conditions / S. Vojnovic et al. Vojnosanitetski pregled. 2014. Vol. 72. P. 30-30.
DOI: https://doi.org/10.2298/VSP140121030V

11. Dunn S. E., Lee H., Pavri F. R., Zhang M. A. Sex-Based Differences in Multiple Sclerosis (Part I): Biology of Disease Incidence. Current Topics in Behavioral Neurosciences. Springer. 2015. Vol. 26. P. 29-56. DOI: https://doi.org/10.1007/7854_2015_371

12. Gomez F. P., Steelman A. J., Young C. R., Welsh C. J. Hormone and immune system interactions in demyelinating disease. Hormones and Behavior. 2013. Vol. 63, No. 2. P. 315-321. DOI: https://doi.org/10.1016/j.hbeh.2012.10.014

13. Seasonal variations of 25-OH vitamin D serum levels are associated with clinical disease activity in multiple sclerosis patients / C. Hartl et al. Journal of the Neurological Sciences. 2017. Vol. 375. P. 160-164. DOI: https://doi.org/10.1016/j.jns.2017.01.059

14. Sex hormones modulate brain damage in multiple sclerosis: MRI evidence / V. Tomassini et al. J. neurology, neurosurgery, and psychiatry. 2005. Vol. 76. P. 272-275. DOI: https://doi.org/10.1136/jnnp.2003.033324

15. Sicotte N. L., Giesser B. S., Tandon V. Testosterone treatment in multiple sclerosis: A pilot study. Arch Neurol. 2007. Vol. 64. P. 683-688. DOI: https://doi.org/10.1001/archneur.64.5.683

THE CONTENT OF CYTOKINES IN THE BLOOD SERUM OF PATIENTS WITH EARLY LATENT SYPHILIS IN PROCESS OF TREATMENT

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The urgency of the latent syphilis problem is caused by the fact that in the structure of syphilis incidence its part amounts more than 50%, the mechanisms of its pathogenesis remain unstudied completely, and after the treatment of such patients the serological resistance arises [1, 3, 4, 7, 9].

Among numerous factors contributing to the increase of the number of cases of the early latent syphilis, a significant part belongs to [1, 2, 4, 11]:

- the significant spread of antibiotics using, both for the treatment of syphilis and for the treatment of other STIs;
- expansion and introduction into practice of a number of highly sensitive methods of examination (immunoenzyme method, immune blotting, the reaction of passive hemagglutination (RPGA));
- the reduction of the virulent properties of the pale treponema itself and its resistance to therapy.

The concentration of IL-10 remained 1.8 times higher. The concentration of IL-6 was increased by 6.5 times in patients with latent early syphilis and was also dependent on the period of the infection, and also even 1.5-2 years after treatment the IL-6 content remained elevated. It was also found that in patients with latent early syphilis the concentration of IL-2 was increased by 2.3 times and it did not normalize in 24.5% of patients even two years after treatment. In patients with latent early syphilis, the concentration of TNFα was increased by 3.6 times. After treatment, the concentration of TNFα decreased, but exceeded the control values by 1.35 times. Further analysis of the concentration of TNFα revealed that, with a disease period of up to one year, the concentration of this cytokine was normal during ten months after treatment, and in patients with the disease period of more than one year, after treatment normalization of the TNFα level was absent in 64.5% even after 18 months. It was found that the concentration of ILNFγ in patients with early latent syphilis before treatment was increased by 3.8 times in comparison with the control group. After treatment, almost 25% of patients with the duration of the infection more than one year revealed no normalization of INFγ and it was increased by 1.5 times. In patients with early latent syphilis there was a significant increase in the concentration of cytokines TNFα and INFγ, an imbalance of IL-2, IL-6, IL-10 as well as. The dependence of the cytokine concentration on the period of infection is noted. Based on the study of the cytokine status in patients with early latent syphilis with periods of infection of more than one year, the use of immunomodulatory therapy may be recommended. Increasing the concentration of such cytokines as TNFα, IL-6, IL-10 after treatment can be used as prognostic tests of serological resistance.
In addition, some researchers believe that L- and cyst-forms of the pale treponema itself can be one of the reasons of the latent course of syphilis [4, 18]. At the same time, none of the researchers studying the mechanisms of the syphilitic infection pathogenesis has doubts as to the fact that the prognosis of the disease depends on the state of the immune system [7, 12, 15, 16, 17]. Until now, there is no consensus among specialists on understanding the mechanism of immunity disorders under the latent syphilis [2, 4, 5].

The above data indicate that the issue of the classification and mechanisms of the immune system disorders initiation under this form of syphilis remains unresolved [2, 16, 17]. Studies of the content of anti-inflammatory cytokines in patients with early latent syphilis, which have been conducted earlier, are highly contradictory and incomplete [4, 5, 8-13].

Under the chronic inflammation peculiar to syphilitic infection in particular, the normal cytokine profile changes, and that is manifested by increased secretion of pro-inflammatory cytokines [3, 5, 6].

However there is another view on the role of interleukins created in the cells of a sick person under the influence of pale treponema due to the activation of Th1 cells [12, 13].

To this day almost no studies have been conducted on the content of IL-2 in the blood serum of patients with latent syphilis, while IL-2 plays a significant role in the activation of the immune system through the stimulation of the synthesis of INFγ, IL-6. Unlike IL-2, IL-6 is produced by different types of cells by activation of CD4+ and CD8+ and belongs to the proinflammatory cytokines. One of the most important cytokines determining the immune response is IL-10. Under its influence, cellular immunity (Th1) is inhibited and humoral immunity (Th2) is stimulated, the secretion of INFγ, TNFα, IL-1, IL-8 decreases. TNFα is a polypotent immunomodulatory cytokine, namely a mediator of a specific and non-specific immune response that depends on its concentration. TNFα is capable of activating EK-cells, increasing the secretion of IL-6. TNFα is synthesized mainly by Th1-lymphocyes and EK-cells and has a significant antibacterial and immunomodulatory effect [5, 6].

A comprehensive study of the cytokine profile in patients with early latent syphilis before and after treatment can give a more detailed idea of the mechanism of the immune response and allow further prognosis of the disease [10, 19-22].

Objective – to study the concentration of pro- and anti-inflammatory cytokines in patients with latent early syphilis before and after treatment.

MATERIALS AND METHODS OF RESEARCH

The study was conducted in 112 patients (52 men and 60 women) aged 18-43 (mean age 31.1±0.7 years) with early latent syphilis who were on treatment at the skin and venereal disease clinic of the State Establishment "Dnipropetrovsk Medical Academy of Health Ministry of Ukraine". The comparison group consisted of 15 practically healthy persons with similar sex and age distribution.

The criteria for inclusion in the study were: age up to 45 years, diagnosis of early latent syphilis. The criteria for exclusion from the study were: age over 45, pregnancy, presence of tuberculosis, viral hepatitis, HIV / AIDS, other infectious diseases; diabetes, as well as antibiotic treatment in the last three months before the study.

For the diagnosis of syphilis serological tests were used: the classical complex of serological reactions (CSR), ELISA (IgM, IgG), the reaction of passive hemaggulitation (RPGA), immunofluorescence reaction with absorption (RIF-abs) and RIF-200. The serum levels of IL-2-, IL-6-, IL-10-cytokone, TNFα, and INFγ were measured by the method of enzyme immunoassay [11]. The analysis of the data received was carried out with application of the program package Statistics 6.0. The difference in indices with p<0.05 considered as probable one.

To identify the relationships between the indices, Friedman's nonparametric variance analysis with the definition of χ² was used. The coupling between indices was considered significant if χ² value exceeded the critical one (χ²=3.84) [3, 4].

RESULTS AND DISCUSSION

The concentration of IL-10 in the blood serum of patients with latent early syphilis before treatment was probably (p<0.05) increased to 14.9±0.9 pg/ml in comparison with the control group (4.11±0.5 pg/ml), that is by 3.7 times. When analyzing this anti-inflammatory interleukin in patients with an infection period of more than one year, its concentration exceeded the normal values by 2.4 (p<0.05). If before treatment the concentration of IL-10 was increased by 3.7 times, after treatment the content of this interleukin significantly decreased to 10.1±0.2 pg/ml and exceeded the normal values by 2.4 (p<0.05). On further observation after treatment, the further decrease in IL-10 concentration to 7.5±0.1 pg/ml was marked only after 12.3±1.2 months. That is, even one year after treatment there was no normalization of the IL-10 concentration (it remained 1.8 times higher than one in the control group).

In patients with early latent syphilis before treatment, the concentration of IL-6 was 31.3±1.2 pg/ml,
that is it was increased by 6.5 times in comparison with the control group.

When analyzing the concentration of IL-6, it was found that in patients with a period of infection up to one year it exceeded the norm by almost 10 times (48.3±1.5 compared to 4.8±0.2, p<0.05). Under the longer duration of the disease, the concentration of IL-6 was almost three times less (15.6±0.5 pg/ml).

After treatment the serum concentration of IL-6 remained elevated (7.4±0.8 pg/ml, p<0.05) even 1.5-2.0 years after.

The concentration of IL-2 in the blood serum of patients with latent early syphilis before treatment was 37.8±4.1 pg/ml while a control group score was 16.5±3.2 pg/ml, that is, it was increased by 2.3 (p<0.05) times. When analyzing the concentration of this cytokine depending on the duration of the disease to one year and more than one year, the difference was unreliable. After treatment the normalization of IL-2 secretion was lacking in 24.5% of patients even two years after.

When analyzing the secretion of tumor necrosis factor (TNFα), we obtained such results: in patients with latent early syphilis the concentration of TNFα was 18.8±0.6 pg/ml while a control group score was 53.7±3.1 pg/ml vs. 16.1±1.3, p<0.05). After treatment almost 75% of patients revealed normalization of this cytokine and only 25% of patients with period of infection more than one year, revealed no normalization of INFγ and it was increased by 1.5 times.

CONCLUSIONS
1. Under the early latent syphilis there is a significant increase in the concentration of cytokines that are synthesized Th1 type of the (TNFα, INFγ), as well as the imbalance of IL-2, IL-6, IL-10.
2. The dependence of the cytokines concentration on the terms of infection was established; so under duration of the infection of more than one year the imbalance of pro- and anti-inflammatory cytokines was more pronounced.
3. Based on the study of the cytokine status, patients with early latent syphilis with terms of infection of more than one year should be treated with medications causing a positive effect on the immune system.
4. An increase in the concentration of such cytokines as TNFα, IL-6, IL-10 after treatment can be used as prognostic tests of serological resistance.

REFERENCES
1. Bondarenko HM, Unuchko SV, Hubenko TV, Matyushenko VP. [Clinical and epidemiological features of syphilis at the present stage]. Dermatologiya ta venerologiya. 2014;2(64):65-71. Ukrainian.
2. Bondarenko GM, Unuchko SV, Nikitenko IN, Gubenko TV, Kutovaia VV. [Syphilis: the current state of the problem]. Dermatologiya ta venerologiya. 2018;1(79):8-12. Russian.
3. Burmeister GR, Pecotto A, Ulrichs T, Aikher A. [Visual immunology]. Moskva, Binom. 2014;320. Russian.
4. Dmitriev GA, Dolya OV. [Diagnosis of syphilitic infection]. Klinicheskaiia dermatologiiia i venerologiiia. 2012;6:10-15. Russian.
5. Drannik GN. [European Declaration of Immunotherapy]. Klinichna imunologiiia. Alerholohiiia. Infektolohiiia. 2011;6:7-13. Russian.
6. Drannik GN. [Modern ideas about the mechanisms of innate and acquired immunity and their interaction (part 1)]. Liky Ukrainy. 2013;4:22-29. Russian.
7. Zakharov VK, Dyudyun AD, Zakharov SV. [Hidden syphilis]. Dnipropetrovsk. 2011;119. Ukrainian.
8. Zaharov SV, Zaharov VK, Djudjun AD. [Features of the level of interleukin-6 inpatients with latent syphilis]. Conference “Dermatovenereology in the aspect of a family doctor”. Kyiv. 2008;35. Ukrainian.
9. Zakharov SV. [Early latent syphilis: focuses on social, epidemiological and medical factors]. Dermatologiya ta venerologiiia. 2018;1(79):44-50. Ukrainian.
10. Zakharov SV. [Cytokine profile in patients with early latent syphilis]. Medicin perspektivi. 2018;23(4):71-5. Ukrainian.
11. Kamyshnikov VS. [Clinical laboratory diagnostics (methods and interpretation of laboratory studies)]. Moskva, MEDpres-inform. 2015;720. Russian.
12. Mavrov GI. [Outpatient treatment of patients with early syphilis with durant penicillins in combination with doxycycline]. Dermatovenerologiya. Kosmetologiya. Seksopatologiya. 2016;1:4:214-9. Russian.
13. Mavrov GI, Mironyuk VI, Shcherbakova JuV, Osinskaya TV. [Some indicators of cytokine status in
СПИСОК ЛІТЕРАТУРИ

1. Бондаренко Г. М., Унучко С. В., Губенко Т. В., Матюшенко В. П. Клініко-епідеміологічні особливості сифілісу на сучасному етапі. Дерматологія та венерологія. 2014. Т. 64, № 2. С. 65-71.
2. Бондаренко Г. М., Унучко С. В., Никитенко І. Н., Губенко Т. В. Сифіліс: современное состояние проблемы. Дерматология та венерология. 2018. Т. 79, № 1. С. 8-12.
3. Бурмейстер Г.-Р., Пенцутто А., Улрихс Т., Айхер А. Наглядна іммунологія. Москва: Бином, 2013. 320 с.
4. Дмитриев Г. А., Доля О. В. Диагностика сифилитичної інфекції. Клінічна дерматологія та венерологія. 2012. № 6. С. 10-15.
5. Дранник Г. Н. Европейская декларация по иммунотерапии. Клініча мімунологія. Алергологія. Інфектологія. 2011. № 6-7. С. 5-13.
6. Дранник Г. Н. Современные представления о механизмах врожденного и приобретенного иммунитета и их взаимодействие (часть 1). Ліки України. 2013. № 4. С. 22-29.
7. Зацаров В. К., Дюдон А. Д., Зацаров С. В. Приховані сифіліс. Дніпропетровськ. 2011. 119 с.
8. Зацаров С. В., Зацаров В. К., Дюдон А. Д. Особливості рівня інтерлейкіну-6 у хворих на прихованій сифіліс. Дерматовенерологія в аспекті сімейного лікування: матеріалі наук.-практ. конф. Київ. 2008. С. 35.
9. Зацаров С. В. Ранній прихованій сифіліс: у фокусі соціальної, епідеміологічних та медичних чинників. Дерматологія та венерологія. 2018. Т. 79, № 1. С. 44-50.
10. Зацаров С. В. Цитокіновий профіль у хворих на ранній прихованій сифіліс. Медичні перспективи. 2018. Т. XXIII, № 4. С. 71-75. DOI: https://doi.org/10.26641/2307-0404.2018.1.124933
11. Камышников В. С. Клінічна лабораторна диагностика (методи та трактова лабораторних ісследовань). Москва: МЕД-пресс-інформ, 2015. 720 с.
21. Knudsen A., Benfield T., Kofoed K. Cytokine expression during syphilis infection in HIV-1-infected individuals. Sex. Transm. Dis. 2009. Vol. 36, No. 5. P. 300-304. DOI: https://doi.org/10.1097/OLQ.0b013e318193ca26

22. Lusiak M., Podwińska J. Interleukin 10 and its role in the regulation of the cell-mediated immune response in syphilis. Arch. Immunol Ther. Exp. 2001. Vol. 49, No. 6. P. 417-421.

CLINICAL FEATURES OF PREGNANCY IN MULTIDRUG-RESISTANT TUBERCULOSIS AND TYPE 1 DIABETES MELLITUS COMORBIDITIES (a case report)

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Ключові слова: вагітність, мультирезистентний туберкульоз, цукровий діабет 1-го типу

Abstract. Clinical features of pregnancy in multidrug-resistant tuberculosis and type 1 diabetes mellitus comorbidities (a case report). Raznatovska O.M., Fedorec A.V., Shalmina M.O., Grekova T.A. Objective – to update the literature data with the clinical features of pregnancy in multidrug-resistant tuberculosis (MRD-TB) and type 1 diabetes mellitus (T1DM) comorbidities based on an example from own clinical experience. A clinical case of pregnancy course in MRD-TB and T1DM comorbidities was described based on our own clinical experience. We report the clinical case of newly diagnosed MRD-TB in a 38-year-old woman suffering from T1DM. Her general condition was unstable from satisfactory to moderately severe despite an adequate treatment of MRD-TB and T1DM with manifestations of intoxication syndrome and nephropathy. Adenomyosis with periodic bloody vaginal discharge was diagnosed. There was no clinical-radiological dynamics and sputum culture conversion. After an intensive phase of antymycobacterial therapy within 3 months, the patient got pregnant. Based on the medical indications (MRD-TB, absence of sputum culture conversion and clinical-radiological dynamics, moderate severity of T1DM, nephropathy) and adenomyosis with bloody vaginal discharge, the patient was requested to induce the pregnancy termination, and she consented. On month 7 of antymycobacterial therapy, an extensive drug-resistance of Mycobacterium tuberculosis was detected.