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0521529069 - Handbook of Pediatric HIV Care, Second Edition
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Handbook of

Pediatric HIV Care

This portable and practical handbook provides a concise guide to the essentials of pediatric HIV care. During the past few years, many agents for the treatment and prophylaxis of HIV infection and the opportunistic infections that accompany HIV infection have been developed, and many new ways of monitoring HIV infection in children have been produced. These new therapies and approaches to management are complicated, but the long-term health of HIV-infected children depends on their correct application. This handbook presents the core information and guidelines necessary for effective management of infected children.

Dr. Stephen L. Zeichner received his undergraduate and graduate degrees at the University of Chicago. He trained in pediatrics and infectious diseases at the Children's Hospital of Philadelphia. An investigator in the HIV and AIDS Malignancy Branch, National Cancer Institute, NIH, and an adjunct family member of the George Washington University School of Medicine. Children's National Medical Center, Washington, DC, and the Uniformed Services University of the Health Sciences, he studies the basic biology of HIV and Kaposi's sarcoma-associated herpesvirus, and directs clinical trials of new therapies for HIV-infected children.

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Handbook of Pediatric HIV Care

Second Edition

Edited by

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For Rachel, Sarah, and Elizabeth

For Alex, Samantha, and Geoffrey

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Frontmatter
[More information](#)

Contents

List of contributors	page xi
List of abbreviations	xvi
Foreword	xxvii
Preface	xxix

Part I Scientific basis of pediatric HIV care

1 The scientific basis of pediatric HIV care	3
Sherilyn Smith, Ann Melvin, Steven L. Zeichner, Elizabeth McFarland, Paul Palumbo, and Grace Aldrovandi	
2 The epidemiology of pediatric HIV disease	78
Mary Lou Lindegren, Teresa Hammett, and Marc Bulterys	

Part II General issues in the care of pediatric HIV patients

3 Diagnosis of HIV infection in children	99
Paul Krogstad	
4 Prevention of mother-to-child transmission of HIV	107
Jennifer S. Read	
5 Routine pediatric care	134
Elaine Abrams, Rachel Y. Moon, Lisa-Gaye Robinson, and Russell B. Van Dyke	
6 Emergency evaluation and care	177
James M. Callahan	
7 Adherence to antiretroviral therapy in children and youth	206
John Farley	

Cambridge University Press
0521529069 - Handbook of Pediatric HIV Care, Second Edition
Edited by Steven L. Zeichner and Jennifer S. Read
Frontmatter
[More information](#)

8 Adolescents and HIV	219
Ligia Peralta, and Bret J. Rudy	
9 Growth, nutrition, and metabolism	273
Caroline J. Chantry and Jack Moye, Jr.	
10 Neurobehavioral function and assessment of children and adolescents with HIV infection	309
Pamela L. Wolters and Pim Brouwers	

Part III Antiretroviral therapy

11 Antiretroviral therapy	335
Ross McKinney, Jr.	
12 Antiretroviral drug interactions	360
Thomas N. Kakuda and Courtney V. Fletcher	
13 Metabolic complications of antiretroviral therapy in children	382
Carol J. Worrell	
14 HIV drug resistance	397
Frank Maldarelli	
15 Initiating and changing antiretroviral therapy	415
Lynne M. Mofenson and Leslie K. Serchuck	
16 Therapeutic drug monitoring	439
Stephen C. Piscitelli	
17 HIV postexposure prophylaxis for pediatric patients	450
Peter L. Havens and Kenneth L. Dominguez	

Part IV Clinical manifestations of HIV infection in children

18 Cutaneous diseases	473
Andrew Blauvelt	
19 Neurologic problems	503
Lucy Civitello	
20 Ophthalmic problems	520
Howard F. Fine, Susan S. Lees, and Michael R. Robinson	

Cambridge University Press
0521529069 - Handbook of Pediatric HIV Care, Second Edition
Edited by Steven L. Zeichner and Jennifer S. Read
Frontmatter
[More information](#)

21 Oral health and dental problems	535
Jane C. Atkinson and Anne O'Connell	
22 Otitis media and sinusitis	543
Ellen R. Wald and Barry Dashefsky	
23 Cardiac problems	554
Gul H. Dadlani and Steven E. Lipshultz	
24 Pulmonary problems	567
Lauren V. Wood	
25 Hematologic problems	588
William C. Owen and Eric J. Werner	
26 Gastrointestinal disorders	602
Harland S. Winter and Jack Moye, Jr.	
27 Renal disease	618
Somsak Tanawattanacharoen and Jeffrey B. Kopp	
28 Endocrine disorders	630
Daina Dreimane and Mitchell E. Geffner	
29 Neoplastic disease in pediatric HIV infection	637
Richard F. Little	

Part V Infectious problems in pediatric HIV disease

30 Serious infections caused by typical bacteria	653
Shirley Jankelevich	
31 Tuberculosis	674
Rohan Hazra	
32 Disseminated <i>Mycobacterium avium</i> complex infection	685
Robert N. Husson	
33 Fungal infections	695
Corina E. Gonzalez	
34 Herpesvirus infections	721
Richard M. Rutstein and Stuart E. Starr	
35 <i>Pneumocystis jiroveci</i> pneumonia	740
Leslie K. Serchuck	

Cambridge University Press
0521529069 - Handbook of Pediatric HIV Care, Second Edition
Edited by Steven L. Zeichner and Jennifer S. Read
Frontmatter
[More information](#)

Part VI Medical, social, and legal issues

36 Medical issues related to the care of HIV-infected children in the home, daycare, school, and community	759
Stephen J. Chanock	
37 Contact with social service agencies	772
Sandra Y. Lewis and Heidi J. Haiken	
38 Psychosocial factors associated with childhood bereavement and grief	781
Lori S. Wiener	
39 Legal issues for HIV-infected children	796
Carolyn McAllaster	
Appendix 1: Formulary of antiretroviral agents	807
Paul Jarosinski	
Appendix 2: National Institutes of Health sponsored clinical trials for pediatric HIV disease	821
J. G. McNamara	
Appendix 3: Selected HIV-related internet resources	826
Leslie K. Serchuck	
Appendix 4: Selected legal resources for HIV-infected children	835
Carolyn McAllaster	
Index	844

Cambridge University Press
0521529069 - Handbook of Pediatric HIV Care, Second Edition
Edited by Steven L. Zeichner and Jennifer S. Read
Frontmatter
[More information](#)

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 Frontmatter
[More information](#)

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Cambridge University Press

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Frontmatter

[More information](#)

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Cambridge University Press

0521529069 - Handbook of Pediatric HIV Care, Second Edition

Edited by Steven L. Zeichner and Jennifer S. Read

Frontmatter

[More information](#)

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Cambridge University Press
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 Frontmatter
[More information](#)

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Abbreviations

AAP	American Academy of Pediatrics
ABC	abacavir
ABCD	amphotericin B colloidal dispersion
ABLC	amphotericin B lipid complex
ACCAP	AIDS Community Care Alternatives Program
ACEI	angiotensin enzyme inhibitors
ACIP	Advisory Committee on Immunization Practices
ACOG	American College of Obstetricians and Gynecologists
ACTG	AIDS Clinical Trials Group
ACTH	adrenocorticotropin hormone
ACTIS	AIDS Clinical Trials Information Service
ADCC	antibody-dependent cell-mediated cytotoxicity
ADDP	AIDS Drug Distribution Program
ADEC	Association for Death Education and Counseling
ADHD	attention deficit/hyperactivity disorder
AEGIS	AIDS Education Global Information System
AFB	acid-fast bacilli
AFXB	Association François-Xavier Bagnoud
AGCUS	atypical glandular cells of undetermined significance
AIDS	acquired immune deficiency syndrome
ALRI	acute lower respiratory tract infection
AmFAR	American Foundation for AIDS Research
AMP	amprenavir
ANC	absolute neutrophil count
ANRS	Agence Nationale de Recherches sur le SIDA
AOM	acute otitis media
ACP	antigen-presenting cell
APV	amprenavir
ARB	angiotensin blockers
ARDS	acute respiratory distress syndrome

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Frontmatter
[More information](#)

ARF	acute renal failure
ARL	AIDS-related lymphoma
ARN	acute retinal necrosis
ART	antiretroviral therapy
ASCUS	atypical squamous cells of undetermined significance
AST	asparate aminotransferase
ATN	adolescent medicine trials network
ATP	adenosine triphosphate
ATZ	atazanavir
AUC	area under the curve
AZT	zidovudine (also known as ZDV)
BAL	bronchoalveolar lavage
BBB	blood-brain barrier
BCG	Bacille Calmette–Guerin
βHCG	serum beta human chorionic gonadotropin
BIA	bioelectrical impedance analysis
BMC	bone mineral content
BMD	bone mineral density
BMI	body mass index
BUN	blood urea nitrogen
BV	bacterial vaginosis
CARE	Ryan White (Comprehensive AIDS Resources Emergency) Act
CAT	computerized axial tomography
CBC	complete blood count
CD	cluster of differentiation
CDC	Centers for Disease Control and Prevention
CDC-GAP	Centers for Disease Control and Prevention Global AIDS Program
CHF	congestive heart failure
Cho	choline
CHOP	cyclophosphamide, doxorubicin, vincristine and prednisone
CIN	cervical intraepithelial neoplasia
CIPRA	Comprehensive International Program of Research on AIDS
C _{max}	maximum concentration/peak blood concentration
CMT	cervical motion tenderness
CMV	cytomegalovirus
CNS	central nervous system
CPAP	continuous positive airway pressure
CRF	case report form
CRH	corticotropin-releasing hormone
CRP	C-reactive protein

CSF	cerebrospinal fluid
CSOM	chronic suppurative otitis media
CT	computed tomography
CTL	cytotoxic <i>T</i> -lymphocytes also cytotoxic memory T-cells
CVC	central venous catheter
CXR	chest X-ray
d4T	stavudine
DC	dendritic cells
DC-SIGN	dendritic cell-specific intercellular adhesion molecule-grabbing non-integrin
ddC	zalcitabine
ddI	didanosine
DEXA	dual energy X-ray absorptiometry
DFA	direct fluorescent antibodies also direct immunofluorescence assay
DHEAS	dihydroepiandrosterone sulfate
DHFR	dihydrofolate reductase
DHPS	dihydropteroate synthase
DHSS	Department of Health and Human Services
DIC	disseminated intravascular coagulation
DLBCL	diffuse large B-cell lymphoma
DL _{co}	diffusing capacity
DLV	delavirdine
DMAC	disseminated <i>Mycobacterium avium</i> complex
DMPA	depot medroxyprogesterone acetate
DNA	deoxyribonucleic acid
dNTPs	triphosphorylated nucleosides
DOT	directly observed therapy
DOTS	directly observed therapy (short course)
DSMB	Data Safety Monitoring Board
DTH	delayed type hypersensitivity
DTP	diphtheria–tetanus–pertussis
DTaP	diphtheria–tetanus–acellular pertussis
DUB	dysfunctional uterine bleeding
EBCT	electron beam computed tomography
EBV	Epstein–Barr virus
EC	emergency contraception also enteric coated
ECG	electrocardiogram
ECHO	echocardiography
ED	Emergency Department also end diastolic

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[More information](#)

EEG	electroencephalogram
EFV	efavirenz
EGPAF	Elisabeth Glaser Pediatric AIDS Foundation
EGW	external genital warts
EIA	enzyme immunoassay
ELISA	enzyme-linked immunosorbent assays
EMEA	European Agency for the Evaluation of Medicinal Products
ENF	enfuvirtide
Env	viral envelope
EP	extrapulmonary pneumocytosis
ERCP	endoscopic retrograde cholangiopancreatography
ES	end systolic
ESR	erythrocyte sedimentation rate
ESRD	end-stage renal disease
5-FU	5-fluorouracil
FACS	fluorescent antibody cell sorting
FAMA	fluorescent antibody membrane antigen
FDA	Food and Drug Administration
FEV ₁	forced expiratory volume in 1 second
FFA	free-fatty acids
FFM	fat free mass
FRS	fat redistribution syndrome
FSGS	focal segmental glomerulosclerosis
FSH	follicle stimulating hormone
FTC	emtricitabine
FTT	failure to thrive
FVT	forced vital capacity
G-6-PD	glucose-6-phosphate dehydrogenase
GCP	good clinical practices
g-CSF	filgrastim
G-CSF	granulocyte-colony stimulating factor
GER	gastroesophageal reflux
GH	growth hormone
GI	gastrointestinal
GM-CSF	granulocyte-macrophage colony-stimulating factor
GnRH	gonatropin releasing hormone
HAART	highly active antiretroviral therapy
HAIRAN	hyperandrogenic-insulin resistant acanthosis nigricans
HAMB	HIV and AIDS Malignancy Branch

HAM/TSP	HLTV-1-associated myelopathy/tropical spastic paraparesis
HAV	hepatitis A virus
HAZ	height-for-age Z-scores
<i>hbhA</i>	heparin-binding hemagglutinin adhesin
HBIG	hepatitis B immunoglobulin
HBV	hepatitis virus B
HCP	healthcare personnel
HDL	high-density lipoprotein
HDL-C	high-density lipoprotein cholesterol
HHV-6	human herpesvirus-6
HHV-8	human herpesvirus-8
HIB	<i>Hemophbilus influenzae</i> type B
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HMOs	health maintenance organizations
¹ HMRS	proton magnetic resonance spectroscopy
HPA	hypothalamic-pituitary-adrenal
HPTN	HIV Prevention Trials Network
HPV	human papillomavirus
HRCT	high-resolution computerized tomography
HRIG	human rabies immunoglobulin
HSI	HIV/AIDS and sexually transmitted infections
HSV	herpes simplex virus
HTLV-1	human T-cell leukemia virus 1
HUS	hemolytic-uremic syndrome
ICASO	International Council of AIDS Services Organizations
ICD	immune complex dissociated
ICMA	immunochemiluminescent assay
IDU	injection drug use
IDV	indinavir
IFA	immunofluorescence assay
IFN	interferon
Ig	immunoglobulin
IGFPB-3	insulin-like growth factor binding protein-3
IgFBPs	IGF binding proteins
IgF-1	insulin-like growth factor 1
IL	interleukin
ILD	interstitial lung disease
IMCI	integrated management of childhood illness
INH	isoniazid

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[More information](#)

INR	international normalized ratio
In V	intravaginal
IP	interferon inducible protein
IPAA	International Partnership Against AIDS
IPI	invasive pneumococcal infections
IPV	inactivated polio vaccine
IQ	inhibitory quotient
IRB	Institutional Review Board
IRU	immune recovery uveitis
ISA	induced sputum analysis
ITP	immune thrombocytopenia purpura
IUDs	intrauterine devices
IUS	intrauterine system
IVIG	intravenous immunoglobulin
KOH	potassium hydroxide
KS	Kaposi's sarcoma
KSHV	Kaposi's sarcoma-associated herpesvirus
LBM	lean body mass
LDH	lactate dehydrogenase
LDL	low-density lipoproteins
LDL-C	low-density lipoprotein cholesterol
LFT	liver function test
LGE	linear gingival erythema
LH	luteinizing hormone
LIFE	leadership and investment in fighting an epidemic
LIP	lymphoid interstitial pneumonitis
LIPA	line probe assays
LP	lumbar puncture
LPN	licensed practical nurse
LPV	lopinavir
LPV/r	lopinavir plus ritonavir
LTNP	long-term non-progression
LTR	long terminal repeat (HIV promotor)
LV	left ventricular
MAC	<i>Mycobacterium avium</i> complex also mid-arm circumference
MACS	Multicenter AIDS Cohort Study
MALT	mucosa-associated lymphoid tissue
MAMC	mid-arm muscle circumference

MCP	monocyte chemoattractant protein
MDI	Mental Developmental Index also metered dose inhaler
MDR	multi-drug resistance
MEMS	medication event monitoring system
MESA	myoepithelial sialadenitis
MHC	major histocompatibility complex
MI	myo-inositol
MIG	monokine induced by interferon gamma
MIP	macrophage inflammatory protein
MIRIAD	mother–infant rapid intervention at delivery
Mo	month
MMR	measles, mumps and rubella
MRI	magnetic resonance imaging
MRS	magnetic resonance spectroscopy
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
MSM	men who have sex with men
MTCs	multilocular thymic cysts
MTD	<i>Mycobacterium tuberculosis</i> direct test
MTCT	mother-to-child transmission
NAA	<i>N</i> -acetyl aspartate
NAHC	National Association for Home Care
NAMs	nucleoside associated mutations
NAAT	nucleic acid amplification tests
NASBA®	nucleic acid sequence-based amplification
NCHS	National Center for Health Statistics
NCI	National Cancer Institute
NF-kappa B	nuclear factor kappa-B
NFV	nelfinavir
NHL	non-Hodgkin’s lymphoma
NIAID	National Institute of Allergy and Infectious Diseases
NICHD	National Institute of Child Health and Human Development
NIH	National Institutes of Health
NK	natural killer
NMDA	<i>N</i> -methyl-D-aspartate
NNRTIs	non-nucleoside reverse transcriptase inhibitors
NPA	nasopharyngeal aspirate
nPEP	non-occupational postexposure prophylaxis
NPO	nothing by mouth
NRTIs	nucleoside reverse transcriptase inhibitors
NSAIDs	non-steroidal anti-inflammatory drugs
NSS	normal saline solution

NUG	necrotizing ulcerative gingivitis
NUP	necrotizing ulcerative periodontitis
N/V	nausea/vomiting
17-OHP	17-hydroxyprogesterone
OCs	oral contraceptives
OD	optical density
OGTT	oral glucose tolerance test
OHL	oral hairy leukoplakia
OHRP	Office of Human Research Protections
OIs	opportunistic infections
OLA	oligonucleotide ligation assays
oPEP	occupational postexposure prophylaxis
OPV	oral polio vaccine
OSHA	Occupational Safety and Health Administration
PACTG	Pediatric AIDS Clinical Trials Group
PACTS	Perinatal AIDS Collaborative Transmission Study
PAHO	Pan American Health Organization
PAP	Papanicolaou (Smear)
PBLD	polymorphic B-cell lymphoproliferative disorder
PBMC	peripheral blood mononuclear cells
PCM	protein–calorie malnutrition
PCNS	primary central nervous system
PCOS	polycystic ovary syndrome
PCP	<i>Pneumocystis jiroveci</i> pneumonia also primary healthcare provider
P Cr	plasma creatinine
PCR	polymerase chain reaction
PCV	pneumococcal conjugate vaccine
PCV7	heptavalent pneumococcal conjugate vaccine
PEL	primary effusion lymphoma
PENTA	The Pediatric European Network for the Treatment of AIDS
PEP	postexposure prophylaxis
PFC	persistent fetal circulation
PFTs	pulmonary function tests
PGE ₂	prostaglandin E ₂
PGP	p-glycoprotein
PHA	phytohemagglutinin
PHC	preventive health care
PHS	public health service
PI	pentamidine isothionate
PIs	protease inhibitors

PIC	pre-integration complex
PID	pelvic inflammatory disease
PIT	pills identification test
PJ	<i>P. jiroveci</i>
PLH	pulmonary lymphoid hyperplasia
PMDD	premenstrual dysphoric disorder
PML	progressive multifocal leukoencephalopathy
PMPA	9-[2-(R)-(phosphonylmethoxy)propyl] adenine
PMS	premenstrual syndrome
PMTCT	prevention of mother-to-child transmission
P Na	plasma sodium
PNS	peripheral nervous system
PORN	progressive outer retinal necrosis
POS	point of service
PPD	purified protein derivative
PPOs	preferred providers organizations
PPV	pneumococcal polysaccharide vaccine
PMN	polymorphonuclear leukocyte
PRA	peripheral renin activity
PRAMS	pregnancy risk assessment monitoring system
PSD	Pediatric Spectrum of Disease
PT	prothrombin time
PTH	parathyroid hormone
PTT	partial thromboplastin time
PTX	spontaneous pneumothorax
PWAs	persons with AIDS
PZA	pyrazinamide
RAD	reactive airway disease
RBC	red blood cells
RDA	recommended dietary allowance
REACH	reaching for excellence in adolescent care and health
RER	rough endoplasmic reticulum
RN	registered nurse
RNA	ribonucleic acid
ROspA	recombinant outer surface protein
RPE	retinal pigment epithelium
RR	relative risk
RRE	rev responsive element
RSV	respiratory syncytial virus
RTI	reverse transcriptase inhibitor

RT-PCR	reverse transcription-polymerase chain reaction
RTV	ritonavir
SBI	serious bacterial infections
Sc	subcutaneous
SDF	stromal-cell derived factor
SHBG	sex hormone-binding globulin
SIADH	syndrome of inappropriate secretion of antidiuretic hormone
SILs	squamous intraepithelial lesions
siRNA	small interfering ribonucleic acids
SIV	simian immunodeficiency virus
SMM	Sooty Mangabey monkey
SOIs	sharp object injuries
SPECT	single photon emission computed tomography
SPNS	special projects of national significance
SQV	saquinavir
SSDI	Social Security Disability Income
SSI	Supplemental Security income
SSRIs	selective serotonin reuptake inhibitors
STIs	sexually transmitted infections
SUDS	single use diagnostic system
3TC	lamivudine
T4	free levothyroxine
TAMS	thymidine analogue mutations
TANF	temporary assistance for needy families
TAR	transactivation responsive
TB	tuberculosis
TCA	trichloroacetic acid
TCR	t-cell receptors
Td	tetanus and diphtheria toxoids
TDF	tenofovir disoproxil fumarate
TDM	therapeutic drug monitoring
Th	T-helper
TIG	tetanus immunoglobulin
TMP/SMX	trimethoprim-sulfamethoxazole
TNF	tumor necrosis factor
TOA	tubo-ovarian abscess
TPN	total parenteral nutrition
TREAT	treatment regimens enhancing adherence in teens
TRH	thyrotropin-releasing hormone

Cambridge University Press
0521529069 - Handbook of Pediatric HIV Care, Second Edition
Edited by Steven L. Zeichner and Jennifer S. Read
Frontmatter
[More information](#)

TSF	triceps skinfold thickness
TSH	thyroid stimulating hormone
TST	tuberculin skin test
TTP	thrombotic thrombocytopenia purpura
U Cr	urine creatinine
UDPGT	uridine diphosphoglyconyltransferase
U Na	urine sodium
URIs	upper respiratory infections
USAID	United States Agency for International Development
USPHS	United States Public Health Service
UTI	urinary tract infection
VCAM-1	vascular cell adhesion molecule-1
VGC	valganciclovir
VLA-4	very late activation antigen-4
Vif	virion infectivity factor
VLDL	very low density lipoprotein
VZIG	varicella-zoster immunoglobulin
VZV	varicella-zoster virus
WAZ	weight-for-age Z-scores
WBCs	white blood cells
VVC	vulvovaginal candidiasis
WHO	World Health Organization
WITS	Women and Infants Transmission Study
XR	extended release
ZDV	zidovudine (also known as AZT)

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Frontmatter
[More information](#)

Foreword

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More than two decades have passed since this devastating infection was first identified. We have come from a time when no diagnosis could be made and there was no treatment, to an era when the development of multiple therapeutic agents and advances in the prevention of HIV infection is commonplace in the developed world. Foremost amongst these accomplishments is our ability to prevent mother-to-child transmission of HIV infection. Seldom is it possible to chronicle such advances in knowledge, which materially affect the lives of thousands of people on a daily basis. All of this speaks to the commitment of scientists and care providers and the rapid evolution of information and technology. There is, however, a pervasive recurrent theme of needing to advocate for the health of children infected and affected by HIV infection.

This handbook provides accessible information at a time when the developed world has succeeded in dramatically decreasing the number of children who acquire infection from their mothers. The need for this information is greater now than ever before. First, because the evolution of information continues at a rapid rate. Second, because the complexity of treatment requires expertise and access to the most current information. Third, because the numbers of HIV-infected children have decreased in the USA and the probability that a physician will have cumulative experience with substantive numbers of these children has diminished. It is important that pediatricians continue to be sensitive to the possibility that a child is HIV-infected and be attuned the specific medical needs and support systems required.

There is an index to Web sources of information, convenient summary tables, and eloquent discussions of antiretroviral drugs conveniently separated from therapeutic decision making. The material is readable, concise, and thorough.

I would wish that this information was accessible, in demand, and essential in the parts of the world where there is so much HIV infection of adults and children. One must reflect on the fact that as many infants are born with HIV infection in sub-Saharan Africa every day as were born in the USA in an entire year prior to the availability of interventions to prevent mother-to-child transmission. Progress is being made to bring

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Frontmatter
[More information](#)

these effective interventions to the developing world. We would hope we can entice a new generation of pediatricians, public health authorities, and other providers to devote their lives to addressing the problem as effectively in the developing world as has been done in the developed world. This handbook contributes to the knowledge, and hopefully will provide additional incentive to take these advances to the entire world of children.

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0521529069 - Handbook of Pediatric HIV Care, Second Edition
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Frontmatter
[More information](#)

Preface

When Cambridge University Press decided to undertake the publication of the second edition of the *Handbook of Pediatric Care*, they told us that they were very enthusiastic about the book, but that they thought that, while the handbook was too large to be a true “handbook,” they still valued and appreciated the more comprehensive content of the book. The Press therefore asked us, for the second edition, to both shorten the material to a more manageable size to make a new handbook and to augment the material in the handbook to make an even more comprehensive *Textbook of Pediatric HIV Care*. We hope that we have achieved these goals in these two books, a second edition of the *Handbook of Pediatric HIV Care* and the first edition of the *Textbook of Pediatric HIV Care*.

Our goals for both books are to provide the clinician with the information needed to provide excellent care to children infected with HIV. Neither book is meant to be an exhaustive treatise on the subject of pediatric HIV disease, covering all the many societal and policy issues that are involved necessarily in a complete discussion of HIV and children. Rather, we aim to provide helpful management information for the frontline clinician. While we have focused on the management of pediatric HIV disease, we believe that effective management requires a solid understanding of the basic and applied virology, immunology, and pathophysiology of the disease, so that the practitioner can thoughtfully and rationally apply the management information supplied in the other chapters. Our authors have included more detailed discussions in their *Textbook* chapters, and have tried to condense their presentations in their *Handbook* chapters to include the most clinically pertinent details. Some of the information presented in more than one *Textbook* chapters has been condensed into a single chapter for the handbook, but we hope that we have been able to include the information in the handbook that will enable clinicians to provide optimum care for their HIV-infected patients.

The HIV epidemic changes quickly. The authors of the individual chapters have attempted to include a significant amount of new information, including new basic science findings, new information concerning the pathogenesis of the disease and the opportunistic infections that affect children with HIV, descriptions of recently

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0521529069 - Handbook of Pediatric HIV Care, Second Edition
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Frontmatter
[More information](#)

approved drugs and recently developed drugs that may be close to approval, both for HIV and for HIV-related opportunistic infections, new information concerning the management of children infected with HIV, and information concerning the social welfare of children infected with HIV. In some fields, so much new information has become available that we included entirely new chapters in the book. There are new chapters about the evolutionary biology of antiretroviral drug resistance and the assessment and management of antiretroviral drug resistance, the interruption of mother-to-infant HIV transmission, metabolic complications of HIV infection and antiretroviral therapy, therapeutic drug monitoring for HIV infection, and the gynecology of the HIV-infected adolescent. Neither book has chapters discussing, in detail, HIV vaccines because both prophylactic and therapeutic vaccines are only in the earliest stages of clinical development, but the basic science chapters about virology, immunology, pathogenesis, and natural history describe some of the fundamental information that vaccine developers are using in their efforts. We hope that we will be able to include in a future edition chapters that outline the use of prophylactic and therapeutic vaccines for HIV infection.

The book does not include a specific chapter on the management of pediatric HIV disease in resource-poor countries. We initially contemplated including such a chapter in the book, but soon came to realize that the spectrum of resources available in 'resource-poor' countries varied tremendously from one country to another. For example, in some countries there are government-mandated commitments to essentially universal access to antiretrovirals, while in others only a tiny fraction of the population has access to the drugs, and these circumstances are changing month by month. We look forward to the day when everyone will receive the best care possible, but until then we thought it wisest to describe state-of-the-art care as practiced in the world's richer countries, and acknowledge that providers elsewhere will know best how to adapt these principles to their own local circumstances.