ISSN 2617-409X *Actual problems of modern medicine. Issue 12, 2023*

REVIEW

DOI: https://doi.org/10.26565/2617-409X-2023-12-06
УДК 616.594.12-03-07-08

I. Serbina [A, B, C, D, F], ***K. Khobzei*** [B, C], ***T. Liadova*** [E, F], ***O. Litus*** [E], ***S. Vozianova*** [E], ***Y. Andrashko*** [E], ***S. Galnykina*** [E], ***T. Sviatenko*** [E], ***I. Svistunov*** [E], ***O. Syzon*** [E], ***I. Kadyhrob*** [B, C], ***Y. Ovcharenko*** [A, B, C, D, F]
serbinaim@gmail.com

CLINICAL GUIDELINES OF UKRAINIAN HAIR RESEARCH SOCIETY. DIAGNOSIS AND TREATMENT OF ALOPECIA AREATA

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

ABSTRACT. Alopecia areata is an immune-mediated disease resulting from the interaction of genetic factors and exogenous triggers, leading to the activation of the Janus Kinases - Signal Transducer and Activator of Transcription signaling pathway, the formation of non-specific autoimmune inflammation and disruption of immune tolerance of hair follicles. Alopecia areata has an unpredictable course with a non-scarring type of hair loss, it can affect the hair part of the head and/or hair in other areas, it can be manifested by damage to the nail plates. The psychotraumatic impact of this disease can be compared to the consequences of life-threatening or disabling diseases. For this reason, the degree of negative impact of alopecia areata on the quality of life may not correlate with the objective condition of patients, which is often not taken into account in the diagnosis and treatment of the disease. Despite the variety of treatment options available, achieving effective and safe disease control is not always straightforward. Treating patients with alopecia areata and comorbid conditions can be particularly challenging and may require close collaboration between specialists from various fields. For these and other reasons, there is significant dissatisfaction among patients regarding alopecia areata and its treatment. The systematic organization, unification, and adaptation of modern knowledge about alopecia areata have led to the creation of two algorithms: a diagnostic algorithm and a therapeutic algorithm. These algorithms provide a differentiated approach to patient management, with age, disease severity, clinical form, disease activity stage, comorbid pathology, prognostic factors, and patient quality of life taken into account. Agents with immunosuppressive action belong to the main group of drugs in the treatment of alopecia areata, according to the antigenic concept of the pathogenesis of the disease. Ongoing work is being done to update treatment protocols to include JAK inhibitors and other preparations, taking into based on new developments and the expanding pharmaceutical market.

Keywords: *alopecia areata, autoimmunity, quality of life, guidelines, algorithm, diagnosis, treatment*

Для цитування: I. Serbina, K. Khobzei, T. Liadova, O. Litus, S. Vozianova, Andrashko Y., Galnykina S., Sviatenko T., Svistunov I., Syzon O., Kadyhrob I., Ovcharenko Y.. CLINICAL GUIDELINES OF UKRAINIAN HAIR RESEARCH SOCIETY. DIAGNOSIS AND TREATMENT OF ALOPECIA AREATA. Actual problems of modern medicine. 2023;12:47-68. DOI: https://doi.org/10.26565/2617-409X-2023-12-06

INFORMATION ABOUT AUTHORS

Inessa Serbina, MD, PhD, Professor at the department of infectious diseases and clinical immunology, medical faculty of V. N. Karazin Kharkiv National University, 6 Svobody sq., Kharkiv, Ukraine, 06122, e-mail: serbinaim@gmail.com. ORCID ID: https://orcid.org/0000-0001-7870-206X.

Kuzma Khobzei, graduate student of the department of infectious diseases and clinical immunology, medical faculty of V. N. Karazin Kharkiv National University, dermatovenerologist, trichologist, chief physician of Khobzei Clinic, Kyiv, Ukraine. e-mail: khobzey@gmail.com. ORCID ID https://orcid.org/0009-0002-2879-9240.

Tetyana Liadova, MD, PhD, Professor of the department of infectious diseases and clinical immunology, Dean of the medical faculty, V. N. Karazina Kharkiv National University, Svobody Square, 6, Kharkiv, Ukraine, 61022, e-mail: t.lyadova@karazin.ua, ORCID ID https://orcid.org/0000-0002-5892-2599.

Oleksandr Litus, MD, PhD, Professor, Head of the department of dermatovenerology, allergology, clinical and laboratory immunology of the Shupyk National Healthcare University of Ukraine, Kyiv. e-mail: aleksandr.litus@gmail.com. ORCID ID https://orcid.org/ 0000-0002-3708-2666.

Svitlana Vozianova, MD, PhD, Professor, Professor of the department of

dermatovenerology, allergology, clinical and laboratory immunology of the Shupyk National Healthcare University of Ukraine, Kyiv. e-mail: s.vozianova@gmail.com ORCID ID https://orcid.org/0000-0002-6445-3442.

Yuriy Andrashko, MD, PhD, Professor, Head of the department Skin and Venereal Diseases of the Uzhhorod National University. e-mail: andrashkoy@gmail.com. ORCID ID https://orcid.org/0000-0001-8608-6754.

Svitlana Galnykina, MD, PhD, Professor, Professor of the department of infectious diseases with epidemiology, skin and venereal diseases of the I. Gorbachevsky Ternopil National Medical University. e-mail: dr.lana08@yahoo.com. ORCID ID https://orcid.org/0000-0003-2062-5529.

Tetiana Sviatenko, MD, PhD, Professor, Head of the department of Skin and Venereal Diseases of the Dnipro State Medical University. e-mail: tatsvyatenko@gmail.com. ORCID ID https://orcid.org/0000-0003-4303-2937.

Igor Svistunov, MD, PhD, Professor, Professor of the department of dermatovenerology, allergology, clinical and laboratory immunology of the Shupyk National Healthcare University of Ukraine, Kyiv. e-mail: svistunov.iv@gmail.com. ORCID ID https://orcid.org/0000-0002-3916-354X.

Orysya Syzon, MD, PhD, Professor, Head of the department of dermatology, venereology of the Danylo Halytskyi Lviv National Medical University. e-mail: syzon-orysya@ukr.net. ORCID ID https://orcid.org/0000-0002-7011-2521.

Iryna Kadyhrob, PhD, associate professor of the department of infectious diseases and Clinical Immunology, V. N. Karazin Kharkiv National University, 6 Svobody sq., Kharkiv, Ukraine, 06122, e-mail: kadygrob13@gmail.com. ORCID ID https://orcid.org/0000-0002-2551-0256

Yuliya Ovcharenko, MD, PhD, Professor at the department of infectious diseases and clinical immunology, V. N. Karazin Kharkiv National University, 6 Svobody sq., Kharkiv, Ukraine, 06122, e-mail: ukrhrs@gmail.com. ORCID ID: https://orcid.org/0000-0002-2412-2251..

Introduction

Alopecia areata (AA) is a chronic recurrent autoimmune inflammatory disease mediated by T-lymphocytes in conditions of impaired immune tolerance of hair follicles and activation of the Janus Kinases - Signal Transducer and Activator of Transcription (JAK-STAT) signaling pathway. The manifestation and clinical diversity of AA are influenced by a complex combination of triggers and genetic factors. The disease has an unpredictable course with a non-scarring pattern of hair loss, which can affect the scalp and/or other areas of the body, including nail involvement. It is characterized by various psychosocial disturbances, social maladjustment, and a significant reduction in the quality of life of patients [6, 56].

Epidemiological characteristics, genetic factors, and the immunopathogenesis

According to epidemiological studies conducted in various countries, approximately 1.7% of the population suffers from AA, with prevalence ranging from 0.1 % to 0.2 % worldwide. AA can start at any age, but it typically presents before the age of 40. Most commonly, patients between the ages of 10 and 25 are affected (60 %). Recent research indicates that 1-2% of individuals with AA are younger than 2 years old, and 21-24 % are under the age of 16. AA is rare in adults over the age of 60 [60, 66].

Most patients experience more than one episode of the disease. Recurrence can occur as small, localized patches of hair loss or large areas of hair loss with complete hair loss. Severe forms of AA, such as total alopecia (TA) and universal alopecia (UA), can manifest even during the first episode of the disease. Approximately 5-10% of patients with patchy alopecia develop complete scalp hair loss (TA), and in 1-2% of cases, there is complete loss of hair on the scalp and body (UA) [33].

For localized AA, the rate of spontaneous remission is 30-50 % within the first 6-12 months of the disease, with complete disappearance observed in 66 % of patients within 5 years. For TA, the rate of spontaneous remission is less than 10%. Over 20 years, 100% of patients with AA experience disease recurrence [38, 56, 73, 76]. The lifetime risk of developing AA in relatives with the condition is 7.1% for siblings, 7.8 % for parents, and 5.7% for offspring [14].

AA is a disease involving complex interactions between different genes. External environmental factors, including the influence of pro-inflammatory substances, and possibly other modulators, such as neurogenic, metabolic, endocrine disorders, allergic conditions, and infectious agents, play a significant role in the manifestation of genetic susceptibility to AA. During the COVID-19 pandemic, an increasing number of patients reported recurrences or new manifestations of AA after infection or vaccination [7].

The disease is characterized by polygenic inheritance. Complex interactions between the environment and genes determine the onset and manifestations of the disease for each individual (type of hair loss and disease severity) [9]. Polymorphisms of genes such as IL2RA and TNF/LTA [65], SPATA5 on chromosome 4 [32], and certain SNPs, STX17, Cxcr3, Cxcl9, Cxcl10, CTLA4, PRDX5, and IKZF4/ERBB3,

as well as TNF-α-308G/A [13,52,53], have been associated with AA. Polymorphisms of the IL-17A and IL-17RA genes (IL-17A receptor) have also been identified [49]. These results indicate that the pathological presentation of antigens and the regulation of autoimmunity may play an important role in the initiation of AA.

Recently, multiple genetic polymorphisms, such as short tandem repeat (STR) polymorphisms and copy number variants (CNVs), have been investigated and are implicated in the pathogenesis of AA. Additional loci with genes related to the apoptosis activation pathway, regulatory T-cells (Treg), and JAK-STAT signaling, some of which are involved in the development of other autoimmune diseases, have been identified [55, 61].

Cytokines are considered a mediator in the formation of the pathophysiological stage of autoimmune reactions in AA, disrupting the mechanisms that maintain immune tolerance in hair follicles [16, 36]. New evidence suggests the significance of the JAK-STAT signaling pathway in the development of AA. CD8+ T cells + NKG2D produce IFN-γ, which binds to its receptor on the surface of hair follicles in AA and activates the JAK1/2 - STAT1 pathway. This, in turn, leads to the production of IL-15, which, by binding to its receptor on the surface of T cells, activates JAK1/3 - STAT5 and induces the production of IFN-γ, maintaining immune inflammation. Biopsy analysis of the skin of AA patients has revealed the overexpression of JAK3, although to a lesser extent than JAK1 and JAK2 [58, 63, 78].

Stress, neuroinflammation and adaptive regulatory mechanisms

The persistent nature of immune disorders, the connection between the development and recurrence of the dermatosis with psychotraumatic factors, indirectly indicates the inadequacy of the adaptive potential of patients [51]. The skin and hair follicles have a local neuroendocrine axis similar to the hypothalamo-pituitary-adrenal system. During periods of stress, the axis is activated to release corticotropin-releasing hormone, substance P, nerve growth factor, leading to degranulation of mast cells, accelerating the catagenic regression of hair follicles, and possibly promoting neurogenic inflammation, which results in the loss of immune privilege in hair follicles [12, 43, 77].

The controversial issue is whether stressful events in life can contribute to the development of AA. There have been documented cases where psychosocial stress clearly preceded the onset or recurrence of AA. However, it is challenging to objectively distinguish stress as a real trigger of the disease from distress caused by the disease, which can retrospectively and mistakenly be identified as the cause of hair loss in AA. It can be assumed that even if stressors play a minimal role in the onset of AA, anxiety and depression directly caused by different forms of AA may negatively affect the course of the disease through stress mediators. For such patients, particularly those with pathological adaptation disorders, an avoidant behavior is typical. AA often leads to the development of anxiety and depressive reactions, as well as social phobias related to low self-esteem. Thus, one can speak of the existence of a vicious circle: stress - AA - the patient's psychosocial status - AA - stress [12, 15].

Diagnosis

A unified diagnostic algorithm should be used for diagnosing AA to determine the clinical form, disease severity, stage of activity, comorbid pathology, quality of life index, and prognostic factors for a severe course, which are important criteria for prescribing differentiated therapy (Table 1.).

The unified examination protocol for patients with AA enables more effective disease monitoring, and the outpatient card, developed in accordance with international recommendations, contains data with epidemiological and prognostic significance, as well as key stages in disease progression. This approach to AA patients improves patient management and medical care and serves as the foundation for the All-Ukrainian register of AA patients [1].

ISSN 2617-409X Актуальні проблеми сучасної медицини. Випуск 12, 2023

Table 1. Diagnostic algorithm for alopecia areata

History, evaluation of trigger factors, clinical examination

Differential diagnosis

Special diagnostic methods:

- pull test
- trichoscopy

Additional research methods:

- fungal testing (scraping, plating, Wood's lamp)
- antinuclear antibodies, antibodies to native DNA
- syphilis serology screening
- skin biopsy

Diagnosis of alopecia areata, determination of the clinical form, stage and affected area

Clinical form

- local scalp
- local beard
- supra- and ciliary
- ribbon-like (ophiasis, sisaipho)
- subtotal (multifocal)
- totalis
- universalis
- diffuse
- incognita
- canites subita
- with nail involvement

Stage (trichoscopy, pull test)

- **Active** (black dots, broken hairs, exclamation marks, tapered hairs, Pohl Pinkus constrictions (moniletrix-like hairs), coudability hairs); positive pull test
- **Chronic** (no signs of activity, yellow dots, vellus); negative pull test
- **Hair regrowth stage** (regrowing hair, twisted hair, poliosis); negative pull test

Affected area (SBN)

Affected area of the scalp (S) and other parts of the body (B), the degree of nail plate (NP) changes (N):

- S0 – without hair loss
- S1 – <25 % hair loss
- S2 – from 25% to 49% hair loss
- S3 – from 25% to 74% hair loss
- S4 – from 75% to 99% hair loss
- S5 – 100% hair loss
- B0 – no body hair loss
- B1 – some body hair loss
- B2 – 100% body hair loss
- N0 – no nail involvement
- N1 – some nail involvement
- N1a – 20-nail dystrophy

Definition of severity

Mild:	Moderate:	Severe:
$S_1B_0N_0$; $S_0B_1N_0$	$S_1B_{0\text{-}1}N_{0\text{-}1a}$; $S_2B_0N_0$	$S_2B_{1\text{-}2}N_0$ - $S_2B_0N_{1\text{-}1a}$ - $S_2B_{1\text{-}2}N_{1\text{-}1a}$; $S_3B_{0\text{-}2}N_{0\text{-}1a}$ - $S_5B_{0\text{-}2}N_{0\text{-}1a}$
▪ local (scalp) ▪ local (beard) ▪ supra- and ciliary	▪ local (scalp) (+ NP damage and/or envelopment other parts of the body) ▪ multifocal ▪ ribbon-like (ophiasis, sisaipho) ▪ diffuse ▪ incognita ▪ canites subita	▪ ribbon-like (ophiasis, sisaipho) ▪ diffuse ▪ incognita ▪ canites subita ▪ multifocal ▪ totalis ▪ universalis (±NP damage and/or involvement of other parts of the body)

Assessment of comorbid pathology

Laboratory and instrumental research methods

As per indications (presence of complaints, clinical manifestations) and before treatment:

- Clinical and biochemical blood test;
- Serological diagnosis of celiac disease, autoimmune diseases (IgA and IgG to tissue transglutaminase, to deaminated peptides (gliadin));
- Acute phase proteins, antinuclear antibodies, antibodies to native DNA and etc.
- Deficiencies (iron, ferritin, serum total iron binding capacity, 25 (OH) D, selenium, zinc, etc.);
- Cortisol; TSH, free T3 and T4, antibodies to structures of the thyroid; prolactin;
- Fluoroqraphy;
- Interdisciplinary consultations.

Determining patients' quality of life on DLQI scale (0-30 points)

Identifying of risk factors for severe disease course

- Early disease onset;
- AT, AU or ribbon-like hair loss;
- Nail involvement;
- Hair loss on the body associated with localized forms on the scalp;
- Disease duration more than 5 years (the absence of yellow dots on trichoscopy);
- Presence of atopy;
- Presence of other autoimmune diseases;
- Positive family history.

Development of a treatment plan

Therapy monitoring

Clinical Forms and Stages of the Pathological Process

Clinical examination reveals alopecia foci, presented as completely hairless areas on hair bearing skin (scalp, eyebrows, eyelashes, body) with marked boundaries, smooth surface, without signs of scaling, infiltration, and atrophy. Depending on the area and extent of involvement, the following clinical forms of AA are distinguished: localized scalp and beard, supra- and ciliary, ribbon-like (ophiasis and sisaipho), subtotal, TA, UA, diffuse, incognita, canites subita.

Clinical forms can transform from one to another, especially in cases of severe disease. In some cases, there may be spontaneous hair regrowth, while in others, there are severe, therapy-resistant forms or cases where hair regrowth occurs only with continuous treatment, and hair falls out again within a few days after treatment is stopped. Nail involvement in AA is not a constant feature. The frequency of nail involvement accompanying AA ranges from 7 % to 66 % [9]. Nail damage can occur before, during, or after hair loss.

In clinical presentation of AA, successive stages are distinguished: active, chronic and hair regrowth. It is noted that the disease duration often does not correlate with the activity of the pathological process [34].

Special Diagnostic Methods

Special diagnostic methods (hair pull test, trichoscopy, and, if necessary, biopsy) are auxiliary for differential diagnosis and are key to determining the stage of the pathological process.

Trichoscopy reflects the pathophysiological process of AA, with markers being almost the same for all clinical subtypes, while the main differences are determined by disease activity. Observing the dynamics of the process in the affected areas is the basis for the differential diagnosis of AA, providing additional evidence for prognosis and treatment efficiency [68].

In the active stage of AA, trichoscopy shows features such as black dots, broken hair, exclamation mark hairs, coudability hair, and monilethrix-like hair, which reflect the dystrophic process. The absence of the above-mentioned signs of dystrophic activity is the main criterion for the chronic stage. However, yellow dots and vellus hairs are variables – not specific, but characteristic signs of this stage**.** According to Rudnicka et al, the number of yellow dots is proportional to patient's age and usually is uncommon in prepubertal children and elderly patients [68]. They may be absent in patients with a duration of AT and AU for more than 5 years, which is an unfavorable prognostic factor for treatment response. Vellus hair is also considered a marker of disease severity. Their presence in the chronic stage indicates the inability of the hair follicle to produce terminal hair.

Trichoscopy also reveals signs of hair regrowth, such as vertically grown and coiled hairs ("pigtail" hair), which may be observed in the presence of long-standing active disease. "Pigtail" hairs, coiled into oval or round shapes with pointed ends, indicate the regeneration of terminal hair from partially damaged hair follicles [68]. The regrowth of unpigmented vellus hairs in areas of alopecia regression is a well-known feature. It should be noted that AA usually does not affect white or gray hair. After regrowth, initially, unpigmented hair shafts appear, and their repigmentation occurs later in the presence of clinical and trichoscopic signs of poliosis [1].

The trichoscopic pattern of diffuse forms of AA reflects the peculiarities of the pathophysiological processes of these patterns and demonstrates differences from the characteristics of the classic forms of the disease described above. AA incognita (AAI) due to diffuse thinning, more noticeable in the androgen-dependent area, may clinically resemble not only telogen effluvium but also androgenetic alopecia (AGA). According to the study by Tosti et al, AGA was identified in 95.23% of cases of AAI [72]. These data may be associated with Rebora's hypothesis, which confirms that the concealed form is more common in patients with AGA since they have a high proportion of hair follicles in the telogen phase and a small number of hair follicles in the anagen phase with high mitotic activity [64].

The role of trichoscopy in AAI was first described by Tosti et al, who documented the presence of diffuse yellow dots in 95% of patients [72]. Another trichoscopic feature of AAI is short regrowing hair. In a small number of patients, hair in the shape of an exclamation mark, black dots, and dystrophic hair were found, confirming that this form is a variant of AA. According to Inui et al [42], the trichoscopic combination of yellow dots and/or short regrowing hair is characterized by a diagnostic sensitivity for the concealed form of AA at the level of 96 %.

Among the characteristic trichoscopic features of the diffuse form of AA are black dots and diffuse yellow dots. In this case, black dots result from acute damage to the hair follicles not grouped in clusters but spread over the entire scalp surface [72].

Biopsy - the histological picture depends on the stage of the disease. Peribulbar lymphocytic infiltration in the form of a "swarm of bees" characterizes the acute period of the disease. A significant proportion of hairs are in the catagen and telogen phases (up to 50%). During the chronic phase of the process, hair follicles undergo miniaturization with minimal or absent inflammation [9].

Severity Assessment

The Severity of Alopecia Tool (SALT), a mathematically based tool to assess the severity of scalp baldness, was developed by Olsen and Canfield. In terms of alopecia, the SALT score ranges from 0% to 100%. (complete hair loss). SALT ALT 0-30% denotes a mild case of AA, SALT 31-50% a moderate case, and SALT > 51% a severe case. An international consensus of hair research experts has developed a special standardized SBN system that allows objectifying the assessment of hair loss - S (Scalp), body - B (Body), nail plate damage - N (Nail), and controlling the treatment effectiveness [57]. The SBN scale was used to determine the severity of AA, considering hair loss on the scalp, other parts of the body, and nail plate involvement [1]:

- ***Mild:*** $S_1B_0N_0$, SoB_1N_0, which corresponds to AA clinical forms: local of scalp, beard, ciliary and supraciliary;

Moderate: $S_1B_{0\text{-}1}N_{0\text{-}1a}$, which corresponds to AA clinical forms: - local of scalp, beard or ciliary and supraciliary (+ damage to the nail plates and/or other parts of the body); $S_2B_0N_0$, which corresponds to AA clinical forms: ribbon-like forms (ophiasis, sisaipho), subtotal (multifocal), diffuse, incognita, canites subita;

Severe: $S_2B_{1\text{-}2}\ N_0$ - $S_2B_0N_{1\text{-}1a}$ – $S_2B_{1\text{-}2}N_{1\text{-}1a}$, which corresponds to AA clinical forms: ribbon-like forms (ophiasis, sisaipho), subtotal (multifocal), diffuse, incognita, canites subita (± damage to the nail plates, other parts of the body); $S_3B_{0\text{-}2}N_{0\text{-}1a}$ – $S_5B_{0\text{-}2}N_{1\text{-}1a}$, which corresponds to AA clinical forms: subtotal (multifocal), total, universal (± damage to the nail plates, other parts of the body).

In order to assess the severity of AA, in addition to the area of the scalp lesion and the involvement of other parts of the body and nails, the duration of the pathological process, torpidity to therapy, and quality of life are important. Thus, the ciliary and supraciliary forms, according to the area of the lesion, represent to mild severity, but a significant decrease in the quality of life of the patient with this localization of the disease, as well as the lack of response only to local therapy, is the rationale for assessing them as moderate, and in some cases, severe degree of AA and requires the appointment of appropriate systemic therapy.

Thus, the ciliary and supraciliary forms, according to the area of the lesion, represent to mild severity, but a significant decrease in the quality of life of the patient with this localization of the disease, as well as the lack of response only to local therapy, is the rationale for assessing them as moderate, and in some cases, severe degree of AA and requires the appointment of appropriate systemic therapy.

Differential diagnosis

The clinical heterogeneity of AA poses difficulties in diagnosing this condition. Trichotillomania, trichomycosis, lupus erythematosus, and, in pediatric patients, congenital triangular alopecia and aplasia cutis are all differential diagnoses for local and multifocal AA. The reticular form must be distinguished from secondary syphilis; the ribbon-like AA from frontal fibrosing alopecia; and diffuse forms of AA from

anagen effluvium of various origins and androgenetic alopecia. In pediatric cases, AT and AU may be distinguished from congenital hypotrichosis, universal atrichia, hereditary vitamin D-resistant rickets, and syndromal alopecia [1, 25, 68, 70].

Comorbid pathology

Evaluating comorbid conditions is a significant step in the diagnosis and can provide important etiological information, indicating a cause-and-effect relationship between different diagnoses in AA, which may necessitate therapy adjustments, offer insights into the clinical prognosis, and potential additional triggers.

Possible associations of AA with autoimmune diseases such as thyroid disorders exist, but the presence of thyroid antibodies in the blood doesn't necessarily correlate with the severity of AA; vitiligo; psoriasis; rheumatoid arthritis, discoid lupus erythematosus, atopy, although atopic constitution is considered a prognostic sign of an earlier onset with a tendency to develop severe forms of the disease; ophthalmological disorders (corneal opacity, fundus changes); Down syndrome; Addison's disease; autosomal recessive autoimmune polyglandular syndrome; chronic hypoparathyroidism; autoimmune adrenal insufficiency; celiac disease; ulcerative colitis, metabolic disorders, and others [1. 37, 62].

A high frequency of psychiatric/psychological comorbid pathology, such as anxiety disorders, depression, and sleep disturbances, has been observed among AA patients. The "distortion effect" of the dermatosis is considered a factor that triggers a spectrum of "secondary" psychological disorders [15, 57].

The first systematic examination of comorbid conditions in AA was conducted by Ikeda T. (1965), who classified the types of diseases into prehypertensive, atopic, autoimmune, and mixed categories [41].

Laboratory and instrumental methods of examination

Dermatological symptoms play a dominant and indicative role in diagnosing AA. However, determining the status of organs and systems whose disturbances most often correlate with AA is also essential. There are no screening laboratory tests for AA. Laboratory and instrumental methods are used as needed (based on complaints and clinical manifestations) and help identify comorbid pathology [21, 22, 40] (Table 1).

Assessing the impact of alopecia areata on quality of life

Under conditions of relatively minor changes in physical health, AA significantly impairs the emotional and social aspects of quality of life, often leading to depression, dysmorphophobia, and, in some cases, suicide attempts.

To assess psychosocial disorders in patients, the Hospital Anxiety and Depression Scale (HADS) is used, the scoring of which allows to identify the degree of disorders and provide timely correction. A score of 8-10 points indicates subclinical depression, while 11 points or higher correspond to clinically pronounced anxiety and depression [79].

The extent of AA's negative impact on quality of life is not always directly related to the objective condition of patients, which is often not considered during the diagnosis and treatment of the disease. Furthermore, there is a discrepancy between the perception of AA by the patient and the physician. As a result, standard indicators used to assess the severity, such as the percentage of hair loss, inadequately describe the level of psychological stress in AA patients.

The Dermatology Quality of Life Index (DLQI) is the most widely used tool for assessing the quality of life in AA patients due to its high objectivity and reliability [27,31]. A score of 0-1 is interpreted as no impact of the skin condition on the patient's quality of life; 2-5 points indicate a slight impact; 6-10 points indicate a moderate impact; 11-20 points indicate a significant impact; and 21-30 points indicate a very significant impact on the quality of life [67].

Determining prognostic criteria for a severe course

Predicting the course and response to therapy in AA is very challenging, so determining criteria for a severe disease is important. Prognostic criteria for a severe course of AA include early age of onset (before puberty); TA, UA, or linear forms; nail involvement; body hair loss in localized forms on the scalp; disease duration of more than 5 years; the presence of atopy; a positive family history; and the presence of other autoimmune diseases [1, 18].

Principles therapy

When selecting treatment for AA, criteria such as age, severity, disease activity stage, and quality of life indicators should be considered. It is important to balance the risk of side effects of medications with the expected therapeutic effect (Table 2).

In AA treatment, it is important to consider the following: the disease does not pose a direct threat to the patient's overall health; in localized forms, spontaneous hair regrowth can occur within a year after the onset of the disease even without treatment; the impact of the disease on the physical and emotional state of the child and adult, including aspects such as self-confidence and social relationships; the evaluation of the patient's quality of life; and the system of measures to overcome anxiety, disappointment, feelings of helplessness, and guilt in parents, which should be part of a comprehensive approach to the treatment of children with AA; comorbid pathology in AA.

Extremely important in assessing the effectiveness of AA treatment with different methods (results determined after 6 months of therapy) is to focus on the dynamics of the Quality of Life Index.

Leaving AA untreated (a "wait-and-see" approach) is an acceptable option and probably the most appropriate in certain cases of AA due to the following facts: spontaneous remission occurs in 80% of patients with limited focal hair loss within a short period (<1 year); patients with severe forms of AA may undergo various types of therapy for an extended period without any improvement; the prognosis for a protracted course of severe AA is unfavorable, and in such patients, the best option may be the use of wigs (prostheses) rather than continuing therapy, which is unlikely to be effective.

Methods of treatment

In the modern arsenal of AA therapy, both strong acting pathogenetic pharmacological agents and various adjuvants are included. According to the antigenic concept of AA pathogenesis, glucocorticoids (GCS) and other immunosuppressive drugs belong to the main group of drugs for pathogenetic therapy [13, 57].

Topical therapy

Topical glucocorticoids (Class B, Level of Evidence 2+)

Topical glucocorticoids (TGCS), due to their simplicity and convenience of use, are considered "first-line" therapy for both adults and children with mild to moderate AA, either as monotherapy or in combination with other forms of treatment. In adults with severe AA, TGCS are considered as adjunctive to systemic treatments [8]. The most commonly used is 0.05% clobetasol propionate, a super-potent steroid, available in the form of ointment, lotion, foam, or shampoo. Betamethasone dipropionate 0.05% in the form of cream was found to be an effective treatment for AA patients [24].

In the developed algorithm, different TGCS are prescribed depending on the patient's age. For children up to 6 years old, strong-acting steroids are used, such as hydrocortisone 17-butyrate and mometasone furoate. For ages 7-12, mometasone furoate and betamethasone dipropionate (Class III and IV, very strong) are prescribed, while for ages 13-18, betamethasone valerate, betamethasone dipropionate, and clobetasol propionate (Class III and IV, very strong) are preferred. In adults, highly active TGCS (clobetasol propionate) are favored. A switch to less active TGCS may be considered to avoid skin atrophy.

Table 2. Therapeutic algorithm for alopecia areata

Group of patients aged 0-6 years.	
Mild, moderate, and severe	
Active stage	Chronic stage
TGCS	TGCS
From 6 months: hydrocortisone 17-butyrate 0.1% From 2 years: mometasone furoate 0.1%.	From 6 months: hydrocortisone 17-butyrate 0.1% From 2 years: mometasone furoate 0.1%. Topical minoxidil 2% once a day.
Lack of therapeutic effect for 6 months: a "wait-and-see" approach.	
Group of patients aged 7-12 years	
Mild	
Active stage	Chronic stage
TGCS	TGCS
Mometasone furoate 0.1%, betamethasone dipropionate 0.05%.	Mometasone furoate 0.1%, betamethasone dipropionate 0.05%. Topical minoxidil 2% twice a day.
Moderate	
Active stage	Chronic stage
TGCS	TGCS
Mometasone furoate 0.1%, betamethasone dipropionate 0.05%.	Mometasone furoate 0.1%, betamethasone dipropionate 0.05%. Topical minoxidil 2% twice a day.
Lack of therapeutic effect for 6 months: a "wait-and-see" approach, hair replacement system, psychological support, social adaptation	
Severe	
Active stage	Chronic stage
Systemic GCS	TGCS
Per os: prednisolone 0.4–0.6 mg/kg/day with a gradual dose reduction, 3–6 months (methylprednisolone at an equivalent dose); ± TGCS: mometasone furoate 0.1%; betamethasone dipropionate 0.05%	Mometasone furoate 0.1%, betamethasone dipropionate 0.05%. Topical minoxidil 2% twice a day.
Lack of therapeutic effect for 6 months: a "wait-and-see" approach, hair replacement system, psychological support, social adaptation	
Group of patients aged 13-18 years	
Mild	
Active stage	Chronic stage
TGCS	TGCS
Betamethasone valerate, betamethasone dipropionate 0.05%, clobetasol propionate 0.05% ± Intralesional GCS (suspension of betamethasone sodium phosphate/betamethasone dipropionate 1 ml; eyebrow area: 0.2 ml; suspension of triamcinolone acetonide 5–10 mg/ml; eyebrow area: 2.5 mg/ml)	Betamethasone valerate, betamethasone dipropionate 0.05%, clobetasol propionate 0.05% ± Intralesional GCS (suspension of betamethasone sodium phosphate/betamethasone dipropionate 1 ml; eyebrow area: 0.2 ml; suspension of triamcinolone acetonide 5–10 mg/ml; eyebrow area: 2.5 mg/ml). Topical minoxidil 5% twice a day.

Continuation of Table 2

Lack of therapeutic effect for 6 months: refer to therapy for a moderate degree	
Moderate	
Active stage	Chronic stage
Intralesional GCS*	Intralesional GCS*
(suspension of betamethasone sodium phosphate/betamethasone dipropionate 1 ml; brow area: 0.2 ml; suspension of triamcinolone acetonide 2.5–10 mg/ml; brow area: 2.5 mg/ml). ± TGCS: betamethasone valerate, betamethasone dipropionate 0.05%, clobetasol propionate 0.05%. Systemic GCS**: prednisolone 0.4–0.6 mg/kg/day per os with a gradual dose reduction, 3–6 months (methylprednisolone in equivalent dose).	(suspension of betamethasone sodium phosphate/betamethasone dipropionate 1 ml; brow area: 0.2 ml; suspension of triamcinolone acetonide 5–10 mg/ml; brow area: 2.5 mg/ml). ± TGCS: betamethasone valerate, betamethasone dipropionate 0.05%, clobetasol propionate 0.05%. Topical minoxidil 5% twice a day.
Lack of effect from the therapy for 6 months: see therapy for severe degree	
Severe	
Active stage	Chronic stage
Systemic GCS	Steroid-sparing therapy
Prednisolone at a dose of 0.4-0.6 mg/kg/day with a gradual dose reduction over 3-6 months (or methylprednisolone in an equivalent dose) is recommended. ± TGCS: betamethasone valerate, betamethasone dipropionate 0.05%, clobetasol propionate 0.05%.	Prednisolone 15 mg/day in combination with concurrent methotrexate at a dose of 10-15 mg/m2 of body surface area per week for 6-8 months is recommended. ± TGCS: betamethasone valerate, betamethasone dipropionate 0.05%, clobetasol propionate 0.05% Topical minoxidil 5% twice a day.
Lack of therapeutic effect for 6 months: a "wait-and-see" approach, hair replacement system, psychological support, social adaptation	
Adults (18 years and older)	
Mild	
Active stage	Chronic stage
TGCS	TGCS
Clobetasol propionate 0.05%. ± Intralesional GCS.	Clobetasol propionate 0.05%. ± Intralesional GCS. Topical minoxidil 5% twice a day.
DLQI > 10. lack of therapeutic effect for 6 months: see therapy for moderate severity	
Moderate	
Active stage	Chronic stage
Intralesional GCS *	Intralesional GCS *
± TGCS: clobetasol propionate 0.05%. Systemic GCS:** Per os: prednisolone 0.4–0.6 mg/kg/day with a gradual dose reduction, 3–6 months (methylprednisolone in equivalent dose); Dexamethasone 0.1 mg/kg/day on two consecutive days per week, 8–12 months; Intramuscularly: suspension of betamethasone dipropionate and betamethasone sodium phosphate 1–2 ml with a 3–4 week interval, 3–6 months; Triamcinolone acetonide suspension 40 mg/ml with a 4-week interval, 3–6 months.	± TGCS: clobetasol propionate 0.05%. Systemic GCS:** Per os: prednisolone 0.4–0.6 mg/kg/day with a gradual dose reduction, 3–6 months (methylprednisolone in equivalent dose); Dexamethasone 0.1 mg/kg/day on two consecutive days per week, 8–12 months; Intramuscularly: suspension of betamethasone dipropionate and betamethasone sodium phosphate 1–2 ml with a 3–4 week interval, 3–6 months; Triamcinolone acetonide suspension 40 mg/ml with a 4-week interval, 3–6 months. Topical minoxidil 5% twice a day

Continuation of Table2

DLQI > 10. Lack of therapeutic effect for 6 months: see therapy for severe severity	
Severe	
Active stage	Chronic stage
Systemic GCS*	Steroid-sparing therapy
Prednisolone 0.4–0.6 mg/kg/day with a gradual dose reduction, 3–6 months (methylprednisolone at an equivalent dose); Dexamethasone 0.1 mg/kg/day on two consecutive days per week, 8–12 months; Intramuscularly: Betamethasone dipropionate and betamethasone sodium phosphate suspension 1–2 ml with a 3–4 week interval, 3–6 months; Triamcinolone acetonide suspension 40 mg/ml with a 4-week interval, 3–6 months. ± TGCS Steroid-sparing therapy** Prednisolone 15–30 mg/day + cyclosporine at a dose of 3–5 mg/kg/day, 6–12 months; Prednisolone 20 mg/day + methotrexate at a dose of 15–20 mg per week, 6–8 months.	Prednisolone 15-20 mg per day + cyclosporine at a dose of 3–5 mg/kg per day, 6–12 months. Prednisolone 20 mg per day + methotrexate at a dose of 15–20 mg per week, 6–8 months. ± TGCS Topical minoxidil 5% twice a day.
Lack of therapeutic effect for 6 months: a waiting approach, hair replacement system, psychological support, and social adaptation	

Notes: * - first-line therapy; ** - second-line therapy.

TGCS are used in the form of ointment, cream, or lotion. In case the condition progresses, ointment forms are used to increase penetration depth, and a transition to cream or lotion is possible. The ointment is applied as an application to the balding area twice a day or overnight with an occlusive dressing for 6 nights, followed by a one-day break. Treatment should last for at least three months and should be discontinued if there is no response within six months. The side effects of TGCS are temporary and may manifest as itching, burning, folliculitis, telangiectasia, and skin atrophy [60].

Topical minoxidil (Class C, Level of Evidence 2-)

Minoxidil acts directly on hair follicles and stimulates the synthesis of vascular endothelial growth factor (VEGF) [35]. The main known mechanisms are realized through the dose-dependent effect of VEGF synthesis activation. In the dermal papillae of hair follicles, VEGF stimulates the proliferation of matrix cells and endothelial cells of the vascular network, forming extracellular matrix substances, thereby supporting follicles in the anagen state. The most common side effects are hypertrichosis and contact dermatitis, headache, and dizziness [23, 30, 39].

Minoxidil accelerates hair shaft pigmentation and increases hair density within the bald spot. It is not recommended to use minoxidil during the active stage of the disease, as it may lead to the spread of the disease and an increase in the area of hair loss. However, this drug should be prescribed to patients after the active phase of alopecia areata of any severity. Minoxidil treatment can last until hair regrowth is observed and continue for 2-3 months. However, therapy should be discontinued if there is no trichogenic response after 6 months. A 5 % minoxidil composition produces better results for alopecia areata than lower concentrations. Due to the dose-dependent nature of minoxidil's action, twice-daily application is more effective [23, 30]. Experience with 5% minoxidil suggests its high effectiveness in

combination with other treatments (GCS) in patients after the elimination of signs of disease activity. TGCS are recommended to be applied 30 minutes after each minoxidil application [8]. Based on the results of several studies, local application of 5% minoxidil reduces the degree of post-steroid recurrence in alopecia areata [2].

After eliminating signs of disease activity, as well as in the case of new depigmented hair appearance, patients can be recommended to use minoxidil lotion or foam externally: for children under 12 years of age, use a 2% concentration once or twice daily for 2-3 months. Adolescents and adults should be prescribed a 5% concentration twice daily. This differentiation is due to the common side effect of minoxidil in children, especially at higher concentrations, including facial and neck hypertrichosis, irritant contact dermatitis, or exacerbation of previously existing seborrheic or atopic dermatitis, and possibly a decrease in blood pressure, especially when used over a large surface area [39].

Intralesional GCS (Class B, Level of Evidence 3)

The anti-inflammatory and immunosuppressive properties of prolonged-action GCS are what determine their use in therapeutic practice for AA. The main properties include a reduction in the number of immune-active cells at the site of inflammation, stabilization of lysosomal membranes, inhibition of phagocytosis, and a decrease in the synthesis of prostaglandins and related compounds [17].

Injections of GCS into the deep dermis of affected areas are the most common method of treating AA with a lesion area of up to 50% in adults. This allows for achieving optimal concentrations in the tissues with minimal systemic absorption [8, 35]. Intradermal GCS are recommended for children aged 12 and older. This method is limited due to the fear of injections and pain. To reduce the pain sensations, smaller gauge needles (30 G or 32 G), ice, and creams with anesthetics can be used. A retrospective analysis of patient outcomes with over 50% of the scalp affected by AA, who received GCS injections, showed better responses in younger individuals and with shorter durations of AA. The results of this therapy were more favorable in patients with signs of active disease [17].

Intradermal GCS as monotherapy are characterized by insufficient efficacy in widespread forms of alopecia AA. However, they can be used as adjunctive therapy alongside systemic glucocorticoids and JAK inhibitors to expedite their action [54, 71]. In the developed algorithm, for adults and children aged 12 and older with mild (second-line therapy) and moderate AA, whether in the active or chronic stage (first-line therapy), intradermal GCS is prescribed as monotherapy or in combination with other medications.

Intradermal preparations are administered in a checkerboard pattern intradermally, in volumes of 0.1–0.2 mL, evenly distributed across the entire affected area. The distance between injections should be 1 cm. When treating an active disease site, injections should not be limited to the balding area but should extend approximately 1–1.5 cm beyond the lesion's edge into the region of hair growth. In case of a positive response to treatment, hair in the affected area may start to appear in the 3rd to 4th week of treatment or later. Subcutaneous injection of the drug is strictly prohibited as it may lead to prolonged atrophy of the subcutaneous fat tissue.

Injections of triamcinolone acetonide suspension are administered in volumes ranging from 2.5 mg/mL to 10 mg/mL, with 2.5 mg/mL used for the eyebrow area, at intervals of 4–6 weeks, reducing the frequency as the pathological process diminishes. If there is no effect within 6 months of starting intradermal GCS treatment, it should be discontinued. The most common side effects of intralesional GCS include pain during injection and transient skin atrophy [20]. To avoid potential side effects in patients of all ages, clinicians may prefer to use lower concentrations of 2.5 mg/mL and limit steroid injections to a maximum of 20 mg per month [7].

The suspension of sodium phosphate betamethasone/diproprionate betamethasone is administered intradermally in volumes of 1–2 mL on the scalp and 0.2 mL in the eyebrow area, at intervals of 3–4 weeks [74].

Systemic therapy

Systemic GCS, cyclosporine, and methotrexate, used as monotherapy or in combination with oral glucocorticoids with cyclosporine or methotrexate as steroid-sparing agents, have demonstrated effectiveness in patients with severe forms of AA. Factors limiting the use of systemic medications for AA are side effects associated with long-term treatment and the risk of recurrence upon dose reduction or discontinuation [54].

Systemic GCS are commonly used for autoimmune diseases and have demonstrated efficacy in the treatment of AA in oral, intravenous, and intramuscular forms of administration. Systemic GCS reduce the risk of developing and progressing severe forms of AA; however, research has shown that they do not affect the long-term prognosis of AA [11, 54, 57].

Cyclosporine is a specific immunosuppressive drug that suppresses the Th1-cell response of hair follicles, selectively acting at the level of cytokines and disrupting the cooperation of immune-competent cells. It initiates and stimulates the transcription and synthesis of the potent cytokine TGFβ1 by T-lymphocytes and macrophages, which ensures immune tolerance in unaffected HFs [5, 10]. Some studies demonstrate the effectiveness of cyclosporine in the treatment of severe forms of AA [47].

Successful treatment of AA with methotrexate has been reported in both adults and the pediatric population [48, 50]. Methotrexate is a cytostatic agent belonging to the antimetabolite group; it inhibits dihydrofolate reductase, which is involved in the reduction of dihydrofolic acid to tetrahydrofolic acid. In addition to its antineoplastic effects, methotrexate also has immunosuppressive properties. Despite the need for further research into the treatment methods of AA patients with methotrexate, its use is considered safe and effective for cases involving a loss of more than 50% of hair [28].

Systemic glucocorticoids (Class C, Level of Evidence 3)

Therapy with systemic GCS is effective for AA; however, there are known adverse effects associated with long-term use of these medications. These adverse effects include hypertension, diabetes, immunosuppression, a predisposition to thrombosis, growth retardation, metabolic disturbances, reduced bone mineral density, and the development of acne. These side effects limit their use in both adults and children.

Before initiating treatment with systemic GCS and during prolonged therapy, the following investigations are mandatory: complete blood count, cortisol levels, carbohydrate metabolism indicators, calcium levels, and a coagulation profile. During the treatment period, monitoring of these parameters should be conducted once every two months.

The analysis of systemic GCS therapy, including relevant doses, regimens, safety, and effectiveness, justifies the use of specific techniques in the therapeutic algorithm: prednisolone per os: 0.4–0.6 mg/kg/day with a gradual dose reduction over 3–6 months (methylprednisolone in an equivalent dose); Dexamethasone per os: 0.1 mg/kg/day for 2 consecutive days per week for 8–12 months; betamethasone dipropionate and betamethasone sodium phosphate suspension (intramuscularly): 1–2 ml with a 3–4 week interval over 4–6 months; triamcinolone acetonide suspension (intramuscularly): 40 mg/ml with a 4-week interval over 6 months.

In children under 6 years of age, regardless of the severity and activity of AA, safety concerns take precedence over treatment effectiveness. Therefore, systemic immunosuppressive therapy is not recommended for this age group. In adolescents aged 13–18 years and adults with a severe course of the disease, systemic therapy options are considered as first-line treatment. The use of oral GCS during active but not chronic AA in children aged 7–12 years can be justified, taking into account the poorer prognosis for AA with a chronic course in this age group and the potential for toxicity due to the likely need for long-term treatment [54].

Steroid-sparing therapy (Class C, Level of Evidence 3)

The use of systemic GCS after the completion of treatment for severe AA typically involves a gradual, sometimes prolonged, reduction of the dosage, which significantly impacts compliance. Steroid-sparing agents are usually used to reduce the risk of side effects associated with long-term use of high doses of systemic glucocorticoids and to optimize AA therapy. According to the International Consensus Expert Group [54], JAK inhibitors, methotrexate or cyclosporine are considered effective in combination with systemic GCS for adults. Steroid-sparing therapy has been added to the therapeutic algorithm for patients with AA, taking into account the consensus group's recommendations, the results of the international experience, and own observations.

The use of cyclosporine and methotrexate is associated with several serious side effects (changes in serum transaminases, blood creatinine levels, and others). Before initiating therapy and monthly throughout the treatment with cyclosporine and methotrexate, it is mandatory to conduct a full complete blood count with platelet count, a biochemical blood analysis to assess liver enzyme levels, bilirubin, albumin, creatinine, calcium levels, chest X-rays, kidney function assessments, and, if necessary, tests for tuberculosis and hepatitis.

Low therapeutic doses of prednisolone, in combination with low therapeutic doses of cyclosporine or methotrexate within steroid-sparing therapy, optimize treatment effectiveness while potentially reducing the number of side effects in patients with AA. For prednisolone, the initial dose is 15 mg/day for 2 weeks, followed by gradual dose reduction by 1/4 of a tablet per week until reaching 5 mg/day. Cyclosporine is administered concurrently with prednisolone at an initial dose of 3.5 mg/kg per day, divided into two doses. From the third month of combination therapy, the cyclosporine dose is reduced by 25 mg every 2 weeks until complete discontinuation [5, 47].

Prednisolone is prescribed at a dose of 20 mg/day, with subsequent gradual reduction, while methotrexate is administered at 15–20 mg per week for 6–8 months. In patients under 18 years of age, the methotrexate dose should be 10–15 mg/m² of body surface area per week. Methotrexate is available in both tablet form (3 doses every 12 hours) and injectable form (in a syringe, administered once a week subcutaneously). Within 12–24 hours, folate supplementation is required at a minimum dose of 5 mg. Individual dose variations for sparing therapy drugs are possible, depending on the patient's weight, body surface area, and response to treatment. The treatment course should last at least 6 months [1, 48].

Adjuvant Therapy

In the case of staged AA therapy, adjuvant measures are equally important and can be applied as part of a differentiated approach, taking into account disease triggers and comorbid pathology, involving specialists from related fields. These methods of AA treatment are not standalone but may be used in specific clinical situations when the main treatment agents cause contraindications or require discontinuation of their use [44].

Metabolic Therapy Medications

Deficiency states of various origins, micronutrient deficiencies, hypo- and dysproteinemias in patients with AA are caused by various comorbid conditions or exogenous factors and can be corrected with metabolic therapy medications. These include amino acids, vitamins, and micronutrients. They can be used as monotherapies or complex compounds in the combined treatment of AA patients [26, 29].

Improving Self-esteem, Overcoming Depression and Anxiety

In addition to the main methods of treatment for AA, it is necessary to employ psychotherapy, aesthetic correction methods, and pharmacological correction of psychological disorders to increase self-esteem and address depression and anxiety. As AA is associated with high levels of anxiety and depressive disorders, sleep disturbances, the effectiveness of antidepressants in AA treatment is currently under evaluation. Small-scale studies involving AA patients

who received antidepressants (selective serotonin reuptake inhibitors) for three months have shown that the treatment in the antidepressant group was significantly more effective. Unfortunately, there haven't been large-scale randomized controlled trials in this direction [4].

In several studies, the effectiveness of using hair prostheses was assessed for patients with AA. According to experts, aesthetic correction is a crucial method of psychotherapy, which has led to its inclusion in AA treatment algorithms. The psychological impact of AA depends on a person's ability to accept their altered appearance and their personal perception of themselves. Cosmetic correction of hairless areas is vital for achieving psychological comfort, allowing patients to look natural. Integrated hair replacement systems, wigs, hairpieces, headscarves, false eyelashes, and trichopigmentation can be used as methods to conceal the effects of AA [59].

Other treatment methods

Other treatment methods include topical immunomodulators (squaric acid or diphenylcyclopropenone), calcineurin inhibitors, topical prostaglandin analogs, systemic minoxidil, and JAK inhibitors [3, 7]. These options have not been included in the treatment algorithm due to insufficient evidence or unavailability in the domestic pharmaceutical market. However, they hold promise and may be considered in future protocol revisions.

JAK inhibitors

JAK inhibitors are currently the most promising targeted agents in the treatment of AA. In patients with refractory AA, pharmacological inhibition of JAK promotes hair regrowth and reverses dystrophic nail changes [58, 63].

The first systemic medication, baricitinib (Olumiant), a selective JAK1 and JAK2 inhibitor, was approved by the FDA in June 2022 for the systemic treatment of severe AA in adults at a daily dose of 4 mg. This decision was based on the results of two phase 3 randomized clinical trials (BRAVE-AA1 and BRAVE-AA2) involving patients with severe forms of AA with SALT >50. Approximately 40% of patients receiving baricitinib at a dose of 4 mg experienced at least 80% hair regrowth on the scalp, in contrast to only 6% in the placebo group after 36 weeks of treatment. Side effects may include upper respiratory and urinary tract infections, acne, elevated levels of low-density cholesterol, creatine kinase, and herpesvirus infections [45].

Ritlecitinib, a highly selective JAK3/TEC inhibitor, suppresses the action of signaling molecules and immune cells responsible for hair loss in AA, including CD8+ T cells, CD4+ T cells, B cells, Treg cells, and NK cells. The advantages of using ritlecitinib compared to other JAK inhibitors include the prevention of clinical consequences of JAK1/JAK2 inhibition, which can lead to pharmacodynamic effects such as increased cholesterol levels, liver enzyme elevation, thrombocytopenia, and anemia [46, 58].

On June 23, 2023, the FDA approved ritlecitinib (Litfulo) for once-daily oral use at a dose of 50 mg for the treatment of severe AA in adolescents and adults. This is the first and only medication approved by the FDA for treating children aged 12 and older with this condition. The approval was based on the results of the ALLEGRO Phase 2b/3 clinical trial, which involved 718 patients with hair loss on the scalp of 50% or more according to the SALT scale. The study evaluated the effectiveness and safety of Litfulo in 18 countries.

In this key study, a statistically significant proportion of patients showed hair regrowth (SALT score ≤ 20) with ritlecitinib compared to placebo. The effectiveness and safety of the drug were consistent in both adolescents (aged 12 to 17) and adults (aged 18 and older). The most common adverse events reported in at least 4 % of patients included headaches (10.8 %), diarrhea (10 %), acne (6.2 %), rash (5.4 %), and hives (4.6 %) [46].

Tofacitinib is a JAK inhibitor that predominantly blocks JAK1 and JAK3 and to a lesser extent JAK2. The drug is approved by the FDA for the treatment of psoriatic and rheumatoid arthritis in adults. It is used "off-label" in the treatment of AA. Oral tofacitinib at a dose of 10 mg per day is an effective treatment for severe cases of AA that have not responded to other treatment methods. Some studies suggest that the dose may be increased to 20 mg per day in stubborn cases. However, it's essential to consider the possibility of side effects, including hematologic abnormalities, elevated liver enzymes and cholesterol, infections (including herpes zoster and tuberculosis reactivation), venous thromboembolism, and acne-like rash [58, 63, 69, 71].

Currently, further clinical trials of JAK inhibitors for AA are ongoing, which will provide more information about their effectiveness, safety, optimal dosages, treatment duration, and the need for adjunctive therapy.

Minoxidil per os

Minoxidil in its oral form is FDA approved for the treatment of resistant hypertension but is used off-label in low doses ranging from 0.25 to 5 mg for AGA therapy. In adolescents and children over 10 years old, the initial dose is typically 0.625 mg per day. While there isn't compelling data in the literature to support the use of oral minoxidil as a monotherapy for AA, it can be considered as adjunctive therapy. Clinicians should exercise caution when prescribing oral minoxidil to patients who have lower baseline blood pressure, a history of orthostasis, or are taking concurrent antihypertensive medications, especially when approaching the minimum antihypertensive dose of 5 mg per day [7].

Psychological support and social adaptation of patients with AA

While AA is considered a relatively benign condition that does not pose a threat to life, its psychological impact can be devastating. Patients with severe forms of AA go through various stages of coping. Initially, there is fear and loneliness, followed by hope, and only then, self-acceptance without hair, which is not achieved by everyone.

23 % of children of different ages have experienced various forms of bullying (aggressive harassment, including physical and verbal abuse, threats, etc.) more than once, with 8% experiencing it 2-3 times a week. 18% have been physically assaulted at least once. The research highlights the importance of the psychological impact on children with AA and the need to discuss the emotional and social consequences of this condition in children of all ages, as well as their family members [19].

Providing psychological support to families and friends is very important. Adapting to society and society's adaptation to people with AA is a complex and crucial task. Support groups that regularly bring together AA patients and their families can be an invaluable resource. Receiving emotional support and information helps develop positive coping strategies, improves quality of life, and enhances the effectiveness of treatment.

These facts motivated the creation of an organization to support people with AA and their families, known as the "Alopecia School" (https://alopecia.org.ua) within the Ukrainian Hair Research Society (http://uhrs.org.ua).

Conclusion

AA is an immune-mediated disease resulting from the interaction of genetic factors and exogenous triggers, leading to the formation of non-specific autoimmune inflammation and disruption of immune tolerance to hair follicles. AA has an unpredictable course, with some cases showing spontaneous hair regrowth while others present severe and treatment-resistant forms. Many patients require continuous treatment, and discontinuation can lead to rapid hair loss within a few days.

While there is no consensus on the role of stress as a trigger for AA, stressful events in life may precede the onset and/or exacerbation of the disease. The impact of AA on the quality of life doesn't always correlate with the objective condition of patients, which is often not considered during diagnosis and treatment. Evaluating the impact on quality of

life is an essential step in the diagnostic process.

The lack of a unified understanding of the mechanisms, causes, and regularities of AA development hinders the development of effective treatment methods. Despite the variety of treatment options available, achieving effective and safe disease control is not always straightforward. Treating patients with AA and comorbid conditions can be particularly challenging and may require close collaboration between specialists from various fields. For these and other reasons, there is significant dissatisfaction among patients regarding AA and its treatment.

The systematic organization, unification, and adaptation of modern knowledge about AA have led to the creation of two algorithms: a diagnostic algorithm and a therapeutic algorithm. These algorithms provide a differentiated approach to patient management, with age, disease severity, clinical form, disease activity stage, comorbid pathology, prognostic factors, and patient quality of life taken into account. Ongoing work is being done to update treatment protocols to include JAK inhibitors and other preparations, taking into based on new developments and the expanding pharmaceutical market.

References

1.Ovcharenko YuS, Serbina IM, redaktory. Menedzhment patsiientiv iz hnizdovoiu alopetsiieiu: klinichni rekomendatsii. Kharkiv: «Kharyzma plius»; 2021. 100 s. [in Ukrainian]

2.Serbina IM. Patohenetychne obgruntuvannia dyferentsiiovanoho pidkhodu v terapii hnizdovoi alopetsii. Dermatolohiia ta venerolohiia. 2018;3(81):46–50. Available from: http://idvamnu.com.ua/wp-content/uploads/2018/11/DIV381.pdf [in Ukrainian]

3.Abbott J, Rapini RP. Totalis Alopecia. In: StatPearls. StatPearls Publishing. StatPearls Publishing LLC.; 2022.

4.Abedini H, Farshi S, Mirabzadeh A, Keshavarz S. Antidepressant effects of citalopram on treatment of alopecia areata in patients with major depressive disorder. J Dermatolog Treat. 2014;25(2):153-5. DOI: https\doi.org\10.3109/09546634.2013.768761

5.Açıkgöz G, Calışkan E, Tunca M, Yeniay Y, Akar A. The effect of oral cyclosporine in the treatment of severe alopecia areata. Cutan Ocul Toxicol. 2014;33(3):247–52. DOI: https\doi.org\10.3109/15569527.2013.839997

6.Aghaei S, Saki N, Daneshmand E, Kardeh B. Prevalence of psychological disorders in patients with alopecia areata in comparison with normal subjects. ISRN Dermatology. 2014;2014(304370):1–4. DOI: https:\\doi.org\10.1155/2014/304370

7.Alhanshali L, Buontempo MG, Sicco KIL, Shapiro J. Alopecia Areata: Burden of Disease, Approach to Treatment, and Current Unmet Needs. Clin Cosmet Investig Dermatol. 2023;16:803–20. DOI: https:\\doi.org\10.2147/CCID.S376096

8.Alkhalifah A, Alsantali A, Wang E, McElwee KJ, Shapiro J. Alopecia areata update: part II. Treatment. J Am Acad Dermatol. 2010;62(2):191–202. DOI: https:\\doi.org\10.1016/j.jaad.2009.10.031

9.Alkhalifah A, Alsantali A, Wang E, Shapiro J. Alopecia areata update: part I. Clinical picture, histopathology and pathogenesis. J Am Acad Dermatol. 2010;62(2):177–88. DOI: https:\\doi.org\10.1016/j.jaad.2009.10.032

10.Al-Salam FA, Azim AA, Darwish H. Alopecia areata: Updates. The Gulf Journal of Dermatology and Venereology. 2013;20(2):1–16. Available from: https://www.gulfdermajournal.net/pdf/2013-10/1.pdf

11.Alsantali A. Alopecia areata: a new treatment plan. Clin Cosmet Investig Dermatol. 2011;4:107-15. DOI: https:\\doi.org\10.2147/CCID.S22767

12.Azzawi S, Penzi LR, Senna MM. Immune Privilege Collapse and Alopecia Development: Is Stress a Factor. Skin Appendage Disord. 2018;4(4):236-44. DOI: https:\\doi.org\10.1159/000485080

13.Biran R, Zlotogorski A, Ramot Y. The genetics of alopecia areata: new approaches, new findings, new treatments. J Dermatol Sci. 2015;78(1):11–20. DOI: https:\\doi.org\10.1016/j.jdermsci.2015.01.004

14.Blaumeiser B, van der Goot I, Fimmers R, Hanneken S, Ritzmann S, Seymons K, et al. Familial aggregation of alopecia areata. J Am Acad Dermatol. 2006;54(4):627–32. DOI: https:\\doi.org\10.1016/j.jaad.2005.12.007

15.Bolotnaja LA, Serbina IM. Adaptive regulatory mechanisms of alopecia areata. Georgian medical news. 2017;11(272):75–80. Available from: https://www.geomednews.com/s/480918712df344a4a77508d4cd7815ab/files/uploaded/V272_N11_November_2017

16.Breitkopf T, Leung G, Yu M, Wang E, McElwee KJ. The basic science of hair biology: what are the causal mechanisms for the disordered hair follicle? J Dermatol

Clin. 2013;31(1):1–19. DOI: https:\\doi.org\10.1016/j.det.2012.08.006
17.Chang KH, Rojhirunsakool S, Goldberg LJ. Treatment of severe alopecia areata with intralesional steroid injections. J Drugs Dermatol. 2009;8(10):909–12. Available from: https://www.researchgate.net/publication/38031609_Treatment_of_severe_alopecia_areata_with_intralesional_steroid_injections
18.Cho HH, Jo SJ, Paik SH, Jeon HC, Kim KH, Eun HC, et al. Clinical characteristics and prognostic factors in early-onset alopecia totalis and alopecia universalis. J Korean Med Sci. 2012;27(7):799–802. DOI: https:\\doi.org\10.3346/jkms.2012.27.7.799
19.Christensen T, Yang JS, Castelo-Soccio L. Bullying and Quality of Life in Pediatric Alopecia Areata. Skin Appendage Disord. 2017;3(3):115–8. DOI: https:\\doi.org\10.1159/000466704
20.Chu T, Aljasser MI, Alharbi A, Abahussein O, McElwee K, Shapiro J. Benefit of different concentrations of intralesional triamcinolone acetonide in alopecia areata: An intrasubject pilot study. J Am Acad Dermatol. 2015;73(2):338–40. DOI: https:\\doi.org\10.1016/j.jaad.2015.04.049
21.Collaku L, Resuli M, Gjermeni I, Tase M. Comorbidity and multimorbidity in the medical practice: A literature review. Alban Med J. 2017;4:55–9. Available from: https://www.ishp.gov.al/comorbidity-and-multimorbidity-in-the-medical-practice-a-literature-review/
22.Conic RZ, Miller R, Piliang M, Bergfeld W, Mesinkovska NA. Comorbidities in patients with alopecia areata. J Am Acad Dermatol. 2017;76(4):755–7. DOI: https:\\doi.org\10.1016/j.jaad.2016.12.007
23.Darwin E, Hirt PA, Fertig R, Doliner B, Delcanto G, Jimenez JJ. Alopecia areata: Review of epidemiology, clinical features, pathogenesis, and new treatment options. Int J Trichol. 2018;10(2):51–60. DOI: https:\\doi.org\10.4103/ijt.ijt_99_17
24.Devi M, Rashid A, Ghafoor R. Intralesional Triamcinolone Acetonide Versus Topical Betamethasone Valearate in the Management of Localized Alopecia Areata. J Coll Physicians Surg Pak. 2015;25(12): 860–2. Available from: https://www.researchgate.net/profile/Rabia-Ghafoor/publication/287999122
25.Doche I, Hordinsky MK, Valente NYS, Romiti R, Tosti A. Syphilitic Alopecia: Case Reports and Trichoscopic Findings. Skin Appendage Disord. 2017;3(4):222–4. DOI: https:\\doi.org\10.1159/000477415
26.Dompson JM., Mirza M., Park M., Qureshi A. The Role of Micronutrients in Alopecia Areata: A Review. Am J Clin Dermatol. 2017;18(5): 663-679 DOI:10.1007/s40257-017-0285-x
27.Dubois M, Baumstarck-Barrau K, Gaudy-Marqueste C, Richard M-A, Loundou A, Auquier P, et al. Quality of life in alopecia areata: a study of 60 cases. J Invest Dermatol. 2010;130(12):2830–2833. DOI: https:\\doi.org\10.1038/jid.2010.232
28.English JC, Heinisch S. Methotrexate Treatment for Alopecia Areata with Greater than 50 % Involvement. Hair Ther Transplant. 2015;5(3):1000138. DOI: https:\\doi.org\10.4172/2167-0951.1000138
29.Esfandiarpour I, Farajzadeh S, Abbaszadeh M. Evaluation of serum iron and ferritin levels in alopecia areata. Dermatol Online J. 2008;14(3):21. Available from: https://www.researchgate.net/publication/51402802_Evaluation_of_Serum_Iron_and_Ferritin_Levels_in_Alopecia_Areata
30.Estefan J, Ribeiro M, Abad E, Saintive S, Ramos-E-Silva M. Alopecia Areata – Part III: Prognosis and Treatment. Skinmed. 2016;14(5):361–5. Available from: https://www.researchgate.net/publication/313337016_Alopecia_Areata-Part_III_Prognosis_and_Treatment
31.Fabbrocini G, Panariello L, De Vita V, Vincenzi C, Lauro C, Nappo D, et al. Quality of life in alopecia areata: a disease-specific questionnaire. J Eur Acad Dermatol Venereol. 2013;27(3): e276–80. DOI: https:\\doi.org\10.1111/j.1468-3083.2012.04629.x
32.Forstbauer L, Brockschmidt F, Moskvina V, Herold C, Redler S, Herzog A, et al. Genome-wide pooling approach identifies SPATA5 as a new susceptibility locus for alopecia areata. Eur J Hum Genet. 2012;20(3):326–32. DOI: https:\\doi.org\10.1038/ejhg.2011.185
33.Fricke ACV, Miteva M. Epidemiology and burden of alopecia areata: a systematic review. Clin Cosmet Investig Dermatol. 2015;8:397–403. DOI: https:\\doi.org\10.2147/CCID.S53985
34.Fuentes-Duculan J, Gulati N, Bonifacio KM, Kunjravia N, Zheng X, Suárez-Fariñas M, et al. Biomarkers of alopecia areata disease activity and response to corticosteroid treatment. Exp Dermatol. 2016;25(4):282–86. DOI: https:\\doi.org\10.1111/exd.12918
35.Gilhar A, Etzioni A, Paus R. Alopecia areata. N Engl J Med. 2012;366(16):1515–25. DOI: https:\\doi.org\10.1056/NEJMra1103442
36.Gilhar A. Collapse of Immune Privilege in Alopecia Areata: Coincidental or Substantial? Invest Dermatol.

2010;130(11):2535–7. DOI: https:\\doi.org\10.1038/jid.2010.260
37.Gong J, Lim SW. Alopecia areata as a paraneoplastic syndrome of Hodgkin's lymphoma: A case report. Mol Clin Oncol. 2014;2(4):596–8. DOI: https:\\doi.org\10.3892/mco.2014.274
38.Harries M, Macbeth AE, Holmes S, Chiu WS, Gallardo WR, Nijher M et al. The epidemiology of alopecia areata: a population-based cohort study in UK primary care. Br J Dermatol. 2022;186(2):257–65. DOI: https:\\doi.org\10.1111/bjd.20628
39.Herskovitz I, Freedman J, Tosti A. Minoxidil induced hypertrichosis in a 2 year-old child. F1000Research. 2013;2:226. DOI: https:\\doi.org\10.12688/f1000research.2-226.v1
40.Huang KP, Mullangi S, Guo Y, Qureshi A. Autoimmune, atopic, and mental health comorbid
44.Jin W, Zheng H, Shan B, Wu Y. Changes of serum trace elements level in patients with alopecia areata: A meta-analysis. J Dermatol. 2017;44(5):588–91. DOI: https:\\doi.org\10.1111/1346-8138.13705.
45.King B, Ohyama M, Kwon O, Zlotogorski A, Ko J, Mesinkovska NA, et al. Two Phase 3 Trials of Baricitinib for Alopecia Areata. Engl J Med 2022;386(18):1687-99. DOI: https:\\doi.org\10.1056/NEJMoa2110343.
46.King B, Zhang X, Harcha WG, Szepietowski JC, Shapiro J, Lynde C, et al. Efficacy and safety of ritlecitinib in adults and adolescents with alopecia areata: a randomised, double-blind, multicentre, phase 2b–3 trial. The Lancet. 2023;401(10387):1518-1529. DOI: https:\\doi.org\10.1016/s0140-6736(23)00222-2.
47.Lai VWY, Chen G, Gin D, Sinclair R. Cyclosporine for moderate-to-severe alopecia areata: A double-blind, randomized, placebo-controlled clinical trial of efficacy and safety. J Am Acad Dermatol. 2019;81(3):694–701. DOI: https:\\doi.org\10.1016/j.jaad.2019.04.053.
48.Landis ET, Pichardo-Geisinger RO. Methotrexate for the treatment of pediatric alopecia areata. J Dermatolog Treat. 2018;29(2):145–48. DOI: https:\\doi.org\10.1080/09546634.2017.1341608.
49.Lew BL, Cho HR, Haw S, Kim H-J, Chung J-H, Sim W-Y. Association between IL17A/IL17RA gene polymorphisms and susceptibility to alopecia areata in the Korean population. Ann Dermatol. 2012;24(1):61–5. DOI: https:\\doi.org\10.5021/ad.2012.24.1.61.
50.Lucas P, Bodemer C, Barbarot S, Vabres P, Royer M, Mazereeuw-Hautier J. Methotrexate in Severe Childhood Alopecia Areata: Long-term Follow-up. J Acta Derm Venereol. 2016;96(1):102–3. DOI: https:\\doi.org\10.2340/00015555-2173.
conditions associated with alopecia areata in the United States. JAMA dermatology. 2013;149(7):789–94. DOI: https:\\doi.org\10.1001/jamadermatol.2013.3049
41.Ikeda T. A new classification of alopecia areata. Dermatologica. 1965;131(6):421-45. DOI: https:\\doi.org\10.1159/000254503.
42.Inui S, Nakajima T, Itami S. Significance of dermoscopy in acute diffuse and total alopecia of the female scalp: review of twenty cases. Dermatology. 2008;217(4):333–6. DOI: https:\\doi.org\10.1159/000155644.
43.Ito N, Sugawara K, Bodó E, Takigawa M, van Beek N, Ito T, et al. Corticotropin-releasing hormone stimulates the in situ generation of mast cells from precursors in the human hair follicle mesenchyme. J Invest Dermatol. 2010;130(4):995-1004. DOI: https:\\doi.org\10.1038/jid.2009.387.
51.Lugović-Mihić L, Ljubesić L, Mihić J, Vuković-Cvetković V, Troskot N, Situm M. Psychoneuroimmunologic aspects of skin diseases. Acta Clin Croat. 2013;52(3)337–45. Available from: https://www.researchgate.net/profile/Liborija-Lugovic
52.McElwee K, Spiers E, Oliver R. In vivo depletion of CD8+ T cells restores hair growth in the DEBR model for alopecia areata. Br J Dermatol. 1996;135(2):211–7. DOI: https:\\doi.org\10.1111/j.1365-2133.1996.tb01149.x.
53.McPhee C, Duncan F, Silva K, King LE Jr, Hogenesch H, Roopenian DC, et al. Increased expression of Cxcr3 and its ligands, Cxcl9 and Cxcl10, during the development of alopecia areata in the mouse. J Invest Dermatol. 2012;132(6):1736–8. DOI: https:\\doi.org\10.1038/jid.2012.17
54.Meah N, Wall D, York K, Bhoyrul B, Bokhari L, Sigall DA, et al. The Alopecia Areata Consensus of Experts (ACE) study: Results of an international expert opinion on treatments for alopecia areata. J Am Acad Dermatol. 2020;83(1):123–30. DOI: https:\\doi.org\10.1016/j.jaad.2020.03.004
55.Mingorance Gámez CG, Martínez Chamorro A, Moreno Casares AM, Sánchez JT, Arias-Santiago S, García-Lora E, et al. Joint study of the associations of HLA-B and the transmembrane short tandem repeat polymorphism of MICA protein with alopecia areata shows independent associations of both with the disease. Clin Exp Dermatol. 2020;45(6):699–704. DOI: https:\\doi.org\10.1111/ced.14208
56.Mirzoyev SA, Schrum AG, Davis MDP, Torgerson RR. Lifetime incidence risk of alopecia areata estimated at 2.1% by Rochester Epidemiology Project, 1990–2009. J Invest Dermatol. 2014;134(4):1141–2. DOI: https:\\doi.org\10.1038/jid.2013.464

57.Olsen E, Hordinsky MK, Price V, Roberts JL, Shapiro J, Canfield D, et al. Alopecia areata investigational assessment guidelines. Part II. National Alopecia Areata Foundation. J Am Acad Dermatol. 2004;51(3):440–7. DOI: https:\\doi.org\10.1016/j.jaad.2003.09.032

58.Papierzewska M, Waśkiel-Burnat A, Rudnicka L. Safety of Janus Kinase inhibitors in Patients with Alopecia Areata: A Systematic Review. Clin Drug Investig. 2023;43(5):325-34. DOI: https:\\doi.org\10.1007/s40261-023-01260-z

59.Park J, Kim D-W, Park S-K, Yun S-K, Kim H-U. Role of hair prostheses (wigs) in patients with severe alopecia areata. Ann Dermatol. 2018;30(4):505-7. DOI: https:\\doi.org\10.5021/ad.2018.30.4.505

60.Pratt CH, King Jr. LE, Messenger AG, Christiano AM, Sundberg JP. Alopecia areata. Nat Rev Dis Primers. 2017;3:17011. DOI: https:\\doi.org\10.1038/nrdp.2017.11

61.Rajabi F, Abdollahimajd F, Jabalameli N, Nassiri Kashani M, Firooz A. The immunogenetics of alopecia areata. Adv Exp Med Biol. 2022;1367:19–59. DOI: https:\\doi.org\10.1007/978-3-030-92616-8_2

62.Ramot Y, Gural A, Zlotogorski A. Alopecia Areata as a Manifestation of Systemic Lymphoma: Report of Two Cases. Skin Appendage Disord. 2016;2(1–2):63–6. DOI: https:\\doi.org\10.1159/000448379

63.Ramot Y, Zlotogorski A. Jak inhibitors for the treatment of alopecia areata. Harefuah. 2020;159(1):38-42. Avaulable from: https://www.researchgate.net/publication/338582544_JAK_INHIBITORS_FOR_THE_TREATMENT_OF_ALOPECIA_AREATA

64.Rebora A. Alopecia areata incognita: a hypothesis. Dermatologica. 1987;174(5): 214–8. DOI: https:\\doi.org\10.1159/000249182

65.Redler S, Brockschmidt F, Tazi-Ahnini R, Drichel D, Birch MP, Dobson K, et al. Investigation of the male pattern baldness major genetic susceptibility loci AR/EDA2R and 20p11 in female pattern hair loss. Br J Dermatol. 2012;166(6):1314–18. DOI: https:\\doi.org\10.1111/j.1365-

2133.2012.10877.Rencz F, Gulácsi L, Péntek M, Wikonkál N, Baji P, Brodszky V. Alopecia areata and health-related quality of life: a systematic review and meta-analysis. Br J Dermatol. 2016;175(3):561–71. DOI: https:\\doi.org\10.1111/bjd.14497

66.Ring J. Quality of life – an essential parameter for dermatology. J Eur Acad Dermatol Venereol. 201731(4):573–9. DOI: https:\\doi.org\10.1111/jdv.14184

67.Rudnicka L, Olszewska M, Rakowska A. Atlas of Trichoscopy. Dermoscopy in Hair and Scalp Disease. London : Springer Ltd; 2012. 507 p.

68.Sanchez-Diaz M, Diaz-Calvillo P, Rodriguez-Pozo J-A, Tercedor-Sánchez J, Cantudo-Cuenca M-R, Molina-Leyva A, et al Tofacitinib for Treatment of Alopecia Areata: Real-world Evidence and Factors Associated with Therapeutic Response. Acta Derm Venereol. 2022;102:adv00736. DOI: https:\\doi.org\10.2340/actadv.v102.2036

69.Slowinska M, Rudnicka L, Schwartz R, Kowalska-Oledzka E, Rakowska A, Sicinska J, et al. Comma hairs: a dermatoscopic marker for tinea capitis: a rapid diagnostic method. J Am Acad Dermatol. 2008;59(5 Suppl):S77–9. DOI: https:\\doi.org\10.1016/j.jaad.2008.07.009

70.Strazzulla L, Avila L, Lo Sicco K, Shapiro J. Image gallery: treatment of refractory alopecia universalis with oral tofacitinib citrate and adjunct intralesional triamcinolone injections. Br J Dermatol. 2017;176(6):e125. DOI: https:\\doi.org\10.1111/bjd.15483

71.Tosti A. Dermoscopy of Hair and Scalp Disorders: with Clinical and Pathological Correlations. London: Informa Healthcare; 2007. 168 p.

72.Trüeb RM, Dias MF. Alopecia areata: a comprehensive review of pathogenesis and management. Clin Rev Allergy Immunol. 2018;54(1):68–87. DOI: https:\\doi.org\10.1007/s12016-017-8620-9

73.Ustuner P, Balevi A, Özdemir M. Best dilution of the best corticosteroid for intralesional injection in the treatment of localized alopecia areata in adults. J Dermatolog Treat. 2017;28(8):753–61. DOI: https:\\doi.org\10.1080/09546634.2017.1329497

74.Vélez-Muñiz RDC, Peralta-Pedrero ML, Jurado-Santa Cruz F, Morales-Sánchez MA. Psychological profile and quality of life of patients with alopecia areata. Skin Appendage Disord. 2019;5(5):293–8. DOI: https:\\doi.org\10.1159/000497166

75.Walker SA, Rothman S. A statistical study and consideration of endocrine influences. J Invest Dermatol. 1950;14(6):403–13. DOI: https:\\doi.org\10.1038/jid.1950.52

76.Zhang W, Yu M, Yu W, Weinberg J, Shapiro J, McElwee KJ. Development of alopecia areata is associated with higher central and peripheral hypothalamic-pituitary-adrenal tone in the skin graft induced C3H/HeJ mouse model. J Invest Dermatol. 2009;129:1527-1538. DOI: https:\\doi.org\10.1038/jid.2008.371

77.Zhou C, Li X, Wang C, Zhang J. Alopecia areata: an update on etiopathogenesis, diagnosis, and

management. Clin Rev Allergy Immunol. 2021;61(3):403–23. DOI: https:\\doi.org\10.1007/s12016-021-08883-0

78.Zigmond AS., Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361–70. DOI: https:\\doi.org\10.1111/j.1600-0447.1983.tb09716.x

Received: 03.10.2023
Accepted: 09.11.2023

І. М. Сербіна [A, B, C, D, F], ***К. М. Хобзей*** [B, C], ***Т. І. Лядова*** [E, F], ***О. І. Літус*** [E], ***С. В. Возіанова*** [E], ***Ю. В. Андрашко*** [E], ***С. О. Галникіна*** [E], ***Т. В. Святенко*** [E], ***І. В. Свистунов*** [E], ***О. О. Сизон*** [E], ***І. В. Кадигроб*** [B, C], ***Ю. С. Овчаренко*** [A, B, C, D, F]
serbinaim@gmail.com

КЛІНІЧНІ РЕКОМЕНДАЦІЇ ВІД УКПАЇНСЬКОГО ТОВАРИСТВА ДОСЛІДЖЕННЯ ВОЛОССЯ. ДІАГНОСТИКА ТА ЛІКУВАННЯ ГНІЗДОВОЇ АЛОПЕЦІЇ

A – концепція та дизайн дослідження; B – збір даних; C – аналіз та інтерпретація даних; D – написання статті; E – редагування статті; F – остаточне затвердження статті

АНОТАЦІЯ. Гніздова алопеція – імуноопосередковане захворювання, обумовлене взаємодією генетичних факторів та екзогенних тригерів, що призводить до активації сигнального шляху JAK-STAT, формування неспецифічного автоімунного запалення та порушення імунної толерантності волосяного фолікула. Гніздова алопеція має непередбачуваний характер перебігу з нерубцевим типом втрати волосся, може зачіпати волосяну частину голови і/або волосся на інших ділянках, проявлятися ураженням нігтьових пластин. Психотравмуючий вплив цього захворювання може бути зіставлений із наслідками життєзагрожуючих або інвалідизуючих захворювань. З цієї причини ступінь негативного впливу гніздової алорпеції на якість життя може не корелювати з об'єктивним станом пацієнтів, що часто не враховується при діагностиці та терапії захворювання. Незважаючи на наявність різноманітних методів терапії, не завжди легко досягти ефективного і безпечного контролю захворювання. На сьогоднішній день не існує універсального методу лікування, який гарантує відсутність рецидиву в майбутньому. Лікування пацієнтів із гніздовою алопецією з коморбідною патологією може бути особливо складним і вимагати тісної співпраці між фахівцями кількох спеціальностей. З цих та інших причин є значна незадоволеність серед пацієнтів щодо гніздової алопеції та її лікування.

Представлені клінінчні рекомендації з менеджменту пацієнтів із гніздової алопеції розроблено на підставі аналізу протоколів міжнародних і національних рівнів, адаптовані під вітчизняний фармацевтичний ринок і є результатом наукових досліджень, проведених в Україні, які обґрунтували необхідність розширення критеріїв вибору і контролю ефективності терапії, що раніше не враховувалося. Основна робота із систематизації, уніфікації та адаптації сучасних знань про гніздову алопецію призвела до створення двох алгоритмів – діагностичного і терапевтичного, які логічно вибудовують диференційований підхід до менеджменту таких пацієнтів із рандомізацією за віком, ступенем тяжкості, клінічною формою, стадією активності процесу, з урахуванням коморбідної патології, прогностичних чинників і впливу на якість життя пацієнта. Відповідно до антигенної концепції патогенезу гніздової алопеції до основної групи препаратів відносять засоби з імуносупресивною дією. Продовжується робота по оновленню протоколів лікування з включенням JAK – інгібіторів та інших препаратів, з урахуванням нових досягнень та розширення фармринку.

Ключові слова: *гніздова алопеція, автоімунітет, якість життя, настанови, діагностика, лікування, алгоритм*

Для цитування: Сербіна ІМ, Хобзей КМ, Лядова ТІ, Літус ОІ, Возіанова СВ, Андрашко Ю В, Галникіна СО, Святенко ТВ, Свистунов ІВ, Кадигроб ІВ, Сизон ОО, Кадигроб ІВ, Овчаренко ЮС. CLINICAL GUIDELINES OF UKRAINIAN HAIR RESEARCH SOCIETY. DIAGNOSIS

AND TREATMENT OF ALOPECIA AREATA. Актуальні проблеми сучасної медицини. 2023;12:47-68. DOI: https://doi.org/10.26565/2617-409X-2023-12-06

Інформація про авторів

Інесса Михайлівна Сербіна, д. мед. н., доцент, професор кафедри інфекційних хвороб та клінічної імунології медичного факультету, Харківський національний університет імені В. Н. Каразіна, майдан Свободи, 6, Харків, Україна, 06122, e-mail: serbinaim@gmail.com. ORCID ID: https://orcid.org/0000-0001-7870-206X.

Кузьма Миколайович Хобзей, аспірант кафедри інфекційних хвороб та клінічної імунології медичного факультету Харківського національного університету ім. В. Н. Каразіна, лікар-дерматовенеролог, трихолог, головний лікар «Khobzei Clinic». e-mail: khobzey@gmail.com. ORCID ID https://orcid.org/0009-0002-2879-9240.

Тетяна Іванівна Лядова, д. мед. н., професор, декан медичного факультету Харківського національного університету ім. В. Н. Каразіна, майдан Свободи, 6, Харків, Україна, 06122, e-mail: t.lyadova@karazin.ua, ORCID ID: https://orcid.org/0000-0002-5892-2599.

Олександр Іванович Літус, д. мед. н., професор, завідувач кафедри дерматовенерології, алергології, клінічної та лабораторної імунології Національного університету охорони здоров'я ім. П. Л. Шупика. e-mail: aleksandr.litus@gmail.com. ORCID ID https://orcid.org/ 0000-0002-3708-2666.

Світлана Віталіївна Возіанова, д. мед. н., професор кафедри дерматовенерології, алергології, клінічної та лабораторної імунології Національного університету охорони здоров'я ім. П. Л. Шупика. e-mail: s.vozianova@gmail.com ORCID ID https://orcid.org/0000-0002-6445-3442.

Юрій Володимирович Андрашко, д. мед. н., професор, завідувач кафедри шкірних і венеричних хвороб із курсами ВІЛ-інфекції, патоморфології та фтизіатрії медичного факультету Ужгородського національного університету. e-mail: andrashkoy@gmail.com. ORCID ID https://orcid.org/0000-0001-8608-6754.

Світлана Олександрівна Галникіна, д. мед. н., професор кафедри інфекційних хвороб з епідеміологією, шкірними та венеричними хворобами, Тернопільського національного медичного університету ім. І. Я. Горбачевського. e-mail: dr.lana08@yahoo.com. ORCID ID https://orcid.org/0000-0003-2062-5529.

Тетяна Вікторівна Святенко, д .мед. н., професор, завідувачка кафедри шкірних та венеричних хвороб, Дніпровський державний медичний університет. e-mail: tatsvyatenko@gmail.com. ORCID ID https://orcid.org/0000-0003-4303-2937.

Ігор Ваніфатієвич Свистунов, д. мед. н., професор кафедри дерматовенерології, алергології, клінічної та лабораторної імунології Національного університету охорони здоров'я ім. П. Л. Шупика. e-mail: svistunov.iv@gmail.com. ORCID ID https://orcid.org/0000-0002-3916-354X

Орися Орестівна Сизон, д. мед. н., професор, завідувачка кафедри дерматології, венерології Львівського національного медичного університету ім. Данила Галицького. e-mail: syzon-orysya@ukr.net. ORCID ID https://orcid.org/0000-0002-7011-2521.

Ірина Володимирівна Кадигроб, к. мед. н., доцент кафедри інфекційних хвороб та клінічної імунології медичного факультету Харківського національного університету ім. В. Н. Каразіна, e-mail: kadygrob13@gmail.com. ORCID ID https://orcid.org/0000-0002-2551-0256.

Юлія Сергіївна Овчаренко, к. мед. н., доцент, професор кафедри інфекційних хвороб та клінічної імунології медичного факультету Харківського національного університету ім. В. Н. Каразіна, президент Українського товариства дослідження волосся, майдан Свободи, 6, Харків, Україна, 06122, e-mail: ukrhrs@gmail.com. ORCID ID: https://orcid.org/0000-0002-2412-2251.

Отримано: 03.10.2023 року
Прийнято до друку: 09.11.2023 року