C. J. (Clarence) Peters, MD

Director for Biodefense
Center for Biodefense and Emerging Infectious Diseases
The University of Texas Medical Branch at Galveston

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What are emerging infectious diseases and how do you work with them?

When you think about emerging infectious diseases, it's important to stand back and look at it from a distance of maybe four or five hundred years. Anything that crops up tomorrow is emerging and different.

About 1500, when the Age of Exploration struck and ships started crossing the oceans with a great frequency, we began to see a mixing of infectious agents that were carried from one continent to another by mosquitoes, ticks that transmitted them and animals that could carry them. We began to see the evolution of a continuous spectrum of emerging infections.

This began really, most dramatically in North America with the European and Asian infectious diseases, which had already mixed because Europe and Asia were in close connection. When these infections were carried to the New World, we saw an absolute decimation of the Indian populations. Probably one of the reasons why Cortez could conquer Mexico City or why the Pilgrims were able to settle in Plymouth Rock [was] because the Native American populations suffered greatly from these new infections.

Now the dramatic, huge changes that we saw initially have modulated, but we're still seeing a continuous movement of infectious agents, evolution of new infectious agents, and also, quite importantly, evolution of niches for infectious agents to move into.

If you look at the earth's surface from satellites, more than half of the earth's surface has been modified by human colonization, housing developments, agriculture, felled forests. We all know this story. But the fact is that it's happening at an ever accelerating rate. So this drives the emergence of new infections. When I say "new," I mean "new to us," because we haven't had to suffer with them before.

We go into the forests and we find agents there that can be very nasty for humans, even though they're innocuous for the animals that they naturally infect. We clear forests and we make fields. When we do that, rodents that carry infections come into these agricultural fields and pose a risk to the people who are working in those fields. We move mosquitoes from one continent to another. Sometimes those mosquitoes are infected with viruses. So they come with a virus that they're already familiar with. These things are happening at an ever-increasing rate. Put that together with air travel, the introduction of new species and a whole variety of other issues, you've got a recipe for a boiling cauldron of emerging infections.

Tell me about emerging infectious diseases that occur naturally compared to those being used as a biological weapon.

There are a large number of infectious agents that circulate in nature, both the classical, old bugs that we know, like plague, as well as new bugs that are emerging. That's where the terrorists can go to find the organisms that they can use to cause human disease and high economic impact.

I think it's important to realize that if a bioterrorist is going to do something, he has to have the agent to start with. And where is he going to get it? Well, I think, in the future, they'll make some of their own. But for now and the immediate future, that's just not possible.

For now, they [bioterrorists] get them from nature, and they often choose dramatic, emerging infections. Emerging infections feed into bioterrorism in that they provide agents that can be used by a person who wants to cause a lot of mischief with a biological weapon, or a bioterrorist weapon. At the same time, there's a feedback in the other direction, because these bioterrorists are going to use these agents to harm people.

Incidentally, by the way, those agents may set up their own cycles in the environment under these new situations. Some of them we don't think can do that, like anthrax. Anthrax is worldwide. We don't think you have to worry [that] if someone disseminates anthrax in this country that it's going to be a big problem. We have cases of anthrax in Texas every year. We don't think that's going to disturb things.

But if someone took one of the new viral agents, like Nipah Virus from Malaysia and Bangladesh, and disseminated it in this country, we don't know what little niches it could find to survive in. We do know that it would be a tremendous agricultural impact on the pork industry, and it would be a tremendous impact on the humans who were infected.

What is your role in biodefense and emerging infectious diseases?

I worked with the Army for about thirteen years in biodefense and then with CDC (Center for Disease Control) for about ten years in emerging infections and high-hazard pathogens. I have a background [that helps me] try to understand the context of these different agents — what we can expect from them, what have they done in the past, and what should we be prepared for in the future.

I think that my job here is to work with other scientists who are experts in their own agents and try to provide some perspective for them. And then, of course, I have my own research program with Rift Valley Fever, one of the emerging infections that is a potential bioterrorist threat, as well as SARS.

Where has your work taken you in terms of traveling around the world?

Over the years, I've worked in most parts of the world for some time, a few years in Latin America, a few months in Africa, few weeks in Asia. Now that I'm settled in here at UTMB, I maintain those contacts, but I try to travel less than I used to in the past because it eats up your time.

There are two aspects to dealing with infectious diseases: the research you're doing here to try to find what causes them and develop vaccinations, and emergency preparedness. Can you tell me about these two aspects?

I think in any aspect of public health — and our response to bioterrorism is really going to be based on public health — you have two pieces. You have the piece where you find out what's going on. You do the research. You develop vaccines. You develop diagnostics. You look for drugs.

Then there's the piece where you apply what you have. Maybe you don't have the research fruits and you have to deal with this strictly on the basis of preparedness. That puts preparedness as sort of the floor from which you work to apply these other things.

I think one of the things that I enjoy about this job is that I have a background in both areas. So, I can work with people like Scott Lillibridge at the University of Houston, as I did at CDC, and we can try to bring preparedness and the demands of preparedness into the research agenda.

What are some of the main elements of preparedness?

Public health preparedness, regardless of what you're preparing for, requires a bottom line understanding of the phenomena that you're going to deal with. And, it also requires a bottom line understanding of the tools that are always present, or should be present, in the public health agenda.

[It includes] things like surveillance. That means, you look to see where the disease is. It means laboratory testing. You apply the available laboratory tests at whatever level you have them to be able to confirm what you have. You have to be able to communicate with the public. The people who are on your team — state and local public health people — have to

be trained. They have to understand how to do these things, and they have to have a rudimentary knowledge, at least, of epidemiology and public health response.

When you suspect an outbreak of a disease, what are the various steps?

You know, it's often underappreciated that our first line of defense against bioterrorism and emerging infections is the clinician. I mean, everybody thinks of CDC — the federal government. Well, I'm sorry. CDC is not there when the sparrow drops in the forest. When the sparrow drops in the forest, it's the clinician that sees that, and the clinician has to have the background, which, fortunately in the U. S., most physicians do. He has to have the curiosity and the awareness, which increasingly is the case. And, he has to have access to tools that he can use to diagnose unusual conditions. That's somewhat handicapped, frankly, because of medical economics today.

But nevertheless, these physicians often seek out those tools. They have access to a tier of CDC laboratories, and they have access to their state health department, which provides them with a strong backup. So when the clinician sees something going on, then he can refer samples for definitive diagnosis. Those samples, once diagnosed, can then go into the pipeline for the overall state and local health response.

The universities become involved at this point if there's no diagnosis and we have a real unknown. There has to be a search for the unknown, which could be an infection or a bioterrorist agent. And, they become involved in mobilizing science to help respond to the threat, whichever that threat might be, because there's always things to learn.

We never know enough to completely deal with these threats. Some things are pretty routine. You go to the church picnic. You get food poisoning. We understand that. But somebody dies under unusual circumstances or with an unusual disease syndrome, then we always have to find out more about that, as well as dealing with the public health consequences.

Do you think we are at greater risk for exposure or outbreaks now than, say, twenty to thirty years ago?

Certainly we're a lot better off today in terms of infectious disease in general than we were ten, twenty, thirty years ago. We have antibiotics. We have improved diagnostic methods and so on. And, we've applied vaccines to control many of the bad, old public health threats. But at the same time that I say that we're better off, we're also at a greater risk for emergence of new problems.

These new problems emerge because of changes in society — sex and drugs, and changes in medical care practices. We have more immune-suppressed people who are extremely vulnerable to infections. We have the pressures from managed care, and so on, to minimize diagnostic tests and treat on basic protocols. We have changes in the environment. We're fragmenting the ecosystem. We're changing the nature of the land cover. We're suffering global warming, be it anthropogenic or not.

We also have the big mixing bowl of travel. We have travel and trade that bring humans around the globe [and] redistribute them, bring arthropods, bring vertebrates and allow them to invade new areas, and possibly bring new viruses with them.

What does the pace of change in our world have to do with infectious diseases?

I think there are two aspects to this. One aspect is that not only is the pace increasing, the rate of change of the pace is increasing. In other words, we're in an exponential phase where things are happening faster and faster, and the rate of increase is faster.

Furthermore, we are shrinking the buffers around us. In other words, we can't spare a river for this or that or the other because we need it to irrigate. We need it to get water to Los Angeles. We need it to get water to San Antonio. We cannot afford to change the environment.

In the past, this country occupied a vast piece of a vast continent, and we had rivers and forests and lakes. And, we had a lot of buffer zones around us. So when something changed, we always had a place to spillover to. Now, we've dammed most of the rivers. They're under control. This results in things like floods and so on. Well, it does the same thing with diseases.

If you want to have fresh water for human consumption, and you want to have hydroelectric power, and you want to have wild salmon that can go up some of these wild rivers to breed, you can't have it all. And that's happening with infectious disease as well.

We can't have it all. We can't use antibiotics indiscriminately and plan on having them useful for tomorrow. We've got to be much more careful about how we're controlling infections and how our interactions with the environment can affect the emergence of infectious disease.

Can you tell me a little bit about the history of the development of biological weapons?

There are a lot of arguments and discussions about the origins of biological weapons. Did biological weapons begin when Central Asian tribes catapulted dead plague victims into cities in Italy? Did it start when the Indians in North America were given blankets that contained small pox crust from people who had died of small pox? I really don't think so. I think those are episodes. I think it really started between World War I and World War II when national programs were instituted to produce biological weapons that would kill tens of thousands or hundreds of thousands of people.

It [the development of weapons] entered a new phase — the modern phase — where we tried to kill lots and lots of folks. The competition was with nuclear bombs. The competition was not with the machine gun. The competition was with weapons of mass destruction. And frankly, you know, nuclear and bio are the weapons of mass destruction.

If you look at the chemical weapons, they're horrible. You can kill a lot of people with them but you require enormous amount of logistics and tons of agent to do it. It's only when you get into nuclear and bio that you can kill so many people with kilograms of agent. So I think that that really went into play in the 1950s and '60s, and was perfected in the '60s and '70s.

One of the things that these people found was that most germs that are used, or they contemplated using, in biological warfare can't kill huge numbers of people unless they're disseminated in a special way — by aerosols. They're disseminated in very fine particles that have been manufactured and specially stabilized so that they're airborne. They don't settle out, they're invisible. They're inspired. They enter through the lung — they may cause pneumonia in the lung or they may just enter through the lung — and they have a high fatality rate. These so-called breakthroughs are what really moved us into the area where biological weapons assumed special significance.

I think that if you want to worry about things like Ricin, which is a toxin —it's very potent, that's fine. But I wouldn't think that a big, national program against Ricin would be of very much interest because it's hard to kill more than a few dozen or maybe a few hundred people with Ricin.

But if you move into anthrax, plague, small pox and some of these other agents, you've gone up several orders of magnitude. Those are things that I don't think we can afford to ignore. Whatever the likelihood of their use, if they are used, we just can't live with the consequences.

In the 1960s, when the U.S. and Russia were developing nuclear weapons, the Russians were also developing biological weapons. What happened when the Wall fell and what happened with the agents they developed?

Curing the Cold War, the U. S. and Soviet Union were, as everyone knows, in a continuous arms race. The focus publicly was on the nukes. Did we have more nukes than the Russians? The Russians have more nukes than we do. Can we deliver them? Can they deliver them? But really, something happened in the '60s and '70s. The U. S. rejected the use of offensive biological warfare. Nixon said, "We will not pursue these weapons. We will destroy the weapon stockpiles that we have," and we did.

The Soviets thought about this and accelerated a program of offensive biological warfare. And I think their reasoning, and this came out with a defector named Ken Alibek who talked a lot about a lot of this, their reasoning was: "They have nukes. We have nukes. They're not going to have biological agents. If we have biological agents, we've got a trump card and we're going for it."

So they worked very hard to build large stockpiles of biological agents. They had thirty to fifty thousand people working in these very secret industries with factories all over the Soviet Union with highly-sophisticated research groups working on this. They produced tons of biological agents that could be delivered on intercontinental ballistic missiles, not as tactical

agents on the battlefield, as the U. S. had envisioned most of their biological agents, but rather as strategic weapons to destroy the base of the United States. And this program accelerated markedly after we stopped our offensive program.

The U. S. continued to do research in defensive biological warfare, in how to defend against these agents, but we frankly never deployed these defenses. It was not until the first Iraq War that we realized we were going up against someone who was trying to — and having modest success in — producing biological agents. And at that point, we realized that we hadn't really thought through our defenses against anthrax [or] botulinum toxin.

It caused a sea change in our attitude. It caused people to look again at the problem and realize, "Hey!" There's a saying in the Army: "You have three bins on your desk: in, out and too hard," and suddenly 'too hard," which was biological defense, went into "must do." And there was a really remarkable change at that point.

Was anthrax some kind of a wakeup call?

This is a true story. I was working at Fort Detrick at the time that Saddam Hussein invaded Kuwait. And, like a lot of Americans, I stayed up watching CNN that night and saw the tanks. I went in the next morning and got a call from a guy at headquarters and he said, "There's something that I've got to tell you, but you're not cleared to know it." I said, "Oh, what?" So they cleared everyone quickly and he said, "You know, Saddam Hussein has an active program in developing biological agents, particularly anthrax, and we don't know exactly how far he's gotten. But, we have to defend the troops against anthrax."

This is the first time that the U. S. military had seriously undertaken to defend U. S. forces overseas against a biological agent — the first time. There'd been research done in the background. It's a little bit like what we talked about on the split between public health, practice, policy and research.

There was research going on. There was a modicum of understanding of the issues, but there was nothing practical in terms of protecting troops. And suddenly, we had to think about, "What would we really do," and that was a real wakeup call, as they say.

After there was no use of biological weapons and the first Iraq altercation, things kind of slipped down into the background a little bit. Then, the attacks in 2001, with anthrax directed against media and politicians, put things right back on the radar scope and couldn't be ignored.

I think the scariest part of that was the powder that came in the letter to the Hart Office Building. That was an extremely dangerous powder. If that had been put in to the air conditioning system without warning, there would've been dozens if not hundreds of casualties — people dead.

Why it was delivered the way it was in a letter with a note and so on, and who did, it remains a mystery to me. And I personally believe that no one knows exactly what went on, except, perhaps, one guy who did it. I think that that really said, "Wake up! We've got to do something about this." That was the real watershed moment.

Do you have a personal theory on that?

I have personal theory, but it differs from day to day and week to week. I don't see how someone could make that powder in this country. If they'd made it at a military facility, I think it would've been picked up. People would know about. You can't keep that big a secret under those circumstances. And if it had been made in a home or some improvised facility, I think we would've had some dead neighbors. So, I really think 60/40 evidence says it was made overseas somewhere. That really changes everything, doesn't it?

What do you think about people actually using this with nefarious means?

The thing that puzzles me is, if you wanted to hurt a lot of people, you wanted to make a statement — which is kind of what terrorists like to do, isn't it? — why would you wrap it up in a little piece of paper that said, "Take penicillin or die." Why would you use penicillin-sensitive anthrax?

We know that the U. S. and the Russians weaponized anthrax and it was penicillin resistant. They made it penicillin resistant. We know that it's not hard to make antibiotic-resistant bacteria like anthrax. So there's the disconnect between how did somebody succeed in making a very dangerous powder that required some technical know-how but didn't bother to make the bug antibiotic resistant? It doesn't quite compute.

Let's talk philosophically about biological weapons being used by human beings to kill other human beings. In your work, you are, in a way, battling against that. Do you ever think about your work in those terms?

I don't know if evil has size, but, I think, that if you kill a lot of people, it's worse than killing a few people. And I think that, to me, the evil of biological weapons is in the number of people you can kill just as the evil in nuclear weapons goes in that direction. The way they die? I don't know. Is that any worse than dying from a nuclear blast, from radiation sickness, from burns? Since I know infectious diseases better than I know nuclear casualties, I tend to think it's maybe not as bad.

I just think that the general opprobrium [reproach] that we reserve for nuclear, biological, and chemical [terrorists] has great value because it puts them [terrorists] outside the pale [beyond limits of decency]. It means that if we are going to be part of the civilized world, and the civilized world doesn't do these things, it gives us an opportunity to tell other people, "You can't do them either," and form an international consensus, whether that's absolutely enforceable or only enforceable in part. If you can enforce it in part, that's better than nothing.

I think that the issue really is twofold: the number of casualties and the rules that we make to try to prevent having any casualties. Sometimes it's better to have a convention that you can't enforce than to have no convention. You just don't rely on it.

What is your motivation for pursuing your work in this field?

I got interested in science in high school. I loved science and I got interested in infectious diseases in medical school. Then I spent five years at an NIH (National Institute of Health) lab in Panama working with infectious disease and it was absolutely the most interesting thing that I could think of to do. I mean, there wasn't anything that looked like it was more fun or more absorbing. And as time evolved, I also became interested in the humanitarian effects.

I went to the Army, not for biological warfare defense, but because I just thought these diseases were fascinating. They [Army] were very interested in studying these diseases and finding out how to defend against their use as biological warfare agents, but they [diseases] were also emerging infections.

You have to realize that until the Iraq War, the first Iraq War, which is about the time I left USAMRID (United States Army Medical Research Institute for Infectious Diseases), nobody was doing anything really serious about biological warfare. But all the things that we were working on as biological warfare agents were, indeed, emerging infections. So, I could satisfy the Army master by dealing with these. I could satisfy humanitarian urges and the issue of emerging infections by dealing with the same bugs. And, I could satisfy my curiosity by dealing with the same bugs. So it was kind of a big package.

By now, you know, the motives are all mixed. I would like to help defend this country against biological warfare, and I'm certainly dedicated to that in my current job. But I would like to see this country defended against emerging infections, as well as countries overseas that are having to deal with these infections all the time. It's still fun.

Did you see the movie *Outbreak* based on the book *The Hot Zone*?

I read *The Hot Zone*.

And was there anything familiar in that story to you?

Yeah, I was in the story. So a lot of it was familiar.

What did it take from your life?

Well, *The Hot Zone* was a dramatization of the history of one virus, called Ebola Virus, that's gotten everybody's imagination fired up because 80 or 90 percent of the people who are infected die. So it's very dramatic. But the total number of deaths were actually quite small.

I was in the book because we were involved, myself and a team of people who worked at USAMRID, in dealing with an introduction of Ebola virus into this country in Reston, Virginia, about thirty miles from the White House, brought in with infected monkeys. And it was quite an exciting time for me, and Richard Preston made it seem even more exciting when he wrote *The Hot Zone*.

How did he do that?

I think the basic sketch of what happened in *The Hot Zone* book corresponds to reality. But I think it's a little overdramatized and a little exaggerated. Nevertheless, it's a good read. The basics are actually correct and it's a fun book.

The Bioweapons Limitation Treaty, the Biological and Toxic Weapons Convention. Does that sound doable?

The U. S. had a really active biological weapons program developing, essentially, weapons of mass destruction for use on the battlefield against troops. Then, in 1969, President Nixon unilaterally stopped the biological weapons program and announced that publicly. Later, the U. S. pushed through, in 1972, the Biological Weapons Convention, which is an international treaty [that's] not particularly enforceable, but is still providing a force of will against the use of these weapons.

When we did that, what were the Russians doing?

Unfortunately the Russian, although signatories to the BWC (Biological Weapons Convention), ramped up their weapons program after we had dis-established our program. They felt that this provided them with a potential ace in the hole, a trump card they could play if we were equal or nearly equal with nuclear weapons.

What are some of the different ways to disseminate airborne diseases?

If you want to injure a large number of people with a biological agent, you have to figure out how you're going to get the agent to them. There's a whole list of ways you could try, but there are really only two that lend themselves to mass casualty scenarios.

One is transmission from human to human, where you start a chain off and it takes care of itself. The only agent that we're worried about, that can do that and cause a lot of casualties, is small pox.

On the other hand, there are a number of agents that could be disseminated in what we call "aerosols." In other words, they could be disseminated in very fine particles that are carried by the wind, that can go downwind invisibly, be inspired, reach the deepest recesses of the lung and setup an infection — maybe a pneumonic infection, but maybe not [or] maybe just gain access to the body through the lung.

We call this "aerosol spread." There are some natural diseases that spread by aerosols: measles, tuberculosis, for example, [and] influenza. And it's exceedingly difficult to protect against these diseases. You don't know when an aerosol attack occurs because it's, as I said, invisible. There's no odor.

On the other hand, if you did know, you can't really protect yourself easily unless you have special filters to take these very fine particles out of the air. We use these filters to construct masks for use in the hospital for people who are taking care of influenza patients. But the ordinary surgical mask provides some, but limited, protection against this sort of situation.

How does it help us to know that aerosols can be dangerous?

I think a citizen who wants to understand the elements of biodefense has got to understand how he'll be attacked. And this understanding only comes about if you understand the issue of aerosols.

Understanding the aerosol threat means that you don't misdirect your energies in other areas. It means that you don't believe that there are false ways to take care of yourself. It also leads to the understanding that we have to have special labs to study aerosol infectious agents. In other words, the person who is working with these agents in the laboratory can become infected by aerosols also. It's very easy to generate a small aerosol in a laboratory, not a large aerosol that's going to infect the community, but a small aerosol that's a danger to the person who's working with it.

So we have to have BSL-4 and BSL-3 laboratories (Bio Safety Level 4 and Bio Safety Level 3) to deal with these aerosol infectious agents. Therefore, if we're going to have a biodefense program, and if we're going to work with many of the emerging infectious agents that also happen to be aerosol-infectious, we must have these laboratories.

It also helps the citizen understand why these laboratories are more of a help than a hindrance to his health. Many people believe that these high-containment laboratories are there [to contain the agent] because if the agent gets out, it'll run through the population and everyone will die. In fact, that's not the case. They're there to protect the laboratory worker, and also because the aerosols might infect individual people, not that it would be transmissible from person to person, but they could infect individual people.

So by having the filtration and the air handling that we build into these laboratories, we protect the community. If the laboratory worker, for some reason, should become infected — maybe he's protected against aerosols but he accidentally cuts himself, or injects himself with a needle, or is bitten by an infected animal — that laboratory worker poses minimal risk to the community because these agents are not transmissible from person to person. That's an important distinction both in understanding biodefense and in understanding the role of the laboratory and the relationship of the laboratory to the community.

Describe a Bio Safety Level-4 Laboratory and its purpose.

The BSL-4 laboratory is constructed, first and foremost, to retain aerosols inside. You have a relatively small volume that's dedicated to the laboratory, and that volume is maintained by air-handling equipment under negative pressure so that any aerosol that's generated — remember aerosols [are] airborne, carried on the wind — are kept inside, then pulled out through plenums into HEPA filters, High Efficiency Particle Filters, that will take out the aerosol. And then there's a second filter in case the first filter should not get everything. So, you have redundancy. You have negative pressure and you have redundancy.

Then you have mechanical interlocks. So, if for some reason, the electricity fails and the backup generator fails, you have mechanical fail-safes that flop shut and trap the aerosols inside. So you have a layered system of security.

Then, because some of these viruses are exotic to the U. S., you also pull all of the liquid effluent from this laboratory, bring it down into big holding tanks, and there you essentially cook it to sterilize it.

If you look at a Bio Safety Level 4 laboratory, you essentially have three floors. You have a floor on top that has all the air handling equipment to maintain everything under negative pressure and all the fail-safes. You have the floor with the laboratory, which, by the way, has a corridor around it, which is another safety layer. And then you have the ground floor, which is where the effluent goes and where it's sterilized. So they're very expensive to build and to maintain. But, they provide not just safety but also redundancy.

The person inside has to be protected against these aerosols, so they wear a plastic suit, which is kept under positive pressure. You use various primary containment devices so that if you generate an aerosol, it's trapped already. But if any of it should get out, then you have the suit that protects you against the aerosols.

To be sure the suit's clean, when you leave, you go through a shower, which has a door on either side of the shower. You go in one door and close that door. Then you have spray nozzles that spray disinfectant over your suit. These viruses are not particularly resistant to disinfectants. They're very dangerous by aerosol but they're not particularly able to withstand ordinary disinfectants. Then, when your suit's been sprayed down, you come out the other door, take your suit out, take a shower, just to be sure, and leave the laboratory putting on your street cloths.

What is your ten second version of that what you do in a BSL-4 lab?

When you're in the BSL-4 lab, you work with infectious agents that could be dangerous to you and cause fatal disease if you accidentally generate an aerosol. [In the lab,] you have all this protection. What you do in the lab is grow virus, do experiments with live virus, do experiments with animals. And then you take the samples from those experiments and you process those so they're not infectious any longer. [You] take them out to an ordinary laboratory to perform the kind of scientific analyses that you would for any other infectious agent.

There's nothing magic that you do in the BSL-4 lab. It's just that while we're working with live agent, you need special protection and you want to be sure the community is protected. When you're at the end of the experiment and you take

the material out to analyze, it's inactivated and you do the same thing that you would with any other common virus or bacteria.

Tell me about the big lab project ahead of you.

Because you can do the infectious work inside a BSL-4 lab and then take materials out that are rendered noninfectious and do the final analysis, you don't necessarily have to have a huge amount of space to get a lot of leverage from a BSL-4 lab.

The lab we have now has 2,000 square feet. Half of it we use for work and half of it we use for propagating virus under different conditions. We're able to leverage that through the use of other labs in the building. In a year or so, when we have this new lab opened, we're going to have six times the amount of BSL-4 space, and we're going to be able to do an incredible amount of work on these biological agents and emerging pathogens. It's extremely important to be able to put this into a university setting and work with it in a basic academic fashion, because the basic science behind these bugs has not been worked out.

Remember, the Army had a small program relative to NIH's program in infectious agents. The emerging infections are often neglected relative to common infections. I'm not criticizing that. I'm just saying they have been neglected relative to common infections that occur in the U. S. So we have a lot of spadework to do on these viruses to work out the basics of their replication — their molecular biology — and to develop animal models that will allow us to test drugs and vaccines.

Can you think of anything that we have not mentioned that is important?

I think there are two ancillary issues here. One is that, in the future, we're going to face new challenges and new threats. I don't mean tomorrow, but, in the not too distant future, we're going to have some remarkable achievements by biotechnology that are going to bring us incredible health benefits and are going to be worldwide achievements — worldwide technology. And, this technology could be applied to malevolent intent [or] ideas, and it could generate new and novel threats — threats that we don't have names for today. So we're going to need a place we can take whatever comes along and be able to work with it and be able to focus scientific effort on that area. So I think that's one issue.

Another issue that I think people have to keep in mind is that emerging infections are not going away. It's an exponentially-increasing problem. West Nile was just a little introduction. We're going to have other problems.

I work primarily with two viruses: Rift Valley Fever virus and SARS virus. Rift Valley Fever virus has just as good a likelihood of being able to establish itself in the U. S. as West Nile did. SARS virus, as you know, emerged in 2002, and almost got out of the bag and became a worldwide problem.

It'll be back because these emerging infections have two qualities. One quality is, you always think you can predict them but you never can. There's always something brand new. And the other quality is, once they've been there, they'll be back because the conditions that brought them out will recur and we'll have SARS again — just like Ebola came out in 1976. It didn't recur until 1995, but it was back and now it's an even bigger problem. So I think that we can count on meeting old friends again and making new enemies.

Does a virus have a role in nature?

We tend to think in sort of simple systems, like predator/prey. You know, if you don't have enough coyotes and you have too many rodents, you get rodent-borne diseases and so on. But it's a multi-component system.

I think that viruses do have an important role in controlling population when population densities spring up to very high levels. But their role in general is not that simple. Because most of these viruses are transmitted in nature, there's sort of a fluctuating, semi-equilibrium. Some of the viruses we can't find any selective role for at all. We've thought about this a lot with viruses of rodents, where we can study rodent populations, and we don't see those viruses regulating rodent populations. When the rodent populations are high, the viruses spread among the rodents and spillover into humans. But they don't really regulate the rodent populations and they don't regulate the human populations.

What you do see, occasionally, is a virus that will take out a species. Look, and once again we're talking history here, at Hawaii. Islands are notoriously-fragile ecosystems. If you go to Hawaii, there are no native bird species below seven or eight thousand feet. And the reason is that a mosquito was introduced that was extremely effective in spreading bird malaria. The bird malaria knocked [out] all the native species. Killed them. You can catch the native species at higher

altitudes and bring them down, and they die in a cage because this vector is so effective. So, the only species at the lower altitudes are introduced species that are resistant to the malaria.

Microorganisms can really affect populations. The other place that they're extremely dangerous is in endangered species. Take cheetahs. There's a feline virus called Feline Infectious Peritonitis Virus that almost finished off the cheetahs. They just barely squeaked through and it's from domestic cats.

The lions in East Africa are greatly reduced in numbers. [Take] the dog distemper virus. In the game reserves, there are native groups, like the Masai, who have dogs. The dogs get in fights with hyenas and jackals. The hyenas and jackals get in fights with lions over prey, over deceased prey, and they spread the virus to the lions. And it [virus] had a huge impact on lion populations.

Are all biological weapons naturally occurring organisms?

Well they are and they aren't. Anthrax, for example, is virtually always penicillin sensitive, but we can make it penicillin resistant. So the foundation organisms for biological weapons are drawn from nature. They're naturally-occurring organisms. We may modify them, we may tweak them, we may put them into an unusual form to spread to humans, but they all are drawn out of nature. In the future, this may be different because we have the power now to manipulate microorganisms and even create microorganisms that could be actually unique — things that we've never seen before. We don't have a name for them.

One of the good things that has come out of the awareness of the biological threat is a complete sea change in the FBI and the intelligence agencies. The whole biological issue has been on the backburner for them for years, and the amount of expertise they've had has been very thin, very shallow, and has not had much impact on their attitudes.

Since 2001, we've seen a massive ramp up in all of the law enforcement agencies in their ability to think about the biological threat, and to actually deal with a biological threat, and to seek out intelligence against the biological threat. They are actively striving to improve this aspect of their capability.

So has that put us in a safer place or given us more hope?

Not only that, they've reached out to the scientific community. I believe, in the future, we'll have better intelligence and better ways to surveill for these threats. If you think about it, the place to stop all of this is at the level of intell and finding out who's doing the bad things, and stopping it there. If you can't stop it there, then the place to stop it is law enforcement when people are trying to apply it. And it's only if those fail that public health and medical counter-measures come into play. So we've got three layers. All three layers are ramping up. All three layers have some ways to go.