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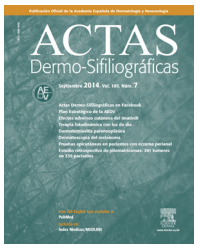

HISTORY AND HUMANITIES IN DERMATOLOGY

Darwinian Medicine and Psoriasis☆

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Abstract Darwinian medicine, or evolutionary medicine, regards some pathological conditions as attempts by the organism to solve a problem or develop defense mechanisms. At certain stages of human evolution, some diseases may have conferred a selective advantage. Psoriasis is a high-penetrance multigenic disorder with prevalence among whites of up to 3%. Psoriatic lesions have been linked with enhanced wound-healing qualities and greater capacity to fight infection. Leprosy, tuberculosis, and infections caused by viruses similar to human immunodeficiency virus have been postulated as environmental stressors that may have selected for psoriasis-promoting genes in some human populations. The tendency of patients with severe psoriasis to develop metabolic syndrome may reflect the body's attempt to react to environmental stresses and warning signs by triggering insulin resistance and fat storage.

PALABRAS CLAVE
Psoriasis;
Medicina evolutiva;
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Síndrome metabólico;
Escudo químico

Medicina darwiniana y psoriasis

Resumen La medicina evolutiva o darwiniana entiende algunos procesos patológicos como intentos del organismo por solucionar un problema o generar mecanismos de defensa. Algunas enfermedades pueden haber representado una ventaja en ciertos estadios de la evolución humana. La psoriasis es una enfermedad poligénica con alta penetrancia y una prevalencia de hasta el 3% en las poblaciones de origen caucásico. Se ha descrito que las lesiones de psoriasis generan una mayor capacidad para la curación de las heridas, y de lucha contra la infección. Se ha postulado que, en ciertas poblaciones, los genes promotores de psoriasis han sido seleccionados ante la presión ambiental de ciertas infecciones como la lepra, el sida y la tuberculosis. La tendencia de los enfermos con psoriasis grave al desarrollo de síndrome metabólico puede representar un intento de reacción ante presiones ambientales y señales de alarma que desencadenan resistencia insulínica y ahorro de grasa.

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''Nothing in biology makes sense except in the light of evolution.''

T. Dobzhansky (1900–1975)

Only in recent decades has the theory of evolution been incorporated into our understanding of diseases through the approach known as Darwinian medicine.[1,2] Viewed through the prism of Darwinism, the organism is the product of trial and error and therefore holds within itself certain instructions and functional processes that might prove useful in some environmental conditions but not in others. As a result, certain events, once set in motion, may eventually generate disease. For a condition to fit into this paradigm, it must be prevalent and heritable. Susceptibility must vary and the potential benefits must have exceeded the costs during a prolonged period in the history of the species. Furthermore, the disease must not hinder reproduction.

The example of obesity provides a way to comprehend the Darwinian perspective on disease.[3] Early hominids evolved in an environment in which food was scarce. The better part of our own evolutionary history has continued to take place under conditions of scarcity. A thrifty genotype was therefore favored, but the abundance of high-energy foods in today's developed world, along with sedentary behaviors, has promoted obesity on a level that has now reached pandemic proportions. Atherosclerosis provides another example, in this case one that shows how certain advantages become disadvantages beyond the reproductive years.[3] Mouse strains with macrophage hyperactivity have been shown to have low rates of infection during the reproductive phase of life. They also display early development of atherosclerosis, however, since macrophages are the main source of foam cells that appear during the initial stages of atheromatous plaque formation. Thus, there is a trade-off between good antimicrobial defenses early in life and the formation of atheromatous plaques later on.

Our reasoning about evolutionary medicine must also take epigenetic mechanisms into account. The environment can affect gene expression and mutations may be heritable. Epigenetics changed the notion that we are merely that which is written in our genes by calling attention to histone interactions with nucleic acid and histone methylation. These processes explain adaptive changes that can take place relatively rapidly—over the course of hundreds of years rather than the millions required for the natural selection of random genotypic variants.

Analysis of Psoriasis From the Vantage of Darwinian Medicine

The worldwide prevalence of psoriasis has been estimated to be around 2%.[4] A recent study in Spain estimates the prevalence at 2.3%,[5] and a north-to-south gradient can be seen in prevalence rates across all Western countries. Like other autoimmune diseases (Crohn disease, lupus erythematosus, rheumatoid arthritis), psoriasis has many pathophysiological pathways. The pathogenesis of psoriasis is fundamentally genetic: at least 9 loci are implicated (PSORS1–9) through the activation of both innate and acquired immune pathways. Because the prevalence of psoriasis is high and susceptibility is variable, it is possible to interpret this disease through the framework of evolutionary medicine. Psoriasis is also a systemic disease that is characteristically associated with insulin resistance and inflammation in other organs.

Prevalence and Distribution

Psoriasis has the highest penetrance of all the polygenic disorders. Heritability is estimated at between 60% and 90%[6]; in contrast, the heritability values for Crohn disease and rheumatoid arthritis are 50% and between 40% and 60%, respectively. Psoriasiform dermatoses have occasionally been described in other primates.[7] The relevant genes can also appear in various other species and their expression can be induced in certain animal models, indications that their presence in the genome dates from prehuman evolutionary stages. However, in spite of rare exceptions, psoriasis seems to be a primordial disease of human populations, particularly Caucasians, suggesting that it is an integral part of human rheostasis and highly peculiar to our species.

Psoriasis is not uniformly distributed across populations. The prevalence is so low in 2 ethnic groups—Alaskan Natives (the Inuit and others) and Australian Aboriginals—that the disease is considered practically nonexistent among them. Alaskan Natives also have a low prevalence of inflammatory joint disease, diabetes, ischemic heart disease, and asthma.[8,9] The traditional explanation cites the protective effect of a diet rich in essential fatty acids from blue fish. This diet is also a reliable source of vitamin D, which would not be effectively synthesized in these peoples given their relatively dark skin and the low levels of solar radiation in their traditional habitats near Arctic and Antarctic latitudes. That the traditional Inuit diet is responsible for this protective phenotype would seem to be demonstrated by individuals' development of the aforementioned diseases on switching to a so-called Western diet. However, all attempts to show a therapeutic effect of fatty acids in psoriasis have failed. It seems that, in addition to environmental factors, there are also specific genetic traits, very probably determined by geographic isolation and genetic drift. Alaskan Natives appear to be representative of the first human migrations across the Bering Strait that led to the colonization of North America.[10]

Australian Aboriginals are the other group in which psoriasis is extremely rare. Recent genetic studies conclude that they are descendents of African hominds who migrated directly to the continent very early.[11] The Aboriginals are therefore a highly homogeneous population from the standpoint of genetics, and they only became influenced by Western lifestyles after the 17th-century colonization of Australia.

Current thinking holds that the lack of psoriasis in such populations is explained by the phenomenon of genetic drift, through which natural selection acted relatively rapidly on certain alleles that provided humans with no advantages in their new environments.[2]

Genetic drift seems to have conserved psoriatic alleles and potentiated their frequency in Caucasian populations,