

## Contents

**About the Editor** *xv*

**Contributors** *xvii*

**Preface** *xxi*

<b>1</b>	<b>Mucosal Immunity in Sexually Transmitted Infections</b>	<b>1</b>
	<i>Jiri Mestecky and Michael W. Russell</i>	
1.1	Introduction	1
1.2	Innate Immunity in the Genital Tract	2
1.2.1	Humoral Defense Factors in Female Secretions	2
1.2.2	Innate Defense Factors in the Male Tract	4
1.3	Immunoglobulins in Secretions of the Genital Tract	4
1.3.1	Female Genital Tract Secretions	4
1.3.2	Origin of Igs in Human Genital Tract Secretions	7
1.3.3	Functions of Genital Tract Antibodies	8
1.4	Cells of the Mucosal Immune System of the Genital Tract	10
1.4.1	Epithelial Cells	10
1.4.2	Immunoglobulin-Producing Cells	10
1.4.3	T Cells and Other Cell Types	11
1.5	Induction of Immune Responses in the Genital Tract	12
1.5.1	Induction of Humoral Immune Responses in Human Male Genital Tract Secretions	14
1.5.2	Immune Responses in the Genital Tract after Infections	15
1.5.2.1	Gonorrhea	15
1.5.2.2	Chlamydia	15
1.5.2.3	Human Immunodeficiency Virus (HIV)	16
1.5.2.4	Human Papilloma Virus	16
1.6	Concluding Remarks	17
	References	17
<b>2</b>	<b>The Role of Circumcision in Preventing Sexually Transmitted Infections</b>	<b>27</b>
	<i>Kouros Afshar, Behnam Kazemi, and Andrew E. MacNeily</i>	
2.1	Introduction	27
2.2	Biological Mechanisms	27
2.3	Methods of Circumcision	28

2.4	Complications	28
2.5	Role of MC in Transmission of HIV	29
2.5.1	Male-to-Female Transmission	29
2.5.2	Female-to-Male Transmission	29
2.5.3	Male-to-Male Transmission	30
2.6	Human Papilloma Virus (HPV)	30
2.7	Nonulcerative STIs	31
2.7.1	Gonorrhea	31
2.7.2	<i>Trichomonas Vaginalis</i> (Tv)	32
2.7.3	Chlamydia Trachomatis (Ct)	32
2.8	Ulcerative STIs/Genital Ulcer Disease (GUD)	32
2.8.1	Syphilis	33
2.8.2	Chancroid	34
2.9	Use of Male Circumcision as a Public Health Measure	34
2.10	Female Genital Mutilation (FGM)	35
	References	36
<b>3</b>	<b>Effect of Probiotics on Reproductive Health</b>	<b>41</b>
	<i>Piotr Kochan, Magdalena Strus, and Piotr B. Heczko</i>	
3.1	Introduction	41
3.2	Definition of Probiotics	43
3.3	Vaginal Microflora (Microbiota)	46
3.4	Applications of Probiotics in Vaginal and Reproductive Health	49
3.4.1	Vaginitis (Aerobic Vaginitis (AV), Bacterial Vaginosis (BV), and Vulvovaginal Candidiasis (VVC))	50
3.4.2	UTI	52
3.4.3	Pregnancy	52
3.4.4	Other Obstetrics and Gynecology (OB/GYN) Uses of Probiotics	53
3.5	Conclusions	53
	References	54
<b>4</b>	<b>Human Immunodeficiency Virus (HIV) Infection</b>	<b>61</b>
	<i>Santosh Kumar Singh and Sunit K. Singh</i>	
4.1	Introduction	61
4.2	HIV Structure/Genome	62
4.3	Routes of Transmission	64
4.3.1	Sexual Transmission	64
4.3.1.1	STDs and Sexual Transmission of HIV	64
4.3.1.2	Vulnerability of Female Genital Tract for HIV Transmission	66
4.3.2	Transmission by Contaminated Blood/Blood Product Transfusion	68
4.3.3	Transmission by Sharing Syringe and Needles	68
4.3.4	Transmission from Mother to Fetus or Newborn Babies	68
4.3.5	Occupational Risk in Healthcare Workers	68
4.4	Host Factors Influencing HIV Infectivity in Sexual Transmission	69
4.4.1	Systemic Host Factors	69
4.4.2	Local Host Factors	69
4.5	Viral Factors Influencing HIV Infectivity in Sexual Transmission	70

4.6	Mechanism of Pathogenesis	71
4.7	Diagnosis of HIV Infections	72
4.8	Therapeutics	73
4.8.1	Antiretroviral Therapies (ARTs)	73
4.8.2	Combinational ARTs	74
4.9	Conclusion	74
	References	75
<b>5</b>	<b>Genital Herpes</b>	<b>83</b>
	<i>Andreas Sauerbrei</i>	
5.1	Introduction	83
5.2	Pathogen	83
5.3	Epidemiology	84
5.4	Pathogenesis and Immunity	84
5.5	Clinical Features	86
5.6	Diagnosis	87
5.7	Treatment	90
5.8	Prevention and Control	93
5.9	Conclusion	94
	References	95
<b>6</b>	<b>Molluscum Contagiosum</b>	<b>101</b>
	<i>Tugba Kevser Uzuncakmak and Ayse Serap Karadag</i>	
6.1	Introduction	101
6.2	Epidemiology	101
6.3	Molecular Pathogenesis	102
6.4	Diagnosis	103
6.5	Clinical Features	106
6.6	Mode of Spread of Infections	107
6.7	Treatment	107
6.7.1	Treatment Options	108
6.7.1.1	Watchful Waiting	108
6.7.1.2	Procedure-Based Treatments	109
6.7.1.3	Chemical Agents	110
6.7.1.4	Immune Modulators	111
6.7.1.5	Antiviral Agents	112
6.7.1.6	Immunocompromised Patients	112
6.8	Conclusion	113
	References	113
<b>7</b>	<b>Genital Warts</b>	<b>119</b>
	<i>Filip Rob</i>	
7.1	Introduction	119
7.2	Human Papillomavirus	119
7.2.1	Taxonomy	119
7.2.2	Life Cycle	120
7.2.3	Interaction with Immune System	120

7.2.4	Transmission	120
7.2.5	Clearance	120
7.3	Epidemiology	121
7.4	Risk and Protective Factors	121
7.4.1	Risk Factors	121
7.4.2	Protective Factors	122
7.5	Clinical Features	122
7.5.1	Physical Signs	122
7.5.2	Symptoms	123
7.6	Diagnostics	124
7.6.1	Clinical Investigation	124
7.6.2	3–5% Acetic Acid	124
7.6.3	Histopathology	124
7.6.4	HPV DNA Detection	125
7.6.5	HPV Antibodies	125
7.7	Differential Diagnosis	125
7.8	Treatment	126
7.8.1	Cryotherapy	126
7.8.2	Laser Therapy (CO <sub>2</sub> laser, Er:YAG laser)	127
7.8.3	Electrocautery	127
7.8.4	Surgical Excision	127
7.8.5	Trichloroacetic Acid (80–90% solution)	127
7.8.6	Podophyllotoxin (0.05% solution or 0.15% gel)	127
7.8.7	Imiquimod (3.75% or 5% cream)	127
7.8.8	Sinecatechins (10% or 15% ointment)	129
7.9	Specific Groups	129
7.9.1	Immunocompromised Patients	129
7.9.2	Pregnant Women	129
7.9.3	Children	129
7.10	HPV Vaccination	130
	References	131

## **8 Chlamydia Trachomatis Urogenital Infections: Epidemiology, Clinical Presentations, and Pathogenesis 135**

*Charles W. Armitage, Alison J. Carey, Danica K. Hickey, and Kenneth W. Beagley*

8.1	Introduction	135
8.2	Epidemiology	135
8.3	Chlamydial Biology	136
8.3.1	The Attachment and Entry of Chlamydial EBs	136
8.3.2	The Chlamydial Inclusion	137
8.3.3	Chlamydial Replication and Persistence	137
8.4	Clinical Features	138
8.4.1	Urogenital Tract Infections	139
8.4.2	Female Urogenital Tract	139
8.4.3	Infection and Pregnancy	141
8.4.4	Male Urogenital Tract	142
8.4.5	Anorectal Tract Infections	143

8.4.6	Gastrointestinal Chlamydial Infections and Persistence	144
8.4.7	Lymphogranuloma Venereum	144
8.5	Pathogenesis of Chlamydial Infections	145
8.5.1	Pathogenesis of Female Genital Tract Chlamydial Infections	145
8.5.2	Lower FRT Pathogenesis	146
8.5.3	Upper FRT Pathogenesis	146
8.5.4	Pathogenesis of Male Urogenital Tract	148
8.5.5	Chlamydial Urethritis and Prostatitis	148
8.5.6	Chlamydial Infections of the Upper MRT	148
8.5.7	Chlamydial Epididymitis	149
8.5.8	Chlamydial Orchitis	149
8.6	Diagnosis and Treatment	150
8.7	Prevention and Control	151
8.8	Conclusion	152
	References	153
<b>9</b>	<b>Donovanosis</b>	<b>167</b>
	<i>Sarita Martins De Carvalho Bezerra, Marcio Martins Lobo Jardim, and Juliana Uchiyama</i>	
9.1	Introduction	167
9.2	Epidemiology	168
9.3	Pathology	168
9.4	Incubation Period	169
9.5	Clinical Pictures	170
9.6	Sites of Involvement	174
9.7	Complications and Sequelae	175
9.8	Diagnosis	175
9.9	Differential Diagnosis	176
9.10	Treatment	176
9.11	Prevention and Control	177
9.12	Disease Control and Prevention	178
	References	178
<b>10</b>	<b>Gonorrhoea</b>	<b>181</b>
	<i>María Teresa Pérez-Gracia and Beatriz Suay-García</i>	
10.1	Introduction	181
10.2	Pathogen	182
10.2.1	Morphology	182
10.2.2	Virulence Factors	183
10.2.2.1	Type IV Pili (Tfp)	183
10.2.2.2	Por Proteins	183
10.2.2.3	Opacity Proteins (Opa)	184
10.2.2.4	Rmp Proteins	184
10.2.2.5	Lipooligosaccharide (LOS)	184
10.2.2.6	IgA Protease	185
10.2.3	Physiology	185
10.2.4	Genome	185

10.3	Pathogenesis and Immunity	185
10.4	Epidemiology	186
10.5	Clinical Features	188
10.5.1	Gonococcal Infection in Men	188
10.5.2	Gonococcal Infection in Women	188
10.5.3	Extragenital Locations	188
10.6	Diagnosis	189
10.6.1	Samples	189
10.6.2	Staining	191
10.6.3	Culture	191
10.6.4	Identification	193
10.6.5	<i>Neisseria gonorrhoeae</i> Genotyping	193
10.6.6	Nucleic Acid Amplification Tests (NAATs)	197
10.7	Treatment	198
10.8	Prevention and Control	200
10.9	Conclusion	202
	References	202
<b>11</b>	<b>Sexually Transmitted Treponematoses</b>	<b>211</b>
	<i>Lenka Mikalová and David Šmajš</i>	
11.1	Introduction	211
11.2	Genetics of TPA and TEN Strains	212
11.3	Virulence Factors of Syphilis and Bejel	214
11.4	Diagnostics of Syphilis and Bejel	215
11.5	Treatment of Syphilis and Bejel	217
11.6	Molecular Typing of Syphilis and Bejel Treponemes	220
11.7	Vaccine Development for Syphilis and Bejel	222
	References	223
<b>12</b>	<b>Genital Mycoplasmas</b>	<b>233</b>
	<i>Suncanica Ljubin-Sternak</i>	
12.1	Introduction	233
12.2	Biology	234
12.3	Pathogenesis	235
12.3.1	Adhesion Proteins	236
12.3.2	Antigenic Variation	236
12.3.3	Production of Enzymes	236
12.3.4	Facultative Intracellular Localization	237
12.3.5	Capacity to Induce Host Immune Response	237
12.4	Epidemiology	237
12.5	Clinical Presentation	238
12.5.1	Urogenital Infections in Women	238
12.5.1.1	Bacterial Vaginosis	238
12.5.1.2	Cervicitis	239
12.5.1.3	Pelvic Inflammatory Disease (PID) and Its Sequelae	239
12.5.1.4	Infections in Pregnancy	240

- 12.5.2 Urogenital Infections in Men 241
  - 12.5.2.1 Nongonococcal Urethritis (NGU) 241
  - 12.5.2.2 Epididymitis and Prostatitis 241
  - 12.5.2.3 Infertility 241
- 12.5.3 Rare Manifestations and Clinical Features in Immunocompromised Persons 242
  - 12.5.3.1 Urinary Calculi 242
  - 12.5.3.2 Systemic Infection and Arthritis 242
  - 12.5.3.3 Infection in Immunocompromised Patients 242
- 12.6 Laboratory Diagnosis 243
  - 12.6.1 Specimen Collection 243
  - 12.6.2 Culture Methods 243
  - 12.6.3 Molecular Methods 245
  - 12.6.4 Serology 246
- 12.7 Treatment 247
- 12.8 Prevention and Control 248
- References 249

### **13 Bacterial Vaginosis 257**

*Aliona Rosca and Nuno Cerca*

- 13.1 Introduction 257
- 13.2 Implication of *G. vaginalis* in Bacterial Vaginosis 258
- 13.3 Epidemiology and Risk Factors 260
- 13.4 Pathogenesis and Immunity 261
- 13.5 Clinical Features 263
- 13.6 Diagnosis 263
- 13.7 Treatment 266
- 13.8 Conclusions 268
- References 268

### **14 Chancroid 277**

*Margaret E. Bauer and Diane M. Janowicz*

- 14.1 Introduction 277
- 14.2 Epidemiology of Chancroid and *H. ducreyi* 277
- 14.3 Clinical Features 278
- 14.4 The Pathogen 279
- 14.5 Pathogenesis and Immunity 280
  - 14.5.1 Overview of Pathogenesis 280
  - 14.5.2 Virulence Mechanisms 280
  - 14.5.3 Regulation of Virulence 282
  - 14.5.4 Immune Response 283
- 14.6 Diagnosis, Treatment, and Prevention 284
- 14.7 Chronic Limb Ulcers Caused by *H. ducreyi* 285
- 14.8 Conclusions 286
- References 287

<b>15</b>	<b>Vulvovaginal Candidosis</b>	<b>293</b>
	<i>Gilbert G.G. Donders, Katerina S. Ruban, Gert Bellen, and Sivtrigaile Grinceviciene</i>	
15.1	Introduction	293
15.2	Etiology	293
15.2.1	Pathogens	293
15.2.2	Morphology	294
15.3	Epidemiology	294
15.3.1	Prevalence	294
15.3.1.1	Asymptomatic Colonization	294
15.3.1.2	Symptomatic Infection	295
15.3.2	Risk Factors	298
15.3.3	Sexual Transmission	298
15.3.4	Young and Elderly Women	298
15.4	Pathogenesis and Immunity	300
15.4.1	Hormones	300
15.4.2	Pregnancy	300
15.4.3	Impaired Glucose Tolerance	301
15.4.4	Genetic Predisposition	301
15.4.4.1	STAT1 Gain of Function Mutations	302
15.4.4.2	CARD9	302
15.4.4.3	AIRE Mutation	302
15.4.4.4	NALP3/CIAS1	304
15.4.4.5	Interleukin-4	304
15.4.4.6	Dectin-1	304
15.4.4.7	Mannose-Binding Lectin (MBL)	304
15.4.5	Other Factors Affecting Pathogenesis	305
15.5	Symptoms and Signs	305
15.5.1	Acute/Episodic Infection	305
15.5.2	Recurrent Vulvovaginal Candidosis	306
15.6	Diagnosis and Differential Diagnosis	306
15.6.1	Clinical Signs	306
15.6.2	Clinical Examination	306
15.6.3	Wet Mount Microscopy	307
15.6.4	Vaginal pH	309
15.6.5	Vaginal Mycological Culture	310
15.6.6	Molecular Biology	310
15.6.7	Histology	310
15.6.8	Differential Diagnosis	310
15.7	Treatment	311
15.7.1	General Principles of Treatment	311
15.7.2	Treatment of Uncomplicated Acute Infection	311
15.7.3	Treatment of Complicated Acute Infection	312
15.7.3.1	Severe Symptoms, <i>C. albicans</i> Vulvovaginitis	314
15.7.3.2	Non- <i>Albicans</i> Candida Infection	314
15.7.3.3	Poorly Controlled Diabetes, Immune Suppression	315
15.7.3.4	Pregnancy and Breastfeeding	315



- 15.7.4 Recurrent Vulvovaginal Candidiasis (RVVC) 316
- 15.7.4.1 Azole-Resistant *C. albicans* 317
- 15.7.4.2 Elimination of Risk Factors of Recurrence in RVVC Patients 317
- 15.7.4.3 Underlying Reasons for Failing Maintenance Therapy 318
- References 319
- 16 Tinea Cruris 329**  
*Anuradha Bishnoi and Rahul Mahajan*
- 16.1 Introduction 329
- 16.2 Etiology and Epidemiology 330
- 16.3 Tinea Cruris as a Sexually Transmitted Infection (STI) 331
- 16.4 Transmission 331
- 16.5 Pathogenesis 332
- 16.5.1 Environmental Factors 332
- 16.5.2 Agent Factors 332
- 16.5.3 Host Factors 332
- 16.5.4 Host Immune Response 333
- 16.5.5 Clinical Features 333
- 16.5.6 Variants 335
- 16.5.6.1 Tinea incognito 335
- 16.5.6.2 Vesico-Bullous Tinea Cruris 335
- 16.5.6.3 White Paint Dots and Pseudomembranous Tinea 335
- 16.6 Differential Diagnoses 336
- 16.6.1 Candidiasis 336
- 16.6.2 Erythrasma 336
- 16.6.3 Hyperpigmented Pityriasis Versicolor 336
- 16.7 Laboratory Diagnosis 336
- 16.7.1 Direct Examination 336
- 16.7.2 Culture 337
- 16.7.3 Nucleic Acid Amplification Tests 337
- 16.8 Treatment of Tinea Cruris and Genitalis 337
- 16.8.1 Topicals 337
- 16.8.2 Systemic 337
- 16.8.3 Recalcitrant/Resistant Tinea: Pathomechanisms and Treatment 338
- 16.8.4 General Measures to Prevent Tinea Cruris 338
- 16.9 Conclusion 338
- Acknowledgments 339
- References 339
- 17 Trichomonas Vaginalis 341**  
*Barbara Van Der Pol*
- 17.1 Introduction 341
- 17.2 Epidemiology of *T. vaginalis* 342
- 17.3 HIV and Trichomonas 344
- 17.4 Biology and Pathogenesis of *T. vaginalis* 345
- 17.5 Clinical Features of *T. vaginalis* Infection 346
- 17.6 Diagnosis of *T. vaginalis* 348

17.6.1	Laboratory Diagnosis	349
17.7	Treatment of <i>T. vaginalis</i>	350
17.8	Conclusion	351
	References	351
<b>18</b>	<b>Scabies</b>	<b>357</b>
	<i>Giuseppe Micali, Giorgia Giuffrida, and Francesco Lacarrubba</i>	
18.1	Introduction	357
18.2	Epidemiology	357
18.3	Etiopathogenesis	358
18.4	Clinical Features	359
18.5	Diagnosis	363
18.5.1	Microscopy	363
18.5.2	Dermatoscopy/Videodermatoscopy	363
18.5.3	Histopathology	365
18.5.4	Other Diagnostic Procedures	366
18.6	Treatment	366
18.6.1	Topical Agents	366
18.6.2	Oral Agents	367
18.6.3	Treatment for Crusted Scabies	367
18.7	Prevention and Control	368
18.8	Conclusion	368
	References	368
	<b>Index</b>	<b>373</b>