
with James Cunningham, David Fedor, and James Timbie

Table of Contents

SPRING SERIES, ISSUE 419

A Letter from the Conveners

Sharp changes are afoot throughout the globe. Demographics are shifting, technology is advancing at unprecedented rates, and these changes are being felt everywhere.

How should we develop strategies to deal with this emerging new world? We can begin by understanding it.

First, there is the changing composition of the world population, which will have a profound impact on societies. Developed countries are experiencing falling fertility and increasing life expectancy. As working-age populations shrink and pensions and care costs for the elderly rise, it becomes harder for governments to afford other productive investments.

At the same time, high fertility rates in Africa and South Asia are causing both working-age and total populations to grow, but that growth outpaces economic performance. And alongside a changing climate, these parts of the world already face growing impacts from natural disasters, human and agricultural diseases, and other resource constraints.

Taken together, we are seeing a global movement of peoples, matching the transformative movement of goods and of capital in recent decades—and encouraging a populist turn in world politics.

Second is automation and artificial intelligence. In the last century, machines performed as instructed, and that "third industrial revolution" completely changed patterns of work, notably in manufacturing. But machines can now be designed to learn from experience, by trial and error. Technology will improve productivity, but workplace disruption will accelerate—felt not only by call center responders and truck drivers but also by accountants, by radiologists and lawyers, even by computer programmers.

All history displays this process of change. What is different today is the speed. In the early 20th century, American farm workers fell from half the population to less than five percent alongside the mechanization of agriculture. Our K-12 education systems helped to navigate this disruption by making sure the next generation could grow up capable of leaving the farm and becoming productive urban workers. With the speed of artificial intelligence, it's not just the children of displaced workers but the workers themselves who will need a fresh start.

Underlying the urgency of this task is the reality that there are now 7.6 million "unfilled jobs" in America. Filling them and transitioning workers displaced by advancing technology to new jobs will test both education (particularly K-12, where the United States continues to fall behind) and flexibility of workers to pursue new occupations. Clearly, community colleges and similarly nimble institutions can help.

The third trend is fundamental change in the technological means of production, which allows goods to be produced near where they will be used and may unsettle the international order. More sophisticated use of robotics alongside human colleagues, plus additive manufacturing and unexpected changes in the distribution of energy supplies, have implications for our security and our economy as well as those of many other trade-oriented nations who may face a new and unexpected form of deglobalization.

This ability to produce customized goods in smaller quantities cheaply may, for example, lead to a gradual loss of cost-of-labor advantages. Today, 68 percent of Bangladeshi women work in sewing, and 4.5 million Vietnamese work in clothing production. Localized advanced manufacturing could block this traditional route to industrialization and economic development. Robots have been around for years, but robotics on a grand scale is just getting started: China today is the world's biggest buyer of robots but has only 68 per 10,000 workers; South Korea has 631.

These advances also diffuse military power. Ubiquitous sensors, inexpensive and autonomous drones, nanoexplosives, and cheaper access to space through microsatellites all empower smaller states and even individuals, closing the gap between incumbent powers like the United States and prospective challengers and giving potentially disruptive capabilities to non-state and terrorist actors. The proliferation of low-cost, high-performance weaponry enabled by advances in navigation and additive manufacturing diminishes the once-paramount powers of conventional military assets like aircraft carriers and fighter jets. This is a new global challenge, and it threatens to undermine U.S. global military dominance, unless we can harness the new technologies to serve our own purposes. As we conduct ourselves throughout the world, we need to be cognizant that our words and deeds are not revealed to be backed by empty threats. At the same time, we face the challenge of proliferation of nuclear weapons.

Finally, the information and communications revolution is making governance everywhere more difficult. An analogue is the introduction of the printing press: as the price of that technology declined by 99 percent, the volume grew exponentially. But that process took ten times longer in the 15th, 16th, and 17th centuries than we see today. Information is everywhere—some accurate, some inaccurate, such that entire categories of news or intelligence appear less trustworthy. The "population" of Facebook now exceeds the population of the largest nation state. We have ceaseless and instantaneous communication to everybody, anybody, at any time. These tools can be used to enlighten, and they can also be used to distort, intimidate, divide, and oppress.

On the one hand, autocrats increasingly are empowered by this electronic revolution, enabled to manipulate technologies to solidify their rule in ways far beyond their fondest dreams in times past. Yet individuals can now reach others with similar concerns around the earth. People can easily discover what is going on, organize around it, and take collective action.

At present, many countries seek to govern over diversity by attempting to suppress it, which exacerbates the problem by reducing trust in institutions. Elsewhere we see governments unable to lead, trapped in short-term reactions to the vocal interests that most effectively capture democratic infrastructures. Both approaches are untenable. The problem of governing over diversity has taken on new dimensions.

The good news is that the United States is remarkably well-positioned to ride this wave of change if we are careful and deliberate about it. We have, as an immigrant nation, always had to govern over diversity. Meanwhile, other countries will face these common challenges in their own way, shaped by their own capabilities and vulnerabilities. Many of the world's strongest nations today—our allies and otherwise—will struggle more than we will. The more we can understand other countries' situations, the stronger our foundation for constructive international engagement.

This is why we have set off on this new project on Governance in an Emerging New World. Our friend Senator Sam Nunn has said that we've got to have a balance between optimism about what we can do with technology and realism about the dark side. So we aim to understand these changes and inform strategies that both address the challenges and take advantage of the opportunities afforded by these transformations.

To do so, we are convening a series of papers and meetings examining how these technological, demographic, and societal changes are affecting the United States (our democracy, our economy, and our national security) and countries and regions around the world, including Russia, China, Latin America, Africa, the Middle East, and Europe.

***

One crosscutting global change whose effects we can now increasingly anticipate with sobering fidelity is the changing environment. This phenomenon has introduced new health risks and challenges to an increasingly interconnected world. Extreme weather events and warming climates affect the spread of infectious diseases or even pandemics, while changing and damaging ecosystems. We further see disruptions to traditional supply chains that support modern economies. The social costs of these phenomena are rising, and individuals, organizations, and governments are struggling to adapt. At the same time, new technologies may give us new tools to address the health issues aggravated by a changing climate and even reduce some of the negative impacts of pollutants on human life.

Experts at the Stanford University schools of medicine and engineering have produced a range of papers to address this important issue. These papers review the consequences of climate change and pollution for public health and identify possible ways—through technology and better governance—to mitigate those effects. They should be read sitting down. But they offer some promising proposals.

The volume begins with a study by Dr. Milana Boukhman Trounce warning that the risk of pandemics continues to grow, driven in part by a warming climate. By reviewing past examples of responses to pandemic outbreaks, she identifies approaches that work and ways technology can help them work better to identify, respond to, and minimize the spread of infectious diseases.

Dr. Kari Nadeau then reviews the health effects of pollution, which can already be seen both here in the United States and around the world. Curbing environmental pollutants is an area where we have some positive experience in the United States, but much more remains to be done. Calling for rapid action to limit further damage to public health, she identifies ways governments, clinicians, and individuals can reduce pollution exposure.

Assessing the global impact of a changing environment, developmental biologist Lucy Shapiro and physicist Harley McAdams write that human-driven increases to CO_2 have created a major biological disruption. They trace the effects of that disruption to some unexpected quarters, from changes in the world's oceans to the spread of animal and plant pathogens to new areas, and they argue for an international political effort to diminish carbon emissions and slow the pace of climate change.

Finally, bioengineer Stephen Quake provides examples of the groundbreaking work being done here at Stanford to address these very health and economic effects and identifies scientific and technological advances that may help humankind adapt to a changing environment.

The authors came together this spring for a roundtable at the Hoover Institution to discuss their ideas, challenge each other's perspectives, and carry the conversation to the broader Stanford University and Silicon Valley community. We conclude this volume with our observations from that discussion, prepared along with Hoover research analysts David Fedor and James Cunningham, and we thank our colleagues at the Hoover Institution who have supported this project, particularly Shana Farley and Rachel Moltz for their work on this volume.

George P. Shultz
Thomas W. and Susan B. Ford Distinguished Fellow

James Timbie
Annenberg Distinguished Visiting Fellow

Potential Pandemics

By Milana Boukhman Trounce, Stanford University

The Threat of Infectious Disease and the Evolution of the Threat

Infectious disease has been a formidable force in shaping human history. In the times past, most people died from two causes: violence and infectious disease, with deaths from infectious disease being many times more common. Bubonic plague killed between a third and a half of the population of Europe in the Middle Ages, thus changing the course of Europe and the world forever. Smallpox killed half a billion people in the 20th century alone before being finally eradicated in 1982.

Oftentimes more people die from infectious disease than from combat even in times of war. Napoleon started the war with over half a million soldiers and only a few thousand staggered back. Most died from trench fever, typhoid and other infections, with immune systems of soldiers weakened by malnutrition, cold and other stressors during movement of the Napoleonic troops through Russia. More recently, more people died due to the Spanish flu pandemic of 1918 than died in combat in World War I.

In the mid to late 20th century, with the advent of antibiotics and dramatic advances in the biological sciences, it seemed that we have conquered infectious disease–and, at least in the western world, we largely have for some period of time. We can now treat, have eradicated or decreased the incidence of infectious diseases. We can now effectively treat plague, cholera and numerous other infectious. We have eradicated smallpox, are close to eradicating polio, and have dramatically decreased the occurrence of other historical killers such as diphtheria, whooping cough, measles, and others through vaccination campaigns. Despite the many remaining challenges including antibiotic resistance and global access to curative drugs, we have developed drugs to treat many infectious diseases.

But now it is time to rethink the notion that we have conquered infectious disease. Due to human activity, the threat of infectious disease is making a come-back. Unfortunately, at this point we are ill equipped to deal with a number of scenarios, particularly those involving large-scale infectious disease outbreaks–pandemics. Pandemics pose some of the biggest threats to humanity, both as far as infectious disease risks as well as overall existential threats more broadly. In terms of impact on human population, this threat is as high as nuclear annihilation, climate change, and global instability for a variety of reasons. Pandemic risk is closely tied to climate change, technological disruption, as well as other factors relating to human activity.

Pandemics challenge our society's ability to withstand them. Severe pandemics can lead to mass panic and disruption of society and governments. In September 2014, the United Nations Security Council declared the Ebola virus outbreak in the West Africa a "threat to international peace and security". The resolution was the first in the history of the Security Council to deal with a public health crisis. In response, the United States sent in troops to assist in disaster response. The prowess of U.S. military in logistics and operations proved critical in helping to stabilize the region during this societal disruption.

Different Patterns of Spread of Infectious Diseases

The risk of pandemics has been increasing and accelerating significantly over the last several decades. Since the 1980s, we have seen a three-fold increase in the number of global epidemics. Climate change has been driving increased risk as mosquitos and other vectors spreading diseases such as dengue, chikungunya, zika moved up north. Also, different ways of using land, increased contact between humans and wild animal populations, urbanization and global travel have all contributed. As a result, we have seen a change in the pattern of spread of infectious organisms: some organisms which historically spread only locally have spread in ways we have never seen before, with dire consequences.

One example of this is the Ebola outbreak of 2014-2015. Historically, Ebola outbreaks involved tens to a few hundred people, and have been limited to one or a few remote villages in Africa. For the first time in history, we have seen this disease affect a continent, claiming tens of thousands of lives and wrecking fear and havoc on the entire world. Notably, this Ebola outbreak was caused by the same Ebola virus as the previous 20 outbreaks of Ebola occurring in Africa between 1976 and 2014. Why was this outbreak different? The difference in 2014-2016 outbreak is attributed to the fact that people are no longer isolated in remote villages–they travel. And when they do, they travel to cities, which, with the rise of urbanization, are now more heavily populated, but still lack the needed health infrastructure. Furthermore, people travel by planes at higher rates. All of this contributed to the number of people infected. It is also an example of a trend which is bound to continue. Although Ebola outbreak was the most recent dramatic example, the same dynamics also apply to the spread of flu and other infectious organisms.

With humans encroaching on traditionally animal habitats, there has also been an increase in the emergence of new infectious diseases affecting humans. This is significant since most pandemics stem from infectious organisms typically infecting animals becoming capable of infecting and spreading between humans.

The Challenges of Preparedness and Response

Medical Countermeasures

Pandemics pose a number of unique challenges to our society's ability to withstand them. One of the challenges is our ability to develop medical countermeasures. Since we know how to develop vaccines and drugs, why can't we just develop drugs and vaccines to control pandemics? To examine this question, let's start with the most common pandemic which predictably happens every year–seasonal flu. In 2018 seasonal flu claimed about 80,000 lives in the United States alone. It would seem that for a pandemic which happens yearly, claims thousands of lives yearly, and results in billions of economic costs predictably every year, we would by now have great medical countermeasures. However, despite the fact that much effort is expended every year in designing and making a flu vaccine, the effectiveness of this vaccine varies significantly year to year.

There are a number of factors which can make creation of good flu vaccine challenging.

Influenza virus is remarkable for its high rate of mutation, compromising the ability of the immune system to protect against new variants. As a consequence, new vaccines are produced each year to match circulating viruses. Currently, vaccine production takes, on average, six months from the selection of seed strains to the final vaccine product. The decision of which influenza antigens to include in the vaccines is made in advance of the influenza season and is based upon global surveillance of influenza viruses circulating at the end of the prior influenza season. In some years certain influenza viruses may not appear and spread until later in the influenza season, making it difficult to prepare a candidate vaccine virus in time for vaccine production. This can make vaccine virus selection very challenging. As a result, sometimes there are mismatches between the vaccine strain and the circulating strain that result in reduced efficacy of the vaccine. Can we come up with a vaccine which would be effective against all flu viruses? Ongoing research is focused on developing a universal vaccine that would elicit protective antibodies directed against conserved viral proteins.

What is the effectiveness of the flu vaccine? It depends on the type of the vaccine and it also varies every year and depends on how good a match is between the viral strains used to make the vaccine and the viral strains actually circulating in the population. During the 2004 to 2005 influenza season, the antigenic match was only 5 percent compared with 91 percent during the 2006 to 2007 season, which resulted in vaccine effectiveness of 10 versus 52 percent, respectively.[1] During the 2014 to 2015 influenza season in the United States, influenza A H3N2 viruses predominated and more than half of these viruses contained H3N2 antigen that was antigenically different (drifted) from that included in that season's influenza vaccines. The adjusted overall vaccine effectiveness for the 2014 to 2015 influenza season was 19 percent; for H3N2-associated illness, the vaccine effectiveness was only 6 percent.[2]

Despite the fact that flu vaccine has varying effectiveness, vaccination does reduce mortality from influenza significantly, and yet only 40% of the population gets the vaccine. The resistance to vaccinations is not unique to influenza. With the rise in anti-vaccination movement, we have recently seen outbreaks of measles and pertussis, both of which are prevented by vaccines with long standing record of safety and efficacy. Given this, what vaccination rates can we expect for newer, less tested vaccines? What percentage of the population would be comfortable getting vaccinated with a vaccine which was developed quickly in response to a novel viral pandemic? What if this vaccine was approved by the FDA under Emergency Use Authorization, which is a legal means for the FDA to approve new therapeutic and diagnostic tools during a declared emergency with more limited testing than it would normally require? How many people would feel comfortable getting immunized with a vaccine with an incompletely understood safety profile? This is one of the many challenges unique to pandemic preparedness and response.

And what about drugs? For immunocompetent population, antivirals like Tamiflu only shorten flu symptoms by a day and offer no mortality benefit. Despite the public panic of trying to get Tamiflu during some of the more severe influenza seasons and the pharmacies running out of Tamiflu, the benefit of Tamiflu and other influenza antivirals is marginal in immunocompetent populations. It does offer more potential benefit to people whose immune systems may be compromised.

How about medical counter-measures such as drugs and vaccines for other viruses and what would it take for us to be prepared for a pandemic due to an emerging infection? Most pandemics caused by emerging infectious diseases are due to organisms which have recently appeared within a population or whose incidence or geographic range is rapidly increasing or threatens to increase in the near future. Most of these arise from human interaction with animals. There are over 200 species of viruses and 500 species of bacteria capable of infecting humans. Focusing on viral infections which are far more likely to cause a pandemic than bacterial infections, there are numerous strains of viruses within each of the specie. This leaves us with thousands of various strains of viruses capable of causing a pandemic. Also, viruses mutate, some very frequently, which increases this number significantly. Additionally, with advances in synthetic biology, it is possible to manipulate viruses to make them more lethal and infectious–those can be released accidentally or nefariously. Although numerous measures have focused on prevention of this occurrence including attempt to regulate biology more tightly and secure it through the NSABB (National Science Advisory Board for Biosecurity) and other governing or advising organizations, ultimately perfect control is not possible. Unless specified beforehand in a grant application or another form of disclosure, it is exceedingly difficult to monitor what kinds of biological experiments one is setting up in their lab or garage, or what kinds of samples one may store in their lab freezer.

This leaves us with a virtually infinite number of viruses to which our population is vulnerable. It costs hundreds of millions of dollars to develop a vaccine or a drug. It would therefore take infinite amount of resources in an attempt to have a vaccine or a drug for every possible pathogen. While it is sensible to have drugs or vaccines to some more commonly occurring organisms, this quick calculation makes it apparent that this strategy will leave large gaps in our preparedness.

How about developing a drug or a vaccine at the very start of an epidemic in order to quickly control it? This reactive approach is politically tempting, and one frequently tried in the past, but which generally fails. The reason is simply the timeframe. It takes years to develop, test, and produce vaccines or drugs. While in an emergency this time may be shortened, it will still likely take a few years to develop and produce a new drug or a vaccine, by which time the epidemic would have already ran out and claimed the lives it was going to claim. It is hard to speed up drug or vaccine development by spending large amounts of money in response to an outbreak. In the past when U.S. Government has reacted to outbreaks by spending large amounts of money, as happened during the Ebola outbreak of 2014-2016, it has not made significant difference. We are still limited by what is possible as far as the speed of development, clinical testing, and production. We still don't have an FDA approved Ebola vaccine, although numerous ones have been developed and some are used, apparently with success, in Africa. Despite significant advances in the biological sciences over the past century, ironically, in the scenarios involving pandemics due to emerging infectious diseases, we are not in a dramatically different place as far as availability of specific countermeasures compared to where we were a century ago.

Surge Capacity

Thanks to the advancement in the medical sciences, even without having specific drugs or vaccines to treat infections, patients today are far more likely to survive thanks to the availability of supportive medical treatments such as fluid resuscitation, ability to help patients breath with the help of respirators, and other medical measures designed to support vital functions while the body's immune system mounts a response to an infectious organism. This is why Influenza or Ebola patients, for example, are far more likely to survive with supportive medical treatment than without it.

In a pandemic scenario, however, the availability of supportive medical treatment is not a given. This has to do with limited ability of hospitals or the medical system more broadly to handle a sudden influx of patients, which is known as surge capacity. In an event of a significant pandemic, our surge capacity will likely be outstripped given limited amount of hospital beds and medical personnel to staff the beds, as well as limited equipment, medications and other supplies needed to care for additional patients. Managing an infectious disease outbreak can also be more complicated since it may require additional kinds of resources such as negative pressure rooms and quarantine facilities.

We have experienced limited surge capacity at Stanford first hand. A number of times over the past several years, for weeks to months at a time, we had to open "The Tent". The Tent is a portable medical tent without running water which Stanford purchased in order to accommodate the influx of patients in disaster situations. We would open the Tent right outside the Emergency Department on the lawn by the parking lot at Stanford hospital in order to accommodate the increase in the number of patients during the flu season. Thus, Emergency Department created extra capacity with 8 additional patient chairs, and an additional physician as well as nurses and techs to take care of patients. We have the luxury of the benign weather in California to be able to operate part of an Emergency Room in a tent during the winter. Given that Stanford hospital has been operating close to capacity, as many hospitals throughout the country do in order to optimize operations and be fiscally responsible, during those times we had insufficient amount of space in the Emergency Department to accommodate the yearly influx of patients. Part of the reason for this is that we had numerous admitted patients being boarded in the Emergency Department due to a lack of availability of inpatient beds. If we have to set up our disaster Tent during the predictable yearly flu season, one can imagine that an influx of patients which is significantly beyond those experienced during the yearly flu season will be challenging and potentially impossible to accommodate as far as medical surge capacity.

We have plans to operate in disaster situations and flex our surge capacity, but the capacity to flex is limited. Our flexing involves putting admitted patients in the hallways, in addition to placing them in rooms, and discharging borderline patients who might be able to be reasonably discharged under these circumstances. Treating patients in the hallways and discharging patients who might be better served in the hospital under normal circumstances puts a stress on the system as well as on the patients. These disaster plans are generally supposed to last for hours to days following disaster, not months, as would be required in a case of a significant pandemic. This does not only apply to Stanford hospital, but is a typical situation in many if not most hospitals throughout the nation.

Another example of the limited medical surge capacity specifically around high consequence infectious disease became apparent during the Ebola outbreak of 2014-2015. During the outbreak, hospitals throughout the country including Stanford were rapidly preparing to receive and treat Ebola patients. Per CDC guidelines, the treatment area for such patients, in addition to the patient rooms, needed a “warm zone” as well as the “cold zone”. The “warm zone” is an area right outside the patient room where providers would take off personal protective equipment (PPE) and which may be contaminated with infectious organisms. The “cold zone” is a zone right outside the “warm zone” where providers would put PPE on, where clean supplies would be contained and where medical charting and other duties not directly involving direct patient contact can take place. The patient rooms themselves would need to have the capacity to suck the potentially infected air out of the rooms and release it into the atmosphere–these are called negative pressure rooms. There are only two such places at Stanford hospital: two rooms in the Emergency Department which are part of the Pediatric area, and the Stanford’s Critical Care Unit for cardiac patients.

If Stanford was to receive one or two suspected Ebola cases, those patients would be placed in the pediatric zone rooms, and if three or more patients would need to be cared for, Cardiac Intensive care unit would be converted into an Ebola care ward. To the chagrin of the cardiologists at Stanford, this would necessitate cancelling all cardiac catheterizations and heart surgeries. Thus, merely three suspected Ebola cases would significantly disrupt Stanford’s normal hospital operations and ability to provide medical care. The Cardiac Intensive care unit could accommodate additional 8 patients. Thus, Stanford as a whole was prepared to accommodate 10 suspected Ebola patients. One can imagine that in an outbreak of highly pathogenic flu or another emerging infection, the number of patients seeking medical care would be hundreds or thousands of times higher, thus overwhelming the system.

Many are under a hopeful impression that in a disaster situation involving pandemic with high consequence infectious organisms Federal Government through agencies like FEMA would step in and provide the medical surge capacity required. While indeed FEMA and other governmental and non-governmental organizations have been instrumental in responding to various disasters in the past such as earthquakes and floods, pandemics are not localized events. We would expect that most if not all areas of the country would be affected, far outstripping the federal and state resources required to provide additional medical capacity. Most of disaster response takes place on a local level, using local resources.

If Not Drugs, Vaccines, or Increased Surge Capacity, Then What?

If we are unlikely to have drugs or vaccines to counter infectious organisms during a pandemic, and if our medical surge capacity may be outstripped, what are we left with? We are left with an approach we have used for centuries to counter infectious disease, namely public health measures such as isolation, quarantine and other forms of infection control. This will be our strongest leverage point and our biggest opportunity. This strategy has a track record of success in a variety infectious disease outbreaks in the past. Despite the fact that it is a centuries-old approach, it makes sound sense to put resources behind it and innovate around it using modern tools.

Rapid Diagnostics and Surveillance: Lessons from Ebola

Rapid diagnostics and surveillance have been challenging for most outbreaks in the past for a variety of reasons, but this is one of our biggest points of leverage in controlling infectious disease outbreaks, and also most realistically doable given the state of technology and the cost/benefit equation. Although this was not available at Stanford hospital during 2014–2015 Ebola outbreak, a time is close when rapid and accurate point of care diagnostic testing for emerging infections will be widely clinically available. This will be very helpful in optimizing utilization of the scarce medical resources and patient outcomes, since a determination could be made quickly whether a patient is infected and therefore whether or not they need to be isolated.

During the 2014–2015 Ebola outbreak, the plan at Stanford was to send samples from suspected Ebola patients to the Center for Disease Control (CDC) lab for confirmation. If the patient was confirmed positive for Ebola, the plan was to transfer the patient to an Ebola-designated treatment hospital—at that time it was

UCSF. And, if the patient could be medically managed at home, to discharge them. The turnaround time given specimen travel and analysis time by the CDC lab was expected to take several days to a week. That would mean that a patient with suspected Ebola would have to be quarantined and treated in the Emergency Room for up to a week, taking up valuable medical resources. Due to high containment, Ebola patient would take up several times more resources than a regularly admitted patient, potentially disrupting provision of intensive cardiac care since the Cardiac Care Unit would be converted to an Ebola ward. All of this could be avoided by having a rapid and accurate point of care diagnostic test. For other kinds of lab testing for clinical purposes, a policy was made by Stanford hospital to only use point-of-care bedside testing for suspected Ebola patients. A rapid point of care diagnostic test which could be used at the bedside would optimize resource allocation.

During the Ebola epidemic in Africa, suspected patients were often quarantined together. Given limited resources, separate rooms were generally not available. Patient with malaria and other viral or bacterial diseases and patients with Ebola were often in the same living quarters: in the beginning of the illness, these diseases can be indistinguishable from each other clinically. This unfortunately made possible transmission of Ebola to patients with non-Ebola infections. A rapid and accurate test which could be used in the field would have precluded this from happening.

This is applicable not only to Ebola outbreaks but to most scenarios involving pandemics. In pandemic scenarios, it is likely that large numbers of patients will present to Emergency Departments and clinics. It would be very helpful to be able to rapidly distinguish between those who are sick due to a dangerous pathogen from those who are not and make treatment and quarantine decisions rapidly and accurately. This is key to getting an outbreak under control.

Quarantine, Isolation, and Other Infection Control Measures

Quarantine has been used extensively in the past during epidemics. The word quarantine comes from an Italian term "quaranta giorni", meaning forty days, the period that all ships were required to be isolated before passengers and crew could go ashore during the Black Death plague epidemic. A quarantine is used to separate and restrict movement of people who may have possibly been exposed to an illness or to restrict transport of possibly contaminated goods; quarantine is designed to prevent the spread of communicable diseases. Quarantine is different from medical isolation, which is to separate ill persons who have communicable disease from those who are healthy.

Outbreaks have been avoided in the past using the above measures alone. One example of this involved SARS. On March 7, 2003, two patients with SARS arrived in Canada and both promptly presented to the local hospitals—one in Vancouver and the other one in Toronto. No outbreak resulted in Vancouver. Toronto had a SARS outbreak with 247 probable cases and 44 deaths. Half of these were in healthcare workers. Vancouver is a useful point of reference for Toronto's response to SARS. Main difference? Immediate medical isolation upon presentation to the hospital in Vancouver, which included respiratory isolation and the use of N95 respiratory masks.

This decision was not only a result of a good call by an ER doctor in Vancouver—this was a team effort and no accident. This decision stemmed from months of monitoring, careful planning, and excellent communication by the local public health department, which was on a lookout for a highly pathogenic form of bird flu coming out of Asia and communicated these alerts to the local medical providers. As a result, although SARS and bird flu are caused by different viruses, a sick patient with flu-like symptoms with recent travel to Asia immediately got isolated with respiratory precautions. In Toronto, medical isolation with respiratory precautions was delayed and numerous medical and non-medical staff were exposed, got infected, and died due to a resulting SARS outbreak.[3]

Another example involved using infection control measures in non-medical settings, which were instrumental in mitigating infection rates during the Spanish flu pandemic of 1917–1918. This entailed the loss of civil liberties, especially in U.S. cities. As demonstrated by the research through the National Institute of Health (NIH) and the Centers for Disease Control (CDC), cities using aggressive measures had significantly lower infection and mortality rates.[4,5,6] As documented by numerous historians, the first line of defense was educational campaigns regarding hygiene, such as spitting and coughing into handkerchiefs, and banning common cups and utensils.[7]

The use of more aggressive interventions required the closing of schools, the restriction of large gatherings, and isolations and quarantines.[7,8] While some have argued that cities with rigorous closings and illegal gatherings fared no better than other cities, the examples of positive effects resulting from aggressive interventions are compelling.[7] Cities that implemented social measures within a few days of the first few cases of flu did better than cities that waited a few weeks to respond; the peak weekly death rates of the former were halved compared to the latter.[7,9] St. Louis had implemented measures within 2 days of their first reported cases, which resulted in a death rate I/8 the number of fatalities in Philadelphia, the worst hit city. The City of Brotherly Love failed at keeping people apart by allowing a city-wide parade to be thrown. The results show a necessity for isolation measures. Other examples of these interventions include Kansas City banning weddings and funerals with greater than twenty persons, New York City staggering factory shifts to reduce the waves of commuter traffic, and Seattle ordering its constituents to wear face masks in all public places. A clear negative correlation between the time of implemented measures and mortality can be observed, along with another negative correlation between the number of measures and mortality. The statistics are publicly available and can be found on the CDC's website.

Even with initial control measures, the second and third waves of Spanish flu caught cities that ended their nonpharmaceutical interventions off guard, demonstrating the importance of not lifting nonpharmaceutical interventions prematurely. For example, San Francisco reduced their mortality rate by 25%, but 90% of their deaths occurring between September 1918 to May 1919 could have been avoided if they had kept their initial controls in place.[4,9] They had previously closed schools and theaters and boasted their law mandating the use of masks in all public places. Catchy sayings, such as "protect your jaws from septic paws," were promoted by the Board of Health, the Red Cross, and the mayor himself; violators of public mandates faced jail time. After signs of the flu waned, sirens wailed on November 21st, 1919; masks came off, schools resumed session, and theaters reopened their doors. This also highlights the need for situational awareness and surveillance–the earlier we are aware of a potentially dangerous outbreak, the earlier we can institute infection control measures including isolation and quarantine, thus giving us a chance to prevent or curtail an outbreak. The premature celebrations left members of the public volatile and the next two cycles of flu once again ravaged the city.

While in retrospect it may seem obvious that rapid implementation of these sweeping measures saved lives, they were met with considerable opposition. Significantly, this resistance did not come from specific ethnic or racial groups being made scapegoats for the outbreak, as had happened in previous epidemics. The Spanish influenza moved so quickly and so indiscriminately among the population that it could not easily be blamed on immigrants or the poor.[10] Instead, the lines of resistance reflected divisions between the public health departments and the communities they served.

Implementing social-distancing measures in these big cities presented a massive public health challenge.[11] They had complex economies dependent on both industry and commerce that could easily be damaged by quarantines and closures. As had happened in earlier epidemics, businessmen resisted the idea of mass closures of transportation and businesses that would cause economic distress both to owners and workers. Some employees filed lawsuits to recover lost wages due to such a closure. Big cities also had large public-school systems, flourishing commercial entertainment districts, and extensive systems of mass transit, all of which formed fertile ground for the spread of influenza. School closures left parents with children to provide for during the day. Shutting down saloons and theaters meant not only lost revenue for owners but also lost pleasures for their customers. To inflict such economic damage on a city's economy required a public health emergency without precedent.

Hence, a number of cities including New York felt that the most practical strategy was to move quickly to isolate the acutely ill in hospital wards or at home and to direct an intensive public education effort about personal hygiene to everyone else.

Public-gathering bans also exposed tensions about what constituted essential vs. unessential activities. Those forced to close their facilities complained about those allowed to stay open. For example, in New Orleans, municipal public health authorities closed churches but not stores, prompting a protest from one of the city's Roman Catholic priests. Theater owners often voiced the "why us and not them" argument. In many cities they were the first, and sometimes the only, businesses to be shut down. In response, some of them asked that the closing order be extended to department stores and public transport.[11]

Perhaps the most important "lesson" taught by the Spanish flu pandemic was the realization that those measures that worked the best to control a highly infectious disease—bans on public gatherings, school closures, and strict quarantine and isolation—were precisely the ones most difficult to implement. In the modern times, the amount of resistance to these measures will likely be no different. Also, in an event of a serious pandemic, some measures such as those involving closure of county or state borders in a quarantine may be impractical since they will not be able to be enforced. The manpower required to do so will outstrip the need. Even more so due to the fact that a significant proportion of law enforcement personnel may themselves fall ill or be taking care of their own ill family members or providing for the safety of their families in an event of societal disruption secondary to a massive pandemic. The mandatory quarantines will also likely fuel public distrust in the government and may even fuel public unrest and societal disruption, as we have seen happen in the most recent Ebola outbreak in Africa.

In light of all this, a combination of select public health control measures with empowering individuals and organizations to self-quarantine or use other measures to decrease or stop the transmission of infectious organisms may be the most practical and effective approach.

Other Infection Control Measures and Opportunities for Innovation

As discussed above, due to the fact that we are unlikely to have drugs or vaccines available in time to counter an emerging infection in a pandemic, we will instead need to rely on infection control measures to get ahead of it. This does not mean we cannot utilize modern technology, however—quite the opposite. This is an area which is currently underinvested but which holds much promise and opportunity if we innovate around it. What might this look like? If we are able to keep everybody home for a month or two, we would stop the cycle of transmission and illness and be done containing a pandemic.

How do we enable that? Perhaps people can work or study remotely from home while they get automated delivery of food, water, and basic supplies via driverless cars or drones. Keeping everybody home for a month at this point in time may be an unrealistic goal given the current state of technology, but it may be more achievable as technology advances. Even if part of the population can be isolated in this way for a period of time, this may help us get ahead of an outbreak. Also, perhaps people would prefer to self-quarantine if they face a possibility of catching an infection with high mortality rates if they leave their homes. They would just need to be enabled to self-quarantine, either with the use of technology or simple personal disaster preparedness. If we are prepared in this way, we are also likely to decrease the chances of public chaos and breakdown of society in an event of a deadly pandemic and will significantly decrease the burden on hospitals and medical infrastructure as a side-effect.

How about creative use of UV lights, which we know effectively kill germs? Those could be used in public transport, offices, and schools. Or the use of germicidal ozone? Air filters? Wider use of negative pressure rooms, to remove air with germs and replace it with the one without? Or altering humidity and temperature in hospitals and buildings, since both have been shown to affect the spread of some infectious organisms including influenza?[12] Or creating better personal protective equipment that everybody, not only medical personnel, can safely and easily use? The opportunities to innovate are numerous. The attractiveness of these approaches is that they can be used for every bug or at least a large group of bugs, unlike the traditional pharmacologic countermeasures, which generally use a one bug per drug approach.

Are We Prepared for Pandemics, and What Should Be the Next Steps?

Are we prepared to withstand pandemics due to organisms with high mortality rates? According to the Blue Ribbon Study Panel on Biodefense (BRSPB) in 2015, we are not.[13] The Blue Ribbon Study Panel on Biodefense is a privately funded entity established in 2014 to provide a comprehensive assessment of the state of U.S. biodefense efforts, and to issue recommendations that will foster change. It is the only body of bipartisan high-level policymakers to do so.

The study covered human-generated (terrorist and accidental) and naturally occurring biological threats. The study culminated in a report to the public that Congress released on October 28, 2015. BRSPB's final report had 33 recommendations and over 80 specific items associated with those recommendations. The study assessed biological threat awareness, prevention and protection, surveillance and detection, and response and recovery. Current and former members of Congress, former administration officials, state and local representatives, thought leaders, and other experts provided their perspectives on current biodefense efforts, including strengths, weaknesses, and opportunities. While much good work has been achieved toward biodefense, these meetings have revealed systemic challenges in the enterprise designed to protect Americans from a biological event.

Some of the challenges highlighted include lack of senior national leadership to centralize efforts of the various governmental agencies working on issues related to biosecurity. The Panel proposed empowering the vice president with jurisdiction and authority over biodefense responsibilities. Other recommendations included measures to enhance national biosurveillance capability, improving public health emergency capabilities and hospital preparedness, incentivizing innovation in countermeasure development and deployment, and rapid point-of-care diagnostics, leading the way toward establishing an agile global public health response apparatus. In 2018, the Blue Ribbon Study Panel also issued their budget recommendations to increase return on investment in biodefense.[14] Much is left for us to do to enhance our ability to withstand serious pandemics. Concerted effort with an innovative and collaborative mindset will save lives and enhance our nation's safety, security, and resilience to pandemic threats.

---

[1] Flannery B, Zimmerman RK, Gubareva LV, et al. Enhanced Genetic Characterization of Influenza A(H3N2) Viruses and Vaccine Effectiveness by Genetic Group, 2014-2015. J Infect Dis 2016; 214:1010.

[2] Zimmerman RK, Nowalk MP, Chung J, et al. 2014-2015 Influenza Vaccine Effectiveness in the United States by Vaccine Type. Clin Infect Dis 2016; 63:1564.

[3] Ontario., & Campbell, A. G. (2006). *Spring of fear: The SARS Commission final report*. Toronto: SARS Commission.

[4] Bootsma, M. C., & Ferguson, N. M. (2007). The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proceedings of the National Academy of Sciences, 104*(18), 7588-7593. doi:10.1073/pnas.0611071104

[5] Hatchett, R. J., Mecher, C. E., & Lipsitch, M. (2007). Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proceedings of the National Academy of Sciences, 104*(18), 7582-7587. doi:10.1073/pnas.0610941104

[6] Qualls, N., Levitt, A., Kanade, N., Wright-Jegede, N., Dopson, S., Biggerstaff, M., . . . Jernigan, D. (2017). Community Mitigation Guidelines to Prevent Pandemic Influenza — United States, 2017. *MMWR. Recommendations and Reports,* 66(1), 1-34. doi:10.15585/mmwr.rr6601a1

[7] Schwartz, J. L. (2018). The Spanish Flu, Epidemics, and the Turn to Biomedical Responses. *American Journal of Public Health, 108*(11), 1455-1458. doi:10.2105/ajph.2018.304581

[8] Shanks, G. D., & Brundage, J. F. (2012). Pathogenic Responses among Young Adults during the 1918 Influenza Pandemic. *Emerging Infectious Diseases, 18*(2), 201-207. doi:10.3201/eid1802.102042

[9] Rapid Response was Crucial to Containing the 1918 Flu Pandemic. (2015, September 28). Retrieved March 04, 2019, from https://www.nih.gov/news-events/news-releases/rapid-response-was-crucial-containing-1918-flu-pandemic

[10] Jones EW. Cooperation is all human endeavor. Can Bull Med Hist. 2005;22:57–82.

[11] Tomes N. “Destroyer and teacher”: Managing the masses during the 1918-1919 influenza pandemic. *Public Health Rep*. 2010;125 Suppl 3(Suppl 3):48-62.

[12] Roles of Humidity and Temperature in Shaping Influenza Seasonality. Anice C. Lowen, John Steel. Journal of Virology Jun 2014, 88 (14) 7692-7695.

[13] Blue Ribbon Study Panel on Biodefense. A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts – Bipartisan Report of the Blue Ribbon Study Panel on Biodefense. Hudson Institute: Washington, DC, October 2015

[14] Blue Ribbon Study Panel on Biodefense. *Budget Reform for Biodefense: Integrated Budget Needed to Increase Return on Investment*. Blue Ribbon Study Panel on Biodefense: Washington, DC. February 2018.

Dr. Milana Boukhman Trounce is a clinical associate professor at the Stanford University School of Medicine and an emergency medicine physician.

Climate Change and Environmental Pollutants: Translating Research into Sound Policy for Human Health and Well-Being

By Kari Nadeau, Stanford University

We are intimately connected to the world around us—to the air, water, and soil that envelop us. The average adult constantly replenishes the oxygen within them by taking 12 to 20 breaths per minute; we regularly consume water, which constitutes over 50% of our body weight; we obtain most of our vital nutrients from the soil through the foods we consume. A healthy vibrant biosphere is vital for our wellbeing (see Figure 1).

Industrialization and increased human activity are changing the biosphere in ways that are detrimental to supporting life on earth. Vehicular emissions, power and heat generation, and industrial and agricultural emissions are major sources of pollutants and greenhouse gases. By increasing greenhouse gases, we are trapping heat in the atmosphere and causing global climate changes and shifts in atmospheric and ocean chemistry that affect human health and the health of the planet. Global average temperature increased by about 1.0°C from 1901 to 2016[1] and continues to increase. The last five years, from 2014 to 2018, are the warmest years ever recorded in the 139 years that the National Oceanic and Atmospheric Administration has tracked global heat.[2]

The time to act and find solutions is now. There is a ground swell of evidence that, despite certain government officials damagingly saying otherwise, should inspire and motivate us to find ways to prevent and treat the acute and chronic effects of pollution on our health.

We have seen the face of pollution in the news, wildfires raging through forests and homes, dust storms stretching far and wide, plastic patches the size of California in the ocean, floods wrecking homes and communities. But pollution also has a real human face. People around the globe have seen the human face of pollution and the real costs. The newborn baby with stunted growth born prematurely because her mother was exposed to too much air pollution in Nairobi; the elderly man dying of a heart attack after exposure to wildfire smoke 500 miles away in San Francisco; a young girl going into puberty because of chemicals from plastics in the water supply in India; a young man who cannot remember where his house is because of eating fish with mercury in Norway; a baby in London with extensively dry irritated skin because of the detergents in the washing water; a pregnant mother who drank rice milk with arsenic levels that will affect her unborn child for years to come in New Hampshire; a 56-year-old grandmother who dies due to new onset asthma in a pollen storm in Australia; and a teenager working in the fields and eating at a food stand with vegetables depleted of minerals and iron in South Carolina.

Pollution, its effects, and its consequences on health are all around us—and they reach into the future through our children. Children are particularly vulnerable to pollution. They breathe proportionally more air because of their higher respiratory rate, and they spend more time outdoors where they are exposed to airborne pollutants. The effects of pollution in children are higher as their lungs and other organs are still developing. In fact, the damage caused by air pollution can begin before a child is born. A recent study demonstrated a clear link between air pollution and stillbirths, premature births, and low birth weight infants.[3] In another study, smoke from kerosene stoves was associated with reduced birth weight and micronutrient imbalance in mothers and newborns.[4]

The evidence that current climate change is caused by increased industrialization and human activity is now irrefutable. The detrimental effects of pollutants to human health are well documented. The scientific evidence is clear as is the need for bold and transformative policy change to promote a sustainable and healthy planet for the benefit of future generations. Scientists have identified these pollutants and their sources to understand their effects on health. Clinicians have a duty towards creating a healthier environment and protecting human health. And citizens need to work towards translating the findings from environmental research into sound policies that can create sustainable solutions for the future of our children and the health of the planet.

Pollutants and Their Effects

There are many types of pollutants. Increasing greenhouse gases are a major concern and cause thermal pollution.

Others include air, water, soil, light, noise, and radioactive pollution. As human population and activity increase, there is the potential for the emission of and exposure to these pollutants to grow. If not managed, global pollution growth could have dire consequences.

Atmospheric Pollutants

Indoor and ambient (outdoor) air pollutants consist of both natural and man-made particles and gases; in high concentrations, they can have a deleterious effect both on human health and the health of the planet. Air pollution is measured by Air Quality Index (AQI) with different countries using different criteria. In the United States, AQI is based on concentrations of ground-level ozone, particulate matter (PM), carbon monoxide, sulfur dioxide, and nitrogen dioxide[5]; in India, AQI also includes ammonia and lead[6] (see Figure 2).

Every year 4.2 million deaths occur as a result of exposure to ambient air pollution and 3.8 million die every year as a result of household exposure to smoke from dirty cookstoves and fuels.[7] The World Health Organization (WHO) has identified five air pollutants of major concern: ground-level ozone, particulate matter, carbon monoxide, sulfur dioxide, and nitrogen dioxide. In the United States, the Environmental Protection Agency (EPA) included lead as the sixth major pollutant and has designated these six as "criteria air pollutants." The Clean Air Act requires the EPA to set national ambient air quality standards for these 6 air pollutants.[8,9] Besides the criteria air pollutants, a number of air pollutants that are known or suspected to cause serious health effects, such as cancer, reproductive effects, birth defects, or those that cause adverse environmental effects, have been categorized as hazardous or toxic air pollutants. Examples include gases (benzene, toluene, and xylenes), liquid aerosols (perchloroethylene and methylene chloride), and inhalable particles (polycyclic aromatic hydrocarbons, cadmium, chromium, lead, and mercury). Major gases that are emitted in significant amounts by human activity include carbon dioxide, chlorofluorocarbons (CFCs), methane, and nitrous oxide (see Figure 3).

Particulate matter pollution is a major concern and particles 10mm or below (PM_{10}) are considered harmful to our health as they are inhaled. Those 2.5mm and smaller ($PM_{2.5}$) are small enough to be inhaled deep into the lungs and enter the bloodstream, aggravating both the respiratory and cardiovascular systems.[10] $PM_{2.5}$ is one-thirtieth the width of a human hair (Figure 2). The chemical composition of particulate matter varies and can be made up of both man-made substances (sulfates, nitrates, ammonia, carbon, lead, organic compounds, etc.) as well as natural substances (soil, dust, bioaerosols, etc.). The mid-20th century saw large scale catastrophes. In 1948, in Donora, Pennsylvania, a deadly smog created by industrial pollutants asphyxiated 20 people and made thousands sick.[11] In 1952, the Great Smog in London caused by extensive burning of high-sulfur coal killed around 12,000 people over the course of 5 days.[12] Catastrophic events of that scale have been avoided by actions over the past several decades that have significantly reduced air pollution, but a number of cities still struggle with very high and extremely unhealthy levels of particulate matter. It is estimated that about 92% of the world's population lives in areas where the air quality exceeds the limits set by WHO guidelines.[13]

It is now clear that both long- and short-term exposure of even moderate levels of air pollutants have detrimental health effects. A study in China found short-term exposures to $PM_{2.5}$, nitrogen di oxide and ozone may increase asthma mortality risk.[14] Another study in Africa found that 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentration is associated with a 9% rise in infant mortality.[15] Studies show that $PM_{2.5}$ is associated significantly with increased rates of emergency department visits for asthma. In children aged 6–18 in New York City, intensive care unit admissions rates and hospitalizations increased 26% and 19%, respectively, when $PM_{2.5}$ concentration increased by 12 $\mu g/m^3$.[16] Recent data indicate that nearly 800,000 people die prematurely each year in Europe because of dirty air and that each life is cut short by an average of more than two years.[17]

The seriousness of the effects of air pollution, which can be cumulative with exposure, has sometimes been downplayed. In response to heavy smog in New Delhi in November 2017, India's Minister of Environment urged his people to remain calm, saying that the smog did not constitute a true public health emergency.[18] According to the U.S. embassy's measurements, air in Beijing reached $PM_{2.5}$ concentrations of more than 300 $\mu g/m^3$, and air in New Delhi reached $PM_{2.5}$ concentrations of more than 1,010 $\mu g/m^3$. In comparison, in the United States, due to the Clean Air Act of 1970 and its subsequent amendments in 1990, the air quality standard for the 24-hour average of $PM_{2.5}$ is 35 $\mu g/m^3$.[19] Although there has been some recent setbacks in the current U.S. EPA scientific advisory board's understanding of air pollution and its connection to health, on the whole, over the last 5 decades in the United States, improvements have resulted. For example, from 1970 to 2017, the annual $PM_{2.5}$ has decreased by about 40%. While the United States needs to continue its progress, China and India each are starting to work on proposed solutions for their current air pollution burden, which include 1) replacing existing cook stoves with clean cook stoves, 2) reducing pollution from diesel transport, and 3) restrict open burning of biomass and fossil fuels.[20]

Epidemiological evidence has clearly shown associations between air pollution and mortality. Ella Kissi-Debrah, who lived near a busy street in London, was hospitalized many times for severe asthma attacks and died in 2013 when she was 9 years old. Scientists found that her hospitalizations coincided with local pollution spikes. Her mother wants to put air pollution as the cause of Ella's death on her death certificate.[22]

Other air pollutants also pose serious health effects. Ozone is a pollutant that can have beneficial or harmful effects. In the stratosphere, ozone has a protective effect as it shields the earth from harmful ultraviolet radiations. However, ground-level ozone is an air pollutant that triggers wheezing, shortness of breath, and causes or aggravates other lung disease, such as chronic obstructive pulmonary disease or asthma. Ground-level ozone is formed when pollutants emitted by vehicular and industrial sources react chemically in the presence of sunlight. Exposure to ozone pollution causes increased risk of asthma, asthma exacerbations, and increased emergency room visits. Predictive models suggest that ozone-related emergency department visits for asthma in children are likely to increase by 7.3% across New York City by the 2020s.[23] Nitrogen dioxide also poses documented health risks. A meta-analyses of 12 studies including nearly 100,000 children found that it significantly influences the development of childhood asthma and symptoms of wheezing.[24]

Combustion of coal at power plants results in air emissions of mercury, another extremely harmful air pollutant. Coal plants are responsible for 44% of U.S. mercury emissions.[25] Mercury in particles in the air is a potent neurotoxin and prenatal exposures can lead to decreased motor and cognitive abilities even at low exposures.[26] Mercury exposures have also been linked to higher risks of hypertension, heart disease, and stroke.[27] The Mercury and Air Toxics Standards in the United States protected us to more than 80 dangerous pollutants, but now, with EPA rollbacks, they are in jeopardy. The standards prevent up to 11,000 premature deaths, 13,000 asthma attacks, and nearly 5,000 heart attacks. They deliver up to $90 billion in annual health benefits.[28]

Lead is another serious environmental health hazard, which can be found in air particulates. Environmental contamination occurs due to mining, smelting, manufacturing, recycling activities, and use of leaded paint, gasoline, and aviation fuel. Lead accumulates in the body and can be found in the brain, liver, kidney, and bones. There is no known level of lead exposure that is considered safe. Lead is now known to affect almost every organ/tissue of the human body. With irreversible effects on neurobiological development of young children and fetus, its toxicity has lasting implications for human life.[29]

Although carbon dioxide is released by living organisms, it is an air pollutant when associated with human activities involving the burning of fossil fuels. It is the most common of the greenhouse gases, which trap heat in the atmosphere and contribute to thermal pollution and climate change. Increasing carbon dioxide levels observed with climate change have been associated with increasing pollen levels.[30-33] Pollen data collected in Europe indicate an increasing trend in pollen aeroallergens,[32] and it is predicted that across Europe, sensitization to ragweed is likely to more than double by 2041 to 2060.[31] Other greenhouse gases include methane, CFCs, nitrous oxide, and sulfur dioxide. Methane is released by landfills, the natural gas industry, and gas emitted by livestock. CFCs, are commonly used in refrigerants and aerosol propellants. Sulfur dioxide and closely related chemicals are known primarily as a cause of acid rain. Once nitrous oxide enters the upper atmosphere, it can remain there for more than 100 years before it is naturally destroyed. Over this period, one molecule of nitrous oxide has the same greenhouse warming power of 300 molecules of carbon dioxide.[34]

Thunderstorms during the pollen season have been linked with increased asthma exacerbations and emergency room visits.[35] In 2016, several asthma deaths were observed during severe thunderstorms in Australia and Kuwait.[36,37] During thunderstorms, whole pollen grains are swept into the clouds where they are broken up into smaller allergenic pollen fragments and eventually carried back to ground level.[38] Similarly, dust storms and wildfires have been shown to increase asthma exacerbations.[39-43] Particulate matter £10mm in dust storms are linked with asthma exacerbations.[39] A 5-year study in Kuwait found that dust storm events (defined as events with PM_{10}>200 mg/m^3) were associated with respiratory disease in children.[39] Rising global temperatures can lengthen the season and increase the geographic range of disease-carrying insects. Increased rainfall, flooding, and humidity can create more viable breeding areas.

Climate change fueled by greenhouse gases has already warmed the planet substantially, causing more severe and prolonged heat waves, greater variability in temperature, increased air pollution, forest fires, droughts, and floods—all of which can put the respiratory health of the public at risk.[44] A 2007 WHO report expected that by 2025 the prevalence of asthma will increase by 25% to about 400 million.[45] Wildfire smoke contains carbon dioxide, water vapor, carbon monoxide, particulate matter, complex hydrocarbons, nitrogen oxides, trace minerals, and several other toxic and carcinogenic compounds. California witnessed devasting fires in the last 2 years. In 2017–2018, extreme wildfires occurred in Southern and Northern California, both located at wildland-urban interfaces. Damaging smoke from wildfires have been detected as far as 1,000 miles away. In a study investigating health effects of a 2008 California wildfire, risk of asthma exacerbation as determined by a 4-fold increase in emergency department visits was found to be associated with wildfire $PM_{2.5}$.[43]

In addition to outdoor air pollution, indoor air pollution is also of concern. Sources of indoor air pollution include fuels (oil, gas, coal, wood), molds, tobacco products, building materials, household cleaning products, and heating and cooling systems. Around 3 billion people still cook using wood, crop wastes, charcoal, coal, dung, or kerosene as fuels, which produces high levels of particulate matter. In poorly ventilated dwellings, indoor smoke can be 100 times higher than acceptable levels for fine particles. Exposure is particularly high among women and young children, who spend the most time near the domestic hearth.[46] Access to clean fuels and technologies for cooking is important to lower indoor pollution. Some outdoor substances can enter the home or building and increase indoor pollutant levels. Radon is a colorless, odorless radioactive gas found in soils. It enters through the ground and into the home through openings in the floors and walls. It decays, giving off radioactive particles. Long-term exposure to these particles can lead to lung cancer.[47] Radon detection devices are commercially available and are relatively simple. Sealing cracks and diverting radon away with vacuum or ventilation systems is the best way to prevent radon exposure.[48]

Solutions: The scientific consensus is overwhelming and leaves little room for dispute—increased human activity and emission of pollutants and greenhouse gases are harming human health and the health of the planet. Climate change is real and clearly points to the need for bold and transformative policy change and clear action items to mitigate or reverse these trends. The 2015 Paris Climate Accord represents the world's desire to combat climate change through reduction of greenhouse gas emissions. The central aim of this international cooperation is to strengthen the global response to the threat of climate change with a goal of limiting global temperature rise this century to 2°C above pre-industrial levels and to pursue efforts to limit the temperature increase even further to below 1.5°C.[49] Meanwhile, the first WHO Global Conference on Air Pollution and Health was held in Geneva in November 2018.[50] There was participation from and collaboration with national and city governments, intergovernmental organizations, civil society, philanthropy, research, and academia. Participants at the conferences highlighted a goal of reducing the number of deaths from air pollution by two thirds by 2030. To reach these goals, one of the important items put forward was to continue the joint effort for harmonized air pollution monitoring through initiatives such as the Global Platform on Air Pollution and Health. This initiative aims to strengthen air quality monitoring and the assessment and reporting of related health impacts across nearly 50 such agencies around the world. Another item was to increase efforts to scale up the "BreatheLife" campaign[51] by enlisting 500 BreatheLife cities and 20 countries by 2020, all committing to reaching WHO air quality guideline levels by 2030. One such member is Oslo, Norway, which has focused on promoting the use of zero-emission vehicles in the urban areas through decreased taxes, access to bus and taxi lanes, free tolls on roads and ferries, and free municipal parking.[52] A 2018 Greenpeace report indicated that Oslo was the only city in their analysis that has emissions below both the European Union limit and the World Health Organization guidelines.[53] So it is possible and some cities are leading by example to change the future.

Water Pollution

Water pollution is one of the major crises in public health today, and it affects millions of people who do not have access to clean drinking water. Water pollution is caused by rapidly growing urban developments and improper disposal of household and other chemicals by residents, improper sewage disposal, dumping of chemical wastes by industry and agriculture, silt runoff from construction, discharge of radioactive wastes, detergents, microplastics, medical drugs, and oil spills. These pose health risks for humans, plants, and animals now and in the future. Two major recent oil spill disasters include the Exxon Valdez oil spill in Prince William Sound, Alaska, in 1989 and the BP Deepwater Horizon explosion in the Gulf of Mexico in 2010. The total volume of oil from the Exxon Valdez spill covered more than 1,300 miles of shoreline. Exxon Valdez was a single-hulled ship. Single-hulled tankers are now barred from using U.S. ports and as of 2015 have been phased out throughout much of the world under International Maritime Organization agreements.[54] In the Deepwater Horizon disaster, over 200 million gallons of crude oil spilt from a wellhead at 5000 feet in the deep ocean. The oil flowed over an 87-day period, before it was finally capped.[55] Some of the immediate changes the Bureau of Safety and Environmental Enforcement and the Bureau of Ocean Energy Management implemented after the Deepwater Horizon oil spill were increasing well-design standards, oversight by third parties, and monitoring. However, the Trump administration is planning to reverse these rules, which were enacted to ensure that similar accidents are prevented in the future.[56] In addition to spills in the ocean, major contaminations have occurred in water supplies. In 2014, China's biggest oil company was blamed for contaminated water affecting over 2.4 million people in Lanzhou. Benzene, a known carcinogen, was found at 20 times the national safety limit. In 2014, Flint, Michigan, authorities switched its drinking water supply from Detroit's system to the Flint River in a cost-saving move. Corrosive water caused lead from old pipes to leach into the water system and into people's homes. The contaminated water led to a doubling or tripling of the incidence of elevated blood lead levels in children. After international publicity and court actions, the city switched to a new supplier for water and is replacing lead pipes.[57]

Under the right conditions, such as warmer water temperatures or excessive nutrients from fertilizers or sewage waste runoff, algae can grow out of control and some can produce toxins that can affect humans and wildlife. Even excessive growth of nontoxic algae can decrease oxygen levels in the water and may smother fish and other vegetation. With climate change, scientists expect these so-called «harmful algal blooms» to become more frequent, wide-ranging, and severe.[58] In the Bering Straits, decreases in the thickness of the ice and increased penetration of light has led to toxic algal blooms. Some algal poisons kill fish and may cause brain damage in people. Cases of paralytic shellfish poisoning have increased seven-fold in Alaska over the past 40 years. The state now has one of the highest incidences of shellfish poisoning in the world.[59]

In 2014, harmful algal blooms contaminated drinking water in Toledo, Ohio, with microcystin, a toxin that can cause liver and kidney damage, causing the water system to be shut down for three days. Fertilizer runoff and septic systems from developments alongside Lake Erie have led to a series of annual algal blooms in the area, and local residents are now attempting to save the failing health of the world's 11th largest lake through legal action.[60]

Coral reefs are an important part of the ecosystem and are responsible for providing shelter and food to around a quarter of all ocean species.[61] Coral reef ecosystems are among the most biologically diverse and complex marine ecosystems worldwide. While covering less than 1% of the ocean surface, coral reefs provide a habitat for nearly one third of marine fish species as well as 10% of all fish captured for human consumption. Unfortunately, the World Conservation Institute estimates that 20% of coral reefs are already destroyed, another 25% are at immediate threat, and another 25% will be threatened by 2050. Regenerating ocean life and establishing marine protected areas are vital. At the current time, only 4.8% of the world's oceans are actively managed marine protected areas, and conservation organizations have proposed significantly increasing this share.[62] Other efforts include repopulating coral reefs with reef fish and crustaceans and by coral gardening. Decreasing pollutants is also key in efforts to improve the health of the oceans. In February 2019, Key West voted to ban the sale of certain sunscreens containing chemicals, which are believed to harm coral reefs.[63] The compounds in most sunscreens catalyze the production of hydrogen peroxide, a well-known bleaching agent, at a concentration high enough to harm coastal marine organisms.

Pollution of our waters by plastics is ubiquitous, with an estimated 18 billion pounds of plastic waste entering the world's oceans each year.[64] Great Britain's Royal Statistical Society has estimated that 90.5% of plastic ever made has never been recycled.[65] Trash accumulates in five ocean garbage patches, the largest one being the Great Pacific Garbage Patch, located between Hawaii and California. Many animals ingest plastics and often die of complications or starvation. In 2017, for example, a large sperm whale was found beached with 64 pounds of trash in its digestive track.[66] Plastics degrade on exposure to sun, wind, and rain and form smaller and smaller particles, termed microparticles. It is now evident that microplastics have permeated remote areas of the planet, including our oceans. A recent study has now found microplastics in the stools of humans and their effects on human health and wellbeing are unknown.[67] Microbeads, plastic beads smaller than 5mm or less, are another source of microplastics. They were being used in a number of cosmetics to exfoliate skin. To address concerns of microbeads in the water supply, the U.S. Congress passed the Microbead-Free Waters Act of 2015, which prohibits the manufacturing, packaging, and distribution of rinse-off cosmetics containing plastic microbeads.[68]

Marian Chertow, an associate professor at the Yale School of Forestry & Environmental Studies and director of the program on solid waste policy, noted that in 2008 China passed a law promoting a circular economy. The idea is you make a product with material you know can be recycled rather than make a product and then figure out how to recycle it. In 2017, China banned import of plastic waste. As China was importing about 45% of the world's plastics, countries like the United States now have an economical and environmental imperative to lower use of plastics and recycle them locally.[69,70]. With increasing recognition of the magnitude of the problem, there are considerable efforts to push for legislation to limit the use of plastics (especially single use plastics). In 2018, the European Parliament approved a ban on single-use plastics such as straws and plates in Europe by 2021.[71] Similar bans are in effect or under consideration in many cities and countries.

Soil, Radioactive, Light, and Noise Pollution

Nuclear power plants offer a means of producing energy without the production of carbon-dioxide emissions. Spent fuel from nuclear power plants and other civil and military nuclear waste need to be protected from the environment for a considerable period of time, since some radioactive components decay over very long periods of time. Radioactive wastes are generally placed in interim storage facilities pending further technical and political consideration of long-term solutions.

Soil pollution perhaps gets less attention than that of water or air; as years can go by before the true effect of the damage can be realized. According to the 2018 Food and Agriculture Organization (FAO) report, the total number of contaminated sites is estimated at 80,000 across Australia; 3 million in the European Economic Area and cooperating countries in the West Balkans; and 1,300 in the United States. In China, the Chinese Environmental Protection Ministry, estimated that 16% of all Chinese soils and 19% of its agricultural soils are categorized as polluted.[72] Official estimates say that China produces 12 million tonnes of heavy-metal contaminated grain a year.[73] In 2018, China passed its first law on soil pollution prevention and control and is in the process of setting national standards for soil pollution risk control based on the soil's contamination status, public health risks, and ecological risks.[74]

Based on evidence on the adverse health effects of environmental noise on cardiovascular and metabolic effects, sleep quality, cognitive function, hearing, birth outcomes, quality of life, mental health, and wellbeing, in 2018, the WHO developed guideline recommendations for protecting human health from exposure to environmental noise originating from various sources such as transportation or wind turbines.[75] Noise pollution also affects animal life. Even the oceans are getting louder as a result of increased global shipping and geologic exploration activities. Such noise can disrupt marine life, including migration and lifecycle patterns. A 2017 study found that loud, underwater noises such as those used in marine seismic survey operations, could kill a majority of zooplankton within a three-quarter mile radius.[76] Although limiting the number and intensity of seismic blasts would be in the best interest for marine life in the oceans, the United States is currently pursuing plans increase seismic surveys along the Atlantic coast for energy production.

Light pollution also has effects on humans and other animals. The light of the moon is an important focal point for many organisms. Coral spawn during the full moon in October and November; baby turtles are drawn to the water by the moon's reflection on the ocean waves. Artificial illumination has been shown to mask the moon's phases potentially causing the reefs to release their reproductive cells out of sync, thwarting their chances of producing offspring. Turtles can be directed to artificial light in the direction away from the ocean.[77] In humans, light pollution can disturb a person's circadian rhythm.

Solutions for Global Pollution and Climate Change

Our progress in mitigating climate change has been followed by setbacks. The United States withdrew from the Paris accord in 2018, and now the EPA Scientific Advisory Board in March 2019, with members recognizably conflicted due to their industry ties, has questioned air pollution's effect on health. However, we have historical precedent for how countries, including the United States, have worked together on global environmental issues, yielding significant results. For instance, following the phase out of CFCs through the 1987 Montreal Protocol, the seasonal hole in the Antarctic ozone layer has in recent years started to diminish. This highlights the impact of motivated citizens to speak up, persist, and apply political pressure at the global, national, and local level.

We should be equally concerned about the effects of climate change on human health and are implementing plans to step up and catalyze innovative approaches to address health (both public and individual) associated with increasing levels of pollution. Doing so will require making the social, health, and economic case for taking action now to address the large and growing global burden. Notably, when countries have passed laws to decrease pollution exposure on their citizens, the increases in worker productivity and economic profits have been dramatic.[78]

Importantly, while progress on preventing, mitigating, and managing pollution will need to occur at a global level, we need to see change in companies, hospitals, and public health systems. Movements are occurring to build 'green' industry campuses, build lower energy-using hospital and clinic buildings, and reduce waste from hospitals. University campuses are improving their energy use and recycling processes. Individuals can also help. Online tools, for example, can educate and assist in calculating one's carbon footprint and social media can help motivated individuals find and share ways to reduce their carbon footprints,[79] whether through reducing one's dependence on fossil fuels and plastics, reducing family-level consumption, recycling and energy efficiency, promoting sustainable healthy living, or supporting responsible public policies across different levels of government.

---

[1] U.S. Global Change Research Program. Fourth National Climate Assessment. 2017. https://science2017.globalchange.gov.

[2] Borunda A. The last five years were the hottest ever recorded. 2019. https://www.nationalgeographic.com/environment/2019/02/2018-fourth-warmest-year-ever-noaa-nasa-reports/.

[3] Korten I, Ramsey K, Latzin P. Air pollution during pregnancy and lung development in the child. *Paediatr Respir Rev* 2017;21:38-46.

[4] Arinola GO, Dutta A, Oluwole O, Olopade CO. Household Air Pollution, Levels of Micronutrients and Heavy Metals in Cord and Maternal Blood, and Pregnancy Outcomes. *Int J Environ Res Public Health* 2018;15.

[5] Agency USEP. Monitoring Air Quality Crucial in Western United States. 2003. http://www.njaqinow.net/App_AQI/AQI.en-US.pdf.

[6] The Economic Times. India launches index to measure air quality 2014. https://economictimes.indiatimes.com/news/politics-and-nation/india-launches-index-to-measure-air-quality/articleshow/44855452.cms.

[7] World Health Organization. Air Pollution. 2019. https://www.who.int/airpollution/en/.

[8] United States Environmental Protection Agency. Criteria Air Pollutants. 2017. https://19january2017snapshot.epa.gov/criteria-air-pollutants_.html.

[9] United States Environmental Protection Agency. NAAQS Table. 2016. https://www.epa.gov/criteria-air-pollutants/naaqs-table (accessed March 5 2019).

[10] Air Quality Communication Workshop. Overview of Particle Air Pollution (PM2.5 and PM10). 2012. https://www.epa.gov/sites/production/files/2014-05/documents/huff-particle.pdf.

[11] Jacobs ET, Burgess JL, Abbott MB. The Donora Smog Revisited: 70 Years After the Event That Inspired the Clean Air Act. *Am J Public Health* 2018;108:S85-S8.

[12] Polivka BJ. The Great London Smog of 1952. *Am J Nurs* 2018;118:57-61.

[13] World Health Organization. WHO releases country estimates on air pollution exposure and health impact 2016. https://www.who.int/news-room/detail/27-09-2016-who-releases-country-estimates-on-air-pollution-exposure-and-health-impact.

[14] Liu Y, Pan J, Zhang H, Shi C, Li G, Peng Z, Ma J, Zhou Y, Zhang L. Short-Term Exposure to Ambient Air Pollution and Asthma Mortality. *Am J Respir Crit Care Med* 2019.

[15] Heft-Neal S, Burney J, Bendavid E, Burke M. Robust relationship between air quality and infant mortality in Africa. *Nature* 2018;559:254-8.

[16] Silverman RA, Ito K. Age-related association of fine particles and ozone with severe acute asthma in New York City. *J Allergy Clin Immunol* 2010;125:367-73 e5.

[17] Carrington D. Air pollution deaths are double previous estimates, finds research. 2019. https://www.theguardian.com/environment/2019/mar/12/air-pollution-deaths-are-double-previous-estimates-finds-research.

[18] Soneja. S CA. Death by air pollution: time to take action. https://blogs.plos.org/globalhealth/2018/08/death-by-air-pollution-time-to-take-action/.

[19] Tom Di Liberto. Smog descends on India and Pakistan in mid-November 2017. 2017. https://www.climate.gov/news-features/event-tracker/smog-descends-india-and-pakistan-mid-november-2017.

[20] Organization WH. India takes steps to curb air pollution. 2016. https://www.who.int/bulletin/volumes/94/7/16-020716/en/.

[21] Ministry of Environment FaCC. Government launches National Clean Air Programme (NCAP) 2019. http://pib.nic.in/newsite/PrintRelease.aspx?relid=187400.

[22] BBC News. Ella Kissi-Debrah ‘pollution’ death: New inquest plea lodged. 2019. https://www.bbc.com/news/uk-england-london-47255859.

[23] Sheffield PE, Knowlton K, Carr JL, Kinney PL. Modeling of regional climate change effects on ground-level ozone and childhood asthma. *Am J Prev Med* 2011;41:251-7; quiz A3.

[24] Takenoue Y, Kaneko T, Miyamae T, Mori M, Yokota S. Influence of outdoor NO2 exposure on asthma in childhood: meta-analysis. *Pediatr Int* 2012;54:762-9.

[25] Thanos Bourtsalas AC, Themelis NJ. Major sources of mercury emissions to the atmosphere: The U.S. case. *Waste Manag* 2019;85:90-4.

[26] Carocci A, Rovito N, Sinicropi MS, Genchi G. Mercury toxicity and neurodegenerative effects. *Rev Environ Contam Toxicol* 2014;229:1-18.

[27] Houston MC. Role of mercury toxicity in hypertension, cardiovascular disease, and stroke. *J Clin Hypertens (Greenwich)* 2011;13:621-7.

[28] Waldman S. The EPA’s Climate Rollbacks Could Mean Thousands of Premature Deaths. 2018. https://www.scientificamerican.com/article/the-epas-climate-rollbacks-could-mean-thousands-of-premature-deaths/.

[29] Sachdeva C, Thakur K, Sharma A, Sharma KK. Lead: Tiny but Mighty Poison. *Indian J Clin Biochem* 2018;33:132-46.

[30] D’Amato G, Holgate ST, Pawankar R, Ledford DK, Cecchi L, Al-Ahmad M, Al-Enezi F, Al-Muhsen S, Ansotegui I, Baena-Cagnani CE, Baker DJ, Bayram H, Bergmann KC, Boulet LP, Buters JT, D’Amato M, Dorsano S, Douwes J, Finlay SE, Garrasi D, Gomez M, Haahtela T, Halwani R, Hassani Y, Mahboub B, Marks G, Michelozzi P, Montagni M, Nunes C, Oh JJ, Popov TA, Portnoy J, Ridolo E, Rosario N, Rottem M, Sanchez-Borges M, Sibanda E, Sienra-Monge JJ, Vitale C, Annesi-Maesano I. Meteorological conditions, climate change, new emerging factors, and asthma and related allergic disorders. A statement of the World Allergy Organization. *World Allergy Organ J* 2015;8:25.

[31] Lake IR, Jones NR, Agnew M, Goodess CM, Giorgi F, Hamaoui-Laguel L, Semenov MA, Solomon F, Storkey J, Vautard R, Epstein MM. Climate Change and Future Pollen Allergy in Europe. *Environ Health Perspect* 2017;125:385-91.

[32] Ziello C, Sparks TH, Estrella N, Belmonte J, Bergmann KC, Bucher E, Brighetti MA, Damialis A, Detandt M, Galan C, Gehrig R, Grewling L, Gutierrez Bustillo AM, Hallsdottir M, Kockhans-Bieda MC, De Linares C, Myszkowska D, Paldy A, Sanchez A, Smith M, Thibaudon M, Travaglini A, Uruska A, Valencia-Barrera RM, Vokou D, Wachter R, de Weger LA, Menzel A. Changes to airborne pollen counts across Europe. *PLoS One* 2012;7:e34076.

[33] Ziska LH, Epstein PR, Schlesinger WH. Rising CO(2), climate change, and public health: exploring the links to plant biology. *Environ Health Perspect* 2009;117:155-8.

[34] Scott Waldman. Nitrous Oxide Poses Fresh Threat to the Arctic. 2017. https://www.scientificamerican.com/article/nitrous-oxide-poses-fresh-threat-to-the-arctic/.

[35] D’Amato G, Liccardi G, Frenguelli G. Thunderstorm-asthma and pollen allergy. *Allergy* 2007;62:11-6.

[36] Bousquet J, O’Hehir RE, Anto JM, D’Amato G, Mosges R, Hellings PW, Van Eerd M, Sheikh A. Assessment of thunderstorm-induced asthma using Google Trends. *J Allergy Clin Immunol* 2017.

[37] Woodhead M. Hospitals overwhelmed with patients after “thunderstorm asthma” hits Melbourne. *BMJ* 2016;355:i6391.

[38] D'Amato G, Vitale C, D'Amato M, Cecchi L, Liccardi G, Molino A, Vatrella A, Sanduzzi A, Maesano C, Annesi-Maesano I. Thunderstorm-related asthma: what happens and why. *Clin Exp Allergy* 2016;46:390-6.

[39] Thalib L, Al-Taiar A. Dust storms and the risk of asthma admissions to hospitals in Kuwait. *Sci Total Environ* 2012;433:347-51.

[40] Kanatani KT, Ito I, Al-Delaimy WK, Adachi Y, Mathews WC, Ramsdell JW, Toyama Asian Desert D, Asthma Study T. Desert dust exposure is associated with increased risk of asthma hospitalization in children. *Am J Respir Crit Care Med* 2010;182:1475-81.

[41] Goudie AS. Desert dust and human health disorders. *Environ Int* 2014;63:101-13.

[42] Reid CE, Brauer M, Johnston FH, Jerrett M, Balmes JR, Elliott CT. Critical Review of Health Impacts of Wildfire Smoke Exposure. *Environ Health Perspect* 2016;124:1334-43.

[43] Reid CE, Jerrett M, Tager IB, Petersen ML, Mann JK, Balmes JR. Differential respiratory health effects from the 2008 northern California wildfires: A spatiotemporal approach. *Environ Res* 2016;150:227-35.

[44] Intergovernmental panel on climate change. Climate Change 2013: The Physical Science Basis2013. http://www.ipcc.ch/report/ar5/wg1/ (accessed.

[45] Global Alliance against Chronic Respiratory Diseases (GARD). Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach, 2007.

[46] World Health Organization. Household air pollution and health. 2018. https://www.who.int/news-room/fact-sheets/detail/household-air-pollution-and-health.

[47] Choi H, Mazzone P. Radon and lung cancer: assessing and mitigating the risk. *Cleve Clin J Med* 2014;81:567-75.

[48] Unites States Environmental Protection Agency. A Citizen's Guide to Radon. 2012. https://www.epa.gov/sites/production/files/2016-02/documents/2012_a_citizens_guide_to_radon.pdf.

[49] Helen Briggs. What is in the Paris climate agreement? 2017.

[50] World Health Organization. CLEAN AIR FOR HEALTH: Geneva Action Agenda. 2018. https://www.who.int/phe/news/clean-air-for-health/en/.

[51] Breathlife. A global campaign for clean air. http://breathelife2030.org.

[52] UN Environment. Oslo takes bold steps to reduce air pollution, improve livability. 2018. https://www.unenvironment.org/news-and-stories/story/oslo-takes-bold-steps-reduce-air-pollution-improve-livability.

[53] Greenpeace. Ranking of European Cities in Sustainable Transport. 2018. https://www.greenpeace.de/sites/www.greenpeace.de/files/publications/living.moving.breathing.20180604.pdf.

[54] Wendy Koch. Exxon Valdez oil spill, 25 years later, offers lessons. 2014. https://www.usatoday.com/story/news/nation/2014/03/21/exxon-valdez-25th-anniversary/6707983/.

[55] Environmental Protection Agency. Deepwater Horizon – BP Gulf of Mexico Oil Spill. https://www.epa.gov/enforcement/deepwater-horizon-bp-gulf-mexico-oil-spill.

[56] FULLER A. Eight Years After Deepwater Horizon. 2018. https://blog.nwf.org/2018/04/eight-years-after-the-deepwater-horizon/.

[57] Denchak M. Flint Water Crisis: Everything You Need to Know. 2018. https://www.nrdc.org/stories/flint-water-crisis-everything-you-need-know.

[58] National Oceanic and Atmospheric Administration. What is a harmful algal bloom? 2016. https://www.noaa.gov/what-is-harmful-algal-bloom.

[59] Carolyn G. Disappearing sea ice could disrupt Arctic's food web. 2019. https://www.sciencenewsforstudents.org/article/disappearing-sea-ice-could-disrupt-arctics-food-web.

[60] Timothy Williams. Legal Rights for Lake Erie? Voters in Ohio City Will Decide. 2019. https://www.nytimes.comz/2019/02/17/us/lake-erie-legal-rights.html?rref=collection%2Ftimestopic%2FWater%20Pollution&action=click&contentCollection=timestopics&region=stream&module=stream_unit&version=latest&contentPlacement=3&pgtype=collection.

[61] Ocean Portal Team. CORALS AND CORAL REEFS. https://ocean.si.edu/ocean-life/invertebrates/corals-and-coral-reefs.

[62] Institute MC. Atlas of Marine Protection. 2019. http://www.mpatlas.org.

[63] Karen Zraick. Key West Bans Sunscreen Containing Chemicals Believed to Harm Coral Reefs. 2019. https://www.nytimes.com/2019/02/07/us/sunscreen-coral-reef-key-west.html.

[64] Randy Olson. A running list of action on plastic pollution. 2019. https://www.nationalgeographic.com/environment/2018/07/ocean-plastic-pollution-solutions/.

[65] Royal Statistical Institute. 2018 Statistics of the Year. 2018. http://www.rss.org.uk/RSS/Get_involved/Statistic_of_the_year/RSS/Get_involved/Statistic_of_the_Year_.aspx?hkey=e5008987-fab9-4385-9110-4287e487b8d6.

[66] Brigit Katz. Dead Sperm Whale Had 64 Pounds of Trash in Its Digestive System. 2018. https://www.smithsonianmag.com/smart-news/dead-sperm-whale-had-64-pounds-trash-its-digestive-system-180968776/.

[67] Laura Parker. In a first, microplastics found in human poop. 2018. https://www.nationalgeographic.com/environment/2018/10/news-plastics-microplastics-human-feces/.

[68] U.S. Food and Drug Administration. The Microbead-Free Waters Act: FAQs. 2017. https://www.fda.gov/cosmetics/guidanceregulation/lawsregulations/ucm531849.htm.

[69] O'Donnell N. What Happens When China Doesn't Want Our Recyclables. 2018. https://www.nbclosangeles.com/news/local/US-Struggles-With-What-to-Do-With-Tons-of-Recycled-Material-489971551.html?_osource=taboola-recirc.

[70] WATSON SK. China Has Refused To Recycle The West's Plastics. What Now? 2018. https://www.npr.org/sections/goatsandsoda/2018/06/28/623972937/china-has-refused-to-recycle-the-wests-plastics-what-now.

[71] Ceylan Yeginsu. European Parliament Approves Ban on Single-Use Plastics. 2018. https://www.nytimes.com/2018/10/25/world/europe/european-parliament-plastic-ban.html.

[72] Maged Srour. FAO Releases Alarming Report on Soil Pollution. 2018. http://www.ipsnews.net/2018/05/fao-releases-alarming-report-soil-pollution/.

[73] The Guardian. The human cost of China's untold soil pollution problem. 2014. https://www.theguardian.com/environment/2014/jun/30/the-human-cost-of-chinas-untold-soil-pollution-problem.

[74] Danson Cheong. China to enact its first soil pollution law. 2018. https://www.straitstimes.com/asia/east-asia/china-to-enact-its-first-soil-pollution-law.

[75] World Health Organization. Environmental Noise Guidelines for the European Region – Executive summary (2018). 2018. http://www.euro.who.int/en/health-topics/environment-and-health/noise/publications/2018/environmental-noise-guidelines-for-the-european-region-executive-summary-2018.

[76] McCauley RD, Day RD, Swadling KM, Fitzgibbon QP, Watson RA, Semmens JM. Widely used marine seismic survey air gun operations negatively impact zooplankton. *Nat Ecol Evol* 2017;1:195.

[77] Nicholas St Fleur. Illuminating the Effects of Light Pollution. 2016. https://www.nytimes.com/interactive/2016/04/07/science/light-pollution-effects-environment.html.

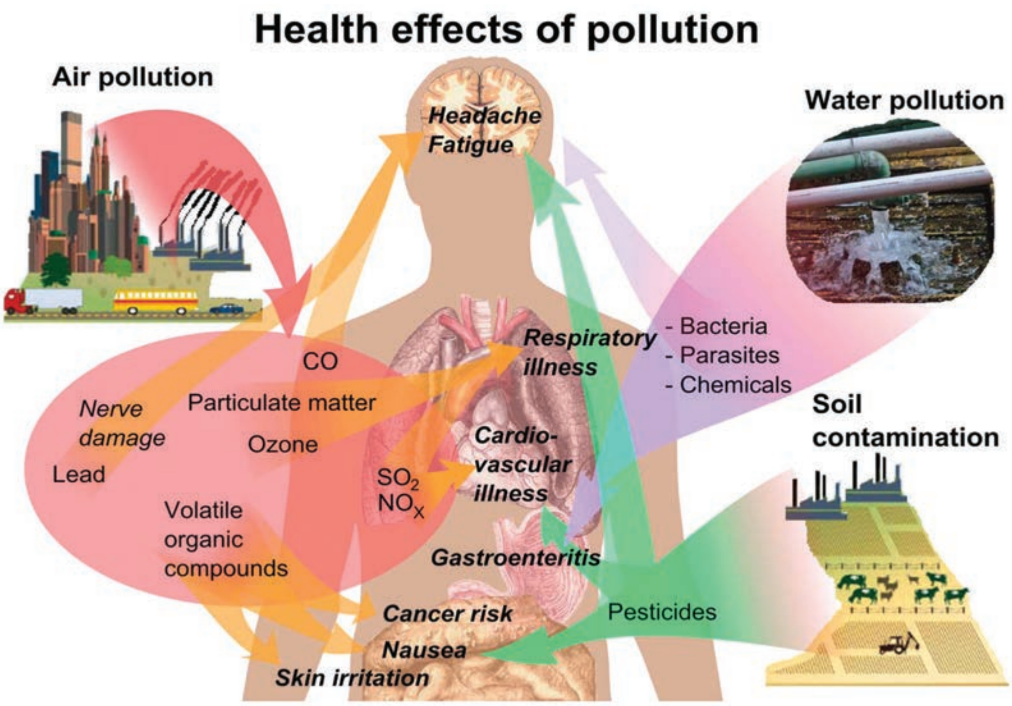
[78] NEIDELL M. Air pollution and worker productivity. 2017. https://wol.iza.org/uploads/articles/363/pdfs/air-pollution-and-worker-productivity.pdf?v=1.

[79] Center for Climate and Energy Solutions. Calculate Your Carbon Footprint. https://www.c2es.org/content/calculate-your-carbon-footprint/

Dr. Kari Nadeau is the director of the Sean N. Parker Center for Allergy and Asthma Research at Stanford University and the section chief of Allergy and Asthma and Naddisy Foundation professor of Pediatric Food Allergy, Immunology, and Asthma at the Stanford University School of Medicine.

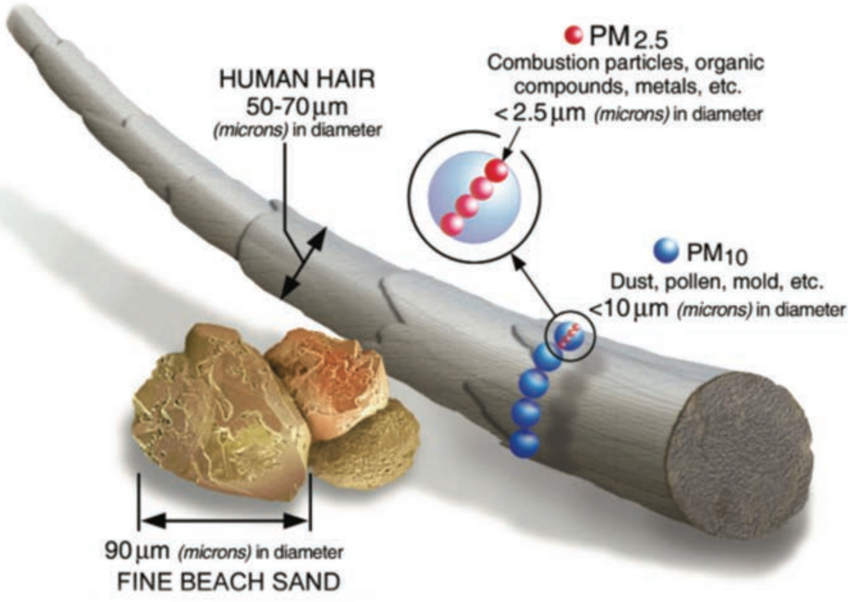
Supporting Data

Figure 1. Pollution Can Modify Our Body at All Levels



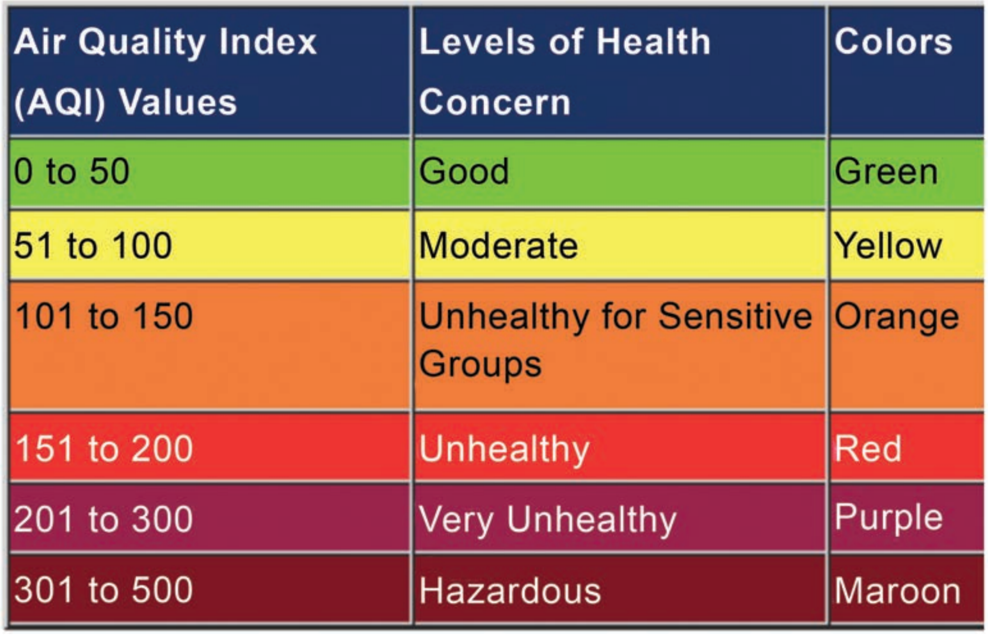
Source: Mikael Häggström, "Medical gallery of Mikael Häggström 2014". WikiJournal of Medicine 1 (2). Public Domain. Available at https://en.wikipedia.org/wiki/Pollution#/media/File:Health_effects_of_pollution.png

Figure 2. Size of Particulate Matter



Source: "Particulate Matter (PM) Basics," U.S. Environmental Protection Agency, available at https://www.epa.gov/pm-pollution/particulate-matter-pm-basics

Figure 3. Air Quality Indices



Air Quality Index (AQI) Values	Levels of Health Concern	Colors
0 to 50	Good	Green
51 to 100	Moderate	Yellow
101 to 150	Unhealthy for Sensitive Groups	Orange
151 to 200	Unhealthy	Red
201 to 300	Very Unhealthy	Purple
301 to 500	Hazardous	Maroon

Source: "Air Quality Index (AQI) Basics," U.S. Environmental Protection Agency, available at https://airnow.gov/index.cfm?action=aqibasics.aqi

Global Warming: Causes and Consequences

By Lucy Shapiro and **Harley McAdams,** Stanford University

Spaceship Earth

The familiar photo of the Earth spinning in the blackness of space that was taken 50 years ago by William Anders, an astronaut on the Apollo 8 lunar mission, starkly illustrated our isolation on this planet. Now we face a crisis as the climate and environmental conditions that support life as we know it become ever more fragile owing to CO_2-induced global warming. The evidence suggests there is significant risk that areas of the Earth in tropical zones may become uninhabitable and that significant food chains will collapse in this century. We agree with those who say that the highest human priority now is to greatly reduce human societies' reliance on CO_2-producing oil and coal. However, even the most optimistic projections of reduced CO_2 production and resulting reductions in climatic warming suggest that future generations will face daunting problems. Fortunately, this growing disruption is occurring at a time of unprecedented breakthroughs in science and technology. Although there are many things that can be done to ameliorate individual events, the worldwide effort is uncoordinated and there is widespread resistance from vested economic and political interest groups. Here, we first survey the consequences of the rapid rise in CO_2 emissions and then consider the possibility that new genetic technologies can help mitigate some of the biological consequences of global changes in climate patterns.

Life on Earth has evolved in an interconnected ecology determined by weather patterns, movements of global tectonic plates, and the dynamic surface chemistry of oceans and land. The creatures on Earth—all the humans, animals, plants, bacteria, fungi, and viruses—are dependent on each another as well as on this enveloping ecosystem. Since the Earth is an integrated system, significant changes in any internal component or in external influences induce movement toward a new equilibrium. Throughout the history of the Earth there have been long periods of cooling leading to growth of massive continental ice sheets, interspersed with warm intervals. While the causes of these ice ages are not fully understood, the principal contributing factors have been identified. The composition of the atmosphere, particularly the concentration of carbon dioxide and methane, is important. Also changes in the Earth's orbit around the sun, changes in the tilt in the Earth's axis, impacts of large meteorites, and eruptions of super volcanoes. The latter two phenomena can both put massive amounts of particulate matter and carbon dioxide into the atmosphere.

In two instances, biological phenomena have disrupted the composition of the atmosphere with global consequences. One was the Great Oxidation Event or the Oxidation Catastrophe, around 2.45 billion years ago. This occurred after a bacterial species, an ancestor of contemporary cyanobacteria, evolved the ability to produce oxygen as a byproduct of photosynthesis. This event had extraordinary consequences for ocean chemistry and eventually for the slow accumulation of atmospheric oxygen to contemporary levels over an interval of several million years. The newly oxygenated atmosphere was toxic to virtually all the anaerobic organisms that then populated the earth. These organisms died and were replaced by creatures that could thrive in the new oxygenated atmosphere.[1] Now, the current human-induced increase in atmospheric CO_2 is the second biological disruption of atmospheric composition that is producing global warming with credible predictions of ever more dire consequences in coming decades. Consequences we are already seeing include:

- Accelerating rise in global sea level owing to irreversible melting of glacial ice in the European Alps, melting of arctic ice, and of greatest concern, melting of the land ice sheets in Greenland and Antarctica.
- Large changes in climate patterns that have led to cataclysmic wild fires encouraged by the hottest summers on record and extreme floods stemming from new and disruptive storm patterns.
- Acidification and warming of the oceans leading to decimation of coral reefs and other changes that are disrupting the marine food chain.
- The global redistribution of bacterial, fungal, and viral pathogens and their vectors out of the tropics and into temperate zones and the emergence of previously unknown pathogens.

As the Earth's climate continues to warm owing to increasing levels of atmospheric CO_2 the mean sea level will rise.[2] The mean sea level has risen about 8 inches since the late 1800s, and projections suggest an accelerating rise of between 2 and 6 feet by 2100.[3] The predominant contributor to the future sea level increase will be melting of the enormous land-based ice sheets and glaciers on Antarctica and Greenland. The amount of the rise will be strongly dependent on mankind's success in limiting future CO_2 emissions. However, even the lowest estimates portend devastating consequences:[4] loss of arable land owing to flooding and salt water intrusion (e.g., Vietnam, Bangladesh, California's Salinas valley[5]); major population displacements (100 million people will be displaced by a three-foot rise); many coastal areas may have to be abandoned (e.g., South Florida and Miami[6]).

We are already experiencing changes in global weather patterns. Regions accustomed to temperate temperatures and predictable periods of rainfall are seeing prolonged drought and periods of extreme high temperature, while other regions are experiencing excess rain and snowfall along with lower ambient temperatures. In parts of Australia, drought and peak summer temperatures nearing 116°F are causing vast wildfires. Simultaneously, U.S. states around the Great Lakes have experienced winter temperatures of -34°C (-29.2°F) that are significantly colder than temperatures in the Arctic. This skewing of ambient temperatures in North America is due to changes in the jet stream that have allowed polar air from the Arctic to flow into zones normally buffered against temperature extremes. Global warming contributes to these unusual weather patterns through its influence on the polar vortex, a wide expanse of swirling cold air near the pole.[7] Over a surprisingly short time, the average temperature rise at the north polar region has been higher than in some more southerly areas. While average temperatures across the globe have now increased to 1.2°C above preindustrial revolution levels, the poles have seen an average increase of 3°C. During March 2018, temperatures in Siberia were 15°C (59°F) above historical averages, and Greenland experienced a period of 61 hours above freezing (three times longer than any previous year), while temperatures were unusually low in Europe. These disruptions in global weather patterns have caused long-term drought conditions in some regions and unprecedented floods in others, leading to loss of arable land and precipitous reductions in agricultural production. Those who deny climate change often point to periods of extreme cold in unexpected regions as evidence supporting their views, without understanding that the large-scale changes in weather patterns are a central consequence of global warming. When the oceans warm, global weather patterns are disrupted in many areas in unexpected ways.

It is important to recognize that these global events are interconnected. For example, consider the consequences of sustained rainfall on degraded farmland: Increased rainfall leads to soil erosion, that in turn results in the release of phosphorous from fertilized soil into rivers and the oceans. That release, in turn can stimulate algal blooms and red tides, further reducing the ocean oxygen levels that are already lowered by warming waters. These phenomena add to the impacts of warming and acidification on food chains in the ocean.

What will be the impact of global warming on our land-based food supply and our ability to maintain the animals and plants we depend on? Warming is already slowing yield gains in most wheat-growing locations, and global wheat production is expected to fall by 6% for each 1°C of further temperature increase while becoming more variable.[8] Global production of corn is similarly at risk.[9] Global warming will alter world food production patterns, with crop productivity reduced in low latitudes and tropical regions but increased somewhat in high latitude regions. This will lead to trade changes with expanded sales of food products from the mid-to-high latitudes to lower latitude regions.[10]

Extinction of species owing to expanding human activities around the globe has been accelerating over the last two centuries. Now the onset of changes in the climate is accelerating the rate of extinctions. Disruptions of habitats, loss of food sources, and the spread of infectious diseases are happening at a rate that cannot be accommodated by evolutionary adaptation. The number of species that have gone extinct in the last century alone would have taken between 800 and 1000 years to disappear in previous mass extinctions.[11] During one of these extinctions, the Permian-Triassic extinction 250 million years ago,[12,13] the earth lost 96% of all marine species, 100% of the coral reefs, and 70% of terrestrial vertebrates. In that event, the accumulation of carbon dioxide in the atmosphere led to ocean warming and to ocean acidification that together played a key role in the global loss of life. Recovery from that extinction event took more than 10 million years.

Currently, we are experiencing a 6th mass extinction,[11] and we are approaching up to 100x higher rates of extinction than the background rate. There are two critical differences now. First, the current rate of change to the earth's ecosystem is occurring in a few decades rather than over thousands of years as in the previous five extinction periods. Second, the events underlying the current cataclysm are man-made. Metaphorically, we are riding a runaway climate train with no one at the controls.

Effects on the Oceans

In the past there have been few established populations of invasive species identified in the high northern latitudes, that is, the northern coasts of Canada or Russia. With the continuing loss of Arctic sea ice, this situation will change. There has been rapid growth of shipping traffic along the northern coast of Russia in recent years, a large cruise ship went through the Northwest Passage in 2016, and now multiple arctic cruises are advertised each year. We can expect continuing expansion in arctic shipping activities, mineral/energy exploration, fishing, and tourism in future years. These new northern transport routes offer shorter and less expensive connections between northern hemisphere ports, so the shipping traffic will inevitably grow as more ice melts and warmer weather seasons get longer. Introduction of invasive species into these Arctic regions will follow rapidly. This will bring new challenges to the native inhabitants—humans, wildlife, and plants—of these northern ocean and terrestrial habitats. There will be greater competition for food sources and introduction of new infectious diseases. This sequence of events has occurred innumerable times before when alien populations expanded into new regions.[14]

Currently, the oceans absorb 93% of the heat trapped by greenhouse gases in the atmosphere, thus slowing warming of land masses. But the resulting rapid warming of the oceans directly impacts marine life and related food chains. Consider, for example, the coral reefs along over 93,000 miles of coastline rimming the oceans—one of the largest ecosystems on the planet.

A thriving coral reef is comprised of groups of millions of identical tiny polyps a few millimeters wide and a few centimeters long, each with a calcite skeleton. Millions of these tiny stony skeletons accumulate over generations to form the large hard coral reefs found along tropical shorelines. Many of the coral species obtain most of their nutrients from photosynthetic algae plants called *zooxanthellae*. When the sea around them warms excessively, the polyps expel the *zooxanthellae* and the coral becomes completely white—a condition called coral bleaching. Corals can survive bleaching events and restore the *zooxanthellae*, if conditions normalize quickly enough. But the bleaching events are highly stressful, and the corals will die if occurrence of bleaching events persists. When this happens, only the dead coral skeletons—which can be immense—are left.

The Great Barrier Reef, 500 feet thick at some points, extends discontinuously for over 1500 miles off the coast of eastern Australia. By 2018, half of the Great Barrier Reef had died from heat stress. Similar damage is occurring in the Caribbean and the rest of the world's tropical shorelines.[15,16]

Loss of the ocean reef ecosystems could substantially compromise the Earths ability to sustain the health and well-being of its inhabitants. Fish populations in the coral reefs are the source of food for hundreds of millions of people. Loss of the reefs disrupts the marine food chain which causes loss of local food supplies, stressed populations, and conflicts over fishing rights.

There is now a global sense of urgency to develop methods to restore and maintain the health of the reefs considering their increasing destruction. Corals can evolve to survive in changed conditions—warmer, more acidic, etc. However, the rate of natural adaptation is too slow relative to the current rate of changes in their ocean environment, so there is widespread devastation of established reefs. This has led to efforts to accelerate the rate of adaptation. In some stressed reefs, small coral colonies are found that have successfully adapted to the local changes in temperature and increased acidity. Reef preservationists have shown that corals harvested from these colonies can be nurtured in coral "farms" and then used to seed new growth in damaged areas. Scientists are also experimenting with selective breeding to develop coral strains better adapted to changed conditions.[17–19]

In Indonesia another attempt at coral reef remediation involves attaching optimized coral polyps to metal rods planted within the compromised reefs. The application of a mild electric shock causes minerals in the water to precipitate and adhere to the metal structures, thus stimulating calcification with the goal of creating the more native 'cement' of a reef's exoskeleton, referred to as 'Biorock.'[20] The resulting limestone surface increases the growth of the corals under conditions that would normally lead to their death. All these schemes are highly promising, but there are daunting cost and logistical barriers to scaling restoration efforts to address the vast areas of lost reefs.

Global Warming Is Changing the Distribution of Animal and Plant Pathogens

The last century has seen radical changes in the pattern, volume, and speed of transport of people and cargo between widely separated regions on the planet. One consequence has been the increase in direct long-distance human transport of dangerous infectious diseases by person to person transmission. Surveillance of travelers at entry points, coupled with identification, treatment, and when necessary, quarantine of the infected persons and their contacts, has been the response strategy. But diseases that are carried by intermediate vectors, for example, mosquitoes or ticks, present a different and more complex challenge. Any such vector is adapted to thrive in some environmental niche—characterized by a temperature and rainfall range, urban or rural, indoor or outdoor, etc. When a region's climate warms, it may become hospitable to new vectors, which will then inevitably arrive either by expansion from adjacent territories or as accidental hitchhikers in freight shipments or transport vehicles.

For example, in a remarkably short time, human viruses like Zika, Dengue, Chikungunya, Yellow Fever, and West Nile have spread into regions of the Caribbean, Latin

America, and the United States that until recently had ambient temperatures below that required to support their transmission. In addition, fungal infections of food plants, like the blights infecting Cavendish bananas and cocoa trees, have become a global problem. The rapid spread of global disease caused by changes in atmospheric temperature, ocean temperature, erratic and drenching rains, and floods in one geographic location accompanied by droughts in another location is being facilitated by migration of the vectors, such as mosquitoes, ticks, bats, and rats, that carry the pathogens. Insect vectors are exquisitely sensitive to changes in temperature, and warmer temperatures increase their breeding season and life span. Zika, Dengue, Chikungunya, and Yellow Fever viruses soon follow arrival of the common *Aedes aegypti* mosquito and are then transmitted among humans by the female mosquito. Other mosquito species transmit West Nile virus, the malaria parasite, and the parasitic nematode worm that causes the human disfiguring disease lymphatic filariasis (elephantiasis).

Ticks are another rapidly spreading vector. Although most tick species do not harbor pathogens harmful to humans, Lyme disease is caused by a tick-borne bacterial pathogen, *Borrelia burgdorferi*. Until recently, ticks were inhibited over much of North America by cold winters, but with increasing average temperatures and milder winters they are becoming established further north. Lyme disease is now endemic in Canada, so the government has recently established tick surveillance networks.

The vector-borne bacterial pathogen *Candidatus Liberibacter* that causes citrus greening disease is a serious agricultural threat. *Liberibacter* are transferred to citrus trees by an insect vector, the Asian citrus psyllid or jumping plant lice. The disease causes the decline and death of citrus trees by blocking the flow of nutrients and sugars from the leaves to the roots. Once infected, the tree is doomed. *Liberibacter* have recently migrated along with the citrus psyllid vector to warming temperate climate zones worldwide, including ten U.S. states.[21] The resulting Citrus Greening infections have devastated the Florida citrus industry and destroyed citrus groves in Asia, Brazil, and the Dominican Republic. In the United States, the damage has been less in states further north than Florida, probably because of their cooler temperatures, but as the climate warms, the citrus greening infections will likely continue moving northward.

Owing to the huge financial impact of citrus greening, there are multiple biology-based efforts underway to disrupt the infection pathway either by eliminating the psyllid vector, by killing the bacterial *Liberibacter* pathogen, or by developing an infection resistant citrus tree variety.[22] Insect warfare has also been tried by introduction of a wasp that preys specifically on the Asian citrus psyllid. This strategy works, but it only reduces, rather than eliminating, the citrus psyllid population.[23]

Each biological approach tried so far has its pros and cons. Insecticides can kill the citrus psyllid, but they may also threaten beneficial insects. Antibiotics may kill the *Liberibacter,* but their use can also increase bacterial antibiotic resistance and thus loss of antibiotic effectiveness for treating human diseases. This story of the challenges of containing the spread of the citrus greening disease is representative of similar challenges encountered in trying to deal with a myriad of newly encroaching diseases, some carried by other insect vectors. Are there better solutions on the horizon? It may be that recent advances in genetic technology will lead to more effective approaches.

Can New Genetic Technologies Reduce Global Warming Consequences?

Along with the increasing threat of climate change to human health and agriculture, we are experiencing a revolution in genetic engineering technology. Perhaps this will lead to new methods for effective surveillance and for mitigation of the redistribution of vectors that transmit disease.

The new CRISPR Cas9 technology lets us change specific genes in an insect or animal vector, thus making it either unable to serve as a reservoir for a given pathogen (known as a population modification drive) or eliminating the ability of the vector to propagate (known as a suppression drive). A suppression drive targets the reproductive capacity of the insect vector and can lead to a population crash, potentially wiping out a species. A population modification drive does not affect the reproduction capability of the insect, but it prevents the vector from harboring the pathogen or it prevents transmitting the pathogen to the human host. With these technologies, the genetic makeup of a few individuals in a targeted vector species is changed in such a manner that once these individuals are released into the wild, the change spreads rapidly throughout the entire vector population. Gene drives only affect sexually reproducing species, and thus they cannot be used directly on bacterial and viral pathogens.

Malaria transmission has been used as a test case to explore use of a vector gene drive to contain the spread of a disease. The results have been encouraging. In 2015, 200 million people worldwide were infected with malaria and between 500,000 and 700,000 died from the disease. Seventy-two percent of these were children under 5 years of age. In 2016, the number of cases worldwide increased to 216 million. Of 3,500 mosquito species, only those that belong to a subset called *Anopheles* can transmit the malaria parasite, *Plasmodium falciparum*, to a human by means of a bite from a female. The *Anopheles stephensi* mosquito, endemic to India and South Asia, carries the malaria parasite in that region. These mosquitoes were experimentally gene edited so that they could no longer carry the malaria parasite, establishing a population modification gene drive. A key trick in a gene drive is to engineer both copies of the chromosome so that all the offspring of a mating between a normal mosquito and a genetically altered one carry the genetic profile of the desired alteration, rather than just half the offspring, which is normally the case. Under laboratory conditions, it was demonstrated that this population modification drive leads to rapid spread of the desired genetically-altered mosquito and disappearance of the normal mosquitoes. The genetically altered mosquitoes cannot harbor the malaria parasite. This suggests that release of this genetically altered mosquito into the wild would halt the spread of malaria and thus save millions of lives. Eventually the malaria parasite could naturally mutate to overcome the genetic change in its mosquito host allowing it to once again infect humans, but this might not occur for a long time.

Another example is the *Anopheles gambiae* mosquito, which transmits malaria in sub-Saharan Africa. In another series of gene drive experiments, gene editing was used to change genes that the female mosquito needs for egg production, thereby creating female sterility (a suppression gene drive). In this case, the goal was just to reduce the number of mosquitoes transmitting malaria, but the technique could potentially wipe out the entire population of *Anopheles gambiae*. The combined challenge of climate change, which is altering the geographic distribution of the vector mosquitoes, and growing resistance to drugs routinely used to treat malaria-infected patients is making gene editing of the insect vectors an increasingly attractive potential solution. However, the notion of eliminating an entire insect species troubles many people.

In another test case, gene drives are being explored as a way of controlling transmission of Lyme disease by ticks on the U.S. island of Nantucket. Owing to recent increases in the population of island ticks, over 40% of the 10,000 inhabitants of Nantucket have, or have had, Lyme disease. Both deer and the white foot mouse can transmit the Lyme disease pathogen, *Borrelia burgdorferi* bacteria, to ticks, and the pathogen can then be transmitted to humans by the ticks. Ticks feed on the deer or white foot mice carrying *Borrelia* and the infected ticks bite humans, passing on Lyme disease. A plan was proposed by Kevin Esvelt (MIT) and Sam Telford (Tufts U., Cummings School of Veterinary Medicine) to use a gene drive to reduce the population of white footed mice that are infected with *Borrelia*. To do this, the mice would be genetically engineered so that they are immune to infection by the Lyme disease bacterial pathogen and thus could not accumulate infectious *Borrelia*. In this case, there would still be the same number of mice and the same number of ticks, but the number of ticks able to transmit Borrelia would be significantly reduced. Thousands of altered mice would be released on the island. The gene drive would ensure that the genetic alteration would pass down through all following generations of mice on the island, disrupting the cycle of transmission. The plan is to first test the genetically modified mice on an uninhabited island and then, with the concurrence of the inhabitants of both Nantucket Island and Martha's Vineyard, release the genetically altered mice. The first step will be to get the concurrence and support of the inhabitants of these islands, because the gene drive would be altering the environment shared by all inhabitants.

Recently, a new gene editing application has been developed to alter the response of plants to environmental challenges. The proposed scheme involves spraying a field of plants with millions of insect vectors carrying viruses that are programmed to edit the genome of a plant such as maize to become drought resistant, in one growing season. This technique would be significantly faster than a gene drive. Further, this method would not permanently alter the genetic makeup of future plant generations, as is the case with gene drives. The goal is to engineer drought-resistant and temperature-tolerant plants, thereby securing the food supply during times of climate instability. But there is a catch, as once released into the wild, controlling these insect vectors would be difficult, if not impossible. As a result, this work has been limited so far to the laboratory. There is also concern that the method could be adapted as a biological weapon, enabling destruction of targeted food crops over wide areas by adverse genetic manipulation of the plants' chromosomes. In addition to controlling mosquito vectors and tick-borne Lyme disease, gene drives are also being devised to control the nematode worms that carry the parasite causing Schistosomiasis.

Gene drives have not yet been released in the wild to mitigate vector-borne transmission of disease as there are critical questions to be resolved as noted above. Although the biology is ready, there are many questions of governance, safety, and ethics to be answered. Caution is important, since once the genetically-altered vectors are released, there is no assured way of controlling them at this point.

In July 2015, the U.S. National Academy of Sciences convened a meeting to discuss "the promise and perils of gene drives." Critical questions raised at the meeting were:

Will an entire species of vector be wiped out? Methods are being devised to slow the gene drive so that only a portion of the offspring contain the genetically engineered alterations. These "Daisy chain drives," have been engineered to be self-limiting and eventually disappear from the population.

Have techniques been devised that could control a runaway gene drive? By creating a second gene drive that undoes the genetic alterations of the first gene drive, essentially "a molecular eraser," it is hoped a gene drive could be reversed, but not before unintended consequences to the ecosystem become apparent.

Can the altered genetic traits be transferred to other insect species? Unlikely, but possible. If this occurred, the potential for wiping out beneficial insect species would lead to further ecological disruptions, compounding the ravages of climate change.

Global Warming Mitigation Will Require a Coordinated International Effort

Many climate scientists and other thoughtful people have had concerns about the deteriorating global ecosystem for several decades now. The contribution of human activity to this escalating cataclysm is well documented. Predictions of dire consequences have been noted and sporadic attempts by the international community have been made to mitigate the ongoing onslaught of carbon emissions. But global warming is a problem that can only be solved by global cooperation because the world's ecosystem is an integrated system. The causes of environmental degradation cannot be addressed by a patchwork of uncoordinated responses. We are dependent upon achieving international cooperation to mount a coordinated, science-based response.

In the United States today, political calculations relating to oil and coal interests have halted government acknowledgement of the risks of continuing future emissions of CO_2 into the atmosphere. In December 2018, at a UN Climate Change Conference in Poland, Wells Griffith, Mr. Trump's international energy and climate adviser, said "We strongly believe that no country should have to sacrifice their economic prosperity or energy security in pursuit of environmental sustainability." The attendees broke into jeers and mocking laughter.[24] Do not think that the United States is alone in this stance. We are aligned with other major fossil fuel producing nations, including Russia, Saudi Arabia, Kuwait, and Australia. We are now well beyond the time of debating about validity of the predictions about what will happen if climate change is left unaddressed. Rather, we are trying to mitigate what has already happened, while, as a society, summoning the courage and the will to leave fossil fuels in the ground and switch to alternative energy sources. Renewable power resources and improvements in the efficiency of our energy use can be important components of our energy future for the rest of this century. But, practically speaking, nuclear power will probably also have to be a major component of the future energy portfolio in order to meet world energy demands while greatly reducing use of fossil fuels.[25, 26] That too is controversial. These are existential choices that call for an unprecedented level of wisdom and societal responsiveness in the world's political systems. It does seem likely that achieving the necessary global political response will only come when there is widespread public fear and panic as the realization of the danger percolates into public consciousness.[27] It is extraordinary that the current U.S. national leadership both denies existence of the global warming problem and actively promotes more use of fossil fuels. The longer we delay reduction in global CO_2 emissions, the worse the ultimate catastrophe will be.

Authors' Note:

We believe the world energy economy must shift rapidly from reliance on fossil fuels—coal, oil, and gas—to cleaner alternatives or our children and grandchildren will suffer dire consequences. We encourage the reader to personally assess the risks and potential solutions. To that end, we have included references for further reading that are openly accessible on the Internet.

---

[1] Plait, P. *Poisoned Planet*. Slate 2014; Available from: https://slate.com/technology/2014/07/the-great-oxygenation-event-the-earths-first-mass-extinction.html.

[2] Willis, J.K., A. Kemp, and B.H. Strauss. *Sea Level Rise*. [cited 2019; Available from: https://ocean.si.edu/through-time/ancient-seas/sea-level-rise.

[3] Hayhoe, K., et. al. *Sea Level Rise, Introduction*. [cited 2019; Available from: https://nca2014.globalchange.gov/report/our-changing-climate/sea-level-rise#narrative-page-16573.

[4] Harris, G. *Borrowed Time on Disappearing Land*. New York Times 2014 March 28, 2014; Available from: https://www.nytimes.com/2014/03/29/world/asia/facing-rising-seas-bangladesh-confronts-the-consequences-of-climate-change.html.

[5] *California Flood Risk: Sea Level Rise, Salinas Quadrangle*. [cited 2019; Map showing projected flood zones with projected sea level rise]. Available from: http://www2.pacinst.org/reports/sea_level_rise/hazmaps/Salinas.pdf.

[6] Korman, C. *Miami faces an underwater future*. New Yorker 2018 [cited 2019; Available from: https://www.newyorker.com/news/news-desk/miami-faces-an-underwater-future.

[7] Berwyn, B. *Polar Vortex: How the Jet Stream and Climate Change Bring on Cold Snaps*. 2018 [cited 2019; Available from: https://insideclimatenews.org/news/02022018/cold-weather-polar-vortex-jet-stream-explained-global-warming-arctic-ice-climate-change.

[8] Asseng, S. and e. al., *Rising temperatures reduce global wheat production.* Nature Climate Change, 2014: p. 5.

[9] Harvey, C. *Rising Temperatures Could Cut Corn Production*. 2018 [cited 2019; Available from: https://www.scientificamerican.com/article/rising-temperatures-could-cut-corn-production/.

[10] Elbehri, A.-E. *Climate Change and Food Systems*. 2015; Available from: http://pure.iiasa.ac.at/id/eprint/11589/1/a-i4332e.pdf.

[11] Ceballos, G., et al., Accelerated modern human-induced species losses: Entering the sixth mass extinction. Sci Adv, 2015. 1(5): p. e1400253.

[12] Hoffman, H.J. *The Permian Extinction—When Life Nearly Came to an End*. [cited 2019; Available from: https://www.nationalgeographic.com/science/prehistoric-world/permian-extinction/.

[13] *Permian–Triassic extinction event*. [cited 2019; Available from: https://en.wikipedia.org/wiki/Permian%E2%80%93Triassic_extinction_event.

[14] Ricciardi, A., et al., Invasion Science: A Horizon Scan of Emerging Challenges and Opportunities. Trends Ecol Evol, 2017. 32(6): p. 464-474.

[15] Loria, K. *What happens if all the coral reefs die?* World Economic Forum 2018 2019; Available from: https://www.weforum.org/agenda/2018/04/what-happens-if-all-the-coral-reefs-die.

[16] James, L.E. (2018) *Half of the Great Barrier Reef Is Dead*. National Geographic.

[17] Chan, W.Y. and e. al., *Interspecific Hybridization May Provide Novel Opportunities for Coral Reef Restoration*. Frontiers in Marine Science, 2018. 5 p. Article number: UNSP 160.

[18] van Oppen, M.J., et al., *Building coral reef resilience through assisted evolution*. Proc Natl Acad Sci U S A, 2015. 112(8): p. 2307-13.

[19] Albright, R. *Scientists Are Taking Extreme Steps to Help Corals Survive*. 2018 [cited 2019; Available from: https://www.scientificamerican.com/article/scientists-are-taking-extreme-steps-to-help-corals-survive/.

[20] Baragona, S. *This Coral Restoration Technique Is 'Electrifying' a Balinese Village*. 2016 [cited 2019; Available from: https://www.smithsonianmag.com/science-nature/coral-restoration-technique-electrifying-balinese-village-180959206/.

[21] [cited 2019; Information on the Asian Citrus Plyllid.]. Available from: https://www.aphis.usda.gov/aphis/resources/pests-diseases/hungry-pests/the-threat/asian-citrus-psyllid/asian-citrus-psyllid.

[22] Sharp, G.M., Exploration of chemical and biological management strategies for Diaphorina Citr the primary vector of Candidatus Liberibacter Asiaticusi, in Biolog y. 2016, University of Texas at Tyler: Tyler, TX.

[23] Rosner, H. *Can Parasitic Wasps Help Save America's Citrus?* National Geographic 2014; Available from: https://news.nationalgeographic.com/news/special-features/2014/06/140617-citrus-greening-wasp-california-biocontrol-psyllid-science/.

[24] Witte, G. and B. Dennis. *That was awkward — at world's biggest climate conference, U.S. promotes fossil fuels*. [Newspaper] 2018 [cited 2019; Available from: https://www.washingtonpost.com/world/europe/that-was-awkward--at-worlds-biggest-climate-conference-us-promotes-fossil-fuels/2018/12/10/aa8600c4-f8ae-11e8-8642-c9718a256cbd_story.html?utm_term=.2e9a2a553dd2.

[25] *Nuclear Power & Global Warming*. [cited 2019; A balanced discussion of pros and cons of use of nuclear power to reduce reliance on fossil fuels.]. Available from: https://www.ucsusa.org/nuclear-power/nuclear-power-and-global-warming#.XGtXBuhKguU.

[26] Rhodes, R. *Why Nuclear Power Must Be Part of the Energy Solution*. Yale Environment 360 2018 [cited 2019; Available from: https://e360.yale.edu/features/why-nuclear-power-must-be-part-of-the-energy-solution-environmentalists-climate.

[27] Wallace-Wells, D. *Time to Panic*. New York Times[Opinion] 2019 February 16, 2019; Available from: https://www.nytimes.com/2019/02/16/opinion/sunday/fear-panic-climate-change-warming.html?em_pos=small&emc=edit_ty_20190218&nl=opinion-today&nl_art=10&nlid=70792616emc%3Dedit_ty_20190218&ref=headline&te=1.

Lucy Shapiro is a professor in the Department of Developmental Biology at Stanford University School of Medicine where she holds the Virginia and D. K. Ludwig Chair in Cancer Research and is the director of the Beckman Center for Molecular and Genetic Medicine. Harley McAdams is an emeritus professor at the Department of Developmental Biology at Stanford University School of Medicine.

Health Technology and Climate Change

By Stephen R. Quake, Stanford University

As you have heard from the other speakers today, there are numerous health risks associated with global climate change. The Union of Concerned Scientists has analyzed this question and concluded that: "Rising temperatures will likely lead to increased air pollution, a longer and more intense allergy season, the spread of insect-borne diseases, more frequent and dangerous heat waves, and heavier rainstorms and flooding. All of these changes pose serious, and costly, risks to public health."[1] Global climate change is clearly under way, and human society may or may not take actions to mitigate it. From the perspective of preparing for the consequences to our species, we must be investing in science and new medical technologies for those areas of human disease we know will be impacted or increasing due to the effects of climate change. In this talk, I will discuss the role of technology as a tool to mitigate the health impacts of climate change. I will illustrate with both concrete examples using technology that is available today, and I will also speculate a bit about where new technologies can be developed to address these challenges.

We are living in a time of rapid technological change, and there are many revolutionary technologies that can be put to work solving the health challenges which are arising due to global climate change. To set the stage for some of the discussion which is to follow, let me outline some of the important technologies I see playing a role. One technology which you will see coming up again and again is that of genomics and DNA sequencing. We are living in the genome age where biology has become an information science, and this transition was driven by the invention of incredibly powerful sequencing machines. These machines are amazing tools that have dropped the cost of sequencing by orders of magnitude and increased the throughput of sequence data, which we can acquire also by orders of magnitude.[2] These trends are comparable to that of Moore's law in the semiconductor world. As a result, we now have genomes of many major organisms—not just humans but also many of the pathogens which afflict our health. We are able to rapidly sequence novel genomes as pathogens mutate and new pathogens emerge. And we are able to analyze human biology with a power that was only dreamed of a few short decades ago.

An important application of genome sequencing relates to technologies that are used to sequence the genomes and transcriptomes of single cells.[3,4] This has allowed us to gain a much deeper understanding of the diversity of cell types in the human body, and also to use the response of the human immune system as a discovery tool for new therapeutics—several examples of this will be described below. We are also able to use high throughput sequence data to monitor the emergence of new pandemics and even new pathogens which have never been characterized before. These experiments can be done with all sorts of human samples: blood, saliva, biopsies, cerebrospinal fluid, and so forth. One of the most useful in my own research has been to use blood samples to study circulating cell free DNA and RNA. These are small fragments of the genome and transcriptome which provide information not only about the health of the individual but also about the microbes and infections that may be colonizing a person.

Another set of technologies, which I believe are going to be important in the battle against global warming related health crises, are electronic and computer technologies. The ability to monitor physiology through wearable or implantable devices, and to have these devices networked to the internet and cloud computing, will provide numerous new approaches to coping with the health challenges which will accompany more extreme weather events.[5] For example, global climate change is expected to produce more frequent and more intense heat waves. The challenge here is that the elderly and young are disproportionately affected and often don't realize they are dangerously dehydrated and overheated. There are many examples of fatalities due to this in recent years in the developed world; for example, during the heat wave that struck Europe in the summer of 2003, more than 70,000 people died due to overexposure. This could in principle be helped by better physiological monitoring—wearable devices such as the Fitbits and Apple Watch can have sensors and apps designed to alert individuals, their families, and caregivers that they are in a dangerous condition. These devices will take advantage of automated cell phone and internet communication to share physiological updates either with the affected individuals or those responsible for caring for them. As an extension of this, research into implanted sensors could yield new devices which are permanently part of our bodies and which don't require separate accessories or charging.

The same emissions that cause global warming also increase levels of air pollution, which is a problem that human society already has extensive experience with and data from.[6] Cities such as Los Angeles, Mexico City, Athens, and Beijing all have a history of dealing with air pollution and its health consequences, and there is by now substantial data on the effect of air pollution on human health. It is known that the increased ozone levels, which are a consequence of air pollution, end up causing increased levels of respiratory disease, exacerbate asthma, and cause cardiovascular problems. Some of the consequences of increased air pollution can be managed by reducing exposure—filters and masks will become ubiquitous, and we expect that this will motivate development of new technologies to improve air quality, particularly indoors, and to protect individuals from unhealthy air in the outdoors. There are opportunities for geo-engineering here—massive air filtration systems placed on top of buildings which scrub the air in entire neighborhoods, for example. Another option may be the construction of large domes which enclose entire towns and provide filtered air for the occupants. At the level of individual homes, one can expect that people will begin to live in sealed environments and each home will have its own air quality control and filtration system. Possibly some of these will be bio-engineered and use living organisms such as bacteria, algae, or plants which have been engineered to improve air quality.

These efforts to control exposure will help manage the consequences of increased air pollution, but it seems inevitable that levels of respiratory disease will increase and that we will see increasing populations of individuals with compromised breathing and damage to lung tissue. Therefore, there is also a need to develop new treatments for pulmonary disease. This suggests that increased investment in regenerative medicine—to understand the basic biology of lung development, the cell types, pathways, and molecules involved, and how they can be manipulated to promote repair of damaged tissue—should be a societal priority. We can imagine that advances in regenerative medicine will play a role in mitigating the effects of these diseases—for example by finding ways to reverse oxidative damage to lungs and perhaps repair cardiovascular damage, thus lowering the burden of disease due to global warming.

Asthma is an already widespread respiratory disease whose incidence and severity will increase dramatically. We will need better treatments for asthma as well as new diagnostic monitors to know when to be taking medicine, perhaps even proactively based on environment or early symptoms. These are all opportunities for the development of new bioengineered devices, new therapeutics, and better understanding of the clinical aspects of the disease.

Another direct health consequence of global warming will be a dramatic increase in environmental allergies. The Union of Concerned Scientists explains it this way: "Three main factors related to climate change fuel increases in allergens. Carbon dioxide, the heat-trapping gas that is the primary cause of our warming planet, increases the growth rate of many plants and increases the amount and potency of pollen. Rising temperatures extend the growing season and the duration of allergy season. And an extended spring season alters the amounts of blooms and fungal spores that are known to exacerbate allergy symptoms."[1] While this increase in environmental allergies is not expected to be life-threatening, it will have an enormous economic cost. Currently, it is estimated that about 60 million Americans are affected by allergic disease, making it the third leading chronic disease for the under-45 age group. The costs of allergies in the United States reach nearly $20 billion per year and result in roughly 6 million school and work days lost per year as well as 16 million doctors visits per year.[7] If allergies increase ten-fold, this becomes $200 billion per year—well above the peak yearly cost of the Iraq War.

Currently we lack all but the simplest understanding of how allergies are caused. Treatment has largely been empirical and is based either on treating the symptoms or by controlled exposure to the allergens for desensitization. Therefore, it would be prudent to invest in basic research in immunology as well as in clinical studies related to allergies. There are hints of novel treatments already, which should be further explored and brought to market. One dramatic example of this is a novel biologic drug developed by the biotechnology company Regeneron. Regeneron has developed an antibody-based therapeutic against the environmental allergen cat whiskers. Allergic individuals treated with these antibodies showed a dramatic decrease in allergy symptoms and allergic response.[8] These results, while the result of only a small clinical trial, provide a blueprint for a class of therapeutics aimed at treating allergies and reducing the economic cost of allergies in the world economy.

The key to expanding such a program of novel anti-allergy therapeutics is the development or discovery of antibodies against the important environmental allergens. Here we have the opportunity to apply emerging technologies such as single cell genomics to analyze the antibody-producing cells of individuals. The philosophy is that the solution lies within the disease—the very antibodies which cause allergic disease can be used to help cure it, if only they can be identified and produced in a slightly different molecular form. Kari Nadeau and I have taken this approach and developed a way to isolate the cells which produce the allergy-causing antibodies from allergic individuals.[9] This has enabled my student Derek Croote to discover numerous antibodies which cause food allergies, and we are now engineering those antibodies to turn them into therapeutics which might cure allergies. While it is still quite early, we believe this provides a potential roadmap to making a broad new class of therapeutics.

Another expected consequence of global climate change is heavier rainstorms and increased flooding. The World Health Organization has found that floods can potentially increase the transmission both water-borne disease and insect vector-borne disease.[10] Examples of water-borne diseases include typhoid fever, cholera, leptospirosis, and hepatitis A. These diseases all have effective vaccines, but only a small fraction of the global population is fully vaccinated. This suggests that resources be invested into a global vaccination campaign to preemptively protect against the expected increase in outbreaks. It would also be prudent to invest in the development of a new generation of vaccines which will be longer lasting, have longer shelf life, and be more broadly protective. The situation is more complicated for insect vector-borne diseases, such as malaria, dengue and dengue haemorrhagic fever, yellow fever, and West Nile Fever. Vaccines exist for only a few of these pathogens, and therefore we should invest in the development of new vaccines against this class of diseases. Many of these already present a substantial health burden on human society. For example, dengue infects 400 million people annually around the world in more than 100 different countries, and there is no particularly effective vaccine or specific antiviral therapeutic treatment. There are also challenges in diagnosing some of these diseases. For example, in the case of dengue infection, only a subset of infected individuals proceed to severe dengue. If we had diagnostics not only for dengue infection, but which had the ability to predict who was going to go on to severe dengue, we would be better able to know who should be treated in the hospital or receive intense medical attention. There are also opportunities to develop novel small molecule therapeutics to treat these diseases, especially from the perspective of blocking host (i.e. human) proteins, which the viral infections are dependent on.

As an example of how to develop new vaccines and therapeutics, I will again turn to the observation that humans who have survived an infection will often make antibodies that protect them. If only we can identify and produce those antibodies outside the body, they could be administered either as treatment or as prophylactic vaccines to protect people from the pathogen. There are some excellent examples of this in the scientific literature; one of the most dramatic is the discovery of broadly neutralizing antibodies against HIV. HIV is a pernicious virus which attacks the immune system to prevent the body from regulating it, and it also seeks to evade the immune system through constant mutation. However, some people's bodies are able to make what are called "broadly neutralizing" antibodies, which is to say that their antibodies neutralize all the various mutant forms of HIV. Scientists have managed to clone these antibodies, which is to say that they have discovered and sequenced the gene which makes the antibody, and then have produced protein versions of the antibody which can be used as an anti-HIV vaccine or as a therapeutic to treat HIV. There has been proof of principle of these approaches using mouse models as well as non-human primates, which have been promising enough that the first human trials are now underway. There is a large vaccine trial in sub-Saharan Africa supported by the NIH currently underway, and there have been small proof-of-principle therapeutic studies with positive results.[11]

The HIV broadly neutralizing antibodies are the result of decades of research, and it is natural to ask if they provide any useful lesson for emerging pandemics, which might require a more rapid response. We can look to the Ebola outbreaks in recent years for an example on a more rapid time scale. In the 2018 outbreak in Congo and Central Africa, three antibody-based therapeutics were tested in the field and were shown to roughly halve the Ebola fatality rate from 68% to 32%.[12] While the results are still early and much work remains to be done, this is an example of how such therapeutics can be deployed in outbreaks and on times scales substantially shorter than decades. One of the therapeutics was developed in 2014 in the space of just a couple of years—six months for development followed by a phase I clinical trial. It was then produced and shipped over a period of 21 days for the 2018 outbreak.[13] This is a dramatic improvement in time scale from the development of HIV broadly neutralizing antibodies, and it seems reasonable to expect even more compression as technologies improve over time.

While there are multiple approaches to generating therapeutic antibodies, I am particularly enthusiastic about using the human immune system as the source. I discussed an example of this earlier in the context of allergy therapeutics, and a similar approach works for infectious disease. Modern single cell transcriptomics technologies continue to accelerate the field, and what was heroic in the case of HIV or Ebola a few decades ago is now becoming commonplace. As an example, a recent collaboration between my lab, Leslie Gu at the Chan Zuckerberg Biohub, and Shirit Einav at Stanford demonstrates how this approach can be used in the context of Dengue. Shirit established a patient cohort in Colombia, which was undergoing an outbreak of dengue fever. Working with colleagues at a hospital there, patients who were admitted in the local hospital with evidence of dengue infection were enrolled in the study. Their blood was sent to Stanford, where my postdoc Fabio Zanini performed single cell transcriptomic analysis of immune cells.[14] We discovered clues that some of the antibodies might be connected to the response to dengue, and we cloned and expressed those antibodies. It turns out that one of the antibodies is broadly neutralizing against all four strains of dengue, with better efficacy than anything reported thus far in the literature. It is therefore a strong candidate to be used either as a therapeutic or as a vaccine.

Single cell transcriptomics of blood cells from infected patients can also be used to discover new diagnostic signals. In the case of dengue, the majority of symptomatic patients experience flu-like symptoms. Five to twenty percent of these patients progress to severe dengue, manifested by bleeding, plasma leakage, shock, organ failure, and sometimes death. Early administration of supportive care reduces mortality in patients with severe dengue, however, there are no accurate means to predict which patients will progress to severe disease. The currently utilized warning signs to identify dengue patients at risk of progressing to severe disease are based on clinical parameters that appear late in the disease course and are neither sensitive nor specific. This promotes ineffective patient triage and resource allocation and continued morbidity and mortality. Our single cell transcriptomic study with Shirit Einav described above enabled us to discover what we think might be a sensitive diagnostic tool which enables us to predict which patients will progress to severe dengue and therefore to provide them with supportive care before they become severely ill. While the patient numbers were small and more work needs to be done to understand if this can become a practical diagnostic tool, it does illustrate the power these technologies bring to the challenges of handling emerging infectious diseases.

I would now like to turn from the question of diagnosing individual patients to the larger question of how to recognize the causes of pandemics and infectious disease outbreaks that affect public health more broadly. This is an area which is ripe for technological revolution, particularly by incorporating hypothesis-free approaches based on genomic sequencing to public health surveillance. While sequencing hardware has become mature and inexpensive, the software and database tools required to make this technology useful in public health has lagged behind. As part of a collaboration between the Chan Zuckerberg Biohub and the Chan Zuckerberg Initiative, my colleague Joe DeRisi has led the development of a cloud-based software tool called IDseq, which enables anyone to compare their sequence data to the collection of all known genomes of infectious pathogens. The beauty of this approach is that you do not need a hypothesis or a preliminary diagnosis—you are testing for all possible pathogens at the same time, including those that are rare or unusual.

As an example, which shows the power of this approach, Joe led the application of IDseq to understand the causes of a meningitis outbreak in Bangladesh.[15] Globally there are 10.6 million cases of meningitis and 288,000 deaths every year, and the majority of meningitis cases occur in low-and middle-income countries. At least a quarter of survivors suffer from long-term neurological consequences. In a World Health Organization-supported meningitis surveillance study in Dhaka, Bangladesh, Joe's collaborators collected 23,140 cerebrospinal fluid (CSF) samples from patients with suspected meningitis and were able to detect a bacterial etiology in only 20% of these cases despite the use of multiple diagnostic tools including culture, serologic and antigen assays, and pathogen-specific qPCR. Such low rates of microbiological diagnosis are common in many settings globally, hampering implementation of evidence-based policy decisions for optimizing local empiric treatment protocols and disease prevention strategies. The challenges of obtaining a microbiological diagnosis may be due to a combination of multiple factors, but one of the most consequential is that meningitis is is caused by a wide variety of microbes, some of which are uncommon and lack diagnostic assays.

In analyzing 66 samples with known infectious cause, IDseq found 83% concordance with conventional testing. In 25 idiopathic cases (i.e. without known cause), IDseq identified a potential etiology in 40%, including several bacterial and viral pathogens. There were three instances of neuroinvasive Chikungunya virus (CHIKV). The CHIKV genomes were >99% identical to each other and to a Bangladeshi strain only previously recognized to cause systemic illness in 2017. Molecular testing of all 472 remaining stored CSF samples from children who presented with idiopathic meningitis in 2017at the same hospital revealed 17 additional CHIKV meningitis cases. Therefore, IDseq revealed a previously unrecognized outbreak of CHIKV caused meningitis.

Although IDseq is very powerful, it has the limitation that it is only as good as what is in the database—which is to say that it can only be used to detect known pathogens. With increasing global warming, we expect new pathogens to emerge and in particular to jump from one species to another. How do we detect those? Fortunately, the combination of sequencing technology and computation offers a solution. Mark Kowarsky in my lab led the analysis of more than 1,000 patient samples whose blood had been drawn and the circulating cell-free DNA purified and sequenced.[16] He mapped all of the sequence reads to all known genomes—human, microbial, and viral—and then discarded them. He wanted to focus on what was left—the sequence reads that don't map to anything in any known database. He then took all of those sequence reads and tried to assemble them like a jigsaw puzzle. In doing so, he discovered something amazing—the remnants of genomes from several thousand organisms, many of which appear to by new microbes and viruses whose evolutionary history is quite divergent from everything studied to date. Among the torque teno virus family, we discovered numerous new species that were quite divergent from all other related viruses which infect humans, and in fact were closer in relationship to ones which only infect non-human animals.

Mark then applied the same approach to non-human primates in an attempt to get a sense of which potential pathogens might be ready to jump species. In collaboration with Nathan Wolfe from Global Viral, we assembled and annotated non-host sequences derived from cell-free DNA from blood samples of 221 individuals from an assortment of both Great Apes (two species) and Old World Monkeys (15 species) from three wildlife refuges in the West African nation of Cameroon.[17] Multiple sequences were detected from the Apicomplexa phylum, which includes the parasites Plasmodium, which causes malaria, and Babesia, which causes babesiosis. In addition, many fungi including known pathogens in the Tremellales order (such as cryptococcus) and fungal orders containing highly prevalent genera such as Candida, Cladosporium, Aureobasidium, and Saccharomycetales also had novel and divergent sequences present. The majority of viral families known to infect primates were found in the de novo assemblies including: adenoviridae, anelloviridae, hepadnaviridae, herpesviridae, parvoviridae, polyomaviridae, and retroviridae. Thirty-nine individuals across ten species were observed with hepatitis B virus, and this study provided the first sequence-based evidence that eight species in the Papionini and Cercopithecini tribes can be infected with HBV. The ability to observe high coverage of viral diseases such as HBV, while providing new lineages and infection patterns, demonstrates a benefit of applying an untargeted approach to microbiome sequencing.

I hope that these vignettes have helped to give a sense for the role technology might play in mitigating the effects of global warming on human health. While I wish we lived in a world where there was a stronger collective commitment to prevent global warming, I think it is only prudent to prepare for what might be the inevitable result of short-sighted policy decisions. There are clearly both short-term and long-term investments that can be made in basic science and technology research which could act as a hedge against the effects of global warming and prepare humans to live in quite a different world.

Stephen R. Quake is the Lee Otterson Professor of Bioengineering and professor of applied physics at Stanford University. He is also the co-president of the Chan Zuckerberg Biohub.

---

[1] https://www.ucsusa.org/our-work/global-warming/science-and-impacts/global-warming-impacts

[2] E.R. Mardis *Nature* 470, pages198–203 (10 February 2011)

[3] D.J. Burgess *Nature Reviews Genetics* 19, page739 (2018)

[4] C. Gawad, W Koh and S.R. Quake *Nature Reviews Genetics* 17, pages175–188 (2016)

[5] M. Haghi et al *Healthc Inform Res*. 2017 Jan; 23(1): 4–15.

[6] M. Lippman *Ann Rev Public Health* 1989. 10:49-67

[7] http://www.worldallergy.org/UserFiles/file/Economic-Burden-of-Allergy.pdf

[8] J.M. Orengo et al *Nature Communications* 9: 1421 (2018)

[9] D. Croote et al *Science* 14 Dec 2018: Vol. 362, Issue 6420, pp. 1306-1309

[10] https://www.who.int/hac/techguidance/ems/flood_cds/en/

[11] D. Sok and D.R. Burton *Nature Immunology* 19, pages1179–1188 (2018)

[12] https://www.nytimes.com/2018/10/31/health/ebola-congo-treatments.html

[13] https://www.regeneron.com/perspectives/making-ebola-drug

[14] F. Zanini et al *PNAS* December 26, 2018 115 (52) E12363-E12369

[15] S. Saha et al https://doi.org/10.1101/579532

[16] M. Kowarsky et al *PNAS* September 5, 2017 114 (36) 9623-9628

[17] M. Kowarsky et al https://doi.org/10.1101/481093

Observations from the Roundtable

Human societies have generally made great progress over the course of history in the mastery of their surrounding environments, climates, and biomes. And the experience of the United States is emblematic of this, across a variety of measures—with significant reductions in air and water pollution, in weather-related mortality, in malnutrition, and in the burden of disease. Progress has been driven by a combination of technology, markets, and governance. Oftentimes difficult social and regulatory choices over the past half century, enabled by technological innovation and ongoing incentives for investments, have allowed this country to stay one step ahead of the variety of environmental and health risks it faces.

It is perhaps indicative of the consistency of this progress that the continued fragility of modern man's relationship with the environment goes unappreciated. But with anthropogenic climate change and other human-ecosystem impacts, some of these natural risks are set to grow faster, stronger, or in newly unpredictable ways. Our exposure to damages may also increase in the United States, which has an increasingly prosperous society with more built assets at risk, alongside an ageing population that could be more impacted by extreme weather or other ecological events. Even today, despite major successes in recent decades, conservative estimates still ascribe more than 10,000 American deaths each year to pollution. The environment is not a solved problem. Governments will have to find new ways to stay ahead of these changes and protect their populations from threats, whose mitigations may now be taken for granted.

Our expert authors and roundtable discussants identified a number of such under-appreciated environmental risks going forward. And while many of their observations are not scientifically novel, they are put in terms that make them accessible to citizens and politicians, who tend to prioritize today's policy problems before tomorrow's. Moreover, they propose to use new technologies, particularly in diagnostics, to facilitate implementation of traditional approaches to countering many of these increasing risks.

Pandemics

American governance and private innovation have of course helped public health make great strides over the past century. In 1900, it is estimated that at least 10,000 Americans died each year from malaria, and at least that many from smallpox. Domestic transmission of both pathogens was essentially eliminated by 1950. U.S. life expectancy rose from 50 years in 1900 to 79 today—and over the same period mortality for children under five fell from nearly 2,000 deaths per 100,000 children, to 140 in 1950, and just 25 today. Since 1980, U.S. infectious disease deaths of all types have fallen by nearly one-fifth.

But infectious diseases, which had declined during the 20th century, are making a comeback, and our discussants argued that pandemics once again pose a major threat to humanity. Part of this is due to growing global human contact. Mobility is increasing everywhere alongside the growing affordability of longer distance travel. Since the 1980's anthropologists have posited the concept of a "travel-time budget": that on average individuals in societies spend approximately the same amount of time each day, roughly one hour, devoted to traveling to and from work. As technologies improve, people become richer, and the price of mobility falls, this results in people choosing to travel longer distances at higher average speeds for leisure or economic activity. This improves the productivity of labor markets, but it also creates new pathways for the spread of infectious disease.

Global urbanization rates are also rapidly increasing, especially in the developing world, due in part to demographic shifts. In parallel, increased immigration to developed countries in temperate regions from source countries across the global tropics—and ongoing family ties to home—has increased the prevalence of tropical sickness in northern hospitals. As our panelist and emergency room physician Milana Boukhman Trounce put it, ubiquitous global air travel has become an infectious disease "super vector."

Meanwhile, human populations are also changing the nature of their contact with animal disease pools or vectors, due in part to climate change. Changing precipitation and temperature patterns, for example, are redistributing the spatial and temporal incidence of disease spreading mosquitos—perhaps lower incidence than today in some areas, but higher in others, including the introduction of tropical diseases into the United States. For another example, African Ebola outbreaks are not new, but the 2014–2015 Ebola outbreak ended up affecting far more people than previous outbreaks, spreading across the entire continent rather than within a single village, with even worldwide impacts due to international travel. Similar dynamics now apply to the spread of predictable outbreaks like the annual flu as well as other infectious organisms.

Beyond these natural drivers, the future also holds the risk of disease outbreaks from accidental or even deliberate means as the cost of genetic engineering rapidly declines. Humans ourselves are at risk from this, but so are our livestock and other agricultural economies.

What can governments do about this threat to mitigate new risks and extend the significant progress in public health made over the past century? Our discussants considered what has worked in the past, what has not been effective, and the potential for new approaches.

Prevention could take two forms. One promising route would be mitigating the newly evolving activity of vectors. Mosquito population control has been practiced for over one hundred years to immense human benefit. Going forward, newly-developed genetic engineering "gene drives" offer numerous new options, with varying tradeoffs between efficacy and ethical concerns or the risk of unintended consequence: such techniques can reduce vector (i.e. mosquito) populations, limit vector reproduction, or inhibit the ability of the vectors to transmit a pathogen. In many cases the biology to do so has already been developed. In weighing the governance framework for deployment of such technologies, we would urge that their potential costs and benefits be considered not against a standard of perfection but of a status quo in which the human burden of infectious disease is already large—and set to grow in a changing world.

Preventing new infection through new vaccines is harder. Humans and the animals we value are potentially vulnerable to thousands of strains of viruses, which can mutate rapidly. Developing vaccines or drugs for all of them, which can easily cost over $1 billion each, is not feasible. Even today's widely administered flu vaccine, for example, which is developed ahead of each flu season based on predictions of the form the virus will take, is of uneven effectiveness because the virus mutates rapidly. And anti-viral drugs like Tamiflu have shown to be of little value in easing virus symptoms, apart from in patients with already-compromised immune systems.

But could new technologies help speed the development of disease treatments once an outbreak has already begun? Traditional vaccines may take a few years to develop, but our panel discussants advised that even a large infectious disease outbreak will generally run its course in 12–18 months—before conventional vaccines would ever be ready.

One strategy that could help is more rapid detection and early characterization of an outbreak. Panelist and biotechnologist Stephen Quake described how biology has become an information science—that is, one driven by data—enabled by low-cost and scalable cloud-based computing and data storage. Meanwhile, the cost of sequencing DNA has dropped by orders of magnitude over just the past 10–15 years, at rates comparable to "Moore's law" improvements through the 1980s, 1990s, and 2000s in the cost performance of microchips. Together, these two advances mean that biologists have rapid access to the genomes of many organisms, including human or animal pathogens at an early stage of a pandemic. When using the right tools, this can cut months out of the detection process.

These same technologies can help develop rapid therapies. Quake described, for example, how his team was able to take DNA samples from a population at an early stage of a novel dengue outbreak and rapidly sequence them against a cloud database of known DNA patterns to look for new strands—including disease antibodies that had been generated through the immune response of some of the infected individuals. Reproducing those highly targeted antibodies and delivering them to other infected or at-risk individuals offers a new path to rapid, almost "in the field" treatments.

Some challenges are less amenable to technological solutions. A large pandemic would of course have direct costs on U.S. citizen health. But even a smaller infectious disease outbreak with high mortality rates could be debilitating given the somewhat prosaic difficulty in providing surge capacity—additional hospital beds, clean rooms, water supplies, etc.—in the health care system. Our discussants described from their firsthand experience how even a very large regional trauma facility, such as the Stanford Hospital, could host, at most, ten Ebola patients at one time—and that even that would require the complete shutdown of the hospital's cardiac wards.

While the development of rapid and accurate diagnostic tests such as those described above would be crucial—i.e. "at home pregnancy tests for Ebola"—the historically effective solution in such circumstances would be public health measures: isolation (of those with the disease) and quarantine (of those exposed). Local governments at the county or city level would be responsible for creating and enforcing bans on public gatherings, school and business closures, and strict home quarantine and isolation. Doing so has always been difficult, with one panelist observing that during the 2003 SARS outbreak, "even Canadians in Vancouver didn't want to comply [with quarantines]."

New, quick, and accurate diagnostic tests could enable effective implementation of isolation and quarantine. In addition, panelists speculated whether new information and communication or logistics technologies could facilitate such difficult-to-enforce measures through location tracking, telemedicine, or the automated delivery of food, water, and supplies. Overall the panelists argued that "the public sector is not sufficiently preparing for this." While local public health departments have protocols, do drills, and receive guidance from the federal Centers for Disease Control and Prevention (CDC), "there are too many cooks in the kitchen." A large-scale disease outbreak is not just a medical event, but also one of public safety and security: "It's chaos every time, and it is always reactive." Looking at how warehousing and logistics technologies are developing, panelists considered how the U.S. private sector might end up delivering many needed services in such an outbreak, and the market incentives and coordination that governments could consider to help enable that.

Climate Change and Environmental Pollutants

A combination of technology and policy within a market incentive framework has led to a reduction in many environmental pollutants in the United States, including ozone, particulate matter, carbon monoxide, sulfur dioxide, nitrogen dioxide, lead, benzene, and mercury. But our panelists asked how much of a threat remained and if that progress might be reversed through interactions with concurrent global climate change.

The detrimental impacts of small particulate matter remain severe in the developing world. While Beijing and New Delhi are extreme examples, 92 percent the world's population lives in areas where air quality does not meet WHO standards. Particulate matter can be inhaled deep into the lungs, bringing hazardous substances into the bloodstream. Exposure can have economy-wide impacts, with a range of estimates in China attributing annual GDP growth rate losses of between one and four percentage points to health and childhood developmental costs associated with air pollution. Meanwhile, indoor cooking with wood or dung, a method relied upon by over a billion people in Africa and South Asia without access to cleaner commercial fuels, produces smoke with particulate levels 100 times higher than acceptable levels and results in millions of deaths annually.

Even in the United States, the changing risk of and exposure to regional drought, floods, and wildfire smoke under changing regional climate regimes may put the respiratory health of the public at risk. Going forward, discussants argued for increased use of controlled burns, for example, which burn less intensely than uncontrolled wildfires and therefore result in fewer health impacts for those exposed to resulting smoke. Rising temperatures may increase Americans' environmental exposure, broadly defined: a longer and more intense allergy season, the spread of insect-borne diseases, more frequent and dangerous heat waves, and heavier rainstorms. One emerging area of policy attention has been ingestion of mercury and microplastics through seafood consumption.

There is reason for optimism that we can successfully handle these risks. In the United States since the 1970s, we have seen substantial, sustained reductions in per capita emissions of air pollutants such as sulfur dioxide, nitrogen oxides, and chlorofluorocarbons, as well as reductions in exposure to toxics such as asbestos and lead—despite overall economic activity quadrupling over that same period. Today's per capita energy-related sulfur oxide emissions in the United States, for example, are about 85% below levels just 25 years ago, while nitrogen oxide emission intensity has fallen 60%. At that time, particulate air pollution from U.S. coal fired power plants alone were thought to contribute to 30,000 American deaths annually; today, with market-driven fuel switching to natural gas as well as improved (and often government-mandated) emissions controls, that number has fallen by 90 percent.

In addition to conventional pollution mitigation measures, our panelists suggested other emerging technologies that might help reduce these public health risks going forward. Even in developed countries, the elderly remain at risk from heat waves, and heat is already the largest weather-related killer in the United States: low-cost wearable devices that automatically report on cumulative heat exposure, hydration, and body response could help in an ageing U.S. society (while deaths from extreme temperatures are difficult to measure, studies suggest that extreme heat deaths have already gradually declined in a variety of U.S. cities over the course of the 20th century, and this progress could be further extended). Emerging technologies over the last decade now show promise for using the same antibodies that cause allergies—which already affect 60 million Americans at a cost of $20 billion per year in lost work days—to create effective therapies for them. And going forward, advancements in regenerative medicine may also be able to play a role in mitigating the effects of pollution-related diseases such as lung disease. Our discussants noted that where markets for such services or therapies exist, U.S. industry is already moving rapidly in using these technologies to develop valuable new consumer products. They should be encouraged.

Ecosystem Services

Our panel leader, biologist Lucy Shapiro, observed that even optimistic projections of reductions in greenhouse gas emissions over the next century are likely to results in significant climatic changes, including potential disruptions to valuable ecosystem services such as environmental pollution filtration, groundwater, seasonal precipitation storage, pollination, biodiversity, agricultural productivity, and other food chains. Since before the founding of our country, we have struggled against weather and environmental threats, sometimes at great cost—consider the plight of early European colonists, for example. Today's climate change is perhaps unique though in the number of ways it will affect various aspects of human prosperity. It is also unique in that the development of modern climate science tools helps us to anticipate these changes with some degree of reliability. From a policy perspective then, as societies strengthen their efforts to reduce warming, they should also be planning for—and budgeting for the costs of—how to ameliorate the expected human impacts of these damages.

We are already seeing the consequences: rising relative sea levels alongside coastal subsidence, causing major population displacements; extreme fires and storms; acidification and warming of ocean waters, leading to decimation of coral reefs; changes in food production; and accelerated extinction of species.

Consider tropical coral reefs, about half of which according to our panelists have experienced heat stress or bleaching, with adverse consequences for fish and other marine life they shelter and support. Recently, scientists have discovered how some corals have naturally adapted to warm water and acidification, and that these populations might be used to help seed new growth in damaged areas through transplantation. While some may find this an unsatisfying concept, it echoes the history of human cultivation of the terrestrial plant biome through intense forestry or cultivation practices.

Another example is storms. Extreme precipitation events have increased in the United States over the last century. But the incidence of floods in this country has remained essentially flat, and deaths from floods have declined on a per capita basis. This is due in part to proactive efforts to control runoff and waterways through infrastructure development or complementary management practices. Similarly, despite incidences of extreme weather, tornado and lightening deaths declined on an absolute basis in the second half of the 20th century, aided by upgrading building codes, detection technology, and emergency response. This has not been a cheap course of action, but it has been worthwhile.

Similarly, we may find ourselves in the United States forced to take novel steps to avoid increased economic climate damages. For example, this country has seen enormous successes in improving the productivity of our agricultural system: U.S. corn farmers produced 30 bushels per acre of farmland in 1900, 40 per acre in 1950, and over 150 bushels per acre today; soybeans and wheat have seen similar productivity growth; and each U.S. milk cow today produces 2.5 times more milk than its predecessors of 50 years ago. And in recent years, agricultural biotechnology has been largely focused on extending the gains of the Green Revolution by further improving those yields. With a changing climate, however, the field may now need to shift more towards the development of drought-, heat-, or disease-resistant crop varietals instead, with the associated opportunity costs of doing so.

Or, in parts of the country that will experience drought, new water infrastructure development may be necessary to both store seasonal runoff and improve end use efficiency, such as in agricultural irrigation, industrial, or residential use; the economics of undertaking new capital investments in an era of declining overall utilization are daunting.

Day to day human activity is likely to be affected too, which can result in a sort of constant tax on normal livelihoods and commerce. Heretofore in modern U.S. history, for example, vector population controls and a generally temperate climate have insulated us from debilitating tropical diseases, with all their ensuing healthcare costs and drains on productivity. But with climate change, mosquitos are moving north. We will need to redouble our diagnostic, treatment, and eradication capabilities in order to hold our ground.

Going forward, maintaining our relationship with our environment—and obtaining the services it provides for us—may simply take more effort.

The Intersection of Technology, Markets, and Policy in an Emerging World

The concrete nature of the challenges presented in this volume drive home the point that policies to address climate and the environment should focus less on what may or may not happen in the future, or on abstract numerical targets and complex agreements, and more on what can feasibly and responsibly be done today to reduce our risk. Many of the steps we could take today in anticipation of any future risks would start accruing benefits even now given that we already manage or mitigate our environment on many fronts.

This was one of the lessons of what is perhaps the most effective coordinated international environmental strategy in history, the Montreal Protocol. At first, the science was uncertain, but it was compelling enough that were the scientists to be right, the environmental results would be unacceptable. So at first we took obvious, easier policy steps to addressing the chlorofluorocarbon problem—but we also got American companies started on the technology development to give us better options to address the more difficult aspects of the problem in the future. By the time that the Antarctic ozone hole was observed, those new technologies were close enough to being mature that we could go ahead with a specific and binding agreement we were confident that we could actually fulfill. We've done this before.

Similarly, one recurring theme in the day's discussions was the growing relationship between climate change and other «conventional» environmental concerns like air, water, and soil pollution. Some of these systems have scientific links. But they are also increasingly linked in the minds of the public and in policymaking. Consider key recent federal «climate» regulations such as the 2015 proposed Clean Power Plan, or even some vehicle fuel economy standards, where cost-benefit analyses in their favor were actually dominated by co-beneficial reductions in local and regional air pollution. And whereas public polling by Pew Research suggests year after year that climate change remains relatively low on U.S. voters' list of priorities for Washington, D.C., maintaining an overall healthy environment consistently ranks highly across party affiliations. Globally speaking, contemporary America's natural environment is one of our country's best assets, and we should be looking to maintain that alongside vibrant economic growth.

Some of the problems are not even so complicated. Think of the existing nuclear power plants in this country, which provide substantial amounts of clean energy. Some are now unexpectedly having to be shut down by their operators because they are losing money in today's low-cost electricity markets. But we know that when those plants get shut down, they are replaced by polluting alternatives. Fixing this doesn't take some aspiration for the future (though we should be investing in even better nuclear power technologies for the future, too). Instead, this is the sort of three-way intersection of technology, markets, and policy that we will increasingly encounter in a changing environment. While these are the sorts of questions state and federal agencies have always had to respond to, as the natural pace of change gets faster on the other two of those three dynamics, government will need to get faster at identifying and responding to change as well.

Importantly, while some of these challenges described in this volume are new, and others are as old as civilization, our panelists—themselves scientists, doctors, or engineers—remained compelled by the optimism of an American spirit of discovery and innovation to take them on. This was tempered only by their regret in the strained relationship between science and policy in this country, where knowledge and promise are too often selectively ignored or weaponized by both political parties.

They concluded with a plea for the foundational long-term importance to the nation of investing in science and engineering. Markets enable a host of groundbreaking science and health innovation by private entities. But public funding is still crucial in serving earlier stage research that does not offer good near-term private investment prospects, and for which socially valuable intellectual property can be made more widely available. In a time of newly emerging challenges, our discussants particularly called for a shift in public funding towards riskier but potentially game-changing forms of research and development that get sidelined by conventional funding processes, which tend to emphasize lower-risk, marginal advancements. Where governments have dialed back those risky research ambitions, philanthropy has tried to fill the funding gap, but its reach is more limited. At the same time, discussants sought to rebalance the working relationship between Washington, D.C., and the optimism of labs such as theirs around the country. As mentioned above, Stephen Quake's contribution to this volume reviews the many groundbreaking research projects being conducted here at Stanford and partner institutions, as well in industry. We are fortunate to be at the center of such great work, and the vibrant culture of investigation and discovery here speaks to the value of fostering such efforts. To conclude with one panelist's summation:

"This argument—about if you should do very basic research with no obvious endpoint and just deal with things that you know how to manipulate and apply them to a different project—is a strange argument.

If you don't push the boundaries of understanding this world that we are living in, then when we are faced with a complete skewing of the ecosystem of the globe (which we are dealing with now) without new kinds of understandings of how living beings, living organisms can survive changes in their environment—we are being, if not short-sighted, then we are being criminal. It just makes no sense whatsoever.

But somehow, we have to do both. We have to continue digging for new ways of understanding the world around us, so that we can mitigate disasters, *and* we have to cleverly use what we already know about to create ways of dealing with them and the immediate situation. So you have to deal both with the future, and with the present, and have enough science, and enough people who are making decisions listening to the science, so that we make intelligent choices.

And right now, both the world ecosystem is skewed, and our political system is skewed, and these things must come together, or I fear for what's going to happen to life on this earth."

Notes

About

New and rapid societal and technological changes are complicating governance around the globe and challenging traditional thinking. Demographic changes and migration are having a profound effect as some populations age and shrink while other countries expand. The information and communications revolution is making governance much more difficult and heightening the impact of diversity. Emerging technologies, especially artificial intelligence and automation, are bringing about a new industrial revolution, disrupting workforces and increasing military capabilities of both states and non-state actors. And new means of production such as additive manufacturing and automation are changing how, where, and what we produce. These changes are coming quickly, faster than governments have historically been able to respond.

Led by Hoover Distinguished Fellow George P. Shultz, his Project on Governance in an Emerging New World aims to understand these changes and inform strategies that both address the challenges and take advantage of the opportunities afforded by these dramatic shifts.

The project features a series of papers and events addressing how these changes are affecting democratic processes, the economy, and national security of the United States, and how they are affecting countries and regions, including Russia, China, Europe, Africa, and Latin America. A set of essays by the participants accompanies each event and provides thoughtful analysis of the challenges and opportunities.

Hoover Institution,
Stanford University
434 Galvez Mall
Stanford, CA 94305-6003
650-723-1754

Hoover Institution in Washington
The Johnson Center
1399 New York Avenue NW, Suite 500
Washington, DC 20005
202-760-3200

HOOVER
INSTITUTION
ONE HUNDRED YEARS