## Contents

		(CRIP)	
List of Contributors Series Preface Preface			
1	Chro	onic Wound Healing: Molecular and Biochemical Basis	1
	Soph	tha late and Keith Harding	1
	1.1	Introduction	1
	1.2	Catagories of Chronic Wound	1
	1.5	1.3.1 Pressure Ulcers	3
		1.3.2 Venous Stasis Illears	
		1.3.2 Venous Stars Oreers	4
		1.3.4 Diabetic Foot Illeers	
	14	How a Chronic Wound Develops: Intrinsic Components	4
	1.1	1.4.1 Cell Phenotype	5
		1.4.2 Immune Cells and Inflammatory Mediators	6
		1.4.3 Reactive Oxygen Species	8
		1.4.4 Growth Factors	8
		1.4.5 The Role of Matrix Metalloproteinases	12
	1.5	How a Chronic Wound Develops: Extrinsic Factors	13
		1.5.1 Infection	13
		1.5.2 Nutrition	13
		1.5.3 Tobacco Smoking	14
		1.5.4 Hypoxia and Ischaemia–Reperfusion Injury	15
	1.6	Concluding Remarks	15
	Refe	rences	16

vi	Contents

Clini	ical Perspectives for Treating Chronic Wounds	21			
Barun Majumder, Kirstie Lane, Diane Beck, Sandeep Singh and Duniya					
Маји	ımder				
2.1	Background	21			
2.2	Aetiology of Diabetic Foot Ulcers	22			
2.3	Standard of Care for Treatment of Diabetic Foot Ulcers	22			
2.4	Commonly Used Wound Dressings for Diabetic Foot Ulcers and Their				
	Mechanism of Action	22			
2.5	Absorbent and Superabsorbent Dressings	23			
2.6	Alginates	23			
2.7	Films	23			
2.8	Foams	24			
2.9	Honeys	24			
2.10	Hydrogels	25			
2.11	The Role of a Split Thickness Skin Graft in Diabetic Foot Ulcers	25			
2.12	Negative Pressure Wound Therapy	25			
2.13	Larval Therapy	27			
2.14	Clinical Case Studies from Multidisciplinary Diabetic Foot Clinic	27			
	2.14.1 Neuropathic Wound	27			
	2.14.2 Ischaemic Wound	29			
	2.14.3 Neuro-Ischaemic Wound	31			
	2.14.4 Osteomyelitis	33			
	2.14.5 Charcot's Foot	35			
	2.14.6 Necrotising Fasciitis in a Patient with Diabetes	36			
2.15	Summary	39			
Ackn	nowledgements	39			
Refe	rences	39			
Pred	iction, Prevention, Assessment, and Management of Skin Tears in				
the A	Aging Population	43			
Kimk	perly LeBlanc and Karen Campbell				
3.1	Introduction	43			
3.2	Skin Tear Prevalence and Incidence	44			
3.3	Predicting Skin Tears	45			
3.4	Prevention	47			
3.5	ISTAP Risk Reduction Program	49			
	3.5.1 General Health	49			
	3.5.2 Mobility	50			
	3.5.3 Skin	51			
3.6	Assessment	52			
3.7	Management	54			
3.8	Treatment	54			
3.9	Conclusion	55			
Dafa	rences	55			
	Clini Baru Maju 2.1 2.2 2.3 2.4 2.5 2.6 2.7 2.8 2.9 2.10 2.11 2.12 2.13 2.14 2.15 Ackr Refer <b>Pred</b> the A Kimb 3.1 3.2 3.3 3.4 3.5	Clinical Perspectives for Treating Chronic Wounds   Baran Majumder, Kirstie Lane, Diane Beck, Sandeep Singh and Duniya   Majumder   2.1 Background   2.2 Actiology of Diabetic Foot Ulcers   2.3 Standard of Care for Treatment of Diabetic Foot Ulcers   2.4 Commonly Used Wound Dressings for Diabetic Foot Ulcers and Their Mechanism of Action   2.5 Absorbent and Superabsorbent Dressings   2.6 Alginates   2.7 Films   2.8 Foams   2.9 Honeys   2.10 Hydrogels   2.11 The Role of a Split Thickness Skin Graft in Diabetic Foot Ulcers   2.12 Negative Pressure Wound Therapy   2.13 Larval Therapy   2.14 Clinical Case Studies from Multidisciplinary Diabetic Foot Clinic   2.14.1 Neuro-Ischaemic Wound   2.14.2 Ischaemic Wound   2.14.3 Neuro-Ischaemic Wound   2.14.4 Osteomyelitis   2.15 Summary   Acknowledgements   References   Prediction, Prevention, Assessment, and Management of Skin Tears in the Aging Population   Kimberly LeBlanc and			

4	Imp	ortance	of Debriding and Wound Cleansing Agents in Wound	50		
	Gwa	ndolvn (	Carandar Bianca K. dan Ottalandar Sandra Kamaa	37		
	Mar	iiin C H	A Doomen Tim HC Damen and Anne Marie F van Well			
	A 1	What i	S Debridement?	50		
	4.2	The H	istory of Debridement	59		
	43	Why I	Indertake Debridement?	60		
	4.4	Debrid	lement Techniques and Wound Cleansing Agents	62		
		4.4.1	Mechanical Debridement	62		
		4.4.2	Biological Debridement	72		
		4.4.3	Enzymatic Debridement	74		
		4.4.4	Autolytic Debridement	77		
		4.4.5	Wound Cleansing	79		
		4.4.6	Other Debridement Therapies	80		
	4.5	What i	s the Future of Debridement?	81		
	Refe	rences		82		
5	Trea	tment o	f Mixed Infections in Wounds	91		
	Asif Ahmed and Joshua Boateng					
	5.1	Introdu	uction	91		
		5.1.1	Wound Healing Process	92		
		5.1.2	Types of Chronic Wounds	92		
	5.2	Preval	ence of Mixed Infections	94		
		5.2.1	Bacterial–Fungal Interactions	95		
		5.2.2	Bacterial-Bacterial Interactions	98		
		5.2.3	Host Responses to Mixed Infections and Drug Resistance	99		
	5.3	Manag	gement of Mixed Infected Wounds	100		
		5.3.1	Clinical and Microbiological Diagnosis	101		
		5.3.2	Debridement and Cleansing	101		
		5.3.3	Antimicrobial Therapies	102		
		5.3.4	Hyperbaric Oxygen Therapy	104		
		5.3.5	Phage Therapy	104		
	5.4	Summ	ary and Future Perspectives	104		
	Refe	rences		105		
6	Trea	tment o	f Biofilms in Infected Wounds	115		
	Philip Debrah, Awo Afi Kwapong and Mansa Fredua-Agyeman					
	6.1	Introdu	uction	115		
	6.2	Why a	nd How Biofilms Form	116		
	6.3	Wound	1 Biofilms	118		
		6.3.1	Wound Healing	119		
	6.4	Biofilr	ns and Wounds	119		
		6.4.1	Simulation of Biofilms in Wounds	120		

	6.5	Treatment of Biofilms in Wounds	126		
		6.5.1 Biofilm Eradication	126		
		6.5.2 Current Treatment Protocols	128		
	6.6	Clinical Examples	128		
	6.7	Summary	128		
	Refe	rences	130		
7	Free	ze-Dried Wafers for Wound Healing	137		
	Shio	w-Fern Ng			
	7.1	Introduction	137		
	7.2	Wafer as a Modern Wound Dressing	138		
	7.3	Freeze-Drying Process	139		
	7.4	Wafer Preparation	140		
	7.5	Wafer Assessments	141		
		7.5.1 Morphology	142		
		7.5.2 Swelling Index	144		
		7.5.3 Mechanical Properties	145		
		7.5.4 In Vitro Drug Release	145		
		7.5.5 Cell Viability	146		
	7.6	Wafer Biopolymers	146		
		7.6.1 Alginate	147		
		7.6.2 Chitosan	148		
		7.6.3 Carboxymethylcellulose	149		
	7.7	Conclusion	150		
	Refe	rences	150		
8	Silver and Silver Nanoparticle-Based Antimicrobial Dressings				
	Josh	ua Boateng and Ovidio Catanzano			
	8.1	Introduction	157		
		8.1.1 Brief History of Silver as an Antibiotic	159		
		8.1.2 Mechanism of Action	160		
		8.1.3 Bacterial Resistance to Silver	164		
	8.2	Silver Dressings in Wound Healing	167		
		8.2.1 Silver-Based Antimicrobial Dressings	169		
		8.2.2 Silver Nanoparticle-Based Antimicrobial Dressings	170		
	8.3	Cost-Effectiveness of Silver Dressings	175		
	8.4	Concluding Remarks	176		
	Refe	rences	177		
9	Hyd	rogel Dressings	185		
	Galiya S. Irmukhametova, Grigoriy A. Mun and Vitaliy V. Khutoryanskiy				
	9.1 Introduction				
		9.1.1 Classification by Origin of Materials Used to Prepare			
		Hydrogels	186		
		9.1.2 Classification by Composition and Structure of Hydrogels	186		
		9.1.3 Classification by the Type of Cross-Linking	187		

		9.1.4	Classification Based on the Shape and Dimensions of			
			Hydrogels	187		
		9.1.5	Classification Based on the Charge of Macromolecules			
			Forming Hydrogels	187		
		9.1.6	Classification Based on Functional Properties of the			
			Hydrogels	187		
	9.2	Mecha	nism of Hydrogel Swelling	187		
		9.2.1	Swelling of Temperature-Sensitive Hydrogels and Their			
		<i>&gt;</i> . <u>_</u>	Application in Wound Healing	189		
		922	Swelling of Light-Sensitive Hydrogels	190		
		923	Swelling of Electro-Sensitive Hydrogels	191		
	93	Applic	ation of Hydrogels as Wound Dressings	191		
	9.5	Industr	ial Methods for the Synthesis of Hydrogels for Wound	171		
	7.4	Dressir	an methods for the synthesis of frydrogers for wound	103		
		Q 4 1	Polymerization Methods	103		
		9.4.2	Cross-Linking of Polymers	105		
	95	Δntimi	crobial Hydrogels with Special Additives	108		
	9.5	Conclu	ision	200		
	9.0 A okn	owledge	nents	200		
	Dofor	owieugii	lients	201		
	Kelei	ences		201		
10	Gene Therapy for the Treatment of Chronic Wounds					
	Marc	os Garci	ia-Fuentes			
	10.1	Introdu	uction	209		
	10.2	Pharma	acodynamics of Gene Therapy in Chronic Wounds	210		
		10.2.1	Signalling Supplementation	210		
		10.2.2	Pathway Inhibition	211		
	10.3	Admin	istration Routes and Methods	212		
		10.3.1	Systemic Delivery	212		
		10.3.2	Topical Delivery	212		
		10.3.3	Intralesional Delivery	213		
	10.4	Gene D	Delivery Systems	213		
		10.4.1	Physical Methods	214		
		10.4.2	Viral Vectors	215		
		10.4.3	Chemical Delivery Systems	217		
		10.4.4	Gene-Activated Matrices	220		
	10.5	Clinica	l Evaluation	221		
	10.6	Conclu	ision	226		
	Ackn	owledge	ements	226		
	Refer	rences		227		
11	Honoy in Wound Hooling					
11	noney in wound nearing					
	11 1	The Ui	nn story of Honey	225		
	11.1		story of fioncy	233		
	11.2	Longe	Desearch	200		
	11.3	попеу	Research	230		

Х	Contents

	11.4	Medical Grade Honey	237			
	11.5	Modes of Action	238			
	11.6	Applications and Specific Wound Types	242			
	11.7	Practical Considerations	246			
	11.8	Novel Concepts and Conclusions	247			
	References					
12	Rege	neration Using Tissue Engineered Skin Strategies	255			
	Lucíl	ia P. da Silva, Mariana T. Cerqueira and Alexandra P. Marques				
	12.1	Introduction	255			
	12.2	Skin Physiology and Wounding	256			
	12.3	Skin Tissue Engineering	258			
	12.4	Evolving Skin Tissue Engineering Strategies	259			
		12.4.1 Balancing the Inflammatory Phase	261			
		12.4.2 Enhancement of Re-Epithelialization	263			
		12.4.3 Target of Dermal Matrix Synthesis and Remodeling	269			
		12.4.4 Re-Establishment of the Vascular Network	270			
		12.4.5 Innervation Shaping	280			
		12.4.6 Appendages and Pigmentation	281			
	12.5	Conclusion	282			
	Refer	ences	283			
13	Loca	l Delivery of Growth Factors Using Wound Dressings	291			
	Ovidi	o Catanzano and Joshua Boateng				
	13.1	Wound Dressings as Delivery Platforms for Growth Factors	291			
	13.2	Growth Factors Involved in the Wound Healing Process	292			
	13.3	Local Delivery of Growth Factors Using Wound Dressings	296			
	13.4	Integration of Platelet-Rich Plasma in Wound Dressings	299			
	13.5	Enhancing Local Growth Factor Expression Using				
		Gene Therapy	300			
	13.6	Wound Delivery of Growth Factors from Living Systems	302			
	13.7	Regulatory Considerations	305			
	13.8	Conclusions and Future Perspectives	306			
	Refer	ences	307			
14	Elect	rospinning Technologies in Wound Dressing Applications	315			
	Giuse	eppina Sandri, Silvia Rossi, Maria Cristina Bonferoni, Carla Caramella				
	and Franca Ferrari					
	14.1	Introduction				
	14.2	Basic Concept and Electrospinning Set-Up				
	14.3	Parameters Affecting the Electrospinning Process	318			
	14.4	Process Parameters	319			
		14.4.1 Electric Field Strength	319			

		14.4.3	Needle-to-Collector Distance	320
		14.4.4	Collector and Needle Types	320
	14.5	Solutio	on Parameters	321
		14.5.1	Molecular Weight and Polymer Concentration	321
		14.5.2	Surface Tension	322
		14.5.3	Conductivity/Surface Charge Density	322
		14.5.4	Environmental Parameters	322
	14.6	Biomed	dical Applications of Nanofibrous Membranes	323
		14.6.1	Wound Dressings and Wound Healing	323
		14.6.2	Electrospun Dressings	325
	14.7	Chemic	cophysical and Biopharmaceutical Characterizations	325
	14.8	Dressin	ng/Scaffold Parameters Affecting Cell Functions	327
	14.9	Materia	als for Fabricating Nanofibers	328
		14.9.1	Biopolymers	328
	14.10	Conclu	ding Remarks	333
	Refer	ences		333
15	The I	Place of	Biomaterials in Wound Healing	337
	Anna	lisa Bian	nchera, Ovidio Catanzano, Joshua Boateng and Lisa Elviri	
	15.1	Introdu	ction to Biomaterials for Wound Healing	337
		15.1.1	Definition of Biomaterials	337
		15.1.2	Functional Requirements of Wound Repair Biomaterials	338
		15.1.3	Classification of Biomaterials Commonly Used in Wound	
			Healing	338
	15.2	Synthe	tic Biomaterials for Wound Healing	339
		15.2.1	Polyurethanes and their Derivatives	340
		15.2.2	Poly L-Lactic Acid	340
		15.2.3	Poly(Ethylene Glycol)	341
		15.2.4	Polycaprolactone	341
		15.2.5	Poly(Glycolic Acid) and Poly(Lactic-co-Glycolic Acid)	342
	15.3	Natural	Biomaterials for Wound Healing	343
		15.3.1	Polysaccharide-Based Biomaterials	343
		15.3.2	Protein-Based Biomaterials	348
	15.4	Applica	ation of Biomaterials in Wound Healing	350
		15.4.1	Traditional and Impregnated Dressings	350
		15.4.2	Hydrogels	352
		15.4.3	Film Dressings	353
		15.4.4	Foam Dressings	354
		15.4.5	Nanofiber-Based Dressings	355
		15.4.6	Three-Dimensional Printed Dressings	356
	15.5	New Ti	rends in Biomaterials for Wound Healing	357
		15.5.1	Extracellular Matrix-Derived Biomaterials	357
		15.5.2	Tissue Engineered Skin Substitutes	357
	15.6	Conclu	sions and Future Perspectives	358
	Refer	ences		359

16	Wou	nd Dressings and Pressure Ulcers	367		
	Michael Clark				
	16.1 Overview				
	16.2	Introduction to Pressure Ulcers	367		
	16.3	The Impact of Pressure Ulcers	369		
	16.4	Managing Pressure Ulcers	370		
	16.5	Wound Dressings in Pressure Ulcer Treatment	371		
	16.6	Pressure Ulcer Prevention and Wound Dressings	377		
		16.6.1 Pressure Ulcers at the Nose	378		
		16.6.2 Pressure Ulcers at the Heel	378		
		16.6.3 Pressure Ulcers at the Sacrum	378		
	16.7	Conclusions			
	Refei	rences	380		
17	3D Printed Scaffolds for Wound Healing and Tissue Regeneration				
	Ataba	ık Ghanizadeh Tabriz, Dennis Douroumis and Joshua Boateng			
	17.1	Introduction	385		
	17.2	3D Printing	386		
	17.3	Laser-Based Bioprinting	387		
	17.4	Jet-Based Printing	389		
	17.5	Extrusion-Based Printing	391		
	17.6	Hybrid Printing	393		
	17.7	Conclusions	395		
	Refe	ences	395		
Ind	ex		399		