Part I Introduction

1 Introduction: development of skin substitutes 3

D. P. ORGILL, Brigham and Women's Hospital, USA

C. BLANCO, Joseph M. Still Research Foundation, USA

1.1 Historical development 3
1.2 Skin regeneration 5
1.3 Intellectual property and financial issues 6
1.4 Changing medical practice 7
1.5 References 7

2 Skin replacement products and markets 9

E. GARFEIN, Montefiore Medical Center, USA

2.1 Introduction 9
2.2 Indications for skin replacement 10
2.3 The products 12
2.4 The marketplace 15
2.5 Conclusion 16
2.6 References 16

3 Biomechanics of skin 18

V. SAXENA, Massachusetts Institute of Technology, USA

3.1 Skin biomechanics 18
3.2 Structure of skin 19
3.3 Definition of mechanical properties 20
3.4 Wounded skin contraction 21
3.5 Modeling skin using finite element methods 22

3.6 Forces on cells 23
3.7 Conclusion 23
3.8 References 23

4 The pathophysiologic basis for wound healing and cutaneous regeneration 25
D. T. NGUYEN, D. P. ORGILL and G. F. MURPHY, Brigham and Women's Hospital, USA.

4.1 Introduction 25
4.2 Skin microanatomy and physiology 26
4.3 Wound repair and scar formation 32
4.4 Pathologic wound healing 38
4.5 Comparison between fetal and post-natal skin 39
4.6 Wound repair versus regeneration: fundamental differences 41
4.7 Issues of stem cells and cellular plasticity 45
4.8 Historic developments and future trends 49
4.9 References 51

5 Skin grafts 58
S. D. IMAHARA and M. B. KLEIN, University of Washington, USA

5.1 Definitions 58
5.2 Skin anatomy and physiology 58
5.3 Autologous skin grafts 61
5.4 Principles of allogeneic skin grafts 67
5.5 Principles of skin xenografts 72
5.6 Future trends 73
5.7 Summary 74
5.8 References 74

6 Understanding the cellular basis of skin growth 80
L. GUO, Brigham and Women's Hospital, USA

6.1 Introduction 80
6.2 Structure of the skin 80
6.3 Skin development and growth 83
6.4 Experimental models for predicting cellular interactions 85
6.5 Conclusions 86
6.6 References 86

7 The regulatory approval process for biomaterials for treating skin loss 87

J. E. O'GRADY, Integra LifeSciences Corporation, USA

7.1 Introduction 87
7.2 Regulatory requirements 88
7.3 Medical device approval in the European Union 91
7.4 Combination products 93
7.5 The Global Harmonization Task Force (GHTF) 101
7.6 Quality system 101
7.7 Clinical trials 102
7.8 Humanitarian device exemption 107
7.9 Human tissue and cellular based products 108
7.10 User fees 109
7.11 Future trends in the regulatory process 109
7.12 References 110

Part II Epidermal and dermal replacement technologies

8 Alternative delivery of keratinocytes for epidermal replacement 115

F. M. WOOD, McComb Research Foundation, Burns Service of Western Australia, University of Western Australia, Australia

8.1 Introduction 115
8.2 Methods of keratinocyte delivery 117
8.3 Direct application 117
8.4 Carrier systems 118
8.5 Summary 119
8.6 References 120

9 Enhancing skin epidermal stability 124

J. R. SHARPE and N. R. JORDAN, Blond McIndoe Research Foundation, UK; L. J. CURRIE, Derriford Hospital, UK

9.1 Introduction 124
9.2 Fibrin as a repair material 125
9.3 Hyaluronic acid and Laserskin® as a repair material 129
9.4 Summary 136
9.5 Future trends 137
9.6 References 138

10 Human-derived acellular matrices for dermal replacement 142
C. T. WAGNER, R. T. OWENS, J. R. HARPER and D. J. MCQUILLAN, LifeCell Corporation, USA
10.1 Introduction 142
10.2 Processing native tissues 146
10.3 Material characterization 149
10.4 Functional evaluation 159
10.5 Universality of acellular regenerative tissue matrices for soft tissue replacement 164
10.6 Future trends 167
10.7 Sources of further information and advice 168
10.8 References 168
10.9 Disclosure 173
11 Lyophilized xenogenic products for skin replacement 174
N. MELO and R. SHERIDAN, Massachusetts General Hospital, USA
11.1 Introduction 174
11.2 Temporary skin substitutes 174
11.3 Permanent skin substitutes 175
11.4 Conclusions 178
11.5 References 178
Part III Combined dermal and epidermal replacement
12 Cultured skin substitutes 183
H. M. POWELL, Shriners Hospitals for Children, USA
S. T. BOYCE, Shriners Hospitals for Children and University of Cincinnati, USA
12.1 Introduction 183
12.2 Medical and surgical objectives for cultured skin substitutes (CSS) 184
12.3 Design and composition of cultured skin substitutes 185
12.4 Clinical considerations 191
12.5 Clinical assessment 193
12.6 Regulatory issues 194
12.7 Future trends 195
12.8 Conclusions 200
12.9 References 200

13 Use of keratinocytes in combination with a dermal replacement to treat skin loss 207
G. PIETRAMAGGIORI, Brigham and Women's Hospital, USA

13.1 Simultaneous substitution of dermis and epidermis: from two-step to one-step skin replacement 207
13.2 Cell seeding 208
13.3 Methods of delivery of keratinocytes 208
13.4 References 210

14 Principles of skin regeneration 212
I. V. YANNAS, Massachusetts Institute of Technology, USA

14.1 Introduction 212
14.2 The central problem of skin regeneration 213
14.3 Experimental variables in studies of skin regeneration 213
14.4 Applications of the wound closure rule 215
14.5 Scar formation may be secondary to wound contraction 216
14.6 Experimental studies of partial regeneration of skin 217
14.7 Regeneration of adult organs other than skin 219
14.8 Antagonistic relationship between contraction and regeneration 219
14.9 Mechanism of regeneration by use of scaffolds 221
14.10 Future trends 225
14.11 Sources of further information and advice 226
14.12 References 226

15 Summary: biomaterials for treating skin loss 231
D. P. ORGILL, Brigham and Women's Hospital, USA
C. BLANCO, Joseph M. Still Research Foundation, USA

15.1 Technological advances 231
15.2 Changes in the market for skin substitutes 231
15.3 A more normal skin – regenerative response 233
15.4 References 234

Index 237