CONTENTS

Preface by Nicolò Scuderi

Introduction by Claudio Ligresti

CHAPTER 1
Anatomy of the skin p. 18
Elda Feyles

CHAPTER 2
Biology of cicatrization p. 26
Claudio Ligresti

CHAPTER 3
Elderly patients and their comorbidities p. 38
Graziano Iraldi

CHAPTER 4
Medications, comorbidities, and difficult wounds p. 44
Claudio Nuti

CHAPTER 5
Nutrition in patients with skin ulcers p. 50
Stefania Bianchi

CHAPTER 6
Pain in patients with chronic skin ulcers p. 68
Alfonso Motolese, Alberico Motolese

CHAPTER 7
Scales and protocols p. 78
Clara Maino

CHAPTER 8
Patient intake, general and local wound assessment p. 88
Giovanni Papa, Evelin Makuc, Martina Pangos, Michele Blasina

CHAPTER 9
Vascular instrumental diagnostics p. 102
Andrea Monti

CONTENTS

CHAPTER 10
The TIME p. 122
Andrea Bellingeri

CHAPTER 11
The TIME-H protocol p. 130
Claudio Ligresti

CHAPTER 12
Soft tissue necrosis p. 156
Claudio Ligresti

CHAPTER 13
Skin and soft tissue infections p. 174
Luigi Toma

CHAPTER 14
Surgical site infections p. 184
Adriana Cordova, Vitalba Giacalone, Greta Tondini

CHAPTER 15
Surgical wound dehiscence p. 194
Claudio Ligresti

CHAPTER 16
Osteomyelitis p. 208
Domenico Aloj, Rosalba Tortia

CHAPTER 17
Burns p. 224
Antonio Di Lonardo

CHAPTER 18
Exudate and its forms in patients with cutaneous ulcers p. 256
Sara Sandroni

CHAPTER 19
Facial wounds p. 264
Rosario Emanuele Perrotta

CHAPTER 20
Wounds of the limbs p. 278
Bruno Battiston, Davide Ciclamini, Andrea Audisio, Fulvio Antonino Nicolò

CHAPTER 21
Inflammatory skin ulcers p. 300
Carlo Salvarani, Chiara Marvisi, Francesco Muratore, Simonetta Piana

CHAPTER 22
Antiblastic drugs extravasation injury p. 322
Sara Carella, Maria Giuseppina Onesti

CHAPTER 23
Ambulatory management of diabetic foot p. 332
Carlo Caravaggi, Andrea Garghetti, Daniele Simonetti

CHAPTER 24
Diabetic foot in emergency p. 344
Carlo Caravaggi

CHAPTER 25
Arterial vascular ulcers p. 358
Marina Muncinelli

CHAPTER 26
Venous ulcers p. 378
Claudio Ligresti

CHAPTER 27
Lymphatic ulcers p. 394
Alberto Macciò

CHAPTER 28
Neoplastic ulcers p. 414
Virginia Caliendo

CHAPTER 29
Notes on paediatric vulnology p. 430
Serena Crucianelli, Guido Ciprandi, Mario Zama

CONTENTS

CHAPTER 30
Pressure injuries p. 458
Manlio Ottonello

CHAPTER 31
Pressure ulcers in patients with spinal cord injury p. 474
Antonino Massone

CHAPTER 32
Skin lesions during the Covid-19 pandemic p. 486
Claudio Ligresti

CHAPTER 33
The scar and its pathological forms p. 500
Paolo Persichetti, Rosa Salzillo, Silvia Ciarrocchi, Carlo Mirra, Giovanni Francesco Marangi

CHAPTER 34
Debridement: general concepts p. 516
Luca Grimaldi

CHAPTER 35
Chemical debridement p. 526
Giuseppe Giudice, Pasquale Tedeschi, Alessio De Cosmo, Marcello Del Zotti

CHAPTER 36
Surgical debridement p. 538
Fabrizio Malan

CHAPTER 37
Lower limb amputations p. 550
Domenico Aloj, Rosalba Tortia

CHAPTER 38
Physical therapies p. 566
Cesare Brandi

CHAPTER 39
Light therapy p. 578
Claudio Ligresti, Sara Sandroni

CHAPTER 40
VAC therapy p. 590
Franco Bassetto, Carlotta Scarpa

CHAPTER 41
Compression therapy for venous ulcer p. 604
Giovanni Mosti

CHAPTER 42
Hyperbaric oxygen therapy p. 618
Lidio Maffi

CHAPTER 43
Orthopedic footwear and biomechanics concepts p. 632
Gabriele Montini

CHAPTER 44
Anti-decubitus devices p. 646
Antonino Massone

CHAPTER 45
Traditional and advanced dressings: general aspects p. 660
Andrea Bellingeri

CHAPTER 46
Antiseptic and absorbent dressings p. 668
Sara Sandroni

CHAPTER 47
Bioactive dressings p. 680
Deborah Cesura Granara

CHAPTER 48
Regenerative medicine with blood components for non-transfusional use p. 690
Laura Mazzucco, Valeria Balbo

CHAPTER 49
Fat grafting in difficult wounds p. 702
Valerio Cervelli, Barbara De Angelis

CONTENTS

CHAPTER 50
Treatment of challenging wounds with dermal matrices p. 716
Giuseppe Giudice, Alessio De Cosmo, Aurelia De Pascale, Pasquale Tedeschi

CHAPTER 51
The operating field p. 730
Adriana Cordova, Giulio Borraccino, Mauro La Bruna, Walter Raffaele Milia

CHAPTER 52
Skin autologous and allogenic grafts p. 740
Francesca Romana Grippaudo, Edoardo Bruno, Sara Carella, Diego Ribuffo

CHAPTER 53
Flaps in the pelvic region p. 752
Manlio Ottonello

CHAPTER 54
Flaps in the lower limb p. 758
Bruno Battiston, Davide Ciclamini, Andrea Audisio, Fulvio Antonino Nicolò

CHAPTER 55
Medical-legal aspects p. 776
Massimo Navissano

CHAPTER 56
Psychological and psychiatric aspects in the management of difficult wounds p. 784
Riccardo Oliva

CHAPTER 57
Organizational management of patients with skin lesions at home p. 790
Marco Marchelli, Sara Sandroni, Laura Stefanon

INTRODUCTION

The decisive inspiration for writing this text stemmed from the commemoration of the tenth anniversary of the establishment of the Italian Academy Wound Care (IAWC), an institution that has trained hundreds of doctors, nurses, physiotherapists, podiatrists, and pharmacists in the intricacies of treating challenging wounds. The Italian Academy Wound Care's program is extensive, covering the entire spectrum of wound care through theoretical and practical lessons delivered by experienced instructors, whom I extend my heartfelt gratitude for their support in crafting this text.

In essence, this book serves as a tangible representation of the Italian Academy Wound Care program on paper. It is designed to simplify the educational journey for students over the two years of study leading to the coveted title of "Expert". Additionally, it caters to experienced healthcare professionals seeking to compare and verify their knowledge in specific treatments for various types of skin lesions.

Authoring a scientific book on challenging wounds is never a simple task due to the complexity encountered in describing the diverse types of skin lesions and their origins. These complexities are often compounded by intertwined pathological conditions, which can be further exacerbated by the implementation of unsuitable therapies.

This volume aspires to guide the reader in studying the various treated pathologies and the most suitable therapies through practical examples of clinical cases. It is crucial to emphasize that the care of patients with cutaneous ulcerative pathologies and even deeper tissues relies heavily on the necessary anatomical and physiopathological understanding of the problem, as well as validated therapeutic protocols to be implemented in suitable facilities with specialized healthcare personnel.

The idea of creating a book beneficial to the reader had to address the challenge of varying educational levels among readers, with different clinical potentials and divergent scientific interests. For this reason, I deemed it appropriate to

divide each chapter into three sections: Pathologies, Therapies, and Clinical Cases. Readers can consult descriptions of various types of lesions and possible therapies within the chapters, delving into the topic with the consultation of clinical cases based on their curiosity and desire for information, which may be broad or “niche” depending on their needs.

Hence, prior knowledge of phenomena related to the healing process, various levels of diagnostic investigation, and the diverse care activities, differentiated based on the intensity of the pathology and the need to expedite healing time when possible, is crucial.

Significant emphasis has also been given to the section regarding diagnostic and therapeutic technology, selecting, among many, activities that are well-established and validated by international literature.

Finally, some in-depth explorations concerning pain and the psychological and psychiatric aspects that patients may present due to prolonged illnesses are included. Equally important is the chapter addressing disputes between healthcare professionals and patients, for malpractice and/or the increasingly frequent requests for compensation in this medical field.

I extend special thanks to the Publisher, who believed in the utility of writing this text in the suggested format, making it more easily accessible while maintaining the scientific rigor required in describing pathology and therapy in the everyday clinical practice.

Good reading to all.

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STRUCTURE	ALTERATION	DESCRIPTION
Epidermis	Orthokeratotic hyperkeratosis	Thickening of layer of corneal lamellae
	Parakeratotic hyperkeratosis	Thickening of keratinocytes with residual nuclei
	Acanthosis	Thickening of the Malpighian layer
	Atrophy	Thinning with disappearance of the basal ridge profile
	Apoptosis	Involution of single cells
	Dyskeratosis	Early keratinization
	Spongiosis	Accumulation of plasma in intercellular spaces
	Acantholysis	Destruction of intercellular junctions
Dermis	Elastosis	Abnormal organization, structure and quantity of elastic fibers
	Fibrosis	Abnormal amounts of collgene and extracellular matrix
	Lichenoid inflammatory infiltrate	Dense infiltration of small lymphocytes affecting the superficial dermis and obscuring the dermo-epidermal junction
	Diffuse	Inflammatory cells scattered throughout the dermal area
	Perivascular	Inflammatory cells arranged in a "cap" around the vessels, without infiltrating the wall
	Granulomatous	Rounded structures consisting of a crown of histiocytes and multinucleated giant cells with a sometimes-necrotic central area
	Eosinophilic component	Presence of eosinophils, suggestive of immunological reaction
	Neutrophil component	Presence of granulocytes suggestive of acute inflammation
Skin appendages	Alopecia	Atrophy of the hair bulbs
Subcutaneous tissue	Septal inflammation	Inflammatory cells present in the fibrous septa that border the lobules
	Lobular inflammation	Inflammatory cells in adipose lobules.

Table 2 Main histological changes of the structures that compose the skin

The epidermis, of ectodermal origin, is a stratified squamous keratinized epithelial tissue (fig. 2). The layers that make up the epidermis are as follows: basal layer (stratum basale), spinous layer (stratum spinosum), granular layer (stratum granulosum), eosinophilic clear layer (stratum lucidum), and cornified layer (stratum corneum).

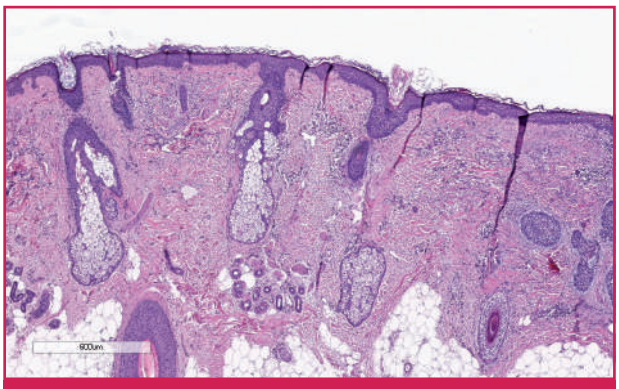

Figure 1 Subdivision of the skin into the three anatomical layers: epidermis, dermis, hypodermis

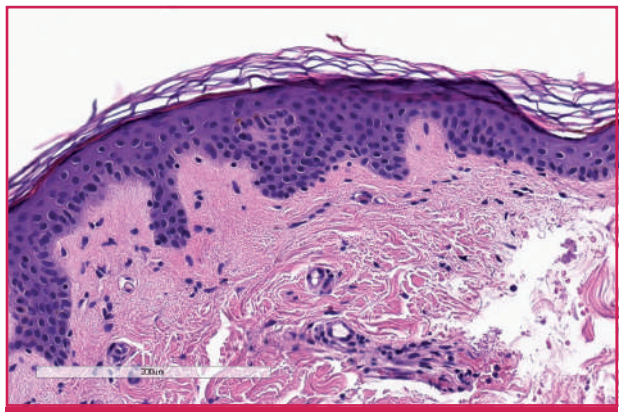

Figure 2 Epidermis

Figure 3 Ulcerated sternal neoplastic lesion

Figure 4 Ulcerated basalioma, tibial region, right lower limb

Objective examination of the wound

Local wound assessment is therefore the final and decisive step, because on its proper execution depends the turning of wounds toward healing and must therefore be performed by experienced personnel. This can avail itself, in addition to TIME for wound bed preparation (Wound Bed Preparation), to tools and schemes of approach such as the Wound Assessment Triangle [6], as outlined in the Wuwhs 2016 (World Union of Wound Healing Societies) position paper, which brings the clinician's attention back to the following points, considering each possible condition found, possible causes, and suggestions for planning a management plan for these three elements:

- perilesional skin;
- edges of the lesion;
- bed of the lesion.

A further assessment that the clinician can adopt is that of the "prevailing sign", defined as "the clinical sign most evident on objective examination of the lesion and perilesion" [7], as an indicator of the current state of the lesion, for example, a profuse exudate or a very reddened perilesional in the case of an infection. Treating the prevailing sign is itself a simple and effective approach, especially in choosing the best dressing to apply in that specific case (fig. 5).

The following will be noted in the objective examination of the lesions.

Size and number. The size of a lesion generally provides an indication of the underlying damage. Size is important because it is the main indicator of improvement and worsening and thus of success or failure of therapy. The number of lesions may suggest their etiology or indicate the presence of a worsening infection or incorrect therapy.

Margins. The shape that the margins have is often

Second-level examinations in lymphatic pathology

The techniques used in second-level instrumental lymphatic diagnostics have an ancient history. Due to the lack of usability and immediacy of the methods, however, recommendations not to forego them in the study of the patient with lymphedema with or without trophic lesions have only recently appeared in the literature.

Lymphography with indocyanine green (fluorescent pigment) has been most widely used over the years both to image lymphatic vessels (fig. 11), before and during surgical procedures, and for the diagnosis of lymphedema and functional assessment of lymphatic drainage in the extremities.

To date, guidelines stipulate that for the proper management of lymphedema, and thus also of the patient with chronic lymphedema skin ulcers, lymphoscintigraphy is indicated as the test of choice (fig. 12); the test is also recommended for treatment monitoring, as it can be repeated serially.

Diagnostic techniques

The following section reviews the details of different diagnostic technologies and was designed by the authors for reference use, so the subsections appear in alphabetical order.

Ankle-Brachial Index (ABI - Winsor Index, WI)

The examination is performed with the patient in clinostatism. The sphygmomanometer cuff is placed four fingers above the malleoli (fig. 1). An acoustic signal of the pedidian artery is sought with the Continuous Wave Doppler (Doppler-CW) possibly in a pocket version

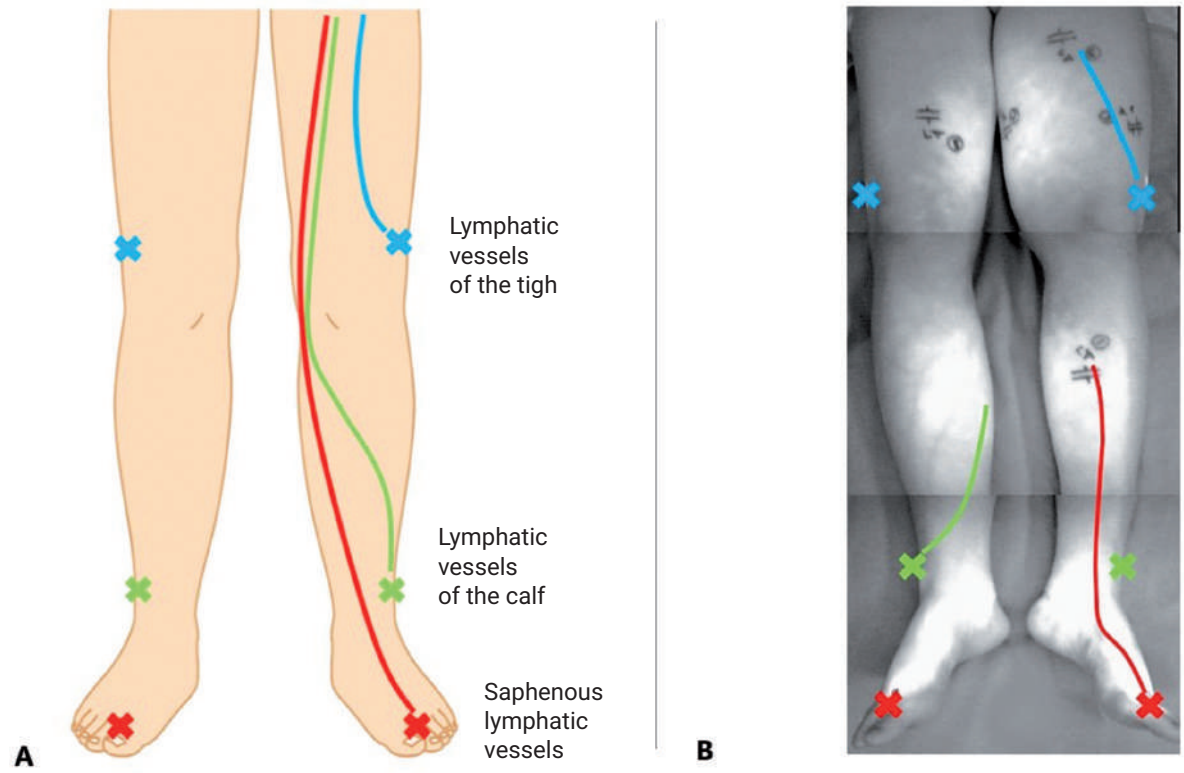

Figure 11 Multiple injection lymphography. A) Schematic diagram of injection sites in the multiple lymphosome technique. B) Lymphoscintigraphy with indocyanine green at multiple lymphosomes one day after injection makes one lymphatic vessel on the left and two on the right identifiable. *Source: modified from Hara H et al. J Plast Reconstr Aesthet Surg. 2020;73:1025-1030.*

CAUSES OF TISSUE NECROSIS
• Pressure (ischemia)
• Ischemia (reduced arterial flow)
• Infection (colliquative action)
• Inflammation (enzymatic coagulative action)
• Trauma (crush syndrome)
• Cancer (enzyme activity)

Table 1 Causes of tissue necrosis

TYPES OF NECROSIS FROM A HISTOLOGICAL POINT OF VIEW
• Coagulative necrosis: ischemia-hypoxia
• Liquefactive/colliquative necrosis: bacterial infections
• Gangrenous necrosis: coagulative hypoxia-infection
• Caseous necrosis: coagulative/colliquative fungal infection
• Adipose necrosis: enzymatic lipase
• Fibrinoid/immunologic necrosis: immune complexes

Table 2 Types of necrosis from a histological point of view

Types of necrosis

Coagulative necrosis

It usually occurs in an oxygen-poor environment. Cell shape and tissue architecture are preserved after their death for a minimum of several days. Affected tissues exhibit well-established architecture. The damage presumably denatures not only structural proteins but also enzymes, blocking proteolysis of dead cells. It is then possible to observe the persistence of eosinophilic anucleated cells for days or weeks. Eventually, necrotic cells are removed by phagocytosis of cellular debris by leukocytes from the inflammatory infiltrate and digestion by lysosomal enzymes of leukocyte origin.

It can be observed with a microscope (as in myocardial infarction, pycnosis of the nucleus, hypereosinophilia of myocytes, contraction band necrosis, initial neutrophilic infiltrate, and of the spleen and in the kidneys). Ischemia caused by vessel obstruction can lead to coagulative necrosis of vascularized tissue in all organs except the brain. An area of localized coagulative necrosis is termed an infarct. In wound care it is observed in burns.

Colliquative or liquefactive necrosis

It occurs by digestion of dead cells. Normal tissue gives way to a viscous liquid mass containing an accumulation of leukocytes and enzymes with formation of pus (dead leukocytes), as in pneumonia. It is usual in infections, results in the formation of pus, mixture of cellular debris and altered polymorphonucleates (white blood cells).

Figure 1 Dry necrosis, eschar with surrounding maceration in sacral pressure injury

Figure 2 Necrosis-slough: devitalized tissue in septic state

Figure 1

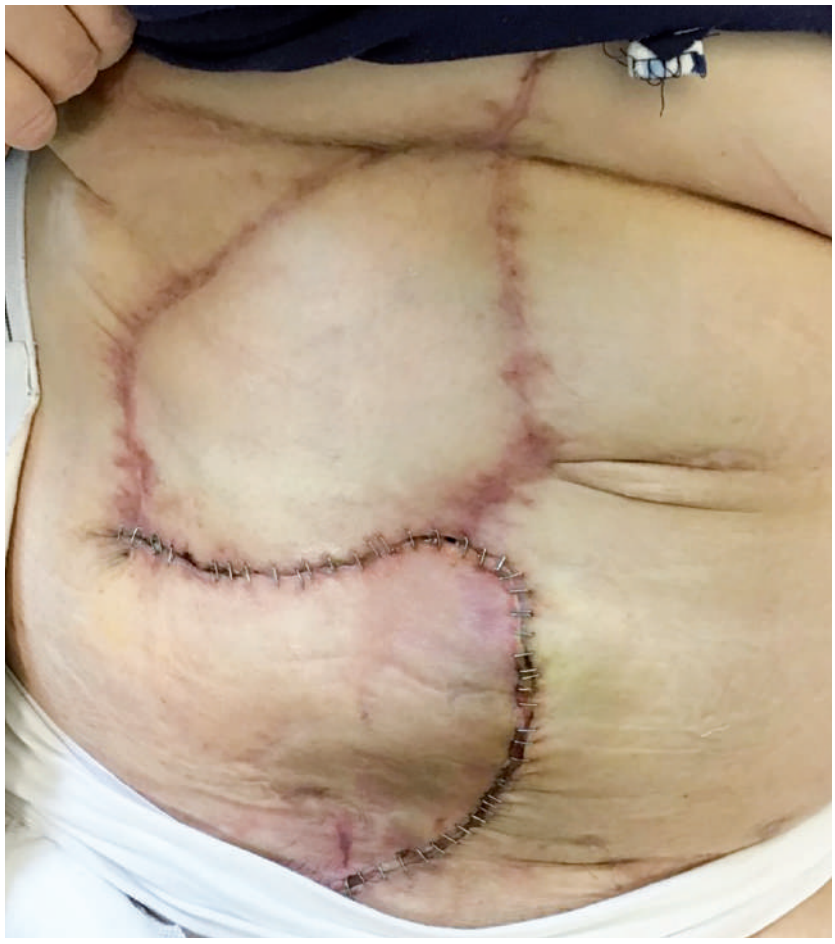

Figure 2

CASE REPORT 1

Post-surgical infection after reconstruction with myocutaneous flap

Post-surgical infection following abdominal wall reconstruction with a vastus lateralis myocutaneous flap (fig. 1). Outcome following a course of antibiotic therapy based on susceptibility testing, surgical debridement, and coverage of the resulting tissue loss due to infection and tissue necrosis with a local advancement flap (fig. 2).

Figure 1a

Figure 1b

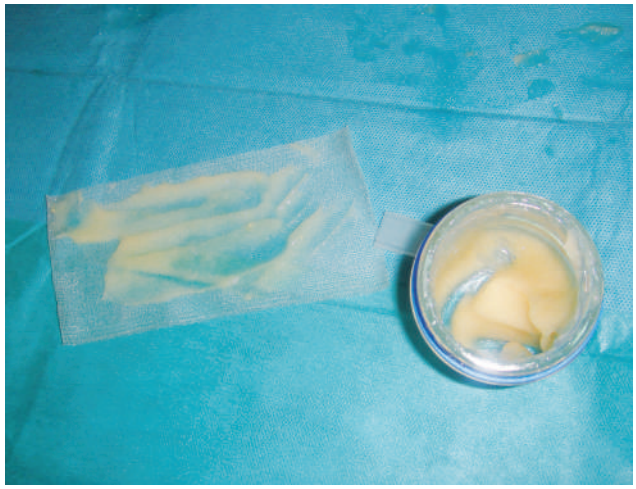

Figure 2a

Figure 2b

Figure 3a

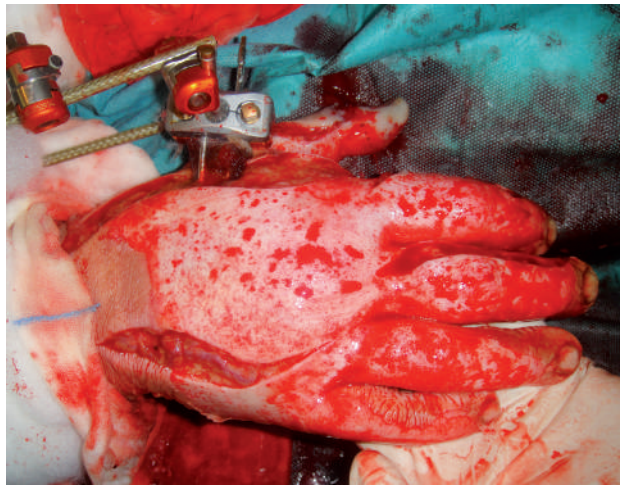

Figure 3b

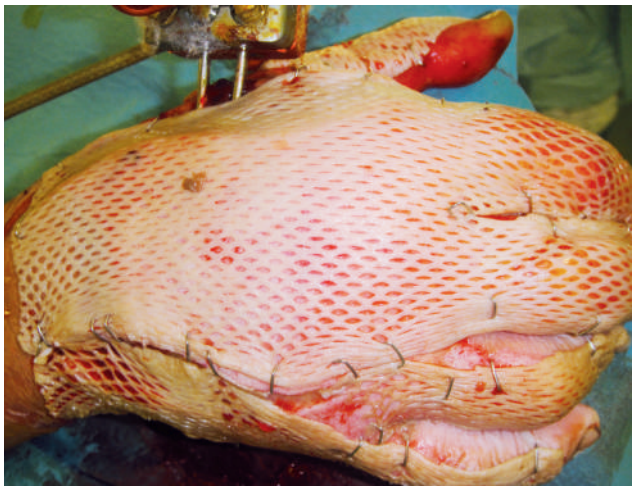

Figure 4a

Figure 4b

Figure 5a

Figure 5b

Figure 5c

CASE REPORT 1

Enzymatic escharolysis on intermediate-deep burns

A 48-year-old male patient suffered from intermediate-deep and deep flame burns, extending to the trunk, upper limbs, and lower limbs (TBSA 60%). The hands exhibited intermediate-deep burns (figs. 1a-1b), which, according to standard care, would have required early excision and repair with autologous grafts. The limited availability of autologous skin precluded this procedure, leading to the decision to undergo enzymatic escharolysis (5 g of NexoBrid were used). The day after enzymatic escharolysis, the treated areas were temporarily protected with allogenic skin, awaiting autologous grafting (figs. 2a preparation of enzymatic gel, 2b application to lesions, figs. 3a-3b result after 4 hours of enzymatic action). Why was this treatment chosen? The goal was to leverage the specific characteristics of enzymatic escharolysis. This method is a highly selective debridement technique that, in the case of intermediate-deep burns, unlike traditional tangential excision, completely removes the necrotic dermal layer while leaving the partially damaged dermal portion intact. This residual dermal portion, if well-protected from infection and desiccation, can act as a “scaffold”, similar to dermal substitutes, ensuring better morphological and functional outcomes. In our experience, allogenic skin coverage is considered the most effective in protecting the dermal scaffold, preventing desiccation (figs. 4a-4b). After 6 weeks, thanks to the survival of a good number of skin appendages in the dermal scaffold, complete spontaneous healing of the treated areas was achieved, avoiding autologous skin grafting. The excellent morphological and functional outcomes were entirely unexpected, given the extent of the damage and spontaneous healing (figs. 5a-5b-5c).

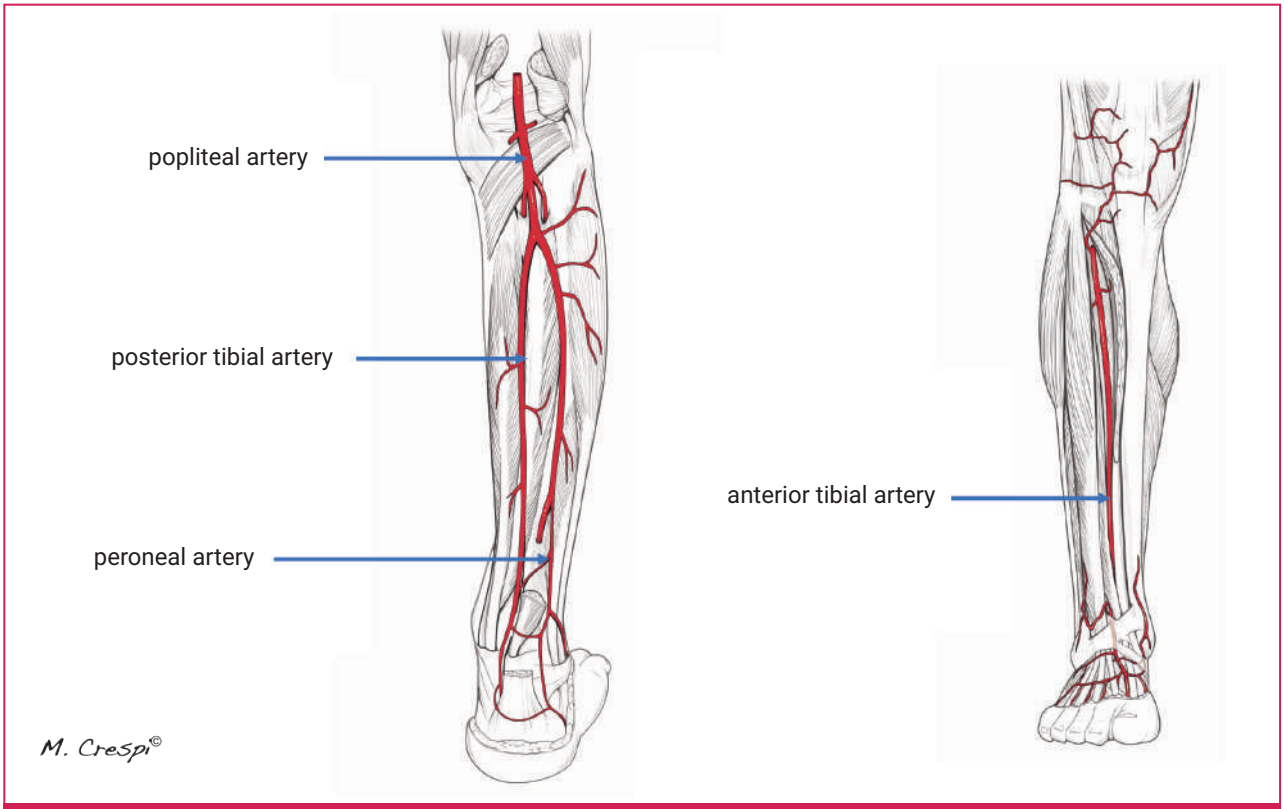

Figure 3 Anterior tibial and posterior tibial artery

the pelvis, and the external iliac arteries, originate. These, passing through the inguinal ligament, proceed in the thigh with the femoral artery and then at the level of the knee with the popliteal arteries which, subsequently, divide into the tibioperoneal trunks from which the vessels that supply the foot originate. The anterior tibial artery, which continues on the dorsum of the foot with the dorsalis pedis artery, and the posterior tibial artery, which plantarly divides into the lateral plantar artery and the medial plantar artery; and finally, the interosseous artery (fig. 3).

Innervation

The muscles of the leg and foot are innervated by the sciatic nerve, which is made up of two nerves: the common peroneal nerve (L4-S2) and the tibial nerve (L4-S3).

The terminal branches of the common peroneal nerve are in the superficial peroneal nerve and the deep peroneal nerve.

The superficial peroneal nerve provides motor innervation of the lateral compartment of the leg and sensation of the dorsum of the foot and toes; the deep peroneal nerve provides innervation to the anterior muscles of the leg (extensor digitorum longus, extensor hallucis longus, tibialis anterior and peroneal third) and the sensitivity of a small area of the foot, descends to the flank of the anterior tibial artery continues with the dorsalis pedis artery and then divides into two terminal branches: the medial branch, which constitutes the lateral dorsal digital nerve of the big toe and the dorsal digital nerve of the second toe; the lateral branch innervates the tarsometatarsal and metatarsal phalangeal joints.

The terminal branches of the tibial nerve (fig. 4) are the medial plantar nerve and lateral

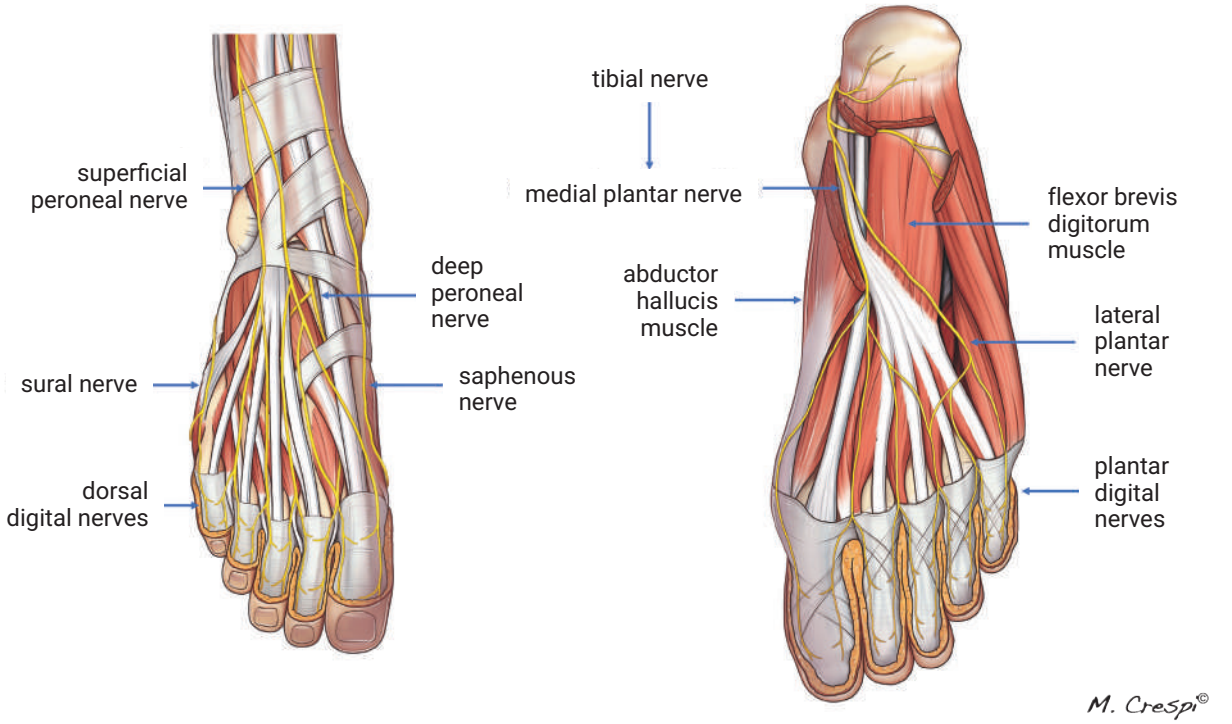

Figure 4 Innervation of the foot

plantar nerve. The medial plantar nerve with its medial branch forms the medial plantar digital nerve proper of the big toe, while with its lateral branch at the level of the first intermetatarsal space it divides into the three common plantar digital nerves of the toes. The lateral plantar nerve runs distally and at the level of the fourth intermetatarsal space divides into its two terminal branches: the superficial branch, which innervates the common and proper plantar digital muscles, and the deep branch, which innervates the interosseous muscles of the first three intermetatarsal spaces and the fourth and fifth lumbrical muscles.

Joints

The tibiotalar joint (fig. 5) or ankle is the most proximal joint that connects the leg with the foot. It consists of the distal end of the tibia

Figure 5 Tibiotarsal joint: fibular and tibial malleolus, talus

Diabetic foot dressing
Courtesy of Prof. Claudio Ligresti

Surgical excision of tiloma of the foot with underlying plantar ulcer
Courtesy of Prof. Claudio Ligresti

Diabetic foot clinic
Courtesy of Prof. Claudio Ligresti