

## VIRUS MENINGO-ENCEPHALITIS IN SLOVENIA

### 1. Epidemiological Observations

J. KMET, M.D.

*Central Institute of Hygiene,  
Ljubljana*

J. VESENJAK-ZMIJANAC, M.D.

*Institute of Microbiology, Faculty of Medicine,  
University of Zagreb ;  
Central Institute of Hygiene, Zagreb*

M. BEDJANIČ, M.D.

*Clinic for Infectious Diseases,  
Faculty of Medicine, University of Ljubljana*

S. RUS, M.D.

*Clinic for Infectious Diseases,  
Faculty of Medicine, University of Ljubljana*

Manuscript received in August 1954

#### SYNOPSIS

The authors describe the main epidemiological features of the meningo-encephalitis observed in Slovenia since 1946. It is endemic there with occasional epidemic outbreaks ; close study has been made of the epidemic which occurred in 1953. The disease is markedly seasonal, 95% of all cases in 1953 occurring from May to September. Another characteristic feature is the mention of tick bites in a very large number of case-histories ; although the Slovenian tick fauna has not yet been systematically investigated, the generally incriminated vector is the tick *Ixodes ricinus*. In close association with this feature, the disease appears primarily among persons whose work lies in the woods where the ticks are found. This consequently affects the age distribution of patients, 56.2% of whom in 1953 were 11-30 years old. No spread of infection from person to person has been noted.

The disease closely resembles the tick encephalitis observed in Czechoslovakia and the meningo-encephalitis described in western Russia and Austria. The authors consider it probable that the virus circulates in enzootic foci between rodents and ticks and that man is accidentally infected.

A special form of meningitis of unknown origin was observed in Slovenia, the north-western part of Yugoslavia, as early as 1946, but the data on it were scarce. Study of this disease was started in 1947, and its



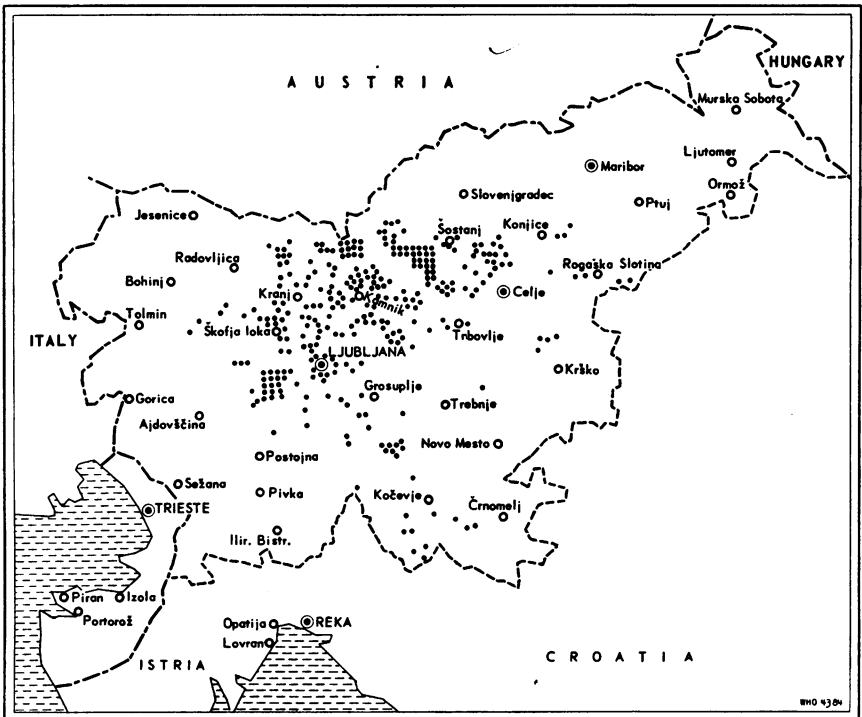


the area, forestry is a highly developed industry. The standard of hygiene of the population is very high.

The endemic area known since 1946 extended towards the north-east in 1953, always maintaining a close connexion with the infected area of earlier years. No cases occurred in 1953 in previously non-endemic areas where there had only been a few sporadic cases in earlier years. Many patients came from villages where the disease had appeared in earlier years, and many from other villages of the endemic area where there had been no cases of disease until 1953. The disease has not so far been noticed in other parts of Yugoslavia.

The second epidemiological characteristic of this disease is its seasonal incidence, which was clearly observed in 1953. There were no cases in the first three months of the year, the first patient falling ill on 12 April. During May and June the number of cases increased rapidly and reached its peak in July. In August and September the number of cases decreased, and in October the last few cases appeared. The last patient fell ill on 20 October.

FIG. 3. ENDEMIC MENINGO-ENCEPHALITIS IN SLOVENIA, 1953



Each dot represents one case.

There were no cases in November or December. From May to September 95% of all cases occurred, while in July, which represents the seasonal peak, 33% of all cases occurred.

A comparison of the seasonal incidence of meningo-encephalitis in the Ljubljana area in 1953 with the seasonal incidence of epidemic meningitis in Slovenia during 1949-51 is given in fig. 4.

**FIG. 4. SEASONAL INCIDENCE OF MENINGO-ENCEPHALITIS IN LJUBLJANA AREA IN 1953 AND OF EPIDEMIC MENINGITIS IN SLOVENIA IN 1949-51**

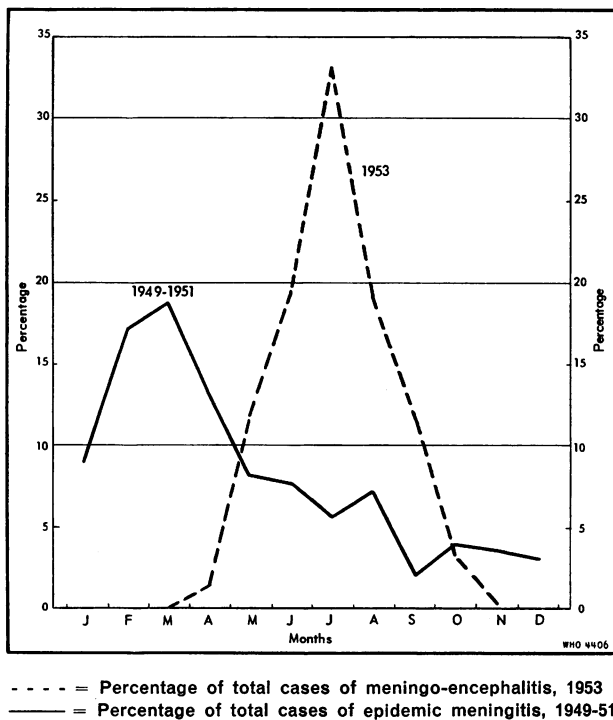
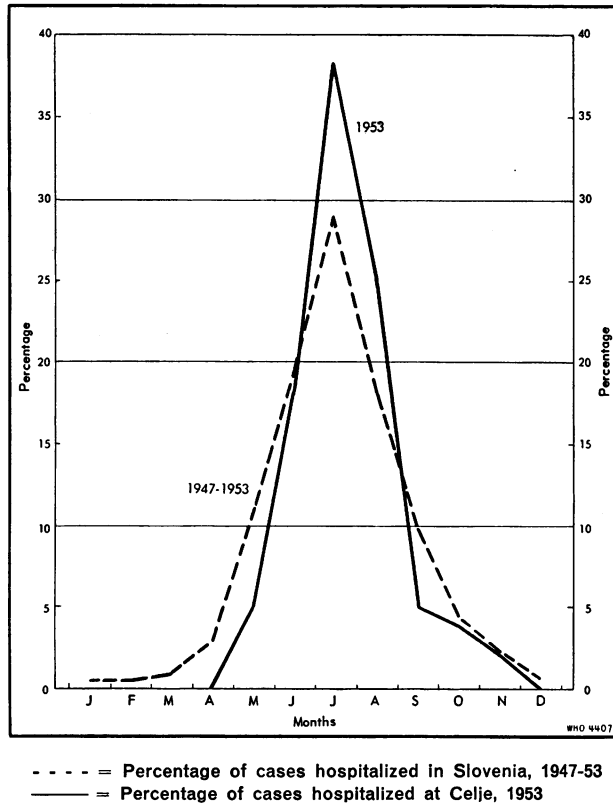


Fig. 5 shows the seasonal incidence of all cases hospitalized in Slovenia in 1947-53 and, for the sake of comparison, cases hospitalized at Celje in 1953. These curves correspond essentially to the curve of the seasonal incidence of cases from Ljubljana in 1953. Single cases that appeared in earlier years (1947-52) in the winter months were probably of different etiology.

Cases occurred simultaneously in different parts of the endemic area. Within villages, cases did not occur at particular periods but singly at sporadic intervals. Several weeks, or even several months, might elapse between the appearance of two cases in the same village.

**FIG. 5. SEASONAL INCIDENCE OF MENINGO-ENCEPHALITIS IN SLOVENIA**

The third epidemiological characteristic is that tick bites appear in the histories of a majority of patients. We found a history of tick bite in 129 patients out of 208, or 62%. However, among the 79 patients who denied tick bite were 36 woodsmen and peasants, who might have been bitten by a tick while working in the woods, and they agreed to this possibility.

With regard to tick bites, the most interesting patients are those who are thought to have had no connexion with ticks or woods for a considerable period of time before the onset of the disease. Table I shows data on 10 cases from Ljubljana; in six cases we could ascertain that they had been in the woods within the endemic area and had been bitten by ticks within 2-3 weeks before the onset of illness. A seventh had been in the mountains during that period, but does not remember having been bitten by ticks. Two patients gave a negative answer, and one could not be questioned.

From these 10 cases we may cite two in particular. The first was a 28-year-old nurse from the Cancer Institute of Ljubljana, who visited her parents in a small village on 21 June. (Cases of meningo-encephalitis were

reported from the neighbourhood of this village in 1946, 1947, 1951, and 1952.) While she was gathering hay and picking bilberries, she was bitten by several ticks. She fell ill on 5 July with a headache and vomiting which lasted three days. For seven days she was well, but on 15 July she developed typical symptoms of meningitis. The second case was a 22-year-old house-

**TABLE I. DATA ON 10 CASES OF MENINGO-ENCEPHALITIS FROM LJUBLJANA IN 1953 EPIDEMIC**

Case	Age (years)	Sex	Occupation	Connexion with woods	Date of tick bite	Date of onset of disease
M. M.	12	male	schoolboy	none	not bitten	4 May
I. M.	9	female	schoolgirl	data not available	data not available	24 June
D. B.	12	male	schoolboy	picking bilberries	3 June	10 July
S. F.	28	female	nurse	picking bilberries	21 June	5 July
V. B.	6	male	child	picking bilberries	13 July	16 July
K. C.	19	male	forestry student	working in woods	1 July	13 July
L. M.	13	male	schoolboy	camping in woods	7 July	19 July
Š. F.	22	female	housewife	day's excursion	22 July	26 July
Š. Š.	35	female	bank official	none	not bitten	10 August
K. B.	17	male	schoolboy	mountaineering	15 September (possibly)	30 September

wife from Ljubljana who went for a day's excursion on 22 July to a mountain resort in the most infected area. On returning home in the evening she found ticks on herself. She fell ill on 26 July with a headache and vomiting that lasted only three days. On 7 August she fell ill with meningitis.

During the epidemic—i.e., in July and August—a group of 20 forestry students from Ljubljana were engaged in practical work in the same resort. Three of them became ill after four weeks of work there. The students were daily exposed to tick bites.

The fourth epidemiological characteristic of this disease is the typical distribution of cases among the towns and villages. This is illustrated by the following tabulation, which shows the 208 cases hospitalized in Ljubljana in 1953 analysed by residence and by profession :

<i>Analysis by residence</i>		<i>Analysis by profession</i>	
Villagers . . . . .	189	Peasants, woodworkers, and their families . . . . .	111
Inhabitants of Ljubljana . . . . .	10	Industrial workers . . . . .	54
Inhabitants of small towns . . . . .	9	State employees . . . . .	21
Total . . . . .	208	Craftsmen . . . . .	16
		Others . . . . .	6
		Total . . . . .	208

Thus, 90.9% of the cases occurred among villagers and 9.1% among town dwellers. Besides the 10 cases from Ljubljana considered earlier, there were nine cases from small towns with 5,000 - 10,000 inhabitants; in seven of these nine, a connexion with the woods within 2-3 weeks of the onset of the disease was proved. In four of these seven a tick bite was ascertained, while the remaining three admitted the possibility of a tick bite.

Among the professions, 53.4% of cases occurred among woodsmen, peasants, or their families and 26% among industrial workers. The high percentage among the latter is explained by the fact that most of them live in villages and engage in rural work as well in their spare time.

The fifth epidemiological characteristic is shown in the typical age distribution of cases. Most cases are found in young or middle-aged persons, and very seldom in small children or old people, as will be seen from the following tabulation, by age-group, of the 208 cases admitted to the Clinic for Infectious Diseases in Ljubljana in 1953:

<i>Age-group (years)</i>	<i>Number of cases</i>
0 - 5	11
6 - 10	15
11 - 20	75
21 - 30	42
31 - 40	26
41 - 50	28
51 and over	11

Thus, 56.2% of patients were found in the group aged 11-30 years; children under 6 years of age amounted to only 5.3%, and children 1 or 2 years old to only 1.9%. Only 2.4% of the patients in 1953 were older than 60. The age distribution found in our cases would seem to indicate that there is a close relationship between this disease and woods and the ticks found in them.

The distribution of cases according to sex was very nearly equal (108 men and 100 women).

The sixth epidemiological characteristic is the fact that no spread of infection from person to person could be found: 196 cases (94.2%) were sporadic, i.e., one case per family. In only six families were there two cases per family (12 cases, or 5.8%). On analysing these six families, it was found that in two families the onset of illness of both cases occurred on the same day, which excludes infection by personal contact. As to the remaining four families, where the persons fell ill within an interval of 2-7 weeks, in three families we found a history of ticks having bitten the second person in the family to fall ill.

During this epidemic there were no cases of the disease among the hospital staff. There were also no infections among patients suffering from other diseases and lying in the same room as our cases.



In the above-mentioned resort where three forestry students fell ill, a group of 18 seasonal workers worked from spring to autumn in 1953 clearing the wood and planting new wood. In the period from 12 April to 13 June seven workers fell ill, and between 20 June and 3 July two workers who were employed all the year round, and who worked close to the seasonal workers, also fell ill. All nine patients (7 women and 2 men) bicycled daily to work from villages 10 km away. These were all the only cases in their families, and the only thing they had in common was their daily work in the woods, where they were bitten by ticks several times a day.

It is difficult to say for how long meningo-encephalitis has been appearing in Slovenia. Many of the inhabitants of the endemic area have told us that they had had severe meningitis before the second World War, but that they had recovered quickly. Analysis of the official statistics of epidemic meningitis for the years 1925-40 shows a very high morbidity rate in 1940. While in the preceding years the morbidity rate ranged from 0.05 per 10,000 to 0.5 per 10,000, in 1940 it was as high as 5.5 per 10,000. All documentary material about the 1940 epidemic was lost during the war. From the statements of doctors who worked in this epidemic, however, we can conclude that the disease was probably serous meningitis, that mortality was very low, and that the disease appeared mostly in districts which are known to us now as the area of endemic meningo-encephalitis. The 1940 epidemic began in April and lasted several months. From all this, we may surmise that the disease we are discussing in these papers had probably already appeared before the war, but under a different diagnosis.

### Discussion

The epidemiological characteristics of endemic meningo-encephalitis, together with its clinical picture (see page 503) and the antigenic properties of the virus isolated from a patient's blood in the 1953 epidemic in Slovenia (see page 513) show a great resemblance to the tick encephalitis described by Czechoslovak authors,<sup>2-4</sup> who succeeded in isolating the virus from the blood and spinal fluid of patients and also from ticks collected in endemic areas. There is also a great resemblance to the meningo-encephalitis described in western Russia,<sup>1</sup> and to that found in Austria (F. Lasch and G. Grinschgl—personal communications).

In the Czechoslovak and Russian encephalitis, viruses have been repeatedly isolated from *Ixodes ricinus*, the patients come chiefly from villages, and a close connexion with woods has been proved. The seasonal peak is in July and August. In the different parts of the endemic areas in Slovenia where ticks have been collected, only *Ixodes ricinus* has so far been found; however, the tick fauna has not yet been systematically studied.

In addition to such features as the seasonal incidence of meningo-encephalitis in Slovenia, and its close connexion with woods and ticks, we consider its endemic occurrence, which points to the probable reservoir of infection in nature, as very characteristic. In Russian spring-summer encephalitis, viruses have been successfully isolated not only from the blood of patients, from brains of lethal cases, and from the tick *Ixodes persulcatus*, but also from the brains of different wild rodents, which proved to be the reservoir of infection in nature.<sup>5</sup> In spite of the fact that we have not so far succeeded in isolating the virus from ticks and that we must grant the possibility that there may be other carriers of this illness, we consider the ticks to be the most probable carriers and surmise that they become infected in nature from animals, probably from wild rodents. The virus probably circulates between rodents and ticks, and so enzootic foci are created. Man is accidentally infected and serves as an indicator of the existence of natural enzootic foci.

### RÉSUMÉ

En 1946 déjà, une forme particulière de méningite d'origine inconnue, décrite alors sous le nom de méningite séreuse, a été observée en Slovénie. Les recherches entreprises dès 1947 montrèrent son endémicité et ses fluctuations saisonnières. En 1953, une grave épidémie éclata. Les auteurs de cet article ont étudié l'épidémiologie de la maladie, d'après 208 sujets hospitalisés cette année-là dans la Clinique pour maladies infectieuses de Ljubljana, et considérés comme atteints de méningo-encéphalite.

La maladie est endémique. La principale zone d'endémicité, rurale et forestière, connue en 1946 déjà, se trouve au centre de la Slovénie; elle s'est étendue vers le nord-est en 1953. La maladie n'a pas été signalée dans d'autres parties de la Yougoslavie.

L'incidence saisonnière est très nette : 95% des cas se sont manifestés de mai à septembre, avec un maximum en juillet (33% du nombre annuel des cas). Dans diverses parties de la zone endémique, des cas ont apparu simultanément, ce qui n'est pas en faveur de l'idée d'une progression de la maladie. Dans les villages, les cas ont été sporadiques, séparés les uns des autres par des semaines, parfois des mois.

Dans 62% des cas étudiés, des piqûres de tiques ont été incontestablement à l'origine de l'infection. Ce sont les villageois qui sont le plus touchés (90,9% des cas contre 9,1% parmi les citadins). Les personnes jeunes ou d'âge moyen sont les plus fréquemment atteintes (56,2% des cas dans le groupe d'âge de 11-30 ans).

On n'a constaté aucune contagion directe d'homme à homme; 94,2% des cas ont été sporadiques. Aucune contagion d'hôpital n'a été signalée.

Il est difficile de dire depuis quand la méningo-encéphalite sévit en Slovénie. D'après les données dont on dispose, on peut estimer que la maladie existait avant la deuxième guerre mondiale — bien que sous un nom différent de celui qu'on lui attribue aujourd'hui — et qu'elle n'a causé qu'une faible mortalité.

Les caractères épidémiologiques, cliniques et virologiques de la méningo-encéphalite épidémique rapprochent cette maladie de l'encéphalite transmise par les tiques, décrite par les auteurs tchécoslovaques qui ont isolé le virus du liquide céphalo-rachidien des malades et du corps des tiques récoltées dans les zones endémiques (*Ixodes ricinus* en particulier). Elle ressemble aussi à la méningo-encéphalite signalée en Russie occidentale et en Autriche. Le caractère endémique et rural de cette forme de méningo-encéphalite semble indiquer qu'il existe un réservoir naturel de virus, constitué peut-être par des

rongeurs sauvages. En effet, ces animaux ont été trouvés porteurs du virus de l'encéphalite verno-estivale russe, dans les contrées où cette maladie sévit.

Le virus circule probablement entre les rongeurs et les tiques. Des foyers d'enzootie prennent naissance, dont la présence est révélée de temps à autre par l'infection accidentelle de l'homme.

### REFERENCES

1. Davidenkov, S. N., Figurina, M. M., Shtilbans, I. I., Kulkova, E. F. & Pokrovskaja, O. A. (1952) *Klin. Med. (Mosc.)*, **30**, 19
2. Gallia, F., Rampas, J. & Hollender, L. (1949) *Čas Lék. čes.* **88**, 224
3. Hloucal, L. (1953) *Schweiz. med. Wschr.* **83**, 78
4. Rampas, J. & Gallia, F. (1949) *Čas. Lék. čes.* **88**, 1179
5. Soloviev, V. D. (1944) [*Spring-summer tick encephalitis*], Moskva