



## Can the United States Cope with Bioterrorism Attacks?

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"I would say certainly we are vulnerable. But I would say we are much less vulnerable, in the sense of being unable to respond, than we were a year ago. It's like night and day even from a year ago. Does that mean we are really well prepared to do all that needs to be done? No! There is a lot to be done, particularly at the local levels."

- D. H. Henderson, M. D.



Smallpox face lesions on boy.

Photograph by Cheryl Tyron, Centers for Disease Control, Atlanta, Georgia.



Man with smallpox. Photograph by Barbra Rice, Centers for Disease Control.

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**January 17, 2003** - Over the past several days, there have been national headlines such as:

- "Flu has turned deadlier in the last decade, new study says."
- "Postal Service tests facility for anthrax, Possible bacteria found in Federal Reserve sample."
- "Bubonic plague suspected in New York City visitors."
- "U.S. is unprepared for germ warfare."

That last headline is a quote from Colonel Erik Henschel, Head of the U. S. Army's Biological Defense Laboratory. He has complained that the military's efforts to develop defenses against biological weapons have not had monetary

support for development from Congress or pharmaceutical companies. Yet, Saddam Hussein has acknowledged in the past that his scientists have made thousands of gallons of toxins such as botulinum, anthrax, plague and viruses such as smallpox for biological weapons of war.

Since the first symptoms of these diseases are often like influenza, some federal monies from the new bio-defense fund are now supporting research at the University of Maryland's Institute of Human Virology. Scientists are now monitoring influenza cases at a Baltimore hospital. The goal is to come up with a genetic test of blood that will rapidly be able to tell the difference between a dangerous disease such as smallpox and the flu.

The head of that research is Professor Maria Salvato, a molecular virologist at the University of Maryland's Institute of Human Virology in Baltimore. Today I asked her to comment on Army Colonel Erik Henchal's statement that the "U. S. is unprepared for germ warfare."

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## **Interviews:**

**Maria Salvato, Ph.D. (Molecular Virology), Professor of Virology, University of Maryland, Institute of Human Virology, Baltimore, Maryland:** "I think it is generally accepted that the U. S. could be better prepared. Current surveillance is very poor. I receive monthly reports of virus infections from our local diagnostic lab at the hospital. They make diagnoses on only about 1 out of 30 patients that come through with flu-like illness. Each diagnosis costs from \$100 to \$500 dollars. And it takes almost two weeks for some of them to come back. So, cheaper diagnostics, faster diagnostics are needed, and a lot more surveillance is needed. More diagnoses need to be made.

SO, IN THE UNITED STATES RIGHT NOW, TRYING TO SEPARATE OUT WHAT MIGHT BE NATURALLY OCCURRING LET'S SAY, A FLU VIRUS FROM SOMETHING THAT COULD BE A BIOTERRORIST ATTACK, IS REALLY NOT HAPPENING?

No. That's a very critical thing that needs to be done.

AS AN INFECTIOUS DISEASE EXPERT, WHAT ARE YOUR GREATEST CONCERNS NOW IN COPING WITH THIS PROBLEM OF DISCERNING BETWEEN NATURALLY OCCURRING DISEASE OUTBREAKS AND A BIOTERRORIST ATTACK?

The biggest problem is speed how fast can all this be done? Once an outbreak has been identified, the biggest difficulty is containing it. People will fly off from the place where the outbreak occurred to another state and start spreading things. The speed of diagnostics and speed of surveillance needs to be stepped up.

HOW ARE YOU TRYING TO HELP WITH THAT?

I have actually received IHS funds which are new bio-defense funds to conduct flu surveillance in our local hospital. So, I know what the current rate of surveillance is. I know that very few diagnostics are done, so I am paying for them from this research grant and I am trying to make a more rapid form of diagnostic, one that can detect the infection before the pathogen builds up in the bloodstream.

HOW DO YOU DO THAT?

What we believe is that the blood cells change their messenger RNA once they are exposed to a virus. So, we know that in monkey models, for example, if you expose them to flu virus, monkeys have a temperature change in two days of the exposure. And yet you can only detect the virus in day 7 or later. That means the body is going through a lot of changes way before the pathogen builds up and causes disease. We want to look at blood cell messenger RNA changes using micro technology in order to determine what type of virus or pathogen is

affecting the body.

HOW DO YOU THINK THE UNITED STATES CAN COPE WITH TRYING TO SCREEN FOR SOMETHING LIKE AN UNEXPECTED SMALL POX OUTBREAK?

That's a very big, almost a political problem because responders are stretched thin and the U. S. government has to somehow make incentives for more surveillance and set up a health care system that can cope with bio warfare outbreaks.

SO, YOU WOULD AGREE THAT WITH MEDICAL DOCTORS QUITTING UNDER INSURANCE PRESSURES AND PUBLIC HEALTH SERVICES STRUGGLING TO JUST COPE DAY-TO-DAY, THE UNITED STATES IS VULNERABLE TO A BIOCHEMICAL ATTACK, MAYBE EVEN MORE SO THAN BEFORE 9/11?

Yeah, I would say. It's very stretched."

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## Flu Turned Deadlier in the 1990s

Complicating the American challenge to know the difference between a flu bug and a bioterrorist disease, influenza has been deadlier in the United States since 1992. A new study about flu mortality in the United States conducted by the Centers for Disease Control and Prevention in Atlanta, Georgia, was published in the January 8, 2003 *Journal of the American Medical Association* (JAMA). When decades were compared, in the 1970s and 1980s, flu killed fewer than 5,600 people in three separate years.

But in the 1990s, from the fall of 1992 through the spring of 1999, annual flu deaths never dropped below 27,000 and reached a high of 51,296 in the 1997 to 1998 season. Final numbers aren't in yet for 1999 to 2000 which some medical experts think will show an even higher flu death rate. For the first time in American history, one influenza strain reached epidemic levels four years in a row from fall 1996 to spring 2000. That's the Influenza A, subtype H3N2, and doctors still don't know why that particular virus affected so many people in the 1990s.

Flu and pneumonia together are now the 7th leading cause of death in America, after heart disease, cancer, stroke, chronic lung diseases, accidents and diabetes. W. Paul Glezen, M. D., Professor of Molecular Virology, Microbiology and Pediatrics at Baylor College of Medicine in Houston, Texas, says the four years of epidemic Type A/H3N2 influenza were unique and he, like many other epidemiologists, wonder if the trend will continue.

This week I asked Dr. Glezen if something has changed in the H3N2 virus that makes it more lethal to humans.

**Paul Glezen, M. D., Professor of Molecular Virology, Microbiology and Pediatrics, Baylor College of Medicine, Houston, Texas:** "What happens constantly with flu virus that the surface coat changes, so even if you had flu last year, you may not be immune to this year's flu. The flu virus is unique in that none of the surface antigens are conserved like they are for other respiratory viruses. Therefore, our immunity is short-lived because the virus escapes our immune system. This happens constantly. This is nothing new.

Now, what the CDC was saying in this report that was published in the JAMA on January 8 is that in the period since 1968 when H3N2 viruses appeared, most of the excess mortality that has occurred in the last 34 years can be attributed to epidemics with the influenza A, H3N2 sub-type. Perhaps there has been some change in the virulence of that virus because I think in the period of 1993 to 2000, 6 out of 7 epidemics were caused by H3N2. That's unusual to have, as occurred then, four consecutive H3N2 epidemics. Usually we saw them every other year, rather than every year. And there is no good explanation for why we had so many H3N2 epidemics in the decade of the 1990s.

DO YOU HAVE ANY EDUCATED GUESS?

There are some theories. One is that it's been shown in the last few years that influenza virus makes an anti-interferon. Remember interferon is part of our innate immunity, part of our natural ability to control all virus infections, or most virus infections. It allows time for specific immunity to develop.

Well, influenza virus has a component which makes an anti-interferon and if this is particularly strong, then this would block the individual's ability to control the infection when it first occurred, as ordinarily we hope it will and allow the specific immunity to take hold.

There are other factors that may impinge on this. One of them is air pollution. Any time you damage a mucosa with a virus infection, you make yourself for vulnerable to pollutants that are in the air. So if these people are living in a city where air pollution is bad, that's going to continue to aggravate. If you're allergic, then there are a lot of factors. All of these things can be initiated by a virus infection. But there are other processes that can take over to prolong the illness.

IS IT FAIR TO SAY THAT FROM AN EPIDEMIOLOGY POINT OF VIEW THAT THE INFLUENZA VIRUS DOES SEEM TO BE HARMING MORE PEOPLE AND CAUSING MORE DEATHS SINCE THE MID-1990S?

Well, the main reason it's causing more deaths is because there are more vulnerable people. You have to also work into this the population thing. Our population is increasing, our population density is increasing, and viruses love that because they can spread much more readily. When we are living in urban areas and our population has become urbanized considerably in the last 50 years. So, instead of living on small farms, we are all crowding into the city. That allows viruses to spread much readily in the population.

The other factor is our population is aging. Most of the excess deaths I talked about are in people over 65 years of age. If you look at the population statistics, you know that population has doubled in the last few years so many more people are vulnerable. In fact, the death rate has not increased. It's the number of deaths that have increased simply because there is a larger pool of people who are in the vulnerable age group.

SO, THAT 85% INCREASE IN DEATHS SINCE THE MID 1990S TO DATE IS RELATED TO THE FACT THAT WE HAVE A LARGER POPULATION OF PEOPLE OVER AGE 65?

Right, and it's going to get worse. Baby boomers are just starting to reach that age and over the next 20 or 30 years, the population over 65 is going to double again. So, if we're up to 51,000 excess deaths in the 1990s, we're going to probably be at 100,000 excess deaths at 2030 if we don't do something else to control influenza.

WHAT CAN WE DO IF THE DEATH RATE ITSELF IS LARGELY RELATED TO OPPORTUNISTIC BACTERIA THAT GETS INTO A SYSTEM AFTER AN INFLUENZA VIRUS HAS TAKEN HOLD AND CAUSES BRONCHITIS AND PNEUMONIA?

We can prevent the influenza infection. You prevent the initiator of the process and that's the way you can control it.

YOU'RE TALKING ABOUT FLU SHOTS.

Right. Or nasal spray flu vaccine which we hope will be licensed soon.

WHAT DO YOU THINK WOULD BE A SMART AND LOGICAL PROGRAM FOR THE UNITED STATES?

I think that universal influenza immunization would be important. We're interested in the possibility that giving flu vaccine to school children will

dampen influenza epidemics and reduce the chance of exposure of high risk patients to influenza. Because school kids are generally the main spreaders of flu in the community.

WHY IS IT THAT OLDER PEOPLE DON'T SEEM TO HAVE AS MUCH RESISTANCE TO FLU IF THEY GET A VACCINE?

It looks like the immune system becomes less responsive. Cell immunity seems to be diminished. What we know is that antibody response to flu vaccine goes down as we age.

WHAT DO YOU SAY TO PEOPLE THESE DAYS AFTER 9/11 AND BIOTERRORISM AND THE GULF WAR SYNDROME 'LOOK, I DON'T WANT ANYTHING BEING PUT INSIDE OF ME BECAUSE I DON'T TRUST THE GOVERNMENT ANYMORE.'

I think when we look at our ability to establish bio -security, one of the things we need to do is to diminish influenza type illnesses. One of the disease syndromes that is under surveillance now because so many disease start with flu like illnesses if we are going to be able to recognize when something unusual occurs like airborne anthrax spores.

OR SMALL POX?

Small pox. It would be good not to have influenza to worry about. So if we could set up good methods for surveillance and control of influenza, we'll be in much better shape IF a bioterrorism occurs.

WHAT IS YOUR MEDICAL PERSPECTIVE ON THE EFFECTIVENESS OF SOMETHING LIKE SMALL POX OR ANTHRAX BEING ABLE TO BE DELIVERED THROUGH THE AIR AND CAUSE PEOPLE TO GET SICK?

I think it's very possible, pretty frightening, the possibilities.

DO YOU THINK WE ARE GETTING ANY CLOSER TO BEING PREPARED FOR A BIOTERRORIST ATTACK?

I think we're getting closer, but we have a long way to go to really be protected.

SO MAYBE THAT'S WHERE THIS COUNTRY'S GREATEST VULNERABILITY IS NOW?

I think that we are always going to be vulnerable to these types of attacks simply because it's much less expensive to produce these agents of bioterrorism to, say, atomic bombs or other things. So, we have to be very wary of this and keep up our defenses.

AS AN EPIDEMIOLOGIST FOR SEVERAL DECADES, WHAT IS YOUR GREATEST CONCERN NOW AS WE SEEM TO BE IN A NEW COUNTRY WITH GREATER CONCERNS HAVING TO DO WITH BIOTERRORISM. WHAT IS YOUR PERSONAL GREATEST CONCERN?

My concern is that we concentrate on the things that we CAN prevent and use our resources wisely so we don't spend billions of dollars on remote possibilities, but develop I think my big concern now is that we strengthen our public health infrastructure so we are better able to cope with any sort of bio emergency, no matter what it is. What this requires is a strong public health that has good surveillance, good laboratories and good communications so that we can be alert and know when something unusual happens and be right on top of it. So, I think that a lot has to be invested in our public health infrastructure because this will provide dividends no matter what happens, you know? There are remote possibilities that we could have serious attacks. But with a strong public health infrastructure, our health will improve overall and we'll be better prepared if those emergencies arise.

BUT WITH ALL THE COMPETITIONS FOR FEDERAL DOLLARS FOR HOMELAND SECURITY AND ALL OF THE OTHER BURDENS THAT



HAVE BEEN PLACED SINCE 9/11, IS PUBLIC HEALTH GETTING THE KIND OF MONEY AND SUPPORT THAT IT NEEDS?

I haven't seen that it is.

SO WHERE DOES THAT LEAVE US?

We have to order our priorities and think about this and see what our leaders are suggesting and see if we agree.

HOW DO YOU LEVERAGE SUPPORT FOR ORGANIZING PRIORITIES AROUND LOGIC INSTEAD OF POLITICS?

(laughs) That's pretty difficult! I don't have the answer to that because I'm not a politician. All I can do is voice the concerns, particularly for the areas where I have some expertise and hope that things move in the right direction."

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## United States Is Still Vulnerable to Bioterrorism

**Donald H. Henderson, M. D., Principal Science Advisor in the Office of Public Health and Emergency Preparedness for the Secretary of Health and Human Services, Washington, D. C.:**

"I think the man from Baylor is right in the sense that the public health infrastructure is still weak. But the President has asked for another \$1 billion this year. We talked with both Republicans and Democrats and there is really strong bilateral support and understanding that we are not going to create what we think is best overnight or even in a couple of years. This is going to have to go on out over the future. When you let a system deteriorate for 40 or 50 years, you can't build it back in just a couple of years. It's going to take time. We are moving as fast as we can on that, but there are real shortages, shortages of people to fill slots, shortages of money. But I think the commitment is there. It is a big change already to what it was.

BUT WHAT YOU ARE SAYING IS - AS THE DOCTOR FROM BAYLOR POINTED OUT - THE UNITED STATES IS STILL VERY VULNERABLE IF WE DID HAVE SOME KIND OF MAJOR BIOTERRORISM ATTACK?

I would say certainly we are vulnerable. I would say we are much less vulnerable in the sense of being unable to respond than we were a year ago. It's like night and day even from a year ago. Does that mean we are really well prepared to do all that needs to be done? No! There is a lot to be done, particularly at the local levels. But we receive now reports on a regular basis from the states and local areas and we just finished a review of the reports that came in the first of November and I'm very impressed that they are really making great progress.

WHAT IS YOUR OWN PERSONAL GREATEST CONCERN RIGHT NOW IN JANUARY 2003 BEING A PERSON WHO IS HAVING TO SIT IN ALL THESE MEETINGS ABOUT AMERICAN EMERGENCY PREPAREDNESS AND GOING HOME AT NIGHT AND WORRYING?

I go home at night and worry! No question about it.

WHAT DO YOU WORRY THE MOST ABOUT?

Well, it is very difficult to deal with an outbreak. I've been throughout all my life working on epidemics in various places. Any epidemic of a disease is not easily handled. It's something new, it's strange, people are concerned. And the problem is trying to put into place very rapidly measures which are effective and at the same time to keep the communication with the public very open and keep them very much aboard and explain to them what it is and getting that message out in a very clear way: what is really the problem, what can you do about it, what are we doing about it. These are very difficult things to handle.

I think one of the problems is that in regard to bioterrorism, we're anticipating and worried about a number of diseases about which very few physicians know

anything, or have known anything. I don't think there are more than a handful physicians who have dealt with any one of the major diseases we are concerned about: small pox, botulism, plague, tularemia, or Ebola. The physicians are just not familiar with it and it's understandable: we don't have those diseases. So, it's important for us and we recognize this to get information out to them the best, the latest, the most comprehensive information that we can. We're very much involved with that at the present time.

ANY ONE OF THOSE DISEASES SHOWING UP IS SORT OF A HAIR TRIGGER THAT SOMETHING MIGHT BE WRONG.

That's right. But the thing that is often the problem is there comes a point of enormous fear of, let's say, that exaggerates the seriousness of the problem. And there is the concern not to appreciate how likely a disease is to spread. For example, is plague. People think of the Black Death of the Middle Ages and they think, 'Oh, my goodness, we're going to have huge epidemics and people are going to be dying right, left and center.' Well, we've been very active in trying to understand what is plague like in today's contemporary world and we have been working on all the data from 1900 outbreaks that have occurred. What has become perfectly clear is that plague does not spread very well. It does not spread at all well. In the Middle Ages, it spread for a very different set of reasons. We've got good antibiotics to treat the cases.

IN THE MIDDLE AGES, IT SPREAD EASILY BECAUSE?

The problems of housing, of the rats, the whole standard of housing, crowding, people living very packed into areas with poor sanitation and poor nutrition. When you put everything together, it really requires a lot of factors like this for it to really spread.

SO WHEN THESE ISOLATED CASES SHOW UP IN PLACES SOMETIMES LIKE NEW MEXICO AND IN THIS CASE IN NEW YORK CITY WHERE THERE IS A COUPLE FROM NEW MEXICO NOW CONFIRMED TO HAVE BUBONIC PLAGUE, YOU AND OTHERS YOU'RE NOT LOOKING AT THIS AS A WORRY THAT THEY COULD SPREAD BUBONIC PLAGUE BY BEING IN NEW YORK CITY?

No, not at all. I wouldn't be the least bit worried.

WHAT DO YOU SAY TO PEOPLE WHO ARE SO AFRAID OF GETTING A SMALLPOX VACCINATION?

Well, I think they forget that up until 1972 every child in this country, virtually every child, got vaccinated. It was required in most states for entry into school. We have since then, there have been a number of others who have been vaccinated. As adults, you had to be vaccinated successfully within the previous three years to go to most countries of the world. The military was regularly vaccinated. I think the point is that vaccination has been very extensively used in this country. We were doing about 12 to 15 million vaccinations a year. But it is a procedure which has not been performed for quite a long time.

Just myself in calculating this, I thought about it. In 1972 we stopped. Let us say that the youngest physicians then who would have been administering the vaccines at that time would be about 30 years old, so that now they are 60 years old. So physicians themselves have not seen vaccination, they have not seen what (smallpox) looks like. It is recognized that there are complications with the vaccine, but it's hard to keep this in perspective. Is everyone who is going to get the vaccine going to have a severe reaction, the answer is no.

RECENTLY THERE WAS RELEASE OF INFORMATION FROM ONE OF THE MEDICAL JOURNALS THAT SINCE THE MID-1990S, THERE HAS BEEN AN INCREASE OF MORTALITY FROM INFLUENZA, ESPECIALLY TYPE A INFLUENZA, AN INCREASE OF 85% MORTALITY SINCE THE LAST DECADE. DO YOU LOOK AT THAT AND HAVE ANY CONCERN ABOUT INFLUENZA A VIRUSES BEING USED FOR BIOTERRORISM?

What we are really worried about is that the virus might change and may start to behave like the swine flu, or what we call the 1918 influenza where you had a lot of deaths. That has been a very great worry. That's why there is right now a global network of laboratories that has been in existence for many years to try to pick up anything unusual so that if something, a new virus does pop up, we would be able to retrieve it and move to produce new vaccines.

WASN'T THE STRANGENESS OF THE SWINE FLU IN THE 1918 PERIOD BECAUSE IT TARGETED AND KILLED THE YOUNGER, SAY BETWEEN 18 AND 30, AND THAT MOST OF THOSE DEATHS WERE CAUSED BY PNEUMONIA?

Yeah, it killed an unusual number in that age group. It's a very unusual phenomenon and they died primarily of an influenza pneumonia.

WHAT CAUSES PNEUMONIA TO SUDDENLY TAKE OVER A HEALTHY BODY?

It's a virus. It depends on the characteristics of the virus. If you have an influenza virus which has unusual characteristics of pathogenicity, it might do that. We've had recently about 3 to 4 years ago in Hong Kong a new strain of influenza called H5N1. In all there were 18 cases that occurred, and 6 of those people developed pneumonia and died. But fortunately, that strain did not seem to spread very well. But this is what everybody keeps a close alert out to be sure that we get and detect as soon as possible and are ready to move quickly and do something."

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## Websites:

<http://www.bt.cdc.gov/agent/smallpox/index.asp>

## Credits

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