DEPARTMENT OF BIOLOGICAL CHEMISTRY
HARVARD MEDICAL SCHOOL

Professor Matt Meselson
Harvard University

Matt:

Here is a copy of my letter to The Wall Street Journal which was sent last Thursday.

Elkan

Enclosure

Date: 5/7/84

HARVARD MEDICAL SCHOOL
DEPARTMENT OF BIOLOGICAL CHEMISTRY

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"Letters to the Editor" Editor
The Wall Street Journal
22 Cortlandt Street
New York, New York 10007

To The Editor:

The article "Surveying the Lethal Literature" (The Wall Street Journal, Friday, April 27, 1984) requires comment. Its main thesis is that Soviet scientists are now using modern biological and biochemical methods to develop "previously undreamed of biological weapons" and that this work is due in large part to Professor Yuri A. Ovchinnikov. The basis for the argument is that Ovchinnikov and his colleagues have been studying the chemical components of highly toxic venoms from cobras, scorpions, bees, and other natural sources, and that their papers in the open scientific literature are "the exposed tip of a new (Soviet) germ warfare program". However, your editorial writer, William Kucewicz, does not mention the large volume of similar work that has been and is going on in many laboratories in countries other than the Soviet Union -- including my own laboratory.

The interest in this field is evident from a recent review article (CRC Critical Reviews in Biochemistry, 14, 113-171, 1983) which lists 180 references from more than 60 laboratories in 12 countries. Obviously, this scientific area has excited the imagination of many scientists around the world. Yet in none of these instances, including work in the U.S., is there evidence to suggest motives other than straightforward scientific ones. The fact that all of this work is in the open literature, including the Soviet contributions, is a clear indication that no secrecy is involved in these studies.

There are many sound reasons for the work on toxins. They are extraordinarily interesting, stable proteins which show significant biological properties at very low concentrations. Scientists want to relate the structure of these molecules to their function. Medical uses for this knowledge include: using toxins, in combination with antibodies, to destroy diseased cells without destroying normal cells; learning about the protein

interactions that occur in blood coagulation and in degenerative diseases of the nervous system. The same protein chemistry and gene-splicing methods mentioned in the Journal article are standard in modern biochemistry and molecular biology, and are used world-wide. They are the bases for the exciting developments occurring throughout biological science and medicine today.

Nevertheless, as in many other biochemical fields, the work with toxins could conceivably be perverted to military uses. However, as a member of the National Academy of Sciences of the U.S. and a foreign member of the Soviet Academy of Sciences, I am familiar with the scientific literature and know many of the scientists in the U.S., the U.S.S.R., and other countries carrying out these research efforts. The publication of these results in the open literature and the common goals of scientific discovery suggest to me -- and to colleagues with whom I have spoken since your April 27 article appeared -- that the perversion to military use is not, and was not, an objective of the published Soviet work.

Without access to hard evidence, a similar article could have been written by a Soviet editorial writer about my research, and that of the 60 other laboratories cited above, which have worked in this scientific area but are clearly not involved in biological warfare research. "Guilt by implication" journalism serves no useful scientific or societal purpose and, in fact, may unnecessarily damage our already fragile relations with the other nuclear superpower.

Yours sincerely,

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Surveying the Lethal Literature

By William Kucewicz

Scientific literature from the Soviet Union has often provided a window into its closed society. Soviet scientists, like those elsewhere, are keen to see their work in print, for reasons of peer recognition and communication.

So although the authorities try to guard Soviet secrets, a careful look at the available open literature can provide evidence on Soviet research priorities and problems. In particular, the literature is useful in confirming emigre reports that provide the initial clues on what to look for.

For example, in 1976 a Russian emigre geneticist, Zhores Medvedev, claimed that a massive nuclear accident had occurred in the Soviet Union in 1957. After meeting initial skepticism from Western scientists, he turned up about 100 Soviet studies in the open literature that proved his claim.

Now emigres report a Soviet program to use recombinant-DNA technology to develop previously undreamed of biological weapons. For instance, they cite efforts to implant cobra snake genes into otherwise innocent bacteria and viruses, which could then direct the production of deadly venom in a victim's body.

The quickest way to review the Soviet literature on genetic research on venoms and bacteria is to consult a publication called "Biological Abstracts." Among the titles of Soviet papers, it lists: "Complete amino-acid sequence of phospholipase A2 (isozyme E-3) from the venom of the Central Asian cobra, *Naja naja oxiana*" (1979) and "Interaction of the photoreactive derivative of the neurotoxin from the venom of the Central Asian scorpion (*Buthus eupeus*) with neuroblastoma cell membranes" (1980).

'Sanitized' Results?

A selective search of the literature turns up at least three dozen such papers, dealing with not only Central Asian cobras and scorpions but also honeybee venom, South African cobra venom, Bulgarian viper venom, tetrodotoxin from puffer fish and saxitoxin from marine algae. Most of these toxins are as lethal as the "classic" nerve agents—soman, sarin and tabun—invented but not used by Hitler's Germany. Each report lists several Soviet scientists as authors. The one name that invariably appears is Yuri A. Ovchinnikov, a vice president of the Soviet Academy of Sciences and a member of the Communist Party Central Committee.

Do these papers represent bona fide basic research by Soviet scientists, who may be looking for some new wonder drug? Or are these the "sanitized" results of work on germ warfare? Any single one of the published Soviet research articles would not appear greatly different from basic genetic-engineering research conducted in the West. Beyond doubt there are good scientific reasons to study toxins; genetically engineered drugs could perhaps kill cancer cells while not affecting healthy cells. Yet the volume and structure of the Soviet literature points to another, hideous intention.

"If you just take Ovchinnikov's group, for example, you see them publishing genetic-engineering studies of membrane penetration and various kinds of studies you would expect them to do if they were in the business of 'improving' chemical and biological weapons," said San Diego biochemist Richard Lukens. He has extensively reviewed the Soviet open literature for IRT Corp., a research firm and government consultant. He concluded from the "matrix" of Soviet studies that they are indeed the exposed tip of a new germ-warfare program.

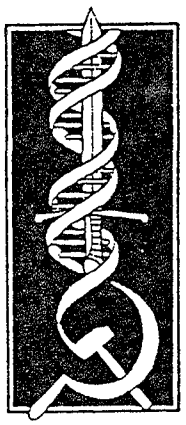
Soviet scientists, for instance, are conducting intensive work on botulin, the most deadly poison known to man, and ricin, an extremely toxic protein of castor beans. Botulin is "10 orders of magnitude" more toxic than the mycotoxins found in "yellow rain," noted Mr. Lukens. And ricin was identified as the poison used in the famous "umbrella assassination" in London in 1978 of a renowned Bulgarian dissident, Georgi Markov, who had been broadcasting scathing commentaries for the BBC.

Just because these poisons are extremely toxic, however, doesn't necessarily make them good military weapons. "There are a lot of properties that a 'bug' has to have to be usable in a military sense, and the intersection between those qualities is not common [in nature]," said one military expert. He noted that a germ-warfare agent has to be able to survive in the environment and to have the capability of being "vectored" to the target—"How do you get your 'bug' from where it is to where you want it to go?" This requires a complete understanding of the genetic "blueprint" of the poisons, the ability to enhance the penetration of membrane and a knowledge of where in the body specific toxins take their effect.

Over more than 15 years, Soviet papers on genetics have followed this exact course. In the late 1960s, the Soviets published works on "mass spectrometric determination of the amino-acid sequences of peptides" and the "synthesis of peptides." This research on genetic structure provided them with a solid foundation to capitalize on the genetic-engineering revolution once the first recombinant-DNA experiments were successfully performed in the U.S. in the early 1970s.

At this point the research emphasis turns from peptides to the amino-acid sequences, or genetic makeup, of various venoms and other neurotoxins. The Soviet scientists next investigated the genetic structures of viruses and bacteria, such as *E. coli*, which exists naturally in the intestines. This is precisely the research path to pursue in order to splice genes producing the venoms into common viruses or bacteria, which in turn would direct the host to begin making the neurotoxins.

BEYOND 'YELLOW RAIN'



THE THREAT OF SOVIET GENETIC ENGINEERING

THIRD OF A SERIES

To aid in this task, the Soviet scientists turned to finding ways of improving membrane penetration and locating the receptors, or "action sites," in the body where different venoms take their deadly hold. "There's a good reason for identifying the action sites," explained Mr. Lukens. "If you know where it's going, you can put on a director that will help it get there." He elaborates: "Say you wanted to hit nerve cells. Then you can put on, say, an antibody for certain molecules that you find on the surface of nerve cells." Once in the body, the antibodies would naturally seek out the molecules on the nerve cells and then the toxins would attack the nervous system. "It would make your nervous system inoperable and you die," he said.

Not everyone who has investigated the Soviet papers is so certain that they necessarily indicate a germ-weapons program. "I think the open literature you can go either way on," said one Pentagon science expert, who like other government officials interviewed for this series asked not to be named. "There are so many commercial, practical, medicinal applications for the damn thing, all of those in essence could be misused in some way if somebody wanted to do it."

Other military experts are impatient with such explanations. An Air Force specialist in biochemical warfare observes, "We're still trying to get the military to face the 1944 threat" of nerve agents such as soman and tabun. With the advent of genetic engineering, he adds, "you're talking about a subject where I can make anything I please, and it expands to the point of boggling the mentality of people who are trained to think about it—much less the military. It's a very difficult problem to get them to cope with it."

At the very least, the open literature is fully consistent with the emigre reports of a genetic-warfare program. In Soviet society, the priority given Prof. Ovchinnikov's program in terms of money and manpower points to a military emphasis. And another kind of Soviet literature—military writings—bears this out. In particular, the 1983 edition of the Soviet Military Encyclopedia, as translated by the U.S. government, has some highly relevant passages.

"The rapidly developing industry in microbiology can be switched over from its peacetime mission of producing antibodies, vitamins, enzymes, proteins, amino acids, and microbiological organisms for protecting plants to the production of pathogenic microorganisms," it says. "This considerably complicates the capability for effective international monitoring of the ban on biological weapons."

Scientific achievements such as genetic engineering, the military document continues, "have led to an increase in the effectiveness of biological agents as a means of conducting warfare." Moreover, it warns that "the threat of biological-weapons employment by the imperialist states demands that effective preparation be made for the sanitary and anti-epidemic protection of the troops and civilian population. . . . The readiness of the troops to conduct combat operations in a situation in which biological weapons are being used and familiarization of the entire population with protective measures against infection make it possible to considerably reduce losses from this weapon of mass destruction." (It should be noted that the U.S. began to expunge references to biological warfare in its military handbooks after the Biological Weapons Convention took effect in 1975.)

Contrary to Weapons Convention

Furthermore, the Soviet Military Encyclopedia rejects the sharp distinction made by Western officials between chemical weapons and biological or toxin agents. The Soviet document says that due to the developments in biotechnology, "the boundaries between the biological and chemical weapons are erased, since all biological processes depend on chemical or physiochemical reactions. Bacterial toxins (botulin, for example) produced by living organisms, but themselves not reproducing, and previously considered to be biological (bacteriological) weapons, are now classed as chemical means of destruction."

This interpretation is contrary to the Biological Weapons Convention, signed by 111 countries including the Soviet Union. The framers of the convention specifically classified toxins as prohibited biological weapons, and banned their manufacture or possession in anything beyond small quantities for research.

Most revealing of all, the Soviet Military Encyclopedia specifically discusses neurotropic toxins, which attack the nervous system, including botulin, staphylococcal enterotoxin, ricin, crototoxin, taytoxin, bungarotoxin and cobra neurotoxin. "The neurotropic toxins are the most toxic chemical substances of all known toxic agents," it says. "Their harmful effect is based upon their capacity to inhibit the membrane receptors responsible for nerve impulse transmission. Under combat conditions they can be used as an aerosol or in a solid or liquid state in mixed elements or ammunition; they can also be used for sabotage purposes."

Mr. Kucewicz is a Journal editorial writer.