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Washington Post August 25, 2004 Pg. 14

N. Korea Continues Criticism Of Bush

Comments Seen in U.S. as Effort to Disrupt Talks on Pyongyang's Nuclear Program By Glenn Kessler, Washington Post Staff Writer

For the second straight day, North Korea yesterday hurled unusually personal criticism at President Bush, calling him a "fascist tyrant" and "human trash." The official statements strongly suggested the communist nation is seeking to disrupt further talks on its nuclear programs before the U.S. presidential election, some U.S. officials said. Senior-level talks are planned for next month, but North Korea has balked at holding working-level talks this month that would pave the way for another six-nation negotiating round. It told the Chinese it has substantive problems with holding such talks now.

North Korea "can no longer pin any hope on the six-party talks, and there is a question as to whether there is any need for it to negotiate with the U.S. anymore," North Korea's official KCNA news agency said.

On Monday, in a statement attributed to Pyongyang's foreign ministry, North Korea likened Bush to Adolf Hilter and said recent comments by Bush on the campaign trail made it "quite impossible" to attend any talks and "deprived [North Korea] of any elementary justification to sit at the negotiating table with the U.S."

North Korea said yesterday that further talks are pointless and pointedly said it would "bolster up its war deterrent" - code for its nuclear arsenal -- "both in quality and quantity in order to beat back any aggressor at a single blow." U.S. intelligence analysts believe that North Korea has in the past year significantly increased its stockpile of nuclear material for weapons.

North Korea's ire was raised when Bush, campaigning last week in Wisconsin, called North Korean leader Kim Jong II a "tyrant" when he alluded to the administration's effort to enlist other countries to restrain North Korea's nuclear ambitions. "I felt it was important to bring other countries into the mix, like China and Japan and South Korea and Russia, so there's now five countries saying to the tyrant in North Korea, 'Disarm, disarm,' " Bush said at a campaign event.

Publicly, administration officials have dismissed North Korea's statements as typical bluster by the reclusive state in advance of negotiations. "I wouldn't make the connection, certainly, between these comments and the talks," State Department spokesman J. Adam Ereli said yesterday. "I would simply reiterate what we said yesterday, that obviously we take issue with those statements. We do not believe they're appropriate to diplomatic discourse." But some administration officials believe Pyongyang is seeking to scuttle the talks in order to deprive Bush of any political advantage from movement on the Korean issue. Democratic presidential candidate John F. Kerry has criticized Bush for not negotiating directly with North Korea, a long-sought goal of North Koreans in more than a year of talks.

"They were looking for an excuse, and Bush calling Kim a 'tyrant' is a ready-made excuse," an administration official said, speaking on the condition of anonymity. He noted that the language in the statements was unusually pointed and personal and appeared designed to give Kerry an opportunity to say the Bush administration had mishandled the negotiations.

"Had Bush [had] even an iota of elementary reason, morality and ability to judge reality as a human being, he would have not dared defile the political system of his dialogue partner so malignantly," the KCNA statement said. "Bush is, in fact, a thrice-cursed fascist tyrant and man-killer as he revived the fascist war doctrine which had been judged by humankind long ago and is now bringing dark clouds of a new Cold War to hang over our planet and indiscriminately massacring innocent civilians after igniting the Afghan and Iraqi wars," the statement said. It added: "It is the greatest tragedy for the U.S. that Bush, a political idiot and human trash, still remains in the presidential office of the world's only 'superpower,' styling himself "an emperor of the world."" http://www.washingtonpost.com/wp-dyn/articles/A30014-2004Aug24.html

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Washington Post August 25, 2004 Pg. 14

World In Brief

SAO PAULO, Brazil -- Police said they had seized a load of uranium and thorium ore taken from a secret mine in the jungle in northern Brazil and destined for sale on the black market.

Based on a lead from an informant, federal police seized 1,320 pounds of ore containing the radioactive metals in a pickup truck about 75 miles from Macapa, capital of Amapa state, near the mouth of the Amazon River. http://www.washingtonpost.com/wp-dyn/articles/A30350-2004Aug24.html

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Bureau of International Information Programs, U.S. Department of State 23 August 2004

Researchers Discover Three Compounds that Inhibit Anthrax Toxins

New drugs being tested for use in humans, University of Chicago says

New screening tools have helped University of Chicago researchers discover three unrelated compounds that inhibit the two toxins -- edema factor and lethal factor -- that have made anthrax one of the most feared potential bioterror agents, according to a press release by the University of Chicago Medical Center.

In the August issue of the journal Chemistry and Biology, the researchers report using a novel screening technique to find the first therapy, a small molecule that prevents edema factor from connecting to its target in the cell. "This is dramatic example of how progress in basic science can be applied quickly, effectively and unpredictably to clinical problems," said Wei-Jen Tang, associate professor at the University of Chicago and an author of the study.

In another study published in the journal Nature, Tang and colleague Milan Mrksich, used the combination of two screening methods they developed to examine a library of 10,000 compounds in search of small molecules that inhibited edema factor. The National Institutes of Health and the National Science Foundation funded the study. The researchers found a compound that kept edema factor from binding to calmodulin, a protein that makes edema factor 1,000 times more potent and kills cells. The compound was toxic, but the researchers modified it to remove the toxicity without altering its ability to block edema factor. They named the non-toxic version Nitro10506-2A. This discovery followed a report from Tang and Mrksich in May that used a similar approach to identify a compound that halts the activity of lethal factor, the other anthrax toxin, in laboratory tests. Lethal factor shreds a protein that helps cells stay healthy. The compound they found, DS-998, blocks lethal factor's harmful cutting action.

Nitro10506-2A and DS-998 could lead to the development of new drugs for treating anthrax, but research is in the early stages. Cell culture and animal testing are under way.

Text of the University of Chicago Medical Center press release follows:

(begin text)

University of Chicago Medical Center

Press release, August 20, 2004

Basic research producing new anthrax therapies

Thanks to new screening tools, and some luck, researchers at the University of Chicago have discovered three unrelated compounds that inhibit the two toxins -- edema factor and lethal factor -- that have made anthrax one of the most feared of potential bioterror agents.

In the August 2004 issue of the journal Chemistry and Biology, the researchers report that they used a novel screening technique, developed at the University, to find a small molecule that prevents edema factor from connecting to its target within the cell.

A similar approach, reported in Nature Biotechnology in May, resulted in a compound that inhibits lethal factor, the other anthrax toxin. And a study published in PNAS in February showed that a drug already approved to treat hepatitis was also effective in the lab against edema factor.

"This is dramatic example of how progress in basic science can be applied quickly, effectively and unpredictably to clinical problems," said Wei-Jen Tang, Ph.D., associate professor in the Ben May Institute for Cancer Research at the University of Chicago and an author of all three studies. "Our lab began working with edema factor as a tool to understand basic cellular metabolism, but the knowledge we gained soon led us to three potential therapies." Because each drug disrupts a different link of the chain of toxic events, the therapies should be complementary. Although all three treatments appear promising in the test tube, none has yet been tested clinically caution the authors. Cell culture and animal testing is underway.

Until 2001, Bacillus anthracis, the bacterium that causes anthrax, was an obscure agricultural pathogen, but that fall someone sent letters stuffed with anthrax spores to several politicians and journalists. Nearly half (5/11) of those infected by breathing in the spores died from the disease. The anthrax mailings triggered a run on antibiotics, but these drugs only work in the early stages of anthrax infection, before the bacteria have had time to spread and secrete toxins.

"These attacks called attention to the need for better therapies for anthrax infection," said Tang.

Fortunately, the Tang lab was already studying edema factor, using it as a molecular probe to understand cell-cell communication. His team had sent a manuscript describing the three-dimensional structure of anthrax edema factor to the journal Nature a few days before the first terrorist use of the microbe became public.

In that paper, Tang and colleagues showed how edema factor did its damage. Inside an infected cell, edema factor connects with a protein called calmodulin. Calmodulin changes the toxin's shape, creating a conformation that functions just like a cellular enzyme called adenylyl cyclase, which helps regulate cell-to-cell signaling. When edema factor connects with calmodulin, however, it becomes a relentless version of adenylyl cyclase -- 1,000-fold more potent -- causing affected cells to become hyperactive. These cells devour their energy stores, lose the ability to regulate their environment, release water, causing edema (swelling) in surrounding tissues, and die. Because of the bioterrorist attacks a few months before, the discovery received widespread attention. A researcher at a pharmaceutical company happened to notice newspaper accounts of the work and suspected that a drug he studied, called adefovir dipivoxil, acted on the same metabolic pathway. He sent Tang several candidate compounds and Tang's lab found that the active metabolite of adefovir also blocks edema factor.

The Chemistry and Biology paper describes a more systematic and less fortuitous approach. Tang and colleague Milan Mrksich, Ph.D., professor in the department of chemistry and the Institute for Biophysical Dynamics at the University of Chicago, used the combination of two screening methods, developed by Tang and Mrksich, to examine a library of 10,000 compounds in search of small molecules that inhibited edema factor.

They uncovered one that very effectively prevented edema factor from binding to calmodulin. Although this compound was itself quite toxic, the researchers were able to make slight modifications that removed the toxicity without altering its ability to block edema factor. They named their non-toxic version Nitro10506-2A. This discovery followed a report from Tang and Mrksich in May that used a similar approach to identify a compound that halts the activity of lethal factor, the other anthrax toxin, in laboratory tests. Lethal factor shreds a protein that helps cells stay healthy. The compound they found, called DS-998, blocks lethal factor's harmful cutting action.

Nitro10506-2A and DS-998 could lead to the development of new drugs for the treatment of anthrax, Tang said, but he cautioned that research remains in the early stages.

"Discovering proteins that have roles in disease processes is the first step in the drug discovery process," added Mrksich, "but still a very long way from the actual development of a drug."

The National Institutes of Health and the National Science Foundation funded the study. Additional authors include Young-Sam Lee, Pamela Bergson and Wei Song He of the University of Chicago. (end text)

http://usinfo.state.gov/xarchives/display.html?p=washfile-

 $\underline{english\&y=2004\&m=August\&x=20040823155911lcnirellep0.8098719\&t=livefeeds/wf-latest.html}$

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U.S. Customs and Border Protection

U.S. Customs and Border Protection Achieves Container Security Initiative (CSI) Milestone Of 25 Operational Ports

(Wednesday, August 25, 2004)

Press Release

Washington — U.S. Customs and Border Protection (CBP) Commissioner Robert C. Bonner announced today a milestone in the Container Security Initiative (CSI) with 25 ports now operational in Europe, Asia, Africa, and North America.

"The 25 ports represent the world's major seaports, but we are not stopping there. We plan to expand the CSI network even farther," stated U.S. Customs and Border Protection Commissioner Robert C. Bonner. "The expansion will extend port security protection to more than 80 percent of all containers coming to the United States." CSI will be expanding to strategic locations that ship substantial amounts of cargo to the United States, and that have the infrastructure and technology in place to participate in the program.

The 25 operational ports include: Halifax, Montreal, and Vancouver, Canada; Rotterdam, The Netherlands; Le Havre, France; Bremerhaven and Hamburg, Germany; Antwerp, Belgium; Singapore; Yokohama, Tokyo, Nagoya and Kobe, Japan; Hong Kong; Göteborg, Sweden; Felixstowe, United Kingdom; Genoa and La Spezia, Italy; Busan, Korea; Durban, South Africa; Port Klang and Tanjung Pelepas, Malaysia; Piraeus, Greece; Algeciras, Spain; Laem Chabang, Thailand.

CSI was proposed by Commissioner Bonner and launched in January 2002. CSI has been accepted globally as a bold and revolutionary initiative to secure maritime cargo shipments against the terrorist threat.

"The primary purpose of CSI is to help protect the global trading system and the trade lanes between CSI ports and the United States. By collaborating with foreign customs administrations, we are working towards a safer, more secure world trading system," Commissioner Bonner said.

The World Customs Organization and the G8 have supported CSI expansion through their adoption of resolutions that support the implementation of the security measures introduced by CSI at ports throughout the world. On April 22, 2004, the European Union and the Department of Homeland Security signed an agreement committing both parties to further cooperate on CSI and related matters.

CSI is a fully reciprocal program. Japanese and Canadian officers are currently stationed and working in key U.S. ports to screen containers destined for their respective countries.

CSI is founded on four core elements: 1) using intelligence and automated information to identify and target all containers that pose a risk for terrorism; (2) pre-screening those containers that pose a risk at the port of departure before they arrive at U.S. ports; (3) using detection technology to quickly pre-screen containers that pose a risk; and (4) using smarter, tamper-evident containers.

Non-Intrusive Inspection (NII) technology allows the screening of a larger portion of commercial traffic in less time. This enables targeting containers that pose a potential risk for terrorism while facilitating legitimate trade. Customs officers use large-scale gamma ray and x-ray imaging systems to safely and efficiently screen conveyances for contraband, including weapons of mass destruction.

These units can scan the interior of a full-size 40-foot container in under a minute.

As part of CSI, inspectors also use radiation detection devices to scan for signs of radioactive materials. If necessary, containers are opened and unloaded by the host government Customs service for a more intensive manual inspection. CSI officers observe this manual inspection.

U.S. Customs and Border Protection (CBP) is the agency within the Department of Homeland Security charged with the protection of our nation's borders. CBP unified Customs, Immigration, and Agriculture Inspectors and the Border Patrol into one border agency for the United States.

http://www.customs.ustreas.gov/xp/cgov/newsroom/press_releases/08252004.xml

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Los Angeles Times August 26, 2004 THE NATION

U.S. Making Preparations for Next Outbreak of Super-Flu

From Associated Press

WASHINGTON — The United States might have to close schools, restrict travel and ration scarce medications if a powerful new flu strain caused a worldwide outbreak, according to federal plans for the next pandemic, obtained Wednesday by Associated Press.

It would take months to brew a vaccine that works against the kind of super-flu that causes a pandemic, although government preparations include research to speed that production.

The federal plans have been long-awaited by flu specialists, who say it's only a matter of time before the next pandemic strikes.

There were three flu pandemics in the last century, the worst in 1918, when more than half a million Americans and more than 20 million people worldwide died.

Concern is rising that the next pandemic could be triggered by the recurring bird flu in Asia, if it mutates in a way that lets it spread easily among people.

"We're all holding our breath," Dr. Julie Gerberding, head of the national Centers for Disease Control and Prevention, said in an interview Wednesday.

About 36,000 Americans die of regular flu every winter.

Pandemics strike when the easily mutable influenza virus shifts to a strain that people have never experienced before.

It's impossible to predict the toll of the next pandemic, but a bad one could kill up to 207,000 Americans, according to the Pandemic Influenza Response and Preparedness Plan.

The plan is a first draft, open for public comment through October.

http://www.latimes.com/news/nationworld/nation/la-na-flu26aug26,1,6540118.story?coll=la-headlines-nation

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Washington Post

HHS Calls for Plan to Counter Threat of Flu

Potential Strains Could Devastate Worldwide

By David Brown

Washington Post Staff Writer

Thursday, August 26, 2004; Page A21

The stockpiling of antiviral drugs, making more flu vaccine and better surveillance for new flu strains were among the suggestions mentioned in a long-awaited draft document, released yesterday by the Department of Health and Human Services, on how the United States can get ready for pandemic flu.

"What we're trying to do from a preparedness perspective is to say this is real, this is serious, and that the time to be complacent about flu is over," said Julie L. Gerberding, director of the Centers for Disease Control and Prevention.

"This is an opportunity to begin to educate the public about what a pandemic is, and what will be necessary to respond to one," said Bruce Gellin, director of HHS's National Vaccine Program and a main author of the 56-page document.

First called for in 1993, the "Pandemic Influenza Preparedness and Response Plan" poses nearly as many questions as it provides answers. HHS is seeking comment from state and local health departments, as well as the medical community and the public, over the next two months before coming up with a final plan.

"Pandemic" influenza refers to a strain of flu virus that is new and capable of being easily transmitted in human populations. The flu virus that circulates each winter in nearly all cases is a genetic variation of a microbe already in circulation. Slightly new strains come and go year to year, some more transmissible or deadly than others. Periodically, however, there is a chance fusion and "recombination" of a human flu virus and a flu virus carried by birds or pigs. If the resulting microbe has the ability to be easily passed person to person -- and most hybrids do not - then it can potentially infect the entire globe, as nobody has immunity to it (or a closely related strain) from past infections.

Such a pandemic occurred in 1918 and 1919 with the "Spanish flu," which killed about 50 million people. There were less severe pandemics in 1957 and 1968. Epidemiologists and virologists believe it is only a matter of time before a new pandemic strain emerges. The H5N1 avian flu virus that killed millions of birds -- and several people -- in East Asia last winter is a candidate, should it become able to be easily transmitted among humans. Experts estimate pandemic influenza might kill between 89,000 and 207,000 people in the United States. Annual influenza mortality is between 20,000 and 40,000.

Many of the actions proposed are underway. Scientists are producing a small amount of vaccine from a "seed virus" made from the H5N1 flu strain now circulating in Asia. When that work is finished in November, the vaccine will be tested in a small clinical trial in people while a larger batch -- perhaps 2 million doses -- of vaccine is made to see how the strain performs in industrial-scale production.

The federal government is also seeking to buy more oseltamivir -- a drug sold as Tamiflu -- from Roche, the company that is its sole manufacturer. Taken for five days, the drug can prevent infection in people exposed to influenza in many cases. There is enough oseltamivir in the government's "strategic national stockpile" of epidemic and bioterrorism drugs to treat about 1 million people. Gerberding said "we would like to have closer to 100 million" treatments but that production bottlenecks make that impossible at the moment.

A major problem is that it takes six months to make large amounts of flu vaccine, which is grown in fertilized chicken eggs. That is too long a delay to stop a rapidly moving virus. Efforts are underway to find alternative methods using cell cultures. That is unlikely to make the process faster, but it may make it easier to rapidly expand the size of production runs, Gellin said.

Anthony S. Fauci, head of the National Institute for Allergy and Infectious Diseases, said "there is really a full-court press going on now to develop" flu vaccines that protect against many strains of the virus, not simply a single strain and its very close relatives, as is now the case.

HHS wants to hear from health departments and the public about who should get vaccines or antiviral drugs if supplies are short. The plan names a number of scenarios, including ones that target the most at risk of death (such as the ill or elderly), the most at risk of infecting others (such as health care workers), or people whose jobs are important (such as police and fire personnel).

The plan says it may be necessary to screen travelers, close schools and quarantine mildly ill people to limit spread of the disease. It noted, however, that given the nature of flu -- which is transmitted much more easily than the virus that causes severe acute respiratory syndrome, which caused a global response last year -- even that might not slow a pandemic much.

http://www.washingtonpost.com/wp-dyn/articles/A33907-2004Aug25.html

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Washington Times August 27, 2004 Pg. 12

California

Anti-Ballistic Missile Misses Target

LOS ANGELES -- An anti-ballistic missile under development by Israel and the United States missed its target yesterday in its latest test off the California coast, a spokesman said. A test last month off California was a success. The Arrow missile failed to intercept an air-launched missile over the Pacific and both fell into the water, said Chris Taylor, spokesman for the U.S. Missile Defense Agency.

"The engineers don't yet know what happened," Mr. Taylor said.

It was the 13th Arrow intercept test and the eighth test of the complete weapon system. Officials have not said how many of the tests have been successful. In yesterday's test, the Arrow was trying to hit a short-range, air-launched target. Mr. Taylor would describe the target only as representative of a threat that Israel might encounter. http://www.washtimes.com/national/aroundnation.htm

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Washington Times August 27, 2004 Pg. 5

Inside The Ring

By Bill Gertz and Rowan Scarborough, The Washington Times

Missile defense

Defense Secretary Donald H. Rumsfeld took a jab at critics of U.S. missile defense efforts during a speech last week in Huntsville, Ala.

When he joined a commission on ballistic missile threats in 1998, "I was stunned by how theological the missile defense debate had become. It was really a hair knot," Mr. Rumsfeld said.

"Everyone felt something very, very strongly about it. Even the proponents disagreed very strongly. And the opponents disagreed very strongly. And things were pretty much on dead center as a result of it. It was a shame." Mr. Rumsfeld said President Bush ended the impasse by junking the 1972 Anti-Ballistic Missile Treaty. He noted that two years after Mr. Bush announced the decision to finally deploy a missile defense system, "in the past few weeks, the first interceptor has been put in place in Fort Greeley, Alaska," and that "by the end of this year we expect to have a limited operational capability against incoming ballistic missiles."

Mr. Rumsfeld said the initial deployment represents "the triumph of hope and vision over pessimism and skepticism." The deployment probably is "somewhat of a disappointment for those who were convinced it would fail," he said.

He noted his cordial discussions days earlier with Russian officials on missile defense and said that critics, primarily liberal weapons-control advocates, who think U.S. missile defenses would be destabilizing were wrong. "The sky-is-falling group was wrong. The sky did not fall. It's still up there."

Mr. Rumsfeld also was asked about the danger of terrorists or rogue states attacking the United States by putting a short-range Scud-type missile on a freighter and firing it close to U.S. shores.

He said one Middle East nation already has "launched a ballistic missile from a cargo vessel."

"They had taken a short-range, probably Scud missile, put it on a transporter-erector launcher, lowered it in, taken the vessel out into the water, peeled back the top, erected it, fired it, lowered it, covered it up. And the ship that they used was using a radar and electronic equipment that was no different than 50, 60, 100 other ships operating in the immediate area."

Other U.S. officials have said the nation was Iran, which tested a freighter-launched missile in the Caspian Sea in the late 1990s.

"It is true that the big distinction we make between intercontinental, medium-range and shorter-range ballistic missiles doesn't make a lot of sense if you're going to move the missile closer to the target," he said. http://www.washtimes.com/national/inring.htm

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