OPINION

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Bioterror focus should be on viruses

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The discussions in the Seattle Post-Intelligencer concerning a proposed new bioterrorism laboratory at the University of Washington serve to emphasize a national dilemma. Should bioterrorism be discussed in detail in public?

Newt Gingrich and Bill Sanders have recently stated: "Biological warfare ... is the largest threat to the human race, a substantially bigger threat than nuclear war. If the United States is hit with an engineered biological agent for which no vaccines are available, we are in for problems of colossal proportions."

Gingrich and Sanders conclude that biothreats are four times as dangerous as nuclear and chemical threats combined. They also argue for public discussion but state, in an initial disclaimer, that nearly all experts consulted were reluctant to comment publicly about the severity of the threat. Quite interestingly, they placed these remarks in the appendix of their book, "Saving Lives and Saving Money."

Public discussion should, I believe, center on two questions:

- What agents constitute the greatest risk?

- Can an epidemic attributable to the most dangerous agents be aborted before it has run its course? In short, can we be survivors?

The supreme threat is from a new lethal highly infectious agent that we initially cannot detect because we lack the proper reagents and for which no treatment exists.

Bacterial agents can cause great damage but can generally be controlled by antibiotics, quarantine and antisera. Fortunately, new lethal bacteria cannot now be created in the laboratory, although existing pathogens can be made more deadly. Growing sufficient bacteria for extensive analyses, including genomic sequencing, and for initial vaccine preparation, can be readily done.

Viruses pose different problems. There are no wide-spectrum anti-viral drugs analogous to the antibiotics effective against bacteria, quarantine may not contain a highly infectious virus, growth conditions may be difficult to find, causing delays in sequencing, and years may be required to produce an effective vaccine. More important, highly pathogenic viruses can now be synthesized in the laboratory from scratch. That is new and may constitute the most important advance in weapons of mass destruction of all time.

One must conclude that any really serious effort in bioterrorism must center on viruses.

In the race to explore agents of bioterrorism, the most deadly known viral genes are being sequenced and can then be synthesized. The technology exists to combine these killer genes with normal genes that disorient our immune systems, to produce new lethal viruses that even eons of evolution would find improbably difficult to make. The kits, reagents and vectors required to do that can be gotten by overnight express. "Cut and paste virology" is an essential element of all modern genetic engineering, which raises us into a new and much higher class of risks.

Very early global detection of new viruses is probably the greatest technological challenge facing the Department of Homeland Security, the National Institutes of Health, the Centers for Disease Control and Prevention, the Department of Defense and all their academic affiliates concerned with biodisasters.

Would anyone actually make, either by design or accident, a new killer strain of virus?

Computer viruses and biological viruses are of similar complexity, and whatever has driven humans to make and distribute at random tens of thousands of computer viruses, all specifically designed to do maximal injury anonymously, will surely drive someone to do the same in human virology. And if man doesn't do it, nature ultimately will.

The average reader has somewhere between one and four (and often more) virus infections per year for his or her lifetime. It is a rare reader who has ever had, or even knows someone who has had, a single one of these viruses completely characterized. You are diagnosed as having a viral infection if you do not respond to antibiotics, and the virus is usually described as "what's going around." Diagnostic virology thus leaves much to be desired, and any means for mass viral screening combined with doctor's office identification could revolutionize the treatment of viral diseases.

The United States has no real-time global surveillance system for viruses, and if it did, newspapers, such as this one, would gladly publish maps showing the spread of all major known human viral pathogens over the United States at weekly intervals. That would prove to the public that "what is going around" is actually known. Every mother would be interested in these maps.

If we cannot detect and follow known viruses quickly, it is unlikely that we can detect and follow new ones early enough to provide an effective response. Humans are now the canaries in this enterprise, and we must wait for multiple deaths to occur before effective notice is taken.

The time between initial infection (the index case), the demonstration that a virus is present by isolating it, completion of tests to know whether it is new or known, culture of the virus to obtain enough material for sequencing, and complete sequence analysis can be longer than an epidemic. Many of the steps in this process depend on accidents of interest and motivation. Once an epidemic is identified as such, there is serious competition to own the relevant patents.

The time required to make a new and effective vaccine, made possible by sequence data, is estimated to be an average of seven years. Only an organization dedicated to assembly line experimental vaccine production can explore means for reducing the delay between detection and vaccination to months or weeks.

In stark and compelling contrast to our approach to bioterrorism, real-time detection and response to an incoming ballistic missile is not designed to depend on a pickup band. Rather the idea is to find out how to intercept and kill a rogue missile in minutes after launch, to reduce the technology to practice in a dedicated 360/24/7 operation, and then, through practice and further research and development, cut every possible second out of the interval between detection and target destruction.

No analogous entity or program exists or is planned in the field of bioterrorism. However, if I did not believe that such was possible, I would not be writing this article.

There are two basic and non-exclusive approaches to organizing rapid detection and response (D/R) for bioterrorism. The first is the Quaker model in which a text (a request for proposals) may be presented, and those moved to respond, do. This sorts out what is believed possible, identifies those interested and absolves the organizers of responsibility for the results. A committee may set priorities for the proposals but will give little attention to actual outcomes. Winners will be chosen by the marketplace.

The second approach to bioterrorism, which has been repeatedly suggested, is a Manhattan Project-style effort, which would ransack all of science to actively find, develop, evaluate and integrate the best ideas and technology. It does not wait for the morning mail. Almost by definition, such a project cannot be done by any existing organization, or it would be under way now and the reader would have heard about it. The aim is an organization that knows from the inside what to do.

In the original atomic-bomb project, access to, and control of, intellectual property was essential; making a profit -- a central concern in Project Bioshield -- was not. There were concrete objectives and extreme flexibility to deal with unknowns along the way. There was also central command, willingness to set up parallel competing projects to ensure that key objectives were actually reached, budgets that matched needs and enforced schedules. And there was a moment of truth at the end, with no confusion between failure and success.

The current response to natural or human viroterrorism (our current paramount threat) provides minimal response and protection. It may be, in effect, an expensive 21st-century Maginot Line in a second "phony war."

It may also be that a Manhattan Project-style operation can be set up only in wartime, leading us to ask whether we are actually in one.

It is interesting that Franklin Roosevelt, with the reins of government in his hands, chose a private foundation to fight a viral disease of great concern to him and to the public, which was polio. This may be the best and possibly the only effective approach now.

Regarding new bioterrorism laboratories, what is actually to be done? How much basic information is useful absent an effective response? It is no consolation to die from something we completely understand.

How about an effective D/R program that yields results visible in the clinic? Whatever really protects us from viroterrorism will also protect us from the scores of viral illnesses that plague us for life now. There must be a plan, and we must all see what it is.

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