Psoriasis—recent advances in understanding its pathogenesis and treatment

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Although not completely understood, there is clearly a genetic component in the development of psoriasis. Twin studies show a 67% concordance for monozygotic twins versus 18% for dizygotic twins. This lack of complete concordance in monozygotic twins suggests multifactorial inheritance and interaction between genetic predisposition and the environment. At present, 8 different psoriasis susceptibility loci have been identified in genome-wide linkage scans, including locations on 15 different chromosomes. Genetic connections have been made between psoriasis and other diseases, including atopic dermatitis, rheumatoid arthritis, and Crohn's disease. A variety of approaches are available for the treatment of psoriasis, ranging from topical agents for milder forms of the disease to phototherapy and systemic agents for severe psoriasis. Despite the importance of systemic therapies and recent advances represented by biologic agents, topical treatments will probably remain the mainstay of psoriasis therapy for most patients. The advent of new, cosmetically attractive vehicles may enhance compliance, add to the use of topical agents, and potentially improve patient outcomes. (J Am Acad Dermatol 2005;53:S94-100.)

Psoriasis is a chronic inflammatory skin condition that varies in severity, which has important implications in terms of medical costs and treatment strategies. The Medical Advisory Board of the National Psoriasis Foundation recently published definitions of mild, moderate, and severe psoriasis (Table I). These definitions are based largely on quality-of-life (QOL) measures, with consideration also given to proportion of body surface area affected.[1]

Although not completely understood, there is clearly a genetic component in the development of this disorder. For example, early onset is related to familiar aggregation and more severe disease.[2] Twin studies show a 67% concordance for monozygotic twins versus 18% for dizygotic twins. This lack of complete concordance in monozygotic twins suggests multifactorial inheritance and interaction between genetic predisposition and the environment for most patients.[3,4] For a small group of patients, plaque psoriasis may be caused by a single gene, inherited in an autosomal dominant pattern with high penetrance.[5]

Abbreviations used:

APC:	antigen-presenting cell
EGF-R:	epidermal growth factor receptor
HEV:	high endothelial venule
IBD:	inflammatory bowel disease
ICAM:	intercellular adhesion molecule
IFN-γ:	interferon gamma
IL:	interleukin
LFA:	lymphocyte functional antigen
MHC:	major histocompatibility complex
PSORS:	psoriasis susceptibility locus
Re-PUVA:	retinoid therapy with psoralen plus ultraviolet A
Re-UVB:	retinoid therapy with ultraviolet B
TGF-α, TGF-β:	transforming growth factor alpha or beta
T_H1, T_H2:	T helper cell type 1 or 2
TNF-α:	tumor necrosis factor alpha
VEGF:	vascular endothelial growth factor
VPF:	vascular permeability factor

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Table I. Quality-of-life–based definitions of mild, moderate, and severe psoriasis

Mild	Moderate	Severe*
• Disease does not alter the patient's QOL • Patients can minimize the impact of disease and may not require treatment	• Disease alters the patient's QOL • The patient expects therapy will improve QOL	• Disease alters the patient's QOL • Disease does not have a satisfactory response to treatments that have minimal risks
• Treatments have no known serious risks (eg, class 5 topical corticosteroids)	• Therapies used have minimal risks (ie, although these therapies may be inconvenient, expensive, time-consuming, and less than totally effective, they are not recognized as having the potential for altering short- or long-term health)	• Patients are willing to accept life-altering side-effects to achieve less disease or no disease

• Generally <5% of body surface area is involved	• Generally 2% to 20% of body surface area is involved	• Generally >10% of body surface area is involved
		• Other factors:
		  • Patient's attitude about disease
		  • Location of disease (eg, face, hands, fingernails, feet, genitals)
		  • Symptoms (eg, pain, tightness, bleeding, or severe itching)
		  • Arthralgias/arthritis

Adapted from Krueger GG, Feldman SR, Camisa C, Duvic M, Elder JT, Gottlieb AB, et al. J Am Acad Dermatol 2000;43:281-5, with permission from American Academy of Dermatology, Inc.
QOL, Quality of life.
*A clinically based definition of severe psoriasis also considers the ways in which the disease alters QOL in various categories, broadly including impact on daily physical activities, social activities, and psychological aspects.

At present, 8 different psoriasis susceptibility loci (PSORS1-8) have been identified in genome-wide linkage scans, including locations on 15 different chromosomes.[5] The most frequently studied locus has been PSORS1, situated within the major histocompatibility complex (MHC) region of chromosome 6, which contains genes coding for immune function-related proteins and which is strongly associated with human lymphocyte antigen genes found within this region.[6-8] Genetic connections have been made between psoriasis and other diseases,[5] including atopic dermatitis (eg, overlap of loci on chromosomes 1q21, 3q21, 17q25, and 20p),[9] rheumatoid arthritis (overlap of loci on chromosomes 3q21 and 17q24-25)[10,11] and Crohn's disease (eg, close proximity of polymorphisms related to psoriasis and Crohn's disease where loci on chromosome 16 have been linked to candidate genes.[12] While there is a locus on chromosome 16 that is near this region, it is unclear whether proriasis shares these associations.[13]

Epidemiologic data also suggest common genetic links among these diseases. For example, an analysis of 5 case-control studies indicates that the prevalence of psoriasis in the general population is about 1.4%, but the prevalence of psoriasis in patients with Crohn's disease is 8.9% ($P < 1 \times 10^{-9}$).[13] In addition, there are a host of common pathologic links among these inflammatory diseases, such as overproduction of TNF and interferon gamma (IFN-γ) that suggest other common genetic linkages that may come into play when triggered by, for example, environmental factors.

PATHOGENESIS

Psoriasis is characterized by hyperproliferation and abnormal differentiation of epidermal keratinocytes, lymphocyte infiltration consisting mostly of T lymphocytes, and various endothelial vascular changes in the dermal layer, such as angiogenesis, dilation, and high endothelial venule (HEV) formation.

T lymphocytes and the cytokines and chemokines they release appear to be the principal driver of lesion development and persistence, although endothelial cells, neutrophils, and natural killer T cells may play an adjunctive role along with other cytokines and selectins such as intercellular adhesion molecule (ICAM)-1.[14,15]

T lymphocytes

Focus on T lymphocytes came with the discovery that psoriatic lesions in patients receiving

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