Conclusions. Defined have been the major internal epidemiological threats to the entities involved in FWC-2018. Advance, forehand assessment of risks allowed for carrying out targeted and effective complex of prophylactic activities. Sanitary-epidemiological welfare of the participants, guests of the sports event was provided despite the coincidence of FWC-2018 terms with the period of seasonal morbidity rate increase as regards endemic, natural-focal infectious diseases of bacterial and viral etiology.

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CLINICAL PECULIARITIES OF MYASTHENIA GRAVIS IN KRASNODAR REGION

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КЛИНИЧЕСКИЕ ОСОБЕННОСТИ МИАСТЕНИИ В КРАСНОДАРСКОМ КРАЕ

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Among 344 myasthenia patients living in the Krasnodar Territory were examined. Of these, 246 were women (71.5 %) and 98 men (28.5 %), the ratio of men to women was 1:2.5. The average age of patients with myasthenia gravis at the onset of disease was 46.2±0.97. In the majority of cases, the generalized form of the disease prevailed (82.8 %). The eye shape

was revealed in 16.3 % of cases, craniopharyngeal in 0.9 % of cases, respectively. The pathology of the thymus gland was revealed in 36 patients. Early onset (up to 40 years) of myasthenia gravis was observed in 142 patients, 114 debut women and 28 men respectively. The ratio of men to women was 1: 4. Oculomotor disorders in the form of asymmetric ptosis and diplopia (weakness in extraocular muscles) with minimal lesion in the bulbar group of muscles and skeletal muscles prevailed in the clinical picture of the disease debut in these patients. 93 patients were diagnosed late onset (after 60 years) of myasthenia gravis, including 60 women and 33 men. The ratio was 1: 1.8. At the onset of the disease, weakness and pathological fatigue in the masticatory muscles, the muscles of the extensor muscles of the neck, and in the deltoid muscle, with minimal damage to the triceps brachii muscle and extraocular muscles prevailed in this group of patients.

Keywords: myasthenia gravis, diagnosis, clinical picture, thymus gland

Обследовано 344 больных миастенией, проживающих на территории Краснодарского края. Из них женщин – 246, мужчин – 98, что составило 71,5 и 28,5 % соответственно (2,5:1). Средний возраст начала заболевания у зарегистрированных больных составил 46,2±0,97 года. Преобладала генерализованная форма (82,8 %), глазная форма была выявлена в 16,3 % случаев, краниофарингеальная в 0,9 % случаев. У 105 пациентов выявлена патология вилочковой железы. Раннее (до 40 лет) начало миастении наблюдалось у 142 пациентов, из них женщин было 114, мужчин – 28 (1:4). В клинической картине дебюта заболевания у этих пациентов преобладали глазодвигательные нарушения в виде асимметричного птоза и диплопии (слабость в экстраокулярных мышцах) при минимальной заинтересованности бульбарной группы мышц и скелетной мускулатуры. Обследовано 93 пациента с поздним (после 60 лет) началом миастении: 60 женщин, 33 мужчины (1:1,8). У этих пациентов в начале заболевания преобладали слабость и патологическая утомляемость в жевательных мышцах, разгибателях шеи и в дельтовидной мышце при минимальном поражении трехглавой мышцы плеча и экстраокулярных мышц.

Ключевые слова: миастения, диагностика, клиническая картина, вилочковая железа

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Recently there has been a rapid increase in the incidence of autoimmune diseases, including myasthenia gravis. Myasthenia gravis is a classical autoimmune disease caused by the formation of polyclonal antibodies directed to various antigen targets of the neuromuscular junction, such clinical manifestations as weakness and pathological fatigue of the striated muscles, lead to disability and, often, to death as a result of myasthenic crisis [1].

Myasthenia gravis was first mentioned as an independent disease in the 17th century. S. Wilks in 1877 thoroughly described the clinic bulbar paralysis involving respiratory muscles, leading to death of the patient, while at autopsy, no morphological changes were found. Later, Erb W. described in detail three cases of myasthenia gravis, in the clinical picture of which the absence of muscle atrophies and sensitive disorders was first noted. The next stage in the clinical study of the disease pattern was a description of fluctuations in such symptoms as muscle weakness during the day and a tendency to spontaneous remissions (Goldflam S., 1893). The disease was named after the researchers who initiated the study of this nosological form – the Erba-Goldflem disease.

The total incidence of myasthenia gravis in the world ranges from 0.5 to 20.0 per 100,000 of population [2]. Over the past 60 years, the increased prevalence of this pathology both in Russia and around the world has been registered [3, 4, 5, 6]. The disease often affects young people, it being of a high social significance [7].

The diagnosis of «myasthenia gravis» is often made with a great delay, despite the simplicity of clinical manifestations and the availability of the developed diagnostic criteria for this disease. This is more often due to the fact that the pathological fatigue inherent in myasthenia gravis can occur in the defeat of the most diverse structures of the peripheral neuromotor apparatus, as well as with the variety of clinical manifestations of myasthenia gravis. [1, 7]. According to some authors, the share of diagnostic errors can reach from 50 to 75–80 % [8]. All this makes the present study relevant.

Objective: to study clinical features of myasthenia gravis in the Krasnodar region in the adult population and compare the results with the data of Russian and foreign authors.

Material and Methods. The work was carried out on the basis of State budgetary health care institution «Region Clinical Hospital № 1 named after Professor S. V. Ochapovsky» of Ministry of Health of Krasnodar Region. In 2011 the peripheral nervous system pathology cabinet was created, where patients with myasthenia gravis living in the Krasnodar Territory are being monitored. By the 1st of January, 2017 three hundred and forty-four patients with a diagnosis of myasthenia gravis have been registered. The diagnosis was made on the basis of anamnestic data, features of the neurological status (syndrome of pathological muscle fatigue), the results of proseryl test and electromyographic examination (decrement test), computed tomography of chest organs for the detection of pathology of the thymus gland, as well as consultations of related specialists for the detection of somatic pathology.

Statistical processing of data was performed in MS Excel (USA) spreadsheets and the software package STATISTICA 6.0 (StatSoft, USA). Processing methods were descriptive statistics, and nonparametric methods of analysis (Wilcoxon test).

Results and Discussion. The data of 344 patients (246 women and 98 men) with the diagnosis of myasthenia gravis were analyzed. Percentage was 71.5 % and 28.5 %, respectively. Ratio between men and women was 1: 2.5.

The average age of debility of the diseased patients was 46, 2±0.97: in men – 50.6±1.6, in women – 44.4±1.1 respectively. These data are given in Table 1.

Table 1

Distribution of patients with myasthenia gravis according to sex and age in the Krasnodar Territory

Age, years	Women, n (%)	Men, n (%)	Total, n (%)
10–19	27 (11)	9 (9)	36 (10.5)
20–29	51 (20)	8 (8)	59 (17.2)
30–39	36 (16)	11 (11)	47 (13.6)
40–49	28 (11)	15 (15)	43 (12.5)
50–59	44 (18)	22 (22)	66 (19.2)
60–69	42 (17)	24 (25)	66 (19.2)
70–80	18 (7)	9 (10)	27 (7.8)

At the age of 20 to 40 years, 36 % of women fell ill, and in the same period19 % of men fell ill. In men, the variation in incidence between the ages of 10 and 50 was significant. After 60 years, 35 % of men and 24 % of women fell ill. Thus, we have revealed a clear bimodality of incidence in women with peaks at 3–4 and 6–7 years of life. Men, on the contrary, are more likely to get sick after 60 years. The data obtained by us on the debut age of the disease are consistent with the results of many researchers of myasthenia gravis [1, 2, 7]. However, in the Samara region there was no clear bimodality of myasthenia gravis in women [5].

We diagnosed myasthenia gravis in 68 % of cases during primary treatment of patients in medical institutions. 17 % of patients with the appearance of the first symptoms of the disease did not apply for medical aid because of their insignificant manifestations or independent regression. According to VD Kosachev, when patients were first treated Myasthenia gravis was diagnosed only in 29.9 % of cases. More accurate diagnosis of myasthenia gravis occurs in the stage of a detailed clinical picture [7].

Most often, myasthenia gravis manifests as oculomotor disorders in the form of ptosis and diplopia. These symptoms appear, as a rule, by the end of the day and regress independently. In a large percentage of cases, this fact leads to delayed diagnosis and treatment of the disease.

Table 2 shows the distribution and characteristics of motor disorders in the myasthenia gravis in patients in the Krasnodar Territory in comparison with the data of Russian and foreign authors.

Table 2

Disribution and character of motor disorders during the myasthenia gravis in Krasnodar Territory and according to the data of domestic and foreign authors

Symptoms	Frequency of occurrence in Krasnodar Territory, (%)	Frequency of occurrence, Osserman K. E., (%)	Frequency of occurrence, Cousin M. I., Hecht B. M. (%)
Ptosis	84	67	62
Diplopia	56	43	73
Bulbar disorders	23	27	78
Fatigue of the neck muscles	25	–	54
Fatigue of the proximal muscles of the hands and feet	27	25	82
Fatigue of the muscles of the trunk	16	15	78

On medical examination we revealed both generalized form of the disease and local forms of myasthenia gravis. In the majority of cases, the genealized form of myasthenia gravis prevailed (82.8 %). At the same time, weakness and abnormal muscle fatigue were observed both in craniopharyngeal and in skeletal musculature. In 100 % of cases the syndrome of pathological fatigue in the proximal group of muscles of the upper and lower extremities involving distal muscles of the extremities was revealed in 42 % of patients, in the muscles of the extensor muscles of the neck in 43 % of patients. In 97 % of patients with the generalized form of myasthenia gravis, weakness both in the circular eye muscle, and oculomotor muscles was revealed. Weakness and pathological fatigue are also found in other groups of facial muscles, particularly in the circular muscle of the mouth, buccal muscles, and chewing muscles (62 % of patients). The lesion of lingopharyngeal musculature was observed in 44 % patients. The clinical manifestations of the generalized myasthenia gravis in patients residing in the Krasnodar Territory are correlated with the data of Russian and foreign authors [9, 10]. The predominance of generalized form of myasthenia gravis is noted by the majority of myasthenia gravis researchers [1, 7, 9]. Of the local forms eye and craniopharyngeal myasthenia were observed. The data are presented in Table 3.

Table 3

The occurrence of various forms of myasthenia gravis in patients in the Krasnodar Territory

Myasthenia's form	Number of patients	Percentage (%)
Generalized	285	82.8
Eye	56	16.3
Craniopharyngeal	3	0.9
Total	344	100

Weakness and pathological muscle fatigue in oculomotor muscles of varying severity were observed in 100 % of patients with an ocular myasthenia gravis, while 32 % of patients complained of persistent diplopia, to a transient 68 %. Kraniofaringealnaya form was observed in 3 patients (0.9 %), while weakness and pathological glossopharyngeal and facial fatigue were observed in the muscles.

To exclude the pathology of the thymus, all the registered patients underwent computed tomography of the thoracic organs. The pathology of the thymus gland was revealed in 82 patients, it accounts for 23, 8 % of the total number of patients. Thus, the pathology of the thymus is found, practically, in every 4 patients. These data are fully consistent with Russian and foreign studies [7, 10]. The data are presented in Table 4.

Table 4

Types and frequency of pathologies in patients in the Krasnodar Territory

Type of pathology	Number of patients	Percentage (%)
Thymomas	42	40
Persistent thymus gland	37	35.2
Hyperplasia of the thymus gland	24	22.9
Involutive thymus	2	1.9
Total	105	100

Nondifferentiated thymomas were detected in 14 (33.3 %) patients; while they had a generalized myasthenia gravis clinic. 10 patients (71.4 %) undergo surgical treatment (thymectomy), and 2 (14.3 %) undergo chemotherapy.

Thymoma type B1 was detected in 10 (23.8 %) patients with thymectomy. Later, in 10 % of cases, radiation therapy of the thymus or chemotherapy (10 %) was performed. All patients in this group had a generalized myasthenia gravis.

Thymoma type B2 was detected in one patient with a generalized form of myasthenia gravis (2.4 %), which was treated with thymectomy and chemotherapy.

Thymoma type B3 was detected in 4 patients (9.5 %) with a generalized form of myasthenia gravis, all with thymectomy. Two-patient (50 %), with thymectomy, underwent chemotherapy.

Thymoma type AB was detected in 9 patients (21.4 %). Thymectomy was performed in 100 % of cases; in 11.1 % of cases thymectomy was followed by chemotherapy.

Persistent thymus gland was found in 37 patients with a generalized form of myasthenia gravis. 9 patients (24.3 %) underwent thymectomy.

Hyperplasia of the thymus gland was detected in 24 patients, 22 (91.7 %) of them underwent the surgical treatment for out-tectomy.

Involutive thymus was detected in two patients; one (50 %) produced thymectomy.

Early onset (up to 40 years) of myasthenia gravis was observed in 142 patients, including 114 women and 28 men. The male to female ratio was 1: 4. In the clinical picture of the disease debut in these patients, oculomotor disorders in the form of asymmetric ptosis and diplopia (weakness in extraocular muscles) prevailed with minimal lesion in the bulbar group of muscles and skeletal muscles.

We identified 93 patients with late onset (after 60 years) myasthenia gravis, including 60 women and 33 men. The ratio was 1:1.8. In this group of patients, at the onset of the disease, weakness and pathological fatigue prevailed in the masticatory muscles, the muscles of the extensor muscles of the neck, and in the deltoid muscle, with minimal damage to the triceps brachii muscle and extraocular muscles. The similar features of the clinical picture of myasthenia gravis, depending on the age of the disease debut, are indicated by Russian and foreign authors [7, 11].

Conclusions. The clinical manifestations of myasthenia gravis differ greatly in their variability.In this connection, awareness of this disease will contribute to earlier and timely diagnostics and treatment of patients with myasthenia gravis. The clinical features of myasthenia gravis among the adult population in the Krasnodar Territory correspond to the data of Russian and foreign authors and meet global trends.

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