

## Lepra vulgaris. History of Psoriasis

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### Abstract

**Background:** The history of psoriasis, remains highly speculative for the time before Willan (1757-1812), and can be reliably assigned only for the last 200 years. Terms such as "Leprosy", "Impetigo" and "Psora" have been used in the centuries before. Hebra (1806-1880) gave a morphological and nosologic definition, in which also the histopathology appearance was taken into account. In the early 20th century, it was the biochemistry and histochemistry, which provided new insights. In the second half of the 20th century, immunocytochemistry and immunology shed some light on the pathogenetic processes of the disease. At the end of the 20th and at the beginning of the 21st century, it is the triumph of genetics and immunology, which have opened new therapeutic possibilities due to the interesting insights into the pathogenesis of psoriasis. However besides the new therapeutic modalities, which harbor some health and some economic threats, classical approaches still remain valuable tools.

### Introduction

Psoriasis is one of the most common diagnoses in dermatology; therefore it is justified to provide some information on the historical background of this frequent disease.

One has to admit however, that talking about historical aspects of diseases and especially of dermatoses is always somehow speculative. It is clear, that most of the diseases we see today already existed 2000 and more years ago and one has to be aware of the fact, that legends and mystery easily melt into "history". The perception of the diseases in ancient time was rather religious or mysterious than scientific, as we see it today.

Much has been written about the history of psoriasis, which roughly can be divided into 3 periods, looking back 2000 years, 200 years and to the past 20 years.

The following citations characterize the challenge, which psoriasis imposed and still does on physicians and patients: *William James Erasmus Wilson* (1809 – 1884) stated «...it is not a disease, on which to build a medical reputation...» and *Paul Bechet*, New York (1936) pointed out that «Psoriasis is an antidote for dermatologists' ego. » (cited from [1])

There are several reviews, on the subject, which have been a major resource for this review article [2, 3, 4, 5, 6, 7].

### Ancient Times: Egypt, Greece and Rome

In Ancient Times diseases were deemed an individual punishment for blasphemous conduct of life or a consequence of low sanitation and hygiene. "Psoriasis" at that time like other diseases was an issue of ignorance, confusion of nomenclature and terminology

When looking 2 or 3'000 years back, religious texts sometimes may give interesting views or at least some arguments for speculations.

In one of the most famous documents conserved today, the *Ebers Papyrus* (around 1500 BC), do not mention Psoriasis but give some remedies for treating skin diseases in general.

*Hippocrates* (460-370 BC) refers to "impetigo" without specific mentioning of psoriasis even though he must have seen the disease.

*Aulus Cornelius Celsus* (25BC-50 AD), who probably was not a physician, but a roman encyclopedian, in his "De Re Medica Libri Octo" describes psoriasis, but calls it "impetigo".

The "Corpus Galenicum" was the basis for teaching and learning medicine over centuries. *Galen* (133-200) introduced the term «psoriasis» to designate diseases (scaling of eyelids and scrotum with erosions; seborrhoeic eczema?), entirely different from psoriasis.

### Medieval Ages from 6<sup>th</sup> till 15<sup>th</sup> Century

In the Medieval Ages (600 – 1500 AC), *Avicenna* (*Ibn Sina*) (980-1037) - a Persian physician, physicist, scientist and philosopher - was the most influential representative of Medieval medicine. His encyclopaedic Canon of Medicine, completed in 1025, comprises five books compiling the medical knowledge of the time. It is considered one of the most famous books in the history of medicine and it provided the basis for teaching and learning medicine not only in the orient but also in Europe. It also contains the first careful description of skin diseases. Avicenna very much followed *Galen*.

*Hildegard von Bingen* (1098 – 1179) was a in-subordinate Abbess and polymath ( music, natural sciences, medicine, theology). She

used to pass out if she wanted to pursue her aims against the opposition of the authorities. The medical treatise ascribed to *Hildegard* were *Causae et Curae* (causes and treatments) and *Physica*, in which she compiles the folk and monastic medicine of her time using herbs, stones and animals on the principle of contraries (*contraria contrariis curantur*) for the treatment of diseases [8].

She differentiates various types of "Lepra" (skin rashes, most probably including "psoriasis") caused either due to acoria and drunkenness or due to irascibility and "Lepra contagiosa sanabilis" due to lasciviousness.

The first universities and medical schools were founded in Europe in Salerno, Bologna, Montpellier, Paris and Oxford in the 12<sup>th</sup> and 13<sup>th</sup> century. Little attention was attributed to changes of the skin, which still at that time in the context of "humoral medicine" were thought to be just an "excretion organ" rather than the manifestation of diseases. Paintings from that time do not show specific skin lesions but just dots and spots on or within the skin

In "De morbis cutaneis, et omnibus corporis humani excrementis tractatus locupletissimi" (Venedig 1572) *Girolamo Hironymus Mercurialis* (1530-1606) classifies diseases of the skin according to their localisation [1] in the head and neck or [2] at other sides of the body. He paid little attention to morphology of the single lesions and described psoriasis under the name of "lepra grecorum" and for other conditions used the term "psora"(itch) [9].

The first ones to look for morphology of skin changes and probably showing psoriasis for the first time were artists, like *Ferdinand Bol*, a flamish painter, who in his work "The Director of the Lepra House in Amsterdam" depicted the social situation of a young boy showing his capillitium covered with dense white scales, which from a medical point of view today might be interpreted as psoriasis or rather as Favus (Figure 1) [10].

In summary, in the Middle Ages there was no scientific pathogenetic or morphologic perception of the disease, we refer to today as psoriasis and we should be cautious in over-interpreting descriptions from this time.



**Figure 1.** *Ferdinand Bol* (1616 – 1680). The Director of the Leprosy House in Amsterdam. Le Petit Palais, Paris. Lepra or Favus on the capillitium of a young boy

### The Beginning of Academic Dermatology in the 18<sup>th</sup> Century

*Josef Plenck* (1735-1807), was an Austrian surgeon and obstetrician. In his book “*Doctrina de Morbis Cutaneis*” (1776) [11] he classified 120 skin diseases into 14 classes based on the works of *Carl von Linné* (1707-1778) and *Francois Boissier de Sauvages de la Lacroix* (1707-1767). Some remarks in Class VI: *Lepra crustosa* and in Class VII about squamous diseases might refer to psoriasis, [11]

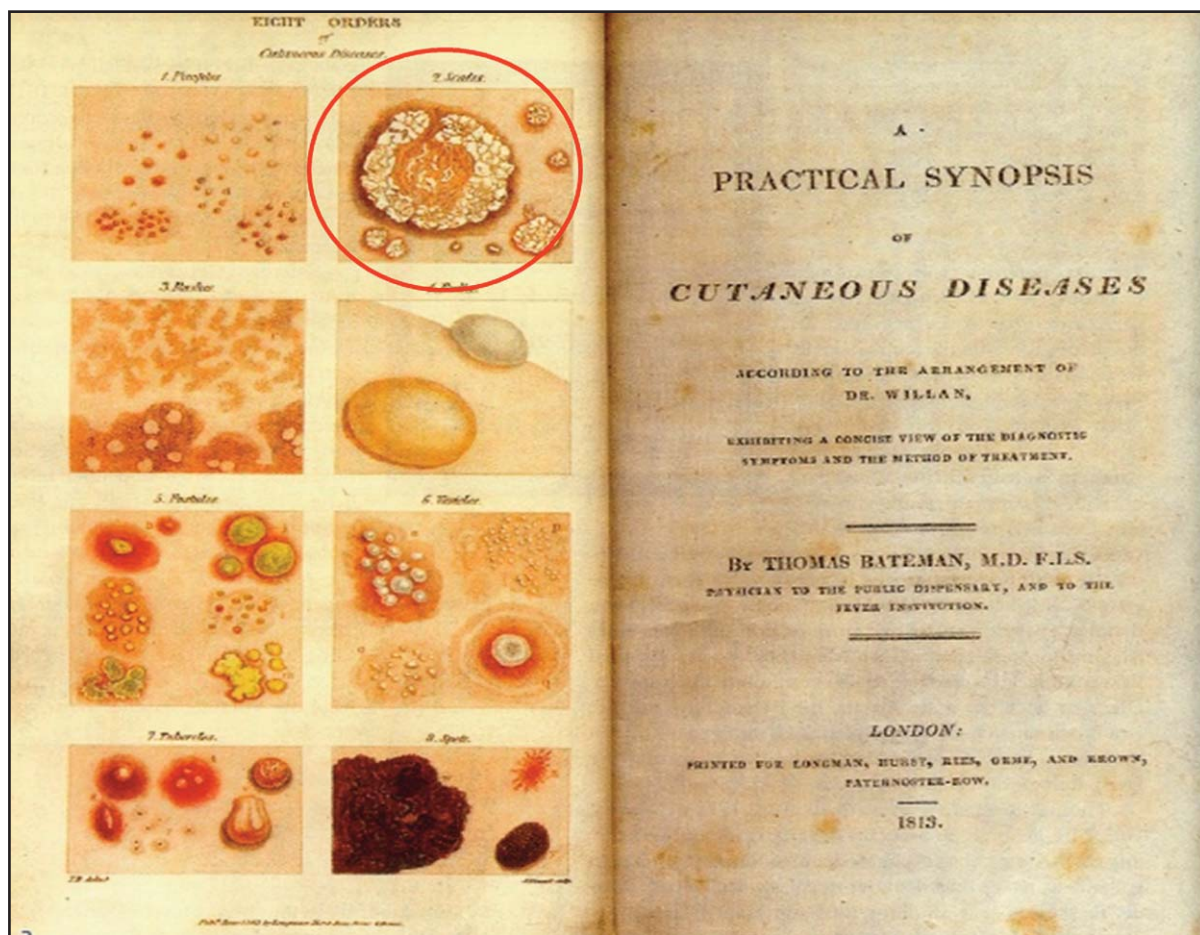
*Robert Willan's* (1757-1812) [12] improved the classification of skin disorders based on morphologic criteria of *Joseph Jakob Plenck* (1735-1807) [11]. The second of the 8 classes in his treatise dealt with “Scales” (Figure 2). He differentiated psoriasis from leprosy (*psora leprosa* and *lepra grecorum*) and described different forms of psoriasis: *guttata*, *diffusa*, *gyrata*, *palmaria*, *unguium*, *inveterata*. He also noticed that the disease begins

on the knees and elbows, attacks the scalp and also the finger and toe-nails [9]. In his book there we find the first medical painting of *lepra vulgaris* that can be identified as psoriasis. (Quelle: Willan, Robert: “*Description and Treatment of Cutaneous Diseases*” Order I. papulous eruptions, London 1798)

*Charles Anne Lorry* (1726-1783) was a contemporary of Willan and a physician of Louis XVI. In his book “*Tractatus de morbis cutaneis*” he presents an etiologic classification of dermatoses, mentioning also a phenomenon, later described by *Carl Heinrich Auspitz* (1835-1886) [13].

Another contemporary of Willan, was Baron *Jean Loius Alibert* (1768-1837) in Paris. He tried to consider morphologic, pathogenetic, metabolic and other aspects in order to create a systemic, kind of pattern-organization of diseases of the skin. However the result, the “*Arbre de Diagnoses*” generated a big confu-





**Figure 2.** Willan, R. and T. Bateman (1813). A Practical Synopsis of Cutaneous Diseases. London. The second of the 8 classes dealt with “Scales”

sion, placing “psoriasis” as “darte squameuse” besides other “dartres”. *Wilkinson* (1822), an admirer of Willan commented *Alibert’s* work with the following writing (cited

acc to [14]): “From the perusal of *Monsieur Alibert’s* inflated fustian in his 'Description des Maladies de la Peau' I rise, as I think every sober man must rise, puzzled and dis-

**Table 1.** Perception of “Psoriasis” through the Centuries

Ancient Hebrews (Old Testament)	«lepra» covers various dermatoses including, ichthyosis, elephantiasis (true lepra), vitiligo («alpos»), eczema, syphilis(?) and psoriasis
<i>Hippocrates</i>	impetigo, no specific mentioning of «psoriasis» even though he must have seen the disease
<i>Celsus</i> (25 BC-45 AD)	first description of psoriasis as second species of «impetigo»
<i>Galen</i> (133-200 AD)	introduced the term «psoriasis» to designate diseases (scaling of eyelids and scrotum with erosions; seborrhoeic eczema?), entirely different from psoriasis
Medieval Ages/authors (500-1600)	No clinico-morphologic description. «Leprosy» -like in ancient times- covered various diseases
<i>Lorry and Plenck</i>	no accurate description or differentiation
<i>Willan</i>	first morphologic description after Celsus and differentiation between true leprosy and lepra vulgaris («Psoriasis»)
<i>Alibert</i>	big confusion: names darte sèche, darte squameuse lichénoïde and darte furfuracée. <i>Alibert</i> used the term psoride pustuleuse as a synonym for scabies
<i>Gibert</i> (1834)	one year before Hebra had stated, that lepra vulgaris is just another form of psoriasis
<i>Hebra</i> (1841)	eliminated the term “lepra” and gave a scientific conception to “psoriasis”

gusted; ... he has continued ... to render this department of the science (Hôpital St. Louis in Paris) more confused and incomprehensible than he found it.”

The following table summarizes the history of the perception of what today we refer to as psoriasis [Table 1]

Prior to *Hebra*, the skin was seen as a place for relief of bad fluids according to the concept of humoralism and skin disorders were not treated in order to let the bad fluids out.

*Ferdinand Hebra* (1816-1880) (Figure 3), who is deemed as the one of the “fathers” of dermatology as a self-standing discipline, was a surgeon. At the age of 29 he was appointed chairman of the department of Dermatology, which had been established by and for him. He confirmed the high reputation of the Vienna School for dermatology.

*Hebra* cut the Gordian knot and defined psoriasis as a distinct disease entity in 1841. Hebra described many diseases and in self experiments proved scabies to be exclusively due to mites, which could be treated [15].

### Variants, Diagnostic Signs and Histopathology of Psoriasis

In the Atlas on Skin Diseases edited by *Pringle* in 1897 [16]. *Jacquet* considers “psoriasis figurate” a special disease, related to Unna’s seborrhoeic eczema and to be different from the psoriasis vulgaris, described and depicted by *Feulard* in the same atlas.

*Von Zumbusch* observed a male patient, who had had classic psoriasis for several years and finally developed multiple pustules [17, 18]. *Andrews* at the Annual Session of the American Medical Association in Milwaukee 1933 presented patients with pustular eruptions of the palms and soles and described fifteen cases [19], which had clinical features similar to the description of pustular psoriasis of the extremities, given by *Barber* [20].

*Heinrich Köbner* (1838-1904), who 1861 founded his own Institute for Dermato-Venereology in Breslau, presented a case in whom psoriatic lesions developed at the site of a bite by a horse (isomorphic reaction) [21, 22] (cit acc [23]). This observation initiated an intense academic discussion on the impact of



Figure 3. *Ferdinand Hebra* (1816-1880), the «Father of Dermatology»

external influences in the pathogenesis of psoriasis.

The histologic hallmarks of psoriasis [Table 2] are known for >200 years.

*Carl Heinrich Auspitz* (1835-1886) was an Austrian dermatologist. He described and explained the phenomenon, which is due to the small bridge of epidermis above the psoriatic papillae [9].

*Paul Gerson Unna* (1850-1929) was one of the first dermatopathologists. In his voluminous book in a brief chapter on psoriasis he describes the basic characteristics of the disease (parakeratosis, proliferation of the epidermis, and changes of vessels) [24].

The 19<sup>th</sup> century was the time, when great progress in medicine came from great discoveries in microbiology: favus (*Schönlein* 1839), Lepra (*Hansen* 1872), gonorrhoea (*Neisser* 1879), Tbc (Koch 1892), chancre (*Ducrey* 1889), syphilis (*Schaudinn* and *Hoffmann* 1905). In speculating about the pathogenesis of psoriasis, *Unna* during his histopathologic studies observed “micrococci” and commented his findings as follows: “...unfortunately



**Table 2.** The Histologic Hallmarks of Psoriasis

* Epidermal hyperproliferation with loss of proper stratified differentiation of the affected epidermis (parakeratosis)
* Expansion of the dermal vascular bed, elongation and tortuous dilatation of postcapillary venules in the st. papillare
* Accumulation of (T-) lymphocytes and other inflammatory cells (dendritic cells/macrophages) in both the dermis and epidermis

the sparseness of the micrococci in the horny layer of psoriasis renders their identification not impossible but difficult...». *Unna's* observations however were critically questioned by other investigators [25, 26].

Another histopathologic hallmarks of psoriasis are the intraepidermal microabscesses and spongiform pustules, as described by the Australian physician *William John Munro* (1861-1908) in 1898 [27] (Figure 4) and *Franjo Kogoj* (1894-1983) from Zagreb in 1928 respectively.

*Woronoff* at the department of dermatology in Moscow described ring like anaemisation of the skin around lesions of psoriasis and secondary syphilis, which he called "pseudoatrophic zones" [28] (Figure 5).

**History of the Pathogenesis of Psoriasis**

Like in other diseases, pathogenetic concepts always have to be seen in the context of the medical knowledge of the time, and technologic and scientific progress [Table 3]. It therefore is not surprising, that a disease

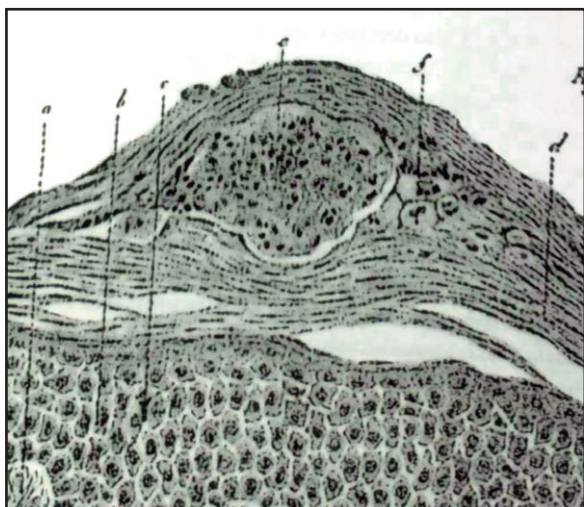
presenting with so many various clinical and morphologic features like psoriasis has been and still is a highly interesting issue for speculations as well as for solid clinical and laboratory investigations; even more since it got clear, that psoriasis is not just a disease of the skin but evolves on a systemic pathogenetic background.

A genetic background already has been assumed for a long time (*Wutzdorf* [29], *Köbner, Hebra*, cit acc [23]). More recent work has shown that there are at least 2 genetic constellations: (1) a juvenile exanthematic form and (2) an adult form which presents as large stable plaques [30, 31].

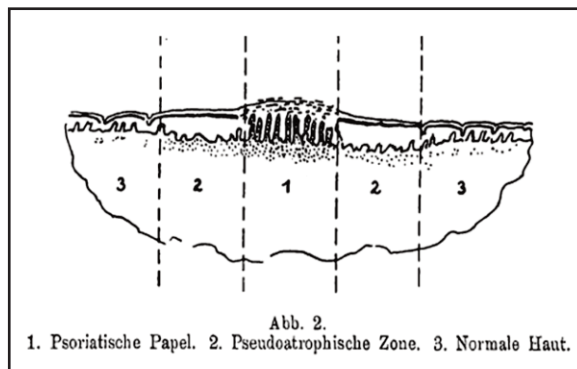
Because of the symmetry of the disease, *Pringle* and his contemporaries also thought of a pathogenetic impact of the nervous system [16].

A major breakthrough was the detection of the acceleration of the epidermal turnover by cytogenetic studies [32, 33].

Immunocytochemical studies in the 1970s showed the involvement of dermal dendritic cells (macrophages) [34]. and of prominent blood vessels in the papillary dermis [35].



**Figure 4.** Microabscess as described by *Munro* in 1898 [27]



**Figure 5.** *Woronoff*-rings as schematically depicted in his original paper on his observation [28]

**Table 3.** History of the Pathogenesis of Psoriasis

<p><b>Old age:</b> no attention</p> <p><b>Rome and Greece:</b> dyscrasia of fluids (blood, yellow and black bile, slime),</p> <p><b>Middle Ages (500-1500).</b> Little attention, mystification, «dark century» of science</p> <p><b>19th century:</b></p> <ul style="list-style-type: none"> <li>Genetic predisposition plus external factors (Wutzdorff 1876; Köbner 1872; Hebra1860)</li> <li>Nervous origin (Pringle 1897)</li> </ul> <p><b>20st century:</b></p> <ul style="list-style-type: none"> <li>Cellular origin. Epidermal (cellcycle) vs dermal vs vascular and inflammatory (leucocytes) micro environmental factors</li> <li>Cytogenetic studies on epidermal turnover (v. Scott 1963, 1973, Weinstein 1978)</li> <li>1970 metabolic disorder (histochemistry, biochemistry)</li> <li>1980 immunologic disorder                     <ul style="list-style-type: none"> <li>Clinical observation (accidently) from immunosuppressive treatments</li> <li>Inflammatory cells (cytochemistry)</li> <li>T-cells (immunocytology)</li> <li>Cytokines</li> <li>Autoimmune process</li> </ul> </li> </ul>
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Today there is significant evidence, that the immune system plays an important role in the pathogenesis of psoriasis [Table 4].

Evidence for the immunologic background also came from accidental clinical observations or from clinical studies, in which patients with psoriasis responded well to cytostatic or immunosuppressive drugs [36].

Looking for some review articles on psoriasis during the past 20 years, the following citations in some way reflect the step by step progress in our understanding of this multifaceted disease:

\* 1995: “Recently, progress has been made in understanding the pathogenesis of psoriasis... There is at present no cure, only suppressive therapy... The presumptive involvement of T cells in psoriasis is leading to intense interest in immunotherapy...and in identifying the genes (PSOR1)... In the future, psoriasis may be amenable to gene therapy.” [37].

\* 1999: “Therapies for psoriasis ... tend to have a remittent effect (inducing long-term remission) or a suppressive effect (improving

**Table 4.** Role of the Immune System in the Pathogenesis of Psoriasis

<p>Increased</p> <ul style="list-style-type: none"> <li>Dendritic cells and IFN-alpha</li> <li>T-cells</li> <li>Th1-cytokines</li> <li>Vascular endothelial growth factor (VEGF)</li> </ul> <p>Cytokines</p> <p>Therapeutic effect of PUVA</p> <p>Therapeutic effectivity of immunosuppressive drugs : cyclosporine (Müller 1979; Ellis et al 1991) and Rifampicin (Tsankov 1993,2011)</p> <p>Therapeutic effectivity of anti-CD4 (Morel et 1992)</p> <p>Clearing after bone marrow transplantation</p> <p>Transfer from transplant donor to recipient</p>
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lesions but with a prompt recurrence when the treatment is discontinued)” [38].

\* 2005: «The most promising compounds are monoclonal antibodies, cytokines, and fusion proteins» [39].

\* “Numerous other biologic agents and immune response modifiers are under development; all of them use at least one of the mechanisms mentioned above» (inhibition of T-cell activation, depletion of pathogenic T-cells, inhibition of leucocyte recruitment, correction of immune deviation)[39].

\* 2009: “The evolution of a psoriatic lesion is based on a complex interplay between environmental and genetic factors that sets the scene for disease initiating events.” [40].

\* “...However, major issues remain unresolved, including the primary nature of the disease as an epithelial or immunologic disorder, the autoimmune cause of the inflammatory process, the relevance of cutaneous versus systemic factors, and the role of genetic versus environmental influences on disease initiation, progression, and response to therapy.” [40].

### History of the Therapy of Psoriasis

It is an unwritten law in medicine that the less understood a disease is the larger is the list of our armamentarium for therapeutic approaches, which have been recommended over the decades and centuries. This holds true also for psoriasis as summarised in [Table 5].

One of the most curious recommendations, which are mentioned in the *Ebers papyrus*, has been the use of excrements from cats and dogs. In the Middle Ages a concoction from snakes (Viper-broth) was applied and coal tar which in some instances still may be an appropriate remedy today and which already has been recommended by *Pedanius Dioscurides* (40-90 AD) from Anazarbos in Kilikien, which belongs to Turkey today. He was a Greece military physician, who served for *Claudius* and *Nero* in Rome and was one of the most famous pharmacists of the antique.

Arsenic (Asiatic pills and *Fowler’s solution*) has been very effective in the treatment of psoriasis and other diseases, including syphilis. It has been used extensively during the 19<sup>th</sup> and first half of the 20<sup>st</sup> century, till the

**Table 5.** Selection of Therapeutic Measurements From Ancient till Modern Time

<i>Ebers Papyrus</i> (1500 BC): topical cats and dogs dung (faeces)
<i>Galen</i> : Viper-broth; Coal tar
<i>Daniel Turner</i> 1723: Galens remedy (boile viper-broth) and ammoniated mercury (topically)
<i>Balmanno Squire</i> 1876: Chrysarubin (Goa powder)
<i>Thomas Fowler</i> . Solution of potassium arsenite
<i>Thomas Gridlestone</i> 1806: <i>Fowler’s solution</i> in psoriasis
<i>E. Tipp</i> 1869: sc-injection of arsenous acid
<i>Hebra and Kaposi</i> : «Asiatic Pills»
Roentgentherapy for psoriasis in 1900 in Europe
1933 Low fat diet
1950 <i>Sulzberger</i> : Corticosteroids
1970-1990 UVA and PUVA
1990’s Vitamin D <sub>3</sub>
1990-2000 Immunological treatment modalities
1993, 2011 <i>Tsankov</i> : Rifampicin
2000 on Biologicals



hazardous effects of this substance got obvious.

Another treatment approach which still is employed today is keeping diet. The rationale for this is the observation that during World War II the incidence of psoriasis decreased [41], the biochemical composition of psoriatic scales and the high blood levels of cholesterol and other lipids in the blood in patients with psoriasis. This therapeutic approach was supported by several laboratory investigations [42, 43].

Glucocorticosteroids (have revolutionized therapy and early in time also have been used in Dermatology, topically and systemically, although the first reports on the topical use in psoriasis were not very enthusiastic [44].

An early description of “balneotherapy” can be found in the Old Testament (Lukas 4.27), even though we do not know which skin disease Naaman, the commander of the army of the king of Arman was suffering from (the term “Lepra” at this time covered many dermatoses and there is a risk that this text was meant as a metaphor and did not describe an practical treatment at all): “...so he (Naaman) went down and dipped himself in the Jordan seven times, as the man of God (Elisha) had told him, and his flesh was restored and became clean like that of a young boy.” [45].

For centuries in India chrysarobin (2-methyl dithranol), the active ingredient of Goa-powder (natural; synthetic: anthralin or cignolin) was used for the treatment of “ringworm” (dermatomycoses). The English physician *Balmano Squire* in 1876 inadvertently discovered its use for psoriasis [9, 46].

*Hippokrates* and other ancient physicians treated skin diseases with pine coal tar [47]. During the first half of the 20th century it was found to be particularly useful in psoriasis [48], either alone or in combination with light and anthralin [49].

The mode of action of anthralins and coal tar is not completely elucidated. They probably function by retardation of the altered epidermal cell kinetics.

Arsenic and mercury have been used in order to treat not only syphilis but also psoriasis. *Fowler's* solution containing 1% arsenic was very effective [50].

The beneficial effect of aminopterin (Methotrexat) in psoriasis has been detected accidentally when clearing in a patient treated for his rheumatoid arthritis [51]. The approval by the FDA for the use in psoriasis was given in 1972 [47].

Cyclosporine (Sandimmune) originally has been developed to prevent rejection of organ transplants. Like with methotrexate it was fortuitously found to clear psoriasis in patients being treated for severe longstanding rheumatoid arthritis [52]. In 1997 cyclosporine was FDA approved for the treatment of psoriasis [53].

Another less hazardous immunomodulator recommended recently is Rifampicin [54].

Retinoids have been used for treatment of keratosis [55]. While first generation and synthetic topical retinoids (1940ies) did not have significant antipsoriatic activity, the efficacy of second generation retinoids (1990ies), etretinate and its derivative acitretin was much better [56].

Vitamin D and its analogues also were found by chance to be beneficial in the treatment of psoriasis in a patient who received Vitamin D<sub>3</sub> for the treatment of osteoporosis [57]. A topical form of vitamin D has been formulated for this indication [58].

At the end of the 19<sup>th</sup> century first reports of UV-Light in the treatment of tuberculosis and wound healing arouse interest in phototherapy. At the same time sunlight as a natural healing force became a main pillar of the arising reform movement and naturopathy [59]. The photochemotherapy (PUVA, psoralen and long wave ultraviolet light A) of psoriasis has been reviewed in an autobiographically tinged monography [5]. At least 3 roots can be followed: (1) Egypt [60]. Ammi majus or Bishop's weed has been recommended in the Ebers papyrus (1500 BC) to be rubbed directly into the skin or taken orally and then to stand naked in the sun (2) Europe. There have been experiments in Switzerland with selective spectra of UV-light [61]. In Germany studies with topical photosensitizers have been performed [62, 63]. In Austria methoxsalen was applied orally [64], following successful studies in (3) the United States [65].

A very special and regional approach to the therapy of psoriasis is bathing with fishes from Sivas-Kangal [66].

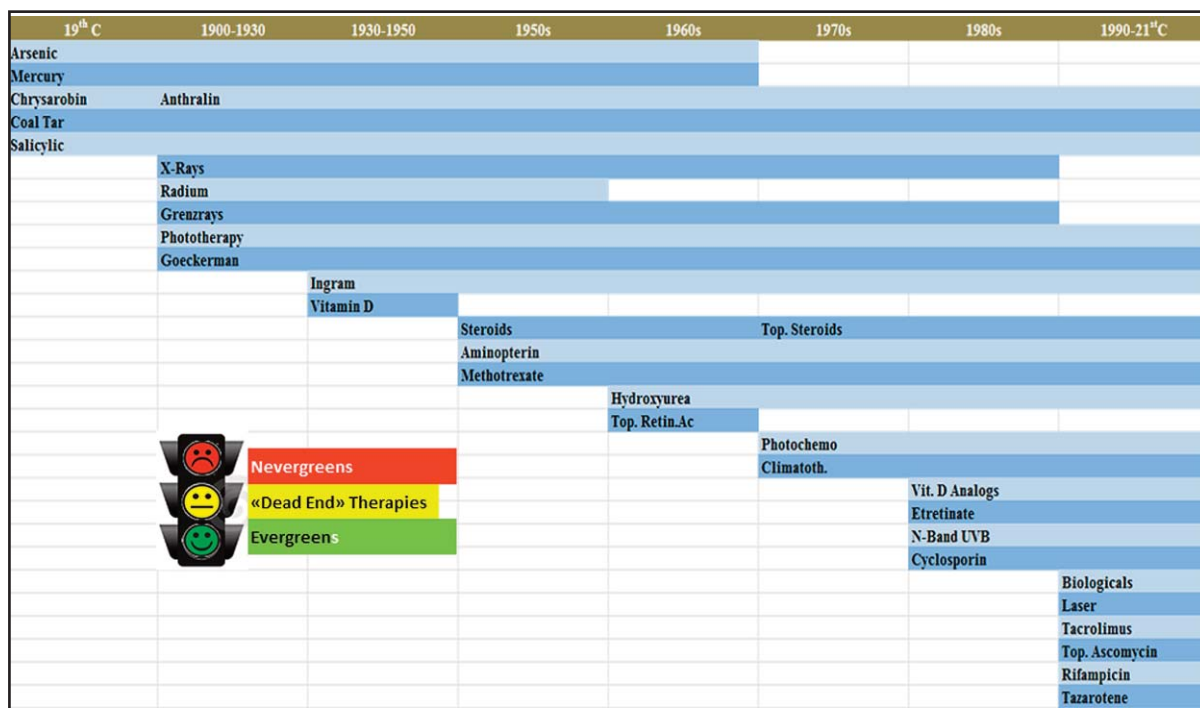


Figure 6. Historical view on evergreens, nevergreens and «dead end» therapies in psoriasis (not comprehensive)

An early immunologic approach to the treatment of psoriasis was with monoclonal antibodies [67]. The mode of action was considered to be different from the pathway in photochemotherapy: “We conclude that anti-CD4 mAb administration can induce a rapid and major improvement in psoriatic lesions (.. of 3 patients with severe psoriasis...), with immunohistochemical changes different from those induced by cyclosporin A or 8-methoxypsoralen plus long wave UV light (PUVA) therapy. Our data provide strong evi-

dence for a critical role of CD4<sup>+</sup> lymphocytes in psoriasis” [67].

Clinical observations and laboratory investigations of the past decade have pointed to the fact, that psoriasis is a T helper (Th)17/Th1-mediated autoimmune disease affecting the skin and joints [40]. Based on the understanding of the immunologic processes, several substances for a targeted therapy have been developed (Biologicals) [68] and have been approved by the FDA in 2003 for the treatment of psoriasis [57].

Table 6. Celebrities, Who Possibly have Suffered from Psoriasis

<b>Artist</b>
Zarah Leander
<b>Poets</b>
John Updike*
Dennis Potter**
<b>Revolutionizer</b>
Jean Paul Marat***
<b>Politicians</b>
Josef Stalin
Winston Churchill
* Report on the treatment with retinoids, Methotrexate and light in the book “Self-consciousness: Memoirs”, 1976
** Movie: The singing Detective (trailer: <a href="http://www.youtube.com/watch?v=wwwhtUdGOVM">http://www.youtube.com/watch?v=wwwhtUdGOVM</a> )
*** Suffered possibly from chronic eczema (neurodermatitis)

**Table 7.** History of Psoriasis. Milestones and Protagonists

<p><b>Old Age:</b> Ignorance no scientific basis, skin rash and impurity, punishment by God</p> <p><b>Greece:</b> Neglectance, <i>Hippocrates</i> (460-377): psora= itch</p> <p><b>Roman Empire 1<sup>st</sup> Century:</b> lack of consistent terms and nomenclature</p> <p>Cornelius Celsus (25 BC-50): first description of psoriasis</p> <p>Galen (131-201 AD): first use of the term psoriasis (probably for seborrhoeic dermatitis)</p> <p><b>Middle Age (500-1500):</b> Neglectance, clerical mysticism. «Dark» age for Science</p> <p><b>Arabian Medicine (Avicenna 980-1037)</b></p> <p><b>Early 18<sup>th</sup> Century:</b> «Protodermatologists»</p> <p><i>Charles Anne Lorry</i> (1726-1783): «Tractatus de morbis cutaneis».</p> <p><i>Joseph Jacob Plenck</i> (1738-1807): Surgeon and obstetrician. Term Impetigo (Latin «atack»)</p> <p><b>Late 18<sup>th</sup> Century:</b> «Dermatologists»: Nosologic Descriptions</p> <p><i>Robert Willan</i> (1757-1812): differentiation between psora leprosa and psora grecorum</p> <p><i>Jean Louis Alibert</i> (1768-1837): Psoriasis in the group of «dartrous dermatoses «</p> <p><b>Early 19<sup>th</sup> Century:</b> Nosologic definitions, impact of histopathology</p> <p><i>Ferdinand Hebra</i> (1806-1880): definitely separated psoriasis from leprosy; histopathology</p> <p><i>Heinrich Auspitz</i> (1835-1886): histopathology; sign already seen by Willan and Hebra</p> <p><i>Ernest Henri Besnier</i> (1831-1909): Histopathology; term «arthritis psoriatica»</p> <p><i>William John Munro</i> (1861-1908): Microabscess (1898)</p> <p><i>Paul Gerson Unna</i> (1850-1929): Histopathology; Micrococci</p> <p><b>Late 19<sup>th</sup> and early 20<sup>st</sup> Century:</b> Description of Variants of Psoriasis</p> <p><i>Leo von Zumbusch</i> (1884-1940): Psoriasis pustularis 1910</p> <p><i>Königsbeck</i> (1917), <i>Barber</i> (1936): Psoriasis pustulosa palmoplantaris</p> <p><i>Heinrich Köbner</i> (1838-1904): isomorphous effect of irritation</p> <p><i>DL Woronoff</i> (1926): rings around lesions in psoriasis and in corymbiform syphilis</p> <p><b>20<sup>st</sup> Century:</b> Biochemistry, Histochemistry, Cytogenetics, PASI, Biologics</p> <p>Carbohydrate Metabolism in psoriatic epidermis (<i>Halprim, Vorhees, Rassner, Braun-Falco</i>)</p> <p>Epidermal turnover: <i>van Scott, EJ</i>, 1963,1973; <i>Weinstein</i> 1968</p> <p>Multifactorial: different chromosomes (PSOR1-PSOR9)</p> <p>HLA-association; Type 1 and Type 2 (<i>Henseler and Christophers</i> 1985)</p> <p>PASI 1972 (<i>Fredriksson and Pettersson</i>)</p> <p>Treatment with Biologics, anti CD4 1992</p> <p><b>21<sup>st</sup> Century:</b> Genetics, Immunology, Autoimmunity, Targeted Therapy (Biologics)</p> <p>Mode of inheritance: chromosomal loci with linkage to psoriasis (PSOR1(Chr 6p)-PSOR9)</p> <p>Dendritic cells and T-cells, type I interferons</p> <p>Dysregulated immune system in psoriasis; role of plasmacytoid dendritic cells, IFN-<math>\alpha</math></p> <p>Antimicrobial peptides from keratinocytes: defensin, psoriasin (<i>Schroeder</i>)</p> <p>Alteration of the innate and adaptive immune response in psoriasis</p> <p>Targeted therapy with biologics</p> <p><b>Future Issues:</b> Safety, Economics; Controlled Studies; Psoriasis-Registries</p>
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The many substances and procedures recommended or used for the treatment of psoriasis roughly can be designated as evergreens (successful use up today), “nevergreens” (anecdotic reports) and obsolete (including hazardous substances like arsenic or mercury) (**Figure 6**). This review is not comprehensive and many issues are missing.

### Famous Persons Suffering from Psoriasis

Psoriasis is one of the most frequent dermatoses, affecting about 2% of the population, including average people and celebrities, among them artists, poets, revolutionizer, politicians, and others. Most of them tried to hide their disease. Only Dennis Potter very frankly presented the psychological distress of his disease in the



movie “The Singing Detective” (trailer: <http://www.youtube.com/watch?v=wwwhtUdGOVM>).

An incomplete list of famous persons suffering from psoriasis is given in [Table 6].

### Timeline of Psoriasis through the Ages

The time line over the centuries reflects a cloudy image which has to be seen in the context of the perception of diseases in the respective time periods [Table 7].

There was ignorance no scientific basis on the nature of the disease in ancient time and confusion lack of consistent terms and nomenclature still through the Middle Ages. For the first time, *Lorry* in France and *Plenck* in Austria, subsequently *Alibert* and *Willan* payed more attention to the disease and defined it as a nosologic entity, which finally was labelled with the term “psoriasis vulgaris” by *Hebra*. Many important contributions on the histopathologic changes came from *Hebra*, *Auspitz*, *Besnier*, *Munro*, *Unna*, *Kogoj* and others in the late 19th and early 20st century. During the same time, some clinical variants of psoriasis were described. Studies on psoriasis in the 20st century were driven by new laboratory technologies (biochemistry, histochemistry, immunohistochemistry), which all generated some interesting results and figures, however without elucidating the basic pathogenetic nature of the disease. Only the last decade of the past and the first decade of the 21<sup>st</sup> century shed some light on the complex genetically predetermined and immunologically driven systemic disease with its major manifestation on the skin. These new insights into the pathogenetic processes facilitated the development of targeted biologic therapies. Since the new therapeutics are extremely expensive and also imply some threats and side effects, a pivotal challenge for the future will be controlled clinical studies on safety, efficiency and economic accountability and collection of data in “psoriasis registries”.

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8<sup>th</sup> March, 2014. Even though extensive and thorough studies of the literature were undertaken, they were not completely comprehensive and due to the obscure profiles of the disease-descriptions in the pre-diagnostic era, some of the conclusions drawn and statements made in this article have to remain speculative in many respects and are not necessarily historically authentic.

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