Michael Osterholm

Nobel Conference 42

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Thank you. Thank you, Barbara. I must admit, as many introductions as I've had, I will never forget that one. I just wish my mother could've been here. Ladies and gentlemen, distinguished guests, it's a true honor to be here today to share with you a message that has already in a sense been laid out for you. Before I begin, though, I want to acknowledge two specific groups of individuals who are in the audience today.

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First, I have to acknowledge he many soulmates I have in this room today who lived with me through what was one of Mother Nature's very worse curveballs, the meningitis outbreak in this area some years ago. It also was the very best of the human spirit. And I know there are a number of you in here today and I must tell you that every day that I live, I carry that experience with me. Grant you, it took a few years of my life expectancy off that I'm not sure genetic manipulation will get back. But at the same time, I have used that experience over and over again to remind why it is we do what we do.

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Second of all, my remarks are aimed very specifically at the students in the audience today. I will tell you at the outset that I am not proud to be part of a generation that's turning the world over to you much, in much worse shape than we received it. The issues I want to talk about today are part of that. It's about what we can do about, what we must do about it, and what are some of the consequences if we don't. We will talk a bit about the fact that hope and despair are not strategies. That issues before us are in fact workable solution situations. But we are going to talk about what I would consider to be some very tough times.

Now I last count had about 9,500 slides in my repertoire of slides that I keep. And if someone asked me and said, Mike, you know, you gotta rid of all your slides but one to tell a story, what would that slide be? This is it. This is the world we live in today. On the bottom you see the last 150 years. On the left vertical bar you see days to circumnavigate the globe. What you see on the right vertical bar is population of the world.

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Well, 150 years ago, it took us a year to get around the world, even on fast sail boats. By 1950 with the advent of the jet plan, we had that down to a little over 40 hours. Not much has changed in terms of speed to get around the world since that time. But what has changed is even more dramatic. We now live in a global just-in-time economy where many of the critical products and services that you count on every day right here in St. Peter, wherever you're at in the United States, originates in an off-shore location. Last year 1.4 billion people – 1.4 billion people – physically crossed an international border. By airplane, by boat, by 4-wheel vehicle, by walking, by any number of different ways. We live in a mobile world that moves around in a way that has tremendous implications for infectious diseases.

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And then I look at that blue line and I remain stunned. This month we are quote unquote acknowledging we have just reached the 300 millionth American to be alive. At the same time, we've just surpassed 6.5 billion people on the face of the earth. One out of every nine people who has ever lived since the caves is now on the face of the earth. That has tremendous implications also for infectious diseases.

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The point being today, in many of the developing world countries, we have situations that if Charles Dickens were alive today, he was be aghast at how things had gone downhill, not improved, from the time that he wrote about the terrible conditions of Europe. In addition, I will add, there are a whole lot of other problems with that blue line. At what point are we going to realize Mother Earth has only so much capacity? That in fact we are challenging the very essence of our ability to live on this planet. Note that infectious diseases will play a part in that whole discussion.

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Now we came up with a term almost some 14 years ago called emerging infections. It was a way to describe the concept of new, re-emerging, or drug-resistant infections whose incidents in humans has increased in the past 2 decades or whose incidents threatens to increase in the near future. So it's brand new ones. Ones that we had never heard of before or at least recognized. Old ones that are finding ways to come back because of changes in our everyday living conditions. And of course that issue of drug-resistance. This morning in what I consider one of the most elegant talks I've ever heard in my career on the genetics of our life, we also understand that microbes have the genetics and the ability to change also, as we just talked about. The difference is, they go through more changes in one year of 20-minute generations than we may go through dating back to the caves. So the point being is they can accommodate. They can acclimate. They can adjust to everything gets throw, thrown at them. And drug resistance, what relatively almost short-lived phenomena of drug susceptibility is something we have to understand.

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Now if you look at this map, you see for the last few years any number of new emerging infectious disease issues that have come forward. And note that they are all over the world. It's not just the developing world or the developed world. It varies from multi drug-resistant organisms. The E.coli infection to intentional events such as Anthrax and what it means for the future of potential events. You'll see, today I'll talk about the few of these in the context of examples of why systematically we have to understand and respond to this issue of infectious diseases.

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Now the National Academy of Science Institute of Medicine put together a group in 1991 that not only coined the term Emerging Infections, but on that left side of the book really laid out a clarion call to all of civilization, not just the public health community, not just medicine, not even just governments, that you had to wake up. That that air of infectious diseases being gone and eliminated was not true. We had that very, very short respite where we thought we had infectious diseases in

control. But in fact, we didn't. The point being is is that today we recognize that these infections are coming back. So the point being is is that now we have a second group that's looked at this issues, that published a document in 2003, which I was part of that group, and we went back and looked at the fact that if we understand Emerging Infections from 1992, we didn't really even understand them compared to today. Because all of the things that we said would happen that were horrible bad happened and a lot of things we hadn't anticipated.

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So today we have to understand that nothing looks bright in terms of the advances we're making. But it doesn't mean it has to be that way. Unlike some things, it is not inevitable that we have to live in this world of infectious diseases as we do. Now there were a number of factors that we put forward that really contribute to that whole, what I'd call perfect storm. The term is, unfortunately, often overused, for the emergence of infectious diseases. Human demographics and behavior. We obviously understand from the world population standpoint what we're talking about. But with human demographics, you've got to feed people. When you've got to feed people, you've got to have a lot of domestic animals. You start challenging water systems for water, things like that. All the things that you don't think about that contribute.

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The issue of behavior, issues of sexual behavior, issues of I.V. drug use, a behavior that virtually didn't exist 100 years ago because the advent of the needle was not there yet for people to routinely do intravenous drug abuse. The issue of technology and industry. Today we have created all kind of new things that add actually to the risk of infectious diseases we hadn't' thought about. I never thought back in 1980, when our group first discovered the relationship between tampons and toxic shock syndrome, that the oxygen capacity of the tampon might have a lot to do with how staph aureus grows. Or how it produces toxin. And in fact it did. Because as we thought more and more absorbent tampons, we just basically jacked up the risk of toxic shock syndrome.

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I could go through a long endless line of examples of industrial-related activities that have increased our risk. Economic development and land use. Today we are basically changing the face of the earth. We happen to live in an area right now, I don't know if you know this or not, but the Upper Midwest is the single most quote, unquote, ecologically devasted location in the world. We devasted 98 percent of the native prairie in this area 150 years ago to make way for the breadbasket, which you can argue is a good thing. But the point is, the rain forests, no other area of the world has been as ecologically changed in modern history as where we sit right now.

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But today how many of you know that there are more forests, there are more trees in the eastern part of the United States today than there ever was when the first white man set foot on this continent. As a result of that, we see major changes in animals. Which wildlife are there? We see major changes in vectors. I could go through a laundry list of issues. Economic development and land use with dams. Today you can't build a dam anywhere in the world and not create a major waterborne-related, uh, mosquito, other vector-related crisis. International travel and commerce, I've already hit on that one.

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Microbial adaption and change. You know, the bugs don't wake up in the morning and go read the paper and try to figure out, OK, what are we going to do today? Who are we going to get? They have a much more powerful guide, that of evolution. And as I pointed out earlier, they're using it very well. The breakdown of public health measures. I always get a little nervous on this one because most people in the room say, what are you talking about? Today the basic support for public health in this country has eroded dramatically, even with recent reinvestments. It is not anything to what it was 30 to 40 years ago. We are so focused on curative medicine, that last-minute miracle, that prevention constantly takes a backseat. You're going to hear later about healthcare costs in this country. Last year, to give you a perspective, the increase in healthcare, disease care costs in this country exceeded the entire revenue from the entertainment industry. Meanwhile, the investment in public health was measured in nanometers. That is obviously a problem.

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If we look at the human's susceptibility to infection, as we heard this morning, we grow older. But as we grow older, it doesn't mean we stay young longer. Today we see many more people living with debilitating conditions, not just HIV. Cancers, [inaudible] that predispose them to infections we never heard of 25 years ago. Is it safe to drink the [inaudible] water supply? Well, for the vast majority it is, but there may be microbes in that water supply today that are not pathogens or disease causing bugs to most of us, but to those very view that are immune deficient, it can be a real problem.

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Climate and weather. You know, let's just wake up and acknowledge, climate change is here and it's coming quickly. The point being though is weather is important. Some 15 years ago we got a glimpse of that when we started seeing an el Nino bring the rains to southern part of the United, Southwestern United States. Now you can't call that climate but as a result of a massive greening of the desert, we saw a massive burst in rodent populations, which we then saw a massive burst in an infectious agent we hadn't previously recognized called hantavirus. As a result of this burgeoning rodent population, they sought refuge wherever they could. They left their territories and went into homes. And with that rodent came rodent urine. And with that rodent urine came the virus. And if you swept a floor that frankly a mouse had peed on, you were in trouble. Today we are wondering about that because we have predictions for a major el Nino coming back into the Southwestern United States this winter. That kind of thing is weather related, it's not just climate.

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Poverty and social inequality, infectious diseases as you'll see are largely tied to the world's poverty status. As goes our well-being, as goes infectious diseases. War and famine, I'm going to talk more about particularly the famine case but suffice it to say today there are very few people who are aware that every time we have a war, what makes the front cover of the magazine or the front, the first story of the evening news, is the bloody dead bodies that are lying there in the battlefield, or today in a result of terrorism. What they don't realize is there are many more people who die every day from infectious diseases because they can't get the

vaccines, they can't get safe water, they can't get the kinds of basic infrastructure protections. Eight times as many people died in Kosovo from infectious diseases that ever died from a bullet or a, with a knife. But we never heard about those.

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Lack of political will. As I was state epidemiologist, I served two democratic governors, two republican governors, one independent wrestler. [laughter] And I've served in the last three presidential administrations, and I can tell you quite honestly, my own family cannot tell you my partisan politics. I have believed it is my job to serve as a fair, honest, and hopefully informed voice of science. Don't think it's not hard sometimes. But today I will make comments about some of the political issues out there and please take it in that context. Suffice it to say, I've had about as much as I can stand of Washington, D.C. right now. I have seen inaction based on inaction. [applause] We worry more about the political issues of division than we do about the collective good of our world. And infectious diseases represent that as much as I know.

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Finally, the intent to harm. This is one that's tough for me because I have every reason to believe it's coming back. As many of you know in the room, I wrote a book on 9/11 of 2000 called *Living Terrors*, one year to the day before the event. It was painful because in that book I did talk about why the World Trade Centers Towers would still stay the number one target for the Al-Qaeda and why they wanted to bring it down. I also talked about what would happen if a very limited anthrax hit occurred, which we saw. That one was really just a, just a wake-up to what happened. Today we have to know that there are people who want to hurt us who will have the ability with infectious agents to do catastrophic things. That's hard to think about and plan for.

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Now in terms of some of the examples, let me point out to you why I say these things and what, what they mean. Here's the example of the SARS epidemic that occurred several years ago. We quickly discovered this was caused by a thing called the Corona virus as a possible cause of the severe acute respiratory syndrome. Clearly caught everybody off guard. But I must tell you from the standpoint of the

big picture, it was really just a minor blip. 8,000 cases, 774 deaths. On an everyday public health basis, not big. But I will tell you that in fact what it did to the individual locations where it occurred was devastating. 80 percent of the flights in and out of Singapore and Hong Kong were cancelled for more than 12 weeks. The city of Toronto lost billions of billions of dollars in revenue and income. By the eighth week of the problem in Toronto, 25 percent of health healthcare workers were too afraid to come to work. This is the kind of thing we'll talk more about.

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But I want to point out to you what I mean today about these factors. We live in a world of loose connections that are all connected. This is the chain of transmission that really got that SARS epidemic started and it should serve as a model for a lot of the other infectious agents we're going to talk about.

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What happened was in that red bar right here, we had a businessman from the Guangdong Provence of China who became infected as a result of exposure to animals in his own local city. He then traveled overnight to the Metropole Hotel in Hong Kong and stayed there for 3 days. While he was there, he infected 10 different people who then all left, well at the time that they left. They went to Canada, they went to Ireland, they went to the United States. They went to Singapore, which then went on to Germany. They went to Vietnam. They went to Hong Kong.

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Very quickly, within a matter of days, that particular infectious agent was around the world. That's that connection I talked about with time and the ability to actually intervene is limited. This kind of situation is real for all the infectious diseases we have today where this kind of transmission can and will occur. This is the old days of public health, when you could do things that were basically a little bit, uh, should you say more in control of and less considering the implications of. We now know that this is not necessarily a wise way to quote, unquote, disinfect, or disinfest your airplane. But let me tell you, the next slide may be the saddest slide I have in my entire repertoire of slides I'll show you today. It shows you where we've been, where we're at, and I fear where we're going.

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Aedes aegypti is a type of mosquito that vectors several important infectious disease concerns of humans, yellow fever and dengue, for example. It's what we call the household mosquito. It loves to be with people. It loves to breed in little containers of water, even a discarded McDonald's wrapper in the ditch where a drop of water will collect for more than a day or two, it will lay its eggs and do very fine, thank you.

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This mosquito was in retreat, when in the 1930s the Rockefeller Foundation and a number of other groups said, 'We're going after this thing and we're going to get it. We're going to eliminate the breeding sites.' And look what they did from 1930, where the green reflects where aedes aegypti was in the Americas to 1970. And I might add, that part of the United States was almost absent of the aedes aegypti, hardly any there. And then we got complacent. We re-, we removed resources. We realized, you know, we had won, well before we had won. Now, ladies and gentlemen, look at the distribution of aedes aegypti today. And I will tell you, per location, it is much, much, much more in numbers and locations within any one country than it ever was in 1930. We've lost all that ground because we didn't continue the job. We got complacent. We gave up on public health.

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Why is that important? Well, this is a disease that I think is one of the most fascinating of all diseases because in part it's a manmade concoction. Dengue fever is a viral disease caused by mosquitos. That's what arthropod means. Basically this disease lived in human, with humans for centuries and centuries and was relatively not a big public health issue. It had the nickname of break-bone fever because if you got it, you thought you were going to die for two or three days. Your bones felt like they were breaking. But you recovered.

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Well, today we have a brand-new component to dengue fever we've never, ever realized. It turns out that there were four distinct stereotypes of dengue. All located in four different parts of the world, two different ones in two different parts of Asia, one in the Americas and one in Africa. Basically following World War II and through that time, we began to move the mosquitos around in all the transportation we did,

whether in cargo holds, in, you know, old military vehicles, tires, whatever. Before 1970, only nine countries had experienced hemorrhagic fever. Why did hemorrhagic fever occur? It was because once the full, one serotype occurred in an area and a second, third, and fourth got introduced, it turned out that if you got reinfected the first time with one serotype and then infected a second time later with a second one, and particularly certain seconds ones, you then developed a whole new illness we'd never seen called dengue hemorrhagic fever, which for the lack of a better description is like an Ebola like illness. Basically it's horrible. A case fatality rate approaching 30 to 50 percent. We created that disease because today everywhere dengue ever existed, all four serotypes now exist, all within the last 50 years. That's a huge issue. So when you have students going abroad to one of these areas and they get dengue the first time, I would be nervous as hell if I was going to send a student back a second time. Because the second time could be a very different outcome.

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Today the WHO estimates 50 million infections, 500,000 hemorrhagic fever cases and 12,000 deaths annually. If you look at the global burden of dengue, we now estimate that it could be as significant as malaria and tuberculosis combined. The world impact will likely continue to grow dramatically due to the potential population change in aedes agypti. Everywhere you see in the developing world intercity junk, the deplorable conditions of the inner cities, those are all rich breeding grounds for aedes agypti. Dengue has to be considered the classic emerging infection and today we have virtually no control programs throughout most of the world for this. If you look at the belt where dengue exists, if you also overlay population with the exception of China, we really are where the heaviest populations are. I might also add, for all of your Minnesota snowbirds who enjoy going to the Caribbean, I would suggest you begin to take more note of where you're going as we're beginning to see much more widespread transmission of dengue throughout all the Caribbean vacation locations.

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Factors associated with dengue increase include world population, conditions favoring aedes aegypti include the rural-urban migration as we have these big cities. We live in junk piles, literally, all holding water. Again, one little plastic

wrapper is a wonderful breeding ground. If you don't have running water in your house, you have containers. Aedes aegypti love to breed in there. That unreliable water source is huge. Solid waste, as I pointed out, if we think we got solid waste problems in this country, much of the developing world has solid waste also, but they just don't deal with it. It just stays there, again, breeding ground for aedes aegypti.

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Our infrastructure support has eroded, and I don't go to anyplace that people sit there and go rah, yay, hah, dengue fever prevention. They don't think about it. It's one of many that are orphaned from any constituency out there because it occurs amongst the least of us. In fact, it's just another developing world disease.

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West Nile Virus, this is one that changed on us a bit. This, this turned on us. This was one that we had said the same thing about for quite some time. This was a viral infection that was first isolated in the West Nile district of Uganda in 1937. Hey, no big problem, it's over there. Today we know it's commonly found in humans and birds and other vertebrates in Africa, Eastern Europe, West Asia and the Middle East. But until very recently it was not documented in the Western Hemisphere. It was moving. It was spreading and the mosquitos and the birds that actually are part of this feeding cycle. What happens is an infected bird, a bird gets infected from an infected mosquito. An uninfected mosquito also takes a blood meal on that bird that now is infected and it's just a viscous cycle.

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Infected mosquitos then transmit the West Nile Virus to us when they take a blood meal. You can see it was documented, as I mentioned before, throughout the world. Israel had outbreaks in '51 and '54. And then the virus appeared to change somewhat. In 1957 we saw the first outbreaks of severe disease with meningitis. Mortality rates approaching 10 to 20 percent. France, South Africa, Romania, Italy, Russia, all those, them countries, and then in 1999 it all changed.

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In the summer of 1999, we had introduction of this virus, ironically, during a serious drought in the Northeast. Just so you understand, in the land of mosquitos, you know, where we all know that unofficially it's our state bird, a mosquito is not just a mosquito. There are those mosquitos that do very well in those containers I talked about. There are mosquitos that need flood plains. There are mosquitos that do well in dry years because of the way they actually, where they grow. There are mosquitos that do well in tree holes, in tires. There are mosquitos that do very well in wet years. Well, it so happened in the Northeast, where you would think mosquito populations would be way down, there were several selected types of mosquitos were way up. Why? Because, first of all, everyone was banned from filling their swimming pools. So they had old stagnant water and there are certain mosquitos that love that. There are certain mosquitos that lived in the sewers and because water never rushed through the sewers with rainfall, they never got cleaned out as such, flushed out, and we had little pockets of water sitting down underneath those drains, 6 feet down, in that cool, nice area, all were competent vectors for West Nile.

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How it got here, we don't know. Did it come in mosquitos in a plane? Did it come in wild birds that were brought over illegally? We know that we, as you'll see in a moment, we have all kinds of animal importations couldn't do it [sounds like]. But look what happened with the spread. It followed basically the migratory routes of the birds. Infected birds moved down the east, eastern flyway, the Atlantic coast flyway. By 2001 it had moved back up from the Gulf States coming up now the Mississippi flyway and by 2002 we had both human and bird activity in most of the country.

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If we look at that activity today, there have been over 2,900 cases of West Nile Virus so far this year, over 85 deaths. There have been upwards of a third of those cases had severe neurologic disease. Last year that number was over 3,000 cases. It's now here. There's not much we can do about it because we let it in. We let our guard down. We didn't deal with it when it was in other areas of the world where control would have meant a big impact.

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And just to give you a wake-up, all the farmers in the room, if nothing else, you better pay attention to this slide. Because just as West Nile came, and ironically I was actually at a meeting of vector control people just the year before which I made a prediction that we would see some novel new arbovirus enter the country because I couldn't understand why they'd stay out. I mean, we're bringing them in airplanes every day. I predict this one, I think, could be our next one. And this is going to be a doozie.

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It's Rift Valley Fever. It's a hemorrhagic fever virus. It causes disease in both humans and animals. It's a mosquito -borne disease. There are at least 11 species native to North America that are very well capable of moving this, including the black flies of north, northern Minnesota. Human diseases have up to 10 percent, up to 10 percent have hemorrhagic fever, a 1 percent case fatality rate, even higher than West Nile Virus. And among the animal diseases, cattle-calves have a 10-70 percent case-fatality risk, adults 4-10 percent, sheep and goats less than one week of age, 100 percent case-fatality rate, others 20 to 30 percent. We have no vaccine for it. We don't really care about this disease because it's not us, it's a developing world. But when it gets here, we'll care. We'll care big time. But it'll be too late. We should be caring now. Even if we're not altruistic, we should just be smart.

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Now in terms of, back up here, in terms of that animal importation I talked about, I mentioned, oops, see I can get one more, just one. If you look at the issue of animal importation, these are data that came out of that investigation of West Nile in 1998, '99. These are the animal importations into New York alone. And in this very dark lavender area, what you'll see, these are countries where over 350,000 animals came through just the Port of New York, through legally, for importation to the United States that year. And New York City was one of the smallest ports of entry we have. The point being today, we're moving everything around the world, including animals. This is an example of what happened with that movement of animals. For those who don't recognize this, this shot of disease, you shouldn't on the offhand recognize. This is monkeypox, a distant but very important relative to the smallpox virus. This is a viral infection with about 1 percent case-fatality rate. It has occurred in Africa for years. We have never seen it in the Americas.

And then one day, lo and behold, we suddenly had an outbreak in this country. And it turned out that we ultimately had estimated about 70 cases of monkeypox the summer of 2003, 37 were laboratory confirmed. This was just an incredible situation. What happened? Well, what we saw was up here, rodent shipment from Ghana. Today you can't be a pet store in this country and make it by selling puppies and kitties. You gotta have the latest, most exotic designer animal. I know that very well because my son, today who is 25, when he was in high school, he said, 'Dad, I gotta have an African Dwarf hedgehog. Anybody who's cool has one. I gotta have a Sonic.' I said, no way. Well, after about 6 months of this discussion, I finally relented and I acknowledge I gave in, but I said, only under once condition, we're going to text that thing when he gets in our house. The first three turds out of that animal were in the Minnesota Department of Health Medical Laboratory within a matter of one hour. Within 2 weeks we identified three new strains of salmonella that had never been seen in Minnesota before. Needless to say, I won't say more about the African Dwarf hedgehog or my son's disposition of it. But the point being is today that we basically are bringing animals. And so what happens is this importer imported 50 Gambian giant rats, 53 rope squirrels, 2 brush tail porcupines, 47 tree squirrels, 100 striped mice, and 410 dormas [sounds like]. These are all animals that you and I would never recognize but they're all being sold in pet stores. Well, it so happened that one of the Gambian rats actually had monkeypox. They then were brought into an area, a holding area in the upper Midwest here, they were being held with prairie dogs because little prairie dog pups are really cute little things when they're young. When they get older, they get mean. They basically don't like to live with humans. They weren't basically raised that way.

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And what happened, though, is people acquired these. They went out, and today we actually have companies that have machines that look like the size of this podium, they stick over holes of prairie dog colonies out in the western states and suck up all the prairie dogs in the hole. They kill the adults, take the pups and go sell them in pet stores. Well, these pups and these Gambian giant rats were in the same building. They spread them, the pups were then sold at what was basically called boot fairs, and lo and behold, this happened.

Just so you understand that this is not just a one-way problem either. For up until this time, we were exporting seventy to eighty thousand prairie dog pups annually to Tokyo for sale in pet stores there and as they would get older, they would get out, they would get loose. Prairie dogs also happen to be a very good vector for plague. And we, I'm convinced that now that these prairie dogs have started to take over the sewers of Tokyo, which they literally have, they are now beating Norwegian rats out for space, it wouldn't surprise me one day to see a plague outbreak in Tokyo, totally related to the prairie dogs of North America now taking over the sewers of Tokyo.

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This slide is one that should be a sober wake-up to all of us because it's a very simple slide with a very powerful message. This is the correlation with infant mortality and total fertility in selected countries and areas of the world. What you see on this left bar is infant mortality for 100,000 live births. What you see on the bottom is total fertility rate, in other words, number of children per 100 women, 700 here, down to 100 here, 0 to 125. We have known for some time that there is inverse relationship between fertility and infant mortality. If families do not have to keep having babies because they die, they won't. Why do they die? They die because of infectious diseases. They die from the very simplest of issues, not having clean water, clean food. When you bring the overall sanitation level up of any community, you greatly lower the overall infant, the total fertility rate.

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Look at New York City in 1900, 123 per 100,000 in terms of total fertility, I'm sorry, it's 650 per, per total fertility rate, look at their infant mortality rate. Look at it today. All we did was bring safe water. In 1900, the number one cause of death in kids under age 9 in Minneapolis/St. Paul was typhoid fever related to an unsafe water supply. That's 107 years ago. Today that's gone. Well, why do I talk about this with infectious diseases? Because I think first of all it has a lot to do with world population. You know, just handing out more condoms or telling people, 'Just say no,' is never going to completely solve this problem. There are social, cultural issues that are far deeper, and this is one of them.

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Well, because I think there are other issues around infectious diseases that are key. Ladies and gentlemen, we are obviously aware of losing one resource called petroleum. But we are missing the point that we are losing even more quickly a more vital one called fresh water. This is a chart showing the actual relative development of population growth versus blue water withdrawals over the last century. Blue water is that water either in the ground or in the surface that we can use for fresh water. It's not salt water. It's the water that's available to us.

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What you see here is population growth and it's projected, you see the projection of blue water withdrawals. When you look at those withdrawals, you use where it's going. It's going to irrigation. Why? To feed our population. Ladies and gentlemen, we're in a collision course with famine. Now I'm sure some people would not agree with this issue. None the least, I think that we are also been very blessed to have people who have worked hard to make this not happen. I remember reading Paul Ehrlich's book, The Time Bomb [sic] back some 40 years ago in which we, he said in 20 to 30 years we'd run out of food. Well, then we had wonderful people like I think Minnesota's native saint, Norman Borlaug, who helped grain the world. Who through genetic manipulation of crops was able to grow, greatly, greatly increase production. But that was predicated on there's a place to grow it. What grows food today? Two things. One is water. The second thing is petroleum. Where does your fertilizers come from? Where does your insecticides comes from, your pesticides? Where does your harvest capability come from? It's from petroleum. I won't go into petroleum today. You can understand that. But look at the water issue. We are running out of fresh water, even right here in places in Minnesota.

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This is a map showing how irrigation and well water withdrawals are beginning to have a major impact. What you see in the burgundy, for places like India and even in parts of the Western United States, high overdraft where we're mining the water. The recharge is much less than the actual water we're taking out.

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In some parts of the world, we have 20 to 30 years of fresh water left. And then all that food's going. But equally so is the water itself. And we know water is one of the most critical, important pieces of a public health infectious disease control program. I would urge all of you to read an absolutely spellbinding factually very, very well-researched series of articles this past week in the New York Times.

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You can see from these articles, In Teeming India, Water Crisis Means Dry Pipes and Foul Sludge. India Digs Deeper But Wells Are Drying Up. Often Parched, India Struggles to Tap the Monsoon. We are seeing this around the world. When we lose our water, we'll lose food, which will predispose us even more to infectious diseases. And when we lose water, we'll lose basic hygiene, and if we have any at all, predispose us much more to infectious diseases. I swear to god that if the 1800s looked bad, when you look at some of these issues, they look much worse.

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I can't do any talk without talking about this issue, the area of HIV. This is an area that I have been very involved with, having attended the very first meeting at CDC on June 4th of 1981 when at that time we had 37 cases of what we call KSOI, Kaposi Sarcoma Opportunistic Infections. We later then called it GRID, Gay Related Infectious Diseases. During that time I have lost many, many dear, dear, dear people in my life, including my aunt, a 63-year-old Catholic nun who was the first blood transfusion recipient in this country to die of AIDS. And a very, very dear high school friend of mine who was the first healthcare worker to die as a result of an occupational exposure. I know AIDS. It hurts. And ladies and gentlemen, as much as we have talked about all the wonderful new things with the Gates Foundation and the Clinton Foundation, and these are wonderful things. I can't begin to say how much those gentlemen in those foundations are doing. But we must face the reality of what HIV means.

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If you look at this slide, you can see sub-Saharan Africa, what more can you say? If you look at the numbers, it's very sobering. 68 million people infected, 25 million people have died in the last 24 years. 5 million infected this past year. The rate of new infections continues to rise annually. It is not leveling off. It's getting more.

About 14,000 new HIV infections each day, 13,000 in persons 15-49. A person is infected about every 6 seconds. Now in this country, we've taken a step back and said, well, we can treat it with drugs. It's become more of a manageable chronic disease. Some of that's true. But we are now also beginning to see the long-term impact of being on anti-retral therapy over time. And how long this wonderful gift of these drugs will mean also high quality of life or improved quality of life is questionable.

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But for much of the world, that's not even a point of discussion. 8,200 AIDS-related deaths occur each day. A person dies every 9 seconds. 6 seconds, 9 seconds. More people are becoming infected every day than are dying. The number of total infected continues to increase. There are 13 million orphans. A child becomes an orphan every 14 seconds. Anybody who's ever worked in this area sees the heart tug of losing entire family units relative to the adults but leaving behind young children who are now in many instances literally on their own.

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If you look at the current estimate, there's about 43 million people living with HIV infection of the world, about 4.9 million new infections in 2005, and about 3.1 million deaths due to AIDS in 2005. Anti-retral therapy is getting to a very, very small percentage of those. And we had a major program initiative 2 years ago that in fact we wanted to make sure that we had large numbers of people on these drugs and we've fallen far short. Doesn't mean we can't keep trying.

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I'll never forget some almost 20, or more than 20 years ago when one of the esteemed speakers at this previous meeting and somebody who's a dear friend to this campus was involved in the discovery of HIV or the name of the new virus and then Secretary Margaret Heckler at HHS came forward and said, 'We'll have a new AIDS vaccine within 2 to 3 years. We're in good shape.' I was quoted the next day on the front page of the New York Times saying I did not believe we would see an effective AIDS vaccine in my lifetime. I don't know what I knew back then but I knew enough about retrovirus, is something that our very distinguished speaker this morning knows a lot about. And I stand by that today. I hope I live a very long,

productive professional career. I don't know what it's ever going to take, if we ever will have an effective preventive AIDS vaccine.

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If you look at where AIDS has impacted, I've already pointed out. But you see Sub-Saharan Africa, Asia, and the very rapidly growing number of cases there. This again isn't us but it's the rest of the world and what happens in the rest of the road, because of that global just-in-time economy does impact on us.

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Let me spend my last few minutes talking about this topic of pandemic influenza. As I mentioned earlier, I published in my book, that was published on 9/11 of 2000, that the Al-Qaeda wanted to take down the World Trade Center Towers. At that point, you know, I had no additional information anybody else would've had that was not already available. And as a scientist who has spent his entire life basically dealing with numbers, you know, putting it in rates, putting in those things that people can interpret from a data-driven standpoint, if you had asked me what the risk of a major attack again occurring the World Trade Center Towers would be, I really thought about this and I would've probably told you one in 5,000, one in 10,000, I don't know. But it's real. We now know the answer from 9/11. What I'm here to tell you today is the next pandemic influenza is a one. It is going to happen. It is not discretionary. It is not optional. It is going to happen. I've never said anything like that in my career before. I don't know if more terrorism is going to occur for sure. I think it is. I don't know when the next exotic disease is going to emerge from somewhere. I think it's going to. But I know this is going to happen. Pandemics are like earthquakes, hurricanes and tsunamis, they occur.

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Human influenza pandemics occur when a novel influenza strain emerges from the avian population has the following features. So you got a virus living in wild birds. Basically until recent we thought they did pretty well, birds meaning. That virus now genetically changes, so it's no longer just a bird virus. It can be transmitted by and to humans. So it's no longer about the birds once it becomes a strain transmitted by and to humans. It's genetically unique, meaning we don't have protective antibody. We already have a problem with that. I mean, for what other

vaccine do we have in our infectious disease armaterian [sounds like] that we're constantly reformulating every year because the virus changes that much in one year.

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Now we're talking about a gigantic leap in change, so that we now have no protection at all. And finally increased virulence. Now flu does a job anyway every year. We estimate that between twenty-eight and fifth thousand people a year die in this country from flu. I know it firsthand. My 72-year-old uncle died last February from influenza. The point being is that already happens. What we're talking about is something way above and beyond seasonal flu. Throughout history, influenza pandemics have occurred, but they've occurred in different times of year. There's no one time. The mortality rates are varied. There's no one model. And even the number of the ways, or how it presents in the community has varied.

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This is a cartoon. It basically gives you the seasons of influenza. On the far left side, here, you see the wild birds. We used to think that the influenza virus resided in those birds such that there was never really any problem. Wild aquatic birds emerged about 150 million years ago in the evolutionary process. Somewhere between 150 million years ago and 100 million years ago when domestic poultry emerged, 50 million years later, the influenza virus took residence in the guts of those birds. And they lived happily ever we thought.

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Now if those viruses get a way out of those birds and get in domestic birds, you can have one of several different kinds of influenza, one that's very serious, one that's not as serious. But, again, that's not a big problem to humans. It's clearly an issue to the birds. We now know today that you also can have disease in cats. We didn't know this H5N1, the Asian flu virus, was a problem with cats until 46 tigers and the Bengals, the Bengal tigers in the Bangkok zoo were fed dead H5N1 infected chickens and all of them died within 3 to 4 days after being fed the chickens. Now we know cats can transmit. We didn't know dogs could transmit until we had an outbreak in Turkey last winter and all the dogs eating the dead chickens got sick also.

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But what we really worry about is when it moves down this line towards humans. Now we used to think that it only went this way, a term called reassortment, where basically what happened was this virus that has eight genes in it would infect a pig cell [sounds like]. Because pigs happen to be the universal lung recipient for influenza viruses, at the same time a human virus would coincidentally infect that pig lung and then what would happen is the influenza virus is one of the most sloppy promiscuous viruses we have, it'll swap out genes in a moment's notice, and what would happen is the two viruses get together and create a third virus. That's called reassortment.

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That's what 1957 and 1968 pandemics were caused by. And we now know in retrospect, those are the dumbed-down versions. Those are the best kind of pandemics to have. What we're worried about is what happened in 1918. We now know, because of the resurrection of this virus a couple of years ago from patching [sounds like] all eight genes of the virus from old samples, that in fact that virus didn't reassort. It basically stayed a bird virus that genetically changed enough to become a human transmitter to transmitter agent. That's where the real horsepower behind a pandemic's at, we believe. This is where we worry today. When a pandemic hits, what happens then is the virus gets into the population over a period of 12 to 18 months. It goes through waves of the population, 12 to 16 weeks here, dies down, 12 to 16 more weeks, and by the second or third wave, it basically, you get it, you get it, you get protection, or it just attenuates over time and then it becomes a seasonal flu situation.

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Now the WHO came out with a document last October. They'll be coming out with another one in a couple of weeks which will actually update this one and I'm not at liberty to share the data in that but let me just suffice it to say this one's enough. Pandemic influenza's different from Avian Flu. Yes, we know that. So while we're worried about the situation in Asia right now, it's when it becomes a pandemic that'll be the real issue if it does. Influence pandemics are recurring events. It's going to happen. The world may be on the brink of another pandemic. That's a very strong statement from the WHO. All countries will be affected. That matters to us

because many of the critical products you count on come from offshore. Widespread illness will occur. Medical supplies will be inadequate. I don't have time in the sake of today's talk, but I'll mention a moment, I am convinced we will have no better than 1918 medical care during the next pandemic. Do you realize today that 80 percent of all the pharmaceutical products used in this country come from offshore? Virtually 100 percent of the vaccines. Most of all the IV bags, needles, syringes, all the equipment parts, all the things you count on every day come from some distant country, where when a pandemic hits, they, too, will be in the soup with us and borders will close. I have no doubt about it. And because it's a just-intime delivery system, if your pharmacy doesn't get its drug twice a day, you're out overnight. There's no surge capacity there. Large number of deaths will occur. I'll talk about that in a minute.

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Economic and social disruption will be great. Every country must be prepared. The WHO will alert us. Which I wish I could say that were true. Today the World Health Organization staff around influenza for the world numbers less than 40. It's hardly an army. Vaccines and antiviral drugs have limited impact on this. Why? Because today we, again, have that just-in-time delivery. We now have a worldwide capacity to make 300 million doses of seasonal flu vaccine every year. That's it. And you can't make the flu vaccine until you get the strain circulating, so even for a pandemic, we'd have to wait until we finally got the last one that's coming out. We will have no vaccine. We have not invested in this because no company sees the bright, bright silver dollar light at the end. Yes, we have 36 vaccines for H5N1 in the works right now, all very early preliminary stages. Nothing about big production. It's years off. The same thing is true with drug in the sense that we're not sure this drug will work, the drugs we think of, Tamiflu. And I don't have time to go into that today but there are big differences between season flu, that we currently use Tamiflu for, which works well, and that of H5.

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The Waves. In past pandemics, the first wave has been the worst one, 1890 it was the third wave, 1918 it was the second wave, 1957, '68 was the third waves. When we blow our wad of supplies, we have no clue from a public health perspective, if

you're only going to have one shot of this, what are you going to do, when are you going to use what you have? We don't know. And non-pharmaceutical intervention such as quarantine, infection control, social distancing are going to have a limited impact. Today we just have just enough respirators, the kind of masks that we typically think of to protect ourselves. Gloves, again, a just-in-time delivery product. We'll run out overnight. Our hospitals are already overstressed. We're going to hear more about that.

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Some additional things a global just-in-time economy presents a unique state of vulnerability. I can't begin to, I've been doing a lot of work recently with a number of economists. In fact, if you go read Tom Friedman's, version two of *The Flat Earth* [sic], he and I put whole section together in there just on this issue about why the world has this unique vulnerability now because of global just-in-time economy with flu, 'cuz it'll shut down. What happens when somebody puts the rock in the gears of the just-in-time economy.

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International governments will have limited opportunities to respond. Secretary Mike Leavitt, who I did not know before he took over, is the current Secretary. I had worked for Secretary Thompson. But he's become a big hero of mine. Because he had the courage to go out to 50 states and say, 'We won't be there for you. We're not going to be there.' And everybody thought it was a post-Katrina coveryour-butt statement, when in fact, when every town, every village, every city, every county, every state, every country will be in the soup at the same time. There won't be any reserve capacity. So when we sent 260 people down from Minnesota to Louisiana to help out with the post-Katrina hurricane, we could do that. We weren't affected. That won't happen. But hope and despair are not strategies. We have to get through this. We have to start planning now for this. Business continuity planning's, not, is not, uh, optional. I can just tell you right now that in fact as goes the private sector will go our health. If we don't have food and water, if we don't have the basic services, the implications from the pandemic will be huge. Imagine running out of insulin and not being able to find it for months. We'll get through it, just like every pandemic in our history.

To get a sense of this, pandemics have been recorded since Hippocrates, the 1580 pandemic gives you a sense of this so you just don't think that I'm talking about only severe pandemics. It's a classic example, it started in Asian and in 6 weeks it afflicted all of Europe. Mortality was high, 9,000 of 80,000 residents in Rome died in little over a week. Spanish cities were considered totally depopulated.

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We've had ten pandemics in the last 300 years. They range from 10 to 49 years between pandemics. The average is 24 years. Now they're not normally distributive events. It's not like, you know, the throwing of dice. Basically it's like 100-year floods where you have nothing for 50 years and then four of them in 10 years. I don't know if the next one's going to occur because an average. I know because of H5N1 what's a good likelihood.

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The 1918-'19 pandemic is what I talked about. We know it was caused by H1N1, 200 million to 1 billion people were infected, 50 to 100 million people died. And the highest number of deaths were in healthy people 18 to 25 to 30 years of age. We know now and we were given some information that would suggest this based on the studies of pregnant women, which is a very precarious time immunologically where part of your immune system is trying to protect this thing that's not supposed to be there because it's not all you. And that whole immune relationship is complicated. When that virus got in the middle of that, it was a real problem. Today we now confirm that it's the immune response of the healthiest people that end up killing you with not only this virus infection, but also at H5N1.

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I would urge all of you to read this book from John Barry, a historian, *The Great Influenza*. It is, I think both an incredible discussion of our past and very much a glimpse potentially into our future. Just to give you a sense what this was like, this is a letter from. Dr. Roy Grist to Burt. Roy Grist was a military physician in a camp outside of Boston the fall of 1918. He wrote this to Burt. After Burt dies, this was found by his children in his effects in the attack and submitted to the British Medical Journal.

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These men started with what appears to be an ordinary attack of la grippe or influenza and when brought to hospital, they rapidly developed the most vicious type of pneumonia that's never been seen. A few hours later you can begin to see cyanosis extending from their ears and spreading all over their face until it's hard to distinguish the colored men from the white. It is only a matter of a few hours then until death comes. It is horrible. One can stand to see one, two, or twenty men die, but to see those poor devils dropping like flies, we've been averaging about 100 deaths per day. Pneumonia means in about all cases death. We've lost an outrageous number of doctors and nurses. It takes special trains to carry away the dead. For several days there were no coffins and the bodies piled up something fierce. It beats any site they'd ever had in France after a battle. An extra-long barracks has been vacated for the use of the morgue and would make any man sit up and take notice to walk down the long lines of dead shoulders, all dressed and laid out in double rows. Good-bye, old pal. God be with you 'til we meet again.

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These people died quickly. They died within hours and a couple of deaths. That's not the kind of flu deaths we see today from secondary bacterial pneumonias. But it is what we're seeing with H5N1, doctors and nurses died, we ran out of things. So what's the potential for this to happen? All I can tell you genetically, pathophysiological and clinically, H5N1 and the 1918 virus are kissing cousins. It has an ongoing genetic roulette table in Asia to actually, to basically become genetically capable of being transferred into humans, and I'll show you that in one moment. Anybody who in the audience who says if it was going to happen, it would've happened by now, I remind you of H3N8. In the early 1960s, H3N8 jumped from birds to horses. It was a, basically a bird virus that jumped. Never reassorted. It's been a big problem in equines since then. Two and a half years ago, H3N8 jumped from horses to dogs. We have no reason why. We don't know why. Today it's a major problem of deaths in canine, particularly in central Florida this past summer. Again, basically a bird virus.

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If H5N1 follows this lead, it could be today, tomorrow, next year, 5 years from now, but it could sure happen. The genetic roulette table I talked about, this is that changing world. In 1968, the last pandemic, there was 790 million people in China.

Today there's 1.3 billion. According to the FAO, an annual harvest in 1968, 5 million pigs were harvested. In 2004 508 million pigs, associated with the new social, political, and economic realities in China. Poultry, 12 million harvested in 1968, 15 billion in 2004. The average time from a chicken being hatched until it's eaten is about 40 days. Point being is that we're constantly putting new, fresh birds out there that are basically still susceptible to this virus. We've given this virus unlimited play in these populations.

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This is the current situation, 249 laboratory-confirmed cases, including 146 deaths. Ladies and gentlemen, this is not the problem. What I mean by that is that if, excuse me, is this is a public health issue with people getting it from birds but not ongoing transmission. It's when that virus gets, becomes capable of going person to person. And we're seeing it getting closer, and closer, and closer to that. If I could tell you about the current clusters we have out there, it's like listening to that old John Deere tractor get started in the middle of January in the old days on the farm. There was [makes noise] and about five of those and all of a sudden you heard a pop and away it went. And I am convinced we are in the end stages of the John Deere tractor starting.

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When will it happen? No one can predict if, when, or where H5N1 virus will shift from an avian strain with incidental human infections to a genetically component human-to-human transmitted agent, we don't know. Asia remains the genetic roulette table for this virus mutation. First the evidence will be ongoing transmission, third generation cases, which we haven't had yet. All my science training leaves me unable to answer the question for you any better than this. I wouldn't want to bet my family's life on H5N1 not becoming the next pandemic influenza strain. If you look at what it could do to our country, these are the numbers from the Department of Health and Human Services. I might add, if it's a severe or moderate like pandemic, 90 million illnesses, 45 outpatient visits. But look at the deaths, 1.9 million. 742,000 people need mechanical ventilators. Right now we have 105,000 mechanical ventilators in this country. On any one given day, seventy to eight thousand are in use, and during the flu season we get right up to 100,000. We have no capacity in our healthcare system to respond to this. None.

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This slide really reminds us we can easily go to either camp, Chicken Little or 'We're all going to die.' Earlier this year I was on the Oprah show for an hour talking about this with Oprah and the following day, for the following week my e-mail system chocked the entire University of Minnesota system practically. And the e-mails fell in one of two categories. Even though it was the same words, the same ugly face, the same message, half of them said, 'You know what, guys like you should be hung. You should be fired by your place. You should just go out and shoot yourself for scaring us needlessly. Guys like you are really bad.' The other half over here is saying, 'You're part of the government cover up. We know this is going to be much worse. We're all going to die. Why don't you just tell us that and be honest.' [crowd laughter] Do you know why we do that? Because that's the easy answer. If you believe it's, 'We're all going to die,' take your bottle, go home, get under your covers, we'll come get you when it's done. If you don't believe it's going to happen, just enjoy life. It's the truth that's hard. And this is where it's about you do it for the kids. What kind of world are we going to leave you? And today, ladies and gentlemen, we're doing almost nothing except giving lip service at the state level, at the federal level, we have done very little.

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I just met last week with executives from 10 of the largest trucking companies in the united states. They've virtually done nothing. We held a national summit in February, our center did in Minnesota. The companies there represented almost 4 trillion dollars in annual re-, in revenues. We heard from the oil refinery companies. All of them were there. They said that if we lose 20 to 30 percent of our workers, we can't continue to run our refineries. So not only do we have just-in-time delivery, but we also have just-enough employee delivery. We've done virtually nothing to prepare for that. This is going to make Katrina seem mild.

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Responding to the pandemic. I've mentioned the issue about prevention/patient treatment. We won't have it. Right now we have to understand that. We, we'll have to just get through without it. Like you do if we had nothing following Katrina. Our medical response system already is very weakened. We won't have that. I worry desperately how we're going to get pharmaceutical drugs to you. Today we don't

have that pipeline. You can't stockpile if you wanted to. We've got to change that. But there's no economic incentive. There's nothing happening to make that happen. I worry whether you'll get your lifesaving drugs during a pandemic. Not for the pandemic but for your other condition.

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In terms of worker and patient protection, we're going to have figure out will our healthcare workers come to work? I mentioned earlier 25 percent of them wouldn't go to work in Toronto with SARS by the eighth week. If you don't have vaccine and you don't have effective drug and you don't have masks, who's going to come to work? Some of you may be doing it, in places like this very room, giving care.

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Corpse management. In 1968 the average time from a casket being made until it was in the ground was almost 6 months. Today's it's less than 30 days. Crematoriums creates just-in-time delivery. We saw in Katrina, and we saw in the tsunami, when we treat our dead with disrespect, that's what takes us over the edge. We have no plans. Cities like Seattle have gone out and figured out where they can get all the indoor ice arenas they know, and they're going to stack bodies right where you're sitting. And hopefully keep them until they can process them. We've done none of that planning here.

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Implications. Food and water. Food's a just-in-time delivery system today. I deal with that all the time in the work I do. We have no contingency plan how to get food to people because it is just-in-time.

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Domestic and international security, again, we just did a survey of prison wardens. Most of them told us, if we lose 20 to 30 percent of our workers, we don't know how we'll control our prisons. Again, where are the plans for that? We could do it now. Pandemic implications, just imagine a 12- to 18-month global blizzard with mandatory or voluntary closings of national, state, or even local borders. Public panic and 24/7 media coverage will reign. Governments will have limited resources. I believe at least 20 to 30 percent of people won't go to work. We won't close

schools because parents will take their kids out of them, you won't have to close them. Even under the worst-case scenario the world's population will survive however. We have to start planning how we're going to do that now.

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So what do we do? Well, it's not a matter of IF, just when and where. At a minimum, assume we will not have vaccine for the first 6 months, then supplies will be limited. If it's a 1918-like scenario, 98 out of a 100 of us will get around, get through it, but we'll still lose 1.9 million Americans and up to 150 million people worldwide. Planning is not an option. Yet we keep postponing it.

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So in conclusion, just let me say, emerging infections are a reality of our modern world. They are. The causes are complex and the solutions are difficult. But there is nothing here that should stop us from doing this. We invest today in things that I have to ask myself over and over again as I go to sleep at night, is this really making the world safer? When I know there are things that will and we're doing virtually nothing. Hope and despair are not strategies. I believe that so much. Why do I do this? My whole career today can be stilled down in one very simple answer. I don't do it for the money. I don't do it for the 180,000 air miles I travel a year. I don't do it for [inaudible] I do it for my kids. It's about my kids. And it's about you students in this room. You're all that matter. We owe it to our kids to make a difference. I can't think of a more important legacy. Thank you very much.