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Certain Characteristics of Epidemiological, Clinical and Laboratory Diagnosis of Typhoid Forms of Tularemia, by L. M. Khatenever, Tularemia Section of VIEM

The following data were collected and analysed by us, together with M. N. Ozerova, and with the participation of local doctors Liktevshtei, Ermolinskaya, Ulina, and assistant doctors Zubenko and Rottelmil, in one of the centers of the fall-winter outbreak of tularemia of a mouse origin. This outbreak appeared in conjunction with a wide spread and intensive epizootia among field and house mice. An epizootic, which expanded extensively in October, started among the field mice in September. As a result of the mass death of the rodents from tularemia, very few were alive in November.

The bacteriological diagnosis of the tularemia epizootic was established by a biological method with the isolation of culture of the tularemia agent from house mice. Bacteriological tests of satiability with the tularemia agent, on small mouse type rodents indicated that the infectability of the house mice is no less than 47.2%. Concerning separate objectives; the degree of infectability in these rodents, to tularemia, was 28.6% in house mice, 56.5% in granary mice, 52-59% in mice inhabiting hay-lots and no less than 45% in mice inhabiting warehouses.

Single cases of infection of humans, according to our retrospective laboratory studies, can be attributed to the last part of May, the latter part of August and in September; the outbreak began in early October and maximum infection period was in the first 10 days of November. The curve of infections decreased in middle November. Table 1.

The diagnosis of tularemia in humans was established somewhat late. At the

beginning of the outbreak local doctors diagnosed the illness as grippe.

The outbreak was quite intensive. The death rate, in the villages studied by us, fluctuated in levels from 0.6 to 2.3%, but an average rate was 0.85%. The number of women ill was almost twice the number of men; 64.6% women - 35.4% men. This is explainable by the predominant female population in the villages.

The portals of infection and contamination of humans are various. Because in a large number of the patients, a phenomenon of the upper respiratory system and the lungs was observed, we concluded that the inhalation tract was the path of infection in many cases during this outbreak. Any circumstances could serve the agent in infiltrating the respiratory system. In many populated areas, during thrashing, mice excrement and dead mice in large quantities could be found in the grain. During milling of the grain into flour, the agent of tularemia, evidently, was suspended in the air, in the flour dust, which entered the respiratory system. During the mass invasion of the mice and after their extermination, large quantities of excrement were found in storage spaces (cupboards, pantries and others). While cleaning the rooms, the agent was suspended in the air, with dust, and could be inhaled. Besides the inhalation tract, the mouth and food tracts were portals for the agent. Indicating these as paths of infection are many cases of tularemia, with the affection of the submaxillary glands. In such cases, the agent evidently entered the organism in food or drink.

The portals of infection in humans during this outbreak were not limited by the two given paths. We ascertained single cases of bubonic type tularemia, caused by direct contact with the agent, during cleaning of buildings. Here are data of one such infection.

Patient B. Became ill 19 November, 2 days after cleaning a closet where mice excrement was plentiful. 20 November, patient noticed a blue spot on the palm surface of the right arm. In the next 2 days a suppuration took place, which burst in the latter part of November. 25 November, there was noticed lymphangitis over the whole palm surface of the forearm, from the wrist to the elbow. By the morning of 26 November, the lymphangitis disappeared, but there appeared a painfulness in the region of the ulna glands, and soon, also in the right underarm region. The patient felt a swelling of the glands. In a few days the glands attained the size of a chicken egg. Tularemia infection in this case was confirmed by a skin allergical reaction test.

Liktenshtei discovered the following case of tularemia after the bite of a mouse, on the third finger of the right arm.

The patient X, 2-3 days after the bite felt chilly and a pain in the region of the right ulnar flexion. After several days, there appeared a swelling of the glands, to the size of an egg, and painfulness, which simultaneously appeared in the underarm region, and later a bubo the size of an egg developed under the arm.

Consequently, during this outbreak, a majority of the cases were infected via the respiratory tract - with air, containing the agent in a suspended status and also through the mouth and food tracts via food and drink. With the given paths of infection, a typhoid form of tularemia is predominant, which, as a rule, was observed during this outbreak. Table 2 sets forth the infectability of one village by age groups.

The susceptability in humans was apparent in age groups from 3 months to 80 years. Evidently humans, at all ages, are susceptable to tularemia infection

and can become infected with it; however, tularemia in infants and young children often passes quite mildly.

The clinical course of the typhoid form of tularemia, during this outbreak, was so pathognomonic, that after establishing a diagnosis of tularemia in a large group of patients, with the help of allergical (tularin for intracutaneous or outer skin reaction) and serological reactions (serum agglutination), there was no necessity for the mass application of laboratory methods of diagnosis of the remaining patients during a clinically obvious course of infection. We used a clinical diagnosis in our studies (basically). Laboratory methods of diagnosis (allergical and serological reactions) were used only in cases that were doubtful and also in cases which demanded a confirmation of the diagnosis by laboratory means (as a rule, in each separate case for the diagnosis of latent, symptomless and ambulatory and effaced forms).

Cases, clinically well indicated, began suddenly, as a rule, without any expressed prodromic appearances. The basic symptoms were; severe headaches, muscular and articular pains (rheumatic pain in the entire body) a rise in temperature to 39.5-40°, acute sweating and notable general weakness. Angina was noted often and also the appearance, from the lungs, of a cough. In numerous cases delirium was apparent and nose bleeding was common. Eruptions of various morphological structures on the skin, the upper and lower extremities and also on the chest, spine and neck were noted. Head colds and other indications characterising grippe, were common.

In one hospital, all the hospitalised patients, with a clinically established diagnosis of tularemia, were verified by laboratory methods.

We utilised tularin for allergical intracutaneous and skin surface tests.

Our aims included (along with the clinical goals) the determination of the local and general reaction to tularin. It was disclosed that those patients who reacted positively, to an intracutaneous test with tularin, also reacted positively to the application of the tularin to the scarificated surface of the skin. Local and general allergical reactions, as a result of the application of the above stated preparations, fully coincided and did not exceed the limits of the ordinary. Suppurations and niecrosis on the area of application was not observed. However, it is necessary to note that the intracutaneous test gave a distinct reaction in the area of the regional glands in 80%, while the skin-surface test gave only 50%. As stated above, the typhoid form of tularemia was noted more in this outbreak than was the bubonic type, which, according to our material, was 0.6%.

Important material, which we have available, allows us to analyse it from the point of view of the severity of the course of the given clinical form of tularemia. During severe tularemia outbreaks, a different degree of severity and duration affects the course of infection. A severe course is accompanied by a lengthy fever (39.5-40°) presence of relapses, skin phenomena and a clearly indicated symptomatology. Sometimes a severe course of infection (more often in aged people) ends in death. Along with the severe cases are cases so light, the patient goes through on his feet. A. M. Berinskaya considers courses as light, medium, severe and abortive. A light course is characterised by milder symptoms; the illness usually starts with chills, the temperature rises quickly to 39-40° plus; the fever period lasts 5-8 days, the liver and spleen are not palpable. During forms of mild tularemia the symptoms are clinically indicated and more durative. Severe forms of tularemia are

characterized by clear indications of all symptoms and lengthy fever periods. Borinskaya considers, there are, as if an average of the severe and light forms, cases of abortive tularemia, characterized by the fact that they begin sharply, stop abruptly and end in recovery. According to unpublished data of Tkacheva, tularemia patients with severe courses were 12% - mild courses 57.8% - light courses 30.12%.

We conducted a survey of a large group of tularemia patients, with clinically indicated courses of typhoid form, in two highly infected areas. The group was infected as follows: severely - 16.38%, mildly - 47.64%, lightly - 30.2% and abortively - 5.96%. This calculates mild cases 1/2 - 1/3 light and 1/6 severe, abortive approximately 6%, but factually it is present more often.

During our study of tularemia patients by laboratory methods of diagnosis, we directed our attention to several healthy members of the family, living in the same conditions as those of the family who was ill. The health status of these non-infected members, of infected families, was confirmed by laboratory diagnosis. It soon was apparent, that part of these people responded positively to tularin, and part gave a positive reaction of agglutination with the serum method. Taking into account the specificity during tularemia allergical and serological reactions, these people should be considered as recovered from a latent (asymptomatic) tularemia infection. To establish the number of similar cases, relative to the clinically evident patients, proves highly difficult; this requires a general clinical survey of all the inhabitants of a tularemia infected center with the mass application of allergical and serological methods of diagnosis. Thus, it is evident, that along with the clinically indicated forms of tularemia, once again the presence of latent forms are confirmed.

Consequently, the course of tularemia can be classified as follows,

according to its severity: 1. latent and non-symptomatic forms, 2. ambulatory or effaced forms, 3. forms with a light course, 4. forms with a mild course and 5. forms with a severe course.

The latent forms of tularemia pass without clinical symptoms and the only method of diagnosis is the application of allergical or serological methods.

Ambulatory or effaced forms pass with lightly expressed symptoms and also require laboratory methods of diagnosis.

Light forms are characterized by clinically apparent symptoms, usually lasting one week. Numerous cases can be diagnosed clinically.

Mild forms of tularemia are characterized by clinical symptoms, lasting 2-3 weeks. After establishing an outbreak, this form can be diagnosed predominantly by clinical diagnosis.

Severe cases are characterized by symptoms lasting 3-4 weeks and longer. These forms can, as a rule, be diagnosed clinically.

Symptoms of all patients were; fever 95.5%, headache 96.5%, sweating 68.1%, delirium 22.4%, rheumatism 51.5%, nose bleeding 7.9%, cough 40.3%, angina 4.9%, vomiting 10.9%, and cutaneous phenomenon 15.7%. Tables 3, 4 and 5 show that the symptoms become more intensive and durative with the severity of the disease; these data are not exact or limiting, they are for guidance in future work.

The duration of the acute period of 41 hospitals is given on Table 6. The period of convalescence was 16-30 days in 61% of the cases. The remaining cases fluctuated near 15 days.

The following 8 cases of death are from one village. We could not obtain more data, but we can note that the age group was above [illegible] in most of the cases.

M. 18 years. 12 November, painfulness in the interscapular region, temperature up. Retired at 8 p.m. 13 November, lost consciousness, remained so to death on 16 November.

I. 75 years. Became ill 6 November. Fever. 3 days later, paralysis of the right side, lost consciousness. 3 days later, still unconscious, died.

P. 75 years. Became ill 5 November. Pain in left side, lost consciousness; partial vomiting, paralysis of the extremities. Died on 7th day of illness.

T. 73 years. Became ill 4 November. Sudden fever, headache and cough, was confined to bed 11 days. Died on 16 November after 4 days of unconsciousness.

C. 66 years. Became ill 3 November. Held high temperature 2 weeks. Died on 14th day of illness. 2 days before death her tongue became paralyzed. Had not been ill for 5 years previous.

I. 67 years. Became ill 26 October. 4 days of headaches, rheumatism and severe sweating; did not remain in bed all the time. After 7 days, patient's general condition improved, but he began to lose weight; temperature up, delirium, patient lost consciousness. Died 12 November - 16th day of illness. Day before death left half of body became paralyzed.

I. 75 years. Became ill 15 October. Confined to bed 21 days.

I. 80 years. Became ill 15 October. In bed 4 days. Day before death she lost consciousness.

Tables from Prof. [illegible]'s article [illegible] on the epidemiology, clinical aspects, and laboratory diagnostics of the typhoid form of [illegible], appearing in [illegible], Vol. [illegible], No. [illegible], [illegible], pp. [illegible]

TABLE 1

October		November	
Date	Percentage of Those Who Fell Ill	Date	Percentage of Those Who Fell Ill
1 - 10	1.17	1 - 5	[illegible]
11 - 15	1.64	6 - 10	18.97
16 - 20	2.19	11 - 15	14.16
21 - 25	1.07	16 - 20	19.23
26 - 31	0.35	21 - 25	6.35
		26 - 30	6.73

TABLE 2

Age in Years	Percentage of Patients	Age in Years	Percentage of Patients
0 - 1	2.3	26 - 30	4.6
2 - 3	5.4	31 - 35	6.9
4 - 5	[illegible]	36 - 40	8.9
6 - 7	5.7	41 - 45	0.7
8 - 10	10.7	46 - 60	11.6
11 - 15	12.7	61 - 70	[illegible]
16 - 20	4.4	71 - 80	[illegible]

TABLE 3

SYMPTOMATOLOGY ACCORDING TO SEVERITY OF COURSE

Clinical Course	% of Cases	Fever	Headache	Sweating	Delirium	Rheumatic Pain	Nosebleed	Cough	Angina	Vomiting	[illegible]
	Number of Cases in %										
Ambulatory	5.9	27	78.9	20.8	4.1	20.8	2.0	14.5	2.0	8.0	8.3
Light	30.2	100	95.4	65.7	7.0	58.5	4.1	47.1	4.6	11.1	9.9
Medium	47.64	100	100	76.8	30.9	44.0	9.8	40.3	5.5	12.7	16.9
Severe	16.38	100	100	84.8	37.8	74.2	11.3	29.7	4.6	6.6	37.8
Of all Cases		95.6	97.2	71.7	23.3	50.7	7.9	37.9	4.9	10.6	15.2

TABLE 4

DURATION OF SYMPTOMS IN AMEBIASIS PATIENTS

Duration of Symptoms (Days)	Fever	Head-ache	Sweating	Delirium	Abdominal Pain	Constipation
	No. of Cases in %					
1 - 3	78.5	60.0	63.6	50.0	40.0	100.0
4 - 5	21.4	25.7	27.7	50.0	50.0	0
5 - 10	0	14.2	9.0	0	10.0	0

TABLE 5

DURATION OF SYMPTOMS IN MILD, MEDIUM, AND SEVERE CASES

Duration	FEVER			HEADACHE			[illegible]			[illegible]
(In days)	Mild	Medium	Severe	Mild	Medium	Severe	Mild	Medium	Severe	Mild
1 - 3	33.5	2.6	0.0	37.0	6.1	0.0	44.1	23.0	24.0	62.5
4 - 5	36.2	4.4	0.0	33.8	11.9	0.7	33.5	24.0	24.0	25.0
6 - 10	8.7	52.5	9.7	25.3	50.0	16.4	17.8	37.9	34.0	12.5
11 - 15	1.6	33.4	25.2	3.7	25.9	34.3	4.8	11.2	14.0	0.0
16 - 20	0.0	3.8	31.7	0.0	2.9	26.4	0.0	3.3	4.0	0.0
21 - 30	0.0	6.6	27.6	0.0	2.9	21.4	0.0	1.5	0.0	0.0
31 - 40	0.0	0.0	5.6	0.0	3.2	0.7	0.0	0.0	0.0	0.0

ND SEVERE CASES

ITES		DELIRIUM				Rheumatic Pain RHEUMATIC PAIN		NOSE-BLEED			COUGH		
dium	Severe	Mild	Medium	Severe	Mild	edium	Severe	Mild	Medium	Severe	Mild	Medium	Severe
3.0	24.0	62.5	50.9	24.0	32.8	10.9	2.3	92.8	78.9	73.3	16.0	6.45	1.0
4.0	24.0	25.0	26.8	24.0	34.5	16.1	8.2	7.2	10.5	13.3	29.4	15.6	3.2
7.9	36.0	12.5	21.3	36.0	28.6	53.8	42.3	0.0	10.5	13.3	41.4	40.5	38.2
1.2	14.0	0.0	0.9	14.0	3.1	11.09	24.7	0.0	0.0	0.0	10.7	28.1	25.4
3.3	4.0	0.0	0.0	4.0	1.4	4.3	14.1	0.0	0.0	0.0	1.8	6.9	20.2
1.5	0.0	0.0	0.0	0.0	1.4	2.9	7.0	0.0	0.0	0.0	0.0	2.7	11.7
3.0	0.0	0.0	0.0	0.0	0.0	0.0	1.1	0.0	0.0	0.0	0.0	0.0	0.0

TABLE 6

Duration of Acute Period	Number of Sick	Course
6 - 10	12 (29%)	Mild
11 - 15	15 (37%)	Medium
16 - 20	11 (27%)	Medium
21 - 25	3 (7%)	Severe