



## VITILIGO'S TREATMENT ALGORITHM

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Vitiligo is a disorder of melanin pigmentation, occurring in 0.5–2% of the population, characterized by the sudden appearance of depigmented spots on any part of the skin, tending to peripheral growth, developing due to the disappearance or impairment of the functional activity of melanocytes [1]. According to modern domestic and foreign data, vitiligo is the result of a complex effect of endogenous and exogenous factors, among which neuroendocrine, immune, reduction-oxidation and microcirculatory disorders are most pronounced [2]. In addition, the results of clinical and genetic researches make it possible to associate vitiligo with diseases of a hereditary nature [3]. Important pathogenetic significance in vitiligo is also stress, which is one of the main trigger factors, excessive UV radiation, trauma, beriberi, diseases of the digestive tract, fermentopathy, hormonal imbalance, microelement deficiency, contact with chemicals. It should be noted that the division of the above theories is very conditional, since direct or indirect causal relationships are clearly traced between all processes without exception, which are believed to lead to the development of vitiligo. Moreover, all of them are components of a complex biochemical reactions and cellular interactions that cannot be considered in isolation from each other [1]. The lack of a unified theory of the etiology of this disease and the existence of a complex multifactorial genetic predisposition to vitiligo causes the absence of radical means for its treatment. The treatment of vitiligo is quite complicated, but nevertheless, there are currently many methods that often achieve acceptable results [2].

To treat or not to treat vitiligo? The first, in our opinion, what a doctor should do when a patient is diagnosed with vitiligo (if the patient already knows his diagnosis) or for the first time making this diagnosis, is to assess the patient's psychological attitude to the disease (quality of life), which is directly related to the degree of motivation patient for treatment. Since vitiligo does not lead to any physical suffering and does not shorten life, we believe that the question of the need for its treatment should be decided by the patient himself after the doctor

provides him with all the information about the disease and the available methods of therapy (on the one hand, the doctor should not say the patient that vitiligo is not being treated, on the other hand, there is no need to “scare” the patient and force him to be treated). In our practice, there are many patients who just need to confirm the diagnosis. Such patients include young people of military age in connection with obtaining an exemption from military service, persons undergoing routine medical examinations, patients with vitiligo in order to confirm the diagnosis and make sure that this disease is not dangerous.

This also applies to children, if the parents are not set up for the medical treatment of the child, and the child is not particularly worried about this, then from the point of view of adaptation in society, there is no need to force him to be treated. Such patients should simply be reassured, advised to use sunscreen when exposed to the sun and, if necessary and desired, apply camouflage cosmetics. If the patient has a motivation for treatment (usually this is due to a severe deterioration in the patient's quality of life in one area or another), the patient must be informed about the possibility of successful treatment, but be warned that the treatment will be long and gradual. Before prescribing a treatment course to a patient, the doctor must ask the patient about the characteristics of the region in which he lives, about accompanying (especially autoimmune) diseases, and, if necessary, conduct laboratory tests and consult the patient with relevant specialists. There are no generally accepted, mandatory methods for examining a patient with vitiligo. Nevertheless, with generalized forms of vitiligo, it is advisable to consult an endocrinologist for the condition of the thyroid gland (as a rule, this consultation is accompanied by an ultrasound of the thyroid gland and a hormonal blood test). It should be explained to the patient that this disease can “support” or “provoke” vitiligo, as it has a similar pathogenesis, as well as other concomitant autoimmune diseases. In case of disruption of the digestive tract or when the patient lives in a rural area, especially in the Central Asian region, it is advisable to conduct a study of feces (coprogram) for worm eggs, toxocara, roundworms, which may possibly (although not so often) provoke vitiligo.

Finally, it is imperative to warn the patient that the treatment is long, gradual and begins with the least aggressive (safe) and economical means. The “treatment step” (that is, the time elapsed from the start of a specific therapeutic treatment regimen to the conditionally first control, when it is possible to give a preliminary assessment of the success or failure of the prescribed course) is usually 3 months. Each step should be applied for a sufficiently long period of

time, as repigmentation is usually very slow, and in the case of an effective skin response to therapy, the treatment regimen should be continued until maximum repigmentation of vitiligo lesions is achieved, which can take up to 1–2 years. At the beginning of vitiligo treatment, all patients undergo a course of immunocorrective therapy using Neovir or ozone therapy. The appointment of neovir is especially necessary in the progressive stage of the disease. Neovir (sodium 10-methylene-carboxylate-9-acridone) belongs to the group of low molecular weight synthetic immunomodulators - interferon inducers. The drug is prescribed 2 ml of a 12.5% solution intramuscularly every 48 hours, for a course of 10 injections. In the future, with a stable course of the disease, prophylactic courses of neovir treatment are carried out once a year according to the same scheme [3]. Oxygen-ozone therapy (ozone therapy) is a physiotherapeutic method of using an oxygen-ozone gas mixture with a concentration of gaseous ozone (O<sub>3</sub>) of 1–50 mg O<sub>3</sub> per 1 liter of medical oxygen O<sub>2</sub>. The amount of injected solution is 400 ml, the rate of administration is 60–80 drops per 1 min, the duration of the procedure is 30–60 min. The procedure is performed 3 times a week, 5–9 procedures per course of treatment [4]. At the same time, patients are prescribed:

- folic acid 1 mg 1 time per day for 3 months;
- vitamin B6 (pyridoxine) 10 mg 3 times a day for 3 months;
- essential phospholipids 2 capsules 2 times a day with meals for 1 month.

In spring and summer, when solar activity is increased, all patients are prescribed antioxidants:

- dehydroquercetin, 1 tablet per day, for 3-5 months; or
- cardiomagnyl (acetylsalicylic acid) 75 mg once daily for 3 to 5 months.

Lines of therapy for vitiligo Topical calcineurin inhibitors (eg, protopic 0.1% ointment 0.1% 2 times a day for 3 months) are prescribed as the first line of therapy for patients with vitiligo. With a pronounced clinical effect, treatment is continued until complete (or the maximum achievable) repigmentation of depigmentation foci [5]. Instead of calcineurin inhibitors, it is possible to use topical corticosteroids of average activity, for example, betamethasone ointment (celestoderm, etc.) 2 times a day, for 3 months. With a pronounced clinical effect, treatment is continued until complete (or the maximum achievable) repigmentation of depigmented center. It is also possible to use topical preparations containing corticosteroids and vitamin D analogs, such as Daivobet ointment, in the same way. Given the local side effects of corticosteroids, especially when used on the face, we often recommend starting vitiligo therapy with calcineurin inhibitors.

In the absence of the effectiveness of 1st line therapy, used for 3 months as 2nd line therapy, we recommend narrow-band phototherapy. NB-UVB phototherapy, especially in combination with 1st line drugs, allows to obtain the greatest clinical effect [6]. To achieve a pronounced clinical effect, 100 to 200 phototherapy sessions may be required. Phototherapy has a number of contraindications (for example, if a patient has cancer).

If the disease is limited, topical NB-UVB phototherapy using special lamps for home use is possible, which is very convenient for patients and does not require regular visits to the medical facility. In the absence of any effect within 3 months of using the 2nd line of therapy, it is advisable to proceed to the next stage of treatment. As a 3rd line therapy, we recommend psoralen ultraviolet A (PUVA) therapy. In some patients, PUVA therapy is more effective than NB-UVB phototherapy, especially in combination with topical calcineurin inhibitors or corticosteroids (1st line drugs). This type of treatment, like NB-UVB phototherapy, is long-term (100–200 sessions) and has the same contraindications and inconvenience for patients [7].

To the 4th line of therapy, we include phototherapy using an excimer laser (EL) with a wavelength of 308 nm. This type of therapy can also be used as a 3rd line therapy for limited vitiligo. EL phototherapy can be performed as monotherapy or in combination with first-line topical drugs (corticosteroids, calcineurin inhibitors). On average, successful restoration of pigmentation requires from 45 to 100 procedures, received at a frequency of 3 times a week [8]. The 5th line therapy is not universal and is applicable for a limited area of depigmented center in patients with a stable course of vitiligo for 1 year or more. In this case, it is possible to use intradermal administration of corticosteroids or to introduce platelet-rich autoplasm into depigmented skin by intradermal injection every 2 weeks, up to 12 procedures in total or until the condition improves [9]. In addition to the above therapeutic regimens, if necessary, patients with vitiligo undergo pharmacological psychovegetative correction with neuroleptics, antidepressants, tranquilizers (sonapax, neuleptil, azafen, relanium, dopegit, tovopass, glycine preparations). Thus, the described strategy for the management of vitiligo makes it possible to effectively treat this disease in motivated patients, while at the same time avoiding frequent early termination of treatment courses in the absence of motivation or because of unjustified expectations of the rapid appearance of therapy results. The described algorithm for the treatment of vitiligo used in our practice allows 70–80% of patients to

achieve pronounced repigmentation of vitiligo and ensure long-term, and often life-long, remission of this disease.

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