- Vaccines in bioterrorism -

DA Henderson
Potomac Inst for Policy Studies
Rosslyn VA
24 Mar 1999

Bioterrorism - a growing concern ①

1) Iraq -
2) Aum - $\geq$ 1 bil / 20 000
3) Russia - 1972 BWC
1980 SE

1975 PDD 39 - ②

CB

Funding ③ ④

Result: Minimal involvement of HHS - ō CDC / ō NIH ③ ⑤
ō in academic world. (Many/most - too repugnant to deal with - hangover from 60s - 70s anti Vietnam feelings)

∴ No assessment has been done re: what threats we should be concerned about nor has there been any plan as to what to do vis-à-vis bioterrorism.

April this year - Working Group created - to develop a consensus as to what agents should be of concern and what should be done about them. Ad process

Let us walk thru certain of the steps in assessing this what we should do

Starting point - Russian analysis - production ④
Iraq - anthrax/bot. Aum - sarin

Our conclusion so far - 4, possibly 5

What do we have in the way of vaccines ⑤

Narrow this down to two vaccines -

~~How might the~~

Status of the vaccines —

(6)

ANTHRAX VACCINE

SMALLPOX VACCINE

How procured. —

Stored. / Problems.

How to use the vaccine — what does epidemic look like

ANTHRAX Story of Sverdlovsk.

SLIDES

0-6 days vs. 4+ days. but not contagious. 80% fatal.

DEVASTATION

monkeys.

vaccine.

but >5 years away.

Two uses: ① Pre-event — all 1st responders.
② Post-event — immed. protection?
③ Post-event — longer term resistance?

SMALLPOX Story of Meschede. // Yugoslavia

Highly contagious 30% death rate

long incubation period

Contagious :: like in crowded, prog.

U.S. — virtually 100% susceptible!!

Time of transmission (first week)

Vac. — protects vs. death up to 5 days after exposure.

Possible uses:

- Pre-event — all 1st responders
- Post event

There you have it. The 2 vaccines we now have might will be among the most important vaccines (potentially) ~~available today~~. Neither, however, are available in any quantity ~~and so quick~~ ~~with [illegible] now~~ Much needs to be done before the vaccine will be available.

NY TIME
Aug 7 98
1 of 3

Germ Defense Plan in Peril As Its Flaws Are Revealed

By WILLIAM J. BROAD and JUDITH MILLER

On May 22, President Clinton unveiled an ambitious plan to stockpile vaccines at strategic sites around the country so communities could better fight germ attacks. "We must do more to protect our civilian population," Mr. Clinton told graduating midshipmen at the United States Naval Academy in Annapolis, Md. "We must do more to protect our people."

While such major initiatives usually result from many months and sometimes years of fierce debate, this one, Federal and private experts said in interviews, was developed in record time, rushed through amid worries of rising threats from Iraq and germ terrorists. But today the multimillion-dollar plan is in jeopardy, a victim in part of the haste in which the decision was reached.

Some Government officials are calling for a different approach that initially plays down vaccines in favor of antibiotics. Others defend vaccines, but concede that making them quickly is nearly impossible, given industry's production limits and the need to insure vaccine safety and effectiveness. Still others fault vaccines as offering little or no protection against such deadly threats as smallpox and anthrax, seen as likely weapons in germ attacks.

A review of events leading to the Clinton vaccine decision reveals that the proposal was pushed by a small group of scientists, businessmen and policy makers who largely shared the same views as they struggled to do something, anything about a threat whose dimensions were potentially terrifying but frustratingly unclear. Working in Washington's frenetic, often insular world, they tended to overwhelm or sidestep doubters, and failed to see warning signs.

Among the findings are these:

¶A Presidential meeting where seven scientists endorsed the stockpile plan included two men who stood to gain financially from the decision.

¶The plan was made without consulting leaders of the drug industry about whether companies could fulfill the President's pledge.

¶The apparent consensus on acquiring vaccines masked deep divisions among scientists and military officials.

William C. Patrick 3d, who made germ weapons for the United States before President Richard M. Nixon outlawed them nearly three decades ago, warned that vaccinations against particular germs could be easily countered by foes, making such safeguards potentially useless.

"It's a hell of a problem," Mr. Patrick said. "Defensive measures are much more difficult than offensive ones. There's no easy way around it. You immunize against anthrax and then an enemy just tries something else."

Even the Administration's top public health officials have begun to warn that stockpiling is no quick fix.

"My view is that the stockpile isn't sufficient," said a senior Administration official, who spoke on condition of anonymity. "We need an entire care system in place" to avoid creating a false sense of security.

And Congress, which has strongly supported the Administration's anti-terrorism efforts, is questioning the rationale and structure of the civilian stockpile. A Senate hearing is being considered for the fall.

"The plan," said Senator Lauch Faircloth, Republican of North Carolina, "needs to be more carefully thought out and discussed more publicly."

The Pentagon

In Early Debate, Focus on Troops

For decades, scientists and military officials debated the merits of vaccines as a defense against germ warfare. Worries grew after the 1991 Persian Gulf war, when United Nations inspectors found that President Saddam Hussein of Iraq had studied dozens of microbial agents and had placed at least 180 biological bombs and warheads around his country ready to spray lethal germs on enemy troops.

As the Pentagon discussed an ambitious program to make a variety of vaccines, its officials weighed the possibility that enemies would simply choose new deadly germs or modify old ones to outwit American defenses.

"People asked if we were just making it possible for Saddam to pick another agent," recalled Stephen C. Joseph, a doctor who at the time was Assistant Secretary of Defense for health affairs.

Dr. Joseph added that he and his Pentagon colleagues nonetheless recommended in the mid-1990's that the military embark on a vaccine effort. They were motivated in part, Pentagon officials said, by intelligence reports of rising dangers outside Iraq of germs being used against American troops.

In 1996, the Pentagon began looking for a company to develop and obtain licenses for 18 vaccines other than the standard one for anthrax. The initial ones were to guard against smallpox, which causes fever, boils and can be fatal; tularemia, which causes chills, aches, fatigue and typhoid-like symptoms, and Q-fever, which causes headaches, weakness and coughing.

In November 1997, the Pentagon awarded a $322 million, 10-year contract for the 18 vaccines to Dynport, a British-American venture. The plan sidestepped the knotty issue of immunizing troops, focusing instead on making and stockpiling vaccines for military personnel.

Exactly how the Pentagon would use its stored vaccines would depend on future events and threats.

Late last year, worry in the Pentagon about biological attacks turned to alarm as United States troops prepared to strike Iraq after President Hussein expelled Americans from international teams investigating his germ arsenal. On Dec. 15, Defense Secretary William S. Cohen announced that all 2.4 million American troops would get anthrax shots. Pentagon officials said the effort would take six years and cost $130 million.

Just at that moment, the theory of enemy countermeasures became real publicly for the first time. In December, Russian scientists stunned the biological world by disclosing that they had used genetic engineering to make a new anthrax microbe. It attacked blood cells and made Russia's vaccine useless.

Whether the organism was a laboratory curiosity or a battlefield weapon was unclear. The Russian scientists gave out no samples, so detailed analysis was impossible. But Western military officials were shaken and wondered whether the American anthrax vaccine was now obsolete, and whether the same was true of other vaccines in development.

"It's not just an academic debate anymore," said Jack Melling, director of the Salk Institute in Swiftwater, Pa., a vaccine center that does research for the Defense Department.

The news got worse in February. Ken Alibek, a top Russian defector, went public to assert that Moscow was working on a range of exotic germ weapons, including hybrids of the smallpox virus that cause profuse bleeding. If real, such germs could sow plagues that kill most victims.

The President

Pushing a Plan To Save Civilians

Around that time, President Clinton became fixated on the emerging germ threat and ways to counter it among civilians, aides said.

Influences are said to have included the Iraqi crisis, the Russian claims, the intelligence reports and a novel, "The Cobra Event" (Random House, 1997), about a terrorist attack on New York City with a genetically engineered mix of the smallpox and cold viruses. Mr. Clinton was so alarmed by the book, his aides said, that he instructed his intelligence experts to assess its credibility and urged Speaker Newt Gingrich, Republican of Georgia, to read it.

Aides said the President and his National Security Council increasingly wrestled with the danger of biological attacks not only on troops abroad but also on American cities, states or even the entire country.

In January, in his State of the Union address, Mr. Clinton vowed to confront the hazard of germ weapons obtained "by outlaw states, terrorists and organized criminals."

In March, the White House held a secret exercise to play out what would happen if terrorists struck with one of the theoretical smallpox hybrids. The results of the war game were grim and fueled a Federal drive to find better ways to cope with such an attack.

In April, the President explored ways in which modern biology might help. He and his top officials met at the White House on April 10 with seven private scientists in the Truman Room, where Cabinet meetings are held. For an hour, participants say, the scientists discussed the germ topic and pushed for a vaccine stockpile.

Mr. Clinton's attending officials included the Secretary of Defense, the Attorney General, the Secretary of Health and Human Services, the Director of Central Intelligence and the national security adviser.

The scientists present were Dr. Frank E. Young, a former head of the Food and Drug Administration, who moderated the panel; Dr. Joshua Lederberg, president emeritus of Rockefeller University; Dr. Lucille Shapiro, a biologist at Stanford University; Jerome M. Hauer, head of emergency management for New York City; and Dr. Barbara H. Rosenberg, a biological arms-control expert at the Federation of American Scientists, a private group.

The scientific panel also had two industry experts, both with financial ties to vaccine work.

One was a pioneer of genetic engineering who had decoded the smallpox virus and other microbes and used the meeting to push his own scientific agenda, participants said. But that researcher, Dr. J. Craig Venter, president of The Institute for Genomic Research, a nonprofit biotechnology group just outside Washington, said he simply urged the Government to step up support for the genetic mapping of deadly microbes. The insights, Dr. Venter added, would aid vaccine development and new methods of germ detection and treatment.

"The argument is that if we decipher these genomes it could be the ultimate deterrent," Dr. Venter said, referring to the ability to have so many avenues of defense that germ attacks would become futile.

Over the years, his institute had received millions of dollars in Federal support and is now gearing up to use more Government money to map the anthrax microbe as an aid to germ defense.

At the White House meeting, participants said, the business interests of another scientist were less well known.

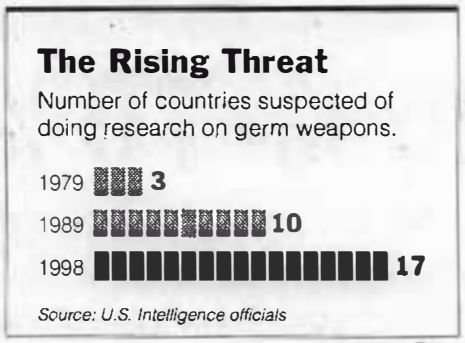
Dr. Thomas P. Monath was identified in a White House announcement as a vice president of Oravax and a former official of the Centers for Disease Control and the United States Army Medical Research Institute of Infectious Diseases, the Government's top body for defensive germ-warfare studies.

A graduate of Harvard College and the Harvard Medical School, a world authority on yellow fever and other epidemics, Dr. Monath had devoted most of his career to public service.

At the meeting, he was viewed mainly through that lens, participants said, who added that they knew little about his company other than it worked on vaccines.

Based in Cambridge, Mass., Oravax was founded in 1990 to tap an emerging multibillion-dollar market in oral vaccines and antibodies to combat infectious diseases. But the small company kept having problems getting beyond research and bringing products to market.

By 1996 and 1997, its survival at stake, Oravax tried to win part of the Pentagon's expanding germ work as a subcontractor to make smallpox vaccines and others. By early this year, that work had failed to materialize and the company's stock price was down 90 percent from $10 a share in the initial public offering.



The New York Times

Memories of meeting participants varied, but no one could recall Dr. Monath telling the President of his company's financial interest in vaccine stockpiles — a step he now insists that he took.

"The way to handle it is to be open, so people understand that I may have a potential bias," Dr. Monath said. "I don't make it a business of taking advantage of situations in which I'm asked to participate to push the Oravax agenda."

Many participants remember Dr. Monath arguing forcefully for stockpiling, a subject he had been asked by the panel's moderator to discuss.

Dr. Venter said the views of Dr. Monath, while strong, reflected the panel's consensus. "Even through he was pushing harder than anyone else," Dr. Venter said, "our recommendations to develop stockpiles of vaccines and medicines would have come out the same."

A retired Army colonel, Dr. Monath was most likely the only scientist in the room who had deeply studied such problems for germ defense as enemy countermeasures.

That topic, participants say, was discussed little and in any case was overshadowed by Dr. Venter's repeated assertions that genetic advances in theory had the power to solve these problems.

The Presidential briefing was such a hit that the experts were asked to take it on the road. In the following weeks, the scientists delivered their views to senior officials involved in vaccine issues at the Pentagon and the Department of Health and Human Services, participants said.

On May 6, the panel delivered a follow-up report to the President that, among other things, called for a stockpile of drugs and vaccines to protect millions of Americans against a variety of germs, up to 40 million against smallpox. The total cost over five years was estimated at $420 million.

Such a stockpile, the report said, could help "reduce the death and illness 10 to 100 fold."

A White House official who spoke on the condition of anonymity said the recommendation by the scientific panel simply encouraged the Administration to do what it was already contemplating. The official added that he saw no conflict of interest in Dr. Monath's participation because his company had signed no Federal contracts for vaccine production.

Government ethics experts say that such private White House advisers are exempt from Federal conflict-of-interest rules and that Dr. Monath, even if he had an undisclosed interest, broke no law.

The White House official called Dr. Monath "very knowledgeable," adding, "The point of the meeting was to get a wide range of opinions from leading experts."

The Pharmaceutical Research and Manufacturers of America, a Washington trade group that represents the nation's top 100 drug companies (Oravax is not among them), said it was never contacted by the White House for advice on the stockpile idea.

The Company

Good News In Stock Market

Oravax at this time was increasingly desperate. In filings to the Securities and Exchange Commission, the company said it had won part of the Pentagon vaccine work.

Its stock price continued to slide. On May 4, the company put out a news release boasting of the contract, and the stock rose that day in heavy trading to $1.31, up from $1.00.

But in fact, Oravax had only a preliminary promise of possible work as a subcontractor to the British-American venture that had won the Pentagon contract, executives from both companies now agree.

Securities lawyers say such misrepresentations in S.E.C. filings are potential violations of Federal securities laws.

Later that month, as rumors and news reports suggested that the President was about to announce a civilian stockpiling effort, Lance K. Gordon, Oravax's president, issued a press release saying the company was prepared to take on the challenge.

"Although there is no guarantee that Oravax will be involved," Mr. Gordon said in the May 21 statement, "the company believes it has the capacity to produce both smallpox and tularemia vaccines for civilian use."

The next day, a Friday, Mr. Clinton announced the new push to create stockpiles of "medicines and vaccines to protect our civilian population." He also praised gene research as "very, very important" to developing new ways of countering germ terror.

The same day, 2,413,100 shares of Oravax changed hands in the Nasdaq market, closing at $1.41, up 28 cents, or 25 percent. It was the stock's heaviest trading day ever. Later, the company issued a statement explaining the sudden activity, which it attributed to the President's action.

For Dr. Monath, who owns or has options on 150,574 shares, the stock's price increase amounted to a profit on paper of $42,160.

The Battle

In Shaping Shield, Emphasis Changes

A quiet war erupted as Federal agencies and experts weighed in heavily for the first time. The Department of Health and Human Services, designated to oversee the stockpile, was ambivalent about the project, officials said. The agency faulted the initiative as simplistic, saying the plan put too little emphasis on the costly, painstaking work of improving the nation's public health network to cope with germ attacks.

Significantly, the agency found that no company was making, or would soon be able to make for civilians, the vaccines scheduled to be stockpiled. It therefore switched the emphasis to antibiotics. Though also potentially vulnerable to enemy countermeasures, these drugs were seen as having the benefit of fighting a variety of noxious germs.

Two weeks after the President's announcement, on June 8, the Government quietly began to back pedal. Even though the White House asked Congress for $51 million in the next fiscal year to develop "a civilian stockpile of antidotes, antibiotics and vaccines," that same day Administration officials disclosed that vaccines had been ruled out for the moment. Why? Cheaper and more effective ones might appear in the next few years, the officials told reporters.

The developing plan has yet to address in detail how and where the medicines would be made, stored or distributed in a crisis.

As for Oravax, its stock is down, closing yesterday at .56 cents. And it still has no Federal stockpile work.

Despite the setbacks, many experts continue to back vaccines as important for germ defense and even hold out the possibility of wide civilian immunizations.

"Preventing an outbreak is always preferable to trying to suppress one after it has started," Senator Faircloth said.

As for the worry that an enemy might outwit vaccines with new or modified germs, vaccine supporters say that most of these enhanced germs are theoretical and would probably be less available and attractive to terrorists than known strains of deadly, dependable germs like unmodified anthrax and smallpox. If so, they say, vaccines are a good deterrent and a relatively cheap insurance policy.

Whatever their flaws or merits, vaccines continue to draw the interest of small companies eager to gain a foothold in an expanding area of the Federal budget.

On July 7, the State of Michigan approved the sale of the nation's only licensed maker of anthrax vaccine to a company led by Adm. William J. Crowe Jr., a former Chairman of the Joint Chiefs of Staff who was an important supporter of Mr. Clinton in the 1992 Presidential campaign.

Admiral Crowe's newly formed company has individuals with extensive drug industry experience and now has an inside track on at least $60 million in Pentagon contracts, officials of the Defense Department said. And while aiming at the military market, it wants to expand to civilian customers as well, company officials said, if that becomes possible in the years ahead. Companies drawn to the germ-defense business see the emerging civilian market as potentialy dozens of times larger than the military one and much more profitable.

Clinton Seeks Additional $300 Million to Fight Bioterrorism

By JUDITH MILLER

President Clinton asked Congress yesterday to add about $300 million to next year's Federal budget to protect Americans better from germ and chemical attacks, the White House announced.

A senior Administration official said the request represented a 30 percent increase in money to fight bioterrorism and was the largest single supplement to the Federal budget ever sought specifically to bolster civilian and military defenses against such terrorism. The Government is spending an estimated $1 billion a year on such efforts.

The supplement reflects President Clinton's growing alarm about the possibility of germ-wielding terrorists crippling the nation by sowing deadly epidemics. Mr. Clinton's personal interest, officials said, has become a powerful force behind a series of secret Federal meetings and directives meant to bolster the nation's anti-terrorism work.

Mr. Clinton recently appointed a national coordinator to guard against attacks using weapons of mass destruction and to better prepare the country for such an emergency. Richard A. Clarke, the coordinator, had pressed hard for the extra money, Administration officials said.

The budget amendment for the 1999 fiscal year, which begins this October, includes $51 million to start a civilian stockpile of antibiotics and other medicines to be administered in a biological or chemical emergency. But the White House did not request money for stockpiling vaccines to immunize civilians against anthrax or other lethal biological agents.

A senior Administration official said the Administration had ruled out buying such vaccines this year in the hopes of developing better ones that could be administered cheaper and more effectively two or three years from now.

But some scientists faulted the Government's go-slow approach on vaccines as unwise given the threat.

"I am extremely disappointed that they have not gone forward vigorously on a procurement program," Dr. Donald A. Henderson, the scientist who led the global campaign that eradicated smallpox, said in an interview. "Two diseases, anthrax and smallpox, represent the biggest problem. We have them to fear the most."

The Pentagon has begun vaccinating every member of the armed services against anthrax, one of the deadliest known biological agents. Administering the six-shot series and yearly boosters to the entire military — which now has 1.4 million troops on active duty and another 1 million reservists — is expected to take six years and cost an estimated $130 million.

That vaccination program will continue, Administration officials said.

One official added that a high-level interagency committee would reconsider the vaccine issue later this year. He also said that the budget amendment requested $10 million more for the National Institutes of Health to help conduct vaccine research, a two-thirds increase in the $15 million a year now allocated for such research. Mr. Clinton has also asked Congress to give the Centers for Disease Control and Prevention an extra $43 million to help public health centers and laboratories better detect outbreaks of suspicious diseases and share information among the centers.

The Administration is also seeking $16 million more for metropolitan medical strike teams, which would bring the office's budget to $20 million, an almost five-fold increase.

But most of the supplement, some $190 million, would go to the Department of Health and Human Services, the Department of Justice, and the Federal Emergency Management Agency for equipping and training state and local officials to deal with a biological or chemical weapons attack. There is no new money for the Pentagon, which spends about $50 million a year training and equipping such officials. The Pentagon, one official said, told the White House that it did not need additional money now. So far, it has trained so-called "first responders" in 28 of the 120 cities chosen to receive such training.

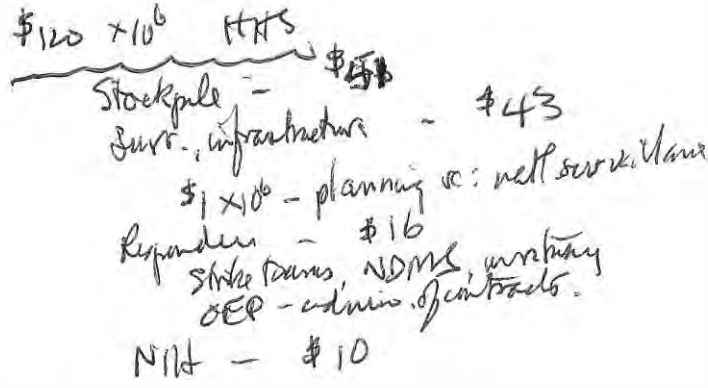
In a statement released by the White House, President Clinton said it was "vital that we take measures to safeguard the health and safety of our civilian population."

The supplement is to be offset by cuts by other agencies, especially the Justice Department, which plans to cut $168 million, mostly from its budget for prison administration.

Reached last night, several aides to members of the House and Senate appropriations committees said Congress would probably support most of Mr. Clinton's request.

"Chemical and biological terrorism has become an equally grave concern here on Capitol Hill," said an aide to a senior Republican on the Senate appropriations committee.

In 1996, Congress approved a $1.2 billion supplement over five years to improve the nation's effort to fight terrorism. Some of that money has been used to help foil chemical and biological weapons attacks.



Smallpox Outbreaks in Europe
Second Generation Cases -- Dec. to May, 1958+

Number of cases	Number of outbreaks
0	8
1-2	7
3-4	2
≥10	7* (13 / outbreak)

* Germany (2); USSR; Poland; Spain; U.K.; Yugoslavia

Viability of Vaccinia Virus at different temperatures and humidities

		% Viable after "x" hours		
Temperature	Rel. Humid.	1	6	23
11	20	82	81	66
	50	83	77	59
22	20	66	45	15
	50	86	57	12

From: Harper, J. H*ygiene, 1961.*

SURVIVAL OF VACCINIA AEROSOLS (%)

Temp F(C)	Rel. Hum.	1 hr.	6 hrs.	23 hrs.
50(11)	20	82	81	66
	50	83	77	59
	83	79	60	27
70(22)	20	66	45	15
	50	86	50	12
	83	66	18	tr
90(22)	20	61	33	13
	50	56	15	tr
	83	36	tr	tr

Harper, J. Hyg. 1961

CIVILIAN BIODEFENSE EFFORT

+ Efforts primarily centered in DOD, DOE, FBI

HHS is a marginal player –

Small staff in Office of Emergency Planning
No funds and no program in CDC or NIH+

Virtually all funds in DOD, DOE
HHS Fy97 expenditures = $ 17 million
Govt. antiterrorist funds FY97 = $ 6 900 million

+ Medical and public health profession generally uninformed as to potential risk and seldom consulted

+ Planning and development meetings

Primarily defense, intelligence, fire, police, emergency response people, occasional biologist

Occasional physician, rarely public health staff and none who have ever dealt with epidemics

+ No comparative threat analysis for civil bioterrorism

+ No consensus as to what the response should be

ANTHRAX VACCINE

Live Vaccine
- Animals
- Russia

Inactivated Vaccine
- Field tested -- 1950s-60s in processing plants
  - 26 cases of cutaneous anthrax
    - 17 placebo; 6 non-vaccinees
    - 3 vaccinees (one adequately)
- Uncontrolled experience 1962-74 U.S.
  - 27 cases of cutaneous anthrax
    - 24 unvaccinated; 3 part immunized

- Licensed (1972)
  - Supernatant of a different strain grown in microaerophilic vs aerobic environment
  - Mainly contains protective factor
    - Varying degrees of purity
    - Guinea pigs - only assay standard
    - No adequate qualitative tests

Vaccinated during Gulf War -- 150 000

Cost $139 000 000

FY 97 FUNDING
UNCLASSIFIED ANTI-TERRORISM PROGRAMS

(millions of dollars)

Defense	3 671
Energy	1 420
Treasury	682
Justice (mainly FBI)	451
Transportation	296
State	162
HHS	14
Total	6 698

Source: GAO/NSIAD-98-39 "Combating Terrorism"