DEFINITIONS IN MEDICINE

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Before entering the labyrinth of panniculars and lymphatic pathologies, of lipoedema and of lymphedema in particular, I consider it useful to review some fundamental definitions that will help us to overcome and understand the many contradictions and misunderstandings generated by an inaccurate dissemination of information on much used channels; given that scientific or scholastic texts are rare and texts addressed to an audience of non-professionals are even rarer, internet has become the first great database in which to search for information about lipoedema and lymphoedema. While it might be true that internet gives us access to anything, including very useful information and very quickly, it is also true that for some information, such as that relating to little known and little studied diseases, internet requires the intermediation of an expert guide and specialised supervision.

Semantics is the science that studies the meaning of words and will be extremely helpful in understanding the definitions that will often be encountered in this text. Let us clarify some doubts about some fundamental definitions often used in Medicine to describe a disease didacticly and exhaustively.

Etiology is the science that studies and investigates the causes of diseases. By etiological classification we mean an ordered list, sometimes by grouping, of all known causes sufficient to determine a disease. There are two large groups of causes:

1. Extrinsic causes, coming from the environment.
2. Intrinsic causes, already inherent within the living organism.

Extrinsic causes can be physical, chemical, biological.

The intrinsic causes of a disease are primarily responsible for alterations in the anatomical-functional development of an organ or a system. Intrinsic causes can be linked to changes in the genetic material that makes up chromosomes (DNA) and be related to physical, chemical, biological agents that cause alterations in development during embryonic or foetal life. Sometimes following these alterations, we only see a hereditary predisposition, an organ *meiopragia*, or rather, a particular fragility or susceptibility to the weakness in a tissue, an organ or a system: the disease itself is not inherited but only the propensity to develop it in presence of environmental factors (triggering causes) capable of revealing this predisposition. Sometimes illnesses can occur at the time of birth (connatal) although they are not necessarily hereditary, that is, transmissible to children. Finally, we must remember that not all hereditary mutations and genetic alterations are connatal, that is, present from birth, but can manifest themselves over following decades.

This is of fundamental importance in the understanding of the complex etiology of lymphoedema and lipoedema.

Histology and **Anatomy** study the structure of tissues, organs, apparatus and systems. To understand and study lymphoedema and lipoedema it is necessary to know the intimate structure of the tissues, organs and systems

affected by this pathology. *Topographic anatomy* in particular describes the exact location and position of the tissues and organs of an apparatus or of a system in our body and their interrelations.

Physiology is the science that describes the normal functioning of a cell, a tissue, an organ or a system. Knowing how normal lymphatic systems and subcutaneous adipose organs work when they are normal helps us to better understand what happens when some part of them no longer functions normally.

By **Pathogenesis** we mean the study of the ways in which the changes in physiological state leading to the establishment and development of a disease happen. It should not be confused with the etiology.

Pathophysiology is the discipline that studies the changes in organ-tissue functions due to a given disease, ie. how a tissue, an organ or a system works when it is sick and how their function deteriorates over time.

Clinical examination is the medical methodology based on the direct examination of the patient. This examination is based on the four pillars of medical semiotics: inspection, palpation, auscultation and percussion. In lymphoedema and lipoedema patients, inspection and palpation are fundamental, but sometimes, in relation to the problems of certain patients, auscultation and percussion can also be very useful. Anamnesis or a detailed collection of information provided by the patient spontaneously and on specific request, is an integral part of the clinical examination. During the evaluation of the patient with lipo-lymphopathies, the medical history and clinical examination are sufficient to make the diagnosis in most cases.

Clinical Staging means the subdivision into stages, generally of increasing gravity, of a morbid process. Staging may be only clinical or clinical-instrumental, ie. performed with the aid of a variety of diagnostic techniques.

Therapies are measures designed to return, where possible, a pathological state to a healthy state and make any uncomfortable symptoms bearable. For some (usually acute) pathologies, causal therapy can promote healing, for other diseases often of a chronic type, therapy should be aimed at favoring a new equilibrium by stabilizing the disease and preventing further resumption or worsening and avoiding complications, as is the case for example Lipoedema and Lymphoedema.

Therapies are usually classified into drug therapies, surgical therapies, preventive (or prophylaxis) therapies, physical and rehabilitative therapies and palliative therapies which alleviate the symptoms but are not aimed at healing (eg pain therapy). In Lymphoedema and Lipoedema, the therapies at our disposal guarantee good results; physical-manual therapy and drug therapy allow us to control most of these pathologies. In certain very select cases, even surgical therapy may be appropriate.

Rehabilitation Medicine or **Rehabilitation** is the branch of medicine that deals primarily with disability, the reduction of disability and the recovery of a function or behaviour. Rehabilitation and Rehabilitative Medicine, should not be confused with Manual Therapy (the therapist uses only their hands, as in manual lymphatic drainage), with Manual Physical Therapy (the therapist uses their hands but also instruments or aids such as bandages to make a multi-layer bandage), with Instrumental Physical Therapy (the therapist uses machines, such as Ultrasounds or TENS) or with active or assisted Kinesiotherapy (the therapist helps the patient carry out some exercises or teaches the patient how to perform exercises such as those for joint mobilization or muscle strengthening).

It is common for definitions like therapeutic program, rehabilitative program, re-

habilitative project, to be a source of confusion and misunderstanding, in fact they are often used as synonyms.
In particular, by **Therapeutic Program or Therapeutic Plan** we mean the planning (an outline of administration, dose, duration) of a given therapy; we might see a pharmacological therapeutic program, a physical-manual therapeutic program, a surgical therapeutic program. The therapeutic plan should not be confused with the rehabilitation program and above all with the rehabilitation project.
The **Individual Rehabilitative Project** is the rehabilitative pathway that a disabled person must follow for a period of their life in order to recover, as far as possible, any lost skills and to strengthen remaining abilities in order to reduce a disability or its progression over time to a minimum. This approach is the most suitable for the treatment of people with chronic and potentially progressive disabilities. An individual rehabilitation project is implemented over time in three specific phases or rehabilitation programmes: a short-term rehabilitation program, a medium-term rehabilitation program and a long-term rehabilitation program. Often in chronic patients the long-term rehabilitation program can last a lifetime.

The individual rehabilitation project, with its related rehabilitative programmes, cannot be defined from the outset nor can it be standardized (the same for everyone) rather it is a dynamic process that takes day-by-day account of the positive or negative changes generated by the therapies in the treatment of specific problems.

In patients with lymphoedema, as example, the *short-term rehabilitation program* would be the intensive decongestion phase or the preparation phase for the therapeutic stocking, while the *medium-term rehabilitative program* would be the clinical stabilization and phase during which the containment garment is checked, while *the long-term rehabilitative program* would be the phase in which obtained results are maintained and the phase of clinical optimization, of prevention of complications and relapses.

The programmes of an Individual Rehabilitative Project are of varying length and are personalised for the type of person, the type of edema, the clinical and pathophysiological conditions at the time of the first visit, age, expectations, working conditions, family situation and distance from the rehabilitation center.

For lymphoedema, each rehabilitation program will include the different therapeutic plans; for example, in a short-term rehabilitative program it will be possible to formulate and propose a pharmacological therapeutic plan, a kinesiotherapeutic plan, a manual therapy plan, a manual or instrumental physical therapy plan, a diet plan, a postural, orthotic and podiatry plan, a skin care plan and medication for any skin lesions and so on.

During the medium-term rehabilitative program, some of the therapeutic planning of the first phase may change in dosage, means and timing of administration while other therapeutic plans may be added; among these are the orthesis plan, which evaluates the suitability of the elastocontenitive garment, and the possible surgical therapeutic plan (plastic-reconstructive-aesthetic or microsurgical) for patients for whom it might be deemed necessary. The long-term rehabilitation program foresees some therapeutic plans will being eliminated, as no longer needed, while the self-management plan will gradually be increased. *Self-management* is not to be confused with self-treatment. *Self-management* consists in the patient's understand-

ing, recognition and learning of environmental and behavioral factors that are useful or harmful for their problems: postures, ways of working, motor activities, sports and hobbies, drugs, food, stress. *Self-treatment* would require a much longer discussion! I have met many patients who have self-treated for years and have come to my attention in the most precarious conditions.

I remain firmly opposed to the proposal, presented by some health professionals, to teach patients some manual lymphatic drainage manoeuvers and some forms of bandaging as sole treatment of the disease, entrusting, in this way, the patients with their own therapy and the management of a disease so complex and potentially progressive, with the illusory end aim of lightening the loads of health facilities. As far as possible, the individual and personalized self-management plan should be included in the rehabilitation project according to the previously stated and described guidelines. Otherwise, patients would find themselves truly alone and abandoned to themselves in the management of a chronic and rather bizarre disease; a disease, remember, burdened by frequently relapsing infectious complications requiring the intervention of specialized and competent health care professionals (preferably at a Reference Lymphological Center) able to help them to deal with and overcome these events in the shortest possible time and in as correct a fashion as is possible. Within the long-term (or maintenance) rehabilitation program which provides specific and individual therapeutic sessions which we call maintenance, in some carefully selected and adequately prepared patients, the self-management therapeutic plan can be considered as the opportunity to teach them some manual lymphatic drainage techniques or some simple types of bandaging that may serve to improve their clinical conditions and promote their autonomy, as far as possible, in the periods between one therapeutic session and the next.

LYMPHOEDEMA AND LIPOEDEMA: A SHORT GENERAL OVERVIEW

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Lymphoedema is generally a progressive condition characterized by continuous changes in the structure and composition of superficial connective tissue, predominantly of the hypodermis and dermis. It is a consequence of an inability of the lymphatic system to completely reabsorb the histolymph that is fed and regenerated deep in the extracellular connective tissue matrix by physiological and continuous, albeit variable, plasma ultrafiltration. A substantial amount of lymph then, with its load of cells and proteins, is trapped in the tissues of the hypodermis and dermis generating a subclinical, chronic, progressive inflammation that, initially sterile or with few passing microorganisms, stimulates the reaction of fibroblasts, the cells of the connective tissue, to produce more dense and resistant fibrous tissue, with characteristics different from normal tissues which are usually much looser and softer to the touch (Fig. 2.1). At the same time there is also a proliferative reaction of adipoblasts, fat cells normally present in the hypodermis, causing an increase in fat tissue. There is a definite increase in thickness of the subcutaneous tissue affected by lymphatic stasis.

This phenomenon explains how the increase in the volume of a limb affected by lymphatic stasis is not only linked to the increase of the fluid content of the lymph (liquid part of the lymphoedema) trapped in the matrix but also to the increase in the connective tissue hosting the stasis

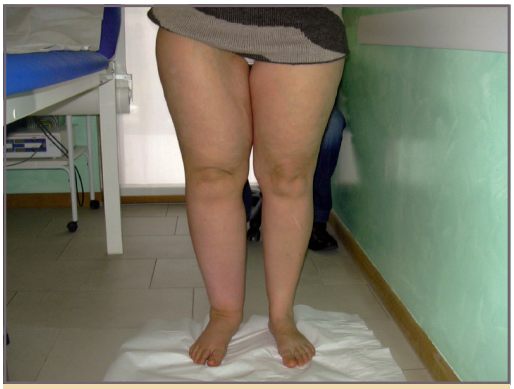

FIG. 2.1 Patient with a secondary lymphoedema of the right lower limb.

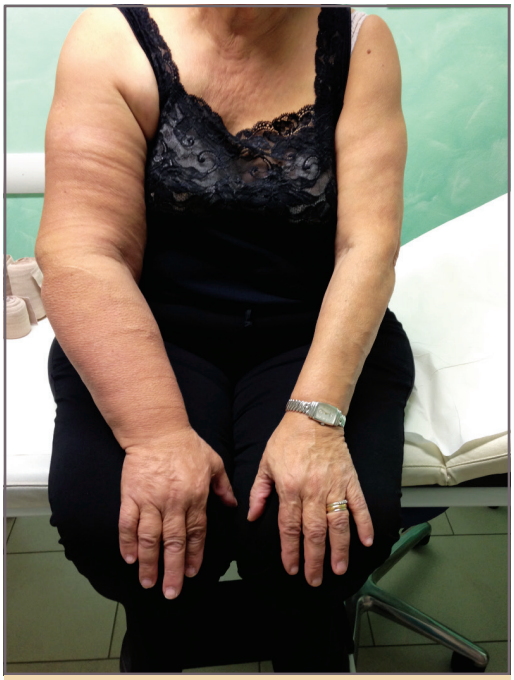

FIG. 2.2 Patient with a secondary lymphoedema of the right upper limb.

through a thickening and hardening of the same connective extracellular matrix (solid part of lymphoedema).

This proliferative reaction is actually very individual. Each case is a case in itself and is different in terms of onset, progression, and response to therapy (Fig. 2.2). As lymphostasis progresses, significant changes can occur in the percentage of cells in the matrix: macrophages, fibroblasts, and adipoblasts increase. Interstitial pressure, usually negative, begins to become positive, especially in advanced cases, reducing the passage of plasma substances from the blood to tissues. Tissue homeostasis is altered and generally, oxygen levels are reduced (hypoxia), the matrix pH tends to be more acidic, toxic substances (exotoxins and endotoxins), which should be eliminated as soon as possible from tissue cells and from the matrix, increase and accumulate. White blood cells, especially in certain types of obstructive lymphoedema, struggle to reach the lymphatic vessels and an increasing number remain trapped in the matrix; some of them die in the matrix and release their cytoplasmic content which is pro-inflammatory. In these conditions the process calls other cells from the inflamation and is amplified and self-sustained, meaning that spontaneous regression of the condition is increasingly unlikely. A normal Lymphatic System, on a 24 hour average, could works at 20-30% of its real total effective capacity; in fact, it has a great functional reserve capacity and could transport much more lymphatic fluid with all its cellular and macromolecular components. However, when a significant part of the lymphatic system has been damaged (as happens with the removal of the lymph nodes and / or radiotherapy), the amount of fluid stagnating in the matrix awaiting reabsorbtion can considerably increase, thus exceeding the residual transport capacity. The interstitial fluid increases and with it the cells and proteins that, due to dehydration, can thicken, concentrate and aggregate triggering the tissue modifications we have just mentioned (tissue fibrosis and proliferation).

Lipoedema is also a chronic and sometime progressive condition, characterized by continuous changes in the structure and composition of the connective tissues that make up the hypodermis. This disease mainly affects women; the few males who are affected have low levels of male sex hormones. The etiology is still unknown. A genetical predisposition is recognised for the most part of the cases and in many cases a familiarity (element of transimitability) can be found through anamnesis or, sometime, directly from the simultaneous examination of family members. In an epidemiological study, some German authors report a percentage of women suffering from lipoedema equal

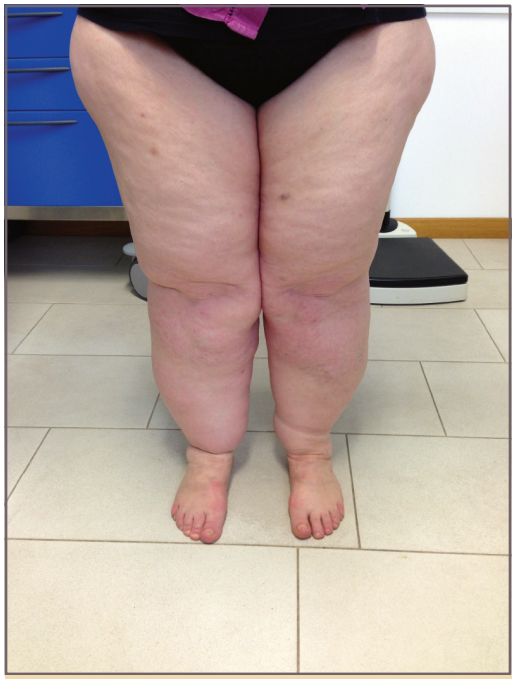

FIG. 2.3 Patient with lipedema of the lower limbs.

to 11% of the female population. Clinically it can be described as a visible and palpable alteration of the subcutaneous tissue; it can strike only the lower limbs, from the waist line down, partially or totally until the ankle, or even the upper limbs and the trunk; the pathology is often confused with obesity but it is imperative to keep the two pathologies entirely distinct (Fig. 2.3). Upon histological examination, in these patients the connective tissues of the hypodermis (lax and adipose) present a characteristic chronic inflammatory process with an increased presence of macrophages, an increased intercellular fibrosis and adipocyte hypertrophy. It is also present a microangiopathy which is responsable for the increased fragility of the blood capillaries, at the root of a predisposition for bruising and hematomas, even after pressure and not necessarily due to trauma. Actually, on palpation the limbs appear large rather than swollen, the fovea remains negative for a long time and Stemmer sign, typical of primary lymphoedema, is usually negative, with the tissues in the foot remaining quite normal even for decades. However, if lipoedema is not adequately treated early, especially where it is associated with other diseases such as obesity it progressively worsens up to a point which, even for competent and well-organized Lymphological Centers, can be unmanageable (Lipo-lymphoedema with elephantiasis). In cases where the pathology is not adequately treated, the histopathological lesions of lipoedema associated to obesity can cause alterations to the lymphatic vascular system which can create an imbalance and an overlap of lymphatic edema with the basic pathology. In some cases, venous changes are also associated and this is where, frankly, the pathology becomes very complex (Lipo-phlebo-lymphoedema).

For both lymphoedema and lipoedema, the prognosis and quality of life remain closely linked to the timely provision of suitable, correct and personalized medical care that is realized through the formulation of an individual rehabilitation project.

This brief overview of the two diseases presents us with the real need to deepen some basic scientific concepts of human biology. It is immediately clear that for a more intimate understanding of what is written here, it is absolutely necessary to have grasped some basic notions of histology, anatomy and physiology. It will subsequently be easier to understand the clinical aspects and to understand the rationale behind the therapy.

3 FLUID CONNECTIVE TISSUES

Lymphoedema and lipoedema are pathologies that develop within and cause significant alterations to the connective tissues.

Blood and lymph should not be considered simple fluids or bodily fluids but real tissues.

From a histological point of view, blood and lymph are classified among connective tissues. Blood and lymph are tissues characterized by having a certain number of cells immersed in an abundant fluid component (blood plasma and lymphatic plasma) which allows them to flow into the blood and lymphatic vessels respectively. In many "posts" found on internet, lymph is usually considered a simple fluid and not a tissue; we usually talk about excess fluid, a fluid full of metabolic waste and toxins, a fluid more like polluted water than a living tissue that is fundamental to our life; lymph has one of the noblest functions of our body: it allows the realization of the immune defense against pathogens. Lymph is not water despite it being a water-rich tissue (about 80-90%)! As such, lymphatic tissue always needs this preponderant quantity of water and can be assimilated to a suspension in water [1]; if for some reason the aqueous component were reduced, the corpuscular part (especially the protein macromolecules) would no longer be normally conveyed; without the right quantity of water, lymph becomes concentrated, increases in viscosity, flows with difficulty, slows down and sediments. We must not forget that lymph moves around and transports not only proteins and many other macromolecules of various types but also all those cells with immune function; we understand from written accounts the sometimes negative effects of certain therapies proposed for lymphoedema which are aimed exclusively at reducing the water component of the lymph (diuretics). Lymph and blood are therefore tissues and as such they must be classified, studied and considered.

We know that organs, apparatuses and systems are made up of tissues, or rather, aggregates of well-differentiated cells performing well-defined functions. The functions of each organ are the sum of the functions of the different tissues that make it up. The functions of a system and of an apparatus are the sum of the functions of all the organs that make up that particular system or apparatus.

In general it can be said that all tissues are made up of cells and extracellular/intercellular living matter known as the extracellular matrix or interstitial matrix; these terms refer to the vital substance present outside the cells and between one cell and another within a

1 In chemistry a suspension is a mixture in which a finely divided and heterogeneous corpuscular material is dispersed in another material so as not to settle in a short time. Suspensions are made up of a minor component in a solid state (in the case of lymph proteins and other macromolecules, white cells) that is finely dispersed within the greater component in a liquid state, in our case, water.