

## Psoriasis: In a War with Your Own Skin

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### Abstract

One hundred twenty-five million people worldwide, among them around 2% to 3% of the total population is having Psoriasis, according to the World Psoriasis Day consortium. It is a genetic disease in which scaly, raised plaques appear on the skin. Psoriasis has been known since biblical times, and since then it is a mystery disease. Now we know many molecular and immune mechanisms for the development of psoriasis, but we still cannot fully understand what is considered the cause and what the effect is. In this article, we will give a general description of the disease, touch on its pathogenesis and tell the history of the study and treatment of psoriasis.

**Keywords:** Psoriasis; Dermatology; Genetic disease; Pathogenesis

### Plaques on the Skin

Psoriasis is a chronic non-infectious disease in which thickened flaky plaques appear on the skin, towering above its surface. This is due to excessive reproduction of epidermal cells and disruption of their keratinization processes. Such pathological changes are accompanied by an inflammatory reaction.

Psoriasis is the most prevalent autoimmune disease in the U.S. According to current studies, as many as 7.5 million Americans—approximately 2.2 percent of the population—have psoriasis.

Almost 2/3 of patients fall ill before the age of 30 years. Nevertheless, there are two peaks in incidence. The first peak in women falls on average by 15.5 years, and in men—by 27.5. The second peak is observed at the age of about 54 years, regardless of gender. Both early and late onset of the disease is associated with a genetic predisposition, but in these two cases different genes may be to blame [1].

The most common form of psoriasis (80-90% of cases) is normal or vulgar. When it appears, red spots appear on the skin, gradually turning into plaques elevated above the skin. Plaques are usually symmetrical and, as a rule, are located on the elbows and knees, on the back and on the scalp. They grow and merge into larger foci, then their growth stops, and the plaques gradually decrease in size. New plaques may occur on the periphery of existing lesions or in places where the skin has been damaged and rubbed (this effect is called *Kebner's phenomenon*). Scales appear on the surface of the plaques that are easily peeled off. At the same time, psoriasis is not contagious and does not pose a danger to others [2].

### There are some more rare forms of psoriasis

**Psoriasis of the palms and soles:** It occurs most often in people engaged in physical labor or often in contact with irritating substances, such as aggressive detergents. When this form of plaque formed on the palms and soles, the skin on them becomes red, cracks may appear. In

some cases, the nails are also affected: pinpoint indentations appear on them, longitudinal grooves, the nail plate itself thickens.

**Guttate psoriasis:** When it appears on the skin multiple small plaques are visible. Usually, shortly before the manifestation of this form of psoriasis, the patient suffers from a sore throat or another disease caused by streptococcus. Probably, streptococcal infection activates a certain type of lymphocytes, provoking skin damage [3].

**Psoriatic arthritis:** In one third of patients with psoriasis, skin rashes can be complicated by joint damage.

**Pustular psoriasis:** Pustular psoriasis of von Zumbush, described by dermatologist Leo von Zumbush in 1910. The skin of these patients is red, and on the plaques and on the unchanged skin bubbles with fluid (pustules) form, pain and burning appear. Skin rashes are accompanied by a pronounced immune response: fever and inflammatory changes in the blood. Often these problems are associated with secondary infection of the skin due to scratching of the pustules.

The classic method for the differential diagnosis of psoriasis is by scraping the surface of a plaque with a glass slide or scalpel. Initially, whitish horny scales easily fly off the surface of the plaque. In dermatology, this is called the phenomenon of *stearic stain*. After peeling off all the horny scales, the surface of the plaque becomes wet and shiny (the phenomenon of the *terminal film*). Upon further scraping, small droplets of blood protrude from damaged capillaries on the surface of the plaque. This phenomenon is called the *Auspitz symptom*, or the *bloody dew phenomenon*. The combination of these three phenomena is called the *psoriatic triad* and is a reliable diagnostic sign of the disease [4].

Psoriasis and its exacerbations are triggered by many factors: stress, smoking, alcohol use, certain infections (streptococcal, HIV). Also known are a number of drugs that provoke the development of the disease and worsen its course: beta-blockers used to treat pathologies of the cardiovascular system, lithium is used to treat diseases of the nervous system, antimalarial drugs, and nonsteroidal anti-inflammatory drugs (painkillers, antipyretic and antispasmodics). Probably, these factors change the immune status of a person, triggering a pathological process in the skin [3].

Since psoriasis is associated with elevated levels of various pro-inflammatory agents systemically circulating in the blood of patients, it is often accompanied by other diseases in which inflammatory processes play an important role:

- all sorts of inflammatory immune-mediated diseases, such as Crohn's disease or ulcerative colitis. The risk of these disorders in patients with psoriasis is 4-7 times higher than in the population on average. According to some reports, people whose families had cases of multiple sclerosis, are more likely to get psoriasis. Perhaps this is because with these diseases the level of cytokines is high in the blood;
- metabolic syndrome and obesity;
- myocardial infarction;
- tumors (in particular lymphoma);
- Tsaraat and leprosy.

Psoriasis has been known to people for a long time: it was difficult not to notice the disease with such bright manifestations as large plaques on the skin, persistent itching and peeling. The first descriptions of a skin disease similar to psoriasis can be found in the Old Testament in the Book of Levitic: there it is called Tsaraat. The book of Leviticus is a set of rules according to which the Jewish people should live. The rules inscribed in the Old Testament contain also descriptions of diseases that need to be able to be recognized by Kohanim (priests). A member of the community suffering from a tsaraat, despite the fact that his skin was covered with strange white spots, was not prescribed to be expelled from the settlement - apparently, it was thought that the disease was non-infectious. It is unlikely that the priests of that time understood dermatology in the same way as modern doctors, therefore the name Tsaraat most likely indicated not only psoriasis, but also a number of other skin diseases [5].

The difficulty of finding descriptions of psoriasis in the past is due to the fact that in medical writings it was often called leprosy. Roman physician Avl Cornelius Celsus confused the situation even more. He described in the work "De Re Medica" psoriasis, calling it impetigo (impetigo), which translated from Latin means "scabs". The same term in the medical books of the time was designated a lichen. In the 16th century, Hieronymus Mercurialis tried his best: with his light hand, psoriasis was combined in clinical descriptions with the same leprosy and some other skin diseases.

The classic description of the disease, made in 1809, belongs to the prominent English physician Robert Willan. The name of the disease "psoriasis" comes from the ancient Greek word ψωριασις ("psoriasis"), which literally translates as "itchy condition". This term was first used in 1841 by the Austrian dermatologist Ferdinand Gebra. The name is completely fair, because itching is one of the symptoms of psoriasis, and patients are often the most worried about patients. The merit of Ferdinand Gebra is also in the fact that he finally separated non-contagious psoriasis from a contagious and deadly leprosy [6].

After a clear description of the disease, dermatologists from different countries began to actively explore it. Heinrich Knebner in 1872 found that skin damage is often preceded by the appearance of psoriatic lesions. This phenomenon was named after him. In 1885, another Heinrich, Heinrich Auschitz, described point bleeding when exfoliating the surface of a psoriatic plaque.

## Immunology of psoriasis

**The main pathological processes that lead to the formation of psoriatic plaques are:**

- inflammatory reaction in the dermis (deep layer of the skin);
- an abnormal increase in the number of epidermal cells (which leads to the growth of the epidermis and the appearance of a plaque raised above the skin);
- together with a violation of their differentiation (on the one hand, keratinocytes more actively divide and do not pass into the terminal differentiation stage in time, due to which the normal stratum corneum of the epidermis does not form, on the other, dead epidermal cells accumulate on the skin surface, which form a flaky layer on the surface of the plaque).

Pathological cell division can be a reaction to skin damage and in this case is considered as an altered process of epithelium repair [7].

At first glance, it is completely unclear where this strange tendency to hyperplasia of the epithelium comes from. If we consider the pathological processes in the skin in detail, it becomes clear that some inflammatory changes in the dermis are observed even when there is no epidermal hyperplasia. Therefore, one of the hypotheses suggests that it is the inflammatory reaction in the dermis that triggers a cascade of epidermal hyperplasia.

Currently, the main role in the "pro-inflammatory" component of psoriasis is assigned to T-lymphocytes and dendritic cells, as well as signaling substances produced by these cells- cytokines (primarily various interleukins and tumor necrosis factor, TNF- $\alpha$ ). The CD4+ lymphocyte fraction is found predominantly in the deep, dermal layer of the skin even at the stage of plaque formation. Due to the misaligned functioning of immune cells (primarily dendritic cells, regulatory and effector T cells) a proinflammatory immune response is activated, provoking epidermal hyperplasia and the formation of a psoriatic plaque.

## Genetics of psoriasis

The predisposition to psoriasis is inherited, so doctors usually ask the patient about a family history of the disease. If one of the monozygous twins suffers from psoriasis, then in the second twin the risk of getting sick is about 70%. But in the case of dizygotic twins, this risk is significantly lower - only 15-20%. If you have a brother or sister with psoriasis, the probability of a disease in your case is close to 6%. If one parent is ill, the risk increases to almost 20%, and if both are up to 65%.

There are more than 40 sites on chromosomes associated with the risk of developing psoriasis, which are collectively called PSORS (psoriasis susceptibility loci), which are predisposition loci for psoriasis. The locus on the 6th chromosome, called PSORS1, has the strongest link: it contains one of the genes of the major histocompatibility complex - HLA-C. This gene encodes a receptor protein on the cell membrane, which is "read" by T-lymphocytes for recognition of "its" and "alien" in the human body. A variant of the HLA-C receptor - HLA-Cw6 - is detected in all familial cases of psoriasis and is a marker for the early onset of psoriasis. According to the presence of this antigen, cases of psoriasis are divided into two large groups. HLA-Cw6-positive psoriasis is a disease with a family history and early onset (up to 40 years). HLA-Cw6-negative psoriasis - late-onset psoriasis. Apparently, in the second case, the primary

pathology of the immune response occurs over time, due to exposure to exogenous factors [8].

The HLA-C gene plays an important role in the epigenetics of psoriasis: there is a relationship between the early onset of the disease and the level of methylation of this gene. Today, scientists have not yet managed to understand whether such a relationship plays a functional role in the development of the disease. Since methylation is a way to fine tune gene expression, it is likely that an increased level of methylation leads to altered expression, which may contribute to the development of the disease. Whether this is so, should we answer the research of the next few years?

### Treatment of psoriasis: Radium jelly, phototherapy and antibodies

Arsenic-based drugs are the first recognized remedy for psoriasis. At the end of the 18th and the beginning of the 19th century, the Englishman Thomas Girdlestone (Thomas Girdlestone) used arsenic for a wide variety of skin diseases and, like any respected scientist, summarized his experience in a journal publication. From that time until the mid-20th century, preparations of this toxic chemical element were used by doctors to treat psoriasis. Mercury and skin irritating substance chrysarobin were also popular. The latter was obtained from the core of the tree of the Araroba and used to treat many skin diseases. Later, expensive chrysarobin was replaced with cheaper and anthralin synthesized commercially [9].

At the beginning of the 20th century, X-ray radiation, the most advanced at that time, joined these excellent methods of treatment. Radiotherapy sessions were performed on the affected skin, and some doctors irradiated the thymus region, an organ critical for the development of T-lymphocytes. A number of experts described the improvement in half of the patients who received this treatment. Furthermore: Maria and Pierre Curie received purified radium. Masters from among the doctors began to use it in the treatment of many diseases, including psoriasis. Fortunately for patients, radium was expensive, and not everyone was able to experience for itself its "life-giving" effect. Unlike Marie Curie. She died of aplastic anemia caused by excessive exposure. It is known that one doctor made radium jelly on the basis of radium bromide and gelatin and placed it on the skin of patients suffering from psoriasis.

Excellent results were reported, but subsequent generations of doctors didn't want to check them. Most likely, the improvements were due to the fact that ionizing radiation damaged fast-growing cells in plaques, which led to their death and the disappearance of the plaque itself.

In the 50s of the 20th century, a breakthrough in the treatment of psoriasis occurred, and this whole set of extreme methods of treatment began to gradually disappear. Synthetic retinoids appeared - substances whose molecules are similar to vitamin A. Doctors and scientists from different countries noticed that when taking high doses of vitamin A patients could have desquamation of the epithelium, that is, the skin, roughly speaking, went off in layers. Vitamin A accelerates the division of epithelial cells and prevents their keratinization - the production of large amounts of keratin. This effect was a sin not to use in the treatment of psoriasis. As in the case of radiation, rapidly dividing cells of the epidermis were targeted. The use of vitamin A itself did not bring the expected result, but various substances structurally similar to it (egretinat, for example) reached the goal. They were taken in the form of capsules, but the drugs often gave unpleasant side effects

(thinning and flaking of healthy skin, brittle nails and hair), so they did not take root in widespread practice. In modern dermatology for the treatment of severe, common forms of psoriasis is used such a representative class of retinoids, as acitretin. Under its influence, the processes of differentiation and keratinization of the skin are normalized [10].

Another "vitamin" drug for the treatment of psoriasis is calcipotriol, a structural analogue of vitamin D. It is applied topically, in the form of ointments. Calcipotriol inhibits the proliferation of keratinocytes in the plaque, and also reduces the level of interleukins 1 and 6 that activate T-lymphocytes.

In the 20th century, powerful weapons appeared in the arsenal of doctors - hormonal substances for local (dermal) use-corticosteroids. They have not lost relevance so far: they are widely used for the local treatment of mild forms of psoriasis, in which the area of the lesion is small. This group of drugs includes betamethasone and prednisone. Ointments and creams based on them are applied to plaques. The effect is achieved due to the effect of corticosteroids on the most diverse parts of the inflammatory process: first, the formation of inflammatory mediators, leukotrienes and prostaglandins, are suppressed; secondly, the activity of T-lymphocytes, the cells that trigger plaque formation, is reduced; thirdly, cell membranes are stabilized, which reduces the release of cytokines. There are ointments containing both glucocorticosteroids and structural analogs of vitamin D. In severe forms of psoriasis, glucocorticoids can be used systemically - in the form of tablets and injections - but in this case they often cause side effects. In addition, systemic use necessitates a gradual increase in the dosage of the drug in the future [11].

Since the immune component is so important in the pathogenesis of psoriasis, immunosuppressive substances are used to treat it. Since 1972, dermatologists have used the drug methotrexate for the treatment of psoriasis in the USA, and since 1997-cyclosporine. Their effect on immunity is not as great as with the administration of glucocorticoids inside. However, the action of drugs is enough to provoke pronounced immunodeficiency in some patients. Due to the powerful effect, immunosuppressants are used only in severe forms of psoriasis.

In addition to medicinal methods of treatment, various types of phototherapy are used for psoriasis. Doctors use ultraviolet light with a wavelength of 280 to 320 nm as an independent method of treatment. Since antiquity, people have known that exposure to the sun improves the course of a number of dermatological diseases, up to a complete cleansing of the skin from rashes. And then there were technologies that allow generating the "useful" part of the spectrum of sunlight - ultraviolet. Currently, in the dermatological offices use a variety of ultraviolet lamps that allow you to be treated without going to the hospital. Irradiation of individual psoriatic plaques with a laser can also be considered as phototherapy.

Popular now and PUVA-therapy - the combined use of a photosensitizing drug (psoralen) and ultraviolet rays with a wavelength from 320 to 400 nm. Psoralen is applied to plaques or taken in pill form. It increases the sensitivity of the skin to ultraviolet radiation and improves the effectiveness of phototherapy. PUVA therapy is effective, but, in addition to some adverse reactions, it can cause a number of unpleasant consequences. First, the risk of developing skin cancer increases, and the threat of tumors does not disappear after the completion of therapy but persists for a lifetime. Secondly, in the intervals between procedures it is necessary to protect

the eyes from sunlight. Third, the skin ages faster. One of the variants of this type of treatment is RePUVA-therapy - PUVA-therapy, supplemented with the use of retinoids.

The introduction of monoclonal antibodies into clinical practice is considered to be a great breakthrough in antipsoriatic therapy. This is the most effective treatment for psoriasis today. Among the drugs are adalimumab, golimumab, ustekinumab and infliximab. They are administered by courses in the form of subcutaneous or intravenous injections and are especially indicated when skin psoriasis is combined with specific joint damage (psoriatic arthritis). These drugs act differently, but what is common is that they are antibodies "targeted" to specific cytokines or other proteins. For example, Ustekinumab achieves a therapeutic effect due to the selective blocking of interleukins 12 and 23, and adalimumab - TNF- $\alpha$ . These drugs are very effective against psoriasis, and their targeted effect on the psoriatic process reduces the number of possible side effects.

### How to live with psoriasis?

Usually the disease does not make our life better, and psoriasis is no exception. In each case, the treatment should be chosen by a qualified doctor, and it should be carried out under his control. The PASI (Psoriasis Area and Severity Index) index of the coverage and severity of psoriasis is used to monitor the effectiveness of therapy by doctors.

About 80% of patients indicate that psoriasis adversely affected their work and personal life. Often patients are ashamed of their appearance, they have signs of depression. There are various drugs that can overcome the disease, but often we want to take control of the disease ourselves and take part in its treatment. This approach makes many of us feel better. To do this, there are several ways associated with lifestyle changes [12].

- Avoid alcohol and smoking. Both of these factors disrupt the patient's immune status, leading to deterioration during the course of the disease.
- Achieve weight loss if it is elevated. Obesity also leads to impaired immunity. Reducing the weight is a beneficial effect on the course of psoriasis.
- Consult a psychotherapist or psychologist to work on problems in your personal and professional life. Often, emotional stress leads to worsening of the course of psoriasis. Learning to resist the difficulties of life, finding a way out of difficult situations will help to cope with exacerbations of the disease.
- In order to prevent exacerbations; be examined by a dentist and ENT doctor to exclude foci of chronic infection, the periodic exacerbation of which may aggravate the course of psoriasis.

- Use natural healing methods. The use of phototherapy for psoriasis is based on the beneficial effects of ultraviolet radiation on the skin. You will not believe, but right above our heads there is an excellent source of ultraviolet radiation. Take a trip to the sea, swim and sunbathe - the methods of balneotherapy for this disease are shown. Salt water combined with the sun helps a lot. You can also try applying a different mud, but here you need to consult with your doctor.

### Conclusion

Now doctors have modern and safe drugs that are ready to help patients in the fight against psoriasis. Constantly conducted research on the development of new drugs, and I want to believe that the victory over this disease is not far off [11].

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