Chapter IX: The Anti-plague System of Ukraine

1. History of Ukraine's Anti-plague System

Unlike other nations covered in this report (with the exception of Belarus and Moldova), Ukraine has no natural plague focus. The republic nevertheless needed to establish an AP system because throughout history its ports have been important passageways for the movement of plague from the Far and Near East to Russia and Europe. In particular, through the centuries ships carrying rodents infected with plague have arrived at Black Sea ports, particularly Odessa, Mykolayiv, and Kherson. The ships offloaded cargo along with plague-infected rodents and the people who then were instrumental in spreading the disease northward. That fact that such incidents occurred many times in the past is evidenced by the presence of eight separate cemeteries in Odessa that only contain graves of plague victims, representing the eight plague pandemics that occurred during 1793 – 1910. So, while the Ukraine AP system is small in size compared to other NIS, with just two facilities, it has a long history and remains important to Ukraine's public health today.

The main mission of the Ukrainian AP system since its establishment has been to interdict plague originating from foreign ports and preventing it from becoming established in Ukraine and spreading elsewhere. Therefore the two Ukrainian AP facilities responsible for fulfilling this mission are located in strategically important cities, namely Odessa and Simferopol.

Odessa

Due to the importance of Odessa as a transit point for plague, possibly the first plague epidemic control facility in the world was established in the city in 1886 by the renown Ukrainian scientists I.I. Mechnikov, M.F. Hamaley, and Y.Y. Bordakh, and named the Odessa Bacteriological Station.[166] After having gone through several name changes, in 1965 it was renamed the I.I. Mechnikov Odessa Scientific and Research Institute of Viral Diseases and Epidemiology.

In a parallel development, the Odessa Port AP Laboratory was founded within the Odessa harbor by epidemiologist M.A. Minchin in 1937. This was apparently done after the League of Nations requested the Soviet government to establish a plague laboratory because of fears of plague being imported into Europe through the Odessa harbor. This laboratory was renamed the Odessa AP Station in 1970 and, in 1997, after Ukraine's independence, was reorganized into the State AP Station of Ukraine.

The latest AP system-related development, in 1999, was that the I.I. Mechnikov Odessa Scientific and Research Institute of Viral Diseases and Epidemiology and the State AP Station of Ukraine were merged and the resulting institution was named the I.I. Mechnikov Ukrainian Scientific-Research Anti-plague Institute (hereafter Mechnikov AP Institute).[167] It is located on Tserkovna Street in Odessa city, a few miles east of a famous landmark, the Potemkinsky Stairs.[168]

Going back to Soviet times, lacking natural plague foci, plague bacteria can be found only at Ukrainian seaports in infected rodents or their ectoparasites. Therefore the most important, and dangerous, task for the Odessa AP Station throughout the Soviet era was to catch rats and mice on ships and around the harbor and culture them and their ectoparasites for pathogens. In addition to plague bacteria, over the years the station has recovered bacteria from rodents that cause cholera, tularemia, leptospirosis, and brucellosis. Beyond Odessa, the station was responsible for monitoring the situation related to plague, cholera, anthrax, tularemia, and leptospirosis in the western and northwestern parts of the USSR, although its activities were mainly undertaken in Ukraine and Moldova. Its major responsibilities were to eliminate these diseases as much as possible and to train local health officials on how to handle and test dangerous pathogens. The station worked under the Rostov AP Institute, and reported to the Ukrainian SSR MOH, which in turn reported to the Soviet MOH.

Before 1985, all of the Odessa station's work was secret, meaning that it had no contacts with any institute outside the Rostov AP Institute and other Soviet AP facilities. The station's scientists were not allowed to publish in the open literature, although some of its staff members published articles in parochial publications, such as those published by Mikrob and the Almaty AP institute. When reporting on its work, Odessa scientists had to use code words for diseases; for example, "Form 10" represented plague. With the institution of *glasnost* soon after Mikhail S. Gorbachev was elected as the General Secretary of the Communist Party Central Committee in March 1985, some of the Odessa AP station's work became public knowledge, but some remained secret. For example, the station was not allowed to reveal the number of victims of cholera, plague, tularemia, and other disease outbreaks to anyone outside the Rostov AP Institute and MOH. The first foreign visitor to the Odessa AP station, from Bulgaria, was received in 1986, but visitors from the West were not allowed until two Israeli scientists came as part of a team from the WHO in 1991. The first U.S. citizen to visit the station did so in 2000.

In the 1980s, the station employed between 120 and 130 staff members on an average, including 30 doctoral-level scientists. Usually, it would dispatch five or six field expeditions per year. Field teams could be as small as three persons or, if there was an active epidemic, up to 40-50 persons. When necessary, the Ukrainian MOH augmented teams with experts from other institutes. Teams were routinely sent to study natural foci of tularemia, cholera, CCHF, and others. For example, there were 24 *oblasts* in Ukraine and the Crimea that possess natural tularemia foci. Periodically, tularemia becomes a serious problem and large-scale outbreaks occur. For example, during 1946-1948, there were two large-scale tularemia outbreaks in the Odessa region. The reasons appears to have stemmed from the recently concluded World War II; due to a shortage of farm workers harvests lay abandoned in the fields, allowing for a tremendous increase in the rodent population that carried tularemia bacteria. Eventually, approximately 50,000 people became ill with tularemia. Although sporadic cases of tularemia occur with some frequency, since the 1940s outbreaks, Ukraine has not suffered any large-scale tularemia epidemics.

The Odessa AP Station was well supported in Soviet times so it could do all the work that it was assigned. This situation continued for the first year of Ukrainian independence, roughly through 1992. At that time, a doctoral-level scientist earned about 500 rubles per month, while a regular scientist was paid about 300 rubles per month. In addition, AP workers were paid extra bonuses when they worked with dangerous pathogens. This was a time when a person living in Odessa paid 10-12 rubles per month for a nice apartment and 20 kopeks (100 kopeks per ruble) per liter of gasoline. In general, in Soviet times scientists were considered members of a highly honored profession and were compensated accordingly.

Since the end of 1992 and beginning of 1993, the station's financial situation became dire because it did not receive funding on a regular basis from the government. Payments of salaries often were delayed and their amounts were substantially less than in Soviet times. In addition, the price of everything rose rapidly, which made it almost impossible for the station to continue doing serious work. There were several years when no field expeditions were sent out or, if one was sent out, its membership was small and remained in the field for no longer than a few days. It has only been in the last couple of years that the station's situation has improved somewhat so that it can at least perform its most important functions. Hence it has had an important role in efforts to control and eliminate cholera in recent times. Although cholera is not endemic to Ukraine, it is often imported; for example, in recent times Ukraine experienced cholera outbreaks in 1991, 1994, and 1995.

The Mechnikov AP Institute, established in 1999,[169] has slowly grown. In 2004, it employed 208-210 persons, including 43 doctors and 10 laboratory assistants who perform scientific research in the first two departments, while 30 doctors and 25 assistants work in the third and fourth departments.

Salaries at the time of the CNS staff's visit for institute workers remain much lower than in Soviet times. For example, in 2004 a deputy director was paid 600 hryvnias (HR) (about $113) per month. A regular scientist received about 400 HR ($75) per month and a new scientist about 250 HR ($47) per month. For comparison, a family needed about 2,500 HR ($472) per month to live decently in Odessa. Of this amount, a worker pays between 80 and 150 HR ($15-28) per month for a reasonably comfortable apartment, although apartment rents continue to climb.

The new institute's organizational structure and responsibilities were as follows. In 2004, the institute's director was Dr. Yurii Boschenko. Under the director, there were three deputy directors. The first was in charge of the administration and accounting, while the other two have scientific responsibilities. The first, Dr. Lev Y. Mogilevsky, was in charge of the Department of Especially Dangerous Bacteria and Virus Research, encompassing all work dealing with Groups I and II bacterial and viral pathogens. The second deputy director of science was in charge of the Department of Prophylaxis of Plague and Other Especially Dangerous Infections, a practical department that performs fundamental research on vaccinations, diagnostics, and the like. In 2004, Dr. George Stepanovich Skriptenko was the deputy director.

The Department of Especially Dangerous Bacteria and Virus Research had the following laboratories:[170]

- Laboratory of epidemiology
- Laboratory of especially dangerous bacterial natural infections
- Laboratory of especially dangerous virus infections
- Laboratory of the ecology of especially dangerous strains
- Laboratory of ecology of carriers and vectors of especially dangerous strains
- Laboratory of slow infections (prions) and AIDS

In general, the Department of Especially Dangerous Bacteria and Virus Research concentrated on performing research to clarify the evolution and development of natural foci of tularemia, leptospiroses, psittacosis, cholera and other vibrios, and arboviruses. In recent years, it developed a particular interest in arboviruses related to birds—such as CCHF virus and West Nile fever virus—because southern Ukraine is a major transit point for birds migrating from Africa to Europe and some are carriers of these viruses. However, until 2004, this department had never studied the CCHF virus directly.

The Department of Prophylaxis of Plague and Other Especially Dangerous Infections has the following laboratories:

- Laboratory of cytopathology and morphology
- Laboratory of genetics and selection of especially dangerous bacteria and viruses
- Laboratory of chemical therapy and immunological preparations

The Department of Prophylaxis of Plague and Other Especially Dangerous Infections' main objectives were to improve vaccines against tularemia and rabies. In addition, the institute had two specialized departments. The Department of Licensing performed research on inventions that result from the institute's work, to determine whether any of it can be patented. If it is determined that a patent is advisable, the department was in charge of filing patent applications. The Department of Organization of Prophylaxis of Plague and Other Infections was responsible for providing expert assistance to the SES regional stations. It had four small laboratories: the Epidemic oversight center, the Bacteriology laboratory, the Virology laboratory, and the Laboratory of carriers and vectors. This department did only practical work, such as identifying microorganisms and helping diagnose diseases.

The institute had a fairly sizeable collection of pathogens, although its administration claimed to never have had, nor have now,[171] any cultures of group I pathogens.[172] Whenever institute scientists work on a group I pathogen, it is destroyed after this work is completed. Further, the institute tries to limit its collection of non-group I pathogens, keeping only reference and atypical strains.

In 2004, the state of the institute's biosecurity was of questionable efficiency. As for physical security, the institute was better guarded than most AP facilities that CNS staff has visited, but not as well as it should be. The wall and fence surrounding the institute could be improved and more surveillance cameras would enhance biosecurity. In 2004, there was no particular threat to the institute from outsiders. There was no terrorist activity in the area. Although Odessa is the home to many criminal enterprises, some of who have international reach, to date none had bothered the institute. As far as the institute security staff was aware, there had been no unauthorized attempt to enter the institute.

Simferopol

The second AP facility in Ukraine is the Crimea AP Station,[173] was founded in 1971 in response to cholera pandemic that originated from Alexandria, Egypt, but that came to affect southern Ukraine. Odessa was especially hard hit, suffering approximately 125 victims, but cholera also spread throughout the Crimean peninsula.[174] The station's original mission was to provide advice, develop standard procedures, and carry out specialized work on cholera. Its first director was Galina Fedorovna Mitsevich, who previously had been the director of the Crimea Region Sanitary Epidemiological Station. The Crimean AP Station was built at Maryino, a suburb of Simferopol, where it remains today. Simferopol is located in approximately the middle of the Crimean peninsula, about 250 kilometers southeast of Odessa. The Crimean AP Station is comprised of a one-story stone building, an infectious material facility, and other working areas.

By 1976, the station's responsibilities went far beyond cholera in the Crimean peninsula; it was responsible for disease monitoring in eight regions of eastern Ukraine, as well as the seaports of Berdyansk, Mariupol, and Kherson. A new branch of preventive medicine at that time was border sanitation, which involves preventing the importation and spread of quarantine diseases from abroad. This work included developing plans for epidemiological surveillance and helping medical institutions prepare for epidemics. This type of work soon became the station's major occupation. By the 1980s, the station had begun monitoring the natural foci of diseases such as tularemia, anthrax, leptospiroses, brucellosis, and yersiniosis. In 1986, the station opened a virology laboratory to study tick-borne encephalitis, CCHF, hemorrhagic fever with renal syndrome, and West Nile fever. In this work, the station collaborated with specialists from many cities in Russia, including Nizhny Novgorod, Kaliningrad, Lipetsk, Murmansk, Rostov-on-Don, Chita, Krasnodar, and Elista, as well as cities in former Soviet republics that now are independent states, including Baku in Azerbaijan; Yerevan and Spitak in Armenia; Tbilisi in Georgia; Almaty, Aralsk, and Kyzyl-Orda in Kazakhstan; Tashkent, Andizhan, and Termez in Uzbekistan; Minsk in Belarus; Vilnius in Lithuania; and Riga in Latvia.

It is claimed that research at the Crimean AP Station led to a number of discoveries, including the identification of five phages that analyze non-01 serogroup cholera vibrios; the first isolation in Crimea from humans and the environment of halophilic and other rare vibrio species, *Yersinia enterocolitica*, and pseudotuberculosis pathogens. In addition, the station's investigators are said to have discovered and mapped natural foci of tularemia, leptospiroses, intestinal yersiniosis, tick-borne encephalitis, CCHF, and hemorrhagic fever with renal syndrome. The station's members have reportedly presented over 300 reports to international, all-union, and republic congresses, symposia, and conferences; published over 230 scientific papers in various journals; and defended 1 doctoral dissertation and 4 candidate dissertations.

In 1991, the Crimean AP Station became a part of the Ukraine MOH. However, as a result of serious economic difficulties in Ukraine, the station was downsized. Most important, the virology laboratory was closed and some experienced senior staff departed. In 1997, Aleksandr B. Khaitovich, Doctor of Medical Sciences and Professor at the Crimea State Medical University, was appointed head of the station and began working to reestablish its reputation in Ukraine (Khaitovich was still the station's head as of December 2004).[175]

In 2001, the station celebrated its 30th anniversary. Attending the ceremonies were the Chairman of the Presidium of the Supreme Council of Crimea Autonomous Republic, representatives of Ukraine's President in the Crimea Autonomous Republic, representatives of the Ukraine and Crimea Ministries of Health, the Chief State Sanitary Physician of Crimea, and directors of various government agencies. The program honored important achievements made by the station. Twenty staff members received recognition and awards from the Supreme Assembly of Crimea Autonomous Republic, the Council of Ministers of Crimea Autonomous Republic, and the Ukraine and Crimea Ministries of Health.

The Crimean AP Station currently provides health-care institutions with advisory, methodological, and practical assistance concerning border controls, prevention, and control of quarantine and other high-risk infectious diseases. Furthermore, it appears that the Crimean AP Station simultaneously serves as the Republic AP Station for the Autonomous Republic of Crimea.[176]

2. Public Health Activities of the Ukrainian Anti-plague System

As in other NIS countries, the state SES has the main responsibility for promoting and sustaining public health, including controlling communicable diseases and assuring environmental protection. Ukraine's AP system appears to have a very small role in public health as demonstrated by the fact that it is not even mentioned in a report published by the WHO Regional Office for Europe, which probably provides the most thorough and current overview of Ukraine's health system.[177]

The SES's main responsibilities are epidemiological surveillance, investigations of infectious disease outbreaks, monitoring food and water supplies, and identifying environmental hazards. In 2000 the SES was comprised of 778 stations and 28 disinfecting stations. At that time it employed approximately 65,000 persons, including about 11,000 medical doctors and 27,000 mid-level health workers. Its budget was part of the national budget administered through the MOH.[178]

Most of the epidemiological studies of the most dangerous infections found in the Ukraine are performed by the SES.[179] There are 30 laboratories at regional SES centers that perform initial investigations of disease outbreaks. The Central Sanitary-Epidemic Station of the Ukrainian MOH in Kiev is responsible for quality control at the regional SES laboratories, investigating errors and mistakes at regional SES laboratories, and assessing the performance of regional SES laboratories. It also provides training to the staff of regional SES laboratories on how to handle and transport samples containing dangerous organisms. It serves as a reference laboratory for all Ukrainian clinical laboratories.

In terms of the public health activities of Ukraine's AP system, there is no available information on the public health activities of the Crimean AP Station. According to the available information on the Mechnikov AP Institute's public health activities, it is probably low. The problem is lack of money; the institute's total budget in 2002 was only 1.2 million HR ($226,000). This sum appears to be sufficient to allow the institute to operate at a low level of activity, but is not enough to purchase new equipment or sufficient supplies. As far as our observations could discern, the station's ability to perform field studies is extremely limited. Our estimate is that many of the functions that were responsibilities of the AP system in Soviet times have been taken over by the SES since Ukraine's independence.

As mentioned previously, Ukraine has no natural plague foci. However, the country has problems with other dangerous diseases including anthrax, listeriosis, tularemia, brucellosis, cholera, rabies, and rickettsiosis. Further, Ukraine has some "polyinfectious" natural disease sites—sites where several types of infection exist at the same time—for example, tularemia and listeriosis. It experiences several cases of human anthrax per year and isolates of *B. anthracis* can be readily recovered from several environmental sites. Ukraine occasionally has had some cases of brucellosis, but they always were imported, usually from Turkey and Italy. Rabies, which is mainly carried by red foxes, is a continuous problem for Ukraine (as well as neighboring Germany and Poland), so AP researchers monitor the main natural reservoirs of this virus.

Waterborne infections have historically presented pressing and difficult problems to Ukraine. Of highest importance has been cholera, although typhoid fever, shigellosis, and hepatitis A and E have also been problematic.[180] In recent times, Ukraine experienced a serious cholera outbreak in 1991, caused by the contamination of the Dunay River, which originates in Rumania. The largest cholera outbreak since the 1920s, was in 1994, affecting over 2,500 persons. Contaminated waters of the river South Bug were responsible for the 1994 epidemic, with the contamination having originated in Dagestan. This outbreak continued in 1995. During 1997-2002, approximately 3,000 persons contracted hepatitis A by drinking contaminated water. Contaminated waters from shaft wells and reservoirs still remained a large problem for public health in Ukraine the time of this report. In general, cholera is most prevalent during June-September; during these months all regional SES stations have to report on local cholera status every two weeks. If any cholera isolates are recovered, the facts about them are supposed to be posted on the World Wide Web.

Ukraine has a national system of epidemiological surveillance that appears comprehensive and well organized, comprised of "…sanitary-epidemiological stations, anti-plague institutions, and scientific and research institutions of epidemiological specializations." In addition, there supposedly are "…91 sanitary units [that] act in international airports, sea and river harbors, highways and railroad stations."[181] However, according to interviews, in general the Ukrainian public health system is neither well run, nor efficient, nor comprehensive. This is mostly due to it being considerably under-funded. As an AP scientist confided, "we usually learn of disease outbreaks elsewhere in Ukraine from newspapers or television, and then in the most sensationalist and unreliable terms."[182] The questioning of other scientists throughout Ukraine elicited similar comments, to the effect that there is no central system of conveying epidemiological information of importance to public health workers and the ability of both SES and AP facilities to undertake epidemiological investigations is very low or non-existent.

It bears noting that one a governmental level, the Soviet era biosafety/biosecurity procedures were starting to be replaced in 2004 as the Ukrainian government was developing its own procedures under the direction of the Chief State Sanitary Doctor.[183] The government was following the WHO biosafety guidelines in this endeavor. The first Ukrainian protocol for biosafety procedures was to come into effect in early 2005; they deal with methods for working with group I and II pathogens. The second protocol was to be completed in late 2005; it deals with preparing for and responding to the importation of especially dangerous infections. We do not know if either protocol has actually been completed and adopted by the Ukrainian legislature.

3. International Activities That Involve the Ukrainian Anti-plague System

Before 2004, the Mechnikov AP Institute received no support from either international or other foreign sources. It had no sources of funding from outside sources at all; for example, it does not rent out space or perform contract research for private parties. Although we are not certain about the funding situation at the Crimean AP Station, as far as the authors are aware no Westerner has ever visited it. It therefore is unlikely that it has any support from international sources.

Perhaps the Mechnikov AP Institute's first involvement with foreign collaborators was in regards to the wetlands restoration projects during 1999-2003 that were supported by the EECNET Action Fund (EAF), whose main sponsors are Dutch agencies and nongovernmental organizations. These projects probably only paid for direct expenses incurred by institute researchers.

Theoretically, any Ukrainian biomedical institution that once had connections to the Soviet BW program could get projects funded by the STCU if they were deemed scientifically valuable. For the first time, researchers from the Mechnikov AP Institute (with collaborators from the I.I. Mechnikov Odessa National University and A.V. Bogatsky Physico-Chemical Institute in Odessa) developed a proposal called the "Elaboration of a system for drug-design and selection of effective anti-herpetic preparations using modern computer technologies," that was funded by the STCU in 2004 for the amount of $183,320. The Mechnikov AP Institute was awarded a second STCU project in December 2005, receiving almost $200,000 for a project on tularemia control, and a third in 2006, again for about $200,000, which involves nanotechnology and vaccine development. It can be expected that as its staff learns how to write proposals, the Institute will become more successful in having its proposals accepted by the STCU.

In September 2005, the Mechnikov AP Institute entered into collaboration with the U.S. Naval Medical Research Unit 3, based in Cairo, Egypt, to sample wild birds for avian influenza. By early 2006, more than 2,000 birds had been sampled.[184] This collaboration continues at the time of this writing, but how it is funded, or the amount of funding, has not been published.

Another promising development for Ukrainian biological sciences in general was that on August 29, 2005, Ukraine and the U.S. signed the Nunn-Lugar Biological Agreement (CTR Program). Under this agreement, the U.S. promises to assist Ukraine to:

- Upgrade the security for pathogens currently stored at various health laboratories throughout Ukraine;
- Significantly reduce the time required to accurately diagnose disease outbreaks in Ukraine and assess whether they are natural or the result of a terrorist act; and
- Allow for cooperation in developing better diagnostic tools and treatments to protect both U.S. and Ukrainian populations against infectious diseases. This includes leveraging U.S. laboratory capabilities to improve detection of endemic diseases in Ukraine.[185]

It is unclear how much funding this agreement will bring to Ukrainian biological sciences. At the time of the agreement, $15 million was promised the Ukrainians. However, this amount has been increased by over 100 percent by 2007, and may be further enlarged. Our estimate is that the Mechnikov AP institute and the Lviv Scientific and Research Institute of Epidemiology and Hygiene of the MOH[186] will receive the lion's share of this new funding.

4. Analysis of the Ukrainian Anti-plague System's Weaknesses and Proliferation Potential

There was no Soviet offensive BW facility in Ukraine, but the Lviv Scientific and Research Institute of Epidemiology and Hygiene was an important Problem 5 institution whose work program was classified. No foreigner was allowed to enter its premises until 2002. Since it did not belong to the Soviet AP system, it will not be discussed here further except to state that since it performed strictly defensive R&D, the proliferation threat it poses is probable low.

As for the Mechnikov AP Institute, its management claimed in 2003 that it knew nothing about either the Soviet offensive or defensive BW program. We question the second since it was in effect a closed facility until the late 1980s and worked on highly dangerous Group II pathogens and, probably, at least at time on some Group I pathogens since at least 1965. It would make sense if at least one of its laboratories worked on Problem 5 projects. Yet, as far as the authors can discern, the institute has a good safety record.

As for biosecurity, the Mechnikov AP institute is fairly well guarded and is surrounded by a high wall. It would be difficult for outsider to gain unauthorized access to its laboratories. Nevertheless, the possibility that insiders could supply pathogens from the institute's culture collection to unauthorized persons is a distinct possibility. In addition, it is equipped with some better than adequate equipment and associated supplies. For these reasons, the Mechnikov AP Institute does pose a not inconsiderable proliferation threat.

Since Ukraine henceforth will benefit from the CTR Program, we expect that the biosecurity aspects of the Mechnikov AP institute will substantially improve by 2009. Already plans are being developed for rebuilding its BL3 laboratory so that is will meet WHO standards for such a facility. When this and other biosecurity measures have been instituted, they will serve to substantially decrease whatever proliferation threat the institute now poses.

As for the Crimean AP Station, the authors have no way to assess its proliferation potential or whether it presents any biosafety or biosecurity threats.