A decade ago, the world learned that the Soviets had built an extensive germ-warfare reserve; today, nations are trying to prevent anyone from trying it again

Down to the Wire on Bioweapons Talks

CAMBRIDGE, U.K.—In the summer of 1994, U.S. experts on biological weapons received a startling invitation to visit a set of secret Russian labs. The offer came as they were delving into a clandestine program revealed earlier by Soviet defectors—one that had employed thousands of scientists and technicians to design and produce weapons loaded with deadly microbes, such as anthrax.

Former Russian President Boris Yeltsin admitted in 1992 that the Soviets had run this vast enterprise, called Biopreparat. He also pledged to dismantle it and adhere to the ban on offensive weapons in the Biological and Toxin Weapons Convention (BWC), which the Soviets had ratified 2 decades earlier but clearly ignored.

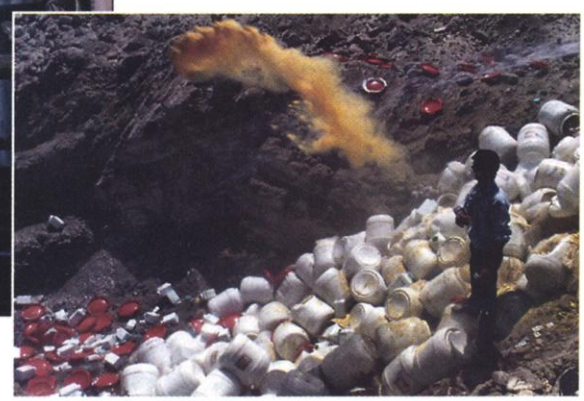
As a gesture of good faith, Yeltsin allowed Western experts to visit the Biopreparat buildings. But another clutch of facilities remained off limits—a shadowy network run by the Ministry of Defense (MOD) for the ostensible purpose of developing vaccines against bioweapons. U.S. and British experts kept asking questions, however, and in June 1994, they got a surprise: Russian officials invited them to visit any lab, including the MOD facilities. "The offer came out of the blue," says a U.S. official.

Over the next few weeks, however, separate talks on Russian visits to U.S. disease-research labs overseas foundered, and by fall, Russia had withdrawn its invitation. The MOD labs remain a closely guarded secret. "We had a chance to learn what they were up to," says the U.S. official, "and we let it slip away."

Today, bioweapons experts say, the entire BWC could also become a lost opportunity. A quarter-century after entering into force, the treaty remains the weakest of the international arms-control agreements. The problem: It has no mechanism for checking on whether states parties are obeying the ban on developing biological weapons. Other agreements on nuclear and chemical weapons have established technical systems for monitoring compliance. But the BWC remains little more than an agreement based on trust.

"We need to have a radar screen to identify spots and follow them up," Ambassador Tibor Tóth, chair of the Ad Hoc Group of the States Parties to the BWC, told *Science*. "Right now our radar screen is blank."

Tóth is hoping to change that. Starting on 23 July, the Hungarian diplomat's Ad Hoc Group will meet in Geneva for a 4-week session to hammer out rules that BWC state parties must abide by. Formally known as the Protocol to the BWC, the measures would include mandatory investigations of facilities suspected of contravening the treaty as well as visits to declared facilities that are not under suspicion, plus export controls on organisms and technologies that might be used to develop biological weapons.



Near miss. U.N. inspection teams found and dismantled biological weapons facilities in Iraq after the Gulf War.

CREDITS: AP/UNSCOM

The challenge will be to win over U.S. policy-makers. They are not alone in having concerns about some of the compromises in Tóth's "composite text," but they have spoken against it strongly and consistently—most recently, before a U.S. House of Representatives national security subcommittee on 10 July. In prepared remarks, Ambassador Donald Mahley, special negotiator for chemical and biological arms control at the U.S. State Department, said that continuing negotiations have become "sterile."

Mahley also described "serious and substantive concerns" with Tóth's compromise language, noting that the United States cannot go along with requirements for "transparency" that could disclose secret data from defense labs or proprietary information from U.S. biotech companies. Restrictions on U.S. industrial exports, he said, would be at odds with trade policy. But he still held out hope, saying the Bush Administration is "grappling with its final decision" on the BWC protocol.

Diplomatic efforts will shift into high gear at next week's meeting in Geneva, where a number of delegations plan an all-out effort to complete the protocol and persuade the U.S. team to go along with it. Rejecting the protocol "would send the message unequivocally that the United States does not care about establishing a stronger regime to prevent biological weapons and their proliferation," maintains Graham Pearson, former director-general and chief executive of the U.K. Ministry of Defence's Chemical and Biological Defence Establishment in Porton Down.

Adds James Leonard, former U.S. ambassador to the United Nations Conference on Disarmament: "A BWC with zero verification provisions stands as a sort of open invitation to do BW, while a BWC with a protocol, even if we think it is rather weak, is a substantial deterrent."

Concealed threat

Biological weapons enjoyed mixed success when they emerged as a strategic threat in World War II. When Japan unleashed fleas infected with bubonic plague on Chinese forces in Manchuria in 1942, for instance, many Japanese soldiers themselves became ill. For the next quarter-century the United States and other countries aggressively developed their biological arsenals, prizing them as potential weapons of mass destruction. In 1969, however, U.S. President Richard Nixon, in a bid to stop other countries from refining their bioweapon capabilities, announced that the United States would dismantle its offensive program. A treaty banning these weapons altogether had great humanitarian appeal; country after country signed the BWC in 1972. In the era of détente, nuclear missiles held the world in thrall, while bioweapons appeared to fade from the military agenda.

That comforting view changed little over the next 2 decades, despite occasional hints that countries were cheating on the BWC. In 1979, for example, dozens of people died of anthrax near the city of Sverdlovsk, now Yekaterinburg. Soviet officials invited suspicious Western experts to Moscow and managed to convince them that the anthrax outbreak came from contaminated beef. (In 1992, Yeltsin acknowledged that anthrax spores had escaped from an MOD lab in Yekaterinburg.)

The mind-boggling scale of Soviet deceit came to light in the 1990s as Western intelligence agencies learned from Soviet defectors Vladimir Pasechnick in 1989 and Kanetjan Alibekov in 1992 about the extent of the Biopreparat operation. By its reported peak in the 1970s, the Soviet bioweapons program, which had begun around World War II, employed an estimated 25,000 or more workers, technicians, and scientists at more than a dozen major facilities.

Russia claims to have made a clean break with the past, but Western experts have lingering concerns about the MOD labs. Russian officials say they cannot shed any light on the MOD lab activities. "They are off limits for national security reasons," says an official with the Agency of Munitions in Moscow. "If I were to ask questions about what goes on in these labs, I could get into trouble." The draft protocol, notes Leonard, would provide "a framework and a trigger" for helping to dispel such questions.

The difficulties of monitoring BWC compliance came into sharper relief after the Gulf War, when the United Nations Special Commission (UNSCOM) went to work in Iraq to ensure the elimination of Saddam Hussein's weapons of mass destruction. With Iraqi officials grudgingly cooperating from 1991 to 1995, the UNSCOM team found loads of circumstantial evidence—facilities with a high capacity for fermentation inconsistent with peaceful purposes as well as irreconcilable records—all pointing to a broad, clandestine program aimed at "weaponizing" bacteria, viruses, and toxins. Despite UNSCOM's sweeping mandate to investigate suspicious activity anywhere and anytime, it wasn't until a son-in-law of Hussein defected in 1995 with damning inside information that the commission was able to further pressure Iraq into acknowledging the extent of its offensive biological weapons program.

The UNSCOM experience crystallizes one of the biggest points of dispute among Ad Hoc Group negotiators at next week's meeting: how to protect national rights while empowering inspectors to determine whether a country is complying with the BWC. The draft protocol—the 16th version of the now-210-page document—would, among other things, allow a future protocol body to mount random transparency visits at declared facilities in precisely defined categories, including maximum containment (biosafety level 4) labs, vaccine facilities, biodefense shops, and plant pathogen containment laboratories. If a facility were suspected of contravening the treaty, the protocol would permit challenge investigations, in which teams of up to 30 investigators would be allowed to remain on site for 84 hours for a lab visit, or 30 days to investigate an alleged field release of a bioweapon.

These provisions, Tóth told the House subcommittee last week, would "create a climate

A Gallery of Rogues

WEAPONS OF MASS DESTRUCTION

Old stand-bys

Anthrax—A staple of bioweapons arsenals for decades, the bacterium *Bacillus anthracis* might be engineered to resist antibiotics.

Plague—In an infamous episode in World War II, the Japanese Army unleashed fleas infected with the *Yersinia pestis* bacterium on Chinese forces in Manchuria. The attack backfired, inflicting heavy tolls on both sides.

Q fever—This disease is transmitted by the highly infectious and heat-resistant *Coxiella burnetii rickettsiae*. Not usually fatal, Q fever could be used primarily as an incapacitant.

Tularemia—One of the most infectious bacteria, *Francisella tularensis* would kill one out of five people in a hypothetical scenario in which 50 kilograms of the weaponized agent were released 2 kilometers upwind from a city.

Smallpox—Eradicated from the wild in 1980, variola major is known to exist in only two restricted laboratories in Russia and the United States. Experts don't dismiss the unlikely scenario of theft or diversion of these stocks.

New possibilities

Aflatoxin—U.S. intelligence reports in 1998 suggested that Iraq was attempting to weaponize aflatoxin, a protein produced by a mold that grows on peanuts and other crops. Aflatoxin is highly toxic in people.

Ebola-influenza hybrid—A flu strain equipped with the hemorrhagic proteins of Ebola, presumably still a fantasy, would be a fearsome weapon.

TOOLS OF ASSASSINATION

Old stand-bys

Botulinum toxin—The most poisonous substance known, a single gram of this crystalline toxin from the bacterium *Clostridium botulinum*, evenly dispersed and inhaled, would kill more than 1 million people.

Ricin—In 1978, Soviet agents used ricin, a lethal toxin extracted from the castor bean, to murder Bulgarian defector Georgi Markov in London.

New possibilities

RNAi—Double-stranded "interference" RNA might be tailored to latch onto specific messenger RNA sequences, thus silencing virtually any gene.

Saxitoxin—Eating shellfish contaminated by this alkaloid neurotoxin, produced by dinoflagellates, can lead to paralysis and death.

Substance P—An aerosolized version of this neurotransmitter could be far more toxic than the potent chemical weapons sarin and VX.

Toxic brews. The United States and other countries are now drafting science briefs describing the state of the black art of bioweapons—including a few of the potential threats highlighted in this table—for the fifth BWC review conference in November. At the conference, signatories will discuss a declaration affirming the treaty that would account for threats that have emerged since the last review conference took place 5 years ago.

SOURCES: CDC, *JAMA*, *JOURNAL OF APPLIED TOXICOLOGY*, WHO

of openness and candor around significant dual-use activities. We are about creating light where there is darkness." U.S. officials disagree. "Illicit biological warfare work could easily be concealed or cleaned up, rendering it highly improbable that international inspectors would detect evidence of noncompliance," asserts the State Department's Edward J. Lacey.

Packaging death. Bomblet filler at Soviet bioweapons plant.

There's the rub, notes a U.S. delegate to the Ad Hoc Group. Weak challenge investigations might provide "a false sense of security," the participant warns. "Under the more restrictive protocol, would you ever really find a smoking gun? ... Is that false sense of security better than nothing?" But negotiators from other countries—and some U.S. experts as well—argue that protocol provisions can deter violators even if they don't necessarily provide access to ironclad evidence. "After all," asks Pearson, "what treaty ever provides such evidence?"

Political endgame

The U.S. is also sparring with its allies over the procedures for facility visits and mandatory declarations of potential dual-use organisms and technologies. Driven by the concerns of the biotech and pharmaceutical industries, the Bush Administration is worried about the inadvertent leakage of trade secrets—vaccines in development, for example. The Administration also fears that visits to government labs could compromise national security. A facility might take pains to ensure that nothing it declares or shows investigators would harm specific security interests. However, claims the U.S. Ad Hoc delegate, by looking at "aggregates of information," an enemy might add things up and find vulnerabilities in biodefenses of the U.S. or its allies.

Negotiators from other countries discount the U.S. objections as primarily politically motivated. When the Ad Hoc Group first began its deliberations in 1995, the British government pressed for more expansive measures that would give the protocol more teeth than the composite text. That put the United Kingdom at odds with the United States on several key issues, including the scope of declarations and site visits. In negotiations since, the British delegates have sought to find compromises that would be acceptable to the United States and other countries without undermining the protocol's effectiveness. The United Kingdom is now solidly in the protocol-enthusiastic camp. "The protocol, in my view, is a very fair compromise," says a senior U.K. official close to the negotiations.

But the protocol has some difficult hurdles to clear. If it wins a vote of confidence in the next few weeks—which will require at least tacit U.S. backing—it would go to a Special Conference in the autumn. If treaty signatories approve it there, the protocol would then go to each country for ratification.

That could be problematic in the United States. Arms-control agreements have not been popular among Republicans in the U.S. Senate, where a two-thirds majority is required to ratify international agreements. It would take a remarkable change of attitude in the Bush Administration to line up enough votes to get the protocol approved.

If the Ad Hoc Group reaches an impasse next month, one U.S. participant doesn't think the years of talks will have been all for naught. The discussions have brought weapons experts from so-called rogue nations that are BWC state parties into the fold and allowed experts from former adversaries to forge more open relationships. "It's much more difficult, in the end, to make a weapon against someone you know," the delegate says, "unless your government compels you to or unless you're truly evil." Of course, without a way to ensure treaty compliance, it will be hard to know who really is evil—until it's too late. **–RICHARD STONE**

INFECTIOUS DISEASES

Malaria's Beginnings: On The Heels of Hoes?

By analyzing DNA of the parasite that causes malaria, researchers are trying to determine the role agriculture played in promoting this deadly disease

How long has the deadly malaria parasite *Plasmodium falciparum* plagued humanity, causing wrenching disease and epidemic death? Since hominids and chimps first went their separate ways? Or only after agriculture created the right conditions for malaria's spread? Scholars have debated this question for decades, but only recently have data become available that might turn theory into fact. By comparing DNA among the various *Plasmodium* species and strains, researchers are attempting to reconstruct when modern *Plasmodium falciparum* first emerged. But, depending on where they look, the DNA is providing different answers—and resolution is nowhere in sight.

Both camps agree that *P. falciparum* has been around in one form or another since the human branch of the primate tree split off from chimps about 8 million years ago. One new analysis, reported on page 482, supports the notion that epidemic malaria traces back to a small population of *P. falciparum* that suddenly expanded exponentially about 20,000 years ago. But another, in press at the *Proceedings of the Royal Society*, suggests the parasite has been common for hundreds of thousands of years, and that malaria took much the same toll on our ancestors on African savannahs as it does today across the globe. "This work is all so new that opinions are unsettled," says Daniel Hartl, a population geneticist at Harvard University.

Although the prevailing view has long

Persistent parasite. After attaching to red blood cells, *Plasmodium falciparum* (yellow) enters the cell, where it differentiates into a gametocyte that is ready to be taken up by the mosquito.

CREDITS: (TOP TO BOTTOM) JUDITH MILLER/*THE NEW YORK TIMES*; MECKES/OTTAWA/PHOTO RESEARCHERS