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TO : Director, Center for Disease Control

FROM : Assistant to the Director
State and Community Services Division

SUBJECT: Smallpox in Yugoslavia

INTRODUCTION

During March and April of 1972, Yugoslavia experienced the largest outbreak of smallpox in the history of Europe since the Second World War and its first smallpox since 1930. The Center for Disease Control sent an observer into Yugoslavia on March 26, and a team for epidemic aid was sent on March 30. The outbreak involved 174 cases of variola major, including 35 deaths.

This memo is divided into four sections. The first (pp. 2-14) describes the outbreak and comments upon certain epidemiologic features. The second (pp. 15-24) examines the strategy and tactics used by the Yugoslav authorities to control the outbreak. The third section (pp. 24-28) is an analysis of aspects of the outbreak which are relevant to the United States' contingency plans for control of smallpox importations, and relevant to the rationale for the recent change in USPHS policy regarding smallpox vaccination. The final section describes the history and actions of the USPHS/CDC team which was involved in the epidemic aid mission. Relevant documents and data are included in an Appendix.

Readers of this memo should realize that the role of CDC advisors in this outbreak was not strictly analogous to that often played by CDC epidemiologists in domestic epidemic aid missions. Administrative, diplomatic, and linguistic reasons prevented the CDC team from obtaining full information about all aspects of the outbreak.

BACKGROUND

Yugoslavia is a nation of 21 million people, comprised of six republics and two autonomous provinces, including Kosovo (Figure I). The people are Serbs, Croats, Slovenes, Macedonians, Bosnians, Montenegrans, and Albanians. Most of the Albanians live near the Albanian border in Kosovo Province, which has a population of 1.1 million, including some 800,000 Albanians. The Albanians are predominantly Moslems, and most of the Moslems in Yugoslavia are Albanian.

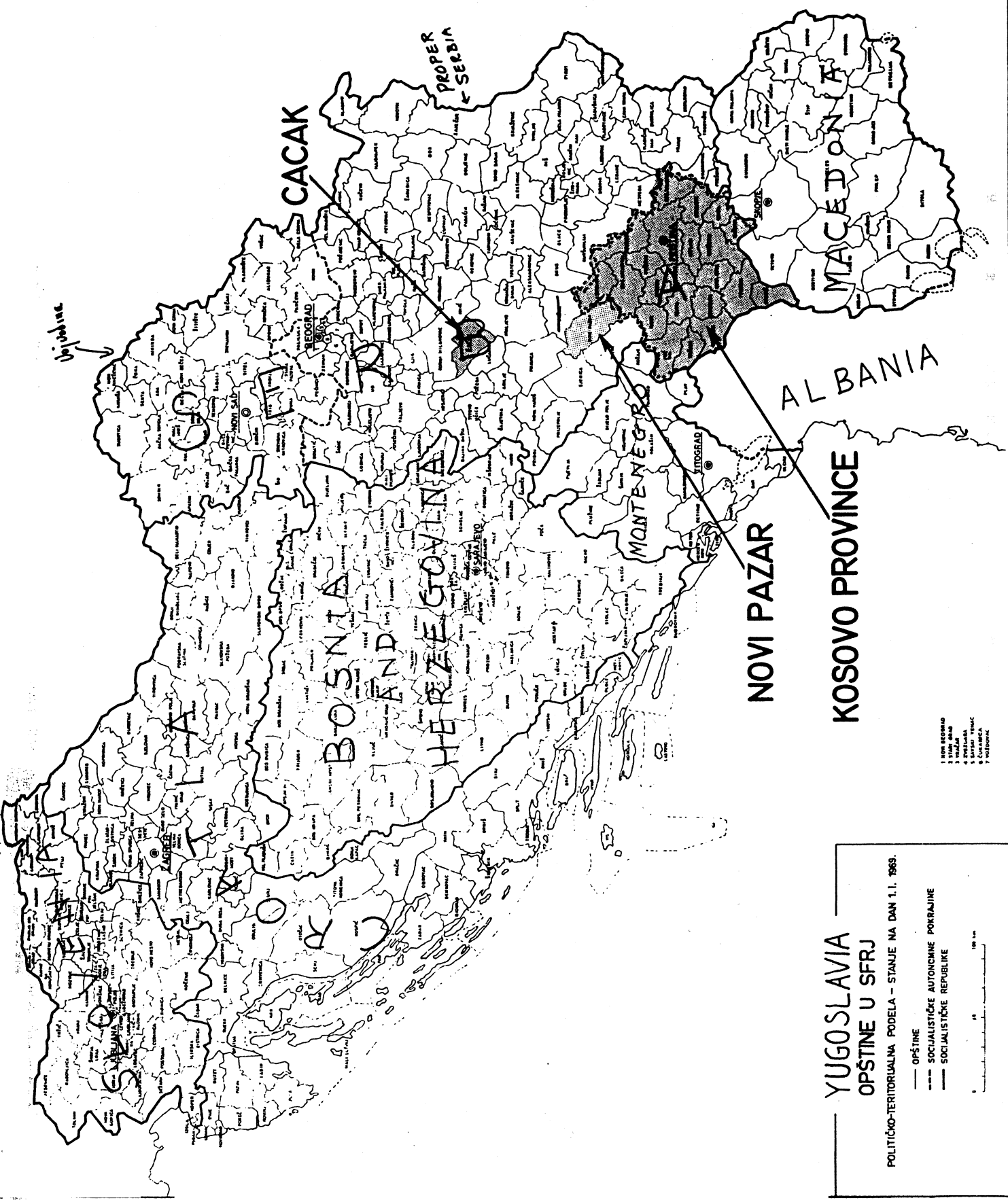
There are historical antagonisms between the ethnic groups of Yugoslavia. One way in which these antagonisms have been handled in modern times is by a vigorous policy of decentralization and autonomy for the republics and provinces. This has worked well in many aspects of medical care, but is potentially detrimental to coordinated large-scale public health actions.

Kosovo Province is the most underdeveloped area in Yugoslavia. Roads and services are poorly developed. Very few people in the other areas of Yugoslavia speak Albanian. The Albanians are at the lowest end of the social spectrum of the nation. The Albanians on their part resent the power and influence of the other parts of the nation, and in 1968, there were demonstrations in the area demanding further autonomy.

Communications and health services in most of Yugoslavia are good. Viral diagnostic services are available in central institutes, particularly at the Serbian Infectious Disease Laboratory in Belgrade.

Section I - THE OUTBREAK

- A. The Importation
- B. The First Indigenous Generation
- C. The Second Indigenous Generation
- D. The Third Indigenous Generation
- E. The Vaccination Status of Cases and Fatalities
- F. The Role of Hospitals in Transmission
- G. The Age and Sex of Patients
- H. The Role of Hemorrhagic and Mild Cases in Transmission
- I. The Use of Thiosemicarbazone Derivatives and VIG
- J. The Immunization Status of the General Population and Medical Personnel
- K. Alternative Importation Hypotheses



A. THE IMPORTATION

About 2,400 Yugoslav pilgrims go to Mecca each winter. They are asked by the authorities to go by plane, with special health precautions observed to prevent the importation of cholera. There is one physician provided by the government for each 100 pilgrims, they undergo a 5-day intensive surveillance upon return, and they are required to take 2 grams of tetracycline orally on return. These measures are avoided, and some money is saved, by those who take special chartered buses.

Ibrahim Hoti, a 35-year-old Albanian Moslem from the village of Danjane, in the commune of Orahovac, Kosovo Provicne, returned to Yugoslavia on February 15 aboard one of the chartered pilgrim buses. He possessed a valid international certificate of vaccination which asserted that he had been revaccinated on December 19, 1971, with Zagreb lyophilized vaccine. This vaccination had not been read. He had also had two injections of cholera vaccine. Hoti traveled with a group through Iraq, and during February 3-7, was in Baghdad, where he visited the market and bought several souvenirs. Hoti denies contact with smallpox patients, although there was smallpox in Baghdad at the time.

Upon his return to Kosovo on February 15, Hoti was visited by friends and relatives who wished to congratulate him on the attainment of the status of Haji. He received visitors and displayed his souvenirs at his home in Danjane intermittently for at least 2 weeks after his return. He was required to visit a physician on February 18 to give a stool specimen for a cholera check, and was referred by this physician to the polyclinic in Orahovac to give a stool specimen. He was not noted to be ill. He visited the town of Djakovica on February 21 to do some marketing and have his automobile repaired.

Hoti has always maintained that he was never ill. His friends and relatives agree with him. He displayed a minimal reaction each time after being revaccinated several times in April 1972. Blood specimens taken on March 16 before his revaccinations, and on April 4 and April 9, yielded unusually high HAI (1/160, 1/320) and neutralizing (1/100, 1/500) antibody titers. The other 37 pilgrims on the bus had titers considerably lower, except for one 1/160 HAI, and another with 1/1024 neutralizing antibody titer. Hoti's blood gave a positive agar gel diffusion test for precipitins, whereas none of the other pilgrims' bloods were positive. Hoti does not bear scars indicative of variola.

Most observers agree that Ibrahim Hoti is an unreliable historian. Unproven rumors abound that he was told by religious authorities not to admit to his illness, that he was engaged in smuggling, or that he is afraid of an Albanian pogrom. There is no proof of these rumors, and no concrete evidence that the above story is incorrect.

Yugoslav, WHO, and U.S. observers agree that Ibrahim Hoti probably had a very mild case of smallpox and was infectious at least during the period of February 18-22. The most persuasive evidence against this hypothesis is that none of his immediate household of 21, including three of his own children who were unvaccinated, developed smallpox.

B. THE FIRST INDIGENOUS GENERATION

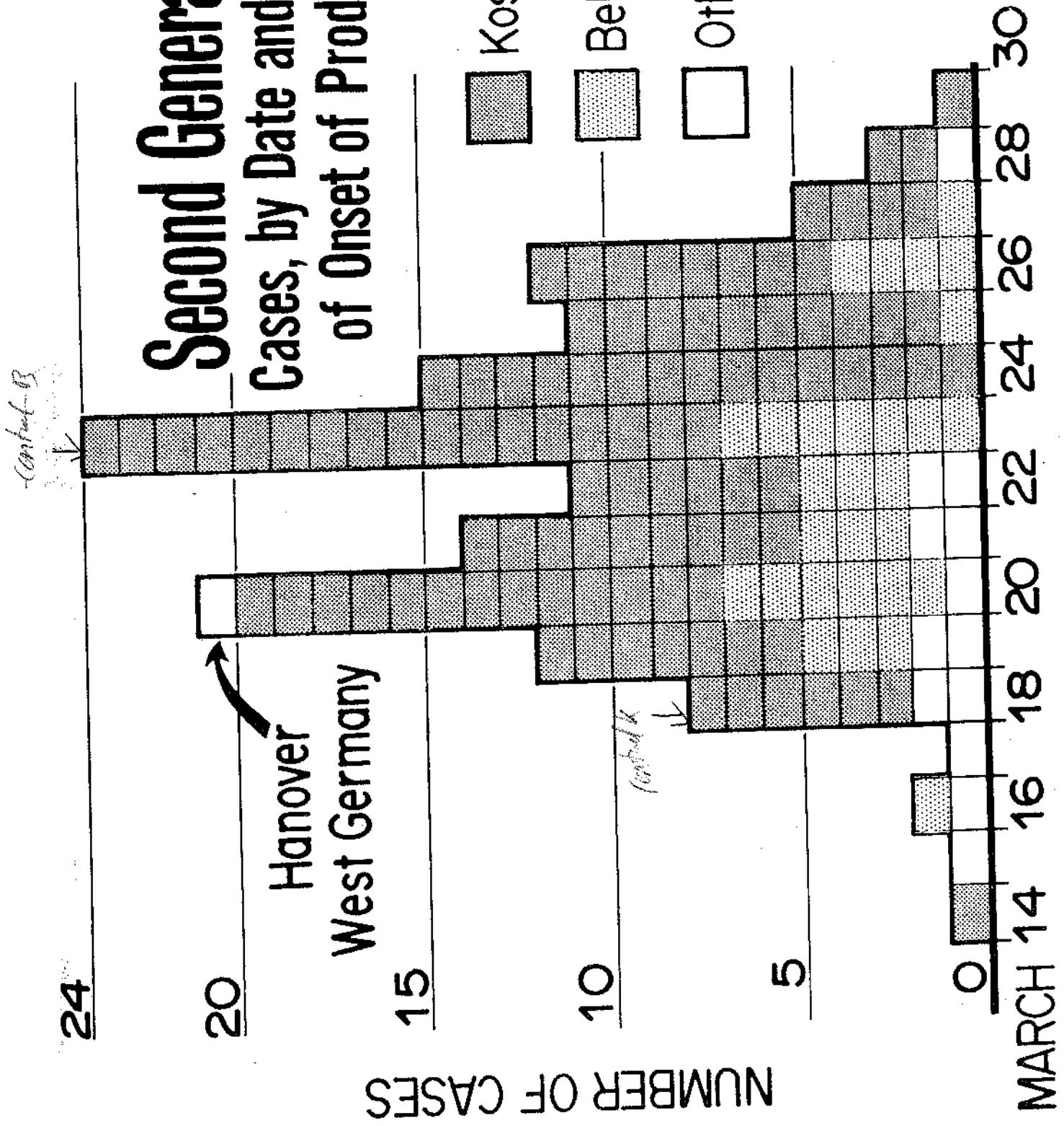
There were 11 first generation smallpox cases who could be traced to Ibrahim Hoti with more or less precision (Figure II).

Hoti had known contact with all six of the patients from Danjane, his home village. The patient from Ratcovac, Orahovac commune, was a relative who visited his home to congratulate him on his Haji status. Hoti was present in the town of Djakovica, Djakovica commune, on the afternoon and evening of February 21, a market day. During this time, he had the opportunity to infect the other four first generation patients, but the contact has not been thoroughly established.

One patient was a painter (AH) from Djakovica who visited the market on February 21. Another was a man (MV) who had come to the market from outside of Kosovo (Bresnica) to sell cheese. A third was an Albanian Catholic woman (PK) from the village of Kusavac in Djakovica commune who was visiting the market (ordinarily there is little contact between the Albanian Moslem and Albanian Catholic groups). The fourth patient (LM) was a young man from Novi Pazar, outside of Kosovo Province. He had come to Djakovica to register for school and to buy a religious gift, such as the artifacts which Hoti brought back from Mecca, for his fiancée. The information on LM is both important, because he was the principal vector of smallpox outside of Kosovo, and suboptimal, because he died before the disease was recognized. His brother had mild encephalitic complications from smallpox, and is confused as to places and dates, so that his sister-in-law is the only source of information about his movements. He is known to have been in Djakovica on February 18 and 20. There are inconsistent and variable stories as to whether or not he was in Djakovica on February 21, when Hoti is known to have been there.

The initial hospitalization was in the hospital at Prizren, in Prizren commune, on March 9. Nine of the 11 first generation cases were hospitalized between March 9 and March 13. PK, the woman from Kusavac, had a very mild illness and did not seek medical care. She was hospitalized on March 24 when her contacts were found to have smallpox. The patient from Bresnica also had a mild illness with onset on March 7, and was not hospitalized until March 26.

Second Generation Cases, by Date and Place of Onset of Prodrome



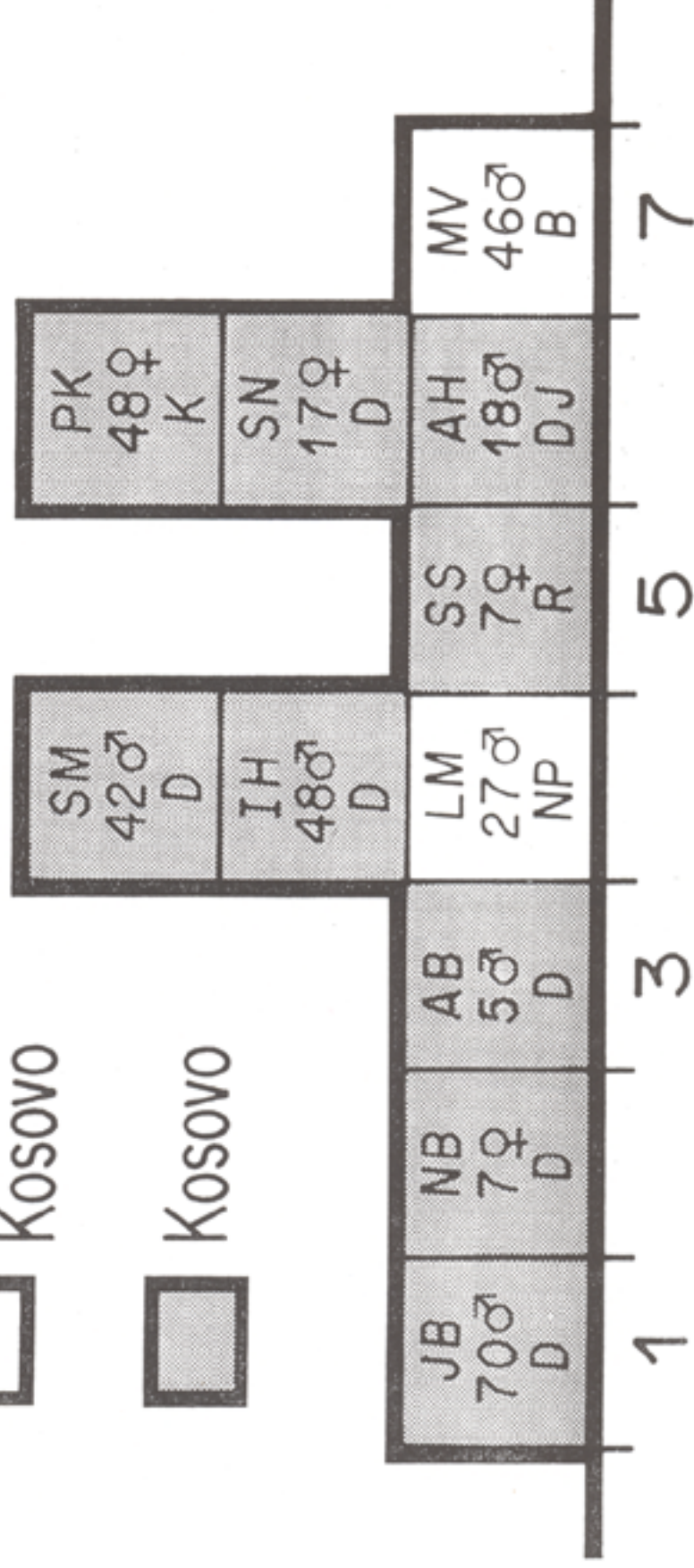
First Generation Cases, by Date of Onset of Prodrome

Outside



KOSOVO

KOSOVO



MARCH

The existence of smallpox was first suspected on clinical grounds on March 14. The diagnosis was confirmed by clinical experts on March 15, and by electron microscopy on March 16. Vaccinations began in Danjane and other limited areas in Djakovica and Orohovac communes on March 16 also. Full-scale immunization of the entire area of these communes was initiated on March 24.

C. THE SECOND INDIGENOUS GENERATION

The second indigenous generation included 140 patients (Figure III). The slight biphasic nature of the curve represents a preponderance of Belgrade cases and Kosovo community-acquired cases in the first half, and of Kosovo hospital-acquired cases in the second half. The source of infection for all of these cases was either community contact with first generation cases in Kosovo, hospital contact with LM from Novi Pazar in Cacak and Belgrade, and hospital contact with patients in the Prizren and Djakovica hospitals in Kosovo.

There were only three patients outside of Kosovo except for those which arose from direct hospital contact with LM in Belgrade and Cacak. One man, a friend of Ibrahim Hoti's brother, was visiting in Djakovica on March 10-12, and then traveled to Hanover, West Germany, looking for work. This man represents the only exportation from this outbreak. The woman from Bresnica gave rise to one case in her immediate family, with onset on March 19. Finally, LM, the man from Novi Pazar, transmitted smallpox to his brother before the start of his historic journey, and his brother became ill in Novi Pazar on March 15.

Hospital Spread in Cacak and Belgrade

LM, the man from Novi Pazar, was an unvaccinated adult male who suffered prodromal symptoms of smallpox on March 6 in his home. He consulted a physician on March 7 and was given penicillin. On March 8, he was very ill and went by bus to the hospital in Cacak. He was kept there overnight, but worsened and developed a petechial rash. He was sent by ambulance, together with an unvaccinated pregnant woman and an unvaccinated ambulance driver, to Belgrade to a Dermatologic Hospital. There he was presented to students and staff as a patient with a severe penicillin reaction. He was given steroids, and began to bleed into his skin and gastrointestinal tract and was transferred to a Surgical and Trauma Hospital, where he died on March 10. His body was taken back to Novi Pazar for burial by his brother before a necropsy could be performed.

Eight people in Cacak, 29 in Belgrade, and the patient's brother all caught smallpox from this man. All except the brother were patients or staff in the three hospitals. None of the passengers on the bus from Novi Pazar to Cacak developed the disease, nor did the driver or woman who accompanied him from Cacak to Belgrade. The 38 patients attributed to this man are nearly twice the number of secondary cases from any one patient in previous European importation outbreaks. There was a mean of 2.1 days lag between onset of prodrome and isolation in the Belgrade second generation cases, with a range from 0 to 7. The corresponding figures for Cacak, Novi Pazar, and Bresnica are 1.0 days mean, with a range from 0 to 7.

One of LM's contacts illustrates the diligence with which the Yugoslav authorities sought contacts outside of Kosovo, and highlights the importance of contact tracing. This boy was a forestry student being treated for scabies in Cacak when LM was admitted. He was subsequently discharged and went home. He received a cable from the army for induction on March 19, the day of onset of his prodrome. He consulted physicians in two hospitals in two towns of the autonomous province of Voivodina and was sent home with the diagnosis of varicella. On March 23, the police in his home town received a cable from the epidemiologist in Cacak notifying them that he was a first ring contact. They immediately took him to the smallpox hospital outside of Belgrade, where he was again told that he had varicella. He might have been sent home had not the police insisted that he had variola. Subsequently smallpox virus was visualized by electron microscopy in his vesicular fluid, and grown from the fluid on CAM.

LM died on March 10. On March 19, after the disease was confirmed in Kosovo, it was suspected that he had had smallpox. Quarantine of some of his contacts began on March 21. Limited vaccination in Belgrade hospitals began on March 20, and mass vaccination began on March 23.

The Second Generation in Kosovo Province

The remaining 99 second generation cases all were located in Kosovo Province. There were four infected villages in the first generation, including Danjane and Ratcovac in Orahovac commune and Kusavac and Djakovica town in Djakovica commune. The second generation spread to two other communes, Pec and Prizren, and involved 14 other villages. Spread was by both hospital acquisition and by community contact.

Hospital spread was facilitated by the fact that the presence of smallpox was not recognized until March 14-16. Isolation of patients in a separate facility was not accomplished until March 16-17, by which time some of the first generation cases had been discharged as varicella cases, and considerable visiting and intrahospital contact had taken place. Community spread was facilitated by the low vaccination status of the community (vide infra), the unrecognized presence of smallpox, and the Albanian cultural trait of visiting sick relatives at home, if possible staying overnight in the sickroom of members of large extended families.

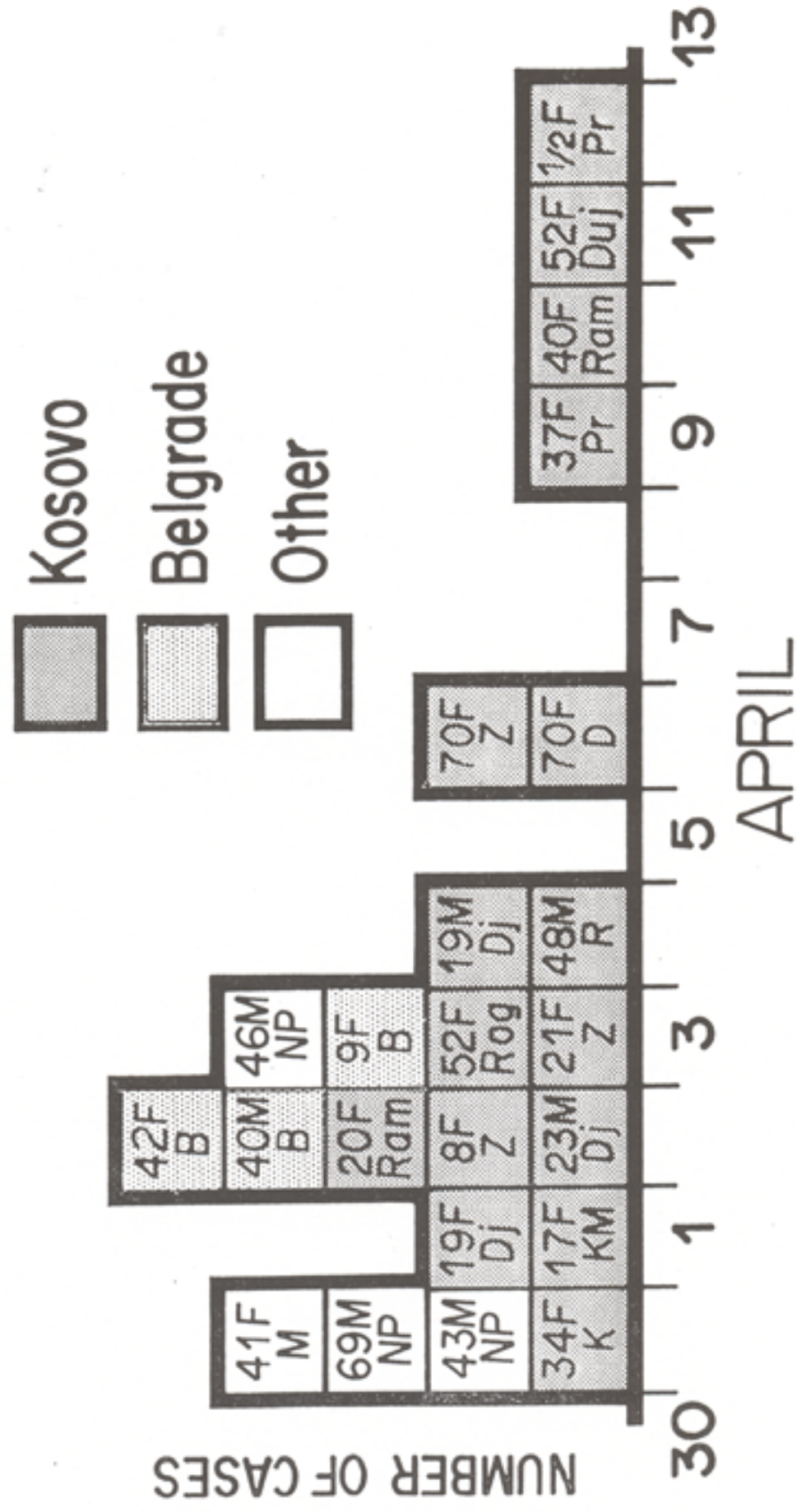
Special mention should be made of the large numbers of second generation cases resulting from contact with PK, the Catholic woman from Kusavac. This woman had been previously vaccinated and had a mild illness. She gave smallpox to six members of her immediate family, and was the source for three other cases in Kusavac. In the nearby Catholic town of Zjum, in Prizren commune, seven people developed smallpox as a result of visiting PK. In addition to these 16 definite cases, at least seven other second generation cases in six different villages apparently had reason or opportunity to have visited PK.

All Kosovo second generation cases are known to have visited villages or hospitals where known first generation cases were present. Most of the second generation cases had definite face-to-face contact with first generation patients. The large number of second generation cases and the language barrier between Serbo-Croatian and Albanian prevented establishment of definite face-to-face contact for every patient. Yugoslav authorities are continuing to search for definite contact histories among these patients.

The large size of the second generation in Kosovo resulted in incidents which were of epidemiologic significance and administrative concern. There were two cases who were missed until contact tracing from third generation cases led to their discovery. These included one mild case, and one child who died of hemorrhagic smallpox undiagnosed. There were three patients who were never hospitalized because they died before they were detected. Some four patients had intervals of 10 days or more between onset of prodrome and hospitalization, largely because they had vaccination-attenuated illnesses.

In general, case detection improved as the outbreak progressed. There was an average lag time of 4 days, with a range from 2 to 24, between onset and prodrome in the patients in the first half of the second

Third Generation Cases, by Place, and Date of Onset of Prodrome



generation (those with onset of prodrome before March 24). The patients in the second half of the second generation, with onset from March 23 through March 29, had a mean lag time of 3 days, with a range from 0 to 13. The overall second generation lag time in Kosovo was a mean of 4 days with a range of 0-24 days. The patients with onsets later than March 26 were carefully scrutinized to make sure they were not early cases in the third generation, but they all had definite contact with first generation patients within 15 days of their onsets. The last date of hospitalization and isolation of a second generation patient was on April 12. Thus the theoretical limits of a third generation, assuming incubation periods from 8 to 15 days, were from March 26 through April 27.

D. THE THIRD INDIGENOUS GENERATION

The third indigenous generation consisted of 23 patients with onset date from March 31 through April 12. Four of these were patients outside of Belgrade and Kosovo, three were Belgrade patients, and 16 were residents of Kosovo (Figure IV). The histories of these patients are important because their onsets were in some cases a full incubation period or more after recognition of the existence of smallpox in Yugoslavia.

The three patients from Novi Pazar were all hospital contacts of the brother of LM. They were all in full isolation and quarantine at the time they developed their illness. While they had all been vaccinated, they had failed to have takes at their initial vaccination. The onset of illness in their source case, the brother of LM, was March 15, but official recognition of his illness as smallpox was not until March 19. There was, therefore, insufficient time to fully immunize the hospital staff, and many patients had also been exposed.

The three Belgrade cases were all contacts of one second generation patient. They were all in full isolation and quarantine at the time they developed smallpox. The source for these three was a man who had been recovering from surgery at the surgical clinic when LM was admitted. He left the hospital against advice on March 15 before the existence of smallpox was recognized, and was not traced as a contact. He developed typical prodromal symptoms on March 20 at home, where he was living with his only child and no one else. The third generation cases consisted of his child, who is assumed to have acquired the disease at home, and two people who took him to the hospital and visited with him before it was realized that he was a smallpox patient.

The last non-Kosovo patient was the mother of the forestry student who had been found in Voivodina by the police. He had become ill on March 19, but had been considered to be a varicella patient until March 23 when the police took him to the hospital. While he was isolated on March 23, his mother was not vaccinated until March 27 because local health authorities were reluctant to go into her home for fear of catching smallpox.

The third generation patients in Kosovo are interesting because they illustrate the ways in which control efforts may fail. Four of them were known contacts of second generation cases, but failed to have "takes" from vaccination (vide infra for discussion of vaccination problems). Four were patients who were inhabitants of infected villages, but who were refused vaccination because they had "contraindications" to vaccination. Two of these were pregnant women, one was "too old" (70), and the last was too old and was under treatment for tuberculosis. One patient was a hospital contact who was not vaccinated because she was pregnant. One patient was a contact of a missed second generation case, whose existence was only discovered by investigating the source of the third generation patient's infection. Specifically, a young girl died on March 25 in Dujak and was not diagnosed. The man who washed her corpse prior to burial subsequently developed smallpox on March 11 in Dujak. Six of the third generation patients represent failure to identify and trace contacts, including two who were hospital contacts and four who were community contacts. The community contacts were apparently missed because they had been visitors in infected villages from other, non-infected villages, and their names and addresses were not elicited on contact tracing. These patients were vaccinated anyway in the mass campaign, but had unsuccessful vaccinations in two cases, and were vaccinated too late into their incubation periods in two others.

One of the unidentified contact cases caused considerable concern because she became ill in a commune which was remote from the infected area. This was a 17-year-old girl from Stari Treg, near the industrial city of Kosovska Mitrovica. She had not been identified as a contact although she had visited Djakovica from March 17-22 to take part in a wedding. She became ill on April 1 and consulted a physician. She visited the polyclinic in Kosovska Mitrovica on April 3 because of prodromal symptoms, during a busy outpatient session. On April 4, she developed an extensive hemorrhagic rash, and an ambulance was called. She died enroute to the hospital, and an alert physician recognized the possibility of smallpox despite the lack of known contact and the geographic remoteness from the infected communes.

One 19-year-old student was a known contact and became ill in quarantine. He had a negative electron microscopic examination, and was released from quarantine. The egg inoculations subsequently grew out a pox virus, and he was picked up by the police on the bus from Prizren to Djakovica, and the bus passengers and his classmates put into quarantine. Subsequent laboratory investigation has shown that the isolation was vaccinia rather than variola.

The date of the last hospitalization of an unquarantined third generation patient was on April 12, so that the theoretical limits of a fourth generation were set at April 18-27.

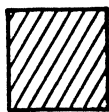
E. THE VACCINATION STATUS OF CASES AND FATALITIES

The vaccination status of cases and fatalities are presented in Table I. The determination of vaccination status was made by examination of the patients for the presence of an old scar of primary vaccination, and may not be completely reliable. The case fatality rate was 35 percent in the unvaccinated, compared with 9 percent in those with old scars. Those who died and had been previously vaccinated included four patients at unusually high risk. One was a child who was recovering from typhoid when he developed smallpox. One was a pregnant woman (the case fatality rate in unvaccinated pregnant women has been said to be as high as 90 percent). Two were over the age of 70 and had probably not been vaccinated for many years. One of these had cardiovascular disease as well as smallpox. If these four patients are excluded, the case fatality rate for those with old scars was only 5 percent.

F. THE ROLE OF HOSPITALS IN TRANSMISSION

As in other European importation epidemics, many of the patients in this outbreak acquired smallpox in the hospital (Table II). All but 12 of the 50 patients outside of Kosovo acquired smallpox by hospital contact with LM, the man from Novi Pazar. Seven of the Belgrade smallpox victims, three of those in Cacak, one in Novi Pazar, and at least four in Kosovo were medical or paramedical hospital workers. The other 58 hospital-acquired cases were patients in, or visitors to, the hospitals. Considerable comment was made in the press and in Parliament about the low immunization status of hospital workers. There has been a policy since 1967 that medical workers should be vaccinated at frequent intervals, but this policy was not enforced.

Only one hospital-acquired case did not have face-to-face contact documented with one or more smallpox patients. This was a young child who was in a room downstairs from LM when he stayed overnight in the hospital in Cacak.



INFECTED COMMUNES

POLITIČKO-TERITORIJALNA PODELA – STANJE NA DAN 1. I. 1969

- OPŠTINE
- SOCIJALISTIČKE AUTONOMNE POKRAJINE
- SOCIJALISTIČKE REPUBLIKE

TABLE IVACCINATION STATUS OF CASES AND FATALITIES,
KOSOVO PROVINCE AND NON-KOSOVO PATIENTS

<u>VACCINATION STATUS</u>	<u>PLACE</u>		<u>TOTAL</u>	<u>CASE-FATALITY RATE</u>
	Belgrade and other non-Kosovo cases	Kosovo Province		
Old Vaccination Scar Present	37 (3)*	63 (6)*	100 (9)*+	9%
Never Previously Vaccinated	13 (6)*	60 (20)*	73 (26)*	35%
Unknown	0	1	1	
TOTAL	50 (9)*	124 (26)*	174 (35)*	

* Fatalities are in parentheses, and are included in the case count.

+ Fatalities in the previously vaccinated include one child recovering from typhoid fever, one pregnant woman, and two patients over the age of 70.

TABLE II

SOURCE AND PLACE OF INFECTION OF
174 SMALLPOX PATIENTS, YUGOSLAVIA 1972

SOURCE OF ACQUISITION	PLACE OF ACQUISITION			TOTAL
	Kosovo Province	Belgrade	Other	
Hospital- acquired	28	31	14	73
Community- acquired	94	1	4	99
Unknown	2	0	0	2
TOTAL	124	32	18	174

TABLE III

AGE AND PLACE OF INFECTION OF
174 SMALLPOX CASES, YUGOSLAVIA 1972

AGE	PLACE OF ACQUISITION					Age Specific Attack Rate*
	Kosovo Province		Belgrade	Other	TOTAL	
	Hospital	Community				
< 1	3	6	0	1	10	29
1-4	1	10	0	0	11	
5-9	1	11	1	0	13	19
10-19	4	19	3	1	27	18
20-29	3	11	3	2	19	15
30-39	6	13	7	2	28	21
40-49	8	14	11	8	41	35
50+	2	12	7	4	25	15
TOTAL	28	96	32	18	174	

*Attack rates expressed as cases per million of the 1970 estimated mid-year population of the Republic of Serbia.

G. THE AGE AND SEX DISTRIBUTION OF PATIENTS

The age distribution of patients is presented in Table III. The patients who acquired the disease in the hospital, particularly those in Belgrade and Cacak, were largely adults. The one Belgrade patient under the age of 10 acquired smallpox at home from his father, the man who had left the hospital and developed symptoms at home rather than under quarantine. The age distribution of the community-acquired cases in Kosovo is much broader, reflecting the wider range of contacts of the unhospitalized patients. The age-specific attack rates are variable but uninterpretable, because they reflect unknown variations in immunity as well as possible differences in exposure.

There were 97 male patients and 77 females. This also reflects the role of hospital spread, because LM was hospitalized on male wards, and his contacts were predominantly male.

Secondary attack rates, using household or ward populations as denominators, cannot be calculated at this time because the data are unavailable. The Yugoslav authorities are in the process of obtaining these rates.

H. THE ROLE OF HEMORRHAGIC AND MILD CASES IN TRANSMISSION

In theory, patients with hemorrhagic smallpox may be inefficient transmitters of the disease because of their prostrating prodrome and short life. On the other hand, they undoubtedly have a high titer of variola virus in the nasopharynx. LM, the man from Novi Pazar, was infectious for 3 days, from March 8-10, yet he spread the disease to 38 contacts, considerably more than any other patient in the cumulative experience of European importation variola. There were five other probable cases of hemorrhagic smallpox, including one girl who died and was buried without being diagnosed. None of these caused more than two subsequent cases.

In theory, patients with mild vaccination-attenuated smallpox are poor vectors of the disease because of their relatively low titer of virus in the nasopharynx. On the other hand, they may be socially mobile because they are not prostrated, and they are frequently not diagnosed and isolated. Two patients in this outbreak represent unusually efficient vectors of the disease despite clinically mild illnesses. The probable index case, Ibrahim Hoti, must have had very mild illness with a minimal rash. Yet he infected 11 others, including at least four with whom he had only casual contact. He also failed to transmit the disease to any of his immediate household including three of his children who were unvaccinated. The woman, PK, from Kusavac had a very mild illness, and was undiagnosed

and remained unisolated until secondary cases occurred traceable to her. She infected at least 16 and perhaps as many as 23 other people. There were many other mild cases in this outbreak, perhaps some 29 (one in Morovic, three in Cacak, eight in Belgrade, and 17 or more in Kosovo) who had illness so mild that they might not have been diagnosed without a definite history of contact, a high degree of suspicion, and good viral diagnostic techniques. Apparently none of these spread the illness further, although this may have been because of their rapid isolation or the immune status of their contacts rather than because of low amounts of virus in their nasopharynges.

In all, at least 65 and possibly 72 patients can be attributed to these three patients, one of whom had classic severe hemorrhagic smallpox, and two of whom had very mild illness.

I. THE USE OF THIOSEMICARBAZONES AND VACCINIA IMMUNE GLOBULIN

After the German outbreak in Merchede in 1970, the Yugoslav authorities obtained thiosemicarbazone (Marboran) from Britain and revised their smallpox control plans to cover its use. In this outbreak, several patients were given Marboran, all of whom were also vaccinated. Forty contacts in Cacak were given Marboran because the disease was not recognized until 11 days after LM had been in the Cacak hospital. Marboran was not used in Belgrade after one woman, otherwise well, went into shock after taking it. None of the contacts who received the drug got smallpox, but this is difficult to interpret because they were also all vaccinated. Some 20 of those given Marboran failed to get a "take," but in view of the general low take rate in initial vaccination efforts, this may not have been caused by the drug. The full details of the use of Marboran will be published by the Yugoslav authorities.

Vaccinia Immune Globulin was used extensively. At least 76 liters of VIG were used, for treatment of cases, for prevention of disease, and for prevention of vaccination complications. Official statements were made in Parliament about speculation and profiteering in VIG, which was in demand because of statements about vaccination contraindications in the press (vide infra). The VIG was largely of Russian origin, and the CDC team did not determine its neutralizing antibody titer. Figures on the results of its use were not obtained by the CDC team.

J. THE IMMUNIZATION STATUS OF THE GENERAL POPULATION AND MEDICAL PERSONNEL

The background immunity level in Yugoslavia is not precisely known. This paragraph should be taken as conjectural in part, as rumor in part, and as overinterpretation of limited CDC surveys in Kosovo province in part.

Yugoslavia has a policy of childhood vaccination before 18 months, revaccination at 7 and 14 years, and vaccination of military recruits (all healthy males serve in the military). Medical personnel are supposed to be frequently vaccinated. The press and medical authorities readily acknowledged that this policy has not been vigorously implemented. Some medical personnel were apparently afraid of vaccination, having received most of their ideas about vaccination from the writings of Herrlich. Magazine and newspaper articles commented on the practice of selling certificates of exemption from vaccination, and named names of physicians who refused vaccination themselves.

Unofficial statements from Yugoslav authorities, the press, and from practicing physicians allege that from 10 to 30 percent of the Belgrade population has never been vaccinated, and that many medical workers had not been vaccinated since childhood.

The CDC teams performed several surveys of take rates in villages in and around the infected communes of Kosovo. These surveys indicated that from 22 to 30 percent of the population had primary reactions and were thus either previously unimmunized, or in some instances were aged people with remote primary vaccinations (see Appendix).

Statistics on the number of vaccinations performed annually are not available for the nation, for Kosovo, or for Belgrade.

K. ALTERNATE IMPORTATION HYPOTHESES

Extensive work was done to determine the cause of the importation. The official and accepted explanation revolves around Ibrahim Hoti who had direct or indirect contact with all 11 first generation cases within the proper incubation period, and had elevated HAI titers and a positive precipitin test. The CDC team was surprised that an individual who had as mild an illness as Hoti apparently had could spread smallpox so effectively. Two alternative hypotheses were considered in detail.

First, Hoti had very mild, basically non-infectious smallpox either in Kosovo or during his travels. This explains his positive laboratory tests. Smallpox was imported by a person or persons unknown who were infectious during the latter half of February. These people could have been missed cases, resulting from an earlier importation, or individuals operating illegally in the area, such as smugglers. Hoti himself may have been involved in smuggling, explaining his reluctance to admit that he knew any ill people and his sometimes contradicting statements concerning his whereabouts. This hypothesis could explain why none of Hoti's susceptible family members developed smallpox. It could also tie in the Novi Pazar and Bresnica cases, both of whom could have been dealing with black market items. The Bresnica man was known to be connected with the black market. The Novi Pazar man was looking for gifts to give his fiancée, which might have been bought on the black market. The lady from Zjum dealt at the market in Djakovica and could have accidentally come into contact with the unknown infected persons.

Second, smallpox virus may have been brought in by Hoti on an article or articles of clothing bought during the pilgrimage. This hypothesis does not explain how the article was infectious for such a long time or how the patients from outside of Danjane became infected. These hypotheses were considered by the Yugoslav authorities. Hoti's possessions were analyzed for variola virus, and none has been found. There is no evidence that Hoti was involved in smuggling or that the intense investigation centered around this epidemic missed one or more cases occurring around February 15. It is quite possible, however, that Hoti himself was sick and was afraid to report his disease, as many of the Yugoslav authorities believe. Whatever the case, the CDC team members find it difficult to accept the fact that a healthy individual could be such an efficient spreader of smallpox.

Section II - THE OUTBREAK CONTROL EFFORTS

- A. Diagnosis
- B. Isolation of Patients
- C. Isolation of Contacts
- D. Contact Tracing and Location
- E. Surveillance for New Cases
- F. Terminal Disinfection and Sterilization
- G. Vaccine, Vaccination Technique, and Vaccination Policy
- H. Administration, Communication, and Decisionmaking
- I. Cultural Problems

A. DIAGNOSIS

The original diagnosis was made by an infectious disease specialist in the hospital at Prizren on March 14. The clinical diagnosis was confirmed by individuals with smallpox experience in India the following day, and laboratory specimens were obtained. On March 16, classical electron photomicrographs were obtained, showing copious amounts of typical pox viruses. The same specimens were positive on egg inoculation.

The laboratory work was performed by the Serbian Public Health Laboratory, which does excellent electron microscopy and egg culture, and which had some experience with agar gel diffusion. Following the use of CDC antigens and antisera starting on April 2, the agar gel diffusion test was 100 percent specific and 100 percent sensitive for cases confirmed by electron microscopy.

Laboratory specimens were only obtained by three workers from the Serbian Public Health Laboratory, who were, if necessary, flown to the patient by helicopter. They took specimens only from patients who had been seen by two specially designated experts, at least one of whom had smallpox experience overseas. Thus most of the irrelevant cases were screened out in advance.

Laboratory confirmation including egg isolation and electron microscopy was made for every patient outside of Kosovo. Within Kosovo, laboratory confirmation was not obtained on clinically obvious cases, and on certain patients with clear histories of contact to proven cases. All suspects, particularly from newly infected villages, were seen by the laboratory people and the diagnosis confirmed by the lab. Some concern was expressed by the authorities at the Djakovica isolation hospital about the lack of rapid and universal lab work on their patients. The Serbian Institute workers did not enjoy going to Kosovo and did not visit the hospital at frequent or regular intervals.

B. ISOLATION OF PATIENTS

Isolation facilities sufficient to handle large numbers of patients were not available in any of the infected areas, and the authorities immediately realized that use of facilities inside major population centers would be unwise. They used a variety of facilities which in retrospect showed imagination, good luck, and the advantages of a system in which health authorities can commandeer whatever facilities they desire.

In Belgrade patients were isolated at a motel some 11 kilometers outside the city. There were four detached pavillions, two for patients, one for suspects, and one for staff. Each pavillion was some 30 yards from the others. There were no other structures within approximately 1 kilometer other than a gasoline station.

The infectious disease hospital in Djakovica was evacuated, and all of the Kosovo patients removed from the Prizren hospital on March 17. Subsequently all Kosovo patients were admitted directly to Djakovica. This facility had an iron fence around it, a military guard at the gate with controlled entry, quarters for staff, laundry, and a make-shift mortuary. It was on the outskirts of the town of Djakovica, a town of some 32,000.

Non-medical facilities such as camping sites, hotels, etc., were used with great success in Cacak, Novi Pazar, and Subotica for patient and contact isolation.

Once the existence of the disease was recognized and isolation procedure initiated, there were no further hospital-acquired cases outside of Kosovo. In Djakovica, seven theoretically preventable cases occurred in hospital contacts. The original patients in the first indigenous generation were transferred from Prizren to the Djakovica Infectious Disease Hospital. There were 14 other patients in the Djakovica hospital at the time of transfer. Instead of removing them, the Djakovica control teams vaccinated them. Eleven of the 14 did not have successful vaccinations; seven of these subsequently developed smallpox. This incident illustrates the danger of hospitalizing smallpox patients, and the inherent difficulty in isolating potentially susceptible patients from patients with smallpox in the same building.

C. ISOLATION OF CONTACTS

Known primary or first ring contacts were isolated in full quarantine. The definition of first ring contacts was never clearly enunciated, but immediate family, known hospital contacts, and others who could be readily identified by the history of the patients' movements were isolated and vaccinated. These individuals were placed under complete isolation until 18 days after successful vaccination or after contact.

In Belgrade contacts were incarcerated in a large hotel in Novi Belgrade across the Danube from the main city, or in an army campsite with rather Spartan facilities some 20 kilometers from the city. At least 725 contacts were isolated in Belgrade. There were complaints from some contacts about the harsh nature of isolation, although they had reasonable creature comforts and were the guests of the government.

Similar arrangements were found in hotels and campsites in Cacak, Novi Pazar, and Subotica, where a total of 419 contacts were isolated. In Kosovo a small number of contacts, specifically those who were in the hospitals in Prizren and Djakovica before the smallpox cases were placed in isolation, were quarantined in the Prizren hospital. The rest of the Kosovo contacts, and the entire village of Morovic in Voivodina where one second and one third generation case were found, were isolated in their home villages.

Village isolation consisted of "100 percent" vaccination of the village (vide infra) and a cordon sanitaire around the village enforced by the police or military. This proved particularly harsh because the villages were agricultural and the outbreak took place during the plowing and planting season. For this reason, a certain number of villagers were allowed to work in those fields in which they could not contact outsiders.

D. CONTACT TRACING AND LOCATION

The CDC team did not obtain permission to review or to participate in the process of tracing contacts. The information in this section is therefore partly conjectural, partly based upon second-hand information, and partly based upon inference.

The criteria for defining contacts were never established. Patients and their families were not always carefully questioned about their movements and visitors. This was particularly true in Kosovo,

where the patients were Albanian, and the epidemiologists did not always speak their language. This difficulty was compounded by the large number of second generation Kosovo patients, and apparently some patients were not clearly interviewed about their contacts. In general, contacts were identified as much by their residence or by the fact that they visited the relevant hospital on the appropriate day than by a history of definite contact. All members of infected villages were considered contacts, but there were failures to detect visitors from neighboring villages. All visitors to or inpatients of hospitals were considered contacts whether or not they had been in proximity to a known smallpox patient.

The hospital visitors were not all located by direct tracing. Instead newspaper, radio, and television announcements called in all persons who had been in the relevant Belgrade and Cacak hospitals on the appropriate days.

While this system of contact identification and tracing worked reasonably well, examination of the third generation patients shows that it was not perfect. Thus, from four infected Kosovo villages in the first generation, the outbreak spread to 17 in the second. In the third generation, there were six patients in Kosovo who had not been identified as probable contacts through the epidemiologic process. The outbreak might have been controlled earlier by more effective contact tracing, but such an undertaking would have taxed the Albanian-speaking staff beyond its limits.

E. SURVEILLANCE FOR NEW CASES

New cases were sought in three ways. First, known contacts under isolation had their temperatures taken daily and were inspected briefly for the presence of a rash. This procedure was carried out both in institutionalized and in village isolated contacts. Second, house-to-house checks and temperatures was accomplished in selected villages in the infected communes of Prizren, Djakovica, and Orahovac. Finally, a manual for smallpox control, which included clinical descriptions of smallpox and the telephone numbers of local consultants and public health authorities, was widely distributed throughout Serbia, and was distributed in other areas to public health officials.

The CDC team was not able to determine how many patients were found by self-referral and how many by active surveillance. In the late second and entire third generation, there were at least eight patients who were not found by active surveillance. The lag time between onset of prodrome and isolation in the third generation cases in Kosovo was 3.7 days, with a range from 0 to 6. Outside of Kosovo, all third generation cases developed their disease in full quarantine and isolation.

F. TERMINAL DISINFECTION AND STERILIZATION

The last member of the CDC team left Yugoslavia before the isolation facilities were disinfected. Plans were to wash all surfaces with soap, water, and a phenolic or formalin disinfectant. They were then to be aired for several days. Authorities feared that the public would refuse to use the motel near Belgrade again.

Laundry of patients and staff was boiled and washed. The other fomites of patients were boiled (dishes, etc.) or burned (papers, certain clothes, etc.).

G. VACCINE, VACCINATION TECHNIQUE, AND VACCINATION POLICY

The vaccination efforts, both in Kosovo and other parts of Serbia, have been critically analyzed in the Yugoslav parliament, the Federal Epidemiologic Commission, and in numerous informal meetings. The authorities were unprepared for a rapid vaccination campaign, and certain problems were encountered in its organization and direction.

The vaccine produced in Zagreb is high quality lyophilized vaccine. However, there were only 1 million doses on hand, of which only 100,000 were in Serbia at the time of the outbreak. The vaccine on hand in Kosovo during the first 8 days of vaccination was of low quality and quantity. Most observers agree that it was dated 1964. There is disagreement whether or not it was glycerinated lymph or lyophilized. The Zagreb Institute did not begin large-scale production of lyophilized vaccine for the domestic market until 1967.

The vaccinators were not trained for their task. They had no needles, and vaccinated with pens and styluses. Because of the shortage of vaccinating instruments, vaccinators flamed their pens until they were red hot, dipped them into the vaccine, and then vaccinated. Reports were frequent of vaccinees crying in pain from the heat of the vaccinostyle. This problem was common both in Belgrade and Kosovo, and was witnessed by many official and unofficial observers.

Long-chain solvents including ether, gasoline, and kerosene were used to cleanse arms, as well as alcohol and acetone.

Most vaccinations in Kosovo were performed on the forearm with three insertions, made with large cross-hatching scratches often resulting in extremely large takes.

Vaccine distribution reflected the political priorities of the republic of Serbia. When smallpox was first recognized in Kosovo on March 16, 45,000 doses were sent to Kosovo. When further vaccine was obtained from other areas (see Appendix), it was to have been shipped to Kosovo. On March 20, smallpox was detected in Belgrade, and vaccine was diverted to mass campaigns in Belgrade and elsewhere. Vaccine did not become plentiful in Kosovo until March 28, when the second round of vaccination in the infected communes was already underway.

Vaccine assessment was not performed until the arrival of the CDC team. Vaccinations had been read prior to then on the third day, by untrained workers. All persons not exhibiting a "positive reaction" were revaccinated. Many people were unnecessarily revaccinated, but in view of the low take rates in initial efforts (vide infra), this may have been a useful practice. There was no attempt to estimate the coverage of the uninfected villages in Kosovo, or in the cities of Cacak and Belgrade. There were no censuses of infected villages in Kosovo. This situation changed after the arrival of the CDC team, so that in early April, at the start of the third round of vaccinations, there were village rosters and attempts were being made to estimate the coverage of uninfected communes (see Appendix). Take rate determinations and assessment of the first two rounds of vaccination were never accomplished, except to the extent that the CDC teams' survey on April 4-9 could be interpreted as reflecting results of the initial vaccination efforts.

It was estimated in the Yugoslav Parliament, and in discussion with local, Federal, and WHO authorities, that the vaccination efforts in the third week of March carried a take rate of about 25 percent. The CDC team feels this estimate may be low because untrained workers in Kosovo were misinterpreting 3-day-old vaccination reactions. The official estimate of the vaccination take rate of vaccinations performed in the fourth week of April is about 60 percent. This agrees approximately with the results of the CDC surveys.

House-to-house vaccination was only performed in known infected villages. Priorities were apparently not influenced by contact tracing or by known social or marketing patterns between infected villages and uninfected ones. Nighttime vaccination was not practiced, although many teams arrived late enough for scheduled daytime sessions so that they were doing evening vaccinations. In general, teams visited schools, vaccinated school children, and then called the villagers to the school to be vaccinated.

VACCINATION CONTRAINDICATIONS

The problems caused by vaccination contraindications require special comment. On March 23 and 24, television and radio interviews with an infectious disease specialist from Belgrade were broadcast regarding contraindications to be used in the Belgrade mass vaccination campaign. On March 24, an article appeared in a widely circulated but unofficial Belgrade evening newspaper citing the contraindications to vaccination. These contraindications were widely quoted, including in Kosovo, and led to debates in the Federal Epidemiologic Commission and to several official attempts to rebut them. The following contraindications were used in the early publicity, and by most of the vaccinating teams up until early April.

Vaccinations were not given to:

1. Patients under 1 year
2. Patients over 60 years
3. Previously unvaccinated patients over 6 years
4. Patients with fever
5. Patients receiving corticosteroids
6. Patients with, or recovering from, infectious diseases
7. Patients with neoplasms
8. Patients with any skin diseases
9. Patients with cardiac or renal illness of a chronic nature
10. Patients with diseases of the central nervous system
11. Patients with tuberculosis
12. Pregnant women.

In addition to this published and circulated list, several widespread myths about the aftercare of vaccination were followed by both medical personnel and the general public. Persons were told not to wash for 20 days after vaccination. This worked particular hardship in Moslem areas, where ritual washing must be performed after sexual intercourse.

Persons were told to abstain from alcohol for one week after vaccination. Persons were informed that standing in the sunlight would kill the vaccinia virus.

The publicity about pregnancy as a contraindication was particularly damaging. Vaccination during pregnancy was added to the official list of indications for abortion on March 27. There were strong statements made in Kosovo when local and Federal officials tried to promote vaccination of pregnant women that such a policy was aimed at genocide of the Moslem subgroup. Pregnant women were vaccinated in Kosovo, Novi Pazar, Cacak, and Subotica (in the autonomous province of Voivodina), but not in Belgrade, Croatia, etc.

The results of this confusion can be seen in the third Kosovo generation, where five contacts had been refused vaccination because of old age or pregnancy developed smallpox.

The numbers of vaccinations performed, in gross figures or by categories such as age, place, or vaccination status, are not available. Teams did not keep accurate records, and any figures coming out of Kosovo or Belgrade must be considered estimates.

H. ADMINISTRATION, DECISIONMAKING, AND COMMUNICATION

The decentralization of decisionmaking and administration in Yugoslavia had a major impact on the outbreak control activities. The day-to-day arrangements for the work of vaccinating teams were made by the staff of the local communes, sometimes with the help of the army. There was little direct contact between even neighboring communes such as Pec and Djakovica. No single individual had access to all of the epidemiologic data, even by May 4, 1972. Novi Pazar, Cacak, Voivodina, Pec, Djakovica, Orohovac, and Prizren all had separate epidemiologists. These men did not meet together, although their information was pooled at weekly meetings of the Federal Epidemiologic Commission. There was a tendency to ignore contacts or movements of people who had left the local jurisdiction, as is illustrated by the late notification of the contact history of the boy from Voivodina who was exposed to LM in the Cacak Hospital.

At the beginning of the outbreak, the Federal Epidemiologic Commission, a policymaking body which ordinarily meets three times a year, decided to meet weekly. The former Minister of Health was named to head an ad hoc committee for the smallpox situation. This group was powerful and apparently was able to ensure adequate supplies of money, men, and vaccine for the control program. It was they who decided to do a nationwide immunization program. However, they did not make decisions which affected daily work schedules, epidemiologic priorities, or the flow of information.

The CDC team was in a fortunate position because at all times there were people in Belgrade and Prizren, and often in other important areas also. Through frequent telephone calls and exchange of information, we found we often had excellent information.

Transportation was a chronic problem, particularly in Djakovica. There was a daily briefing at which dozens of teams were assigned work and some attempt was made to find vehicles. By the second week of April, there was still no reliable source of transport, particularly of four-wheel drive vehicles for the rugged upland roads. The result was late starts, unmet schedules, and bickering among teams.

While the army provided 40 of the 65 teams working in Kosovo, and these were probably the best equipped and most disciplined teams, they were also non-Albanian and had problems both of morale, language, and perhaps even dedication.

I. CULTURAL PROBLEMS

The role of the historical ethnic antagonisms in this outbreak is hard to evaluate. In 1968, there were separatist demonstrations in Kosovo, and in December 1971, there were meetings in Zagreb protesting Serbian authority. The army in Kosovo, as part of an army policy to have people serve outside of their own homeland, was predominantly Croatian and Macedonian. The CDC teams' surveys showed that several communes adjacent to the four infected Kosovo communes, which had been vaccinated by the Albanians without the help of the army, were better vaccinated than the epidemic area itself (see Appendix). The importance of the scarcity of Albanian-speaking epidemiologists cannot be measured, but may have influenced the quality of contact tracing.

The Moslem community was upset by the idea that the Haji pilgrimage could be responsible for the importation. There were rumors that Ibrahim Hoti had been ordered not to admit to any illness. The Moslem tenet requiring ritual washing after sexual intercourse, coupled with the widespread story that vaccinees could not wash for 20 days, caused obvious problems. While Albanians do not practice true purdah, they do not allow strange males into their houses after dark. This was frequently cited as a reason for not scheduling nighttime vaccinations. The Albanian family structure and the architecture of their houses ensured close contacts between some

20 to 40 individuals in an extended family. This undoubtedly contributed to the large size of the second generation in Kosovo. Vaccination was slowed because the Albanians, particularly in the cool hill villages, often wore as many as seven layers of closely fitting clothing, so that 2 or 3 minutes were required to vaccinate a single individual.

Section III - IMPLICATIONS OF THE YUGOSLAVIAN EXPERIENCE FOR THE UNITED STATES' POLICY REGARDING VARIOLA IMPORTATION

The recent change in USPHS recommendations regarding routine smallpox vaccination, and the development of contingency plans for handling a variola importation, were done when the largest single outbreak in Europe was that of Poland in 1963, with 130 cases. This section will briefly outline some of the facets of the Yugoslavian outbreak which may be of importance to the United States.

1. The importation was by land travel, and was apparently brought in by a rural Moslem pilgrim. His revaccination on December 19, 1971, probably did not take. While the reason for and mode of travel would be impossible for the United States, the revaccination failure is possible.
2. Ibrahim Hoti's diagnosis was missed. This would be likely in the United States given the mild nature of his illness.
3. Ibrahim Hoti was an efficient transmitter of smallpox. While it is unlikely that patients with very mild illness excrete large amounts of virus, the experience of Ibrahim Hoti and PK in this outbreak prove that it is possible. The greater opportunity for social mobility and widespread contact of such mildly ill patients constitute a definite threat in the event of an importation.
4. The importation was made into a rural peasant society with a social and familial structure marked by close family ties and intimate living conditions. Most travelers to and from the United States and Asia or Africa would not be found in such circumstances upon return to the U.S.
5. The diagnosis was not suspected until several patients had been hospitalized, some for up to 5 days. While this is possible in the United States, one trusts it is unlikely.
6. The first indigenous generation was both large and geographically widespread by the standards of other European outbreaks. This was largely because of the patterns of visitation of Ibrahim Hoti and his apparent freedom from major symptoms. This must be considered possible but unlikely if the importation case were considerably more ill than was Hoti.
7. Latif Muzza, the man from Novi Pazar, was an unusually efficient transmitter of smallpox. While many European outbreaks have had one or more missed patients with hemorrhagic smallpox, none have had even

half as many cases resulting as did this one. The 38 cases from one missed case must be considered possible but highly unlikely in the United States.

8. Latif Muzza did not spread the illness to any contacts on either his bus ride from Novi Pazar to Cacak, or his ambulance ride from Cacak to Belgrade. This keeps unblemished the European experience that smallpox has not been transmitted on a common carrier such as a bus, plane, or train. The contingency plans for a United States importation should consider such transmission highly unlikely.

9. The background immunity in the Kosovo community, and perhaps even in Belgrade, was low. For the next few years, this will not be the case in the United States, particularly among adults, who bear the brunt of hospital-acquired or importation smallpox. The recent policy change will obviously lead to a gradual reduction in the immunity of the U.S. population.

10. Medical staff were not well vaccinated. At present, there is no concrete evidence that the vaccination status of American medical personnel is better now than it was during the surveys performed in 1963 through 1966.

11. Vaccine was of poor quality and in short supply, and vaccinators were not trained. It is the responsibility of United States authorities, and particularly CDC, to make sure this would not happen in the U.S. This outbreak perhaps shows that a slight delay in starting vaccination will be amply rewarded by better work if the time is used for training.

12. The Yugoslavs had excellent results, as have the British and others, with using remote non-medical facilities as isolation hospitals. Outside Kosovo, there were no hospital-acquired cases once isolation was instituted. The Kosovo cases could have been prevented had reliable vaccine and good techniques been used. The United States' contingency plans for a smallpox importation should encourage care of smallpox victims in isolated, preferably non-medical facilities, although we must anticipate strong pressure to hospitalize them. The Yugoslavian government was able to quickly locate and take over whatever facilities it needed, which might be difficult in the United States.

13. The vaccination efforts were hampered by an irrational set of contraindications to vaccination. This should not happen within the United States.

14. The Yugoslav response to the discovery that smallpox existed in four geographic locations, shortly after the initial diagnosis was confirmed in Kosovo, was to order widespread mass vaccination. This was partly the result of panic and partly of political and administrative demand. The inevitable results were poor coverage of all areas, including infected areas. Personnel who could have been working on contact tracing and surveillance were diverted to the vaccination effort. The plans for the United States should ensure that mass vaccination would be avoided until a reasonably thorough epidemiologic assessment of the situation is made.
15. Contact tracing was suboptimal in this outbreak. Better work might be expected in the United States. The language problem would not be as acute even if the original importer could not speak English.
16. The Yugoslavs quarantined contacts efficiently and rigorously. We might find it difficult to incarcerate over 1,000 U.S. citizens for 14 days or more. Contingency plans currently call for home quarantine with daily surveillance of temperatures. Consideration should be given to more stringent quarantine of definite first ring contacts at some point late into their theoretical incubation periods. The authorities and public took great comfort from the fact that many late second generation and most third generation cases developed prodromal symptoms while in full isolation.
17. Marboran and VIG were used freely and publicized widely. The use of these drugs should be controlled by experienced medical and public health personnel, and of course they must not be allowed as substitutes for vaccination.
18. The current United States contingency plans should be revised to provide for the needs of medical and public health tourists and observers. While WHO and CDC workers in Yugoslavia had certain positive contributions to make, the Yugoslavs also had to host observers from Albania, Rumania, Bulgaria, Austria, Hungary, and the Soviet Union, and honor requests for information from several other European nations. The United States should anticipate similar groups, at least from within the U.S. and from Mexico and Canada.
19. The CDC team was impressed by the lack of information available in Belgrade at the Federal Institute for Public Health, and at the political headquarters of Kosovo Province at Pristina. Many of the field workers knew little of new developments except by rumor. Contingency plans should include an office, one or more telephones, and a full-time person to coordinate communications. Clear lines of authority and communication should be established as early as possible.

20. The economic impact of this outbreak upon Yugoslavia will be estimated at a later date. Several borders were closed, including internal borders between Macedonia and Kosovo. Tourists were harrassed at the Hungarian border, and the Soviet Union refused to let any of its citizens travel to Yugoslavia for several weeks. Some of this might have been averted had a stream of reassuring information been released through the press and other media.

21. While this outbreak was numerically large and geographically widespread, it was rapidly controlled once the diagnosis was confirmed. Serious control efforts did not start until March 18 in Kosovo and March 21 in other areas. By this time, all of the second generation cases were well into their incubation periods. Thus only certain of the third generation cases can be considered failures of the control effort, rather than failure to detect the outbreak earlier. The rapidity of control, despite certain administrative and scientific problems, should be comforting the United States and other smallpox-free nations.

The circumstances which contributed to this outbreak would be difficult to duplicate in the United States, in other European nations, or indeed in most areas of Yugoslavia. However, the occurrence of 174 cases including 35 deaths in three generations of disease, with a missed importation and wide geographic spread, is now established as a possibility which cannot be ignored.

DISTRIBUTION

Mailing Keys 53.1, 2, 3

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APPENDIX

Vaccines Acquired from Other Nations, by Sources

<u>Nation</u>	<u>Doses of Vaccine</u>
Albania	200,000
Bulgaria	600,000
France	225,000
Greece	300,000
Netherlands	250,000
People's Republic of China	3,500,000
West Germany	125,000
Eastern Germany	60,000
Switzerland	2,325,000
USA	3,251,000
USSR	3,000,000
WHO	500,000

APPENDIX

Results of CDC Vaccination Surveys in Dragash and Suva Reca (Non-infected Communes)

April 6 and 7

<u>Village</u>	<u>Major Reactions</u>	<u>No Takes</u>	<u>Percent No Takes</u>
Plava	55	9	14%
Zjum	21	21	0%
Dikance	36	14	28%
Backa	67	18	21%
Suva Reca (school)	456	16	3%
Suva Reca	365	5	1%
Musutiste	900	7	1%
Dulja (school)	142	11	7%
Latze	183	6	3%
Junik	<u>117</u>	<u>30</u>	<u>20%</u>
Totals	2,342	137	6%

APPENDIX

Results of CDC Vaccination Surveys in Djakovica and Orahovic

Infected Communes, April 4, 5, 8

<u>Villages</u>	<u>Primary Takes</u>	<u>Revaccination Positives</u>	<u>No Takes</u>	<u>Percentage No Takes</u>
Vranic	62	105	30	15%
Dobre Vare	122	184	142	32%
Lipovec	78	184	122	32%
Rogovo	48	198	119	33%
Guska	14	128	63	31%
Brekovac	95	279	57	13%
Danjane	36	37	30	29%
Mala Hoca	147	412	182	25%
V. Krusha (school)	99	191	31	11%
V. Krusha (village)	50	173	56	20%
V. Hoca (school)	140	211	51	13%
V. Hoca (village)	<u>35</u>	<u>174</u>	<u>70</u>	<u>25%</u>
Total	926	2,276	953	23%

<u>Villages</u>	<u>Major Reaction</u>	<u>No Takes</u>	<u>Percentage No Takes</u>
Ponoshevac	243	64	21%
Batus (school)	272	26	9%
Batus (village)	153	71	32%
Crmljane (school)	91	65	42%
Crmljane (village)	<u>163</u>	<u>55</u>	<u>25%</u>
Total	922	281	23%

APPENDIX

Official Estimate of Vaccination Status
of Infected Area of Kosovo after Third Round of Vaccination,

4/14/72

Village	Population	+	%	±	%	-	%
Djakovica	34326	33276	97.2	901	2.6	59	0.2
Dujak	872	841	96.4	27	3.1	1	
Morina	344	334	97.0	10	3.0	0	
Korenica	495	480	97.7	10	2.0	1	
Rogovo	2377	2342	98.5	32	1.3	3	
Raskoc	203	171	84.0	31	16.0	0	
Dolj	578	516	89.3	58	10.0	4	
Kusevac	243	197	81.1	45	18.5	1	
Raca	226	216	95.4	7	3.2	3	
Ramoc	955	886	92.7	64	6.6	5	
Danjane	781	768	98.6	8	1.0	5	
Ratkovac	1867	1828	97.9	39	2.1	0	
Sanovac	354	350	98.8	0	0	4	1.2
Pustoselo	536	528	98.5	5	0.9	3	0.6
Nogavac	510	478	93.7	32	6.3	0	
Zjum	1109	1102	99.3	7	0.7	0	
Karasindjerdj	642	630	98.0	12	2.0	0	