CONTACT DERMATITIS, CUTANEOUS BARRIER, AND SENSITIVE SKIN

*Laura Statescu, Laura Gheuca Solovastru

Dermatology Department, “Grigore T. Popa” University of Medicine and Pharmacy, Iassy, Romania
*Correspondence to laura.statescu@gmail.com

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ABSTRACT

Contact dermatitis (CD), one of the most common skin disorders, is one of the oldest but, at the same time, one of the newest diseases in dermatology. Ideas about the pathogenic mechanism, clinical aspects, and the therapeutic and prophylactic methods are always at the centre of the discussion; cutaneous barrier and ‘sensitive skin’ are two of the most important subjects when we refer to prophylaxis. We will try to present the connections between sensitive skin terrain, disruption of the skin barrier, and the development of CD. Establishing these connections, and understanding them, can set some valuable prophylactic methods for CD.

Keywords: Contact dermatitis, cutaneous barrier, sensitive skin.

INTRODUCTION

Dermatology, as a clinical specialty, is part of the ‘border’ domains, being closely linked to several medical disciplines as well as the surgical branch. Whenever we refer to dermatological diseases, pathology, aetiology, pathogenesis, clinical severity, and therapeutic possibilities, we talk about evolution and associated complications, the diagnosis of ‘contact dermatitis’ (CD) is usually met. It is a term used so often that it has been trivialised and forgotten. Sometimes a ‘common’ CD can destroy the entire ‘logic’ of the evolution of a case.

CD has been recognised as an entity since ancient times, being (probably) one of the most common dermatological pathologies of daily life. Perhaps just this increased daily frequency lowers the importance of the diagnosis and the addressability to a dermatologist, with most patients considering that it is ‘normal, not requiring medical consultation, medicines and that they can benefit from empirically solutions or neglecting existing therapeutic options.’ It is this kind of thinking that has led to the emergence of symptoms of chronic and severe aspects, sometimes misleading the cases, and being unable to hinder diagnosis and therapeutic solving.

CD is an inflammatory skin reaction due to contact with a chemical substance; they can be irritant and allergic reactions. Irritant CD occurs in any person who has come into contact with an irritant, if it is sufficiently concentrated, and the period of exposure is sufficiently long. It is not an immunological reaction, but the result of direct injuries caused to the protective layer of the skin - the stratum corneum. The reaction may occur anywhere on the skin and can affect anyone.

Allergic CD occurs only in sensitised individuals, as a delayed hypersensitivity reaction (Type 4, Gell and Coombs) and relapses appear in each subsequent contact with the allergen. The allergen is usually a low molecular weight chemical (hapten) that will bind to a carrier protein. This allergen is processed by Langerhans cells and macrophages, and transported to regional lymph nodes (paracortical area), where it will come in contact with T cells. This process takes about 7-10 days. Further contact with the allergen requires only 48-72 hours for the occurrence of cutaneous reactions.\(^1\)

Photo CD (photoallergic, phototoxic, photoaggravated) is determined by a combination of the photosensitising effect of chemicals and exposure to ultraviolet radiation, resulting in a
toxic or allergic reaction, with non-immunologic or immunologic mechanisms, so that it may appear in any person.\textsuperscript{2,3} Systemic CD, secondary to systemic administration of a substance (drugs commonly), determines prior sensitisation when used as a contact substance (topical applications).\textsuperscript{4}

Cases of CD, some suggestive and anecdotal, are sprinkled throughout the literature, the first mention was made of Pliny the Younger (61/63-113 BC), which refers to the appearance of skin changes in wood cutters (mostly pine) secondary to resins contact.\textsuperscript{1} Over the years, as CD was defined as a clinical entity, it also observed the existence of individual predisposition to the occurrence of contact sensitivity, given that not all people who come in contact with various allergens (fragrances, herbs, medicines, etc.) developed allergic reactions.

The modern history of CD cannot be separated from the epicutaneous testing history, which is currently one of the key tools used to highlight the chemical agent involved in triggering pathogenic mechanisms. Historical aspects of epicutaneous tests were reviewed in 1984 by Jean Foussereau, and respectively, in 1989 by Jean-Marie Lachapelle.\textsuperscript{5} Over the 17th, 18th, and 19th centuries, some researchers have occasionally reproduced CD by applying chemicals, plants, etc. on intact skin.

CD is a frequent pathology in current dermatological practice, but the real epidemiological data are incomplete. Epidemiological studies should be conducted to assess how common this condition is, the existence of at risk population groups, mitigating and aggravating risk factors for CD. All epidemiological studies are helpful in determining the effectiveness of investigative methods (e.g. epicutaneous tests) to establish a positive diagnosis, identifying the allergen involved and therefore, the imposition of characteristic preventive measures.

Usually statistical data are obtained among hospitalised patients or those addressing to hospitals, but most of these cases are severe ones. The number of cases resolved before reaching the dermatology network remains unknown and they are usually not so severe. International studies conducted refer, especially, to the hand CD, one of the most common manifestations of CD. Information about the prevalence of hand eczema, contact sensitisation, and CD in the general population can be obtained from studies conducted in recent years. Johnson and Roberts\textsuperscript{6} estimated that 1-2% of patients hospitalised in the US suffer from CD. In the Netherlands, the rate of incidence of CD as a primary diagnosis is approximately 9 per 100,000 inhabitants per year, representing 6% of all dermatological, and <1% of all admissions in 1988.\textsuperscript{1}

A number of studies conducted in European countries revealed the following results: the Netherlands (women 8%, men 4.6%), Norway (women 13.2%, men 4.9%), Sweden (women 14.6%, men 8.9%). These results indicate that the disease incidence rate is higher in women than in men,\textsuperscript{7} and although the data obtained in different studies could not establish any unanimous conclusion, clinical practice shows that female gender is most affected. In the US the prevalence appears to increase with age, and after a series of publications issued in Sweden, the Netherlands, and Norway, the incidence rate tends to decrease slightly after the age of 50.\textsuperscript{8}

The study conducted by Johnson and Roberts\textsuperscript{6} related to CD prevalence by sex and age groups, showed that there is a clear trend of increasing prevalence in males.\textsuperscript{1} In women, the prevalence rate is increased generally around the age of 40, many of them practicing household chores. All these studies suggest that age and gender - by themselves - are not risk factors for CD, but can become associated with exposure in various occupational and household activities.

It is estimated that 5-10% of all cases of CD from studies conducted in European clinics are determined by plants. The Compositae family comprises more than 13,000 species, of which some are for food consumption and others are grown as ornamental plants (such as chrysanthemums), and others (calendula) are of medicinal use. Schmidt\textsuperscript{9} studied allergic CD induced by lactones from Compositae family plants. He found that repeated exposure frequently causes acute CD, which often recurs and subsequently becomes chronic. When localised to the elbow fold or popliteal space, it can simulate atopic dermatitis (AD). Initially localised lesions on the face, hands, and genitals can spread and cause erythroderma with worse prognosis. Also, remaining dust from the dried plants can induce an ‘airborne’ phytophotodermatitis (windborne), something that is frequently encountered in the desert regions of the US and Australia.

The location of the hand is most likely a work-related dermatitis, in both women and men in a
proportion of 80-90%. Hand dermatitis affects 2% of the general population. In 1989 Goh\textsuperscript{10} published a clinical study involving over 2,000 patients and found that 34% of them had CD of the hand (56% men and 44% women) and in 30% of cases, the cause was occupational.\textsuperscript{11}

**CD AND CUTANEOUS BARRIER**

As we have shown, CD is the consequence of environmental factors and a susceptible terrain. Skin penetration is a key factor in the development of undesirable skin CD, at xenobiotics, as well as drugs or other substances. The most important role of the skin is that of a barrier, but not an ‘inert’ one, rather it is a barrier which participates in the homeostasis of an organism. Skin barrier is designed to control the exchange between inside and outside, in both directions:

- from the inside to the outside - a major role in the control of transepidermal water loss (TEWL) and to prevent drying;
- from outside to inside - a protective barrier against different external aggressor factors - mechanical, physical, chemical, and microbial.

The role of the skin barrier has been adjusted in recent years as studies have revealed its essential role in the occurrence of various professional diseases with cutaneous manifestations. Understanding the physiology and structure of the skin barrier, we can establish proper preventive measures and appropriate treatment of cutaneous manifestations. Skin protection function is ensured by various types of barriers: physical, chemical, or biochemical (innate immunity), and immune (acquired immunity - adapting cutaneous immune system).

In addition to lipids, an important role in the physiology of the skin barrier is played by corneocytes. The most important component of the skin barrier from the permeability point of view is the stratum corneum, which is composed of corneocytes and intercellular lipid bilayer, and is formed during the epidermal differentiation.\textsuperscript{1} Behind this first barrier is the second line of defence represented by cutaneous intercellular junctions in the epidermis and intercellular cement proteins: occludins, claudins, and proteins of the occlusion area (area occluding proteins, zonal occluding proteins).\textsuperscript{1,2} Acute changes occurring in the skin barrier - by mechanical or chemical factors - lead to a repair response involving an increase in epidermal lipid synthesis, accelerated cell proliferation, and the appearance of changes in epidermal cell differentiation.

In patients with CD, the skin barrier is degraded from the onset; alterations persisted throughout the disease course and cause chronic skin lesions. The most important agents that modify the skin barrier are: water, detergents, solvents, chemicals, dry skin, and dehydration. The most important protective mechanism in CD is an intact skin barrier. Destruction of the skin barrier entails increased permeability of the skin, opening the way for the penetration of microbial agents, allergens, and irritants. It starts as an inflammatory reaction in the skin, with the possibility of cutaneous immune activation.

Any injury to the skin (erosion, ulceration, fissure, xerosis, burning, etc.) may precede the occurrence of CD lesions by altering the skin barrier and removing its protective role. Occlusion of the skin, the phenomena of fluid overload, is another factor that can lead to impaired skin barrier, thus favouring the penetration of allergens into the skin. Frequently, allergic CD occurs after an irritant CD due to the existence of some chemical substances which have irritating and allergenic dual functions, or combination products that contain irritants and allergens that have potentiated effects on each other. Destruction of skin barrier leads to proliferation of Langerhans cells in the epidermis, but without changes in the dermis, so only the activation of the skin immune system. Restoration of damaged skin barrier is the main goal of the treatment and prevention of CD, representing the core question of therapist outside flares.

**CD AND ‘SENSITIVE SKIN’**

There are many debates on this notion. Does a population of people with ‘sensitive skin’ really exist? What actually is ‘sensitive skin’? What characterises it and how do we identify ‘sensitive skin’? Exposure to allergens and irritants in the environment, in the same conditions, causes irritation reactions in some individuals, but not in others, the same being observed in the case of allergic reactions. There have been various attempts to standardise methods of identifying people with over-reactive skin that can easily develop allergic reactions or irritation; this feature is especially helpful in implementing preventive measures.
measures, both in everyday life, and especially in the field of occupational medicine.

Frosch and Kligman\(^1\) have identified a group of seven contact irritants that, when applied to the skin, may cause changes (characterised by minimal erythematous dose) suggesting a sensitive, hyperactive area. There have been numerous attempts to establish specific tests to identify extra-sensitive people with ‘sensitive skin’, but the results were contradictory. Several non-invasive techniques have been used in an attempt to determine the biophysical properties of the skin. These include TEWL. This index has been most helpful in establishing a high reactivity in the skin, highlighting the increase in TEWL, with amplification of reactions, and revision obtained secondary to the application to the skin of sodium lauryl sulphate.

Other attempts to cause skin sensitisation have used\(^1\) in particular:

- Measuring skin hydration using skin capacitance and conductivity - low utility in medical practice
- Measurement of skin colour - as predictor for susceptibility to irritants, but intermittent exposure to sunlight interferes with the accuracy of measurements
- pH of the skin
- Epidermal lipid
- Skin thickness - measured by ultrasound

Currently there is not a standardised method to identify ‘sensitive skin’ with increased susceptibility to irritants or allergens. It is necessary to conduct large population studies using various experimental methods to identify a pattern of ‘sensitive skin’ and a method for prediction of increased susceptibility to action as contact skin irritants or allergens.

This approach to CD, in terms of ‘sensitive skin’ and damaged barrier, brings into the spotlight, the association as CD-AD, an association that, until recently, was considered impossible, but now has become a reality, proven by identifying the common pathway represented by LytH2. Given that primary, secondary, and tertiary prevention and education is the cornerstone of the current management of CD, the skin barrier and notions of ‘sensitive terrain’ should be part of health education programmes aimed at the general population.

REFERENCES