Methodological approach to the patient with dermatological lesions

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SKIN

The skin covers the body surface, representing the first area of contact with the external environment. It has an extension between 1.3 and 2 m^2 (average of 1.7 m^2), and it has a thickness that varies between 0.5 mm (eyelids) and 3 mm (hands feet) according to the part of the body. The skin color varies according to ethnicity, age, and body district. The weight of the skin is around 5 kg. Distinctive skin qualities are distensibility and elasticity that increases and decreases with age respectively.

The free surface of the skin is characterized by:

- Folds;
- Muscular skin lines due to contractions of the underlying muscles (Langer's lines);
- Articular skin lines due to joint motility;
- Senile wrinkles secondary to a decrease in elasticity or in adipose subcutaneous tissue;
- Ridges: minute linear reliefs, arranged regularly and parallel, visible at the palm of the hand and at the plant of the feet. At the fingertips of the hand they form tactile rosettes with interindividual variability;
- Furrows: they run parallel to the ridges, demarcating them, or joining the outlets of the hair follicles forming a lozenge-shaped network;
- Orifices: very small and punctiform depressions, corresponding to the opening of hair follicles with sweat glands and of the sweat glands with a spiral form.

CUTANEOUS ADNEXA

The cutaneous adnexa are structures with an intimate functional link and the same embryological origin with the skin. They are:

- Nails: hyperkeratinized structure with protective function;
- Pilosebaceous follicle;
- Hair: partially keratinized structure, contained within the hair follicle;
- Sebaceous gland: glands with holocrine secretion of sebum mediated by contraction of the muscle erectorum;
- Hair erector muscle;

- Sweat glands: tubular glands distinguished into eccrine (sweat secretion for thermoregulatory purposes) and apocrine (pheromone secretion for sexual purposes). Sweat changes in relation to sex hormones during puberty (in sweat glands at armpits, perineum, breast).

SKIN FUNCTIONS

The main functions of the skin are:
- Protective from physical, chemical and biological agents;
- Sensory with receptors for mechanoception, thermoception, and nociception;
- Secretory with sweat glands, sebaceous glands and cells, keratinopoietic with keratinocytes, and pigmentogenic with melanocytes;
- Thermoregulatory with irradiation, conduction, evaporation (sweating), and convection.

MICROSCOPIC CHARACTERISTICS

The skin is composed of two overlapping tissues, separated by a membrane called dermo-epidermal junction (DEJ) and they are:
- Epidermis: superficial parenchymal layer of ectodermal origin;
- Dermis: deep layer of mesenchymal origin.

EPIDERMIS

The epidermis is a multilayered epithelium, formed by keratinocytes that renew continuously, with a cycle of 14–28 days. It is formed by two main compartments:
- Proliferative compartment: constituted by the basal layer containing the stem cells, which have to maintain the homeostasis of the tissue, forming a simple columnar epithelium with cells joined together by desmosomes, and anchored to the lamina lucida of the DEJ by hemidesmosomes.
- Differentiation compartment, constituted by:
  - Spinous layer: most represented layer, formed by cells containing numerous keratin filaments, concentrically arranged around the nucleus and anchored in the periphery to desmosomes;
  - Granulosum layer: formed by cells containing basophilic granules of keratohyalin that undergo apoptosis into the transition to the corneum stratum;
  - Stratum lucidum: particularly visible in the palmoplantar regions, with cells characterized by atrophic nucleus;
  - Stratum corneum: made of keratinocytes without a nucleus and flattened. This stratum can be divided into stratum corneum proper, consisting of cells still attached, and stratum corneum disjunctum formed by desquamated cells. The mucous membranes are devoid of the horny and granular layer, except for the buccal masticatory ones (lips), and also they are poorer in tonofibrils.

Inside the epidermis, it is possible to find the presence of different types of other cells such as:
- Melanocytes: dendritic cells localized at the basal layer, deputies to melanogenesis and to the transfer of melanic pigment (melanin) through dendritic extensions to the stratum spinosum cells;

- Langerhans cells (antigen-presenting cells [APC]): cells distributed in the first three epidermal layers. They are capable of recognizing antigens and haptens inducing the activation of naive T lymphocytes and determining their differentiation into a T helper 1 (Th1) or Th2 cell;
- Th2 cells: they are involved in humoral immunity and produce interleukin 4 (IL-4), IL-5, and IL-10;
- Th1 cells: they are involved in cell-mediated immunity and produce IL-2 and interferon (IFN);
- Th17 and Th22 cells: they are involved in defense against bacteria and fungi and produce IL-17 and IL-22;
- Regulatory T cells: are involved in modulation and suppression of immune response;
- Merkel cells: present in body areas of high tactile sensitivity and they represent type I mechanoreceptors that transduce signals to nerve fibers.

DERMO-EPIDERMAL JUNCTION

The DEJ is an interface between the epidermis and the dermis, which performs the function of semipermeable membrane, allowing the progression of intracellular signals and of nutrients that regulate growth cells. The DEJ is composed of the lamina lucida and lamina densa.

Dermis

The dermis is the layer of skin located under the epidermis, made of proper dense connective tissue, richly vascularized and innervated. It is divided into:

- Superficial or papillary dermis: it presents numerous "saw-tooth" elevations (dermal papillae) interspersed between the corresponding epidermal (ridges);
- Deep or reticular dermis: it differs from the papillary dermis by the presence of connective bundles and elastic fibers.

The dermis has three main components:

- Fibrous component: collagen fibers (75%), elastic fibers, reticular fibers;
- Basic substance: produced by fibroblasts and formed by glycosaminoglycans, proteoglycans, strongly hydrated;
- Cellular component: fibroblasts, monocytes/macrophages, mast cells (papillary dermis).

The deep reticular dermis also contains a vascular component, a lymphatic component, and nervous plexuses that ascend to the surface through the dermal papillae, but they never exceed the DEJ.

Underneath the dermis it is possible to find the hypodermis, an extracutaneous structure formed by islands of connective adipose tissue divided by connective tissue, that acts as a supplementary reserve of energy, elasticity and protective support for the skin ensuring its mobility on the underlying structures.

DIAGNOSTIC METHODOLOGY

The diagnostic method in dermatology is principally based on studying the morphology and topography of lesions as well as the symptoms and anamnesis described by patients. Once you have identified the morphology and topography of the lesion, you can describe what you see and thus interact with

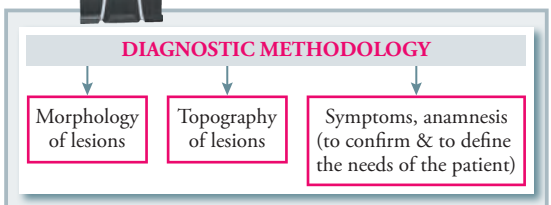

FIG. 1.1. Diagnostic method in dermatology.

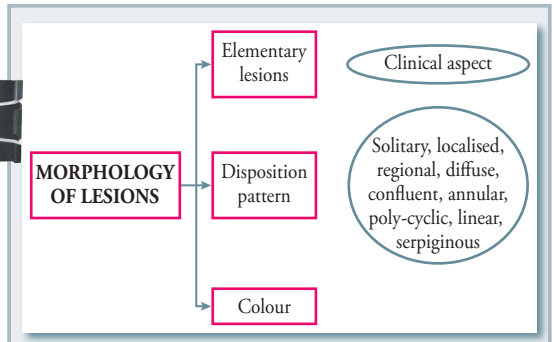

FIG. 1.2. Morphology of lesions.

a dermatologist. The morphology of a lesion depends on clinical aspects and color of elementary lesions and on their disposition pattern (solitary, localized, regional, diffuse, confluent, annular, polycystic, linear, serpiginous) (**Figures 1.1, 1.2**).

Topography of lesions changes in every cutaneous disease. Different dermatoses shows characteristics sites of body involvement that guide our diagnosis:

- Psoriasis: elbows and knees;
- Atopic eczema: perioral and flexures;
- Lupus: sun-exposed areas;
- Pemphigus: oral mucosa.

There are also some diseases that are characteristics of specific sites and exclusively localized in those sites: *i.e.* rosacea: face or Lichen sclero-atrophicus: genitalia.

The identification of morphology and topography allows to define from a clinical point of view the dermatological lesions and constitutes the first step for the diagnosis.

The second step is represented by the association of this specific pattern of manifestations to a disease (*i.e.* patches and scales in the elbows represent psoriasis, vesicular lesions on the flexural areas of elbows represent atopic eczema).

In cases of doubtfull clinical diagnosis, a cutaneous biopsy can be performed. In these cases, it is mandatory to proceed with a carefull clinic-pathologic correlation, in as much as the diagnosis is made considering together the clinical and histological findings.

The clinical history and the symptoms allow the clinician to confirm the diagnosis made on the basis of morphology and topography, and to identify the need of the patients, but do not change the diagnosis.

TABLE 1.I. Elementary lesion of the skin.

Primary	Secondary
Macule, patch	Crust
Papule, plaque	Scale
Nodule	Excoriation
Vesicle	Fissure
Bulla (blister)	Erosion
Pustule	Ulcer
Hive	Scar

TABLE 1.II. Primary elementary lesions.

	Aspect	Consistency	Dimensions	Colour
Patch	Flat-edematous	Cute normale	Variable (patch > macule)	Eritematous/achromic/pigmented
Papule	Raised	Solid	<5 mm - 1 cm	Eritematous/achromic/pigmented
Node	Raised	Solid	>5 mm	Eritematous/achromic/pigmented
Vescicle	Raised	Liquid-exudate/blood	<5 mm	Citrine/haematic
Bulla	Raised	Liquid-exudate/blood	>5 mm	Citrine/haematic
Pustule	Raised	Pus	Variable	Yellowish
Hive	Flat - edematous	Edematous	Variable	Light pink

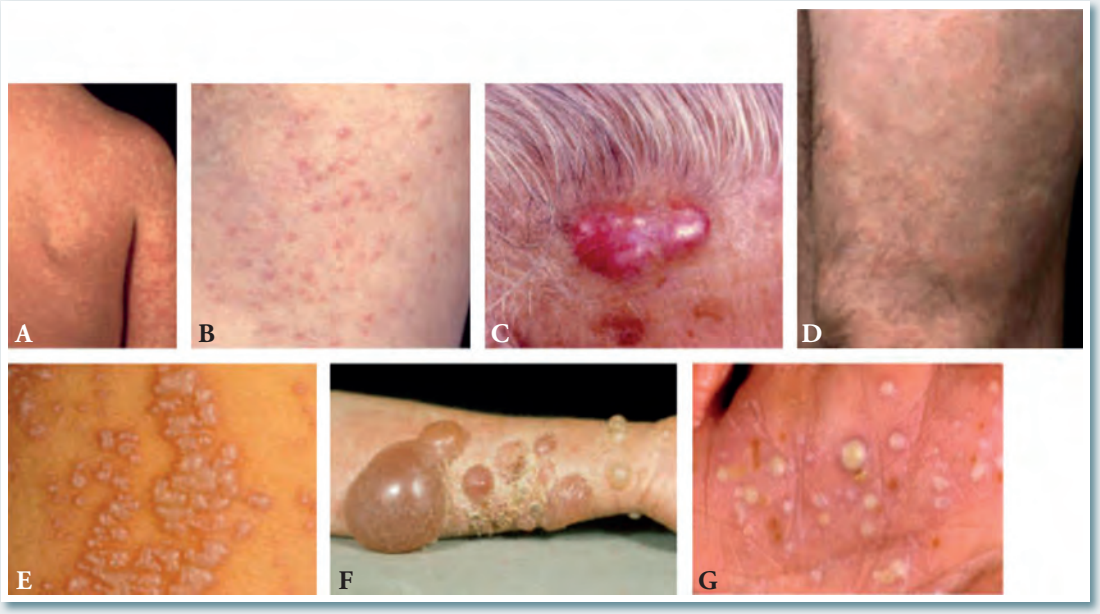

FIG. 1.3. Elementary primitive skin lesions. A) Patch; B) papule; C) Nodule; D) Hives; E) Vesicle; F) Bulla; G) Pustule.

ELEMENTARY LESIONS OF THE SKIN (Tables 1.I, 1.II, Figure 1.3)

The basis of the morphology is the identification of elementary lesions.

The elementary lesions of the skin include a set of alterations of the skin that can be detected during dermatological examination. They are the clinical expression of pathological processes, and their correct interpretation allows to distinguish the main skin diseases. They are distinguished as:

- **Primary or primitive:** represent the direct manifestation of the underlying pathogenetic phenomenon. Even if there can be more primary lesions, at least one is always present and therefore is fundamental for identification of the disease They arise on previously healthy skin.
- **Secondary:** evolutionary phase or outcome of a primary lesion. They can be present or not, and contribute to the disease manifestation.

Therefore, from a clinical point of view, the first step is the identification of the primary lesion(s), and after the evaluation of the secondary lesions whenever present.

PRIMARY LESIONS

Macules and patches

Definition: a spot or macula is a circumscribed modification of the skin color, without appreciable alterations of the other macroscopic epidermal and dermal characters, and without elevation or depression changes. Therefore, a macula is not palpable even if in some cases there can be slight edema. A patch is defined as a large macule (>1 cm). Macules can have precise margins or not, and they can have several causes.

Quantitative/qualitative alterations in blood content

- Erythematous spots or erythema: given by active hyperemia secondary to vasodilation of the arteriolar capillaries; they appear at diascopy (*e.g.*, measles, adverse drug reactions [ADRs]);
- Cyanhematous stains: secondary to erythrocyte diapedesis; they do not disappear on diascopy (*e.g.*, acrocyanosis, ecchymoses, purpura, and hematoma);
- Anemic spots: pale spots due to a vascularity defect; they disappear with diascopy (*e.g.*, Raynaud's phenomenon). With diascopy, we mean the pressure we make with a slide on a margin of a red lesion. If redness disappears, the red lesion is due to capillary vasodilatation; if redness does not disappear the lesion is due to extravasation of erythrocytes;
- Hemorrhagic spots: blood spread to superficial tissues (example: vasculitis);
- Hemangiomas: vascular hyperplasia; flat and mature ones do not disappear in time unlike immature ones (tuberous, cavernous).

Quantitative alterations of melanic pigmentation

- Hyperchromic or pigmentary spots: excess melanic pigment (*e.g.*, nevi, milk-coffee stains, blue like in mongolic scrub);
- Hypopigmented/achromic spots: melanic pigment deficiency (*e.g.*, vitiligo).

Qualitative pigmentation alterations: pseudomacchia

Secondary to the external penetration of pigments in an accidental way, for ornamental purposes such as tattoos or through blood (amyloidosis, xanthochromia, jaundice, drugs such as amiodarone, and sulfonamides).

Papule

Definition: it is a superficial, solid, and circumscribed protuberance of the skin, due to a thickening at epidermal site (epidermal papule) and/or inflammatory infiltration in the superficial layers of the skin (dermal papule or dermo-epidermal) and/or cell hyperplasia. The protuberance of the papule can also be made of metabolic deposits or of local products deposits. Papules can be flattened in lichen planus. A plaque is defined as the presence of multiple papules near one another without distinguishing their edges and borders. It is a prominent area of the skin. It is characterized by the fact that the area involved is major than the skin thickness which is involved in the lesion. The limits of the plaque are usually defined. The limits are more defined in superficial papules than in dermal papules. It generally does not exceed 5 mm in size, and upon palpation it has a solid prominence that differentiates it from vesicles.

Node or nodule

Definition: solid, circumscribed (>5 mm), it is a round type of elementary skin lesion. A nodule is different from a papule based on its larger dimensions. It is a deep dermal or hypodermal formation due to a cellular (inflammatory, neoplastic) or metabolic infiltrate (abnormal accumulation of various substances). Their boundaries are more defined if the nodules are more superficial. On palpation, nodules can be hard or soft. Nodules can have a smooth surface or they can present a depression in their center site.

Vesicle or vesicula

Definition: a small collection of organic fluid (<5 mm) in the epidermis or immediately underneath it. A vesicula is a superficial and prominent cavity with net limits and with a fluid content. Vesicles are due to detachment at different sites of the epidermal or of the DEJ. For the location and the resistance of the vesicle itself to open towards the outside are distinguished as:

- Subcorneal (*e.g.*, eczema, dome-shaped vesicula): it has a greater tendency to break outwards;
- Intraepidermal (*e.g.*, herpes simplex virus [HSV], navel vesicula): greater resistance;
- Subepidermal (*e.g.*, non-acantholytic bullous diseases, flabby vesicula in pemphigus).

Often, the roof of the vesicle is transparent and thus the contents can be seen. The content could be red if there is blood or yellow if there is serum in the vesicula content. Their formation can occur by spongiotic process or ballooning.

Bulla or blister

Definition: circumscribed collection of organic fluid at intra-/subepidermal site larger than that of a vesicle (>5 mm). The roof of the bulla is often transparent. Because of its size it cannot occur at the subcorneal level (intraepidermal and subepidermal site).We find this type of lesion in erysipelas, phlyctena, and autoimmune bullous diseases. According to the different etiopathogenetic processes of detachment are distinguished as:

- Intraepidermal: acantholysis, epidermolysis and spongiosis;
- Subepidermal: trauma (cytolysis), autoimmune (acantholysis), and genetic processes.

Pustule

Definition: a small circumscribed collection of purulent exudate at an intra-/subepidermal site. It can be yellow, white, green, or with an hemorrhagic appearance. Therefore, it differs from the vesicle for the purulent content, formed by cellular debris and polymorphonucleates. The follicles are often involved. There is a high variability in pustule dimensions. Vesicles can become pustules for sovrainfection in pathologies such as HSV and varicella zoster viral infections.

Hives

Definition: a circumscribed and fleeting edema of the skin. Examples include hive lesions, initially pale due to vasoconstriction and then hyperemic due to vasodilation. Hives are characteristic of urticaria.

SECONDARY LESIONS

Crust

Definition: a product of the drying of organic, physiologic, or pathologic fluid (serum, blood, pus) over preexisting skin lesions. Crusts can be thick and tight or thin and brittle. They are yellow when formed by serum, green when formed by purulent exudate and brown, dark red or black when

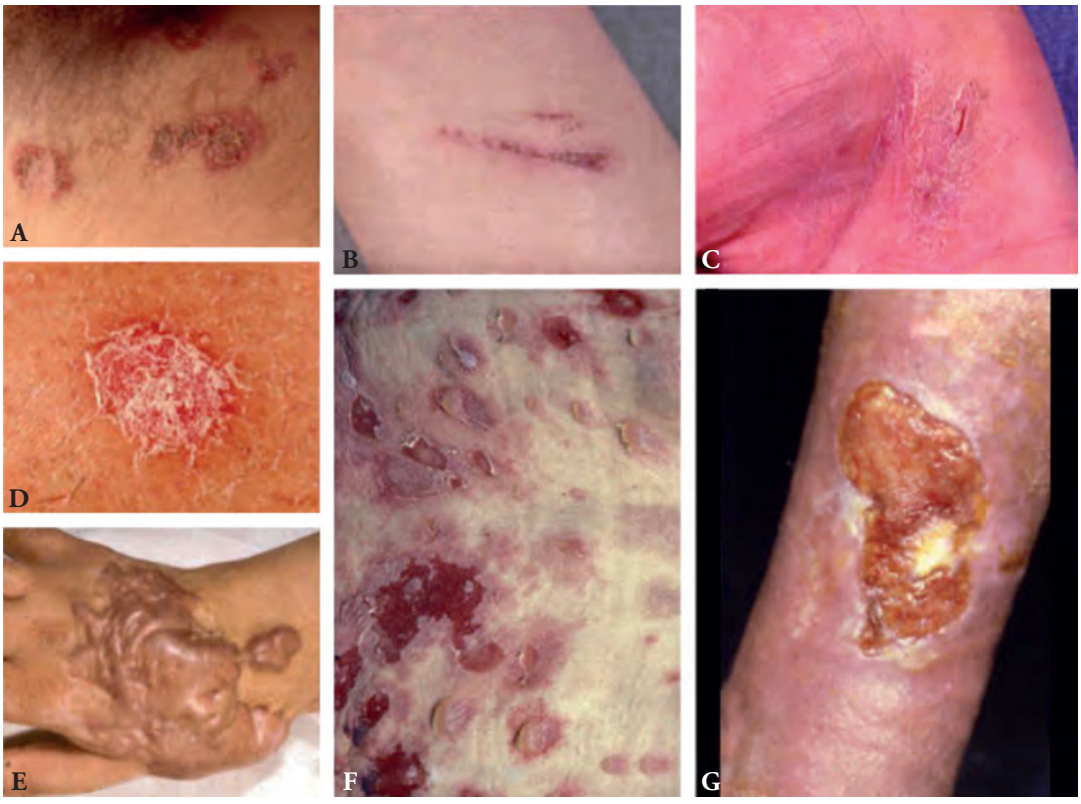

FIG. 1.4. Images of secondary lesions. A) Crust; B) Excoriation; C) Fissure; D) Scale; E) Scar; F) Erosion; F) Ulcer.

formed by blood. Examples: pyoderma causes myelic (yellowish) crusts to form as a result of drying of serum and pus. Superficial crusts are honey-colored with a delicate, shiny surface (impetigo).

Scale

Definition: a product of pathological flaking of the stratum corneum. They can be as large as membranes, as tiny as dust, pityriasiform, adherent, or lax. According to the dimensions they are subdivided into:

- Furfuraceous (dandruff, seborrheic dermatitis);
- Pityriasis (pityriasis versicolor);
- Lamellar (psoriasis);
- Laminar;
- Foliaceous (autoimmune diseases).

Excoriation

Definition: a continuous, often linear, traumatic solution affecting the epidermis and sometimes the superficial layers of the dermis.