

Giovanni Guaraldi · Julian Falutz
Chiara Mussi · Ana Rita Silva
Editors

Managing the Older Adult Patient with HIV

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Editor Biographies

Giovanni Guaraldi, MD, is Assistant Professor of Infectious Disease at University of Modena and Reggio Emilia, Italy, where he also completed his medical training. Dr Guaraldi undertook his residency at Liverpool School of Tropical Medicine, UK, and Jackson Memorial Hospital, USA.

Dr Guaraldi was awarded the Dean's Delegate Cooperation for development projects of Modena University. He has extensive experience in HIV in resource-limited countries and has coordinated the European, Africa, Caribbean, Pacific project CoBaSys (Community-Based System in HIV treatment) focused on antiretroviral access programs in sub-Saharan African countries.

In 2002 Dr Guaraldi started a liver and kidney transplant program for people with HIV at the multivisceral transplant center at Policlinico of Modena, Italy. Since the center opened, he has personally cared for approximately 80 patients with HIV who have received solid organ transplantation. Dr Guaraldi has led the Modena HIV Metabolic Clinic (MHMC) since 2000. This referral center cares for more than 4000 patients and offers a multidisciplinary team consisting of infectious disease physicians, nutritionists, occupational therapists, psychologists, cardiologists, nephrologists, endocrinologists, and plastic surgeons for the diagnosis and treatment of noninfectious comorbidities.

Dr Guaraldi has been the principal investigator in several studies generated by the MHMC, mainly focused on frailty and HIV-associated comorbidities. He has extensive experience in scientific publication, with more than 260

peer-reviewed papers, he is coeditor of *Journal of Antimicrobial Chemotherapy* and serves as reviewer for the major HIV journals and as a consultant for EMA. He supervises PhD students in the Experimental Medicine PhD course at Modena University.

Dr Guaraldi is a panel member of the European AIDS Clinical Society guidelines on prevention and management of HIV-associated comorbidities and has published widely on clinical aspects of HIV treatment and care.

Julian Falutz MD, FRCP(C), is Assistant Professor of Medicine at McGill University and Associate Physician at the Montreal General Hospital Site of the McGill University Hospital Centre (MUHC), Canada. He is the director of the Comprehensive HIV and Aging Initiative in the Chronic Viral Illness Service and a Senior Physician in the Division of Geriatrics at the MUHC.

Dr Falutz attended McGill University School of Medicine, where he completed his residency in General Internal Medicine and received subspecialty training in both internal medicine and geriatrics. He has been actively involved in the clinical care of both HIV and geriatric patients at the MUHC for over 25 years. He is active as a clinical teacher at the undergraduate and graduate levels and was the director of the HIV elective program at the MUHC for 20 years.

His research in HIV has focused on the interaction of immunodeficiency, nutrition, and metabolic complications. He has initiated and participated in numerous studies on the management of HIV-related complications. He was the coprincipal investigator for the pivotal multinational studies investigating a novel growth hormone-releasing factor for the treatment of abdominal obesity in patients with HIV. The investigated drug has since been approved for use in both the USA and Canada. He is the Canadian coordinator for the REPRIEVE study, a multinational study of statins to prevent cardiovascular disease in low-risk treated HIV patients. He has initiated a program for the evaluation of patients aging with HIV and plays an active role in emerging studies evaluating frailty and comorbidities in patients aging with HIV.

Chiara Mussi, MD, PhD, is a Doctor in Medicine within the Modena HIV Metabolic Clinic at the University of Modena and Reggio Emilia, Italy. Dr Mussi earned her medical degree from the University of Modena and Reggio Emilia in 1995, and her graduation thesis centered on orthostatic hypotension in the elderly. In 1999 Dr Mussi specialized in geriatrics, and in 2004 she gained her PhD in biology and pathophysiology of aging, where her main research topic was cardiovascular autonomic changes in older patients. In 2008 she obtained a research grant from the University of Modena and Reggio Emilia to research syncope in the elderly. Dr Mussi has been a researcher and Chair of Geriatrics at the University of Modena and Reggio Emilia since 2009. She also works as an MD at the New S Agostino-Estense Civil Hospital in Baggiovara, Modena.

Dr Mussi has authored more than 100 peer-reviewed papers published in international and national journals, is an expert in multidimensional geriatric evaluation and geriatric syndromes, and has been a consultant in the Multidisciplinary Expert Working Group dedicated to HIV aging population issues since 2013 (sponsored by ViiV Healthcare).

Ana Rita Silva, MD, is an infectious disease specialist in the Department of Infectious Diseases at the Hospital Beatriz Ângelo, Portugal. She works within the infectious disease ward and is a consultant at the outpatient clinic. Dr Silva is currently undertaking her PhD in Clinical and Experimental Medicine at the University of Modena and Reggio Emilia, Italy, where Dr Giovanni Guaraldi and Dr Emília Valadas are her tutors.

Dr Silva attended the Coimbra School of Medicine (Faculdade de Medicina da Universidade de Coimbra) in Portugal and started her residency in Infectious Diseases in 2008. In 2009, after attending a 3-month internship at the Clinica Metabolica, Dr Silva helped to create the Metabolic Consult at the Hospital de Joaquim Urbano, Portugal. Since 2009 she has been involved in several projects in the area of HIV and aging, both in Portugal and with Dr Guaraldi in Italy, and has published several papers in this field. Dr Silva

has also collaborated in the formation of residents and has participated as a lecturer in several courses, community actions, and congresses.

In 2013 she was awarded the certification in travel medicine by the International Society of Travel Medicine (ISTM) after taking the Certificate of Knowledge Examination. Throughout her career, Dr Silva has participated both as principal and coinvestigator in several studies on HIV and HIV/hepatitis C coinfection.

Contributor Biographies

Thomas Brothers is a medical student at Dalhousie University in Halifax, Nova Scotia, Canada.

Marta Calvo, MD, PhD, is the Spanish Medical Affairs manager for HIV and hepatitis at Gilead Sciences, Spain. She trained in medicine at the Universidad Autónoma de Madrid, Spain, and completed her residency in Internal Medicine at Hospital de Móstoles, Madrid, Spain, in 2006. Her academic training also includes a master's degree in AIDS, doctorate degree in medicine, and master's degree in design and analysis of clinical research from the Universidad de Barcelona, Spain.

Dr Calvo was responsible for a start-up hospital, Fundación Vicente Ferrer Hospital de Bathalapallí, dedicated to the care of patients with HIV/AIDS in rural India. She served as infectious disease specialist and medical scientist at the Infectious Disease Unit, Hospital Clínico de Barcelona-IDIBAPS, Spain, from 2007 to 2011, where she was also sub-investigator for several clinical trials. She has also completed a fellowship at the Infectious Disease Unit, University Hospital of Bonn, Germany, and served as an internist at the Emergency Department, Hospital de Fuenlabrada, Spain.

Dr Calvo has published over 20 peer-reviewed papers in international journals, written several book chapters, and spoken at numerous conferences, including the International AIDS Conference. She is fluent in Spanish, English, German, and Catalán.

André Fragoso Gomes, MD, is currently undertaking his residency in Infectious Diseases at the Department of Infectious Diseases of Hospital Garcia de Orta, Portugal, which he started in 2011. Dr Fragoso Gomes attended the Lisbon School of Medicine (Faculdade de Ciências Médicas, Universidade Nova de Lisboa).

Dr Fragoso Gomes has been actively involved in clinical care of patients with HIV at the Hospital Garcia de Orta, both within the wards and the outpatient clinic. He is particularly interested in metabolic disorders and other complications of HIV infection, especially the comorbidities that arise as patients age. Dr Fragoso Gomes worked at the Modena HIV Metabolic Clinic, Italy, for 3 months, where he developed his skills within the field and actively participated in ongoing clinical studies.

Esteban Martínez, MD, PhD, is an Associate Professor of Medicine at the University of Barcelona and Senior Consultant in Infectious Diseases at the Hospital Clínic in Barcelona, Spain. Since 1996, he has devoted his time to outpatient care and the clinical research of HIV infection, and, in 2001, he took up a teaching role in infectious diseases at the University of Barcelona.

Dr Martínez was born in León, Spain, in 1963. He studied at the School of Medicine in Valladolid, Spain, from 1980 to 1986, and specialized in Internal Medicine at Hospital de la Santa Creu i Sant Pau in Barcelona, Spain, from 1988 to 1992. In 1996 he achieved his PhD in neurological infections from the Autonomous University of Barcelona. His fields of interest span opportunistic infections, simplification of antiretroviral therapy, incidence and causes of death in HIV-infected persons receiving antiretroviral therapy, toxicity of antiretrovirals, and noninfectious complications in HIV-infected patients.

Dr Martínez is a member of the Scientific Board of the International Workshop on Adverse Drug Reactions and Co-morbidities in HIV and was the coauthor of the Spanish Guidelines on Antiretroviral Therapy from 2001, Spanish Guidelines for Metabolic Complications in HIV-Infected

Patients since 2003, Spanish Guidelines for Kidney (2010) and Bone (2013) Complications in HIV-Infected Patients, and Guidelines for the Prevention and Management of Non-infectious Co-morbidities in HIV (European AIDS Clinical Society) from 2007.

He is a member of Grupo de Estudio de SIDA (GESIDA), Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC), and European AIDS Clinical Society (EACS). He was elected as Regional (South Europe) Representative for EACS in 2012 for a 4-year period and has been a founding member of the International Symposium on Psychiatry and HIV (<http://www.psiquiatria-vih.com/>), held annually in Barcelona since 2007.

Dr Martínez has authored more than 200 papers and has led nine doctoral students. He has served as a reviewer for Dirección General de Investigación Científica y Técnica (Government of Spain), Agence Nationale de Recherche sur le Sida (France), UK Medical Research Council, South African Medical Research Council, Conselho Nacional de Desenvolvimento Científico e Tecnológico (Brazil), University of New South Wales, and University of Dublin. He has also served as a regular reviewer for major journals on medicine infectious diseases, chemotherapy, HIV/AIDS, endocrinology, bone, kidney, and circulation. He is an editorial board member of *AIDS Research and Therapy*, *HIV Medicine*, and *Journal of Acquired Immune Deficiency Syndromes*.

Preface

The ‘graying’ of the human immunodeficiency virus (HIV) epidemic is an established fact. Regardless of this evolving epidemiological context, no guidelines currently exist to offer a comprehensive view of the management of older patients with HIV.

This concise compendium addresses this gap by describing the aging trajectories of patients with HIV, by describing clinically meaningful end points, including comorbidities, multimorbidity, frailty, geriatric syndromes, and disability. Specific attention is given to the management of antiretroviral drugs in the context of polypharmacy in this special population.

In the context of the older patient with HIV, the model of HIV care is changing, and new strategies are needed to address the unmet healthcare needs of the aging patients. Best practices are presented together with the awareness that patient empowerment will remain at the core of innovative care models.

The authors of this book are infectious disease physicians and geriatricians, who are involved in the daily care of patients with HIV. We hope that this book will help not only doctors, but also allied care providers, including nurses, occupational therapists, social workers, psychologists, pharmacists,

community leaders, families, and especially patients to better understand this changing paradigm and prepare for the future.

Ana Rita Silva
Chiara Mussi
Julian Falutz
Giovanni Guaraldi

Abbreviations

AADL	Advanced activities of daily living
AADL-CDI	Advanced activities of daily living cognitive disability index
AADL-DI	Advanced activities of daily living disability index
AADL-PDI	Advanced activities of daily living physical disability index
ABC	Abacavir
ACC	American College of Cardiology
ADEs	Adverse drug events
ADL	Activities of daily living
AHA	American Heart Association
AIDS	Acquired immunodeficiency syndrome
AIN	Anal intraepithelial neoplasia
ALT	Alanine transaminase
AMPS	Assessment of motor and process skills
ANI	Asymptomatic neurocognitive impairment
ART	Antiretroviral therapy
ARV	Antiretroviral
AST	Aspartate transaminase
AZT	Azidothymidine
BI	Barthel index
BMD	Bone mineral density
BMI	Body mass index
BNCS	Brief Neurocognitive Screen
BUP	Bupropion
CAM	Confusion Assessment Method

cART	Combination antiretroviral therapy
CGA	Comprehensive geriatric assessment
CI	Confidence interval
CIN	Cervical intraepithelial neoplasia
CKD	Chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CMV	Cytomegalovirus
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CSF	Cerebrospinal fluid
CVD	Cardiovascular disease
DDI	Drug–drug interactions
DSM-III-R	Diagnostic and Statistical Manual for Mental Disorders Third Edition Revised
DXA	Dual-energy X-ray absorptiometry
E/C/F/TAF	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
EACS	European AIDS Clinical Society
eGFR	Estimated glomerular filtration rate
EI	Entry inhibitor
EMA	European Medicine Agency
ENDS	Electronic nicotine delivery systems
FDA	Food and Drug Administration
FEV ₁	Forced expiratory volume in 1 second
FRAX	Fracture risk assessment tool
FVC	Forced vital capacity
GALT	Gut-associated lymphatic tissue
GFR	Glomerular filtration rate
GGT	Gamma-glutamyl transphosphatase
HAART	Highly active antiretroviral therapy
HAD	HIV-associated dementia
HANA	HIV-associated non-AIDS
HAND	HIV-associated neurocognitive disorders
HbA1c	Hemoglobin A1c
HCV	Hepatitis C virus
HDL	High-density lipoprotein
HIV	Human immunodeficiency virus

HIVAN	HIV-associated nephropathy
HIV-VL	HIV-viral load
HLA	Human leukocyte antigen
HPV	Human papilloma virus
HR	Hazard ratio
HRM	High-risk morphology
IADL	Instrumental activities of daily living
ICKD	Immune complex kidney disease
IDU	Injecting drug users
IHDS	The International HIV Dementia Scale
IL	Interleukin
INI	Integrase inhibitor
INSTI	Integrase strand transfer inhibitor
IRP	Immune risk phenotype
KS	Kaposi's sarcoma
LDH	Lactate dehydrogenase
LDL	Low-density lipoprotein
LGBT	Lesbian, gay, bisexual, or transgender
LPS	Lipopolysaccharide
MCI	Mild cognitive impairment
MDRD	Modification of Diet in Renal Disease
MHMC	Modena HIV Metabolic Clinic
MM	Multimorbidity
MNA	Mini Nutritional Assessment
MND	Mild neurocognitive disorder
MoCA	Montreal cognitive assessment
MRI	Magnetic resonance imaging
MSM	Men who have sex with men
MVC	Maraviroc
NHL	Non-Hodgkin lymphoma
NICM	Noninfectious comorbidities
NK	Natural killer
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRT	Nicotine replacement therapy
NRTI	Nucleoside reverse transcriptase inhibitor
NtRTI	Nucleotide reverse transcriptase inhibitor
OTC	Over-the-counter
PI	Protease inhibitor

PLWHA	People living with HIV or AIDS
PPI	Proton pump inhibitor
PYFU	Person-years of follow-up
QOL	Quality of life
RDA	Recommended daily allowance
SCA	Successful cognitive aging
SGA	Subjective Global Assessment
STF	Single-tablet formulations
STR	Single-tablet regimen
T2DM	Type II diabetes mellitus
TDF	Tenofovir disoproxil fumarate
TMIG	Tokyo Metropolitan Institute of Gerontology Index
TNA	Total number of activities
TNF	Tumor necrosis factor
TSH	Thyroid-stimulating hormone
VACS	Veterans Administration Cohort Study
VAR	Varenicline

Chapter 1

Introduction

Julian Falutz

Over 30 million people are infected with human immunodeficiency virus (HIV) today, more than 30 years after HIV/acquired immunodeficiency syndrome (AIDS) was first described [1]. AIDS describes a set of usually fatal infectious and malignant diseases that occur in previously healthy individuals and are due to a progressively severe acquired immunodeficiency state. This state is due to infection with HIV, a unique retrovirus. Following exposure (via perinatal, blood-borne, or sexual vectors) to HIV, most people, overall, remain relatively well during a clinically latent phase that lasts on average 10 years. Most infected people may not be aware of being seropositive unless specifically tested for HIV. During the initial 15 year period of the epidemic antiretroviral therapy (ART) was unavailable. Most patients died of poor response to appropriate therapy of often concurrently occurring infectious and malignant complications, usually within 2–3 years of the initial AIDS complication [2]. However, during this period important advances were made and a deep

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understanding of HIV biology and the pathogenesis of AIDS occurred. This led to the progressive development of effective antiretroviral (ARV) drugs by the mid-1990s. These drugs, when used in specific combinations, referred to as highly active anti-retroviral therapy (HAART), transformed AIDS into a mostly manageable chronic disease. As a result few effectively treated patients still develop traditional AIDS-related complications [3].

Since the widespread introduction of HAART in the mid-1990s the survival of treated patients has increased significantly [4]. This has impacted on the mean age of the infected population. Currently, about 50 % of infected persons in high-income countries are older than 50 years of age [5], with similar proportionate increases noted in non-industrialized countries. The age of 50 years has been used in HIV infection as a transition point separating older from younger patients, while recognizing that there is no specific biologic rationale for this precise age to represent older patients. Its use likely stems from the fact that during the first decade of the epidemic only a small minority (<10 %) of affected patients in industrialized countries were older than 50 years of age [6], a proportion that has progressively increased to 50 % at present [7].

Effective HIV risk prevention and education programs have significantly reduced new infection rates since HIV was identified as the etiologic agent of AIDS. However, new infections clearly still occur. The term 'long-term survivors' refers to patients infected early in the epidemic who either did not develop AIDS or survived those complications to benefit from the initial HAART regimens. Their improved survival is the main explanation for the overall increasing age of the majority of currently infected persons [5]. However, the age at the time of HIV seroconversion has also increased [8]. Older persons are at particular risk of exposure to HIV and other sexually transmitted infections for various reasons. Health care workers infrequently discuss sexual issues, including HIV, with older patients [9]; this is associated with a perception of low personal HIV risk among older persons. Also, the relative