

Brief History of Psoriasis

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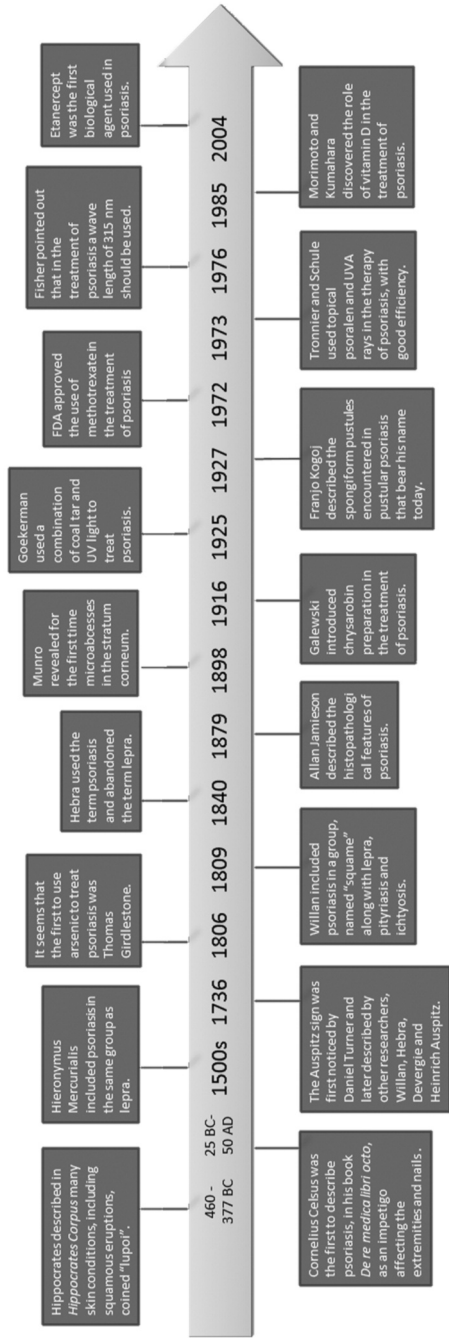
Introduction

PSORIASIS IS an ancient disease with a history that goes back more than 2,000 years (Figure 1). In recent years many discoveries have been achieved, but there are still many gaps in understanding the pathogenesis of psoriasis (Menter 2010). Psoriasis is a chronic inflammatory condition, affecting 2% of the population worldwide, characterized by cutaneous eruptions of red plaques covered by whitish scales. Over time, various speculations have been made on its etiology and many hypotheses were postulated; however, to this day, the etiology of psoriasis is still not fully understood. Present knowledge ascertains that psoriasis is a multifactorial disease with an important genetic determinism, modulated by various environmental factors (Fitzpatrick et al. 2008). In the past, individuals with psoriasis were stigmatized, as it was thought that psoriasis was a contagious disease, being mistaken for leprosy for a long time. However, today psoriasis lesions still remain associated with an important emotional and social impact on patients' quality of life (Menter 2010).

2. First Remarks about Psoriasis

THE EARLIEST writings regarding cutaneous diseases date from ancient times, appearing first in the Egyptian literature, then in Greek, Roman and Arabic literatures. In the Ebers Papyrus, a document dating from the 16th century BC, skin conditions were mostly included in the general medicine. The scholars were focused on methods to cure itching, but cosmetics represented also a concern at that time. The denominations assigned to various skin diseases were not always adequate, constantly leading to subsequent confusion. In the Bible, leprosy was often mentioned, but further studies showed that, in most cases, the described disease was in fact psoriasis; moreover, studies on Egyptian mummies dating from that time found no signs of leprosy (McCaw 1944). In the Bible we can find a disease under the name of "zaraath," which seems to be either psoriasis or leprosy (Gruber et al. 2004); it was thought that Moses and his sister Miriam might have had leprosy, but further research established that the cutaneous lesions they presented were more likely due to psoriasis or a fungal infection (Liddell 2006).

Timeline – History of psoriasis



At that time leprosy was the main disease associated with stigmatization. The individuals with leprosy were marginalized and were forced to wear a bell as a distinctive sign. In fact, probably most of these people had psoriasis. There was a confusion regarding the terminology. In Greek, leprosy was called “*elephantiasis grecorum*,” but later on, when the Arabic literature was translated into Latin, “*elephantiasis grecorum*” was mistaken for “*lepra grecorum*”. In fact, *lepra* was a squamous disease, meaning the same thing as psoriasis. The confusion regarding the terminology continued for a long time; the writings of the 18th century indicate the persistence of these mistakes in the terminology used (Baker 2008).

In Antiquity, the Greeks classified dermatological diseases into three groups: *psora*, *lepra* and *leichen*. *Psora* meant itch, *lepra* included the squamous diseases and *leichen* was related to tuberculous disorders (Ritchlin and FitzGerald 2007, Cowden and van Voorhees 2008).

Hippocrates (460–377 BC) described in *Hippocrates Corpus* many skin conditions, including squamous eruptions, coined “*lupoi*”. He mentioned the occurrence of cutaneous lesions as happening after an episode of sore throat, suggestive for guttate psoriasis (Baker 2008). In the first century AD, Cornelius Celsus (25 BC–50 AD) was the first to describe psoriasis, in his book *De re medica libri octo*, as an impetigo affecting the extremities and nails (Brajac and Gruber 2012). Galen (133–200 AD) defined a pruritic condition located on the eyelids and scrotum, which was originally called psoriasis. However, what Galen described as psoriasis was in fact seborrheic dermatitis (Baker 2008). The Greeks used the term “*psora*” for two disorders: ulcerated psora, characterized by pustular lesions resulting in ulceration, considered contagious, and simply psora, represented by squamous-crusted lesions (Willan 1809).

3. Various Classifications of Psoriasis

MANY CLASSIFICATIONS of skin diseases were established, in most cases according to their similar features. By the 1500s, Hieronymus Mercurialis included psoriasis in the same group as *lepra vulgaris* (Brajac and Gruber 2012). Daniel Turner (1667–1741), in his book *De morbis cutaneis*, wrote that psora was a pruritic eruption made of pustules meaning the same as scabies (Turner 1712). In literature psoriasis was also found under the name of *scabiei sicca*. In Arabic writings, psoriasis, lichen and *lepra grecorum* pertain to the same class, Alkouba (Willan 1809).

Robert Willan (1757–1812), considered the founder of modern dermatology, defined the dermatological elementary lesions, as we know them today. He had an important role in the understanding of psoriasis in the 19th century. Thomas Bateman, Willan’s student, continued his observations. According to the elementary lesions seen in various diseases, Willan classified dermatological disorders into eight groups. Psoriasis was included in the second group, named “*squame*,” along with *lepra vulgaris*, pityriasis and ichthyosis and was also called dry or scaly tetter. Willan presented *lepra vulgaris* and psoriasis as two distinctive diseases. He stressed the differences between the two diseases (Willan 1809, Menter 2010).

By 1800s, Jean Louis Alibert (1768-1837), a famous French dermatologist, devised a classification of cutaneous diseases which comprised psoriasis and leprosy in the dartrous dermatoses group (Gruber et al. 2004). Pierre François Olive Rayer (1793–1867) asserted in his book that the darte furfuracee described by Alibert was in fact psoriasis and darte squamous lichenoid was psoriasis inveterata. Rayer agreed with Willan's concept and defined leprosy and psoriasis as two distinctive entities, although Plumbe and Duffin had an opposite point of view, considering that psoriasis and lepra vulgaris are one and the same disease (Rayer 1833).

In 1840 Ferdinand von Hebra (1806-1880) established a new classification of dermatological diseases based on their histopathological appearance (Baker 2008). Hebra used the term psoriasis and abandoned the term lepra vulgaris, considering that the two conditions described by Willan are the same (Menter 2010, Nicolas and Thivolet 1997). Moritz Kaposi continued his research (Brajac and Gruber 2012). The term psoriasis was included by Fox and Wilson in their writings, but in 1872 Milton suggested the exclusion of this term (Menter 2010, Ritchlin and FitzGerald 2007).

4. Clinical Perception and Histopathological Aspects of Psoriasis

WILLAN CONSIDERED that the distribution and form of the lesions differentiate lepra vulgaris from psoriasis (Willan 1809). Unlike lepra vulgaris, psoriasis lesions did not display elevated borders and peripheral inflammation; lepra vulgaris was characterized by circular patches. Willan described many forms of psoriasis: guttata, diffusa, gyrata, palmaria, labialis, ophtalmica, preputti, scrotalis, unguium, infantilis and inveterata. Psoriasis guttata was more frequent in the spring; before the eruption the patient complained of generalized pain and fever. The disease developed more rapidly in children. Psoriasis diffusa was characterized by pruritic erythematous, ill-defined lesions with fine scales, commonly occurring on the ears, face, back and hands. It was accompanied by malaise, gastralgia, and a skin burning sensation. Psoriasis inveterata was the most severe form, involving the whole body excepting the face (Bateman 1813).

Bateman noticed the involvement of the nails in psoriasis; the nails were thickened, opaque and yellow. Edward Beck (1834) described the psoriatic lesions as painful, itchy, accompanied by locally increased temperature (Beck 1834). In 1853, Romberg described psoriasis lavatricum, in washerwomen (Purdon 1875). In 1878 in the *British Medical Journal*, in an article dedicated to psoriasis, the authors considered that psoriasis might appear at any age, but not in infants. At the end of the 19th century, Radcliffe Crocker defined pustular psoriasis. The forms of pustular psoriasis were subsequently described by Hallopeau (1890), von Zumbusch (1910) and Barber (1927) (Nicolas and Thivolet 1997). In 1930 Barber and Ingram characterized pustular psoriasis considering that there was a link between eczematous reaction and psoriasis, the abscesses of Munro turning into sterile pustules (Ingram 1954).

The Auspitz sign was first noticed in 1736 by Daniel Turner and later described by other researchers, Willan, Hebra, Devergie and Heinrich Auspitz. The sign bears the

name of Heinrich Auspitz (1835-1836), who was the student of Hebra (Sattigeri 2013). The Kobner sign was described by Heinrich Kobner. He noticed the occurrence of psoriatic lesions in association with horse hits, tattoos and excoriations. His observation was disclosed in 1872, at the conference of the Silesian Society for National Culture (Mohan 2004). In 1926 Woronoff described the rings around psoriatic lesions that bear his name today (Burg and Geiges 2014).

In 1879 Allan Jamieson described the histopathological features of psoriasis. He noticed the presence of nuclei in the corneous layer of the epidermis (parakeratosis). He considered that the rete Malpighi plays an important role in the pathogenesis of psoriasis (Baker 2008). Regarding the histopathological findings noted in psoriasis, Hebra described the presence of cellular infiltrate around the vessels, edema and changes in the rete mucosum. In 1878 Robinson published a detailed description of histopathological findings that occur in psoriasis, highlighting characteristics such as dilation of blood vessels, thickening of malpighian layer and enlargement of dermal papillae (Cumming 1878, Thin 1881, Burgess 1934). With regard to the involvement of skin layers in psoriasis, some authors (Munro, Montgomery) believed that the disease had its origin in the epidermis. On the other hand Hebra advocated its dermal origin (Ingram 1954).

Psoriasis was considered an inflammatory disease with cellular hyperplasia, dilated papillae and vessels (Purdon 1875). Rayer defined inflammation as that phenomenon based on the accumulation of blood in a region followed subsequently by healing, desquamation, ulceration, induration or other changes (Rayer 1833). In 1898 Munro revealed for the first time microabscesses in the stratum corneum. However, in 1895, L. Kopytowski had already observed what Munro described later (Don Friday 1979). In 1927 Franjo Kogoj described the spongiform pustules encountered in pustular psoriasis that bear his name today (Brajac and Gruber 2012).

5. The Etiology of Psoriasis – A Dilemma throughout History

THE ETIOLOGY of psoriasis has been the object of concern. Over time many factors which seemed to be involved in the etiology of psoriasis were discussed. Therefore, many theories were formulated.

5.1. Psoriasis – An Internal Disease

IN THE 19th century, many authors agreed that psoriasis was an internal disease (Bateman 1813). They believed that there was an association between gastrointestinal disorders and psoriasis (Beck 1834). Gout, rheumatic disorders, gastritis, dyspepsia, and lactation were advocated as contributing factors in the pathogenesis of psoriasis (Nicolas and Thivolet 1997). Considering that it is a disease with an internal origin, scientists analyzed the urine of patients with psoriasis and identified sulphate and phosphate in urine samples (Purdon 1875). Willan and Bateman also observed that the course of the disease was influenced by the climate, occurring especially in spring and worsening in winter (Bateman 1813). Contributing factors in the pathology of psoriasis were considered the warming-up

that comes after physical exercise, cold weather, diet errors, certain types of food (crude vegetables, citrus, vinegar) and a melancholic personality (Bateman 1813, Beck 1834).

Hebra issued a new theory regarding the origin of psoriasis. He said that the development of psoriasis is not based on internal conditions, but on external factors. He noted that patients with psoriasis are healthy individuals without any other disorders and psoriasis lesions are a consequence of external aggression on the skin. The theories stated by Willan and later by Bateman, regarding the role of climate and geographic area in the appearance of psoriasis, are not accepted by Hebra (Baker 2008). At the middle of the 20th century the idea was preserved that psoriasis had an unfavorable evolution in winter and a better one in summer, which is true to this day (Ingram 1953).

5.2. A Hereditary Component in the Etiology of Psoriasis

THE ORIGIN of psoriasis was unknown, but a hereditary factor was suspected (Bateman 1836). Although it was long thought that psoriasis is a hereditary disorder, Knowles believed that this theory was not true and he stated that in a family there was rarely more than one person suffering from psoriasis. Subsequent opinions were divided. Engman and Pusey embraced the idea of heredity, while Stelwagon explained that the occurrence of many cases of psoriasis in the same family was due to a parasitic infection (Schall 1936). In 1945, Romanus conducted a detailed study which demonstrated the presence of a hereditary component in psoriasis; he revealed the risk of a child developing psoriasis if its parents or grandparents had been affected by psoriasis (Ingram 1954).

5.3. Psoriasis – An Infectious Disease

MANY RESEARCHERS tried to emphasize the role of an infectious agent in the etiology of psoriasis. In 1878, Lang observed in psoriatic scales something that seemed to be a parasite, an epidermophyton. Later studies showed that in fact there were artifacts provided by granules from the cell cytoplasm. In that period many microbial agents were isolated and it was supposed that they played a role in the onset of psoriasis. The concept of an infectious origin was also connected with vaccination (Baker 2008). Beck believed that vaccination was involved in the development of the disease and that it was rarely hereditary. Since ancient times, doctors had supposed there was a link between psoriasis guttate and infections. Hippocrates described the appearance of psoriatic lesions after a sore throat, suggesting guttate psoriasis (Beck 1834). J. Heaney, in 1927, supported the parasitic theory with many arguments, although a microorganism was not detected. Among his arguments, he included the efficacy of antiparasitic medication in the treatment of psoriasis (Heaney 1927). It was also believed that psoriasis was the consequence of syphilis infection. Erasmus Wilson was a proponent of this theory (Burgess 1934).

5.4. The Impact of the Psychological Status in Psoriasis

THE SIGNIFICANCE of psychological factors has been studied since ancient times (Squire 1873). Studies have shown that in 1700 BC, the prince of Persia had psoriasis and his doctor attributed it to his anxiety. In 1891 Brocq and Jacquet advocated that the psychological status and skin lesions were interconnected and defined the concept of neurodermatitis. Today there are numerous studies which attest the role of psychological factors in the onset of psoriasis (Barber 1950, Brufau et al. 2012).

5.5. The Role of Endocrine Dysfunctions in Psoriasis

IN THE early 20th century, some researchers revealed a link between psoriasis and adrenal gland hypofunction. Gruneberg stated that the administration of pituitary corticotropic hormone and cortin resulted in improvements in psoriatic lesions, especially in arthropathic psoriasis (Barber 1950). Byrom Bramwell considered that patients with psoriasis had a deficient activity of the thyroid gland (Baker 2008). Another theory linked psoriasis with the presence of alterations in lipid metabolism (Orr 1937, Ingram 1938).

5.6. Allergies and Psoriasis

IN 1950 Barber suggested the association of psoriasis with food allergies. He illustrated two cases, in which eliminating cow's milk from the diet resulted in the improvement or even the healing of psoriatic lesions (Barber 1930). Meinicki and Ryll-Nardzewski observed that one third of the patients with psoriasis developed a focal reaction in the lesions after the inoculation of staphylococcus vaccine. But this theory was not accepted by other scientists, who considered that it was just a reaction to a foreign body (Orr 1937).

6. Treatment of Psoriasis from Ancient Times to This Day

THE TREATMENT of psoriasis over time underwent many improvements. Therapeutic options progressed from tar baths to biological treatment. Over time it was noticed that when psoriasis patients were treated for various other disorders which affected them, there was also an improvement in their psoriasis lesions. Hence many of the treatments applied in psoriasis were discovered by chance.

First, the treatment was given internally because psoriasis was considered an internal disease. Bleeding, purgatives and diuretics were the methods traditionally used. Subsequently the topical treatment began to gain a more important role (Brajac and Gruber 2012).

Naaman, the captain of the army in Syria, was bathed in the Jordan River to cure zaraath. Later many scholars had different opinions regarding this; Russell considered that the illness involved was psoriasis while Hebra thought it was scabies. Treatment options were extremely diverse (Ritchlin and FitzGerald 2007). In the Ebers Papyrus the treatment with excrements from dogs and cats was indicated (Burg and Geiges 2014). Galen recommended the treatment with broth in which a viper had been boiled (Baker 2008).

6.1. Therapy in the 19th Century

IT SEEMS that the first to use arsenic to treat psoriasis was Thomas Girdlestone, in 1806. He used Fowler's solution with 1% arsenic, a solution made by the pharmacist Fowler in 1780. In 1809 arsenic was introduced in Pharmacopeia of the Royal College of Physicians of London (Orr 1937, Baker 2008). However, arsenic was found to be a therapy with multiple side effects. Patients treated with arsenic developed skin cancers and neoplasms of the internal organs, keratoses, hyperpigmentations, conjunctivitis and gastrointestinal disorders (Gruber et al. 2004). Based on studies conducted by Lipp, in 1869, subcutaneous injections with arsenic were possible (Brajac and Gruber 2012).

Willan individualized the treatment somewhat, in accordance with the type of psoriasis. For psoriasis guttata, diffusa and gyrata he recommended ipecacuanha with antiemetic effect and calomel granules. The patient should follow a diet; avoid citrus fruit and alcoholic drinks. He stressed the importance of treating digestive disorders. In psoriasis inveterata he administered plants such as bark of mezereon root. For palmar psoriasis, ointed silk gloves were used day and night. Hot baths and baths with water gruel, and antimonials were used in children (Willan 1809). Bloodletting proved efficient in the cases of psoriasis guttata with early onset in adults and children. In psoriasis diffusa repeated bleedings near the inflammatory areas were recommended, combined with “fresh emollient narcotic tepid baths”. Other therapeutic options were sulphur baths and frictions with stibial ointment (Rayer 1812). At that time baths and emollients were useful for detaching scales.

Wood tars were discovered by the Vikings and were used as a therapeutic agent since 800-1000 AD (Levell and Peters 2011). Tars have also been used in the treatment of psoriasis since ancient times. In his writings Hippocrates refers to wood tars (Gruber 2004). In 700 AD Paulus Aegineta described in his book the treatment with liquid pitch for leprosy and psora. Sir Admiral Francis Beaufort suffered from psoriasis and used tar for his lesions, which resulted in partial healing. Later on he was cured in Gibraltar, when he exposed his skin to sunlight (Levell and Peters 2011). Tars were used in creams, ointments or baths, but they had an irritant effect (Champion 1966, Gruber 2004).

In 1834 Beck highlighted the usefulness of occlusive dressings. Another therapy involved administering products based on precipitate sulphur and camphor, with good results (Beck 1834). He reported the case of a 40 years-old patient, who suffered from psoriasis diffusa and was treated with ointments containing precipitate sulphur and camphor and the lesions resolved. In 1840, the therapy for psoriasis also included Plummer’s pills and hydrargyrum, but their efficiency was poor. The administration of pitch had a superior effect (Toogood 1840).

Hebra used a preparation known as “spiritus saponis alkalinus” which contained potash soap, alcohol and lavender. After applying the preparation to the lesions the patient had to keep the same underwear on for several days. A longer contact was necessary. Various plants were also used in the treatment (oleum rusci, oleum coniferi, oleum fagi, etc.) (Cumming 1878).

Byrom Bramwell (1847-1931) was the initiator of the therapy using thyroid extract in psoriasis. He formulated the hypothesis that the patient with psoriasis had a thyroid dysfunction (Baker 2008). Thyroid extract served as a therapeutic option. During the 1890s a number of psoriasis cases treated with thyroid extract were described in the medical literature. In patients who failed to achieve results, arsenic was associated to the treatment (Gordon 1894, Auld 1894). Radcliffe Crocker (1846-1909) believed that salicylates represented a therapeutic option in psoriasis, especially when the administration of arsenic was inappropriate and the thyroid extract worsened the disease. Salicylates were used mainly for acute psoriasis guttata. They did not seem to be effective in patients with chronic psoriasis. It was thought that salicylates had an antimicrobial effect (Baker 2008).

There were reports about patients suffering from both syphilis and psoriasis, who experienced an improvement in their psoriatic lesions while being treated with mercury for their syphilis. Mapother mentioned that he considered psoriasis an “atavistic

manifestation” of syphilis and treated the patients with mercury. Mercury had a diuretic and purgative effect (Mapother 1891).

Often, treatments which were given for other diseases to patients with psoriasis were found to be useful to cure psoriasis. In 1878, a patient of Dr. Squire Balmanno used Goa powder for a fungal infection, which resulted in the improvement of the lesions which were in fact of psoriasis. Goa powder contained ditrhanol extracted from a tree that grows in Brasil, called the araroba tree. Later it was revealed that the active ingredient in the powder was chrysarobin, the precursor of anthralin, the first synthetic drug used in psoriasis. In 1916 Galewski introduced this preparation in the treatment of psoriasis. Chrysarobin was toxic, tolerated with difficulty by patients, and expensive (Cameron and Van Voorhees 2014, Coondoo and Sengupta 2015).

6.2. Therapy in the 20th Century

AT THE turn of the century, the patients were bathed in a solution obtained by mixing 90 liters of water and 114 ml of coal tar solution. The procedure lasted ten minutes. Then they used a mercury vapor lamp; the exposure lasted 30 seconds initially from a distance of 0.9 meters. The exposure time increased gradually. This therapy had to be practiced daily. Then a paste containing salicylic acid, zinc oxide and starch was applied to the lesions and the patient was covered with stockinet dressing. That dressing was worn by the patient until the next day. This was considered the first line of treatment, which was efficient in most cases (Ingram 1938, Ingram 1953). The second line of treatment was represented by anthralin (Ingram 1953). Ingram suggested the combination of anthralin with salicylic acid, zinc oxide and UV rays. This treatment formula was used for many years in Europe (Cameron and Van Voorhees 2014).

At that time many remedies for psoriasis were speculated upon. It was known that the skin of psoriasis patients had an acid pH, therefore alkaline baths were helpful. The protein-free diet proposed by Schamberg was also recommended in psoriasis. Another method of treatment was represented by injections with sterile milk (Orr 1937). Danysz believed that psoriasis developed as a result of an exaggerated immune response, a phenomenon that occurs in asthma or urticaria. He also thought that psoriasis was associated with an anaphylactic status. His method consisted in the oral administration of bacterial proteins derived from fecal cultures (Barber 1921). In 1930, Campbell and Frost proposed as treatment for psoriasis injections with a 10% suspension of the scales obtained from the patients with psoriasis. The method was later abandoned (Burgess 1934).

The role of the sun in the treatment of dermatological diseases has been observed since ancient times. The first centers for hydrotherapy were set up at the beginning of 20th century in Italy and England (Stašić et al. 2004). Goekerman noted that combining sunlight with a topical photosensitizer increased the effectiveness of the treatment. Starting from his observations, in 1925 he used a combination of coal tar and UV light to treat psoriasis. There were studies regarding the wavelength of UVB rays used in psoriasis therapy. Hence in 1976 Fisher pointed out that in the treatment of psoriasis a wavelength of 315 nm should be used. Niels Finsen (1860-1904) was the first to use an artificial light source in the therapy of a dermatological disorder, lupus vulgaris. His discovery was established on a lamp based on electric carbon arcs (Kostović and Pašić 2004, Grzybowski and Pietrzak 2012).

Towards the middle of the 20th century, corticotherapy began to be used in several skin diseases. Topical corticosteroid therapy was found to be very useful in the treatment of psoriasis (Cameron and Van Voorhees 2014).

Gubner administered aminopterin, a drug discovered by Farber in 1946, to a patient diagnosed with rheumatoid arthritis. During the administration of aminopterin, the psoriatic lesions of which the patient also suffered were alleviated. Methotrexate is a derivative molecule of aminopterin with fewer side effects (Cameron and Van Voorhees 2014). In 1972, about 20 years after its discovery, the FDA approved the use of methotrexate in the treatment of psoriasis (Cowden and van Voorhees 2008).

The introduction of retinoids in dermatological practice was not initially an effective therapeutic option for psoriasis (Cowden and van Voorhees 2008). Isotretinoin was synthesized in 1955 and used in the treatment of psoriasis without satisfactory results. With the development of the second generation of retinoids an increased efficacy was noticed in the treatment of psoriasis. Third generation retinoids offered the chance for patients with psoriasis to achieve a better healing of their lesions (Cowden and van Voorhees 2008, Chapman 2012). Another molecule used to cure psoriasis is cyclosporine. Jean Francois Borel obtained cyclosporine in 1970 and later in 1990 it was approved in the treatment of psoriasis (Colombo and Di Pietro 2012).

In 1973, Tronnier and Schule, used topical psoralen and UVA rays in the therapy of psoriasis, with good efficiency (Brajac and Gruber 2012). A study conducted in 1974 showed the usefulness of oral methosalen followed by the administration of long wave ultraviolet. In addition it was observed that this combination had greater efficacy than ultraviolet alone. The mechanism of action is based on the inhibition of DNA synthesis in the epidermis (Parrish et al. 1974).

In 1985 Morimoto and Kumahara discovered the role of vitamin D in the treatment of psoriasis. The discovery was accidental. They noticed the improvement of the condition of psoriatic lesions in a patient who was treated with 1 alpha hydroxyl vitamin D for osteoporosis (Coondoo and Sengupta 2015).

6.3. Therapy Today

THE DEVELOPMENT of biological therapy led to dramatic improvements in the treatment of patients with psoriasis. These drugs work against specific mediators involved in the pathogenesis of psoriasis (Coondoo A and Sengupta 2015). Over time, many biological agents have been introduced to treat psoriasis.

Etanercept, approved for use in psoriasis in 2004, was the first biological agent used in psoriasis. It is a fusion protein produced by genetic engineering, which combines the constant region of IgG, the Fc fragment, comprising the CH2 and CH3 constant regions, with two TNF type II receptors (Constantin et al. 2014). Etanercept binds soluble TNF α and TNF β . Two years later, Infliximab was approved in the therapy of psoriasis. Infliximab is a chimeric monoclonal antibody produced by recombinant DNA technology containing a human constant region and a variable murine region, which binds both soluble and transmembrane TNE. This complex leads to complement fixation and

activation, resulting in the induction of antibody mediated cytotoxicity (Mustafa et al. 2013).

Adalimumab is a human monoclonal antibody anti-TNF α , with a mechanism of action that is similar to that of Infliximab, which was introduced in the treatment of psoriasis in 2008 (Tracey et al. 2008). Ustekinumab, recently introduced in the treatment of psoriasis (2009), is a human monoclonal antibody that specifically binds the p40 subunit of IL-12 and IL-23 (Campa et al. 2015). Therefore, blocking the action of IL-12 and IL-23, ustekinumab is involved in the pathogenic mechanism of psoriasis plaque development, reducing neutrophil chemotaxis, angiogenesis, and inhibiting keratinocyte proliferation (Fitch et al. 2007).

Recent studies have highlighted the role of IL 17 in the pathogenesis of psoriasis and the utility of IL17 inhibitors in therapy. Secukinumab, Ixekizumab, Brodalumab, IL 17 inhibitors, have proven effective in various clinical trials (Gooderham et al. 2015). Other studies about inhibitors of IL-23 are underway. Tildrakizumab is a humanized monoclonal antibody targeting IL 23 p19 subunit (Reichert 2013).

In recent years there have been great advances in the management of psoriasis. Traditional therapies are increasingly replaced by more modern therapies with specific mechanisms of action, targeting mediators involved in the maintenance of the psoriasis plaques (Winterfield et al. 2005).

7. A Brief History of Psoriatic Arthritis

IN 1860, Pierre Bazin originally used the name “psoriasis artritique,” the term referring to a type of psoriasis. Psoriatic arthritis was first described in 1918 by Jean Louis Alibert. There is no accurate data about the first cases of psoriatic arthritis. In 1992 Ronald mentioned the discovery of a pelvis and some vertebrae in an ossuary in Israel dating from 2000 years ago, which showed signs of seronegative arthritis (Pasero and Marson 2006, Ritchlin and FitzGerald 2007). A recent study, which analyzed skeletons dating from the 17th century, emphasized changes specific to psoriatic arthritis (erosions and deformities of the distal interphalangeal joints) (Hadjouis 2011). In his book, Bateman mentioned that patients with psoriasis could experience articular pains. In 1818, Alibert believed that there was a link between psoriasis and the joint pain of which patients complained. However the confusion between psoriasis and leprosy was still present, therefore Alibert in his paper wrote that articular changes were encountered in “leper squammeuse” (Moll 1984).

The concept that psoriasis is associated with arthritis was not embraced by all scientists of that time. For this reason Brocq, Margolis, Romanus and Gribble asserted that psoriatic arthritis was in fact a variant of reumathoid arthritis. It was only in 1964 that psoriatic arthritis was classified as a distinct entity (Ritchlin and FitzGerald 2007). The studies continued and concluded that psoriasis is associated with inflammatory arthritis (Moll 1984). In 1973 Moll and Wright classified and defined psoriatic arthritis (Ritchlin and FitzGerald 2007). During the 1900s some authors considered that streptococcal infection plays a role in the occurrence of psoriatic arthritis (Barber 1950).

8. Conclusions

THROUGHOUT HISTORY, we encounter significant confusion concerning the etiology and pathogenesis of psoriasis. It was only in the 19th century that psoriasis was defined as a separate entity and the distinction between psoriasis and leprosy was made, as the two skin conditions have been confused over time, hindering the progress in this medical field. Many discoveries regarding the treatments applied in psoriasis were serendipitous. Today, although the life of psoriasis patients has improved to a great extent, due to recent advances in understanding the pathology and the treatment of the disease, many things are waiting to be discovered. The question still remains: what does the future hold with respect to psoriasis?



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Abstract

Brief History of Psoriasis

Psoriasis is a common disease affecting people worldwide. Although many researchers have tried to understand, throughout history, the mechanisms involved in the pathogenesis of the disease and despite considerable progress that has been made, a plethora of key aspects are still waiting to be discovered. In the last 2,000 years, the treatment evolved from an empirical stage to the modern therapy oriented to targeting molecules shown to be involved in the occurrence of the disease. In this paper we are reviewing the great discoveries that have marked the history of psoriasis, as well as the latest advances in the treatment of the disease.

Keywords

psoriasis, history, etiology, therapy