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# THE TIPHUS FEVER PROBLEM AS REFLECTED IN STUDIES OF ITS CONTEMPORARY FORMS

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[Following is the translation of an article entitled "Problema sypnogo tifa v otrazhenii izucheniya yego sovremennykh form" (English version above) by Prof P. F. Zdrodovskiy in <u>Vestnik Akademii Meditsinskikh</u> <u>Nauk SSSN</u> (Herald of the Academy of Medical Sciences USSR), Vol 15, No 7, Moscov, 1960, pages 3-14.]

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Among the peculiarities of residual forms of contemporary typhus there are included: the sporadic character of the diseases observed, as a rule without the detection of the disease sources and in the absence in the foci of carriers of the infection -- body lice; the primary concentration (in certain localities up to 80%) of the disease in the older age group (41-60 years of age and over) in contrast to past times when, for the most part (45-62\$) typhus affected people in the young and mature years (20-40 years of age); there is an unusual number of recurrent attacks of typhus (40% and higher); there is the benign character of the disease with the extremely rare fatal outcome; there is the absence or obliteration of the winter-spring seasonal prevalence so characteristic of typhus in the past. To the above should be added the relative difficulty of isolating from the blood of the diseased the pathogenic agent which retains all the visual characteristics of Provachek's rickettsia, i.e., of the authentic stimulus of typhus. It is impossible, likewise, to ignore the limited sensitivity of the Weil-Felix reaction in the contemporary forms of typhus, which forms are at the same time serologically well differentiated when Provachek's rickettsia antigen is used. These characteristics of the major portion of contemporary forms of typhus are

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responsible for

Adisorienting, in no small degree, epidemiologists, who from established tradition continue the analysis of these forms from epidemiological points of view, which have been developed for typhus.

As is known, the code of epidemiology, having become established in the minds of the majority of epidemiologists, runs as follows: the sole source of infection in typhus is the human being ill with the typhus; the sole carrier of this infection is the louse (primarily, the body louse), which becomes diseased in sucking the blood of the diseased merson. Aside from the epidemiological chair "louge-human-louse", infection with exanthematous fever (or typhus) cannot occur is natural circumstances. To the facts indicated, established half a century ago by C. Nicolle unquestionably for spidemic typhus, there is being added the absence in typhus fever both of the "obliterated" and "asymptomic" forms of the intection by the majority of our epidemiologiets, led by L. V. Gromashevskiy. In this direction L. V. Gromashevskiy writes

in his work on local epidemiology (1947): "In diseases, which exhibit a wide polymorphic range in the clinical appraisal, proceeding in the direction of increasingly mildly progressing ("obliterated") forms, it may be expected that such conditions will be met when every reaction to the infection from the part of the organism is absent; such a condition is designated as a healthy carrier state (infection corrier state). And, on the contrary, in infections the course of which always progresses in a clinically manifest form and do not give the "obliterated progression", the possibilities of an infection corrier state are excluded" (page 424). Further, proceeding from his numerous observations that the length of the fever in typhus is never less than nine days -- this is the minimum period, which accounts for only 2.1 % of the disease --"This most important u. V. Gromesbevskiy concludes: fact for the clinic (diagnostics) and epidemiology denies with a certitude the possibility of the existence of a healthy carrier state in typhus, for a disease in which the mildest observed forms proceed as a nine-day fever cannot proceed as an asymptomatic healthy carrier state" (page 421).

The indicated thesis of L. V. Gromashevskiy entered the official code of epidemiology for typhus in its entirety, having been confirmed in 1939 by the All-Union Conference of Microbiologists, Fpidemiologists,

and Infectious Disease Specialists. As a result of the report by L. V. Gromashevskiy, "the recently prevailing teaching of virus-carrying in typhus, in the literature of our country" was admitted as groundless, and the estimate of the epidemiological role of this factor was found to be based on "no concrete data whatspever" (quoted from the resolution of the conference). Since then, the question of obliterated forms and virus-carrying in typhus has been relegated to the estegery of Larmful epidemiological mistakes, deserving of the most severe judgment.

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Occasioned by the conflict which had occurred between the prevailing ideas of the epidemiology of typhus and the real state of affairs, and also from considering the data of world-wide experimentation in the field of rickettsial disease and, in part, also in typhus, we decided to subject some of the collected degues in the teaching of this infection to revision. The need for such a revision was supported by the fact that the existing ideas on the epidemiology of typhus, as has already been indicated above, came to our attention as a result of the analysis of epidemic forms of this disease. Also, the study of typhus had previously been carried out with primitive methods of research, while contemporary science makes use of methods which are further perfected, specifically, the method of the highly effective specific flow and the retrospective serodiagnosis aided by the reactions of complement fixation (REM) [reaktsiya svyazyugaiya komplementa - complement fixation resction? with the use of Antigen from cultures of Provached is ricketusia.

At the first stage we examined the thesis indicated above of the absence in typhus of "obliteratcd" and "saymptomatic" forms of the infection. This thesis, is splite of the existence of sufficiently well-founded objections from some Soviet investigators (K. E. Tokarevich and colleagues), continues to prevail among our epidemiologists, in large measure determining their factics relating to typhus, and so it demands therefore an immediate resolution in one direction or the other.

We placed before ourselves the problem of insituting a mass serological investigation of population groups in various regions, which groups have been infected in the past, to one degree or another, with typhus, and paying special attention to the age distribution of the results of serological researches.

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The study of typhus was carried out by immunological methods of retrospective diagnostics, with both wide and narrow application in virus infection (poliomyelitis, encephalitis, and others) and in a number of bacterial infections (diphteria, scarlet fever, and others). We organized, in 1957, in cities of the central

region of the RSFSR corresponding investigations with mass use of contemporary methods of serodiagnostics of typhus infection with the eid of RSK. Designed under one plan, with one method of research, and with the use of one standard antigen for RSK, these observations during 1957 - 1958, and partly in 1959 were carried out on a mass scale by the efforts of the specially prepared scientific workers of local institutes of microbiology and epidemiology, santiation - epidemiological stations and other laboratories under the general leadership of the author and under the method-During 1957ological leadership of E. M. Golinevich. 1958 a collective composed of 30 scientific workers completed, essentially, the work assigned it on a series of questions, having developed a personal re-search initiative (See Note). As a result there was collected unique material on the study of the epidemiology of typhus, the basic results of which are briefly summarized in this article.

(/Note/ The authors of the research material summarized in this article are V. A. Yablonskaya, T. S. Kovreva, A. V. Yeremenko (Moscow); N. I. Stratonovich, A. I. Yakushkina, L. A. Pravdina, G. N. Rozanova, A. I. Kogan, T. A. Manevich, Ye. S. Parfenova, Ye. S. Temryuk (Smolensk); G. R. Gazizova, A. E. Reznik, N. R. Payteryakova, M. P. Lashmanova, F. B. Kolpachikhin, Eayteryakova, M. P. Lashmanova, F. B. Kolpachikhin, F. A. Sergeeva, V. M. Klyuchnikova (Kazan'); G. I. Grenaus, A. S. Antsunova, V. T. Degtyareva, Ye.A. Miloradovakaya, I. S. Soldatova, M. V. Lopatina (Gor'kiy); L. N. Astakhova, M. V. Matveyava, G. P. Setunovskaya (Sverdlovsk); M. A. Kulemina, K. P. Kuznetsova (Kuybyshev). The material of the authors indicated is cited from their manuscripts which are subject to publication.)

A comparison of the objective indices of serological research with the data of anamnesis confirmed that in mass observations the anamnetic data display sufficient authenticity. Thus, among 5124 cases of serological investigation with negative typhus acof serological investigation with negative typhus according to the RSK anamnesis, the RSK with the typhus antigen in 10 % of the diseased was found, on the averlage, to be positive, while among 362 persons with positive typhus the REK anamnesis was recorded to be 41 % on the average, 1. c., four times more frequent See Note7. We will note in passing that K. N. Tokarevich likewise confirms the good correlation of immunological data from observations with the data of ty-

(/Note/The following data convincingly illusphus anamnesig.

trate, at the same time, the RSK specificity.) Before presenting the results obtained and their discussion, we will turn to the elucidation of some features concerning the methodology used in the sero-

logical investigations. As has previously been indicated, serological

investigations were conducted with the aid of RSK, the methodology of foreign countries paralleling the methodology accepted by our laboratory, and, specifically, parallel with the methodology which was used by and colleagues). Rumanian investigators (D. Combiesco As antigens in the RSK arrangement, the so-

called completely soluble antigens suggested by Ye.M. Golinevich were used, which are prepared from hemo-lyzed egg cultures of Provachek's rickettsia (the same type of antigens were used by the Rumanian authors). The RSK was applied with four units of the antigen indicated and with two units of the serum complement --by "hot" (36 to 37 ) or by "cold" (40 ) methods without noticeable difference in the results. In mass observations with the goal of retrospective diagnostics of typhus infection, the seruns under test were usually employed in the following dilutions: 1:5, 1:10, 1:20, 1:40, etc. In this sree, pard of the authors considered as positive (+ + + +) at the 1:5 dilution, the other part of the authors -- at the 1:10 dilu-

Titers of the positive RSK and their correlation. tions in mass investigations of a healthy population with negative anamnesis for typhus are illustrated by table 1, which sums up the results of serological investigations in four cities.

As seen in table 1, positive RSK in a serum dilution of 1:5, on the average, gave us a registration of 18 %. How can the significance of this trial using the 1:5 dilution be evaluated? (1957, 1958), having studied the headed by Combiesco significance of various RSK titers by a methodology paralleling ours, which is one of diagnostic titers for typhus, accepted the dilution 1:16 on the condition

# Tthat it be dynamically raised or lowered with repeated 7 investigations. Parallel with this in their data, pos-

## TABLE ONE

Negati	ve Anamnesis	for	Typhu	8			
Number Trivest sated	Number of RSK Positive		Dist: Tite:	ribut: rs in	lon of Perce	RSK ent	
THACONTOC		1:5	1:10	1:20	1:40	1:80	1:160

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330

3,257

18

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# Titers of Positive RSK in Healthy People with

26.4

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itive RSK figures in the 1:4 dilution observed, on the one hand, at the beginning of typhus attacks and, from the other, in cases of late retrospective diagnostics of typhus infection in subjects with medical documentation of previous typhus experience. In this manner, in retrospective investigations a positive RSK at 1:5 dilution can specifically expose the early-experienced typhus infection.

Together with this, as special investigations of the Rumanian authors show, in separate cases it is impossible to exclude the unspecific RSK delay. Thus, in the deliberate investigation of 90 healthy children with negative anamnesis for typhus these authors once discovered a positive RSK at a 1:4 titer.

Concerning positive REK with a 1:10 titer, we have no doubt of its specificity in retrospective diagnestics of typhus infection. Thus, from the data of N. I. Stratovich, R. I. Yazushkina, L. A. Fravdina, and others (Smolensk), among the 142 people investigated in the three to nineteen year range with deliberately negative typhus anamnesis, positive RSK was not observed in a single case with a serum dilution of 1:10.

We related to positive RSK, in the data presented for the mass retrospective investigation of population groups on typhus infection, the trials with 1:5 titer together with 1:10 trials, and higher dilutions. From this, as is seen from the figures below, we discovered no differences in the general regularity of the age distribution of positive RSK in the cases investigated, starting with a beginning titer of 1:5 (figure 2) or 1:10 (figure 1).



Figure 1. Summary curve of age distribution of positive RNK in population groups with negative enamnesis for typhus (in five cities of the RGFSR) (Upper dashed line reads "Maximum"; lower dashed line reads "Minimum."7 (Abscissa: Age/



Fig. 2. Curve of the age distribution of positive RSK in population groups with negative examnesis for typhus. Minimum RSK titer: 1:10 (Sity M) [Abscissa: Age] Finally, for the character of general and particular RSK specificity with the antigen from Provachek's rickettsia it is necessary to indicate that V. A. Yablonskaya in our laboratory for about 50 cases of retrospective positive RSK to typhus infection carried out researches, using as controls the same serums for RSK, with the antigen from rickettsia of the tick-borne group, and obtained negative results.



Figure 3. Age distribution curve of positive RSK in population groups with negative anamnesis to typhus. Minimum RSK titer: 1:5 to 1:10 (City S) (Abscisse: Age/

The results of the retrospective serological RSK investigation of typhus infection of population groups with negative typhus anamasis are presented in figure 1, where the positive MSK findings are summarized for the 5124 persons investigated in five cities of the central region of the RSFER, with the distribution of positive EDE in various age groups.

In this manner, so is seen from figure 3, the summary curve of positive ESK progressively grows from zero or minium importance in the child and in the younger ages to the mature and elderly age groups with the peak occurring at 41-50 years of age -- the type of curve is observe in the cities and regularly repeats for investigated population groups of different cities (figures 1, 2, and 4). The trustworthiness of the data presented is supported by the presence of 80 % positive RSK results in titers which raise the minimum level of typhus infection in retrospective diagnosis. From the other side, serological data do not occasion any doubt, even in the statistical sense, since every age group, in the material summarized, is represented by highly significant figures (in the range of from 380 to 1156 persons to an age group).



Figure 4. Age distribution curve of positive RSK in population groups with negative anamnesis for typhus (City K) /Abscissa: Age/

Analysis of the data discloses, first of all, the very low percentage of a positive SSK in the younger age groups (7-12 and 13-18 years of age). This circumstance indicates that in recent years the circulation of the typhus virus in the collectives investigated was absent or was insignificantly expressed in contrast to previous years (in particular, during the war period) when it was evidently important, as is reflected in the relatively high percentage of a positive RS K (11.7 to 17 % on the average) in the mature and elderly age groups (31-40 and 41-50 years of age and higher).

Simultaneously, in the 31-60 years of age and higher age group, with a categorical negation of previous typhus illness together with a negation, in general, of its occurrence in infection hospitals (see figure 1), a positive RSK was, in places, registered at 21-25 %, i.e., was present in a very high percentage of the cases investigated (see figures 1 and 4). In connection with this it is necessary to note that the percentage displayed of a positive RSK is evidently understated, since sufficiently trustworthy evidence in the USSE and in foreign countries shows that in cases of clinically expressed typhus the positive HSK can, with time, disappear in a considerable percentage of those who were diseased.

As an illustration of what has been stated, we present the observations of M. A. Kulemnaya and K. P. Kuznetsova (Kuybyshev), which, for 107 cases who experienced typhus of varying remoteness in time, there was determined the loss of a positive RSK, depending on the remoteness of the illness with the following correlations: for the course of one year RSK was retained by 38 of 41 of those who were diseased; for a period of 6-20 years by mine out of 21 persons; for a period of over 20 years by 16 out of 45 persons. Of 107 who had been ill in the periods indicated, a positive RSK loss occurred in 44 persons, or 41 %.

What conclusions should be drawn from the data presented of the mass serological investigation of population groups of older and elderly ages?

Considering the specificity of the RSK, it should be admitted that in the above-mentioned groups where the percentage of a positive RSK reached 21-25%, the investigated cases, in spite of their assertions, were ill in the 30-50 year age range with obvious forms of typhus, which seems absurd, or they were ill with typhus in some light "obliterated" form, having slipped away from recognition, which seems more reasonable and correlates with the observations in other countries (see below).

Direct observations on the length of the fever give a convincing illustration of the clincial polymorphism of contemporary forms of typhus in their general benign character distinguished universally.

As an illustration we present the investigations pertinent here, of M. A. Kulemina and X. P. Kuznetsova (Kuybyshev), who studied the length of fever in 264 ill persons with typhus in contrast to the data of L. V. Gramashevskiy, relating to epidemic typhus (Table 2).

By analogy with the material indicated, according to the date of V. A. Yablonskays, T. S. Kovreva and A. V. Teremanko (1956), among the 184 cases of

# TABLE TWO

# Length of Fever in Typhus (from data of native scientists)

Length of	fever	Number of the diseased (in %)					
(in days	)	From data of M. A. Kulemina and K. P. Kumetsova (Kuybyshev)	From data of L. Y. Groma- shevskiy				
5-8	9. de la calence des ser la calence de la construcción de la construcción de la construcción de la construcción	20	0				
9		18.8	2.1				
10-11		40	12.7				
12-17		21.2	85.2				

### TABLE THREE

D. Combiesco)		ł
Length of fever (in days)	Number of the diseased (in percent)	
	б	ł
7-9	48	
10-11	28	
12-14	18	

Length of Fever in Typhus (from the data of

sporadic typhus studied by them, the length of the fever oscillated within the range of from 6 to 15 days with an average length of 9.4 days. From the similar data of A. N. Astakhova, M. V. Matvayeva and G. P. Setunovskiy (1958), among 153 ill with typhus, the fever length was observed to be 7-9 days in 31.5 %, 10-12

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days in 66 %, and 13-16 days in 6.9 % only (as against 65 % according to the data of L. V. Gromashevskiy). In conclusion we present the data of D. Combieand his colleagues (1957), concerning the length

of rever of repetitive typhus in Rumania (table 3). In other words, D. Combiesco registered even a four-day fover length for typhus.

Thus, we see that in short-fever forms, the atsence of which, in L. V. Gramshevskiy's investigations, is the main argument for the negation of "obliterated" and "asymptomatic" forms of typhus infection, at present are not rare -- rather, they are commonplace. It cannot be doubted that the clinical course of typhus has changed greatly in comparison with the past -- this disease has become considerably more benign, but its clinical expression more polymorphous, which, obviously, explained the difficulties observed in the clinical diagnosis of contemporary forms of typhus in the sporadic category and its frequent registration under an erroneous diagnosis.

In connection with this, the observations of M. A. Kulemina and K. P. Kuznetsova should be observed, who, in the investigation of 862 healthy subjects, retrospectively separated 142 persons with a positive RSK to typhus. It was found that among the latter, 63 persons or 44.3% during the years 1957-1958 had influenza -- the diagnosis which sent such patients often and, evidently, not accidently to the hospitals.

It should be sold that in cases of hospitalization and lengthy observation not so rarely is it that contemporary typhus is clinically observed. Thus, among 52 cases of sporadic typhus studied, who had been hospitalized during the last few years in cities of the R5428, 75 persons, i.e., 9.1 %, had diagnoses which were made only on the basis of serological investigation (R52); also, this figure varied in different hospitals from 4.5 to 15 %.

Thus, light or atypical and orliterated forms of the disease are common for contemporary typhus. Clinical forms of typhus infections of the same type are, underwoodly, encountered even in foci of epideuic typhus, which follows from the considerable number of positive RSK in the older age groups with negative typhus anamnesis and visibly demonstrated in our material.

Evidently the correctness of the suggestions of R. N. Tokarevich (1958), stating that "typhus, in the gense of varied expression and typical development in individual disease cases, does not represent an isolation from the class of other acute infections." Here occurs the similarity with bacterial and virus infections in the appraisal of retrospectively-revealed immunological indices in the province of typhus infection in older population groups with negative anamesis for typhus, out having suffered unfortunate bouts with this infection.

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> As L. V. Gromsshevskiy correctly indicates, if "obliterated" forms were present in typhus, this would predetermine, in the positive sense, the possibility of "asymptomatic" forms of typhus disease, ocrresponding to virus-carrying. Since, as is now determined, "obliterated" forms are, undoubtedly, met in typhus disease, the question of its "asymptomatic" forms is predetermined a priori.

Parailel with this, the possibility has been proven out by foreign investigators of the presence, in all types of the most important rickettsial diseases, of long-lived latent forms of infection in persons who had been ill with the pathogenic agents in sons who had been ill with the pathogenic agents in lymph nodes (Parker; Smedley and colleagues; and Price). Our material does not yet include direct obser-

vations of "asymptomatic" forms of typhus disease if two ceases are not counted which were discovered by the workers of the Gor'kivskiy Institute of Microbiology and Hyidemiclogy (G. 1. Grenaus, and others, 1958) in family foci of sporadic typhus; also, in one healthy subject a positive RSK at 1:20 titer was discovered and hemogelutination at 1:4000 titer, end in the other -- 4 MSK at 1:4 viter and homogelutination at a letter istar. It should be noted that benegglutingthon is the titers noted is obtained only in active infeation or in the early stages of convelescence. The authory who discovered the cases cited are not certain that the gaven subjects did not have a light attack prior to their investigation to which they paid no attention. Thus, if the given case exhibited no "asympatemation infaction proper, then, at least a very light form of typhus wes theseny which was experienced, though the poison was not versition. It is impossible, howevery to can't the out through recentles corried out with positive results in recent years in Rumania under the losdership of the prominent specialist on typhus, Frod D. Quablesco.

The Runanian authors, well-acquainted by past paperience with epidemic typhus, in recent years also encountered the epidemiclogical paradoxes of sporadic typhus. In connection with this, in analogy with us, they carried out mass serological investigations in the unfortunate rayonny with the aid of specific RSK, concentrating especially on the search for obliterated and asymptometic forms in the foci of sporadic and epidemic typhus.

The results which are of interest to us, of the -researches of Prof D. Combiesco who headed the large collective of research participants, are summarized in two theses, which we quote from the original: "The application of R5K allowed the recognition of numerous hidden cases of typhus which play an important role in epidemic typhus, since these forms of the disease are in large measure responsible for the appearance of sporadic forms of the disease"; "With the aid of R2K the hidden epidemiological foci, which had passed for sporadic examples, were exposed as obvious epidemiological foci by numerous cases."

We present an example of the discovery in foci of "asymptomatic" forms of typhus, which were found serologically.

1. In a ten-year old case the diagnosis of typhus was belatedly determined by a RSK at a 1:512 titer. Seven persons were found in contact with the diseased, ranging in age from 14-18 to 36-48 years of age. On studying the, a positive RSK was found in six at titers of 1:128, 1:64, 1:28, 1:32, 1:256, and 1:16. The focus was given special attention. Following the isolation of the ill person, among the remainder, regardless of the RSK presence at diagnostic titers (1:16 and higher), illnesses were not found.

The example given illustrates the actual focus of typhus infection, which in the absence of serological investigations of persons surrounding the diseased, would qualify only as a sporadic case of typhus.

We present another example where a case of clinically-manifest and asymptomatic typhus was subject to a repeated serological investigation.

2. The ill person had the RSK: 25/VI - 1:1024; 22/VII - 1:1024; 30/VII - 1:1024; 4/X - 1:125.

The RSK of the person who had been in contact with the diseased and who had not fallen ill were: 2/VIII - 1:512; 29/VII - 1:1024; 4/X - 1:100; in April of the following year -- 1:128 (Combiesco, 1957). The examples cited pertain to foci of sporadic typhus. Below we present the discovery of "asymptomatic" forms in a focus of epidemic typhus. tic" forms in a focus in Kucha-Voda. During January

3. The focus in Kucha-Voda. During January and February an epidemic outburst of typhus occurred with the appearance of 25 cases of the disease, of which half were found in schoolchildren. In the begwhich half were found in schoolchildren. In the beginning of March a laboratory investigation was made of 168 persons of those who were in contact with the disleased cases, of that number were 33 pupils, ranging in age from 7 to 14 years of age and 135 were persons out of school, from 15 years of age and up.

of the entire group by RSK are presented in Table 4.

Thus, among 33 pupils 14 were found to have positive RSK in titers of the range of 1:16 - 1:2048. In connection with this the authors note that all the cases with a positive serological reaction that were uncovered remained healthy (Combiesco, 1958).

From Combiesco collected data (1958) in 48 epidemic foci (in the presence of a considerable infestation here, judging by the illustrated presented), festation here, judging by the illustrated presented), with the aid of RSK 2108 trials of serums of persons who had been in contact with typhus were investigated; here, in 947 cases (44 %) RSK was found to be positive here, in 947 cases (44 %) RSK was found to be positive with titers in the range of 1:4 to 1:2048, with an age with titers in the range of 1:4 to 1:2048, with an age distribution of 9 % positive in a group of children up to six years of age, and to 53 % positive within the ages of 51-60. Serological findings are detailed in Table 5.

## TAELE FIVE

Compo investigated				RSK	Tit	ers_	1 20	256	2048
Groupe invite in old	0	4	8	16	32	64	120	290	2010
Pupils /-i+ jis ois	2	9	8	3	2	• 6	2	1	
Persons not in scho who are over 15 yr and older	ol 9 13	38	49	27	3	1	2	1	. 1

DAMNITO OF	the Se	rological	1 RSK Investigation In
Hesulus VA		And the Party of t	The second of The States
Ele Trachig	of sn	Enidemic	OUTDMEEK OI LYDNUD

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# TABLE FIVE

RESULTS OF REK SENICLOGICAL INVESTIGATION IN FOCI OF EPIDEMIC OUTBREAKS OF TYPHUS (According to the data of D. Combiesco)

21777/1 <i>2</i> 77								
Studied 0 4 8	16	32	64	3.28	256	512	1024	2048
Absolute 1128 259 26	1 233	116	17	14	6	3	1	2
Pigure	2 , 11	5.68	0,68	0.68	0.24	0.14	0.04	0.09

Thus, to sum up, titers in the range of 1:16 to 1:2048 were encountered in 392 persons, i.e., in 18.5% of those investigated.

of the ill (dans le majorite des cas) with a showing of the ill (dans le majorite des cas) with a showing of positive RSK, the infection was not discovered by clinical observation. However, in 43 out of 46 cases clinical observation. However, in 43 out of 46 cases studied with the aid of RSK the immediate sources of infection were found.

Mith the above-indicated data of the Rumanian With the above-indicated data of the Rumanian authors, concerning the contact with foci of epidemic typhus in the presence of a considerable infestation, typhus in the presence of a considerable infestation, it is interesting to compare the analogous data of M. it is interesting to compare the analogous data of M. A. Kulemina and K. P. Kuznetsova (1958) on the sero-A. Kulemina and K. P. Kuznetsova (1958) on the serological investigation of healthy cases with negative logical investigation of healthy cases with negative negative in foci of sporadic typhus in the enamnesis for typhus in foci of sporadic typhus in the presence of only isolated cases of cephalic pediculosis. These data are presented in summary form in Table

6. As is seen from the data presented, contacts in the foci of sporadic typhus with minimum infestation, evidently, were likewise accompanied by the appearance of immunological indicators of typhus infection, but in considerably lesser degree in comparison with the foci of epidemic typhus.

IOCI OF epidemic syphes. Thus, the question of the asymptomatic forms of typhus from the data of the Rumanian investigators is quite solidly based and, also, there is pertinent to this question sporadic foci as well as epidemic typhus. In any case these data do (indirectly, but sufficiently logically in agreement with our material also, that is presented in this survey) deserve the most intense ettention and influence the execution of corresponding investigations.

## TABLE SIX

Results	of RET	Serologi	<u>cal In</u>	vest178	tions )	11
Foci of	i snora	lic Typhi	is (acc	ording	to the	<u>data</u>
OT M.	A. Kule	aine and	5. • K •	Kuznets	<u>iova)</u>	

Fumber inves-	Positive	REF cases	R	SK Tit	ers	
tisated in the foci	ni these		1:10-	1:20-	1:40-	11:30
	Absolute figure	Percentage	1:20	1:40	1:30	up
851	85	10	29	27	29	0

we will turn now to the additional characteristics of sporadic typhus.

The great majority of foreign investigators in Europe and America identify sporadic forms of typhus with Brill's disease, considering them as relapses of previously experienced typhus. The relapse nature of sporadic typhus is defended here by K. N. Tokarevich and G. G. Mosing.

In Rumanie, D. Combiesco and his colleagues, admitting the relapse nature of repetitive typhus, parallel with this predicts the primary origin of sporadic forms, pointing out that with the aid of RSK the relations between sporadic diseases (by the presence in the foci of hidden forms of the infection) may be shown.

In our opinion it would be a mistake to register the observed cases of sporadic typnus under the generalized term "typnus." At the same time it would be incorrect to limit the category "sporadic typnus" only to cases of repetitive typhus from the data of anomesis. Evidently, all the individual cases of tythus that do not the in with a known source of infection, regardless of their nature, should be viewed and registered as "sporadic typhus" of the corresponding Brill's disease, in official nomenclature, VCZ. The basis for what has been stated is the fact that according to the data of our investigators there is no special difference in the clinic of repetitive and periodicelly sporadic typhus. Evidently they are similar by their relatively low infectiousness.

It may be suprosed that the cause of contemporary typhus, retaining a visual resemblance to Frovachek's rickettsia, is characterized by less effective pathogenic agents. Under our conditions of socio-economic progress, typhus more and more tokes on the characteristics of a waning infection.

According to the joint announcement of all competent investigators -- native and foreign -- reliable diagnosis of contemporary torms of typhus demands the necessary application of scrological diagnostics in the form of agglutination reactions or, better, reactions of complement fixation with Provachek's rickettsis actigen. As has previously been noted, on the average about 10 % of those ill with scoradic typhus, even in conditions of nospital observation, are diagnosed only by RSF; also, in a number of cases typbus was retrospectively diagnosed, after they had already left the hospital where they had been with other diagnoses.

Also, from the most recent data of the Rumanian authors "epidemiological connections between separate sporadic sttacks of typhus may be exposed and clarified only with the aid of serolgical investigations of corresponding contingents" (D. Combiesco).

Thus, on the basis of the material presented above, two needs of principal importance may be formulated: 1) to legislate the nomenclature of "sporadic typhus" in the above-mentioned sense; 2) to facilitate and inculcate into wide practice scrological diagnostics of typhus by contemporary methods, having organized the mass troduction of moderately priced antigens of high quality.

In conclusion, there should be emphasized the pressing need for the most thorough possible study of "residual" forms of typhus from contemporary eptroaches and with the use of contemporary methods of immunological diagnosis of typhus infection. with this, in connection with the observations of the Rumanian authors, special attention should be paid to the detection of obliterated and asymptomatic forms of the infection in foci of typhus, for the clarification of their conditions of origin and epidemiological significance. Use of the hemagglutination reaction (HAR) in parallel with RSK lends a special perspective. This reaction provides the possibility of the differentiation of active forms of typhus infection and their most immediste convalescences in contrast to RSK, which at low titers does not differentiate retrospectively disgnosed forms from fresh ones (V. A. Yablonskaya, L. N. Astakhova, M. V. Matvejeva).

As the experiment of the application of HAR in typhus in comparison with its mass trial use among healthy contingents (over 4000 people investigated) showed, for the diagnostics of active forms of typhus infection HAR is conclusive at titers of 1:1000 and higher.

It is necessary to sever all ties with the widespread and completely unfounded conception of the imaginary mastery of the epidemiology of typhus.

It is necessary to make a few statements concerning "caution" heard in the school of conservative epidemiologists, as though the adrission of obliterated and asymptomatic forms of typhus and the relapse theory of the origin of repetitive typhus is disorganizing and weakening the battle with typhus. To these warnings should be contrasted first of all, the fact that we are obligated in our conceptions to be subject to "Mr. Fact." On the other hand, the admission of the these indicated above are not contributing to the weakening but, on the contrary, to the strengthening of our means of combatting typhus. Sporadic and obliterated forms of typhus infection are potential sources of infection and in unfavorable conditions may produce flareups of epidemic typhus. Therefore, all the generally accepted methods for combatting typhus remain in force with the request that they be unconditionally implemented. Supplementing them, a request is presented for the wide application of contemporary immunclogical investigations, as in the clinic with the sims of diagnostics, thus to epidemiological investigations of foci of sporadic typhus. In other words, the system of methods to be taken, in the battle with the potential threat of typhus is not growing weaker but, on the contrary, is gaining in strength and is being armed with improved methods of work.

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