New Insights into HIV/AIDS for Students and Healthcare Professionals

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Edited by

Esther Olufunmilayo Asekun-Olarinmoye
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This book is dedicated to stakeholders in HIV care

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PREFACE

Human Immunodeficiency Virus (HIV) infection with its attendant Acquired Immune Deficiency Syndrome (AIDS) is a pandemic that has been ravaging different countries of the world despite the colossal resources channelled towards its containment. It is estimated that about 36.7 million people are currently living with HIV/AIDS in the world and the brunt of the infection is mostly felt in Africa. Presently, Nigeria is the second most endemic country in the world after South Africa and about 3.2 million people are living with HIV/AIDS. The infection is more prevalent among the youths (18-49 years) and over 160,000 people die due to the infection and its complications annually. This is indeed, worrisome.

So far, all efforts to find a cure for the HIV/AIDS infection globally have not yielded appreciable results. The containment of the infection has centred on chemotherapeutic management, public health education on the aetiology and transmission of the infection and the enactment of policies to guide Local and National Ministries of Health and other caregivers to stem the tide of the infection.

It is therefore, heart-warming to note that biomedical researchers and medical practitioners from diverse backgrounds have come together to produce a textbook on HIV/AIDS for the utilization of the students and health caregivers involved in the management of HIV/AIDS. The textbook has chapters which cover a broad spectrum of topics in HIV/AIDS such as history, epidemiology, complications, laboratory diagnosis, chemotherapeutic case management, policies and advocacy.

While commending the College of Health Sciences, Osun State University for championing and chatting pathways for the diffusion of knowledge and the containment of the HIV/AIDS pandemic through this effort, it is my fervent hope that this textbook will not only find its relevance in Nigeria but in the entire globe. I recommend it to all and sundry.

Labode POPOOLA, Ph.D, *FFAN*
Vice-Chancellor
Osun State University, Osogbo

FOREWORD

Since the first case of HIV was diagnosed in 1981, several efforts have gone into its prevention and control. Yet HIV remains the leading scourge of our times with its attendant deaths and sickness. There is no cure for HIV as of today despite the international attention and publicity received by the disease. It is one of the few diseases specifically given attention in the Millennium Development Goals (MDG) and now the Sustainable Development Goals (SDGs). There has been little effort by academia in developing countries towards contributing to in-depth knowledge of HIV, as well as stimulating the interest of students at both undergraduate level and in carrying out research on HIV. As the search for a cure continues, the writing of this book is a timely concept, discussing the changing epidemiology of HIV and presenting from the angle of both academics and public health programming. The authors are not only academicians but seasoned programmers who have worked or are currently working in the realm of HIV comprehensive care. HIV has been looked into from multi-disciplinary and multisystem angles including pregnancy, the bodily organs and systems, cancers, and its effects on the general population.

This book presents the current perspective of HIV care. Because recommendations for care are bound to change with time, the authors and reviewers of this book have accurately showcased the present concepts, and shall not be liable for any errors or omissions in information or any perceived inaccuracies to the users of this book as recommendations and guidelines change with time. I am confident that this will just be the first of the books to be written by a team of erudite scholars presented by the College of Health Sciences of Osun State University and their collaborators in other Universities within Nigeria. Thus, students, programme planners, programme managers and policy makers among other stakeholders in HIV care would benefit immensely from this book.

The book would also assist the Nigerian Government in making policy decisions that would further crash the current prevalence of HIV. All the chapters were double-blinded peer reviewed and subjected to plagiarism assessments. With the high level of research interest that this book will

stimulate, there is no doubt that Nigeria is gradually moving towards a pattern of zero prevalence and an HIV-free generation.

Professor Alebiosu C.O.
Visiting Professor of Medicine
Office of Global Health
Department of Internal Medicine
Yale University School of Medicine

ACKNOWLEDGEMENT

Having an idea and turning it into a book is as hard as it sounds. The experience is both challenging and rewarding.

This book was prepared under the auspices of the College of Health Sciences, Osun State University and collaborators in other Universities within Nigeria. Expert reviews, feedbacks and comments were contributed by numerous experts. Outstanding amongst these reviewers are the Special Editors / Editorial Consultants, Professor Adesegun Fatusi and Professor L. Salawu, of the Obafemi Awolowo University, who reviewed and edited every chapter. We appreciate the fact that you are able to create time out of your ever busy schedule to carry out this assignment.

A very sincere note of acknowledgement to all the authors whose works were cited; their contributions have indeed been a source of enrichment with regard to the existing body of knowledge pertaining to the subject.

Writing a book is harder than we thought, our gratitude also goes to the publishers of this book - Cambridge Scholars Publishing.

LIST OF ABBREVIATIONS

AAN:	American Academy of Neurology
ABC:	Abacavir
ACE:	Angiotensin-Converting Enzyme
AD:	Alzheimer's disease
ADRs:	Adverse Drug Reactions
AIDP:	Acute Inflammatory Demyelinating Polyneuropathy
AIDS:	Acquired Immune Deficiency Syndrome
AJOL:	African Journals Online
AKI:	Acute Kidney Injury
ANC:	Antenatal Care
ANI:	Asymptomatic Neurocognitive Impairment
ANUG:	Acute Necrotizing Ulcerative Gingivitis
ART:	Antiretroviral therapy
ARVs:	Antiretrovirals
ATN:	Acute tubular necrosis
AZT:	Azidothymidine
Aβ:	Beta-amyloid
BBB:	Blood–Brain Barrier
BCC:	Behavioural Change Communication

cART: combination antiretroviral therapy

CCF: Congestive Cardiac Failure

CD: Cluster of differentiation

CDC: Center for Disease Control and Prevention

CEDAW: Convention on the Elimination of All Forms of Discrimination against Women

CHAI: Clinton Health Access Initiative

CHER: Children with HIV Early Antiretroviral Therapy

CIDP: Chronic Inflammatory Demyelinating Polyneuropathy

CKD: Chronic kidney diseases

CKD-EPI: Chronic Kidney Disease Epidemiology Consortium

CMI: Cell-Mediated Immunity

CMV: Cytomegalovirus

CPT: Co-trimoxazole Preventive Therapy

CRA: Child Rights Act

CRFs: Circulating recombinant forms

CSF: Cerebrospinal fluid

CT: Computerised Tomography

CVD: Cardiovascular diseases

DBS: Dried blood spot

DILS: Diffuse Infiltrative Lymphocytosis Syndrome

DM: Diabetes Mellitus

DSP: Distal Sensory Polyneuropathy

DTG: Dolutegravir

EBV: Epstein-Barr virus

EID: Early Infant Diagnosis

ELISA: Enzyme-linked immunosorbent assay

ENT: Ear-Nose-Throat

ESRD: End-stage renal disease

FDA: Federal Drug Agency

FGC: Female genital cutting

FP: Family Planning

FSW: Female Sex Workers

GFR: Glomerular filtration rate

GIT: Gastrointestinal tract

HAART: Highly Active Antiretroviral Therapy

HAD: HIV-associated dementia

HAND: HIV-associated neurocognitive disorders

HCT: HIV Counselling and Testing

HCV: Hepatitis C virus

HHV8: Human herpes virus 8

HIV DNA-PCR: HIV DNA-Polymerase Chain Reaction

HIV: Human Immunodeficiency Virus

HIV-1: HIV type 1

HIV-2: HIV type 2

HIVAN: HIV associated nephropathy

HIVICK: HIV-immune complex mediated kidney disease

HIV-SGD: HIV salivary gland disease

HPV: Human Papilloma Virus

HSV: Herpes Simplex Virus

HTC: HIV Testing and Counselling

HTLV-III: Human T-cell Lymphotropic Virus III

HZ: Herpes Zoster

HZO: Herpes Zoster Ophthalmicus

HZV: Herpes Zoster Virus

IDUs: Injection drug users

IDUs: Intravenous Drug Users

IFN-α: interferon α

IgA: Immunoglobulin A

IPT: Isoniazid Preventive Therapy

IUGR: Intrauterine growth Restriction

IVIg: Intravenous immunoglobulin

JC: John Cunningham

KS: Kaposi's sarcoma

LD: Liposomal doxorubicin

LGE: Linear gingival erythema

LTRs: Long terminal repeats

MAC: M avium-intracellulare complex

MALT: Mucosa-associated lymphoid tissue

MDG: Millennium Development Goal

MDRD: Modification of diet in renal disease

MI: Myocardial infarction

MMSE: Mini-mental status examination

MNCH/FP: maternal, child health and family planning

MND: Mild neurocognitive disorder

MRI: Magnetic Resonance Imaging

MRSA: Methicillin-resistant *S aureus*

MSM: Men having sex with men

MTCT: Mother-to-child transmission

NACA: National Agency for Control of AIDS

nef: negative regulatory factor

NF-κB: Nuclear factor kappa B

NGOs: Non-governmental Organizations

NHL: non-Hodgkin lymphoma

NMDA: *N*-Methyl-D-aspartate

NNRTIs: Non-nucleoside Reverse Transcriptase Inhibitors

NRTI: Nucleoside Reverse Transcriptase Inhibitors

NUG: Necrotizing ulcerative gingivitis

NUP: Necrotizing ulcerative periodontitis

NVP: Nevirapine

OHL: Oral Hairy Leukoplakia

PBMC: Peripheral blood mononuclear cell

PCNSL: Primary CNS lymphoma

PCR: Polymerase Chain Reaction

PEP: Post-exposure prophylaxis

PHC: Primary Health Care

PIs: Protease inhibitors

PITC: Provider initiated testing and counselling

PLHIV: People living with HIV

PML: Progressive Multifocal Leukoencephalopathy

PMTCT: Prevention of mother to child transmission

PORN: Progressive outer retinal necrosis

PPAR: Peroxisomal proliferator-activated receptor

PPD: Purified protein derivative

PPE: Pruritic papular eruption

PRN: Progressive retinal necrosis

pTAU: hyperphosphorylated tau

RDTs: Rapid Diagnostic Tests

rev: Regulator of viral protein expression

RH: Reproductive Health

RTI: Reverse Transcriptase Inhibitor

RUQ: Right upper quadrant

SDGs: Sustainable Development Goals

SIVs: Simian immunodeficiency viruses

SPECT: Single-photon emission computed tomography

STDs: Sexually transmitted diseases

STIs: Sexually transmitted infections

tat: trans-activator of transcription

TBAs: Traditional Birth Attendants

TDR: Tenofovir

T_H Cells: T Helper cells

TWGs: Technical Working Groups

UNAIDS: United Nations Agency for AIDS

VCT: Voluntary Counselling and Testing

vif: Viral infectivity protein

VL: viral load

VMMC: Voluntary male medical circumcision

vpr: Viral protein R

vpu: Viral protein U

vpx: Viral protein X

VZV: Varicella-Zoster Virus

WBC: White Blood Cell

WHO: World Health Organization

ZDV: Zidovudine

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Chapter Twenty-Six

HISTORY OF HIV

IBUKUN PETER OYEYIPO, PHD

Human immunodeficiency virus (HIV) originated from the non-human primates in Central and West Africa. HIV type 1 and 2 (HIV-1 and HIV-2) which are lentiviruses are causative agents of Acquired Immune Deficiency Syndrome (AIDS). M, N, O and P are the distinct lineages of HIV-1 with M classified into nine subtypes. On the other hand, HIV-2 has at least eight distinct lineages. The greatest morbidity and mortality of HIV/AIDS have been experienced in the developing countries with young adults in sub-Saharan Africa most vulnerable. Consequently, this has impacted adversely on the working-class raising fundamental issues which are related to unemployment, work rehabilitation, and stigmatization among others.

Human immunodeficiency virus (HIV) is established as the causative agent of Acquired Immune Deficiency Syndrome (AIDS) and it originated from the non-human primates in Central and West Africa. This disease of humans is caused by two lentiviruses; human immunodeficiency viruses types 1 and 2 (HIV-1 and HIV-2). AIDS is an infectious disease which was first recognized in 1981 (1, 2) and ever since then, it has become one of the most challenging diseases to be discovered in recent history (3). Ever since the identification of this virus over three decades ago, the pandemic form of HIV-1 which is also referred to as the main (M) group has caused over 25 million deaths and 60 million infections (4). Thus, AIDS will continue to pose a significant public health threat for decades to come. In 1986, the first clue to the reason for the epidemic's spread and sudden emergence and the unique pathogenicity of HIV-1 was discovered when an antigenically distinct but morphologically similar virus was found to cause AIDS in western African patients. Interestingly, this virus called human immunodeficiency virus type 2 was closely related to a simian virus that caused immunodeficiency in captive macaques (5). Thereafter, other collected viruses termed simian immunodeficiency viruses (SIVs), usually differentiated with a suffix denoting the species of origin, were identified in various primates such as Chimpanzees, sooty mangabeys,

mandrills, African green monkeys and others from sub-Saharan Africa. It was amazing to discover that close simian relatives of HIV-1 were found in Chimpanzees (6) while those of HIV-2 were found in sooty mangabeys (7) therefore this association provides evidence that AIDS had emerged in both macaques and humans as a result of cross-species infections with lentiviruses from different primate species; thus the origin of HIV-1 and HIV-2 has been associated with zoonotic transfer of the viruses from primates to man in Africa. Demographic data also indicate that the HIV-1 pandemic started when there was an expansion of urban populations in west and central Africa (8). At that time, Leopoldville in the Belgian Congo (now Kinshasa in the Democratic Republic of the Congo) was the largest city in the region and thus a likely destination for a newly emerging infection. Moreover, rivers were the major routes for travelling and commercial activity at the time, which might have provided a link between the chimpanzee reservoir of HIV-1 group M in southeastern Cameroon and Leopoldville on the banks of the Congo (9). Thus, all current evidence points to Leopoldville/Kinshasa as the cradle of the AIDS pandemic.

HIV-1 comprises four distinct lineages, termed groups M, O, N, and P, each of these groups is as a result of independent cross-species activities. The first group; M was the first to be discovered, it represents the pandemic form of HIV-1 infecting several millions of people in the world and found in almost all countries (10). It is also currently classified into nine subtypes (A, B, C, D, F, G, H, J and K) as well as over 40 different circulating recombinant forms (11). The origin of Subtypes A and D was central Africa which established epidemics in eastern Africa, while Subtype B, which accounts for most of the HIV-1 infections in America and Europe, was from a single African strain that appears to have first spread to Haiti in the 1960s and then onward to the US and other western countries (12). Subtype C was from Southern Africa from where it spread to India and other Asian countries.

In 1990, Group O was discovered with lesser prevalence, representing less than 1% of global HIV-1 infections with restrictions to a few African countries (13). Group N with a lesser prevalence than O was identified in 1998 with only 13 cases documented in Cameroon (14), while Group P was discovered in France in 2009 in a Cameroonian woman (15) and after that in one other person also from Cameroon (14). Groups M and N of HIV-1 were shown to be closely related to SIV of Chimpanzee origin. HIV-1 group N appears to have originated in the vicinity of the Dja forest in South-Central Cameroon while group M is likely to have emerged in an area near Boumba, Ngoko and Sangha River in the southeastern corner of

Cameroon (16). Phylogenetic data have supported that Group P has a gorilla origin of HIV-1. However, very few SIV of the gorilla strain have been characterized to ascertain the region where transmission occurred. The immediate source of HIV-1 group O is still debatable since to date, no ape viruses are similar to this group. Therefore, HIV-1 group O could either be of Gorilla or Chimpanzee origin.

The mode of transmission through which humans acquired ape precursors of the HIV-1 groups is still unclear but it is most likely that transmission occurred through mucous and cutaneous membrane exposure to infected ape blood and/or fluid from the body such as during bushmeat hunting (16).

HIV-2 is largely restricted to West Africa, with Senegal and Guinea-Bissau having the highest prevalence rates recorded (17). However, HIV-1 is increasingly replacing HIV-2, thus, there is a decline in the overall prevalence of HIV-2 (18). The lower transmission rate and the near complete absence of mother-to-infant infection of HIV-2 could be associated with a lower viral load in infected persons (19). Interestingly, most people infected with HIV-2 do not have AIDS but have clinical symptoms indistinguishable from HIV-1 (20). These facts are all indications that the natural history of HIV-2 infection is different from HIV-1. Since the first isolation of HIV-2, at least eight distinct lineages have been identified, with each representing an independent host transfer. These are groups A–H, and Group A and B have been found to spread to humans. Group A has been isolated in West Africa (21), while group B has been isolated in Cote d'Ivoire (22). Groups C, G, and H have also been associated with Cote d'Ivoire, group D with Liberia and groups E and F with Sierra Leone (23, 24, 25).

The spread of HIV-1 is primarily through sexual intercourse (26), however, perinatal and percutaneous routes have been implicated in the spread (26). The greatest morbidity and mortality of HIV/AIDS have been experienced in developing countries with young adults in sub-Saharan Africa being the most vulnerable. From an epidemiologic point of view, Southern Africa has recorded prevalence rates higher than 10% of the HIV pandemic and it is thus the region of the world that is hardest hit. Surveys across the Southern Africa region indicate that Zambia recorded an HIV prevalence of 15.6% in the Zambia Demographic and Health Survey in the period 2000–2001 (27), Namibia (individuals aged 15–49 years) recorded 10% in 2005, 4.5% in the Democratic Republic of Congo are infected (28), and 14.4% in the Malawi Demographic and Health Survey in 2004

(29). HIV/AIDS was ranked the 5th largest cause of death in Southern sub-Saharan Africa in 1990, whereas in 2010, it was the top cause of death (30). Braveman *et al.* (31) reported that in the United States, 850 000 to 950 000 persons are estimated to be living with HIV and with an increased incidence rate each year and since a large population of the working-class is affected, issues of employment, work rehabilitation, and AIDS are major causes of concern in the workplace.

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