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Can you talk about the work you are doing at UTMB?

We've had a longstanding program in infectious diseases here at UTMB, one that's been growing for well over a decade, and it has had a particular emphasis on what we call *emerging infectious* diseases. These are infectious diseases that appear *de novo* — newly — in our society. They often come from our interactions with various animal hosts that may have viruses that they harbor naturally, that don't normally infect humans, but are able to jump species when we invade their environment.

So that [program] has involved the collection of a group of faculty here, who have strong interests in not only the microbiology, the virology and bacteriology of the bugs that cause these infections, but also the animal vectors and the insect vectors that can transmit them.

West Nile Virus, for example — that most people have heard about — was unknown in this country ten years ago. Now it is a major threat and has changed the way people behave outside in the summertime. Other examples might be the H5N1 Avian Influenza that's been in the news so much.

What has really characterized our program has been our interest in newly-emerging infectious diseases that pose real threats to our society. When the anthrax attacks happened in 2001 and led the U. S. government to invest a great deal in defenses against bioterrorism, we were naturally poised to respond to that challenge because the infectious agents that cause emerging infections are very much the same kinds of agents that one would be worried about that might be used by a terrorist.

So, the NIH issued a call for proposals to build and operate high containment laboratories, like the one behind me here, and, we responded. We competed in a national competition. We were one of two universities selected to build this kind of a facility.

This facility has what we call BSL-3 as well as BSL-4 laboratories. There are high containment laboratories that provide a high degree of safety to the investigator — the scientist — working with these kinds of viruses or bacteria.

The BSL-4 laboratory is the highest, most safe type of laboratory, with an individual spacesuit air supply for each investigator within the facility.

How did you determine that there was a need to do something more than you were doing?

We have had a number of BSL-3 laboratories, a slightly lower category of containment, for a number of years. We work on West Nile virus, for example, in these kinds of facilities. But we recognize that agents like the H5N1 Avian Influenza, agents like Ebola virus that you may have heard about, or Marburg virus — a closely related virus in Africa — pose a much greater risk to the scientist. The risk is really to the scientist working with these bugs, not to the immediate community. We really needed to have more laboratory space at higher levels of containment — BSL-4 — in order to deal safely with those kinds of agents.

So, beginning around 1997, we actually began plans to construct the first BSL-4 laboratory here on campus. This is the Robert Shope Laboratory, which was fully commissioned about two years ago. It's one of four, active BSL-4 labs in the United States today, and the only one on an academic campus in the U. S.

That laboratory is now working at full capacity. We have a number of requests from investigators at other universities and from companies that want us to be able to test vaccines or therapeutics — drugs — that they have developed, say, for influenza. We can only do this in this kind of a facility. There are very few of them available, as I said, in the United States, so the capacity's not really there.

This building under construction now is being built largely with funds provided from the U. S. government to provide that kind of capacity, so we are able to test, effectively, drugs, vaccines and diagnostic tests for these kinds of agents in advance of something happening.

The new lab will allow us to have much more capacity. It'll allow us to use more sophisticated instrumentation at BSL-4. There are imaging capabilities and technical capacities, in terms of image analysis and the way one would be able to analyze an experiment, that are ongoing within the BSL-4 laboratory here that simply don't exist in our existing BSL-4, or really in any BSL-4 now in the country.

What is driving the concern about emerging infectious diseases?

The concern about emerging infectious diseases [is what] really drives the faculty here. Each one of us, when we get up in the morning, worries about this. These are infections that, previously, were unknown to humans.

If you think back over the past thirty years, we've had an average of one per year spring upon the human population. Examples might be AIDS, which was really unknown to medical science prior to the early '80s. West Nile, as I've already mentioned, is another example. SARS is a tremendous example of how humans interacting with an animal reservoir of a virus, that doesn't normally infect humans, led to humans being infected by a virus that was highly pathogenic with a very high mortality rate — about 10 percent worldwide.

There are a number of factors that drive this. One overarching factor is the fact that we're really overpopulating this planet. The human population is increasing globally and we're expanding into environments where we never were before.

We have areas in the Amazon, for example, that are being deforested where there are exotic species infected with exotic viruses that were totally out of contact with humans before. Now humans are coming into contact as they clear that land, plant that land and carry out commerce right where the jungle used to be.

At the same time, we have these very large cities that are developing all over the world — cities of 20 to 25 million or more, often in very poor countries with very poor hygiene, and virtually no sanitation to take care of most of the residents of many of those cities. That trend of mega cities is increasing globally. At the same time now, we have transportation that is incredibly rapid. You can go from any one point on earth to any other point in less than 24 hours by commercial jet travel. If you look back a hundred years ago, if there was an outbreak of plague, say, in Tunisia, it might take eight weeks for it to reach some other continent by ship. Now it can get there in 24 hours or less.

At the same time, we're changing our environment in ways that introduce new insect vectors to our environment. There are now insects in the United States that weren't here previously, that probably were transported here on water and on rubber tires on the decks of ships coming from Southeast Asia, that now have the capability of transmitting viruses in this country — capability that wasn't there previously.

All of these things combine with the fact that these bugs, these viruses, are capable of very rapid evolution. Now no matter what you think about human evolution, there's no doubt that these bugs, these viruses, evolve. We can see it happening right under our eyes. It takes just a few minutes for a virus to replicate itself, whereas it takes thirty years plus for a human generation to occur. So these viruses can adapt to new environments, to new opportunities that face them, and that poses a real risk for us.

Josh Lederberg — a Nobel Laureate who was one of the first to call attention to this problem a couple of decades ago — has likened it to a battle. It's our wits against their genes. Their genes are very fast and evolving rapidly. We have to be smart. We have to stay ahead of that, and we need the facilities to be able to do the kind of research that's necessary to stay one jump ahead of these microbes. That's what's being built outside here.

What has led to and contributed to a "perfect storm of factors" in terms of infectious diseases.

A recent report from the National Research Council called these factors "a perfect storm" of events, trends, human evolution and changes in our society, where it is impacting the environment and how it is doing that. [These changes are] creating a set of convergent factors that are providing wholly new opportunities for microorganisms to inflict great damage on us.

If you look back at our history, human history has been replete with episodes where infections have devastated society. The great Plague of the Middle Ages, for example — the 1918 influenza. Those of us who think about emerging infectious diseases can look forward, and we see this convergent storm — perfect storm of factors on the horizon. We recognize that those who ignore history are doomed to repeat it. I think someone said that once. And, that's what we're trying to avoid. I think, with today's science, we should be able to do that, but it means staying ahead of the race.

Would you say that we're at a greater risk now than 20 to 30 years ago?

There's no question about it. Human society is larger. These risk factors are more extensive. Transportation has increased. The ease of transportation has increased. If you look at the number of people that are now transiting between continents, the speed with which that's happening is increasing exponentially. All of those factors contribute to the ease with which an infectious disease can spread from one corner of the world to another, because these bugs don't recognize any political borders.

The first report on emerging infectious diseases — this threat— came out in the early '90s, and it was followed up by a second report from the National Research Council several years ago. It shows very clearly that the risk has increased in the past twenty years. It's not decreased, and very little has been done, really, to counter those risks.

Discuss emerging infectious diseases in relationship to bioterrorism.

If you look at the threat of emerging infectious disease, all these factors that we talked about, one other factor, of course, is political upheaval. You can look at bioterrorism as one facet of emerging infectious diseases. Bioterrorist is simply a man-made emerging infectious disease threat.

The kind of agents that these terrorists would seek, many people believe, would be the kinds of agents that were worked on in the former Soviet Union in their offensive biological weapons program. That might include small pox, which has been eradicated from the world and only stored in two spots, now, in the whole world, legally, but which many people fear may be held in other labs, clandestinely, in other countries.

Anthrax is another agent that has relatively little risk of naturally-infecting humans, but which has some particular biological properties that allow it to be engineered into a weapon, as we all saw several years ago here in the United States, unfortunately.

Other agents [might include] Tularemia, which is a bacteria that infects rabbits and can be very highly fatal for man if man becomes infected with it, plague, many of the hemorrhagic fever viruses, or Ebola, for example, that you've probably heard about in the outbreaks in Africa. These are viruses that could be worked on, propagated in the laboratory and used as offensive agents.

Many of the techniques and approaches that one would use to control emerging infectious diseases — the creation of vaccines, the creation of better drugs, antibiotics, to fight these infections — have tremendous overlap with the emerging infectious disease arena and the threat we have there. It's really one spectrum of threats, with the manmade bioterrorist agents at one end and the naturally-emerging agents, like pandemic influenza — the Avian/Bird Flu, on the other end.

As a person dedicated to fighting against this, how does it make you feel that infectious disease is used by man against man?

I think anyone that works in the biological sciences and the life sciences, anyone that I know, really abhors the thought of using technologies like this — biotechnology — for nefarious, malevolent purposes.

But, if you look back at human history, we've never been able to imagine a single technology that hasn't been used by humans against humans, be it steam, be it nuclear, be it electrical, [or] gunpowder. All of these technologies have their history as a use in offensive weapons. And I think we

have to be realists to understand that biotechnology and the life sciences are no different. I think that's an emerging concept that people in the life sciences, many scientists today, don't think much about [or] don't want to think much about. But, I think it requires some careful thought and careful preparation.

Do you have a personal mission against these people who are trying to do this?

Well, I'm driven more by the fact that we're fighting an array of microorganisms. There are obviously people who might want to use those microorganisms, but the real threat, I think, is the threat of natural emergence. This is the threat that has the capacity to really destroy the function of our society, to set us back many, many years — something like a pandemic influenza outbreak.

We have to be aware of bioterrorism. We have to do everything we can to prevent and be prepared should it happen, which means having a very strong public health infrastructure to help mitigate the consequences of an attack. I think the attention should be primarily directed towards natural disease emergence. Fortunately, in addressing one you also address the other. I think it's the desire to counter that natural threat at the same time to understand how these things work — how these things actually wreck the human body with severe disease when an infection occurs — and how to interrupt that disease mechanism and reverse it. I think that's what we're all driven by.

Is there going to be a point where we have this licked? How long is this going to go on?

I can't see that we'll ever solve this problem. I've worked in the field of infectious diseases for thirty years plus, and every year it's a new infectious disease. We face infectious diseases today that were not in the textbooks when I went to medical school, and I feel quite confident that anyone entering the field of infectious diseases today will be facing infectious disease threats thirty years from now that aren't in our textbooks today. I'd be very surprised if that wasn't the case.

Tell me about efforts to try to find solutions and vaccines, and discuss emergency preparedness in case of an outbreak.

One of the real needs of our society is to pay more attention to public health infrastructure should there be a natural pandemic of influenza or a bioterrorist attack with an agent capable of spreading from person to person. We need strong public health.

It's not a very sexy thing for government to invest in, because, in the absence of something happening, you don't see the benefits of strong public health departments — public health departments that can communicate rapidly with the state and federal agencies that are their counterparts — or a command structure at the federal level that can deal with it better than we dealt with Hurricane Katrina, Hurricane Rita. So, there is a need for much greater preparedness.

On the medical side, we try to educate our medical students as to these threats, prepare physicians to be able to think about the disease process that's ongoing in their patient, whether it's SARS in Southeast Asia or the anthrax attack. The first case recognized in Florida came from the fact that there was a very smart, astute clinician who recognized something was strange, something was unusual.

So, training physicians and healthcare providers to be able to recognize something, having in place a public health infrastructure that can respond, having the vaccines, the antibiotic countermeasures for

something like anthrax, having a facility like this that can serve an emergency, standby-laboratory function in the event of a bioterrorist attack or a natural pandemic — those are really important steps.

It's prevention. You're putting money in the bank for the future and you're hoping that you're not going to need it. Saving for rainy days is very good, I think, and a wise thing to do.

Was the anthrax threat a wake-up call?

I think the anthrax attack clearly was a watershed event in the United States. The 9/11 episode in 2001, and the anthrax attacks that happened shortly afterwards — where anthrax spores were sent through the mail to a number of members of Congress and the news media — those events really served as wake-up calls for the American public.

The threat of bioterrorism, I think, was not firmly appreciated by many individuals. The fact that members of Congress had to vacate their offices for a period of months while they were decontaminated certainly led Congress to a new awareness of the threat from bioterrorism.

But for those in the field, that threat had been known some time before. In fact, we began working here in Galveston on research aimed at countering some of these bioterrorist threats as early as 1995. That realization has been there, but the funding to support it really did not become available until after 9/11 and the anthrax attacks of 2001.

I think the investment at the level of NIH (National Institute of Health) went from somewhere under $20 million to $300 million, to $1.7 billion over three years.

What might happen in a worst-case scenario?

Well, let's take an example of something we do know about and we're worried about: pandemic flu.

We have now known for about five years that there is a novel strain, a novel variant of Bird Influenza virus. Influenza viruses are primarily bird viruses, extent in Southeast Asia. It has infected a substantial number of humans, who have been in close contact largely with chicken flocks over the past few years, with a very high mortality rate in those who become infected.

This virus clearly is evolving. If we look at its genetics every year, we can see they're changing and we can see it's changing quite rapidly. And we're now actually faced with maybe three different strains in Asia spreading.

What this virus hasn't yet been able to achieve, however, is the ability to be transmitted from one infected individual human to another easily. It happens between birds but not between people. That might be only a single mutation away. So let's say that that happens. Say that that happens and the first case of influenza happens in Houston or Dallas or New York City, and within a few weeks there are many cases.

What one could see, and many experts foretell this, is a return to the situation that we had in 1918 when we had a severe pandemic influenza — when there were, I believe, over ten thousand deaths in Philadelphia in one month, when the mortuary services could not deal with the number of human bodies, [and] when the individuals who were dying were not the elderly and the very young but the middle aged, the healthy, the robust.

We don't have effective, really effective antibiotics for this infection. We don't have a vaccine that we know is protective against this infection. And there's no reason to believe that this shouldn't, couldn't happen again. Our history seems to be replete with perhaps two to three pandemics every century, some more severe than others. And, the very high mortality that you see with the Avian Influenza in Southeast Asia suggests that, should that become the next pandemic strain, we might be faced with the same.

That might lead to a disruption in our ability to ship food stuffs around the country. Our commerce may close. Our air services may drop. The financial impact could be enormous. The financial impact of SARS — SARS alone in Southeast Asia with only 8,000 cases and 800 deaths, I think — was on the order of $80 billion dollars. It would be dwarfed by a pandemic influenza episode.

If you look at graphical curves, if you look at the life expectancy in the United States around the time of the 1918 influenza, it took a severe dip down. You can actually see that on the life expectancy charts of the entire population.

If you had a flu epidemic that infected 20 percent of the population and had a mortality rate of 1 percent, you can do the math. The number of deaths would be enormous and the impact on our society incredible.

Could you give me a real quick worst-case scenario in a bioterror attack?

In terms of the worst-case scenario for a bioterrorist attack, you can look at this one of two ways. You could look at an agent that, once launched, had the ability to spread from person to person. Most bioterrorist agents like anthrax don't have the ability to do that, but small pox does.

So here you have small pox virus, a virus that has been the scourge of mankind for generations — hundreds and hundreds of years — which was eradicated a couple of decades ago, and there have been no natural cases in the entire world since. If that was launched again against the population in the United States that is largely susceptible, does not have immunity, the consequences could be devastating.

That's a very easy infection to recognize, however, and as part of the response to the anthrax attacks in 2001, the U. S. government has invested in a great deal of small pox vaccine. So now we actually do have small pox vaccine stores in the United States that might be able to be distributed fast enough to really counter that threat.

Another perhaps worst-case scenario would be anthrax. The anthrax spores that were sent through the mail infected some of those who opened the envelopes. They infected postal workers who stood near the sorting machines that were sorting this. It was a very inefficient way to deliver those spores.

If someone prepared those spores as well as they were prepared, apparently, in 2001, and introduced them into the ventilator system of a building, for example, the fatality rate could have been the same and the numbers of those infected much, much higher. That's an infection that, once it begins moving, moves so fast that antibiotics or other therapeutics really have very little effect in altering the course. So, one could have many hundreds or even thousands of individuals sick and ill from that, very, very quickly.

What is the function of the BSL-4 lab?

A BSL-4 lab is needed so we can work with these agents safely. One needs to be able to handle these bugs in the laboratory. One needs to be able to develop and utilize, humanely and as minimally as possible — but absolutely necessary — animal models of these infections to be able to determine whether a vaccine or a therapeutic, a drug, is capable of intervening in the course of the disease.

You need to know that information before the disease actually appears in the human population. It's required not only for licensure, but it's required for the doctor to be able to know whether this drug works or that drug works — whether this vaccine's going to protect or that vaccine. You can't do that in a conventional laboratory. It would not be safe to handle those agents in a conventional laboratory.

You need a laboratory, such as the one under construction here, with the containment facilities to protect the scientist, primarily, and the community around the laboratory from any potential of infection and contamination.

If you put a camera inside that lab, what are you going to see?

[You'll see] a lot of concrete all around you. It'll look like a regular lab in many ways, but the windows will all be airtight. All the penetrations coming into the room will be airtight.

You would see individuals working within the high containment lab in what looks like a spacesuit with their air being piped in from the outside. They'll have a spacesuit-like helmet over their heads. And it's not an easy way to do research. It's not an easy way to work in a suit like that.

They would be working at what are called biosafety cabinets, which are ventilated cabinets with the agent inside, so that the infectious agent is not allowed to become airborne in the ambient air within the room.

You would see a tremendous amount of high-efficiency particulate air filters on top of the lab, outside the lab, all the air coming in the lab, all the air going out of the lab being very, very carefully filtered, all of the liquid effluent being decontaminated by high heat, [and] anything exiting the lab, including the surfaces of the spacesuits that these investigators are wearing, being chemically decontaminated.

You'd see a very high level of redundant safety measures that probably is best likened to a 747 jet plane, where you have redundant systems — where, if any one system fails, there's two systems to back it up.

And you can't conduct any [experiments] on humans, of course.

You can't conduct any of this on humans. But it is important to recognize that many of the agents we are concerned about for emerging infectious diseases here in the United States, or that might be used as bioterrorists' threats, are natural, infectious diseases in other parts of the world.

So you have outbreaks of Ebola, for example, or Marburg, which is a very closely-related virus happening in mine workers in Angola that are entering the mine — the mine shift where there are probably bats infected with these viruses — and that virus is then getting into these individuals and infecting this individual.

So it would be possible, perhaps in some cases, to test vaccines and drugs in human populations in those natural settings: Marburg in Angola, perhaps, or some hemorrhagic fever viruses in South America. But many of these diseases, most of them, don't exist appreciably in the United States today in human populations.

What do you have to use to conduct the experiments?

A good example would be the H5N1 Avian Influenza virus. This is the pandemic bird flu virus that we're all concerned about. There are very few models of that human infection. The one that seems to be best is the use of a ferret, which is a small rodent-like animal.

Ferrets, when they're infected with human influenza viruses, develop very human-type illnesses. So, they can be protected by vaccines that work in humans. They can be treated by drugs that work in humans. Understanding how a vaccine or a drug affects influenza in a ferret can help us understand how to protect and treat influenza in a human. A great deal can be done in mice with some of these agents as well.

Here's a hypothetical situation. A virus breaks out. People die. What's the next step? No one knows what it is.

So, a new virus agent has appeared in the population. Well, I think the first step you would do is look diagnostically [at it] to try to determine what kind of virus, what bacteria might be present. We are working with several companies to look at new technologies for diagnosis — technologies that don't require prior knowledge of what the infecting agent actually is. Tremendous advances have been made using molecular techniques where bacteria and viruses have very broad signatures — very broad fingerprints that can be detected.

So what we would want to do would be, first of all, identify what kind of virus. We'd want to identify what family of infectious agents this infecting agent belonged to. We would then want to be able to bring this into the laboratory, into the BSL-4 or BSL-3 laboratory, to grow it in cell culture, in some kind of a culture in the laboratory, to be able to understand how to stop it from growing.

Once we're able to grow it, we can then see which drugs may interfere with it. We can then approach it using molecular techniques, isolate the genes that the infectious agent has and, by characterizing the nucleotide sequence of those genes, understand how this infecting agent is actually working. That can help us design, on a rational basis, drugs or vaccines to mitigate or block its effects.

Then what happens in the public sector?

It's a very close partnership between the scientists who are working in the laboratory, [and] the public health officials who are guiding the public in their response — in terms of the distribution of vaccines — and communicating to the public what can be done to prevent transmission.

In the case of pandemic influenza, it might mean preventing people from getting together at the mall or in schools and so forth. These kinds of measures have been discussed. Or, it might mean staying away from certain types of water or other potential sources of exposure. Therefore, it's a very close partnership and multi-disciplinary approach to get it right.

So those people have to be very prepared?

They have to be very prepared, and they have to have proper investment from society. We have not done that in the United States. We have let our public health infrastructure erode because infectious diseases have been considered licked in the past. We don't worry about polio any more, although many of our parents worried about it when we were children.

We don't worry about small pox anymore, except very recently as a bioterrorist threat. These were infections that, in decades past, mothers worried about their children acquiring. So, as you know, measles, mumps, German measles, chicken pox — these have all disappeared because of vaccines. People have become complacent. It's long past time to get rid of that complacence and be sure we have the public health infrastructure in place that can help us deal with this.

Is the BSL-4 a big deal for Galveston and UTMB?

Oh, I think it's definitely a big deal for Galveston and for UTMB. It's a big deal in the infectious disease community to be building and operating a BSL-4 lab. UTMB is a large organization. Our annual budget's about $1.3 - $1.4 billion, I think. So, on a financial perspective, this is perhaps, a small piece of it all. But I think it's a very substantial part of the intellectual activity here.

Is this is an enormous step for you personally?

This has been a tremendous step for the infectious disease program here and it has really catapulted UTMB to the forefront nationally and internationally in the infectious disease community. We get requests almost every day from scientists around the world who are looking for jobs, who want to come here, who want to be able to access our facilities, work within our facilities, join our faculty, work with our faculty. And that's very, very rewarding to see that.

Does having a family drive your work?

Certainly. I think any physician is driven, to some extent, by caring for their family, worrying for their family for the future. That's just natural for all of us — those of us who look towards our economic welfare in decades ahead. I think those who work in infectious diseases also think about protecting against infectious diseases in the decades ahead.