

DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR BIOLOGY
HARVARD UNIVERSITY

7 Divinity Avenue
Cambridge, Massachusetts 02138



September 9, 1986

Dr. Peter Nicolaevitch Burgasov
Deputy Minister of Health
Rachmanovsky, 3
Moscow, USSR

Dear Dr. Burgasov,

First of all, I would like to express my appreciation for the kind and generous hospitality you and your colleagues extended to me in Moscow.

I enclose a copy of a memorandum summarizing our discussions. If you find in it anything I have misunderstood or if I have neglected any important points, please let me have your corrections and additions.

I do believe that we have already accomplished much that is worthwhile and I am making every effort to complete the three projects we mutually agreed to pursue, as listed at the end of my memorandum.

The manuscript you and Professor Nikiforov prepared is being translated. When this is done, I will immediately read it, acting as a scientific reviewer. I will then return it to you for final revisions before submitting it to a suitable English language journal, as we discussed.

I enclose some photographs which remind me of the pleasure it was for me to meet you and your associates.

Sincerely yours,

Matthew Meselson
Professor of Biochemistry
and Molecular Biology

Burgasar

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DISCUSSIONS IN MOSCOW REGARDING SVERDLOVSK ANTHRAX OUTBREAK

Matthew Meselson
September 5, 1986

At the end of June I visited Dr. Martin Kaplan, Secretary General of the Pugwash Conferences in Geneva. I asked him to renew an earlier request he had made to Soviet officials on my behalf to visit the USSR in order to obtain information regarding the outbreak of human anthrax that occurred in the city of Sverdlovsk in April and May, 1979. On July 7, Kaplan met with Soviet CD Ambassador Viktor Issraelyan and passed on my request. On August 23, I received a call from the Soviet embassy in Washington, inviting me to visit Moscow to speak with scientists at the Ministry of Health. I asked for definite confirmation that the subject would be the one raised with Issraelyan. A few hours later, the Soviet Embassy called back to say that this was indeed the subject, and I agreed to go. I left for Moscow on August 26 and returned home August 30.

On August 27-30 I met in Moscow with four Soviet physicians who attended patients in Sverdlovsk during the outbreak and investigated its origin. These individuals are:

Peter Nicolaevitch BURGASOV
State Hygienist-in-Chief of the USSR
Deputy Minister of Health
Member of the Soviet Academy of Medical Sciences

Vladimir Nikolaevitch NIKIFOROV
Head, Department of Infectious Diseases,
Central Postgraduate Institute,
Corresponding Member of the Soviet Academy of Medical Sciences

Ivan Semenovitch BEZDENEJNICH
Chief Epidemiologist of the Russian Federation

Olga Veriaminovna YAMPOLSKAYA
Assistant to Professor Nikiforov

Bezdeneynich and Nikiforov are the authors of a paper on the Sverdlovsk outbreak published in the Soviet Journal of Microbiology, Immunology and Epidemiology, Number 5, 1980, pages 111-113.

Also participating were:

Viktor S. Voskresenskiy
 Deputy Chief, Department of Infectious Diseases
 Ministry of Health
 formerly Medical attache at Soviet Embassy in Washington D.C.
 Viktor Petrovich Nikulin
 Department of Infectious Diseases
 Ministry of Health

During some meetings and meals and on the way to and from the airport there also was:

Andrey Petuchov
 Protocol Department
 Ministry of Health

Drs. Yampolskaya and Voskresenskiy interpreted. Burgasov, Voskresenskiy and Petuchov have visited the US. The discussions took place Wednesday afternoon and all day Thursday and Friday in the office of Professor Nikiforov at the Botkina hospital and in an adjacent classroom. We also met over meals at the Hotel Sovietskaya, where I stayed. The discussions were informal and proceeded largely in response to my questions. In addition, Bezdenejnich and Nikiforov each gave an organized presentation of about an hour and a half, on epidemiological and clinical aspects, respectively.

I asked my hosts to drive me to the US Embassy on Friday morning. I had breakfast with ~~the charge~~ ^{E.} ~~Mr.~~ ^{Jr.} Richard Combs, and summarized for him the discussions of the two previous days.

Minister - Counselor

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The following is a summary of the discussions:

1) Anthrax is endemic in the Sverdlovsk region. From 1949 to 1978 there were 156 known outbreaks of animal anthrax at 32 sites in the Sverdlovsk oblast, an administrative area of 194,800 square km surrounding the city.

2) Nearly 2 million persons are inoculated against anthrax each year in the Soviet Union, usually in the Spring. Those inoculated are slaughterhouse workers and other groups at risk. In high incidence areas, such as Sverdlovsk, this includes private owners of meat animals. The vaccine used is a live unencapsulated strain developed by Ginzburg. The effectiveness of the vaccination in man is not reliably known. Immunity is thought to develop in 12-14 days and to persist for about a year. Large numbers of animals are also inoculated.

3) In the Spring of 1979 there was a major outbreak of human anthrax in Sverdlovsk. It is the largest on record in the USSR. Altogether, there were 96 cases and 64 deaths. The first case presented April 4 and the last May 18. There were 11 cases of pure cutaneous anthrax and 6 cases of cutaneous with systemic involvement. All of these 17 patients survived. All of the remaining 79 cases and all of the 64 deaths were gastrointestinal anthrax. The largest previously reported outbreak of gastrointestinal anthrax in the USSR occurred at Yaroslavl' in 1927. Consumption of infected sausage caused 27 cases, all of them fatal.

4) The Summer of 1978 was unusually wet. Supplies of fodder were reduced and there were food shortages. It was decided to make available to private owners of meat animals an animal feed supplement known as "bone-flesh powder". This is slaughterhouse waste and grain ground up and dry autoclaved. The autoclaving is done to sterilize anthrax spores and other infectious organisms. Reports of animal anthrax caused by the consumption of such powders exist in the literature, including reports of animal anthrax in Great Britain caused by ~~feed~~ powders imported from Africa. The technology used in the present case was developed at Bogdanovichi, 100 km east of Sverdlovsk. The powder was then made at 11 different slaughterhouses in the Sverdlovsk oblast.

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5) The outbreak of human anthrax was traced to privately slaughtered animals whose owners had made purchases from a single 29 ton lot of contaminated bone-flesh powder. This lot was made at a meat processing plant at Aramil, about 15km southeast of central Sverdlovsk. It was put on sale March 25 and sold out by March 29. The first known associated case of animal anthrax occurred March 29. Later investigation showed that sterilization procedures at the Aramil facility were not properly carried out. Autoclave pressure readings were not taken; the raw material and the autoclaved material were handled in the same area and were transported in the same wheelbarrows, ~~and no~~ ^{and the powder was not} microbiologically ^{tested} ~~analysis was carried out.~~ ^{by me being sold.}

6) In subsequent laboratory tests, Bacillus anthracis was isolated from samples of the Aramil powder, from infected meat and from human victims. All of these isolates were judged to be of the same strain. The tests done were studies of capsule morphology and titrations of virulence in white mice.

7) The animals with anthrax were mainly sheep and some cows. A few pigs had milder cases. The epizootic affected 8 different villages and settlements in the area. The contaminated meat was sold at private markets in southern Sverdlovsk and suburbs. It is estimated (how?) that hundreds or even a few thousand persons ate infected meat. Common cooking methods do not adequately inactivate anthrax spores.

8) Contaminated feed and infected meat were destroyed by open air burning. About 30 buildings where possibly infected animals were slaughtered and butchered were burned. Burning was done after dousing with gasoline. Burning sites were typically left as is, not covered over with asphalt or such. (However, the road from Aramil south to Chelabinsk was being widened and presumably surfaced at the time.) Refrigerators and certain other surfaces suspected of contamination were disinfected with chloramine. As prophylaxis, members of patients' families were given antibiotics. ~~No~~ B. anthracis was found in air samples from hospital wards and apartments of patients or in samples from vacuum cleaners, walls, dishes, and furniture, supporting the ^{generally accepted} view that there ~~was~~ little danger of contagious spread of the disease from anthrax patients.

9) Road-blocks were set up to prevent uninspected meat from entering the city. There were three cases of anthrax among street dogs but none among cats. Approximately 300 street dogs were exterminated.

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10) Warnings against consuming meat from private sources, citing the risk of anthrax, were published in local papers and distributed as posters and leaflets. I requested and was given original copies of these, the earliest of which is dated April 14. Warnings against consumption of privately produced meat were also broadcast by local radio stations.

11) Starting April 4, the number of cases of human anthrax presenting in hospital each day through April 19 was 5,5,5,7,7,6,10,9,7,5,4,4,1,0,0,1. The number of presentations from April 20 to the last case, on May 19, was 20. No two of these last 20 cases occurred on the same day.

12) The age-distribution of cases through April 19 was

under 20 years	1	40-49	32
20-29	11	50-59	10
30-39	10	over 59	12

The only child was a 6 year old girl, who survived. Males accounted for 67% of the cases and females for 33%. Approximately 70% of the cases lived in (or presented in?) the southern half of the city and 30% in the northern half. No two cases occurred in the same household. No transmission from man-to-man was expected and none was found. Anthrax is generally not considered to be contagious. All the cutaneous cases were from the outskirts and were persons who butchered privately owned animals. There were no cases among military personnel. No cases were traced to food consumed in restaurants, cafeterias, canteens or other establishments serving officially inspected meat. About 30% of the cases were among employees of a ceramics factory in southeast (?) Sverdlovsk which has about 3,000 workers. On April 8, this factory received 15 cattle carcasses and the fresh meat was put on sale. At least one of the carcasses was infected. A disproportionate number of gastrointestinal cases occurred among automobile and truck drivers, perhaps because they were particularly likely to know of meat from private sources on sale.

13) The first two cases were initially diagnosed as intestinal blockage. When surgical exploration failed to confirm this diagnosis, Professor Nikiforov was contacted in Moscow. He arrived in Sverdlovsk on April 6 and stayed until early June. At first he did not suspect anthrax because it usually occurs in the summer, not in early spring. Nikiforov made a provisional diagnosis of anthrax on April 7. His assistant, Dr. Yampolskaya, arrived from Moscow on April 8 and remained until near the end of April. The first confirmation of anthrax by bacteriological tests was made on April 10. Professor Nikiforov immediately contacted Dr. Burgasov, who arrived in Sverdlovsk the same day. Professor Bezdenejnich also came to Sverdlovsk and stayed until about April 20. Another member of the group was the son of Dr. Burgasov, a young physician who died a few years ago of pancreatitis.

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 I ~~the~~ ~~was given~~ ~~the~~ ~~report~~ ~~of~~ ~~the~~ ~~Health~~ ~~Secretary~~ ~~of~~ ~~Sverdlovsk~~ ~~and~~ ~~was~~ ~~given~~ ~~by~~ ~~Dr~~ ~~Burgasov~~ ~~on~~ ~~May~~ ~~25~~ ~~1979~~
 the report of the Health Secretary of Sverdlovsk and was given by Dr Burgasov on May 25 1979 and distributed confidentially.

14) Management of the situation was under the direction of Dr. Burgasov. All cases were taken to city hospital number 40. At no time did the military take over or intervene. (X)

I asked and was told that for a list of
15) ~~There were several~~ foreigners in Sverdlovsk during the outbreak. ~~One of these was~~ Professor Donald Ellis of Northwestern University in Evanston, Illinois. He was a US National Academy of Sciences exchange scientist who came with his family and worked at the Institute of Chemistry and Physics from mid-April to mid-May. After travelling to Novosibirsk, Ellis and his family were readmitted to Sverdlovsk to work from mid-June to the end of July. ~~In addition, there were two Japanese, three Finns and three Frenchmen.~~ *I was given the name and affiliation of*

In addition there was

16) After ingestion of contaminated food, animals developing anthrax generally come down with it in 2-3 days. In people, the corresponding time is 3-5 days. A rarer faster course has been observed in animals. Many animals in the Sverdlovsk region were debilitated in the early spring of 1979. Bone-flesh powder contains rather sharp particles of bone. These factors may have facilitated animal infection, since the initiation of gastrointestinal anthrax is thought to require damaged tissue through which spores can enter.



17) All 96 of the human anthrax cases are thought to have resulted from animals consuming the bone-flesh powder from Aramil. This is supported by the finding of the same strain of the organism in samples of the powder from farms where animals had died (10 isolates tested), the bad meat (8 isolates) and the human victims (numerous isolates) and by the various epidemiological findings cited above that trace human cases to contact with or consumption of privately marketed animals fed the Aramil powder.

18) Since the fatality rate in previous outbreaks of gastrointestinal anthrax in the USSR, as recorded in the literature, is close to 100%, heroic therapeutic measures were undertaken. These included intensive antibiotic therapy with penicillin, cephalosporins, chloramphenicol and the administration of corticosteroids, specific globulins, Phillips' solution, various salts and heparin. Even so, the fatality rate for gastrointestinal cases was 81% (64/79). The cause of death was characterized as toxic shock. The cases of gastrointestinal anthrax had a very acute onset. Patients could specify the exact time. Symptoms included chills, high fever (39-41 C), belly pain, swollen gassy belly, acidosis (pH 6.8), dyspnoea, rapid shallow breathing (up to 60/min), rapid then failing pulse, fibrinolysis, almost total loss of blood pressure, cyanosis and death. In some patients, fever followed a hectic course, cycling between 37 and 40 C. Near death, temperature could drop from high levels down to about 32 C within an hour. Belly pain was

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more severe in some patients than in others, corresponding to the extent of lesions seen at autopsy. All fatal cases had at least some belly pain. If fibrinolysis developed, all efforts to save the patient were in vain. All of the dead were buried in a separate area of the cemetery and interment was done in accord with special instructions (what were they?).

20) Professor Nikiforov projected a series of 14 color photographs taken at autopsy. I asked for and was given the first of these, showing the body cavity of a victim who died 48hrs after onset. The photographs showed early stages (48hrs) and later stages (3-4 days). In early stages, hemorrhage was seen in the intestines at several sites. At first, this was mistaken for thrombosis. The intestines were very swollen and there were pockets of gas. At later stages, severe and disseminated hemorrhage was seen over a much wider area, including the inner intestinal surface, the mesenteries and, in some cases, the brain. Nodes throughout the body cavity were black and necrotic. In all cases, however, the inner surface of the lungs was free of hemorrhage. No material aspirated from the lungs was found to contain E. anthracis.

21) The anthrax strain involved had a particularly thick capsule. During development of the disease, the bacterial concentration in blood reached levels up to 500,000 per ml. Later, these lyse and release the anthrax toxin.

22) No sequelae were seen in survivors 1-2 years after the outbreak.

23) The overall conclusion is that the outbreak was caused by inadequate sterilization of the Aramil bone-flesh powder; the failure of certain private animal owners to observe regulations requiring official veterinary approval for slaughter of sick animals; the illegal sale of meat from such animals; and inadequate supervision by the veterinary services.

24) *Report*

In order to facilitate further scientific study and understanding of this remarkable outbreak, we agreed to take the following three steps:

First, since I am not a specialist in the relevant areas, I undertook to organize a return visit of highly qualified US medical specialists interested in the outbreak. These should include, if possible, specialists from the Center for Disease Control and/or the National Institutes of Health, as well as private specialists.

Second, I would arrange to have invitations extended to Burgasov, Nikiforov, Bezdenejnich and Yampolskaya, or some sub group of them, to give scientific lectures and consultations in the US in the areas of their special knowledge, including the outbreak at Sverdlovsk. Two additional topics suggested for Professor Nikiforov are toxic shock and botulism, areas of research and practice in which he specializes.

Third, Bezdenejnich, Burgasov and Nikiforov would write a paper about the Sverdlovsk outbreak suitable for publication in an English language scientific journal. While I was still in Moscow, they completed and gave me a first draft of the manuscript.