MEDITERRANEAN SPOTTED FEVER - CLASSIFICATION BY DISEASE COURSE AND CRITERIA FOR DETERMINING THE DISEASE SEVERITY

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ABSTRACT

INTRODUCTION: Mediterranean spotted fever (MSF) in Bulgaria is caused by *Rickettsia conorii conorii* with a major vector the dog tick, *Rhipicephalus sanguineus*. The first cases of re-emerging MSF were reported in this country in the early 1990s after some 20 years of absence and then registered an annual increase until 2001-2003 after which the disease prevalence declined. MSF still poses a serious health problem in the country as severe, complicated cases with lethal outcome occur.

The aim of this paper was to classify the forms of MSF according to the course of the disease process and to devise criteria for the disease severity in order to enable comparison of clinical manifestations of the disease at different stages of spreading, in different age groups, and between endemic and non-endemic regions in this country and abroad.

PATIENTS AND METHODS: The study was carried out in a comparative aspect during the first phase of increase (1993-2003) with incidence of 11.88 per 100000 population and during the second phase of decline (2004-2011) with incidence of 9.56 per 100000 population. The disease was etiologically confirmed in 883 hospitalized patients by the positive antibody response to the specific antigen - *Rickettsia conorii conorii* by means of the immunofluorescence assay (IFA). The criteria we used for the classification of the forms of MSF included:

1. Typicality: forms having the most characteristic features of the MSF - eschar, fever, papular / maculopapular rash on the trunk and extremities, including hands and feet.
2. Manifestation: forms represented by all or some of the typical symptoms, giving sufficient grounds for preliminary diagnosis.
3. Duration: fulminant, acute and protracted forms.

The criteria for severity differentiate between mild, moderate, severe or malignant forms, and include clinical and laboratory parameters as shown in the present study.

RESULTS: Classification of the forms according to MSF course defines them in order of severity, typicality, manifestation, duration of symptoms, complications and age characteristics. According to the accepted criteria for severity and with respect to the studied I and II phase of the disease the mild forms are 41.16% - 35.62% (p > 0.05), moderate forms are 32.79% - 43.11% (p < 0.01), severe forms are 16.03% - 11.37% (p = 0.05), malignant forms are 6.56% - 8.68% (p > 0.05), and mortality is 3.46% - 1.19% (p < 0.05). The mean age was significantly higher for patients with severe forms of MSF (58.59 ± 4.32 yrs) compared with those with moderate (46.10 ± 3.71 yrs, p < 0.05) and mild forms (42.05 ± 3.50 yrs, p < 0.01). For children up to 14 years old mild forms are more common than in adults over 65 (p < 0.0001). Among children up to 14 years old there were no lethal outcomes, while mortality rate in the patients older than 65 was as much as 10%. All this indicates that MSF runs a milder course in children and a severe, complicated course in the elderly.

CONCLUSION: The criteria for MSF severity we have selected are based on our own experience and the experience of other authors. They are based on the reaction of human organism to the pathogenic agent and can be used during the different phases of emergence and development of rickettsial diseases, regardless of their geographic distribution. Unified use of these criteria would eliminate the differences in the data reported by different researchers regarding the disease development and severity.

Key words: Mediterranean spotted fever, *R.conorii conorii*, criteria for severity, classification
INTRODUCTION

Mediterranean spotted fever (MSF) from the tick-borne spotted fever group (SFG) is caused by *Rickettsia conorii conorii* and is transmitted by ticks of the genus *Rhipicephalus*. First MSF was detected and described in Bulgaria in 1948 in the Plovdiv endemic region by I. Vapzarov who reported a limited number of diseased in a small riverside settlement. In the following years the disease occurred sporadically in mild and moderate forms mainly in southern Bulgaria along the Maritsa River and the Black Sea coast. Thus 240 MSF patients were collected and described without reported death case by 1972. There were no cases of MSF registered or reported for more than 20 years after that, with no acceptable cause for this being suggested (the dog extermination in the 1970s because of rabies in wild animals and the excessive use of toxic pesticides in agriculture at that time were brought up as possible reasons). The early 90s of the XX century mark the re-emergence of the first cases of MSF in the endemic regions of the country, their annual increase and peak in 2001-2003 followed by a gradual decline in the prevalence of disease. It is currently known that MSF in Bulgaria is caused by *R. conorii conorii* (strain Malish), with a major vector the brown dog tick *Rhipicephalus sanguineus*. Despite the decrease in the prevalence, the disease remains a serious public health problem - severe forms with multi-organ involvement, serious complications and death are not uncommon.

The aim of the present study was to classify the forms of MSF according to the disease course and to develop criteria for determining the severity of the disease in order to enable comparison of morbidity rate between the different phases (rise and downturn) of the spread of the disease in various age groups, and in different endemic and non-endemic regions in the country and abroad.

PATIENTS AND METHODS

The study compared the results of the first phase of increase of incidence (1993-2003) and the second phase of a decline (2004-2011) of the two-decade presence of MSF in the country. The data are based on patients hospitalized in the Clinic of Infectious Diseases in St George University Hospital, which is the only facility that hospitalises and treats patients with MSF in Plovdiv region with a population of about 700,000 people. The number of patients infected with and treated from MSF between 1993 and 2011 was 1254. The disease was confirmed etiologically in 549 patients in the first phase and 334 patients in the second phase by a positive antibody response to a specific antigen *R. conorii conorii* by indirect immunofluorescence assay (IFA) carried out in the Referent Rickettsioses Laboratory of the Military Medical Academy, Sofia. The classification scheme and the criteria for determining the severity were based on 883 serologically verified cases of MSF. The criteria for the classification of the MSF forms are presented in Table 1:

1. **Typicality**: forms having the most characteristic features of the MSF - eschar, fever, papular /...

<table>
<thead>
<tr>
<th>By severity of clinical manifestations</th>
<th>Mild forms - typical or atypical (inapparent, without rash, abortive)</th>
<th>Moderate forms (most often typical)</th>
<th>Severe forms – typical or atypical (complicated, protracted)</th>
<th>Malignant forms (severe atypical – with multi-organ involvement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>By manifestation of clinical symptoms</td>
<td>Inapparent forms (mild, atypical)</td>
<td>Forms without a rash (mild, atypical)</td>
<td>Abortive forms (mild, atypical)</td>
<td>Forms with a rash (typical and atypical)</td>
</tr>
<tr>
<td>By typicality of symptoms</td>
<td>Typical forms (mild, moderate, severe)</td>
<td>Atypical forms (mild atypical, severe atypical -malignant)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>By duration of symptoms</td>
<td>Fulminant forms (malignant )</td>
<td>Acute forms (mild, moderate, uncomplicated severe)</td>
<td>Protracted forms (complicated severe and malignant)</td>
<td></td>
</tr>
<tr>
<td>By complications</td>
<td>Uncomplicated forms (mild, moderate, severe)</td>
<td>Complicated forms (severe complicated and malignant)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>By age</td>
<td>In children</td>
<td>In adults</td>
<td></td>
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</tbody>
</table>
maculopapular rash on the trunk and extremities, including hands and feet.

2. **Manifestation**: forms presenting with all or some of the typical symptoms, giving sufficient grounds for preliminary diagnosis.

3. **Duration**: fulminant, acute and protracted forms:
   a. **Fulminant forms** are characterized by infectious shock (IS) and duration of 24-48 h. They belong to the most severe malignant forms.
   b. **Acute forms** have a duration of 7-14 to 21 days, and are efficiently managed by timely, appropriate therapy.
   c. **Protracted forms** manifest multi-organ involvement or different complications. Duration is longer than 21 days and depends on treatment.

**Statistical analysis**

Fisher’s exact test for comparing severity of clinical forms in the two studied periods and the two age groups; independent samples t test and one way ANOVA for comparing the average age of patients with different forms of MSF.

**RESULTS**

The presented classification of the forms according to MSF course includes the criteria of severity, typicality, manifestation and duration of symptoms, complications and age characteristics (Table 1). The typical forms of MSF are characterized by pronounced clinical symptoms including the pathognomonic symptom of tache noire, febrile state and a characteristic papular or maculopapular rash covering the body and limbs, including hands and feet. By the criterion „manifestation“ we have marked rash and rash-free forms of the disease and possibly existing inapparent forms, given the evidence of increasing antibody titer to *R. conorii conorii* in tick-bitten patients, but having no other clinical manifestations. It is possible that these forms may account for the invisible immunization of a part of the population that despite exposure and tick-borne bites, does not suffer from MSF. By the criterion “duration” we mean fulminant, acute and protracted forms. In fulminant forms some authors speak of septic shock but in our opinion infective shock (IS) is better justified pathogenetically. There is no evidence of chronic form of MSF, although latent carrier state exists in some rickettsioses - Brill-Zinsser disease in epidemic louse-borne typhus (*R. prowazekii*). There have been reports of *R. rickettsii* persisting in the lymph nodes within one year after Rocky mountain spotted fever (RMSF). Mild and moderate forms of MSF are usually uncomplicated, while various complications have been observed in severe and especially in malignant forms. These complications include end-stage organ damage leading to cerebral edema, acute renal failure, gastrointestinal bleeding, acute respiratory distress, etc. These were extremely severe atypical form of MSF, some of which ended with IS and had lethal outcome. Since our study involves hospitalized patients, we have observed only three patients without rash, who had tache noire and also an increasing antibody titer to *R. conorii conorii*. Mild atypical forms would be the inapparent and abortive forms as well, but they are probably not diagnosed as MSF and patients are not referred to the hospital.

By severity the MSF forms can be mild, moderate and severe. As early as the early 1980s, it was D. Raoult that used the term «malignant» for the worst forms of MSF, which we now call severe forms with multi-organ involvement, but many authors have retained the designation «malignant». Table 2 shows the criteria for evaluating the severity of MSF. Based on the suggested criteria, we compared forms according to severity during the high incidence phase of MSF (11.88 per 100000 population) for the period 1993-2003 and the decreased incidence phase (9.56 per 100000 population) for the period 2004-2011. The presented classification and the criteria for the severity have enabled us to investigate whether the clinical manifestation of the disease changes in line with its steeply rising distribution (I phase) and gradual decline in morbidity (II phase). Figure 1 compares the percentage distributions of different severity forms of MSF in the two investigated phases, and Table 3 shows

**Figure 1.** Percentage of MSF forms of severity evaluated in two consecutive phases: 1993-2003 and 2004-2011.
Table 2. Criteria for determining MSF forms according to the severity of the disease

<table>
<thead>
<tr>
<th>Forms classified by severity</th>
<th>Clinical and laboratory criteria for determining the severity *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild forms</td>
<td>Fever of 38 °C - 38.5 °C without chills and headache; moderate myalgia and arthralgia; scarce or less abundant macular or maculopapular rash (or without rash); no significant deviations in the laboratory indicators (may show slight variations in peripheral blood count, platelet count about 120-140×10⁹/l or negligible increase in aminotransferases, but without clinically expressed and laboratory confirmed organ damages).</td>
</tr>
<tr>
<td>Moderate forms</td>
<td>Well pronounced toxic-infection syndrome: fever of 38.5 °C - 39 °C, chills, no or mild headache; moderate or abundant maculopapular rash most often without haemorrhagic components; X-ray possibly showing bronchitis or peribronchial changes; minor hepatomegaly, but without clinically manifested organ damages. Laboratory findings: moderate leukocytosis / leukopenia, shift to the left, ALT and AST increased 2-3 fold, platelet count ≥ 100×10⁹/l; Serum sodium around the lower limit (136-135 mmol/l); Serum albumin - around the lower limit - 35 g/l; blood urea nitrogen (BUN) and creatinine normal or slightly above normal levels. The combination of at least one clinical syndrome and one laboratory criterion determines the form as moderate.</td>
</tr>
<tr>
<td>Severe forms</td>
<td>Severe toxic-infection syndrome. Temperatures above 39 °C, chills, severe headache, nausea, vomiting; abundant rash of haemorrhagic character in the legs or on the whole body; Clinically manifested lesions of one organ (lung, liver, kidney, myocardium, etc.). Platelet count &gt; 50, &lt; 120×10⁹/l, but most often ≤ 100×10⁹/l; Serum sodium &lt; 136 mmol/l; Ca &lt; 2.12 mmol/l; ALT/AST increased ≥ 4 times; blood urea nitrogen and creatinine - significantly above normal levels. The presence of at least two of the above clinical criteria and at least one clinical criterion defines the form as severe.</td>
</tr>
<tr>
<td>Forms with multi-organ involvement (malignant)</td>
<td>Extremely severe toxic-infection syndrome. Temperature ≥ 40 °C, chills, severe headache, nausea, vomiting, typhoid mental condition, stupor, coma; abundant haemorrhagic rash. Clinically apparent lesion of more than one organ (pneumonitis, jaundice, renal failure, gastrointestinal hemorrhage, myocarditis, CNS damage); platelet count ≤ 50×10⁹/l or &lt; 100×10⁹/l; Serum sodium ≤ 130 mmol/l; ALT/AST increased &gt; 5 times, hypocalcemia, hypoalbuminemia, hypoxemia. The presence of at least two clinical syndromes and two laboratory criteria of the above, determines the form as malignant.</td>
</tr>
</tbody>
</table>

* The proposed scheme is based on a set of criteria in defining severity;
** The scheme is constructed by the authors based on personal experience (Popivanova N. et al., 2007; Baltadzhiev I. 2012), and on the experience of many researchers, who have advocated one or other criteria in their publications (Raoult D, et al., 1982; Roult D, et al., 1986; George F, et al., 1993; Dignat-George F. 1999; Rovery C, et al., 2008. Cf References 3, 8, 12, 21, 22, 23, and 29.
the statistical values of the differences. Using the severity criteria we found that the mean age of patients was significantly greater in severe cases than in mild and moderate cases ($F = 3.785$ $p = 0.02$) (Table 4). This is particularly clearly seen in the two marginal age groups - children under 14 and adults over 65. Mild forms are more common in children, while severe forms are more common in the elderly patients. Although there were only single cases in childhood, statistically significant differences were not found in the presence of malignant forms in both age groups (Table 5). A possible explanation could be that there were no lethal outcomes among children and mortality rate in the patients over 65 was nearly 10% and is mainly on account of malignant forms of the disease (Fig. 2). This indicates a predominantly benign course of MSF among children and severe, complicated course in the elderly.$^{8,13}$

**DISCUSSION**

The course of the disease and the severity of rickettsial clinical forms are determined by factors related to the causative microorganism and to the characteristics of the host response.$^{14}$ According to some authors, the balance between individual susceptibility to pathogenic mechanisms and resistance of the individual to rickettsial growth and propagation indicates the human risk factors for disease severity.$^{15}$ For people these factors include greater age, glucose-6-phosphate-dehydrogenase deficiency, concomitant diseases, alcoholism, diabetes, immunosuppression of various kinds, etc. Inadequate or delayed therapy should be added to the above factors,$^{3,8}$ although some authors have found that this may have no statistical significance.$^{18}$ Experiments have found that older male animals are killed by lower average dose of rickettsiae.$^{16,17}$ We have not

### Table 3. Comparison of severity in clinical forms of both studied periods of MSF: 1993-2003 and 2004-2011

<table>
<thead>
<tr>
<th>Forms according to severity</th>
<th>1993-2003 (n = 549) n (%)</th>
<th>2004-2011 (n = 334) n (%)</th>
<th>Fisher’s exact test (two tailed p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>226 (41.16)</td>
<td>119 (35.62)</td>
<td>N.S. *</td>
</tr>
<tr>
<td>Moderate</td>
<td>180 (32.79)</td>
<td>144 (43.11)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Severe</td>
<td>88 (16.03)</td>
<td>38 (11.37)</td>
<td>0.05 n.q.s *</td>
</tr>
<tr>
<td>Malignant</td>
<td>36 (6.56)</td>
<td>29 (8.68)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Lethal outcome</td>
<td>19 (3.46)</td>
<td>4 (1.19)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

* n.q.s. – not quite significant; N.S. = non significant.

### Table 4. Age specificity in the MSF clinical forms according to the severity course

<table>
<thead>
<tr>
<th>Forms classified by severity</th>
<th>Patients (n = 334) n (%)</th>
<th>Mean age of patients (yrs)*</th>
<th>With respect to age Independent samples test</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Mild forms</td>
<td>119 (35.62)</td>
<td>42.05 ± 3.50</td>
<td>$p^{1-2} &gt; 0.05$</td>
</tr>
<tr>
<td>2. Moderate forms</td>
<td>144 (43.11)</td>
<td>46.10 ± 3.71</td>
<td>$p^{2-3} &lt; 0.05$</td>
</tr>
<tr>
<td>3. Severe, malignant and lethal forms</td>
<td>71 (21.25)</td>
<td>58.59 ± 4.32</td>
<td>$p^{1-3} &lt; 0.01$</td>
</tr>
</tbody>
</table>

* $F = 3.785$ $p = 0.02$.

### Table 5. Comparison of clinical form severity in two marginal age groups of patients with MSF - children up to 14 and adults older than 65 yrs

<table>
<thead>
<tr>
<th>Forms classified by severity</th>
<th>Children up to 14 years n = 85 n (%)</th>
<th>Adults above 65 years n = 127 n (%)</th>
<th>Fisher’s exact test (two tailed p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>59 (69.42)</td>
<td>27 (21.25)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Moderate</td>
<td>18 (21.18)</td>
<td>45 (35.43)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Severe</td>
<td>4 (4.7)</td>
<td>30 (23.62)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Malignant</td>
<td>4 (4.7)</td>
<td>13 (10.23)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Lethal outcome</td>
<td>0</td>
<td>12 (9.44)</td>
<td>-</td>
</tr>
</tbody>
</table>
detected statistically significant gender differences either between infected people in general or among the worst forms of MSF.

*R. conorii conorii* includes: a) the prototype strain *Malish*, cause of MSF in the Mediterranean area (Southern Europe, northern Africa), Croatia, Slovenia and around the Black Sea: Turkey, Bulgaria, Ukraine, Romania; b) isolate Kenyan, causative agent of MSF in Kenya, Somalia, South Africa; c) isolates, causing Indian tick typhus (ITT) in India; d) Israeli spotted fever (ISF) rickettsia in the Middle East; e) Astrakhan spotted fever rickettsia (AFR) in Southern Russia. All these are transmitted to humans mainly by *Rhipicephalus* ticks. 3 Differences in the course of these diseases have long been the subject of debate among rickettsiologists. Since most of the clinical features of MSF overlap with those of ITT, ISF and AFR some authors thought that these were different names for a single disease characterized by fever and maculopapular rash. 19 Conversely, other authors have identified a number of differences, e.g. less frequent occurrence of inoculation eschar in ISF and AFR compared to the MSF. They claimed they need a separate nosological denomination as the four isolates caused varying clinical presentations with different disease severity and had different geographical locations. 20

The classification we present refers to MSF (*R. conorii conorii – Malish*), which can have a typical or atypical clinical course, acute or protracted course, but chronic forms are not known so far. A number of researchers have developed criteria for assessing the severity of MSF, including clinical and laboratory parameters. 3,8,12,21-23 The thing worth noting here is that the severity criteria for the disease we have chosen on the basis of our own experience and the experience of other authors, are based on the reaction of the body to the etiological pathogens and can be used in various SFG-rickettsiae in various stages of their emergence and development, regardless of the geographic location. Unlike RMSF in America, Mediterranean spotted fever has long been considered a benign disease. In 1982, Raoult et al. described the first severe case resulting in death – a malignant form, involving the kidneys, lungs, liver, pancreas, heart, spleen, skin and the nervous system. 12 In the 1990s, when the disease had a peak in many countries, rickettsiologists and clinicians reconsidered their stance that only a favourable outcome of MSF is possible. 8,22,24,25 It was gradually realized that, in the words of Z. Alioua “… Mediterranean spotted fever has a false reputation of being benign”. 25 The severity of the disease shows temporal and geographical variations. 3 Mortality rate in Oran (Algeria) in 2004 was 3.2%, in Marseille in 2003 - 5.6%, in southern Portugal in 1997 - 32.3% among hospitalized patients without having achieved similar levels in previous years. 18 A similar pattern was observed in Bulgaria: no death was reported in the first wave of MSF (1948-1972); in the first decade of its re-emergence (1993-2003) the mean mortality rate in the endemic Plovdiv region was 3.46%, and among the forms of multi-organ involvement (“malignant” forms) it reached 34.54%. 8 According to the opinion of prominent researchers and experts MSF has become more severe disease than RMSF. 3 There is no exact explanation for such changes observed with other SFG-rickettsiae as well. On the contrary, greater awareness, earlier and improved management should render the disease course less severe. According to existing hypotheses it is possible that: a) MSF, considered a mild disease in the past, was not recognized among severe and lethal cases of unusual course; b) a more virulent strain of *R. conorii conorii* has emerged; c) in many infectious diseases the bacterial load correlates with disease severity and this was demonstrated in scrub typhus; d) there is variable flexibility to the pathogenic effect of rickettsiae among heterogeneous human population, a different type of relationship with the endothelial cells and the different responses of the latter. 15 G Valbuena also refers to other reasons that could explain the differences in severity between separate rickettsioses: cross-protective immunity, due to infection with rickettsiae with variable virulence; exposure to vectors with immunomodulatory activity in saliva; the proliferation of some rickettsiae in the place of inoculation is the time for adaptive immune response, and in rickettsiae that do not form eschar (ISF, RMSF) it is probable that earlier vascular dissemination and more severe disease occur. 15

In immunological aspects it is considered that when rickettsiae run as a serious or fatal disease, that is caused by an imbalance between pro-inflammatory responses that eliminate pathogens and anti-inflammatory responses that reduce immune-mediated tissue damage. The bacteria-emitted lipo-polysaccharide and peptidoglycan can lead to excessive re-stimulation of Toll-like receptors (TLR4 and TLR2) of dendritic cells (DC) and switching the pro-inflammatory cytokine IL-12 production to the anti-inflammatory IL-10 production. IL-10 stimulates regulatory T lymphocytes (Treg) and inhibits the Th1 cell-mediated immune responses and as a consequence uncontrolled bacterial growth leads to
more serious outcomes of the disease.26-29 Wrongly regulated activation and proliferation of lymphocytes may lead to severe and unusual complications. Genetic polymorphism of some cytokines (IFN-γ, TNF-α and IL-10) probably also plays a role in susceptibility to MSF.30

CONCLUSIONS

The classification of the MSF forms according to the course of the disease and development of criteria for determining the severity of disease allows us to compare morbidity rates in different stages of disease spread in different ages and in different endemic and non-endemic regions. Unified use of these criteria would prevent any discrepancy in the data on the course and severity of SFG-rickettsioses allowing clinicians to find their changing clinical manifestations. All this contributes to a more objective surveillance (accurate diagnosis, registration and reporting) and more effective control of the disease.

REFERENCES

СРЕДИЗЕМНОМОРСКАЯ ПЯТНИСТАЯ ЛИХОРАДКА – КЛАССИФИКАЦИЯ ФОРМ В ЗАВИСИМОСТИ ОТ ТЕЧЕНИЯ БОЛЕЗНЕННОГО ПРОЦЕССА И ОТ КРИТЕРИЕВ ОПРЕДЕЛЕНИЯ ТЯЖЕСТИ ЗАБОЛЕВАНИЯ

И. Балтаджиев, Н. Попиванова, Й. Стоилова, А. Кеворкян

РЕЗЮМЕ
ВВЕДЕНИЕ: Средиземноморская пятнистая лихорадка (СПЛ) в Болгарии вызывается Ricketsia conorii с основным вектором собачий клещ rhipicephalus sanguineus. В 90-ые годы XX века отмечены первые случаи снова появившейся (после 20-илетнего отсутствия) СПЛ в стране и ее ежегодное нарастание до 2001-2003 г., после чего наступает некоторый спад в распространении болезни. СПЛ продолжает оставаться проблемой здоровья, так как и не редки тяжелые и комплицированные формы.

Цель: Настоящая работа ставит себе цель классифицировать формы СПЛ в зависимости от течения заболевания, а также и выработать критерии определения тяжести заболевания с целью сравнения клинических проявлений в различных фазах распространения болезни среди различных возрастных групп в различных эндемических и неэндемических регионах страны и вне ее.


Воспринятые авторами критерии классификаций форм СПЛ включают: 1. Типичность: Формы с самыми характерными признаками СПЛ (струп, фебрилитет, папуло-макулярная сыпь по телу и конечностям, в том числе по ладоням и ступням). 2. Проявленность: формы, при которых наблюдаются все или часть характерных симптомов, дающих достаточные основания для предварительного диагноза. 3. Продолжительность: сверхострые, острые и протяженные формы. Критерии насчет тяжесть разделяют формы на легкие, средние тяжелые, тяжелые и малигенные. Критерии включают клинические и параклинические показатели.

РЕЗУЛЬТАТЫ: Классификация форм и течения СПЛ представлены в работе. В зависимости от воспринятых критериев и проведенных исследований легкие формы представляют 41.16% - 35.62% (p > 0.05), средне-тяжелые – 32.79% - 43.11% (p < 0.01), тяжелые формы – 16.03% - 11.37% (p = 0.05), малигенные формы – 6.56% - 8.68% (p > 0.05), а летальный исход – 3.46% - 1.19% (p < 0.05).

Средний возраст пациентов достоверно более высокий среди тяжелых форм СПЛ (58.59 ± 4.32 г.) по сравнению со средне-тяжелыми (46.10 ± 3.71 г. - p < 0.05) и легкими формами (42.05 ± 3.50 г. - p < 0.01). У детей до 14 лет по сравнению с взрослыми до 65 лет чаще встречаются легкие формы (p < 0.0001). Среди детей до 14 лет нет умерших, а летальность среди группы до 65 лет достигает почти 10%. Все это говорит о более легком течении СПЛ среди детей и тяжелое комплицированное течение среди людей в пожилом возрасте.

ЗАКЛЮЧЕНИЕ: Критерии, подобраные на основании собственного опыта и опыта других авторов, основываются на реакции человеческого организма к биознесетворному патогену и эти критерии
можно применять при риккетсиях в различные фазы их появления и развития, несмотря на их географическое распространение. Унифицированное использование этих критериев уменьшило бы разнонаправленность в данных различных авторов по отношению к течению и тяжести заболевания.