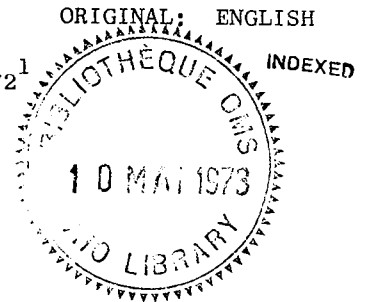




EPIDEMIOLOGIC ASPECTS OF SMALLPOX IN YUGOSLAVIA IN 1972¹

by

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In Yugoslavia, during the period 16 February to 11 April 1972, smallpox affected 175 persons, 35 of whom died. The infection struck the autonomous Province of Kosovo with 124 cases, 26 of which were fatal; Serbia proper, with 49 cases, 8 deaths; the autonomous Province of Voivodina, 1 case and 1 death; and Montenegro, 1 case (Fig. 1).

1.0 COURSE OF THE EPIDEMIC IN KOSOVO

The epidemic was recognized on 14 March, at which time the hospital wards for infectious diseases at Prizren and Djakovica had admitted 4 smallpox cases each. Six patients came from the village of Danjane, one from Ratkovac and one from Djakovica (Fig. 2). On 15 March material for virologic examination was obtained and on the following day, laboratory findings confirmed the presence of smallpox virus. It was later found that in the village of Kušavec, near Djakovica, another person was also ill, as well as one person in Novi Pazar and one in the village of Bresnica, near Čačak. The index case infected a total of 11 persons. The six persons from Danjane and the one from Ratkovac, all of whom became ill between 1 and 7 March, were found to have been in contact with the index case between 16 and 21 February. The remaining three persons who fell ill, on 3, 6 and 7 March, are believed to have been in contact with the index case most probably on 21 March in Djakovica.

After a one week lull in cases, active search in Kosovo disclosed new cases. In the period 15 to 31 March, another 100 persons became ill. These were members of families of those affected by smallpox, as well as hospital patients at Prizren and Djakovica, who had been in contact with the smallpox cases before the disease was diagnosed. They constitute the second generation in Kosovo. An additional second generation case fell ill in Hanover, Germany, on 20 March. He came from the village of Crmljani, near Danjane. The patient was found to have been in contact with the patients of the first generation from Danjane. He left Prizren for Germany on 13 March.

In the period 1 to 14 April, another 14 persons fell ill, the third generation of cases and the end of the epidemic in Kosovo.

Thus, the epidemic in Kosovo consisted of three generations: 9 cases in the first generation, 100 in the second, and 14 in the third, plus the index case, bringing the total to 124 patients, of whom 26 died. (One patient from Novi Pazar and one from Bresnica, as well as the case in Hanover, are not included in the figure for Kosovo).

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2.0 THE INDEX CASE

Epidemiologic and serologic investigations confirmed that smallpox had been imported by a haji pilgrim, Ibrahim H., a resident of the village of Danjane, who had visited Mecca with another 24 pilgrims from Kosovo early in 1972 and had returned via Iraq, by bus. During the period 3 to 6 February, he had visited the holy places in the vicinity of Basra and Baghdad, from where smallpox cases were notified at the time. The haji came back to his village (Danjane) on 15 February and the following day fell ill with a clinically undiagnosed illness (fatigue, shivering and a slightly elevated temperature). He denied having had any rash, and a month later no evidence of lesions could be seen on his body or face. He had been vaccinated against smallpox on 5 December, 1971, at Orahovac, by a physician from the Skoplje Institute of Public Health. No post-vaccinal lesion developed.

A few days after Ibrahim H. returned to his village, he was visited by, among others, the six persons from Danjane as well as the person from Ratkovac, who subsequently became ill. All were close relatives.

Ibrahim H. was the only "haji" from the village of Danjane. Another haji, Skender H., from the nearby village of Crmljane, spent one night in Ibrahim's home (between 15 and 16 February), and came again on 20 February. Serological studies showed no trace of recent smallpox infection.

All epidemiological data indicate that Ibrahim H. imported smallpox into Yugoslavia. No clinical evidence was found on his skin, but his serological findings confirmed the epidemiological diagnosis. Here, as in many other non-typical cases, the epidemiologic diagnosis is most important, particularly with a view to undertaking epidemic control measures.

3.0 COURSE OF THE EPIDEMIC OUTSIDE OF KOSOVO

Concurrent with the described epidemic in Kosovo, an epidemic developed in Serbia Proper.

Novi Pazar Ljatif M., a teacher from the village of Dobri Dub near Novi Pazar, came to Djakovica on 21 February to register for a college there and, in a still undetermined way, he had contact with the index case. On 3 March he developed prodromal symptoms, and until 7 March he was treated with penicillin for a febrile illness by the physician of the Medical Centre of Novi Pazar. During therapy, the patient developed a rash. As his illness became more severe, he was referred to the Čačak hospital, where, accompanied by his brother, he went by the bus which regularly connects Novi Pazar and Čačak. After spending one day in the Skin and Venereal Diseases Ward in Čačak, he was referred to the Belgrade Skin and Venereal Diseases Department because of the severity of his illness. He left Čačak on 8 March by the hospital ambulance together with a pregnant woman (who did not get smallpox). With the development of severe haemorrhagic complications, the patient was transferred after one day to the Surgery Hospital. On the evening of 10 March he died. The diagnosis of the duty physician read as follows:

"Status post anaphylaxiam e penicillino, melaena, anaemia post-haemorrhagica gravis propter haemorrhagian profundam intestini".

No one thought of smallpox. No autopsy was done. The cadaver was taken back to Novi Pazar to be buried with all religious rites on 12 March. Subsequently, his brother who had accompanied him to Čačak, and later accompanied his body to Novi Pazar, fell ill. One other person from the village Požega who had been on the bus connecting Novi Pazar and Čačak, also fell ill. These two second generation patients infected another three persons (third generation), the last cases in the outbreak at Novi Pazar.

Čačak During his one-day stay in the Skin and Venereal Diseases Ward of Čačak, Ljatif infected 9 persons (8 patients and a nurse), one of whom fell ill at his home in Morović (see below). All the others became ill and were treated at Čačak. The nurse died. The epidemic of Čačak ended with this group of cases.

Morović (Voivodina) In the village of Morović two persons developed smallpox. The first was a school pupil, who had been treated for scabies at the Skin and Venereal Diseases Ward of Čačak at the time Ljatif was there. He was infected by Ljatif, but fell ill in his village (Morović). From there he was transferred to the quarantine hospital in Belgrade and was recorded as a Belgrade case. His mother became infected at Morović and died.

Belgrade At the skin and Venereal Diseases Hospital in Belgrade, Ljatif infected 20 patients (including the first case from the village of Morović) and 7 health workers, who, in turn, infected another five persons. Six persons died.

Trnjane The only patient from Trnjane (near Požarevac) was infected by Ljatif at the Surgery Hospital, Belgrade, on 13 March.

In all, Ljatif infected a total of 38 persons (Fig. 3).

Bresnica Of the two cases at Bresnica, one was a first generation patient, who was infected through direct contact with the index case at Djakovica on 21 February. The second case was his wife, the only person whom this patient infected.

Play (Montenegro) The only case from Play resulted from intrahospital infection. He visited his daughter at the Djakovica hospital on 12 March and thus was in contact with the smallpox patients whose diagnosis was not yet known at this time.

Accordingly, including the index case in this epidemic, a total of 175 fell ill, 35 (20%) of whom died. In the first generation there were 11 cases during the period 1 to 7 March; in the second generation, 140 which occurred during the period 15 to 31 March; and in the third generation from 30 March to 11 April, there were 23 cases. There was thus an overlap in the time of onset of cases in the second and third generations.

4.0 COURSE OF THE EPIDEMIC BY SETTLEMENTS AND GENERATIONS

The first generation of patients came from six foci: Danjane, Ratkovac, Djakovica, Kušavec, Novi Pazar and Bresnica (Table I). In the second generation the epidemic spread to cover another 17 settlements, in addition to the six mentioned. In the third generation, the number of foci was reduced to 11: 8 in Kosovo, as well as Novi Pazar, Belgrade and Morović. In all, there were 25 smallpox foci during the outbreak.

Fig. 4 shows the geographic spread of the epidemic.

5.0 EPIDEMIOLOGY

Incubation period

The mean incubation period was 11.3 days, ranging from 7 to 16 days. The length of the incubation period for 171 patients is shown below:

LENGTH OF INCUBATION FOR 171 SMALLPOX PATIENTS

Length of incubation period (days)	7	8	9	10	11	12	13	14	15	16
No. of patients	1	5	20	26	39	39	27	6	7	1

For 88% of the patients, the incubation period ranged from 9 to 13 days. These observations are in accord with those described in the literature. No differences were noted between the length of the incubation period among the vaccinated and the unvaccinated.

Incidence and case fatality rates by sex, age and vaccination status

Of the 175 patients, 99 (57%) were male and 76 female. In Kosovo, however, there were less males than females affected (60 males and 64 females), approximately the ratio in the population. In the Čačak and Belgrade hospitals, males constituted 75% and females 25% of those affected. This also reflects the ratio of patients in these hospitals. Cases by sex and age are presented below:

SMALLPOX CASES IN YUGOSLAVIA BY SEX AND AGE

Sex	Age (years)					Total
	<1	1-6	7-14	15-19	20+	
Male	9	8	11	5	66	99
Female	3	7	8	8	50	76
TOTAL	12	15	19	13	116	175

Cases and deaths by age and vaccination status are shown in the table below. Of the 175 cases, 105 (60%) had previously been vaccinated, 66 were unvaccinated, and in 4 the vaccination status was unknown.

All cases among those less than one year of age were among the unvaccinated. In the age-group 1-6, the age-group in which most children should be protected by primary vaccination, only one of the 15 patients had been vaccinated. In the age-group 7-14, the age-group in which both the first and second revaccinations should have been completed, six cases occurred among the previously vaccinated and 13 among the unvaccinated. In the age-group 15-19 there was an equal number of previously vaccinated and unvaccinated cases. In the age-group 20 and over, 91 patients had previously been vaccinated while 21 were unvaccinated. The relatively large number of previously vaccinated cases among those over seven years of age indicates a substantial decrease in post-vaccinal immunity following primary vaccination, as well as a lack of successful revaccination when they were seven and 14 years old.

CASES AND DEATHS BY AGE AND VACCINATION STATUS

		Age (years)					Total
		<1	1-6	7-14	15-19	20+	
All cases	Vacc.	-	1	6	7	91	105
	Unvacc.	12	14	13	6	21	66
	Total	12	15	19	13	116 ^a	175 ^a
Deaths	Vacc.	-	-	1	1	6	8
	Unvacc.	8	3	3	2	7	23
	Total	8	3	4	3	17 ^a	35 ^a
Case-fatality ratio		67%	20%	21%	23%	15%	20%

^a Includes four of unknown vaccination status.

Case-fatality ratio

There were 35 (20%) fatal cases: 20 males and 15 females. The ratio was the same for both sexes. The highest case-fatality ratio was in the age-group 1-5, where eight of the 12 patients died. In the older age-groups, the case-fatality ratios ranged from 15 to 23%. Among those previously vaccinated, the case-fatality ratio was only 8% while among the unvaccinated it was 35%.

Influence of the length and intimacy of contact on the number of secondary cases

The large number of secondary cases originating from one single source is closely linked with the length and intimacy of contact between the patients and susceptible persons. The number of secondary cases depends also on the clinical form and stage of disease at the time the contact took place.

The first patient from the first generation, Jemin B., a relative of the index case from Danjane, spent the first 12 days at home till he was hospitalized (Fig. 5). Two of his children fell ill, one and two days later. They shared a room with him and all three were admitted to the hospital at the same time. Of the remaining five members of the family who shared a room with him, all became ill between 15 and 19 March. Three other members who slept in separate rooms remained well despite their many daily contacts during the 12 day period the smallpox cases were at home.

Paulina K. from the village of Kušavec (Fig. 6), a first generation patient, with mild clinical smallpox, was detected only on the 18th day of her illness. She infected 16 persons from four villages of Kosovo.

However, Sadeta Š., a six year-old girl from the village of Ratkovac, also a first generation patient, was hospitalized on her fourth day of illness (first day of rash). In her family of 17 persons, none became ill except her mother who attended Sadeta throughout her stay in Prizren hospital. At the hospital Sadeta infected a total of seven persons within seven days at which time her illness was correctly diagnosed.

Patients with pronounced typical changes on the skin and mucosa produced the largest number of secondary cases. Ljatif Lj. who experienced the haemorrhagic form of smallpox, caused 38 infections in three towns among direct contacts - the largest reported number of infections known to have been caused by a single patient. This occurred despite his very short stay in the Čačak hospital and the skin and surgery hospitals in Belgrade. This suggests that he experienced the flat form of smallpox rather than the haemorrhagic form as the haemorrhagic form is usually associated with comparatively few secondary cases. Notably, the haemorrhagic form of smallpox in the nurse from Cačak and Belgrade, as well as in the patients from Djakovica and Stari Trg resulted in no secondary cases. The relatively late time of death of Ljatif, the eighth day, speaks in favour of this hypothesis.

Hospital and ex-hospital infections

In this epidemic, 84 patients (48%) acquired infection in a hospital as shown below:

SMALLPOX CASES BY PLACE OF INFECTION

	Place in which infection occurred		Total
	Hospital	Ex-hospital	
Kosovo	43	81	124
Belgrade	28	4	32
Novi Pazar	3	3	6
Čačak	8	-	8
Other	2	3	5
Total	84	91	175

This is approximately the same proportion as acquired infection in hospitals during European outbreaks between 1961 and 1970.

The largest number of hospital infections was 43 in Kosovo. Belgrade accounted for 28; Novi Pazar, 3, and Plav and Trnjane, one case each. Unlike the other foci, in Kosovo there were twice as many infections acquired outside the hospital as in the hospital. One group of the hospital-acquired infections was made up of patients and hospital staff of Djakovica and Prizren at the time the first eight smallpox cases were hospitalized there. A second group was infected in the maternity unit, the source of infection for this unit being undetermined. The third group consisted of visitors coming to the Djakovica hospital before smallpox was diagnosed. Some persons were infected in the Health Centre of Djakovica where they were in contact with the first generation cases. These persons became ill after returning home and thus created new foci. It is apparent that when smallpox is undiagnosed and the cases isolated, the hospital and out-patient units play an important role in disseminating infection.

6.0 DISCUSSION

Several factors contributed to the development of the outbreak.

Smallpox was last recorded in Yugoslavia in 1930. In the meantime, compulsory vaccination of children (primary vaccination at the age of 3 months to 3 years, and revaccination at 7 and 14 years) has been regularly carried out. A certain proportion of the male population has also been vaccinated during army service. According to available

records, about 80% of conscripts were vaccinated but the success was inadequately or not checked at all in some areas. Of late, the percentage of town children who have been vaccinated is decreasing and physicians have been discussing the desirability of routine vaccination against smallpox. Thus, a rigorous implementation of compulsory vaccination has been difficult. Among the more elderly citizens, the immunity acquired through previous vaccinations had greatly decreased or vanished so that there was a large number of persons susceptible to infection.

Rural families in Kosovo are large, with many children; several members of the family sleep in a single room; they have many relatives who frequently visit each other; and the economic and other standards are unsatisfactory. Adult males often travel from one part of the country to another, as well as outside of Yugoslavia, looking for work.

As there has been no smallpox for over four decades in Yugoslavia, the physicians had no personal experience in its diagnosis, epidemiology or control. Thus, there was a delay before the correct diagnosis was made and control procedures instituted, even though the clinical picture of the first generation of cases was typical.

Such factors made it possible for the imported case to obtain the dimensions of the largest post-war outbreak of smallpox in Europe.

7.0 EPIDEMIC MEASURES

More details on the epidemic measures undertaken by the committees for the control of quarantine diseases will be given in separate papers. Vaccination of the population in the initial foci in Kosovo started on 16 March immediately after the disease was diagnosed. The same was done in other foci in the country. Vaccination was extended in concentric rings spreading to whole territories of the communes in which the cases occurred. In Kosovo, by the end of March, almost the whole population was vaccinated. It had to be continued to the end of April, however, because vaccination was unsuccessful in a proportion of the vaccinees. Vaccinations were repeated until over 95% had been successful. Based on the decision of the Federal Epidemiologic Commission, vaccination was extended to cover the whole population of Yugoslavia, 18 million persons.

Except for four cases, all in the second generation were infected before 15 March, i.e. before the diagnosis was determined. The third generation cases were mostly among those whose first vaccination was unsuccessful and those such as a 70 year-old woman whose general physical state was assessed by the physician to be such that no vaccination should be performed.

Immediately after the epidemic was detected, the Federal Institute of Public Health renewed the Manual on the control of smallpox, previously distributed to all the health institutions in the country. The Federal Epidemiologic Commission met weekly throughout the epidemic to keep the situation under review and to recommend to the federal committee what current measures to undertake.

As regards contact tracing, the interviews in Belgrade alone involved about 3000 persons. To facilitate this activity, special forms were prepared with questions phrased in the form of reminders.

Health surveillance in the Kosovo foci consisted of daily visits to all the inhabitants of a settlement during which temperatures were taken and the skin and mucosa inspected. In the rest of the settlements situated in the infected communes, this measure was implemented every three days.

Contacts were placed in special quarantine facilities (e.g. in the Djakovica hospital and in a motel near Belgrade). There were also quarantine facilities set up in individual houses, as well as in whole villages, as was the case with Danjane and Ratkovac and some other villages.

Other measures consisted of restriction of movement of the population to the infected areas, checking vaccinations at exit and entrance points and prohibition of public meetings.

8.0 CONCLUSIONS

The risk of importing smallpox from infected areas will continue until smallpox has been eradicated from the world.

Notwithstanding the fact that 18 million inhabitants were vaccinated early in 1972, making Yugoslavia one of the most protected countries of the world, the level of population immunity will decrease as time passes. Therefore, it is indispensable to continue compulsory vaccination of particular groups of the population as well as those travelling to endemic countries and potentially infected areas.

This outbreak has shown that all health workers, especially physicians, must have at least a basic familiarity with clinical, epidemiological and preventive measures in smallpox. All health workers must be familiar with vaccination techniques.

The relatively rapid extinction of the epidemic was possible thanks to the efforts made by special control units at all political and social levels, solidarity of the health services of the republics, provinces and the army, as well as international solidarity and assistance provided by the World Health Organization.

In order to ensure a maximum preparedness in case of importations of infection such as smallpox, cholera or other dangerous diseases and with a view to reducing the enormous expenses involved in epidemic control, it is imperative that a system of specialized preventive institutions be created with defined territorial responsibility and tasks, functionally linked both vertically and horizontally, whose work in normal conditions would contribute to reduce the risk of importation and the spreading of quarantinable diseases in general. At the same time their work could be aimed at combating other communicable diseases.

TABLE 1. SPREAD OF EPIDEMIC BY SETTLEMENTS AND GENERATIONS

I Generation	II Generation	III Generation
1. Danjane	1. Danjane	1. Danjane
2. Ratkovac	2. Ratkovac	2. Ratkovac
3. Djakovica	3. Djakovica	3. Djakovica
4. Kusavec	4. Kusavec	
	5. Dujak	4. Dujak
	6. Morina	
	7. Rača	
	8. Ramoc	5. Ramoc
	9. Raškoc	
	10. Sanovac	
	11. Vitromirica	
	12. Korenica	
	13. Rogovo	6. Rogovo
	14. Zjum	7. Zjum
	15. Karašindjerdj	
	16. Pusto Selo	
	17. Dolj	
		8. Stari Trg
5. Novi Pazar	18. Novi Pazar	9. Novi Pazar
6. Bresnica	19. Bresnica	
	20. Čačak	
	21. Beograd	10. Beograd
	22. Trnjane	
	23. Plav	
		11. Morović

FIGURE 1
YUGOSLAVIA: SMALLPOX CASES, 1972

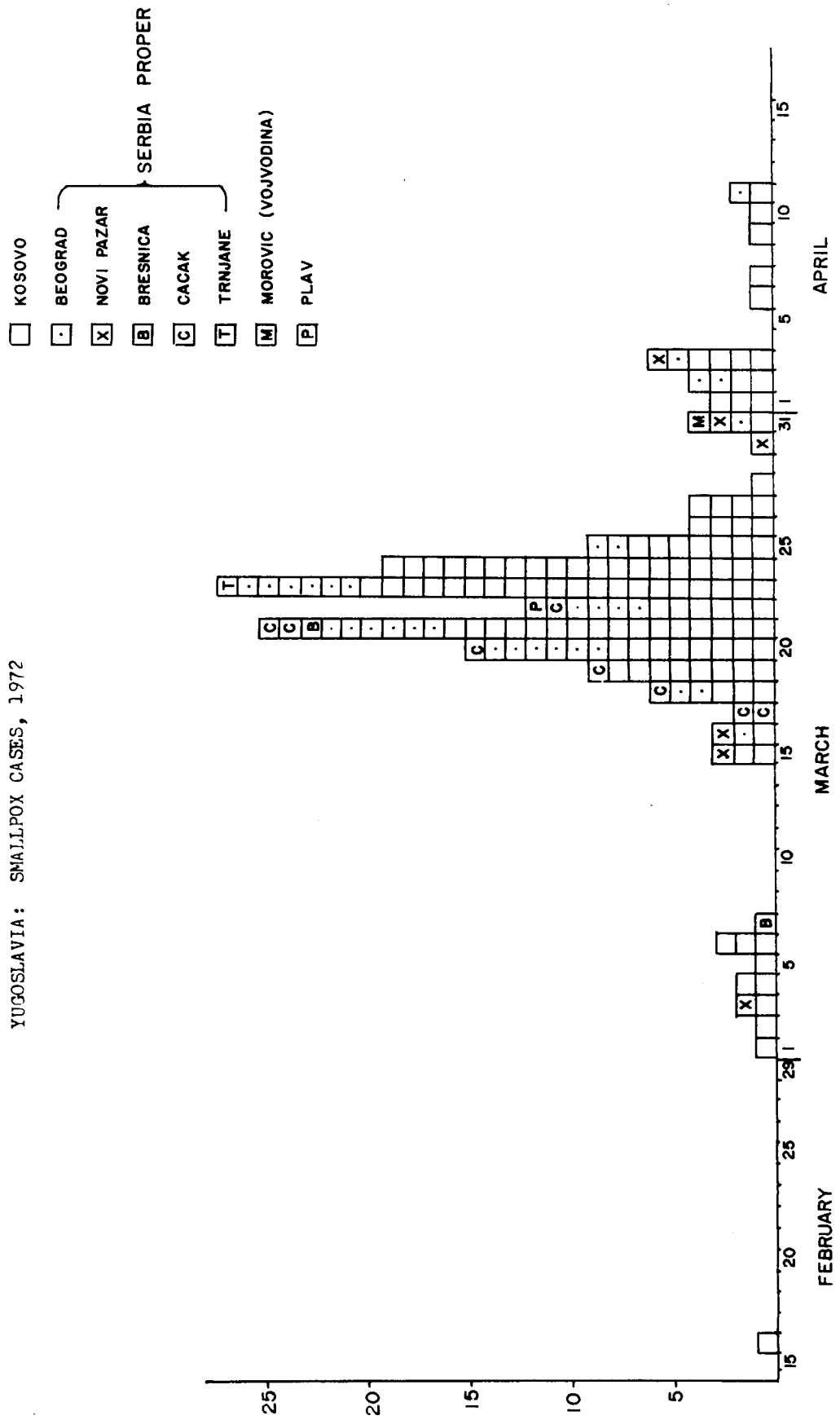


FIG. 2. YUGOSLAVIA: GEOGRAPHICAL
LOCATION OF THE 11 FIRST GENERATION CASES

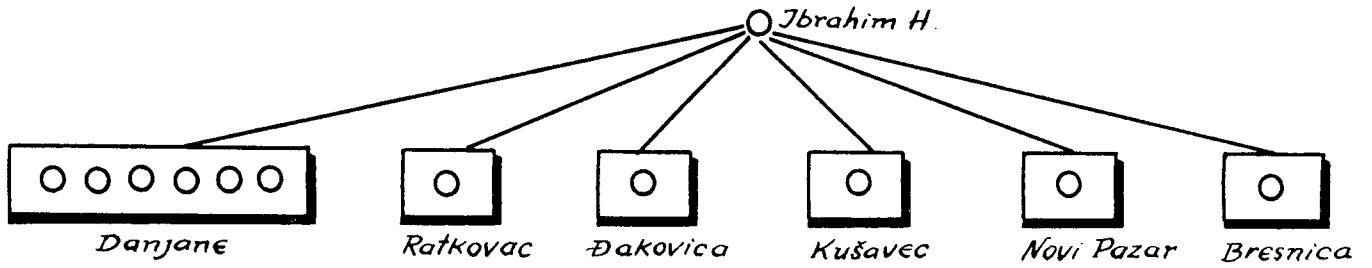


FIG. 3. YUGOSLAVIA: SMALLPOX CHAIN OF TRANSMISSION

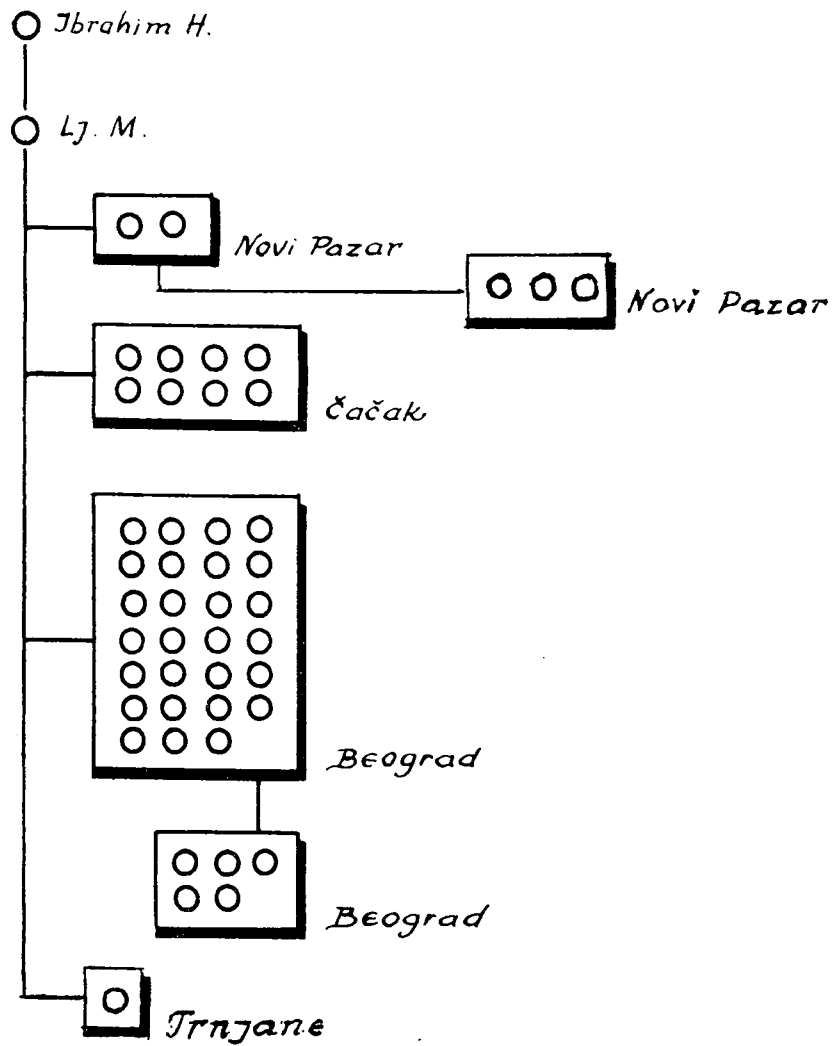


FIG. 4. YUGOSLAVIA: SPREAD OF SMALLPOX EPIDEMIC, 1972

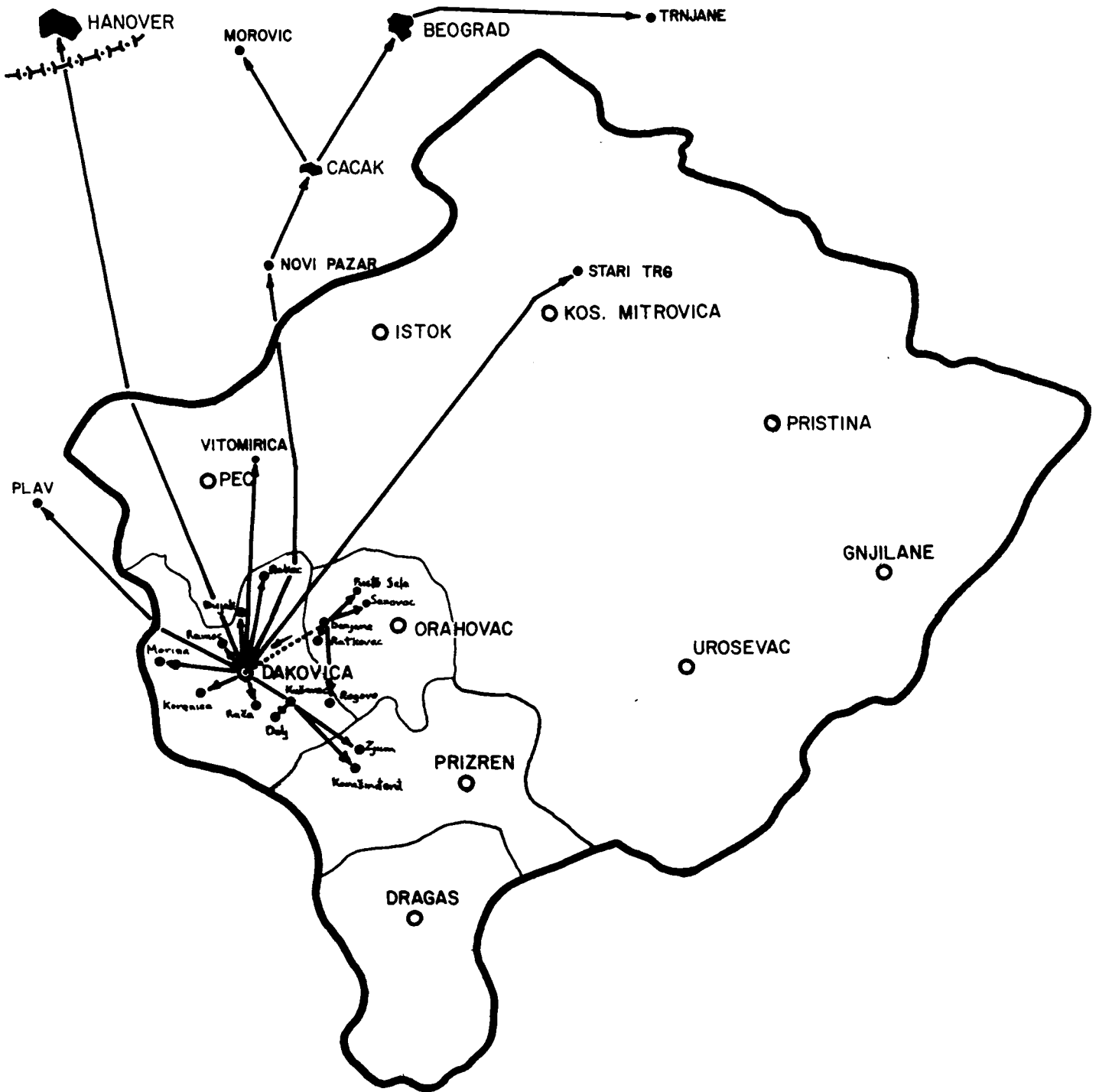


FIG. 5. DISSEMINATION OF SMALLPOX BY JEMIN B. IN HIS HOUSEHOLD

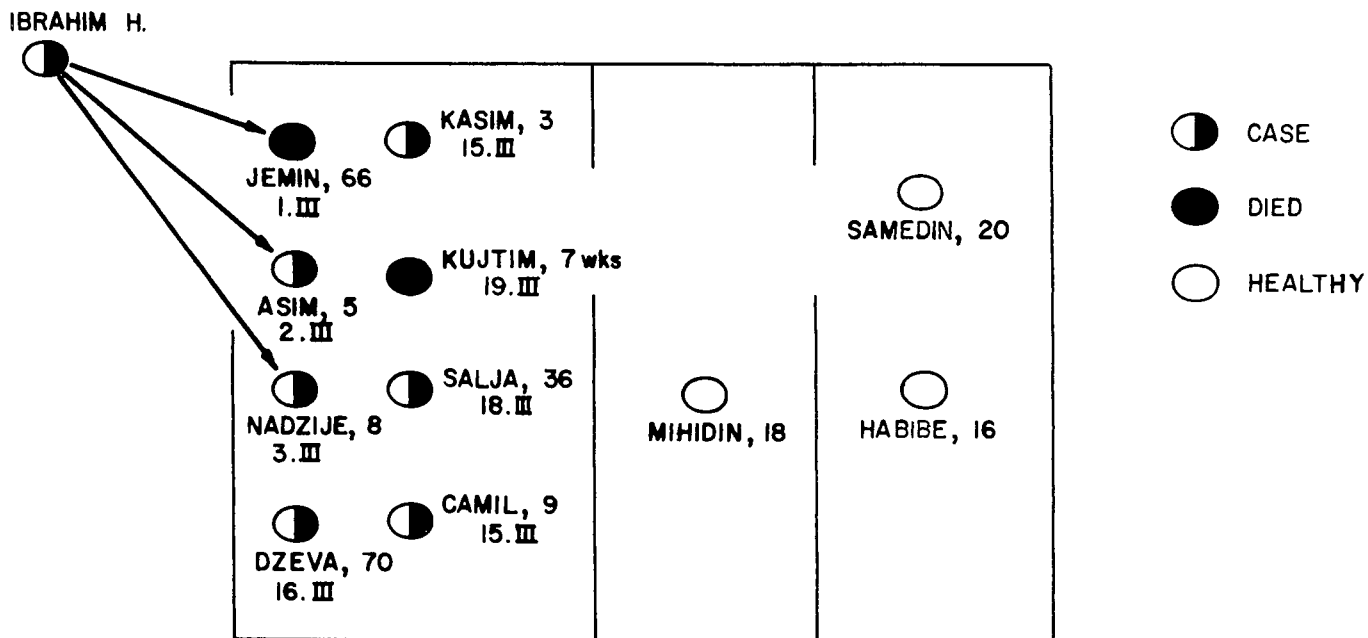
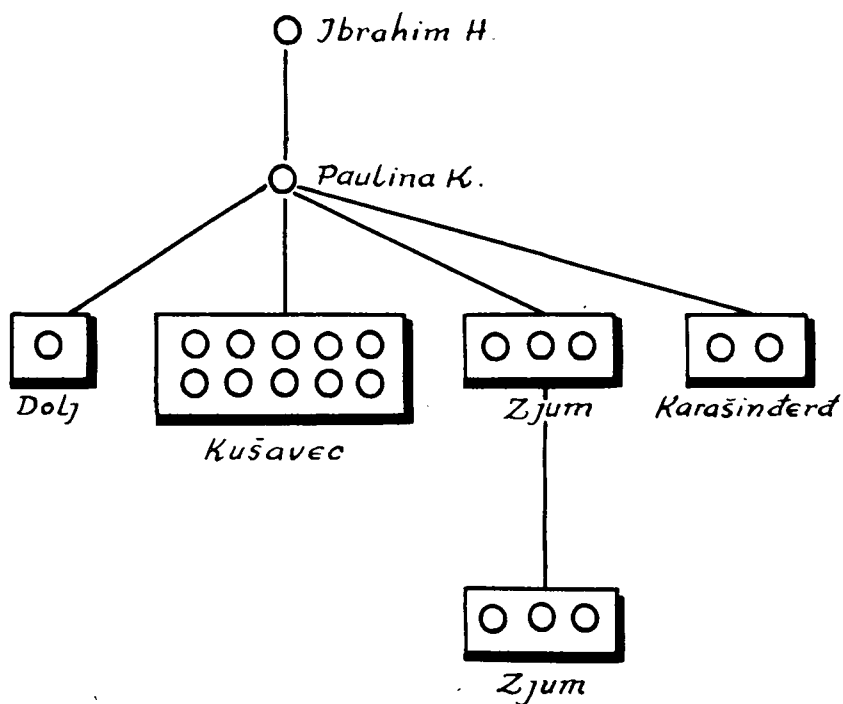


FIG. 6. DISSEMINATION OF SMALLPOX BY PAULINA K.



The purpose of the WHO/SE/- technical information series of documents is to acquaint interested research and public health workers, as well as WHO staff, with the progress of smallpox research and eradication by means of:

- (1) summaries of some relevant problems of fundamental, epidemiological and operational aspects;
- (2) field project reports and other communications on particular research and eradication aspects which would not normally be published by WHO or elsewhere;
- (3) papers that may eventually appear in print but, on account of their immediate interest or importance, deserve to be made known without delay.

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