OECS

HIV/STI

GUIDELINES 2017

The Global Fund

Organisation of Eastern Caribbean States

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1 PREFATORY MATERIALS
1.1 Abbreviations and Acronyms

Acronym	Meaning
3TC	Lamivudine
ABC	Abacavir
ABG	Arterial Blood Gas
AFB	Acid Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
ALT	Alanine Aminotransferase
APV	Amprenavir
ART	Antiretroviral therapy
ARV	Antiretroviral Medication
ASC	Atypical Squamous Cells
ASC-US	Atypical Squamous Cell of undetermined significance
AST	Aspartate Aminotransferase
ATV	Atazanavir
ATV/r	Atazanavir plus ritonavir
AUC	Area under the curve
AZT	Azidothymidine (zidovudine)
BAL	Bronchoalveolar lavage
BCA	Bichloroacetic acid
BID	Twice a day
BIW	Twice weekly
BV	Bacterial Vaginosis
CAREC	Caribbean Epidemiology Center
CBC	Complete Blood Count

Acronym	Meaning
IVIG	Intravenous immunoglobulin
KOH	Potassium hydroxide
LAIV	Live attenuated influenza vaccine
LDH	Lactate dehydrogenase
LDH	Lactate dehydrogenase
LGV	Lymphogranuloma venereum
LPV	Lopinavir
LPV/r	Lopanavir plus ritonavir
LSIL	Low Grade Squamous Intraepithelial Lesion
LTBI	Latent Tuberculosis Infection
MAC	Mycobacterium avium complex
MARP	Most-at-risk populations
MCD	Multicentric Castleman's disease
MCTC	Mother to Child Transmission
MCV	Meningococcal Conjugate Vaccine
MDR-TB	Multi-drug resistant tuberculosis
MMR	Measles Mumps Rubella (Vaccine)
MMRV	Measles Mumps Rubella Varicella (Vaccine)
MPSV	Meningococcal Polysaccharide Vaccine
MRI	Magnetic Resonance Imaging
MSM	Men who have Sex with Men
MTB	Mycobacterium Tuberculosis
NAAT	Nucleic Acid Amplification Test

CCR	Chemokine Receptor
CDC	US Centers for Disease Control
CLD	Chronic Liver Disease
Cmax	Maximum concentration
Cmin	Minimum concentration
CMV	Cytomegalovirus
CNS	Central Nervous System
CPK	Creatine Phospokinase
CrAG	Crytococcal Antigen
CRP	C-reactive protein
CSF	Cerebrospinal fluid
CT	Computed Tomography (Scan)
CXR	Chest X-ray
d4t	Stavidune
DBS	Dried Blood Spot Test
DDL	Didanosine (Videx, Videx EC)
DGI	Disseminated Gonococcal Infection
DLV	Delavirdine
DOT	Directly Observed Therapy
DRV/r	Darunavir plus ritonavir
DS	Double Strength
DTG	Dolutegavir
DTP	Diphtheria, Tetanus, Pertussis (Vaccination)
EFV	Efavirenz
EIA	Enzyme Immunoassay
ELISA	Enzyme-Linked Immunoabsorbent Assay
NAT	Nucleic Acid Testing
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NSAID	Non-Steroidal Anti-inflammatory drug
NVP	Nevirapine
OECS	Organization of Eastern Caribbean States
OI	Opportunistic Infection
OPV	Oral Polio Vaccine
PAHO	Pan American Health Organization
PCP	Pneumocystis jiroveci pneumonia
PCR	Polymerase Chain Reaction
PCV	Pneumococcal Conjugate Vaccine
PEL	Primary Effusional Lymphoma
PEP	Post-exposure Prophylaxis
PHDP	Positive Health, Dignity and Prevention
PI	Protease Inhibitor
PID	Pelvic Inflammatory Disease
PITC	Provider-Initiated Testing and Counselling
PLHIV	People Living with HIV
PML	Progressive Multifocal Leukoencephalopathy
PMTCT	Prevention of Mother to child transmission of HIV
PO	By mouth, oral
PPS	OECS's Pharmaceutical Procurement Service
PPSV	Pneumococcal Polysaccharide Vaccine
PrEP	Pre-exposure prophylaxis
Q[#]H	Every [amount] hour

EMB	Ethambutol
EPT	Expedited Partner Therapy
ESR	Erythrocyte Sedimentation Rate
ETV	Etravirine
FCSW	Female Commercial Sex Workers
FDA	US Food and Drug Administration
FI	Fusion Inhibitor
FPV/r	Fos-amprenavir plus ritonavir
FTA-ABS	Fluorescent Treponemal Antibody Absorbed Test
FTC	Emtricitabine
GUD	Genital Ulcer Disease
HAART	Highly Active Antiretroviral Therapy
HAM	Human T-lymphotropic virus-I associated myelopathy
HAPU	HIV/AIDS project unit of the OECS
HAV	Hepatitis A Virus
HBeAg	Hepatitis B e Antigen
HBIG	Hepatitis B Virus Immunoglobulin
HbSAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HHV-8	Human Herpes Virus-8
Hib	Haemophilus influenzae
HIV	Human Immunodeficiency Virus
HTEP	HIV TB Elimination Project
HIVSTS	HIV Self Testing
HPTN	HIV Prevention Trial Network
QD	Daily
QHS	Every Bedtime
QID	Four times a day
QM	Monthly
QOD	Every Other Day
QW	Once a week
RNA	Ribonucleic Acid
rPI	Ritonavir-boosted protease inhibitor
RPR	Rapid plasma reagin
RSV	Respiratory Syncytial Virus
RTV	Ritonavir
SD-NVP	Single dose nevirapine
SGOT	Serum Glutamic Oxaloacetic Transaminase
SGPT	Serum Glutamin Pyruvic Transaminase
SQ	Subcutaneous
SQV	Saquinavir
SS	Single Strength
START	Strategic Timing of Antiretroviral Therapy
STD	Sexually transmitted disease
STI	Sexually transmitted infection
TB	Tuberculosis
TCA	Trichlroacetic Acid
Td	Diphtheria and Tetanus Toxoids
TdAP	Diphtheria and tetanus toxoids and acellular pertussis
TDF	Tenofovir Disoproxil Fumarate (Tenofovir)
TE	Toxoplasmic Encephalitis

HPV	Human Papilloma Virus
HRSA	US Health Resources and Services Administration
HSIL	High grade squamous intraepithelial lesion
HSV	Herpes Simplex Virus
HTLV	Human T-lymphotropic Virus
HTS	HIV Testing Services
HZV	Herpes Zoster Virus
I-TECH	International Training and Education Center for Health
IBS	Irritable Bowel Syndrome
ICP	Increased Intracranial Pressure
IgG	Immunoglobulin G
IHPS	Infantile Hypertrophic Pyloric Stenosis
IM	Intramuscularly
INSTI	Integrase Inhibitor
IPT	Isoniazid Preventive Therapy
IPV	Inactivated Polio Virus
IRIS	Immune Reconstitution Inflammatory Syndrome
IRU	Immune Recovery Uveitis
IU	International Units
IUD	Intrauterine Device
IV	Intravenous
TID	Three Times Daily
TIV	Trivalent Inactivated Influenza Vaccine
TIW	Three Times Weekly
TMP-SMX	Trimethoprim-Sulfamethoxazole (co-trimoxazole)
TP-PA	T.pallidum, passive particle agglutination
TPHA	Treponema Pallidum Hemaglutination Assay
TST	Tuberculin Skin Test
TWG	Technical Working Group
UWI	University of the West Indies
VCT	Voluntary Counselling and Testing
VDRL	Venereal Disease Research Laboratory Test
VDRL	Venereal Disease Reference Laboratory
VIA	Visual Inspection with Acetic Acid
VL	Viral Load
VVC	Vulvovaginal Candidiasis
VZV	Varicella-Zoster Virus
WBC	White Blood Cells
WHO	World Health Organization
WSW	Women who have sex with women
XDR-TB	Extensively Drug Resistant Tuberculosis
YMSM	Young Men who have sex with men

1.2 Foreword

Given the archipelago of islands of the OECS and the free movement of people within our common heath space, it is vital that clinical standards are established to guide the prevention, diagnosis and treatment of HIV and STI in the region especially for mobile populations. The development of this updated guidelines will not only strengthen clinical care but also consolidate efforts at the integration and decentralization of HIV and STI into primary care. We believe that this is an effective and sustainable public health strategy aimed at preventing and controlling HIV and STI's in the OECS region and contributing to the UNAIDS 90 90 90 target and the SDG Goal 3.3 of ending the AIDS epidemic by 2030.

In the era of emerging infectious diseases, it has become paramount that control measures be instituted to avert potential public health threats so as to protect the health of all citizens. As an appendage to this practice and philosophy is the fervent need to prevent and control those infections that are already creating deleterious effects on our health care system. Now that HIV has moved from an acute centered infectious disease to that of a chronic disease, it becomes even more fundamental that stringent measures be put in place to ensure that there is a sustainable prevention, treatment and care infrastructure to control this debilitating disease. A core element of this effort is the development of clinical guidelines that will provide concise clinical care guidance spanning populations that are directly and indirectly affected by HIV and STI's. These include general and key populations that are disproportionately affected by the stabilized HIV epidemic in the OECS region and require targeted interventions to achieve maximum impact.

These OECS HIV/STI guidelines are written for health care workers, program managers, policy makers, academic, civil society and persons living with HIV/ STI's. They aim to support clinicians in the prevention, diagnosis, treatment and management of patients with HIV and STI's within both the public and private healthcare systems. These guidelines further serve as a reference source for program managers and policy makers to guide the planning, implementation and evaluation of HIV/STI programs. It uses both a clinical and programmatic oriented approach to ensure that clinical practice is harmonized throughout the region. Much of the core evidence has been derived from the recent recommendations from PAHO/WHO and the CDC. The HIV section embraces the latest WHO HIV treatment guidelines. The approach is on HIV testing, primary and secondary prophylaxis, and treatment; with particular attention to high risk groups including HIV/TB co-infected patients, pregnant mothers and their infants. The STI section is centered on a combination of syndromic and etiological management taking into consideration the most recent recommendations from the CDC and experience from local clinical practice. As the OECS moves toward the Elimination of Mother to Child Transmission of HIV and Syphilis, this guideline serve as a cornerstone to guide the clinical and programmatic parameters of this aspiration.

The entire process was built upon the work of dedicated stakeholders from the last guidelines development era and has adopted the same approach of broad sector, multidisciplinary consultation and concise review. This entailed conducting constant review sessions by the multidisciplinary technical working group, the Clinical Care Coordinators Forum made up of project based clinicians. These reviews were conducted under the guidance of an independent regional consultant with over 20 years in HIV/STI clinical and programmatic management. A multi-country, multi-stakeholder consultation comprising of representative from the OECS

member states was convened in St Lucia to review and revise the draft guidelines. Moreover, external peer reviews from PAHO and regional experts have refined the product. It is evidenced based and embedded with concrete recommendations on the management of HIV/STI's according to the latest evidence based research. It is further guided by an implementation plan to guide its roll out in the Member States of the OECS. The guidelines are intended to be revised every 3 to 5 years in keeping with current trends and practices in HIV and STI clinical management

The HIV/TB Elimination project would like to thank all those who have contributed to the development of this important guidelines through their invaluable inputs, comments and feedback.

Dr. Cleophas D'Auvergne
HIV/TB Project Co-ordinator

1.3 Acknowledgements

The guidelines revision process led by the Organisation of Easter Caribbean States (OECS), HIV TB Elimination Project (HTEP) and builds on the work of the HIV STI 2013 guidelines. The OCES gratefully acknowledges the tremendous effort and the invaluable contributions to those persons who shared their technical knowledge and expertise in the revising and updating of the 2013 guidelines.

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In addition to relevant publications from the medical literature, the OECS HTEP acknowledges the following resources were significant in supporting the technical recommendations of these guidelines. These include:

1. Latest WHO HIV treatment Selected guidelines from the World Health Organization (WHO) on HIV, tuberculosis, and sexually transmitted infections (STI)
2. Latest consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations
3. Guidelines from the current US Centers for Disease Control and Prevention on HIV, opportunistic infections, and STIs
4. The treatment and patient monitoring guidelines for HIV/STI in the OECS and other Caribbean countries

Please refer to the works cited section for complete references on these resources.

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In addition to relevant publications from the medical literature, the following resources were used to support the technical recommendations of these guidelines:

- Selected guidelines from the World Health Organization (WHO) on HIV, tuberculosis, and sexually transmitted infections (STI)
- Guidelines from the US Centers for Disease Control and Prevention on HIV, opportunistic infections, and STIs
- HIV care and treatment guidelines for the Caribbean region
- Caribbean *Guidelines for the Prevention, Treatment, Care and Control of Tuberculosis and TB/HIV*
- National HIV care and treatment guidelines from Belize
- *HIV Web Study* FANTA Project's *Nutrition and HIV/AIDS: A Training Manual*
- Please refer to the works cited section for complete references on these resources.

INTRODUCTION

These guidelines revised from the Organisation of Eastern Caribbean States (OECS) 2013 guidelines provide updated guidance on the prevention and diagnosis of Human Immunodeficiency Virus (HIV) infection and the use of antiretroviral (ARV) drugs to treat infected with the virus. In addition, updated guidance is provided on other sexually transmitted infections.

Aligned to 2016 World Health Organisation (WHO) guidelines, it prioritizes earlier initiation of ARVs and expands the use of ARVs for prevention of HIV. New recommendations include lifelong ART to all children, adolescents and adults living with HIV, including all pregnant and breastfeeding women living with HIV, regardless of CD4 cell count. A newer class of ARV drugs is now recommended as an option for first-line treatment option, as well as a reduced dosage of a previously recommended drug, efavirenz, to improve tolerability.

Because of the dynamics between HIV and other sexually transmitted infections, there continues to be a strong focus on the prevention, diagnosis, treatment and control of sexually transmitted infections contained in a separate chapter. Aligned to the CDC 2015 guidelines, new sections are included on proctitits, proctocolitis and enteritis as well as sexual assault. Based on new scientific evidence, treatment of Hepatitis C is also noted.

1.1 Objectives

The objectives of these guidelines are:

- Standardize the management of infants, children, adolescents, and adults in OECS living with HIV.
- Ensure that antiretroviral treatment protocols in OECS reflect evidence-based international standards of practice.
- Present simplified algorithms for the counselling, assessment, diagnosis, treatment, clinical and laboratory monitoring, and follow-up of adults and children living with HIV.
- Provide streamlined information on the benefits and risks of antiretroviral therapy to facilitate a public health approach to implementing highly active antiretroviral therapy (HAART) throughout OECS.
- Provide recommendations on the management of co morbidities.
- Provide recommendations on the care of pregnant mothers with HIV to prevent mother-to-child transmission (PMTCT) of HIV.
- Provide recommendations on the care of individuals co-infected with tuberculosis and HIV and other co infections.
- Provide recommendation for managing post-exposure prophylaxis (PEP).
- Provide simplified guidelines for prophylaxis and management of common opportunistic infections in adults and children (OIs).
- Provide guidelines for the prevention and management of non HIV sexually transmitted infections focusing on a syndromic approach.

1.2 Target audience

The guidelines are primarily intended for use by HIV and STI clinicians but can be extended to all clinical practitioners including nurse practitioners, social workers, pharmacist and others. Additional audiences of interest include:

- National AIDS and STI Programme Managers,
- HIV clinical teams- physicians, nurses, social workers, HIV counsellors, pharmacists and others.
- Primary Health Care practitioners,
- Hospital staff and departments especially Emergency Rooms, Labor and Delivery and Infectious Disease Wards.
- National TB programme managers,
- National maternal and child health programmes,
- National Laboratory managers,
- People living with HIV,
- Persons from the key populations in the OECS,
- Community Based Organisations and
- Technical partners, international and bilateral agencies working in the OECS.

1.3 Guiding principles

The following principles have informed the development of the guidelines and should guide the implementation of the recommendations:

- The guidelines should contribute to OECS fulfilling its commitment to 90-90-90 by 2020, ending AIDS by 2030.
- The guidelines should contribute the elimination of mother to child transmission on HIV and Congenital Syphilis.
- The guidelines are based on a public health approach to scaling up the use of ARV drugs ensuring earlier initiation of ARVs.
- The guidelines emphasize the role of treatment as prevention such as in cases of pre-exposure prophylaxis.
- The guidelines realizes the rights and responsibilities of all people living with HIV and promotes the greater involvement in their care.
- The guidelines will be implemented with respect for and protection of human rights of all persons who need STI and HIV services including the promotion of gender equity and ensuring informed consent where necessary.
- The guidelines emphasizes the importance of providing STI and HIV services with respect for gender identity, without discrimination and with the highest level of confidentiality.
- The guidelines presents technical recommendations that are driven by global scientific evidence but informed by the local context including STI and HIV epidemiology, availability of resources and comorbidities, the organization and capacity of the health system and anticipated cost–effectiveness.

1.4 Methodology for developing the guidelines

- The OECS HIV TB Elimination Project (HTEP) contracted a consultant to review key technical documents focusing primarily but not limited to "***WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, Recommendations for a***

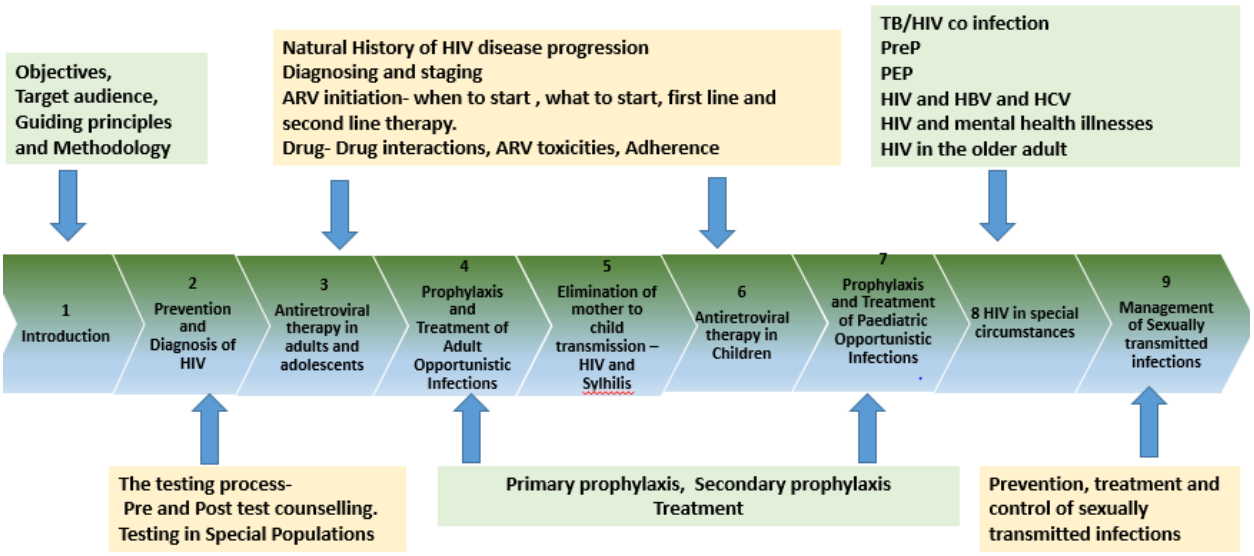
Public Health Approach, Second Edition 2016" for updating of the HIV section and US Centers for Disease Control **"Sexually Transmitted Diseases Treatment Guidelines 2015"** for the STI section.

- The OECS HTEP convened a Technical Working Group (TWG) comprising of clinicians, pharmacist, physiologist, M&E experts, National AIDS Programme Managers and other programme persons to guide the process. Each of the OECS territory was represented on the TWG.
- Clinical practitioners in the various member states were consulted through their representatives on TWG.
- The OECS HTEP clinical care forum comprising of primarily of practitioners in the region and representatives of the HTEP was consulted and provided inputs to the guidelines.
- An OECS HTEP consultation was convened with diverse stakeholders to provide inputs to the revision process. Recommendations from the consultation were inputted into the final document.
- An external review process initiated by the OECS HTEP facilitated feedback and inputs from independent technical experts and PAHO.

1.5 Organisation of the guidelines

The guidelines are organised into 9 parts as outlined in figure 1 below.

Figure 1: Organisation of the guidelines



2 PREVENTION AND DIAGNOSIS OF HIV INECTION

2.1 Screening for and diagnosing HIV infection

Identifying HIV disease and ensuring linkage into care in a timely manner is vitally important to the health of infected individuals as well as to public health, so that disease progression and transmission can be moderated. This is best accomplished through a comprehensive HIV Testing Services (HTS) programme compromising of a full range of services that should be provided together with HIV testing. These include counselling (pre-test information and post-test counselling); linkage to appropriate HIV prevention, treatment and care services and other clinical and support services; and coordination with laboratory services to support quality assurance and the delivery of correct results. Voluntary Testing and Counselling (VCT) that is client initiated has proved insufficient as persons in the OECS who are HIV infected and unaware of their status do no not seek testing. The OECS therefore recommends Provider Initiated Testing and Counselling (PITC).

PITC refers to HIV testing and counseling which is routinely recommended by health care providers to persons attending health care facilities as a standard component of medical care. PITC is the recommended approach as it acknowledges that any contact with the health care system represents an opportunity to offer HIV testing.

All testing, whether client- or provider-initiated, should be conducted using the **'five Cs': informed consent, confidentiality**, **counselling** (whether brief or extended), **correct results and connection** (linkage to prevention, care and treatment services).

Consent: Clients receiving HTS must give their informed consent. Clients should be informed of the process for HIV testing and counselling and of their right to decline (opt out) after which verbal consent should be given.

Confidentiality: HTS must be confidential. There should be no third party disclosure without the expressed consent of the person being tested. Counsellors should investigate who clients wish inform about their HIV status and how they would like this to be done.

Counselling: All clients should be provided with pre-test information and post-test counselling and should have the opportunity to ask questions. This can be done in a group setting, however if requested clients should have the opportunity to ask questions in a private setting.

Correct test results: Providers of HTS should provide high-quality testing services and quality assurance mechanisms that ensure people receive a correct diagnosis.

Connection: All clients testing HIV positive must be linked to prevention, treatment and care services with effective and appropriate follow-up. Clients testing HIV negative should also be linked to other services as appropriate and referred for HIV repeat testing if indicated such as in the window period.

2.2 Process of HIV Testing-PITC

HIV testing should be considered a routine component of primary health care and offered all clients/patients who present for medical services. A PITC approach is recommended, as it is an efficient and effective way to identify people with HIV and should be offered for all clients and in all services.

Box 2.1: Settings for PITC

PITC should be offered in the following clinics

- Routine primary health care services
- Sexually transmitted infection (STI) clinics
- Tuberculosis (TB)Clinics
- Immunization clinics, children under 5 years of age
- Malnutrition clinics
- Reproductive and maternal and child health clinics

PITC should be offered to the following populations

- Key and vulnerable populations (youth; sex workers; men who have sex with men; persons identifying as gay, lesbian, bisexual, or transgender; drug users; prison inmates; migrant workers; physically and mentally challenged; and victims of domestic violence).
- Partners of HIV positive TB patients should be tested and support given for mutual disclosure
- Cases of sexual assault and occupational exposure requiring post exposure prophylaxis.

2.2.1Steps in PITC

2.2.1.1 Step1 Pre-test counselling

In pre-test counselling, patient's knowledge and understanding of HIV should be established. Based in this, patients should be informed of the benefits of knowing one's HIV status, using simple, non-technical language. Patients should be counselled on the implications of the test result, emphasizing that if HIV negative, focus on should be on staying negative and if HIV positive, focus should be on accessing HIC care and treatment. At this point, patient should be asked whether they are ready for the test and a verbal consent obtained.

2.2.1.2 Step 2: HIV Testing

Explain the testing procedure and timing of results (office-based or laboratory). Advise the patient that there may be a need for confirmatory tests that are positive or indeterminate; reassure them that all test results are confidential.

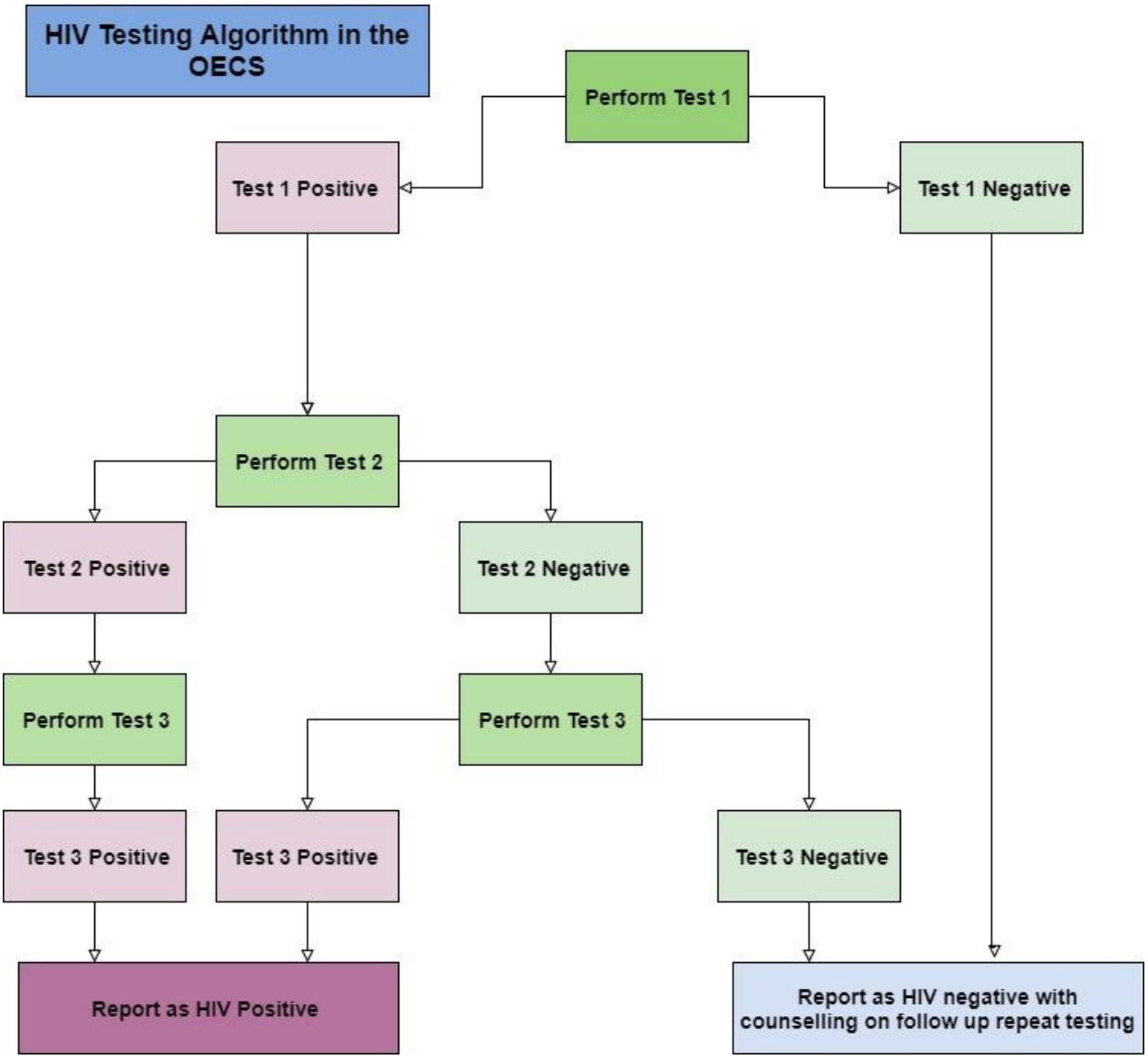
HIV testing for persons older than 18 months is performed using antibody testing including rapid HIV testing such as Determine, Unigold and StatPak and enzyme-linked immunosorbent assay (ELISA)-based HIV antibody (serologic) assays. The test result can be interpreted using the guidance provided in table 1.

***Table 1:** Interpretation of HIV test results*

Test result	Interpretation
Negative	Because these tests are highly specific, a negative test does not require an additional confirmatory test. However, if a patient reports possible exposure to HIV within the past month, HIV testing should be repeated in 1–3 months, as the patient could be in the 'window period' of acute HIV infection. During this time, the patient is infected with HIV but has not yet developed antibodies to the virus, which can be detected by conventional antibody tests.
Positive	HIV antibody testing will require additional testing before being confirmed positive. The confirmatory test can be performed using a different ELISA-based antibody test. 'Laboratory usually perform "Reflexive' confirmatory testing, bypassing the need for the provider to order confirmatory testing. Only (when) if the confirmatory test is also positive is the patient considered to be HIV infected.
Indeterminate	If the initial tests are positive but the confirmatory test is negative, then follow up monitoring and testing will be required.

The algorithm proposed for the OECS is outlined in Figure 2.

Figure 2: HIV testing algorithm in the OECS



2.1.1.3. Step 3: Post-test Counselling

Linked to issuing the results, it is important to verify the patient's identity and patients results.

In cases of an **HIV negative test result,** post-test counselling should focus on prevention messages including safe sex practices such as condom use and partner reduction, in remaining HIV negative. The window period should be discussed and where applicable, patient advised to return in 3 months for repeat testing.

In cases of **HIV positive test result,** post- test counselling should prioritise healthy living including safe sex practices and linkage to HIV treatment services.

Box 2.2 Tips in Post Test Counselling

HIV Negative Post Test Counselling

-Delivering the results: 'You tested HIV negative.

-Discussing prevention options: 'What will you do to remain HIV negative?' Options may include abstaining from sexual intercourse, being faithful to one partner, reducing the number of sexual partners, using a new latex condom at EVERY sexual encounter, encouraging asking partner(s) to be tested and to use condoms, encouraging disclosure and partner notification, and getting tested again in a year's time or sooner if the patient gets an STI, has a new partner, has unsafe sex, becomes pregnant, or becomes sick.

HIV positive PostTest counselling

-Delivering the results: 'You tested HIV positive, which means you have HIV infection.

-Coping with the results: Ask about concerns and respond appropriately. Reassure the patient that knowing their HIV status and getting care can extend their life.

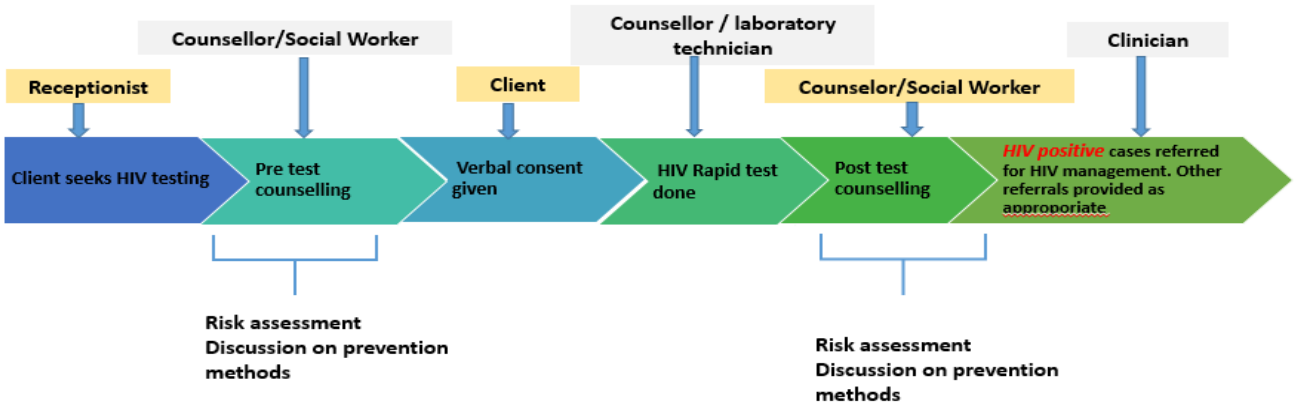
-Living positively: Explain the importance of knowing their CD4 count and HIV stage. Emphasize that this information guides care and treatment (e.g., when to start highly active antiretroviral therapy [HAART]).

-Protecting the patient and their partner: Explain how to avoid reinfection with HIV and new STIs. Encourage condom use at EVERY sexual encounter, disclosure and partner notification. Discuss partner testing and condom use.

2.3 The overall testing process

The overall testing process, commencing from client seeking access to services and HIV testing to post counselling for HIV negative persons and referral and linkage treatment for HIV positive persons is illustrated in Figure 3.

Figure 3: The HIV testing process



2.4 HIV Testing among Special Populations

The following groups and specifics in relation to HTS is noted.

2.4.1 Pregnant and Post-Partum Women

Using a PITC approach, all pregnant women should be tested for HIV twice during the pregnancy: immediately upon enrolment into antenatal care, and during the third trimester of pregnancy. This approach will facilitate the elimination of mother to child transmission of HIV (MTCT). This opportunity should also be leveraged to test for other STI's such as syphilis, viral hepatitis in providing comprehensive STI services to this population.

2.4.2 Infants <18 Months of Age

HIV exposed Infants less than 18 months of age require specialized testing for HIV DNA or RNA. Traditional HIV antibody tests do not provide accurate results for this age group because any HIV antibodies found in infants could actually be maternal HIV antibodies that crossed the placenta. HIV DNA Dried blood spot (DBS) testing is the preferred approach for this age group.

2.4.3 Couples and Partners

Couples and partners testing are recommended in antenatal care settings, facilitating provision of interventions, including ART for prevention in serodiscordant couples. Retesting should be offered at least annually for HIV negative partners in serodiscordant relationships.

2.4.4 Adolescents

HIV testing services, with linkages to prevention, treatment and care, should be offered to all sexually active adolescents and particularly to those from key populations. Adolescents testing positive should be counselled about the potential benefits and risks of disclosure of their HIV status and empowered and supported in determining if, when, how and to whom to disclose.

2.4.5 Key Populations

Community-based HIV testing services is recommended in reaching the key populations. This is preferably done through community testing including testing in closed settings such as prisons and facility based settings. Community testing should be linked to prevention, treatment and care services and couples and partners should be supported for mutual disclosure. Retesting should take

place at least annually for people from the key populations groups, however depending on the risk behaviors' more frequent retesting could be considered.

2.4.6 Other populations

Other populations considered to be at higher risk for HIV include the elderly, homeless, prisoners, mentally challenged and the male population.

2.5 HIV Retesting

The OECS recommends retesting is recommended for following groups:

- All HIV-negative pregnant women in the 3rd trimester, postpartum or during labour because of the high risk of acquiring HIV infection during pregnancy.
- Persons from the key populations groups should be retested annually, however depending on the risk behaviors' more frequent retesting could be considered.
- All people newly and previously diagnosed with HIV before enrollment in care and initiate ART

2.6 Connection- Linkage and Management of a Newly-diagnosed Patient

Individuals who test positive for HIV infection should be immediately linked to HIV care and treatment. Where possible, HIV positive patients should be navigated into the treatment programme. Pregnant women who test HIV positive should immediately be referred for HIV management for her own health and to prevent transmission to the exposed infant.

2.7 HIV testing approaches

The following public health approaches to HIV testing are recommended. Some of these are already implemented in the OECS.

- **Facility-based HIV testing services** – this is the traditional provider-initiated testing and counselling (PITC) described above and is offered routinely in a health facility setting (see details in section above).
- **Community-based HTS** – this approach targets the first-time testers and people who seldom use clinical services, including persons from key populations. Services may be offered in community sites such as community-based organizations, schools, workplaces and religious institutions. With a focus on the key populations, testing can take place in bars, clubs, street venues and other like places where key populations ply their trade or socialize. Mobile services though mobile vans and establishment of temporary tents had proven successful and a community based approach.
- **HIV Self Testing (HIVST)** - HIV self-testing is a process in which a person who wants to know his or her HIV status collects a specimen, performs a test and interprets the result by himself or herself, often in private. This emerging approach can extend HTS to people who may be unable or reluctant to access existing HTS as well as to people who frequently retest such as key and vulnerable populations. HIVST does not provide a definitive diagnosis and therefore requires additional testing according to a national testing algorithm. This is particularly important prior to initiation of ARVS.
  Although Self- testing is not a common practice, the OECS continues to monitor the evidence and developments around the potential risks, public health benefits and its impact on achieving 90-90-90 by 2020. New guidance on HIVST in the OECS will be provided to the relevant stakeholders as this becomes available.

3 ANTIRETROVIRAL THERAPY FOR ADULTS AND ADOLESCENTS

3.1 Introduction

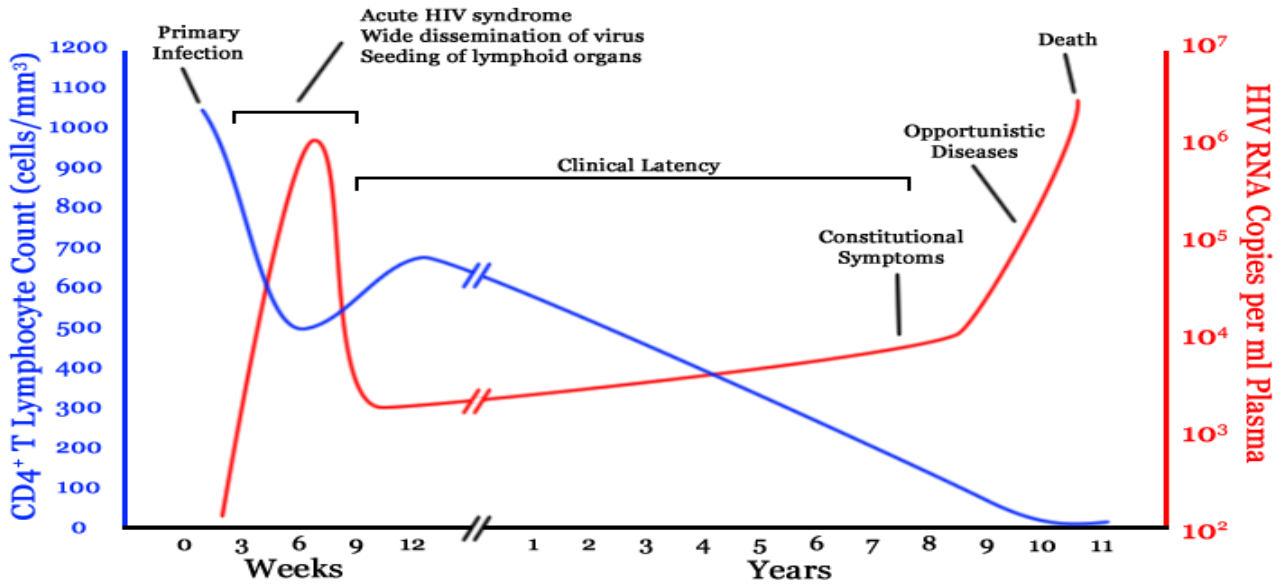
The science of HIV treatment has progressively developed changing the course from a debilitating disease with high mortality rates, to one where persons are now living normal productive lives and achieving normal life expectancies. Like the rest of the world, in the OECS this can be attributed to the expanded access to rapid diagnostic methods, better monitoring strategies and efficacious optimised antiretroviral therapy. The guidelines present evidence based strategies in relation to the provision of antiretroviral therapy and holistic care of the HIV patient. Every health care worker is encouraged to consult with the guidance contained herein, detailing the standard care to be provided in the OECS.

3.2 Transmission and natural history of HIV infection

Transmission of HIV-infection in adults and adolescents occurs mostly through sexual contact. In some context, HIV is commonly acquired through exposure to contaminated blood or blood products, which includes blood transfusion as well as needle sharing among intravenous drug users. Sexual transmission is the predomination mode of transmission in the OECS. Risks for transmission vary by the type of exposure and other factors, such as the presence of other concomitant sexually transmitted infections (STIs). The natural history and disease progression is complex and multiphasic. Throughout the course of HIV infection, viral replication takes place and immunodeficiency steadily progress to end stage disease of AIDS.

Untreated HIV infection usually follows a predictable course. Within the first 72 hours of transmission, HIV is brought to the lymphoid tissues. Viral replication early in the course of HIV disease is partially contained as virions are trapped in the lymphoid tissue. During these first few weeks of HIV infection, there is a rapid spike in the HIV viral load (the amount of HIV in the blood) and concurrent decrease in the CD4+ cell count (the number of circulating CD4+ T-lymphocytes in the bloodstream). During this phase the patient may feel a flu-like syndrome (the antiretroviral syndrome) or may not notice any symptoms at all. A robust immune response steps in between 6-12 weeks after infection, and is marked by significant downregulation of the virus in the blood with a parallel model increase in CD4 cells. The acute phase is followed by a phase of chronic infection with persistent replication of the virus. It is characterised as the asymptomatic period (clinical latency) during which there chronic persistent viral replication resulting in a slow and gradual rise in viral load accompanied by a progressive destruction of CD4 cells. The rate of CD4 cell destruction depends on the viral load, with higher viral loads leading to more rapid CD4 cell loss. The clinical latency period is followed by symptomatic HIV infection (Acquired Immunodeficiency Syndrome or AIDS) which occurs when CD4 counts fall 200 cells/mm3. This is stage is characterized by weight loss, the development of opportunistic infections, and end-organ disease such as neurologic complications or renal failure. The natural history is graphically represented in figure 4.

Figure 4: Natural History of HIV Progression



Source: Fauci, et al, Immu. Mech HIV Inf, 1996

3.3 Diagnosis and Staging

3.3.1 Diagnosis

There are several tests for diagnosing HIV infection in adolescents and adults. Because of the high costs associated with testing for the HIV virus itself (either through HIV DNA or HIV RNA), diagnosis is made by testing for the presence of antibodies to HIV. It is important to remember that it takes 2-6 weeks between infection and the development of a sufficient quantity of HIV-antibodies to be detected. In the OECS, antibody testing using rapid testing and ELISA is used for diagnosis, See Figure 2.0 for detailed algorithm.

Rapid tests used in the OECS include Unigold, Determine and StatPak and like ELISA these are antibody test with high sensitivities and specificities of over 98%. Rapid test also has the additional advantage of providing results to patients within 15-20 minutes and could be a good strategy for increasing testing in the region. Health care workers must familiarise themselves with their country specific algorithms. All HIV testing should be voluntary with conformity to the 5 "Cs" of Consent, Confidentiality, Counselling, Correct test results and Connections to care, treatment and prevention services.

3.3.2 Staging

In addition to CD4 and viral load testing discussed in subsequent sections, clinical staging is useful to gauge the extent of HIV disease progression based on clinical parameters. The OECS recommends the use of WHO Clinical Staging System for staging patients. The WHO Clinical Staging system uses current and past illnesses to categorize patients into four stages, from Clinical Stage I (mild, asymptomatic HIV infection to clinical stage 4 (AIDS). In the development of the classification, adolescents were defined as 15 years or older. WHO Clinical staging is outlined in box 3.1.

Box 3.1 WHO Clinical staging for adults and adolescents

Clinical Stage 1
Asymptomatic
Persistent generalized lymphadenopathy

Clinical Stage 2
Moderate unexplained weight loss (<10% of presumed or measured body weight)
Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulceration
Papular pruritic eruption
Fungal nail infections
Seborrhoeic dermatitis

Clinical Stage 3
Unexplained severe weight loss (>10% of presumed or measured body weight)
Unexplained chronic diarrhoea for longer than 1 month
Unexplained persistent fever (intermittent or constant for longer than 1 month)
Persistent oral candidiasis
Oral hairy leukoplakia
Pulmonary tuberculosis
Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)
Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
Unexplained anaemia (<8g/dl), neutropenia (<0.5x 10^9/l) and or chronic cytopenia (<50x 10^9/l)

Clinical Stage 4
HIV wasting syndrome
Pneumocystis (jirovecii) pneumonia
Recurrent severe bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month's duration or visceral at any site)
Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
Extrapulmonary tuberculosis
Kaposi sarcoma
Cytomegalovirus infection (retinitis or infection of other organs)
Central nervous system toxoplasmosis ,HIV encephalopathy
Extrapulmonary cryptococcosis, including meningitis, Disseminated nontuberculous mycobacterial infection
Progressive multifocal leukoencephalopathy
Chronic cryptosporidiosis
Chronic isosporiasis
Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis)
Lymphoma (cerebral or B-cell non-Hodgkin)
Symptomatic HIV-associated nephropathy or cardiomyopathy
Recurrent septicaemia (including nontyphoidal Salmonella) Invasive cervical carcinoma
Atypical disseminated leishmaniasis

Source *http://www.who.int/hiv/pub/guidelines/arv2013/annexes/WHO_CG_annex_1.pdf?ua=1*.

3.4 Preparing patients for HAART

Retest patient to confirm HIV diagnosis prior to ART initiation. Once confirmed patient should be counselled and the following addressed:

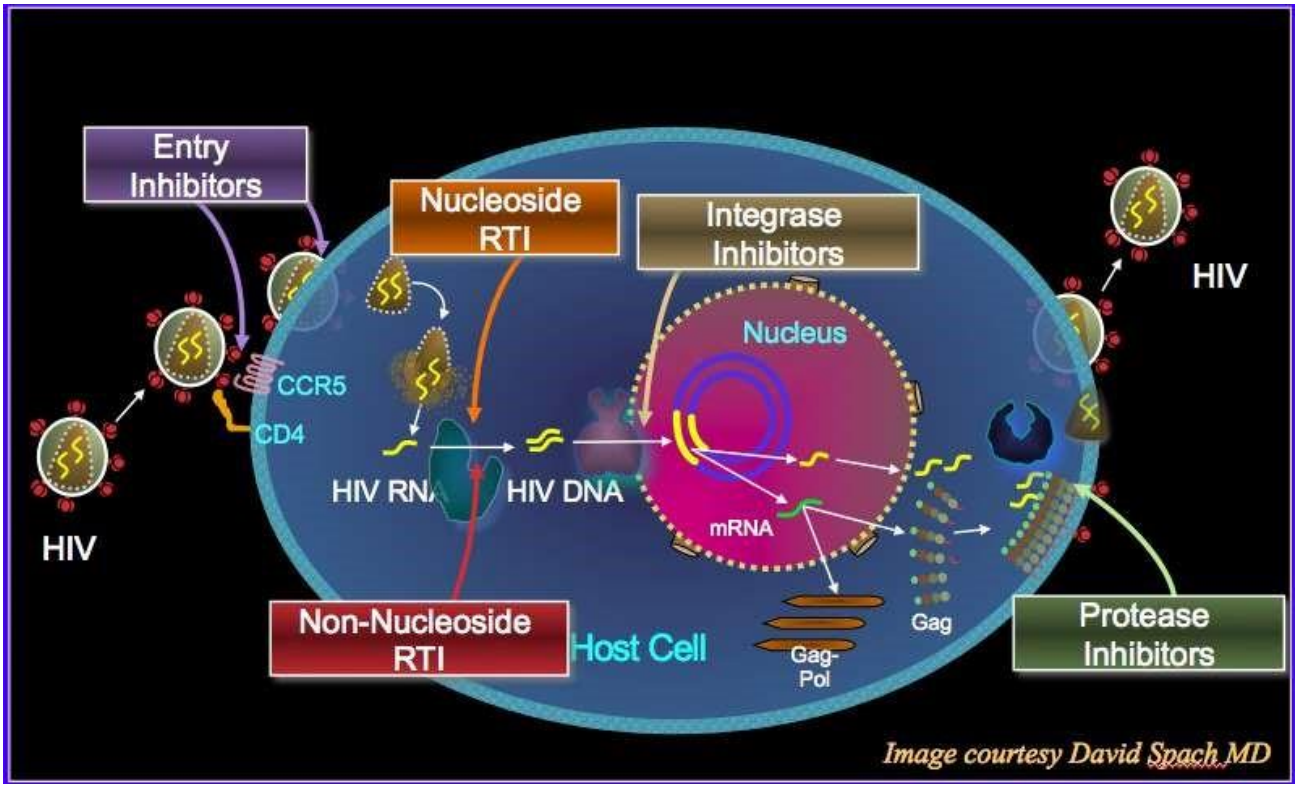
> Retest patient to confirm HIV diagnosis before starting ART

- Establish the patients' willingness and readiness to start ART. The choice to accept or decline ART lies with the patient or care giver. If declined, ART can be offered again at subsequent visits. If the patient has barriers to ART initiation such as mental health, substance use issues, appropriate psychosocial and other support should be given with regular assessment to establish readiness.
- Educate patients on the basics of ARVs- name of drug, regimen, benefits, dosage, scheduling, and any adverse effects. Patients should be informed of the benefits of early treatment, risk of delaying treatment and the need for lifelong commitment. They should be informed that first line ART regimen is the most effective and therefore adherence is paramount in preventing drug resistance.
- Educate patients in the importance of monitoring viral load regularly as the most adequate way of monitoring response and detecting treatment failure.
- Discuss the importance and frequency of follow up visits.
- There are instance where delays in ART can have negative consequences e.g. TB cases and those persons are at a high risk for death. In such cases, patients should be advised that ARV drug related adverse effects are transient and will be managed.
- Initiation of ART should always consider nutritional status, any comorbidities and other medications being taken to assess for possible interactions, contraindications and dose adjustment.
- Ask about the use any herbal or other medicines as these may interfere with the ARVS.
- General counselling on safer sex, including condom use and avoidance of other high-risk activities such as sharing of injecting equipment, to prevent transmitting HIV to other people. Counselling should also focus on healthy life choices such as exercise, nutrition and reduction or cessation of alcohol and tobacco consumption among others.

3.5 Antiretroviral therapy for adults and adolescents

The term **'antiretroviral therapy'** (ART) refers broadly to the use of antiretroviral medications (ARV)—either as individual drugs or in combination with each other—to treat or prevent HIV infection. **'Highly active antiretroviral therapy'** (HAART) refers specifically to the combination of three or more ARVs taken concurrently to suppress HIV replication in persons with chronic HIV infection by blocking key steps in the HIV life cycle (see figure 5).

Figure 5: HIV life cycle and drug classes for treating HIV infection



Highly Active Antiretroviral Therapy (HAART) interrupts HIV replication and significantly reduces morbidity and mortality among HIV positive individuals. The following principles are used to guide the use of antiretroviral therapy:

- HIV is ***incurable*** using currently available antiretroviral drugs, however ARVs prolong lives and significantly reduces morbidity and mortality.
- Treatment should be based on informed consent.
- HAART is hardly ever an emergency. Lifelong ARV treatment should be started with assurance of adherence readiness and support, a strategic follow-up plan, and psychosocial support.
- Earlier initiation of lifelong HAART is associated with improved treatment outcomes and lower rates of mortality.
- Delaying the initiation of HAART may be appropriate if there are medical or non-medical indications.
- CD4 lymphocyte count and viral load tests should be used to monitor the progress of HIV infection and response to treatment.
- Effective to achieve optimal suppression, HAART regimen should include an appropriate combination of three (3) or more ARV drugs given together.
- Effectiveness of HAART is determined by the appropriateness of the ARV drug combination, level of adherence to therapy, management of drug toxicities and interactions and severity of immune suppression at initiation of therapy.

- ❖ Identify and manage active opportunistic infections before initiation of HAART to avoid paradoxical worsening of the patient's clinical condition.
- ❖ Insufficient adherence to therapy, inappropriate combinations or doses of ARV drugs, and drug interactions can all lead to HIV-drug resistance.
- ❖ ARV drugs, particularly protease inhibitors, can have multiple interactions with other medications and should not be prescribed without a careful review of each patient's current
- ❖ Intervention should be made to remove any barriers to adherence.

HAART represents the current standard of care of ART for individuals infected with HIV. This strategy evolved from the recognition that treatment of chronic HIV infection with only one or two ARVs typically results in rapid treatment failure and facilitates the development of drug resistance, thereby compromising future therapeutic options. The standard first-line HAART, two ARVs from the nucleoside reverse transcriptase inhibitor (NRTI) class (e.g., tenofovir [TDF] plus lamivudine [3TC] or emtricitabine [FTC]) are combined with another drug from the non-nucleoside reverse transcriptase inhibitor (NNRTI) class (e.g., efavirenz [EFV] or nevirapine [NVP]). Inexpensive, fixed-dose combination tablets has greatly simplified HAART regimens—most People Living with HIV (PLHIV) in the OECS can now take a single pill once daily to control their HIV disease.
Ultimately, the goal of HAART is to prevent HIV-associated morbidity and mortality. This is most effectively achieved by suppressing HIV replication to a level below the limit of detection by viral load assays (generally less than 50 copies/mL).

3.6 Adherence to HAART

Medication adherence is defined as the extent to which a patient takes a medication in the manner intended by a health care provider and necessary for optimal treatment. Suboptimal adherence is associated with treatment failure and the evolution of resistance to ARVs. A number of factors have been associated with non-adherence to HAART, such as depression, substance abuse and homelessness. These should be addressed in a proactive and ongoing manner, both before and after the initiation of HAART. An adherence assessment tool is presented in Box 3.2 and provides practical tips on assessing and counselling on adherence.
Ongoing support given to those experiencing adherence challenges. Two strategies to monitor adherence should patient self-reporting and pill counting at every visit.

- ❖ ***Patient self-report***ing is a simple and efficient method of assessing adherence in clinical practice. Using visual aids and reviewing the patient's understanding of the prescribed regimen prior to assessing adherence helps to increase the sensitivity of this method. An example of an adherence assessment tool that relies on patient self-report can be found in Box 3.2.
- ❖ ***Counting pills*** requires the patient to bring their medication to each visit and to count the remaining pills to determine whether any doses were missed. The pharmacist can verify adherence as stated by sharing the patient's refill patterns.

Box 3.2 Adherence Assessment Tool

Make an introductory statement. Make a statement acknowledging that many PLHIV have difficulties taking ARVs—it is common and inevitable at some point in treatment. State that you are there to help identify these difficulties and to try to make it easier to take the medication. Consider the following language:

'Taking pills every day is really hard. Most people have problems taking their pills at some point during treatment. I am going to ask you about problems that you may have taking your pills. Please feel comfortable telling me about pills you may have missed or taken late. I am asking because I want to make it easier for you to take them.'

Confirm the patient's understanding of their HAART. Using a visual aid, such as a chart that shows colour images of the available pills, ask the patient which medications they are taking. This is not always useful in situations with white, generic preparations that look similar. For each of the indicated pills, ask the patient how many and exactly how often they take them. Ask if they have special instructions for any of the pills, such as dietary restrictions or extra fluid requirements. If any answers are incorrect, clarify the regimen prior to completing the adherence assessment.

Assess the patient's adherence. Ask the patient about their adherence over the past 3 days, on a day-by-day basis. Start with yesterday and ask them how many of their pills they had missed or taken late that day. Then ask about the 2 days prior to that, addressing each day separately. Next, ask about how many doses they missed or took late over the past 7 days and the past 30 days. If they report no missing doses, ask them how long it has been since a dose was missed.

Ask the patient about reasons for missing doses. For patients who report missing any doses, ask if they know the reasons why. Prompt them if they cannot offer an explanation: Common reasons include forgetting, being away from home, being too busy with other things, having a schedule change, experiencing too many side effects, feeling sick or depressed, and running out of pills.

Ask the patient about medication side effects or other problems. Ask the patient about medication side effects or other problems that they may be experiencing. Prompts can be offered: Common problems include nausea, diarrhoea, and difficulty swallowing the pills, headaches, fatigue, depression, or any other physical or emotional complaints.

Collaborate with the patient to facilitate adherence. Reassure the patient again that problems with adherence are common. Explain that your concern is based on the fact that missing more than 5% of doses in a month (i.e., more than three doses in a month, given a twice daily regimen) can lead to the medications not working well anymore, and that missing less than this would be a good goal. Take all complaints about side effects or other physical or emotional problems seriously and address them concretely. Offer suggestions to overcome specific obstacles the patient may have mentioned. Depending on their concerns, suggestions could include using a watch alarm, storing pills in a medication organiser, keeping extra packages of pills at work or in the car, or storing pills an unmarked bottle for enhanced privacy. Ask the patient if they have any ideas to make taking their medication easier. Finally, do not worry if the problem cannot be solved immediately; uncovering a problem with adherence is an important accomplishment and solutions can emerge in subsequent visits.

3.7 Antiretroviral Drugs

Over time, there have been significant advancements in pharmaceutical science with newer classes of ARVs added to the available treatment. Currently, medications are better tolerated, more effective and require a smaller daily pill burden. There are currently six classes of ARV drugs: Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), protease inhibitors (PIs), Integrase Inhibitors (INSTIs) Fusion Inhibitors (FIs) and Chemokine Receptor Antagonists (CCR5 antagonists). In the OECS, there are three classes of ARVS available; NRTS, NNRTIs and PIs.

Table 2 below provides a list of US Food and Drug Administration (USFDA) approved ARVs, their mechanism of action, adult dosing and possible side effects. Some of these are in use in the OECS.

Table 2: List of Antiretroviral drugs, mechanisms of action, dose and side effects

Drug	Dosage form	Adult Dose	Selected Adverse Effects/Toxicities
1. Nucleoside Reverse Transcriptase Inhibitors (NRTIs)			
Mechanism of action NRTIs interrupt the HIV replication cycle by competitive inhibiting the HIV reverse transcriptase and terminating of the DNA chain. Reverse transcriptase is an HIV-specific DNA polymerase that allows HIV RNA to be transcribed into single-strand and ultimately double-strand proviral DNA and incorporated into the host-cell genome. NRTIs are structurally similar to the DNA nucleoside bases and become incorporated into the proviral DNA chain, resulting in termination of proviral DNA formation. ***Tenofovir, lamivudine, and emtricitabine exhibit activity against Hepatitis B virus (HBV) in addition to HIV and are frequently incorporated into antiretroviral regimens for patients with HIV and HBV coinfection.***			
Abacavir (ABC)	300 mg tablet 20mg/ml	600 mg PO qd **OR** 300 mg PO bid	Hypersensitivity reaction (may include fever, rash, nausea, vomiting, diarrhea, malaise, shortness of breath, cough, pharyngitis)
Emtricitabine (FTC)	200 mg capsule 10 mg/ml oral solution	200mg PO qd **OR** 240 mg (24 mL) oral solution PO qd	Minimum toxicity, Skin discolouration/ hyperpigmentation
Lamivudine (3TC)	150mg, 300mg tablet 10 mg.ml oral solution	300mg PO qd or 150 mg twice daily	Minimal toxicity
Tenofovir DF (TDF)	300mg tablet	300mg PO qd	Nausea, vomiting, diarrhoea, headache, asthenia, renal insufficiency
Zidovudine (AZT)	300mg tablet; 100mg capsule 10 mg/ml oral solution 10mg/ml intravenous solution	300 mg twice daily or 200mg PO tid	Nausea, vomiting, headache, asthenia, anemia, neutropenia
Combinations			
Truvada (TDF/FTC)	300/200mg tablet	300/200mg PO once daily	Renal toxicity
Dimune (AZT/3TC)	300/150mg tablet	300/150 mg PO twice daily	Anaemia, neutropenia

Drug	Dosage form	Adult Dose	Selected Adverse Effects/Toxicities
2. Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)			
Mechanism of Action Chemically different from the NRTIs, they too inhibit transcription of viral RNA into DNA in a noncompetitive manner.			
Efavirenz (EFV)	600mg tablet, 50mg, 200 mg capsule	600 mg once daily, *preferably at bedtime *take on an empty stomach	Rash, CNS (e.g. somnolence, vivid dreams, confusion, visual hallucinations) hyperlipidemia. Possibly teratogenic during the 1st trimester of pregnancy
Etravirine	100mg, 200mg tablets	200mgs PO twice daily	Rash, nausea
Nevirapine (NVP)	200mg tablet, 400mg XR tablet, 10 mg/ml suspension	(200 mg once daily for 14 days, then 200 mg twice daily)	Stevens-Johnson Syndrome, Rash, Hepatotoxicity (potentially fatal)
Rilpivirine	25 mg tablet	25 mg PO once daily with a meal	Depressive disorders, insomnia, headache, rash
3. Protease inhibitors (PIs)			
HIV protease is a 99-amino-acid, aspartic acid protein and is responsible for maturation of virus particles late in the viral life cycle. HIV protease systematically cleaves individual proteins from the *gag* and *gag -pol* polypeptide precursors into functional subunits for viral capsid formation during or shortly after viral budding from an infected cell. HIV protease inhibitors function as competitive inhibitors that directly bind to HIV protease and prevent subsequent cleavage of polypeptides.			
Atazanavir	100mg, 150mg, 200mg, 300mg capsule	400mg PO once daily or 300mg +ritonavir 100mg PO once daily	Indirect hyperbilirubinemia, prolong PR interval, hyperglycemia, skin rash (20%), hyperlipidemia
Darunavir	75 mg, 150mg, 300mg, 400mg, 600mg tablets	800mg PO once daily + ritonavir 100mg PO once daily or 600 mg PO twice daily + ritonavir 100 mg PO twice daily	Hyperlipidemia, Hyperglycaemia
Fosampenavir	700mg tablet, 50mg.ml oral	700mg twice daily + ritonavir PO twice daily or	Rash, nausea, vomiting, diarrhoea, hyperlipidemia, hyperglycaemia

Drug	Dosage form	Adult Dose	Selected Adverse Effects/Toxicities
	suspension	1400 mg PO twice daily or 1400 mg + ritonavir 100-200 mg PO once daily *Suspension – take without food * Boosted with RTV- take with food	
Lopinavir/Ritonavir (LPV/r)	100mg/25mg, 200mg/50mg tablets 80 mg/20mg per mL oral solution	200mg/100mg PO twice daily or 800mg/200mg PO once daily *Oral solution- take with meals	Recommended with food to decrease GI side effects Diarrhea, Nausea, Hepatitis, Metabolic effects
Ritonavir	100mg tablet, 100 mg soft gelatin capsule 80mg/mL oral solution	Boosting dose for other protease inhibitors 100-400 mg/d (refer to other PI for specific dose) Nonboosting dose of ritonavir used as sole PI -600mg twice daily	Nausea, vomiting, diarrhoea, asthenia, hyperlipidemia, paresthesis, hyperglycaemia
Tipranavir	200 mg soft gelatin capsule, 100mg/mL oral solution	Unboosted Tipranavir is not recommended	Hepatotoxicity, rash, hyperlipidemia, hyperglycaemia, intracranial hemorrhage (rare)
4. Integrase Strand-Transfer Inhibitors (INSTIs)			
Mechanism of action: HIV integrase is responsible for the transport and attachment of proviral DNA to host-cell chromosomes, allowing transcription of viral proteins and subsequent assembly of virus particles. INSTIs competitively inhibit the strand transfer reaction by binding metallic ions in the active site.			
Raltegravir	400mg tablet	400mg PO twice daily *With rifampin- 800mg PO twice daily	Nausea, diarrhea, headache, CK elevations, myopathy/ rhabdomyolysis (rare)
Dolutegravir	50mg tablet	With UGT 1A/CY3A inducers (e.g. Efavirenz, fosamprenavir/ritonavir, tipranavir/ritonavir, rifampicin) 50mg PO twice daily	Cholesterol and TG elevations, CK elevations, liver enzymes elevation, hyperglycaemia
Elvitegravir	85 mg, 150mg tablet	85 mg PO once daily + atazanavir or lopinavir plus ritonavir	Immune reconstitution syndrome

Drug	Dosage form	Adult Dose	Selected Adverse Effects/Toxicities
		OR 150 mg PO once daily plus darunavir or fosamprenavir or tipranavir plus ritonavir	
5. Fusion Inhibitors (FIs)			
Mechanism of action Fusion inhibitors act extracellularly and prevent the fusion of HIV to the CD4 cell. It binds to the HR1 region of glycoprotein 41 (gp41) and therefore does not allow HR1 and HR2 to fold properly. This prevents the conformational change of gp41 necessary for the fusion process			
Enfuvirtide	90 mg/mL powder for injection	90mg SC twice daily	Injection-site reactions- subcutaneous nodules, erythema, pruritus, pain, and ecchymosis. diarrhea, nausea, and fatigue. Increased risk for bacterial pneumonia.
6. Chemokine Receptor Antagonists			
Mechanism of action The method by which HIV binds to CD4 cells and ultimately fuses with the host cell is a complex multistep process, which begins with binding of the gp120 HIV surface protein to the CD4 receptor. This binding induces a structural change that reveals the V3 loop of the protein. The V3 loop then binds with a chemokine coreceptor (principally either CCR5 or CXCR4), allowing gp41 to insert itself into the host cell and leading to fusion of the cell membranes. Maraviroc is a small molecule that selectively and reversibly binds the CCR5 coreceptor, blocking the V3 loop interaction and inhibiting fusion of the cellular membranes. Maraviroc is active against HIV-1 CCR5 tropic viruses. It has no activity against CXCR4 tropic or dual/mixed tropic virus.			
Maraviroc	150mg, 300 mg tablet	300 mg PO twice daily 150 mg PO twice daily (CYP 3A4 inhibitors +/- inducers 600 mg PO twice daily (CYP 3A4 inducers)	Constipation, dizziness, rash, increased risk for infections

Source: Adapted from Antiretroviral therapy for HIV infection, R. Chris Rathun, Michelle D. Liedtke accessed on line at http://emedicine.medscape.com/article/1533218-overview on May 1st 2017

3.8 Initiating HAART

3.8.1 What to expect in the first months of ART

ART improves quality of lives and reduces morbidity and mortality. The first three months of starting a patient on ART requires close monitoring. With adherence to treatment, clinical and immunological improvement and viral suppression is expected. In addition to early adverse drug reactions, during this time, patients can develop immune reconstitution syndrome (IRIS). IRIS is discussed in detail under section 3.13.

In most cases of IRIS, HAART should continue and the relevant opportunistic infection treated. In cases of severe inflammatory process, steroids maybe indicated and where IRIS becomes life threatening, HAART should be discontinued.

3.8.2 When to start ART in adults and adolescents

Evidence and programmatic experience have continued to favour earlier initiation of ART because it results in reduced mortality, morbidity and HIV transmission outcomes. Based on findings from the Strategic Timing of Antiretroviral Therapy Trial (START), untreated HIV infection may be associated with the development of several non-AIDS-defining conditions, including cardiovascular, kidney and liver disease, several types of cancer and neurocognitive disorders. Evidence from the HIV Prevention Trial Network (HPTN) O52 Study, ART substantially reduces sexual transmission to HIV-negative sexual partners among heterosexual and homosexual couples.

Box 3.3 When to Start ART?

Aligned to WHO 2016 guidance, the OECS recommends:

1. ART should be initiated in all adults and adolescents living with HIV, regardless of WHO clinical stage and at any CD4 cell count.
2. As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm3

3.8.3 What to start

Effective selection of appropriate ARV medications coupled with good adherence should lead to complete suppression of HIV viremia. This in turn leads to improvements in CD4 counts and the overall clinical status of the patient. "Triple therapy" using three antiretroviral drugs drawn from more than one class provides the most effective suppression of viral replication while preventing the development of resistance. The recommended first-line ARV regimens consist of a combination of two (2) NRTIs and an NNRTI or two NRTIs and INSTI. There are alternate first-line antiretroviral from each class for patients who may have toxicities from or contraindications to the recommended first-line combination regimen. In the absence of any contra-indications, a fixed-dose combination tablet of once-daily TDF + FTC + EFV is preferred due to its potency, tolerability, and ease of administration. This combination is highly efficacious in adults with baseline RNA level >100,000 copies/ml. There is however a high rate of rash and neuropsychiatric adverse effects. There is also an increased risk of suicidality particularly in patients with a history of depression with the use of EFV. The use of TDF requires close monitoring of renal function. Additional consideration when determining what to start are:

- ❖ AZT should be substituted for TDF in patients with preexisting renal disease. However, if AZT is contra-indicated (e.g., in the case of severe anaemia), then TDF should be used with close monitoring of renal function.
- ❖ NVP should be substituted for EFV in patients with poorly controlled psychiatric disease and low CD4 counts (less than 250 cells/mm^3 for women, less than 400 cells/mm^3 for men). Patients with higher CD4 counts and poorly controlled psychiatric disease should receive a ritonavir-boosted protease inhibitor (rPI) instead of NVP or EFV.
- ❖ EFV is no longer contra-indicated in pregnancy (including in the first trimester), and a fixed dose combination of TDF + FTC+ EFV is the preferred first-line agent for pregnant women.
- ❖ Substitution of rPI for EFV may be indicated in women who have received single-dose NVP (SD-NVP) in the past twelve months for PMTCT purposes. EFV may be used if a two-NRTI 'tail' was administered with the SD-NVP.
- ❖ AZT should be substituted for TDF in patients with HTLV-1 co-infection, unless the patient has contra-indications for receiving AZT (e.g., severe anaemia).
- ❖ EFV can lower the seizure threshold. It should be avoided in patients with poorly controlled seizure disorders and used with caution in patients with well-controlled seizure disorders.

Recommended first line regimens are outlined in table 3. The availability of fixed dose combinations and dosing is detailed in appendix 3A.

Table 3: Recommended First Line ARVS and Dosing for Adults and Adolescents1

Target Population	***Preferred first line and dosing***	***Alternative first line and dosing***
Adults and Adolescents	**TDF (300mgs) +FTC (200mgs) +EFV(600mgs)* *TDF (300mgs) +3TC (300mgs) +EFV(600mgs)* **Available in the OECS fixed dose combination of Atripla.*	*-AZT(300mgs) +3TC(300mgs)+EFV(600mgs)* *-AZT(300mgs)+FTC(200mgs)+EFV(600mgs)* *-AZT(300mgs)+3TC(300mgs) +DTG(50mgs)* *-AZT(300mgs)+FTC (200mgs) +DTG(50mgs)* *-TDF(300mgs) + 3TC (300mgs) + EFV(400mgs)* *-TDF (300mgs) +FTC(200mgs) +EFV (400mgs)* *-TDF(300mgs) + 3TC(300mgs) +NVP (200mgs)* *-TDF (300mgs) +FTC(200mgs) +NVP(200mgs)* *-ABC (600mgs)+3TC (300mgs)+NVP (200mgs)* *-ABC (600mgs)+FTC(300mgs)+NVP (200mgs)* ***Safety and efficacy data on DTG for pregnant, breastfeeding women and TB/HIV coinfection are still pending.*** ***Efficacy data for EFV at a lower dose of 400 mg/day in the case of pregnant and breastfeeding women and TB coinfection and adolescents younger than 12 years is not yet available.***
3TC lamivudine, ABC abacavir, AZT zidovudine, DTG dolutegravir, EFV efavirenz, FTC emtricitabine, NVP nevirapine, TDF tenofovir.		

[1] *Source: Adapted from WHO- Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendation for a public health approach. Second Edition 2016. Available from* http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1

Additional Important Information Regarding First-Line ARVs

- ***Tenofovir (TDF):*** Monitor for the development of renal insufficiency. TDF-related renal insufficiency is usually manifested by increases in serum creatinine, though can also be manifest by glycosuria, hypophosphatemia, or rarely proteinuria.
- ***Efavirenz (EFV):*** The most common adverse effects from Efavirenz therapy are central nervous system side effects (dizziness, sleepiness, lethargy, vivid dreams, depression, etc.). These frequently (~95%) improve after the first month of therapy and can usually be managed conservatively. More serious side effects, similar for NVP, but less serious are Stevens Johnsons Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN).
- ***Nevirapine (NVP)*** is contraindicated for women with CD4+ counts > 250 cells/mm3 and men with CD4 count > 400 cells/mm3 due to high rates of serious hepatotoxicity. This usually presents within the first several months of starting the drug, though can present at any time. It is manifested by abnormally high liver enzymes (> 5 times the upper limit of normal) and frequently accompanied by rash and flu-like symptoms. NVP has also been linked to Stevens - Johnson syndrome (Toxic Epidermal Necrolysis) and can be potentially fatal. Screening for jaundice should be combined with liver function testing at 2 and at 4 weeks after starting NVP. Nevirapine should be *abruptly discontinued* whenever this syndrome is suspected and NRTIs continued for one week. ***Nevirapine should never be restarted in these patients.***
- ***NVP*** should not be taken by patients receiving any regimen containing Rifampicin to treat TB, because Rifampicin reduces serum levels of Nevirapine. In these patients, EFV is recommended.
- ***NVP*** - 25% of women who have received single dose **Nevirapine** (sdNVP) develop mutations leading to pan-NNRTI resistance for PMTCT. These women should be started on a PI such as LPV/r, and be carefully monitored for virologic, immunologic or clinical failure.
- ***Nevirapine (NVP)*** *and* ***Efavirenz (EFV)*** have longer serum half-lives than NRTI backbones. For this reason, when *stopping antiretroviral therapy*, it is recommended that the NNRTI be stopped first and the NRTI backbone be continued for 1 week to prevent prolonged exposure to NNRTI monotherapy.
- ***Abacavir (ABC):*** Patients started on ABC containing regimens should be evaluated at 2 weeks, 4 weeks and 6 weeks following initiation of ***ABC for hypersensitivity reaction (HSR)*** and developed within the first six weeks of starting ABC**.** Though rare (2-9%), ABC HSR can be fatal with re-challenge. ABC HSR typically presents with fever, rash, and abdominal pain. **Any patient identified as developing HSR to ABC should *never* be re-challenged with ABC**.
- ***Zidovudine (AZT)*** can cause a macrocytic anaemia and ideally should not be used in patients with severe anaemia or neutropenia. All patients starting AZT should be monitored for potential development of anaemia. The AZT induced macrocytic anemia may improve with folate supplementation.
- ***Dolutegavir (DTG)*** has demonstrated a favourable safety profile and low potential for drug interaction. Serious adverse effects include abnormal liver function, particularly in patients with HBV or HCV coinfection, and potentially serious hypersensitivity reactions. DTG affects renal function, with a 10% serum creatinine increase due to inhibition of renal transport protein and consequently an estimated reduction in creatinine clearance, but without any eGFR modification. No tubulopathy or discontinuation of DTG due to renal toxicity has been reported. In this regard, no dosage adjustment is required for treatment-naïve or treatment-experienced and INSTI-naïve patients with mild, moderate, or severe renal impairment or for INSTI-experienced

patients (with certain INSTI-associated resistance substitutions or clinically suspected INSTI resistance) with mild or moderate renal impairment However in cases of severe renal impairment in for INSTI-experienced patients with resistance, dolutegavir is not recommended. Decrease in dolutegavir concentrations may result in loss of therapeutic effect and development of resistance.

Alternate Antiretrovirals for First-line Regimens

Special considerations when alternate antiretroviral may be preferable as part of the first line regimen include:

- **TDF and Renal Insufficiency-** TDF can exacerbate or cause renal insufficiency. The risk is higher in individuals with pre-existing renal insufficiency. In these cases, it is important to calculate creatinine clearance to determine the appropriate dose of TDF/FTC. When tenofovir cannot be safely used, ABC or AZT in conjunction with 3TC is recommended as the NRTI backbone. 3TC and AZT must also be dosed appropriately based on **creatinine clearance**. Decreased secretion of erythropoietin from kidney cells among patients with renal insufficiency results in anemia. While AZT use does not always exacerbate this type of anaemia, close monitoring is essential to ensure that the anaemia does not worsen. Creatinine clearance is calculated using the Cockcroft Gault method as per formula below in tables 4 and 5.

Table 4: Cockcroft gault formula for calculating creatinine clearance

Creatinine Clearance for MALES =	**Weight (kgs)x (140-age)** **72 x Serum Creatinine(mg/dl)**
Creatinine Clearance for FEMALES =	**Creatinine Clearance for Males x 0.85**

Table 5: Antiretroviral requiring dose adjustment for renal insufficiency

Antiretroviral	Estimated Creatinine Clearance (ml/min)		
	> 50-90	**10-50**	**<10**
Tenofovir/Emtricitabine (Truvada)	1 tab PO daily	1 tab PO every 48 hours	Do Not Use
Lamivudine	150mg PO twice daily	75mg PO twice daily	50mg PO once daily
Zidovudine	300mg PO twice daily	300mg PO twice daily	100mg PO every 8 hrs

- **Nevirapine (NVP) in women-** Hepatotoxicity occurs in about 4% of patients taking NVP and can be life threatening. The risk is higher in females than in males, and higher in patients with higher CD4 counts (>250 cells/μL in women, and >400 cells/μL in men) at initiation of nevirapine therapy. In the OECS where once-daily fixed -dose combination of TDF + 3TC (or FTC) + EFV is contraindicated and nevirapine presents as a viable alternative option, serious consideration must be given to the hepatotoxity associated with its use, particularly in women with CD4 >250 cells/μL

- **CNS Toxicity or Mental Health Illnesses**- A significant proportion (approximately 50%) of individuals starting EFV-based regimens will develop central nervous system (CNS) side effects, including dizziness, headache, sleepiness, insomnia, or depression. Among these, almost 90% will be able to tolerate EFV by the end of the first month of treatment. Thus, reassurance and symptomatic treatment of side effects is sufficient for most patients. In some cases – where destabilization of existing mental illness is a concern, or CNS side effects are intolerable – it may be advisable to change EFV to NVP or DTG. In the rare event that neither EFV nor NVP use is possible, DTG should be considered as the most viable option.

Drug Interactions

Drug interactions between ARVs and medications used to treat other conditions are common. Potential drug interactions must be investigated and appropriate modifications made prior to initiating HAART. Appendices 3B and 3C lists drugs that should not be used in patients on HAART due to potentially severe drug-drug interactions. Drug-drug interactions between antiretroviral and other medications can also be checked at the following website: http://hiv-druginteractions.org[2].

3.9 Laboratory Monitoring

Prior to initiating HAART, it is useful to check haematologic and chemistry indices as well CD4 count and HIV viral load so that the immunologic (and virologic) response to HAART may be measured against pre-therapy baseline levels. If primary drug resistance is a possibility, a resistance assay may be considered. ***However, scarce resources or a lack of laboratory facilities for measuring baseline values should not delay the timely initiation of HAART.*** Pregnancy testing prior to initiation of HAART is strongly recommended for women of childbearing potential. Recommendations for baseline (and follow-up) laboratory monitoring are presented in Table 6.
For patients on HAART, periodic laboratory monitoring is recommended to screen for ARV toxicities and to assess the patient's immunologic and virologic response to the medication.

CD4 testing monitors the immunologic function, determines need to initiate opportunistic infection prophylaxis, assesses the effectiveness of HAART, and diagnoses immunologic failure. For more details, refer to the section of the guidelines that addresses Opportunitic infections among adults and adolescents. An increase in the CD4 lymphocyte count is expected in an ARV-naïve patient who is adhering to the treatment regimen. For individuals not on HAART, larger decreases in CD4 values over time is correlated with higher viral loads and may be an indication for more frequent (i.e. every 3 months) monitoring. Routine CD4 absolute cell count and percentage monitoring for indications of immunologic failure while on HAART is recommended. More importantly, viral load testing should be conducted to establish virologic response. Because concurrent illnesses or immunizations can temporarily distort true CD4 values, it is recommended that CD4 testing be performed 1-2 weeks after an acute illness or immunization.
CD4 count is recommended at baseline and repeated every 6 months thereafter once the patient is stable. More frequent testing can be considered on a case by case basis and depends on the clinician's judgments.

Viral Load testing is the preferred way of monitoring treatment response. Effective HAART results in suppression of viral replication in the blood to levels below the threshold of detection ["undetectable viral loads"]. Changes in viral load precede changes in CD4+ counts and can identify treatment failure earlier than CD4 monitoring alone. Like CD4 testing, concurrent illnesses or immunizations can temporarily distort true viral load values. It is therefore recommended that viral load testing be performed 4 weeks after an acute illness, surgery, hospitalization or immunization. ***In OECS, viral load testing is indicated at pre-initiation of ARVs, repeated at 6 months post initiation and yearly thereafter once the patient is virologically suppressed. More frequent testing can be considered on a case by case basis and depends on the clinician's judgements.*** The OECS defines viral suppression as <1000 copies per milliliter.

WHO defines viral failure as a persistently detectable viral load exceeding 1000 copies/mL (that is, two consecutive viral load measurements within a 3-month interval with adherence support between measurements) after at least 6 months of starting a new ART regimen. Circumstances in which there is a suspicion of treatment failure may require repeat testing. A repeat viral load test may also be required to differentiate between a viral blip or to establish any other reason for the increase. Viremia Blip is defined as an isolated detectable HIV RNA level occurring after virologic suppression and followed by a return to virologic suppression. The blip can occur up to 2000 copies per milliliter.

On the other hand, viral load is ***not recommended*** if the patient had immunization within the last month, severe viral infection or a recent surgery. In these cases, VL testing should be deferred to one month later.

*Table 6: **Recommended monitoring schedule***

Test	Frequency	
	Baseline	**Follow up**
HIV test	YES	N/A
CD4 lymphocyte count	YES	Every 6 months. More frequent testing is determined by the physician on a case by case basis.
Viral Load	YES- at ART Pre-initiations	Every 6 months post initiation and yearly thereafter for virologically suppressed patient. More frequent testing is determined by the physician on a case by case basis.
HIV genotyping	As indicated- in suspected cases of treatment failure.	

Test	Frequency	
	Baseline	Follow up
CBC and differential	YES	As indicated eg- If on AZT, 2 wks, 6wks and 3 months after initiation and then as needed but at least once yearly
VDRL	YES	Annually if sexually active
HBsAg	YES	When clinically indicated
HCV	YES	When clinically indicated
HTLV I	YES	Annually
Pregnancy	YES	As indicated
Chest X-ray	As indicated	As indicated
Liver function test	YES	2 weeks after initiation, 4 weeks after initiation and subsequently every six months.
Renal function test	YES	2,4, 8 and 12 wks after initiation of TDF and then annually
Cervical Cancer Screening- PAP Smear	YES	Annually
PPD	YES	Annually until positive, if never had INH prophylaxis/TB disease treatment. Then monitor with yearly chest x-rays
Toxoplasmosis immunoglobulin (IgG)	YES	Repeat if CD4 lymphocyte count <100 cells/mm^3
Serum amylase, lipase	YES	As indicated
Serum glucose	Baseline	Every 6–9 months for patients taking PIs and if otherwise indicated
Serum lipids	Baseline	Annually for patients with abnormal baseline values or taking PIs or Efavirenz
Serum lactate	When lactic acidosis is suspected	

3.10 Patient Follow-up and Monitoring after Initiation of Therapy

After HAART is initiated, close monitoring of the patient is warranted; the first six months are a critical time for them. During this period, HIV viral load should decline rapidly, by at least 1.0 log per month, and become undetectable by 24 weeks of therapy. It would be important to monitor for medication toxicity, problems with adherence and any signs of developing ARV resistance. Patients may paradoxically worsen clinically due to immune reconstitution inflammatory syndrome (IRIS) and Mortality is higher in this, than any other period while on HAART.

3.11 Timing of Follow-up

A follow-up visit is recommended within two weeks of HAART initiation. This will reinforce the importance of adherence and provide an opportunity for assessment of adverse medication reactions or IRIS.

3.12 Adherence Assessment

Adherence should be measured at each patient encounter. If adherence is sub-optimal, counselling is warranted, including an investigation of adherence barriers. See section 3.5 and Box 3.1 for more details on adherence.

3.13 Treatment Toxicity

Adverse effects from HAART are common and can usually be managed symptomatically without interrupting the regimen; most resolve within 1–3 months of HAART initiation. A clinical toxicity grading system and guidance on managing drug toxicity is outlined in Table 7 and Box 3.4 respectively. If the adverse effect is severe enough to require modification of the regimen, a different ARV can be substituted for the offending drug. Table 8 presents options for managing selected common adverse reactions. Detailed grading of toxicity based on clinical and laboratory parameters is outlined in appendix 3D.

Table 7: Estimating toxicity severity.

Grade 1	**Mild reaction: Transient or mild discomfort, no limitation in activity, no medical intervention/therapy required.**
Grade 2	**Moderate reaction:** Limitation in activity, some assistance may be needed, no or minimal medical intervention/therapy required.
Grade 3	**Severe reaction:** Marked limitation in activity, some assistance usually required, medical intervention/therapy required, and hospitalisation possible.
Grade 4	**Severe/life-threatening reaction:** Extreme limitation in activity, significant assistance required, significant medical intervention/therapy required, hospitalization or hospice care.

Box 3.4 Managing ARV drug toxicity

Determine the seriousness of the toxicity.

1. Evaluate concurrent medications and establish whether the toxicity is attributable to one or more ARVs or to a non-ARV medication taken at the same time.

2. Consider other disease processes (e.g., viral hepatitis in a patient on ARVs who develops jaundice)—not all problems that arise during treatment are caused by ARVs

3. Manage the adverse event according to severity. In general:

Grade 4—severe life-threatening reaction: Immediately discontinue all ARVs, manage the medical event (i.e., symptomatic and supportive therapy) and reintroduce ARVs using a modified regimen (i.e., with an ARV substitution for the offending drug) when the patient has stabilized[a].

Grade 3—severe reaction: Substitute the offending ARV without stopping HAART.

Grade 2—moderate reaction: Consider continuing HAART as long as feasible. If the patient does not improve on symptomatic therapy, consider single-ARV substitutions.

Grade 1—mild reactions: These are bothersome but do not require changes in therapy.

In grades 1 and 2 reactions, stress the importance of adherence.

If there is a need to discontinue HAART because of life-threatening toxicity, all ARVs should be stopped until the patient has stabilized.

Table 8: Symptom-directed toxicity management[3]

Adverse events	Major first-line ARVs	Recommendations
Drug eruptions (mild-to-severe, including Stevens-Johnson syndrome or toxic epidermal necrolysis)	NVP, EFV (less commonly)	In mild cases, provide symptomatic care. EFV rash often stops spontaneously after 3–5 days without need to change HAART. If moderate rash, non-progressing and without mucosal involvement or systemic signs, consider a single NNRTI substitution (i.e., from NVP to EFV). In moderate and severe cases, discontinue HAART and give supportive treatment. After resolution, resume HAART with a boosted protease inhibitor (rPI)-based regimen or triple NRTI if no other choice.
Dyslipidaemia	All NRTIs (particularly d4T) EFV	Consider replacing the suspected ARV.
Anaemia and neutropenia	AZT	If severe (Hb <7.0g/dl and/or Absolute Neutrophil Count [ANC] <750 cells/mm^3), replace with an ARV with minimal or no bone marrow toxicity (e.g.TDF) and consider a blood transfusion.
Hepatitis	All ARVs (particularly NVP)	If ALT is more than five times the basal level, discontinue HAART and monitor. After resolution, restart HAART, replacing the suspected causative drug (e.g., EFV replaces NVP).
Lactic acidosis	All NRTIs (particularly d4T)	Discontinue HAART and give supportive treatment. After resolution, resume HAART with TDF.

[3] Adapted from: World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents. Recommendations for a public health approach, 2010 revision. Geneva: WHO; 2010. Available from: http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf.

Lipoatrophy and lipodystrophy	All NRTIs (particularly d4T)	Replace the suspected ARV early on (e.g., d4T for TDF or AZT).
Neuropsychiatric changes	EFV	Usually self-limited, without the need to discontinue HAART. If intolerable to the patient, replace NVP with EFV or bPI. Single substitution recommended without cessation of HAART.
Renal toxicity (renal tubular dysfunction)	TDF	Consider substitution with AZT.

Occasionally, severe HAART-related toxicity requires the patient to discontinue all ARVs. In such circumstances, it is best to stop all of them simultaneously, because continuing therapy with only one or two ARVs is associated with the development of drug resistance. If the HAART regimen contains an NNRTI (e.g., NVP or EFV), some expert clinicians recommend discontinuing the NNRTI 3–7 days prior to discontinuing the NRTIs, given the prolonged plasma half-life of NNRTIs. HAART should be withheld until the patient recovers, at which time re-initiation of therapy with a different regimen can be considered.

3.14 Immune Reconstitution Inflammatory Syndrome

IRIS is defined as a paradoxical clinical deterioration after starting HAART that results when the improving immune system interacts with organisms that have colonized the body during early stages of HIV infection. It commonly occurs in patients with a CD4 count <200 and is a pathogen specific cellular and humoral response to multiple opportunistic pathogens including mycobacteria, fungi and viruses. Symptoms usually occur after 2-12 weeks after beginning HAART. IRIS could present as two scenarios. Firstly, patients who started treatment for an opportunistic infections and later begins HAART, can develop paradoxical worsening of the treated OI. Secondly, clinically stable patients starting ART, develops signs and symptoms of a dormant and previously unrecgonised OI. It is critical to exclude or treat an OI before initiating ART. Depending on the pathogen, pill burden, drug-drug interactions and adverse effects, there may be value in delaying ART. ***Discuss IRIS with your patient.***

A wide range of conditions have been associated with IRIS. The most common involve mycobacterial disease (especially TB), cryptococcal disease, or viral diseases from the herpesvirus family. Box 3.5 lists some of the pathogens and conditions that have been implicated in IRIS reactions.

Box 3.5. Pathogens and conditions that may present as IRIS

Bartonella henselae		
Chlamydia trachomatis	Histoplasmosis HTLV-1 and -2	*Mycobacterium tuberculosis*(MTB)
CMV	Kaposi's sarcoma	Parvovirus B19
Cryptococcus	Leprosy	PCP
Graves' disease	Lymphoma	PML
Guillain-Barré syndrome	MAC	Sarcoidosis
HBV and HCV	Microsporidia	VZV, HPV, HSV

3.14.1 Differential Diagnosis

Some medication toxicities (e.g., hepatitis, allergic hypersensitivity) present with signs and symptoms suggestive of IRIS. Additionally, the timing typical of IRIS reactions overlaps with that of ARV-associated toxicities. In patients with suspected IRIS, failure of therapy of a pre-existing OI should also be considered. Efforts should be made to diagnose as accurately as possible the pathogen(s) responsible (e.g., aspirating and culturing enlarged lymph nodes).

Key elements that would implicate IRIS include:

- Low pre-treatment CD4 count and/or advanced HIV disease.
- Robust immunologic (and virologic) response to HAART.
- Temporal association between initiation of HAART and onset of illness.
- Presence of clinical signs and symptoms of inflammation.
- Absence of evidence for other causes.

3.14.2 Management of the Patient with Suspected IRIS

Data from clinical trials are limited for determining the appropriate management of IRIS. However, the following steps represent a reasonable general guide for management.

- Consider other possible aetiologies- persistent active infection (e.g., OI treatment failure) of adverse drug reaction(s).
- Continue HAART.
- Attempt to diagnose the infection or condition responsible for IRIS such as aspirate and culture any easily accessible abscesses or lymphadenopathy or obtain bacterial, mycobacterial, and (if available) fungal cultures.
- Initiate pathogen-specific therapy, if not already in place, noting that the development of IRIS does not require reinitiating antimicrobial therapy or changing maintenance therapy for the responsible infection if the patient is already on appropriate therapy. Also, initiating empiric therapy is reasonable for highly suspected conditions when the diagnosis is not immediately apparent.
- Provide anti-inflammatory therapy: nonsteroidal anti-inflammatory drugs (NSAID) for mild-to-moderate cases (e.g., ibuprofen, naproxen, acetylsalicylic acid) and corticosteroids for moderate-to-severe cases (e.g., prednisone dosed at 0.5–1.0 mg/kg/day while the patient is acutely ill with IRIS, then tapered gradually as he or she improves clinically).
- Drain abscesses and infected lymph nodes as necessary; emergency surgical decompression may be indicated for the patient with tracheal or intestinal obstruction.
- Consider interrupting HAART in patients with life-threatening IRIS reactions or who do not clinically stabilize with the above measures.

3.15 Metabolic Complications of HAART and HIV

A number of metabolic disturbances have been described in HIV-infected patients on HAART. Patients who have initiated HAART should be monitored carefully for signs of complications and managed appropriately, as outlined below. The exact aetiology of these complications is not clearly understood, and may reflect a multi-factorial process involving ARVs, HIV itself, and host factors.

3.15.1 Lactic Acidosis Syndrome and Hepatic Steatosis

Lactic acidosis syndrome represents a rare but potentially fatal complication of HAART, linked to the use of NRTIs. NRTIs can inhibit human mitochondrial DNA polymerase gamma, an enzyme crucial for normal mitochondrial DNA replication. This results in a depletion of the mitochondrial DNA, compromising cellular oxidative phosphorylation. Evidence of mitochondrial DNA depletion can also be found in HIV-infected persons who have never received HAART, suggesting that HIV itself may contribute to mitochondrial dysfunction.

Clinically, this syndrome can range from asymptomatic hyperlactataemia to fatal lactic acidosis. The development of lactic acidosis is dependent on the duration of NRTI exposure and specific ARVs used. For example, d4T appears to be most commonly associated with lactic acidosis, followed by ddI and AZT, followed by 3TC and ABC. TDF appears to carry a low risk of mitochondrial toxicity as well. Pregnant women appear to be at greater risk taking the combination of d4T plus ddI. None of these are recommended in the OECS.

Symptoms include nausea, vomiting, abdominal pain and distension, diarrhoea, fatigue, myalgias, weight loss, and dyspnoea. An elevated lactic acid level establishes the diagnosis but a proper diagnosis requires sampling without a tourniquet, rapid transportation to a laboratory on ice, and processing within a few hours. Other laboratory indicators include elevated CPK, LDH, amylase, and aminotransferases, and low serum bicarbonate.

Lactic acidosis is treated by discontinuing the ARVs and providing supportive care until the syndrome is resolved. Case reports have suggested that giving high doses of vitamins involved in oxidative phosphorylation, such as riboflavin or L-carnitine, may hasten the recovery process.

Following resolution of the syndrome, HAART should be reinitiated cautiously. NRTIs such as d4T and ddI—which are strongly associated with mitochondrial toxicity—should be avoided.

3.15.2 Lipodystrophy

Lipodystrophy refers to changes in the distribution of fat and is associated with HIV and HAART. Two distinct lipodystrophic syndromes have been characterised: subcutaneous fat wasting ('lipoatrophy') and central fat deposition ('lipohypertrophy'). Lipoatrophy is typically most apparent in the face and extremities, and has been associated with advanced HIV and with NRTIs, especially d4T. With lipohypertrophy, central fat deposition in the viscera, breasts, and dorsocervical fat pad ('buffalo hump') have been described; its pathophysiology remains unclear. These changes in the distribution of fat are often, though not always, associated with dyslipidaemia and insulin resistance.

The optimal management of lipodystrophy is not known. Lipoatrophy appears to improve, though very slowly, in patients who remove d4T from their ARV regimens and substitute NRTIs like TDF or ABC, which have less potential for mitochondrial toxicity. Similar ARV-switch strategies have failed to consistently demonstrate a clinical benefit for patients with lipohypertrophy, though improvements have been documented following dietary and exercise modifications. Cosmetic

plastic surgery options—such as facial injections with polylactic acid or surgical excision of dorsocervical fat pads—exist but are expensive and not widely available.

3.15.3 Hyperlipidaemia

In the absence of HAART, HIV infection can lead to dyslipidaemia, including lower HDL levels. HAART has been associated with elevated total cholesterol, LDL, and triglycerides. Several (though not all) PIs have been strongly associated with lipid abnormalities, though dyslipidaemia has also been documented in patients on NNRTI-based regimens. Recent data suggest that these abnormalities can lead to accelerated atherosclerosis and cardiovascular complications in PLHIV. In general, patients with HIV/HAART-associated dyslipidaemia should be managed in a similar fashion to patients who are not infected with HIV. Low-fat diets, regular exercise, and smoking cessation represent first-line interventions. Fibrates and HMG-CoA reductase inhibitors (statins) can be helpful, but certain statins (e.g., simvastatin and lovastatin) should be avoided due to dangerous drug interactions with PIs. Pravastatin is the preferred agent; atorvastatin may also be used at reduced doses. See appendices 3B and 3C for common drug drug interactions.

3.15.4 Insulin Resistance

Hyperglycaemia, new onset diabetes, exacerbation of pre-existing diabetes, and diabetic ketoacidosis have all been reported in PLHIV receiving HAART, especially in those receiving PIs. EFV has also been associated with insulin resistance. Routine fasting blood glucose measurements should be performed every 3–4 months for patients who are receiving PIs or EFV and have no previous history of diabetes. Pregnant women receiving PIs should have their glucose levels monitored closely. All patients should be counselled to recognise symptoms of hyperglycaemia, such as polyuria, polydipsia, and polyphagia.

Insulin resistance is usually treated by either switching to a non-PI-/non-EFV-based regimen (if possible), or by adding oral hypoglycaemic agents or insulin to the HAART regimen. See appendices 3B and 3C for common drug drug interactions.

3.15.5 Metabolic Bone Disorders

Avascular necrosis and decreased bone density have been documented in HIV-infected adults and children. Although TDF has been associated with decreases in bone mineral density, the degree to which most ARVs contribute to these disorders is unclear. Some studies have linked PIs to osteopenia and osteoporosis, while other data suggest that PIs have a possible protective effect on bone mineralisation.

Recommended prevention and treatment measures for osteopenia include modifying other risk factors (e.g., smoking cessation, weight-bearing exercise) and ensuring an adequate intake of calcium and vitamin D. Hormone replacement therapy may be considered in postmenopausal

women. Bisphosphonates, such as alendronate, have demonstrated clinical efficacy for PLHIV who have osteoporosis.

Avascular necrosis most commonly involves the femoral or humeral head, leading to hip or shoulder pain. Risk factors for osteonecrosis include corticosteroid therapy, alcohol abuse, hyperlipidaemia, and hypercoagulable states. The diagnosis is typically made by X-ray or CT scan, but may miss early stages of disease; MRI is the most sensitive test. There is no accepted medical therapy, and surgery may be needed to treat severe disabling symptoms. See appendices 3B and 3C for common drug drug interactions.

3.16 Treatment Failure

Monitoring people on ART is important to ensure successful treatment, identify adherence problems and determine whether ART regimens should be switched in case of treatment failure. In the OECS viral load testing is the preferred monitoring approach to diagnose and confirm ARV treatment failure. Viral load provides an early and more accurate indication of treatment failure and therefore the need to switch therapy. It is also used to distinguish between treatment failure and nonadherence, observed when patients on first-line therapy with high viral load becomes suppressed following adherence intervention. Further, in line with the concept of treatment as prevention, viral load can also serve as a proxy measure for the risk of transmission.

Treatment failure refers to the absence of a sustained favourable response to HAART. Treatment failure can be suspected on the basis of clinical, immunologic, or virologic criteria summarized on Table 9. Treatment failure that is suspected on the basis of clinical progression or CD4 count decline should always be confirmed with HIV viral load testing before a patient's HAART regimen is changed. Suspected treatment failure should be confirmed as rapidly as possible to prevent HIV disease progression and the development of further resistance to ARVs.

In the event of treatment failure, reassessment of adherence is indicated. After adherence issues have been adequately addressed, a change in the HAART regimen to second-line therapy is usually warranted. Resistance testing, where available, should be used to guide a change in HAART regimen.

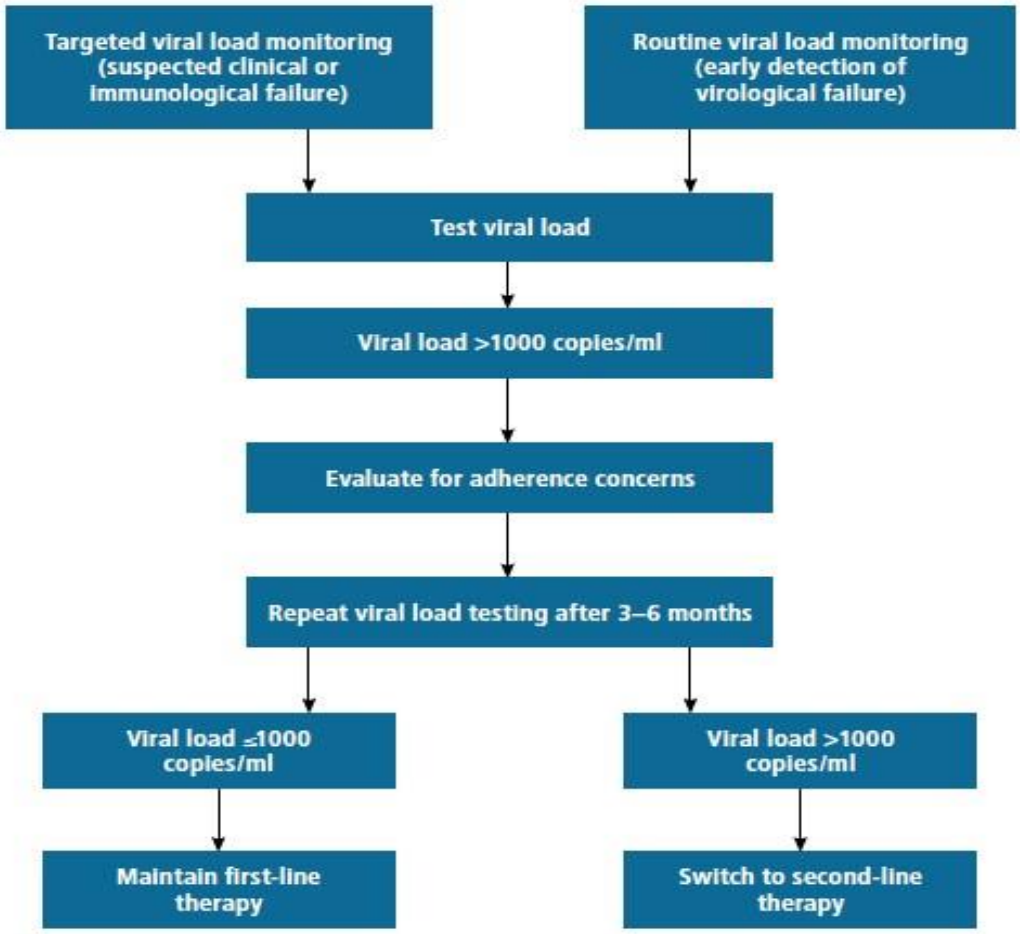
Table 9: *Categorisation and Definition of Treatment failure*

Failure	Definition	Comments
Virologically failure	Viral load above 1000 copies/mL based on two consecutive viral load measurements in 3 months, with adherence support following the first viral load test	A single VL > 1,000 copies/mL should prompt reinforcement of adherence measures with the client and repeat VL testing 3-6 months later. A persistent VL > 1,000 copies/mL should prompt change to second line therapy (see text and Figure 4). An individual must be taking HAART at least 6 months before it can be determined that a regimen has failed.
Immunological failure	CD4 count at or below 250 cells/mm3 following clinical failure **OR** persistent CD4 count below 100 cells/mm^3 Children Younger than 5 years Persistent CD4 levels below 200 cells/mm3 Older than 5 years Persistent CD4 levels below 100 cells/mm3	Verify no concomitant infection is causing transient CD4 count decrease.
Clinical failure	Adults -New recurrent WHO stage 4 condition after 6 months of effective treatment. Children- New or recurrent clinical event indicating WHO clinical stage 3 and 4 clinical condition with the exception of TB, after 6 months of effective treatment	Condition must be differentiated from IRIS. Certain WHO clinical stage 3 conditions (e.g., pulmonary TB, severe bacterial infections), may be an indication of treatment failure.

Source: Adapted from World Health Organisation- Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendation for a public health approach. Second Edition 2016. Available from http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1

When using Viral load to monitor treatment failure the following algorithm outline below as figure 6 should be applied.

Figure 6: Viral load testing algorithm to detect or confirm treatment failure in adults, adolescents and children



3.17 HIV Resistance to HAART

Treatment failure may occur because a patient's strain of HIV has developed resistance to one or more ARV. The manner by which HIV develops resistance to ARVs is similar to the way bacteria or mycobacteria (e.g., TB) develop resistance to antibiotics: insufficiently potent drug therapy selects for mutant strains that are resistant to the medications administered to the patient. These mutant strains then replace the wild-type strain due to their selective replication advantage in the face of drug pressure, thus leading to treatment failure.

Resistance to ARVs most commonly develops in cases of suboptimal adherence but it can occur in patients who maintain very high levels of adherence to their medications. For example, severe diarrhoea can result in the malabsorption of ARVs, potentially leading to treatment failure and ARV resistance.

Laboratory assays have been developed to estimate the patterns of resistance in a given patient's strain of HIV. These assays have demonstrated clinical efficacy in aiding the design of second-line treatment regimens following treatment failure. Hence, where resources permit, a resistance assay is recommended in cases of treatment failure.

Even in the absence of resistance testing, knowledge of the patterns of resistance and cross-resistance that commonly develop in patients failing specific regimens allows for reasonably accurate empiric decision-making in designing a second-line regimen. For example, patients failing an NNRTI-based initial treatment regimen commonly develop one or more mutations that confer high-level resistance to all available NNRTI medications. Therefore, a second-line regimen for these patients should be PI-based rather than NNRTI-based.

3.18 Switching from First-Line to Second- Line HAART

Patients failing first line therapy will require shifting to an adequate second line and at the right time. The following will guide switching:

- Use viral load (VL) to confirm treatment failure, as immunological and clinical criteria for treatment failure are not reliable. When VL is not available, use immunological criteria to confirm clinical failure.
- Where routinely available, use VL every 6 months to detect viral replication.
- A VL of >1,000 copies/mL should prompt the clinician to reinforce adherence with the patient, and repeat VL testing in 3 months, as shown in Figure 3.1.
- A persistent VL of >1,000 copies/ml confirms treatment failure and should prompt change to second line therapy.

3.18.1 Second-Line HAART Regimens

Second-line HAART regimens are indicated for patients who would have failed the initial (first-line) treatment. Second line regimen must be constructed carefully to account for potential ARV resistance. Where available, ARV resistance testing is strongly recommended to help guide the design of the second-line regimen. In the absence of resistance testing, empiric reasoning of the likelihood of resistance to agents in the initial regimen, as well as considerations of cross-resistance, can be used to design a second line regimen. Because the exact nature and extent of resistance is difficult to estimate empirically, these guidelines suggest trying to replace as many of the agents in the initial regimen as possible.

See table 10 for suggested second-line regimens for patients who have experienced treatment failure on their initial regimens, in situations where resistance testing is not available to help guide decision-making.

Table 10: Preferred second-line therapy for adults and adolescents

Failing first line	Failing first line	Preferred Second Line	Alternative Second line
2 NRTIs + EFV/NVP 2NRTIs- DTG	TDF/FTC/EFV or NVP or DTG ABC/3TC/EFV or NVP or DTG	AZT/3TC/ATV/r AZT/3TC/LPV/r	AZT/3TC/DRVr AZT/3TC/RAL/LPVr
	AZT/3TC/EFV AZT/3TC/NVP AZT/3TC/DTG	TDF/3TC/ATV/r TDF/3TC/LPV/r TDF/FTC/ATV/r TDF/FTC/LPV/r ABC/3TC/ATV/r ABC/3TC/LPVr	

Source: World Health Organisation-Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendation for a public health approach. Second Edition 2016. Available from http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1

3.19 Third-line Therapy

The World Health Organisation estimates that approximately 1% of persons on ARVs are on third line therapy and that this will increase wider access to HIV resistance testing.

While previously salvage regimen was recommended for patients failing second line therapy, more recent data supports the efficacy of newer antiretroviral agents such as INSTIs, second generation PIs and NNRTIs as third line therapy. ART-experienced patients who have failed first- and second-line regimens, would have accumulated multiple resistance to NRTI agents. In this regard, when switching patients to a third line regimen, it is important to take in to consideration that NRTI agents are often associated with cumulative toxicity, their maintenance in third-line ART may not be optimal and may involve increased pill burden and risk of drug interactions. Where possible selection of third line therapy should be guided by genotype resistance testing and should include new drugs with minimal cross resistance to previously used regimens such as INSTIs, and second generation NNRTIs and PIs. In the absence of resistance testing, empiric reasoning of the likelihood of resistance to agents in the second line regimen, as well as considerations of cross-resistance, can be used to design a third line regimen. This outlined in table 11.

Table 11: Recommended Third Line Regimen for adults and adolescents>10 years of age

First Line Regimens	Second Line Regimens	Third Line Regimens
TDF+FTC+EFV TDF+3TC+EFV	AZT+3TC+ATV/r AZT+3TC+LPV/r AZT+3TC+DRV/r	DRV/r *+ DTG**(or RAL) ±1-2 NRTIs *for PI experienced patients, the recommended DRV/r dose is 600mgs/100mgs twice daily ** Safety and efficacy in adolescent younger than 12 years of age and pregnant women is not yet available.
TDF+3TC+DTG TDF+FTC+DTG	AZT+3TC + ATV/r or LPV/r AZT+3TC + DRV/r →	DRV/r + 2 NRTIs ± NNRTI Optimise regimen using genotyping

With access to genotyping, a clear determination can be made on the resistance profile. In these cases the following is recommended and detailed in table 12.

Table 12: Recommended third line based on resistance profile

Mutation	Recommended third line regimen
184 V +K65R	DRV/R + DTG + AZT+ 3TC
M184V + TAM	DRV/R+ DTG + ABC/3TC
M184v + TAM	DRV/R + DTG + TDF+FTC

LIST OF APPENDICIES

Appendix 3A: Fixed dose combination of Antiretroviral medications

Generic name	Dose
NRTIs	
Abacavir (ABC)	300 mg twice daily or 600 mg once daily
Emtricitabine (FTC)	200 mg once daily
Lamivudine (3TC)	150 mg twice daily or 300 mg twice daily
Zidovudine (AZT)	250-300 mg twice daily
Nucleotide reverse transcriptase inhibitors (NRTIs)	
Tenofovir (TDF)	300 mg once daily[a]
NNRTIs	
Efavirenz (EFV)	600 mg once daily
Etravirine (ETV)	200 mg twice daily
Nevirapine (NVP)	200 mg once daily for 14 days, followed by 200 mg twice daily[b]
PIs	
Atazanavir PLUS ritonavir (ATV/r)	300 mg PLUS 100 mg once daily
Darunavir PLUS ritonavir (DRV/r)	600 mg PLUS 100 mg twice daily
Fosamprenavir PLUS ritonavir (FPV/r)	700 mg PLUS 100 mg twice daily
Lopinavir/ritonavir (LPV/r)	Fixed dose combination tablets (LPV 200 mg/RTV 50 mg) Two tablets (400 mg/100 mg) twice daily[c]
	Considerations for individuals on TB therapy: • In the presence of rifabutin, no dose adjustment required • In the presence of rifampicin, use RTV superboosting (LPV 400 mg PLUS RTV 400 mg twice daily) or LPV 800 mg PLUS RTV 200 MG twice daily, with close clinical and hepatic enzyme monitoring

[a] TDF dosage adjustment for individual with altered creatinine clearance can be reconsidered (using Cockcroft-Gault formula). Creatinine clearance ≥50ml/min. 300 mg once daily. Creatinine clearance 30–49 ml/min. 300 mg every 48 hours. Creatinine clearance 10–29 ml/min (or dialysis). 300 mg once every 72–96 hours. Cockcroft-Gault formula: GFR = (140-age) x (wt in kg) x (0.85 if female)/(72 x Cr). [b] In the presence of rifampicin, or when patients switch from EFC to NVP, no need for lead-in dose of NVP. [c] LPV/r can be administered as 4 tablets once daily (i.e., LPV 800 mg PLUS RTV 200 mg once daily) in patients with less than three LPV resistance-associated mutations on genotypic testing. Once-daily dosing is not recommended in pregnant women or patients with more than three LPV resistance-associated mutations.

Source: World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents. Recommendations for a public health approach, 2010 revision. Geneva: WHO; 2010. Available from:
http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf.

Appendix 3B: Drug- Drug interaction between antiretroviral medications and other drugs

Drug	NVP	EFV	LPV/r
Antimycobacterial			
Rifampicin	Reduces NVP level by 31–58% Virologic consequences are uncertain; the potential of additive hepatotoxicity exists Co-administration is recommended with careful monitoring	Reduces EFV level by 13-33%	Reduces LPV area under the curve (AUC) by 75% Should not co-administer
Rifabutin	Reduces NVP 16%; no dose adjustment	EFV unchanged Reduces Rifabutin by35% Increase rifabutin dose to 450–600 mg Once daily or 600 mg 3x/week EFV dose remains standard	Rifabutin AUC increases 3-fold Decrease rifabutin dose to 150 mg oncedaily or 3 x a week LPV/r: Standard
Clarithromycin	None	Reduces clarithromycin by 39% Monitor for efficacy or use alternative drugs	Increases clarithromycin AUC by 75%, Adjust clarithromycin dose if renal impairment
Antifungal			
Ketoconazole	Increases ketoconazole level by 63% Increases NVP level by 15– 30% . Do not co-administer	No significant changes in ketoconazole or EFV levels	Increases LPV AUC Increases ketoconazole level 3 fold Do not exceed 200mg/day ketocanazole
Fluconazole	Increases NVP maximum concentration (Cmax), AUC, minimum concentration (Cmin) by 100%	No data	No data

Drug	NVP	EFV	LPV/r
	No change in fluconazole level Possible increase hepatotoxicity with co-administer requiring monitoring of NVP toxicity		
Intraconazole	No data	No data	Increases itraconazole level. Do not exceed 200 mg/day itraconazole
Oral Contraceptives			
Ethinyl estradiol	Reduces ethinyl estradiol by 20% Use alternative or additional birth control methods	Increases ethinyl estradiol by 37% Use alternative or additional birth control methods	Reduces ethinyl estradiol level by 42% Use alternative or additional birth control methods
Anticonvulsants			
Carbamazepin, phenytoin	Use with caution; one case report showed low EFV concentrations with phenytoin	Unknown; use with caution	Many possible interactions: Increases carbamazepine levels when coadministered with RTV. Use with caution and monitor anticonvulsant levels Phenytoin: reduces levels of LPV, RTV, and reduces levels of phenytoin when administered together. Avoid concomitant use or monitor LPV level
Lipid lowering drugs			
Simvastatin, lovastatin	No data	Reduces simvastatin level by 58% EFV level unchanged Adjust simvastatin dose according to lipid response; not to exceed the maximum recommended dose	Potential large increases statin level Avoid concomitant use
Atorvastatin	No data	Reduces atorvastatin AUC by 43% EFV level unchanged	Increases atorvastatin AUC 5.88 fold

Drug	NVP	EFV	LPV/r
		Adjust atorvastatin dose according to lipid response; not to exceed maximum recommended dose	Use lowest possible starting dose with careful monitoring
Pravastatin	No data	No data	Increases pravastatin AUC 33% No dose adjustment needed

Note: Concomitant use of fluticasone with RTV can result in significantly elevated serum cortisol concentrations. Coadministration of fluticasone with RTV or any RTV-boosted PI regimen is not recommended unless the potential benefit outweighs the risk of systemic corticosteroid side effects. Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Washington, DC: Department of Health and Human Services; 2013 [last update]. Available fromhttp://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl

Appendix 3C: DRUGS THAT SHOULD NOT BE USED IN COMBINATION WITH PIs OR NNRTIS DUE TO DANGEROUS DRUG INTERACTIONS										
Drug category[#]	Calcium channel blocker	Cardiac	Lipid lowering agents	Anti mycobacterial[‡]	Anti histamine[∂]	Gastro intestinal drugs[∂]	Neuro leptic	Psycho tropic	Ergot alkaloids (vasoconstrictor)	Herbs
PIS										
Ritonavir (RTV) PIS	bepridil	amiodarone flecainide propafenone quinidine	simvastatin lovastatin	rifapentine	astemizole terfenadine	cisapride	pimozide	midazolam[Σ] triazolam	dihydroergotamine (D.H.E. 45) ergotamine‡ (various forms) ergonovine methylergonovine	St. John's wort
Lopinavir (LPV) + ritonavir	(none)	flecainide propafenone	simvastatin lovastatin	RIF[⊥] rifapentine	astemizole terfenadine	cisapride	pimozide	midazolam[Σ] triazolam		St. John's wort
Atazanavir (ATV)	bepridil	(none)	simvastatin lovastatin	rifampicin rifapentine	astemizole terfenadine	cisapride proton pump inhibitors	pimozide	midazolamΣ triazolam		St. John's wort
NNRTS										
Nevirapine (NVP)	(none)	(none)	(none)	rifampicin rifapentine[‡]	(none)	(none)	(none)	(none)	(none)	St. John's wort

Efavirenz (EFV)	(none)	(none)	(none)	rifapentine‡	astemizole terfenadine	cisapride	(none)	midazolamΣ triazolam	dihydroergotamine (D.H.E. 45) ergotamine‡ (various forms) ergonovine methylergonovine	St. John's wort

#*Certain listed drugs are contra-indicated based on theoretical considerations. Thus, drugs with narrow therapeutic indices and suspected metabolic involvement with P450–3A, 2D6, or unknown pathways are included in this table. Actual interactions may or may not occur among patients.*

‡*HIV patients being treated with rifapentine have a higher rate of TB relapse than those treated with other rifamycin-based regimens; an alternative agent is recommended for this population.*

Δ *Rifampicin and rifabutin are contra-indicated unless SQV is combined with RTV.*

ʃ*In one small study, higher doses of RTV or LPV/r offset RIF-inducing activity of LPV. Of note, 28% of subjects discontinued due to increases in LFTs. The safety of this combination is still under evaluation; further studies are needed.*

Σ*Midazolam can be used with caution as a single dose and given in a monitored situation for procedural sedation.*

†*This is likely a class effect.*

∂*Astemizole and terfenadine are not marketed in the US. The manufacturer of cisapride has a limited-access protocol in place for patients meeting specific clinical eligibility criteria.*

Each 150 mg APV Agenerase® capsule has 109 international units (IU) of vitamin E and 1 mL of APV oral solution has 46 IU of vitamin E. At FDA approved doses, the daily amount of vitamin E in Agenerase® is a 58-fold increase over the federal government's reference daily intake for adults. Patients should be cautioned to avoid supplemental doses of vitamin E. Multivitamin products containing minimal amounts of vitamin E are likely acceptable.

Suggested alternatives:

Cerivastatin (no longer marketed in the US), simvastatin, lovastatin: Pravastatin and fluvastatin have the least potential for drug-drug interactions; atorvastatin should be used with caution, using the lowest possible starting dose and monitoring closely.

Rifabutin: Clarithromycin, azithromycin (MAC prophylaxis); clarithromycin, azithromycin, ethambutol (MAC treatment) Astemizole, terfenadine (no longer marketed in the US): Desloratadine, loratadine, fexofenadine, cetirizine Midazolam, triazolam: Temazepam, lorazepam

Source: Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Washington, DC: Department of Health and Human Services; 2013 [last update]. Available from: http://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

Appendix 3D: SEVERITY GRADING OF SELECTED CLINICAL AND LABORATORY TOXICITIES

For abnormalities NOT found elsewhere on the table below, use the following scale to estimate grade of toxicity:

Grade 1	Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required.
Grade 2	Mild-to-moderate limitation in activity; some assistance may be needed; no or minimal medical intervention/therapy required.
Grade 3	Marked limitation in activity; some assistance usually required; medical intervention/therapy required; hospitalization possible.
Grade 4	Extreme limitation in activity; significant assistance required; significant medical intervention/therapy required; hospitalization or hospice care.

	Grade 1	Grade 2	Grade 3	Grade 4
Haemoglobin	8.0–9.4 g/dL **OR** 80–94 g/L **OR** 4.93–5.83 mmol/L	7.0–7.9 g/dL **OR** 70–79 g/L **OR** 4.31–4.92 mmol/L	6.5–6.9 g/dL **OR** 65–69 g/L **OR** 4.03–4.30 mmol/L	<6.5 g/dL **OR** <65 g/L **OR** <4.03 mmol/L
Absolute neutrophil count	1,000–1,500/mm **OR** 1.0–1.5/G/L*	750–999/mm **OR** 0.75–0.99/G/L*	500–749/mm **OR** 0.5–0.749/G/L*	<500/mm **OR** <0.5/G/L*
Platelets	75,000–99,000/ mm **OR** 75–99/G/L*	50,000–74,999/mm **OR** 50–74.9/G/L*	20,000–49,999/mm **OR** 20–49.9/G/L*	<20,000/mm **OR** <20/G/L*
Hyponatremia	130–135 meq/L **OR** 130–135mmol/L	123–129 meq/L **OR** 123–129 mmol/L	116–122 meq/L **OR** 116–122 mmol/L	<116 meq/L **OR** <116 mmol/L
Hypernatremia	146–150 meq/L **OR** 146–150mmol/L	151–157 meq/L **OR** 151–157 mmol/L	158–165 meq/L **OR** 158–165 mmol/L	>165 meq/L **OR** >165 mmol/L
Hyperkalemia	5.6–6.0 meq/L **OR** 5.6–6.0 mmol/L	6.1–6.5 meq/L **OR** 6.1–6.5 mmol/L	6.6–7.0 meq/L **OR** 6.6–7.0 mmol/L	>7.0 meq/L **OR** >7.0 mmol/L
Hypokalemia	3.0–3.4 meq/L **OR** 3.0–3.4 mmol/L	2.5–2.9 meq/L **OR** 2.5–2.9 mmol/L	2.0–2.4 meq/L **OR** 2.0–2.4 mmol/L	<2.0 meq/L **OR** <2.0 mmol/L
Hyperbilirubinemia	>1.0–1.5 x ULN	>1.5–2.5 x ULN	>2.5–5 x ULN	>5 x ULN
Hypoglycemia	55–64 mg/dL **OR** 3.01–3.55 mmol/L	40–54 mg/dL **OR** 2.19–3.00 mmol/L	30–39 mg/dL **OR** 1.67–2.18 mmol/L	<30 mg/dL **OR** <1.67 mmol/L

	Grade 1	Grade 2	Grade 3	Grade 4
Hyperglycemia (nonfasting and no prior diabetes)	116–160 mg/dL **OR** 6.44–8.90 mmol/L	161–250 mg/dL **OR** 8.91–13.88 mmol/L	251–500 mg/dL **OR** 13.89–27.76 mmol/L	>500 mg/dL **OR** >27.76 mmol/L
Triglycerides	----------	400–750 mg/dL **OR** 4.52–8.47mmol/L	751–1,200 mg/dL **OR** 8.48–13.55 mmol/L	>1,200 mg/dL **OR** >13.55 mmol/L
Creatinine	>1.0–1.5 x ULN	>1.5–3.0 x ULN	>3.0–6.0 x ULN	>6.0 x ULN
AST (SGOT)	1.25–2.5 x ULN	>2.5–5.0 x ULN	>5.0–10.0 x ULN	>10.0 x ULN
ALT (SGPT)	1.25–2.5 x ULN	>2.5–5.0 x ULN	>5.0–10.0 x ULN	>10.0 x ULN
GGT	1.25–2.5 x ULN	>2.5–5.0 x ULN	>5.0–10.0 x ULN	>10.0 x ULN
Alkaline phosphatase	1.25–2.5 x ULN	>2.5–5.0 x ULN	>5.0–10.0 x ULN	>10.0 x ULN
Amylase	>1.0–1.5 x ULN	>1.5–2.0 x ULN	>2.0–5.0 x ULN	>5.0 x ULN
Pancreatic amylase	>1.0–1.5 x ULN	>1.5–2.0 x ULN	>2.0–5.0 x ULN	>5.0 x ULN
Lipase	>1.0–1.5 x ULN	>1.5–2.0 x ULN	>2.0–5.0 x ULN	>5.0 x ULN
Lactate	<2.0 x ULN without acidosis	>2.0 x ULN without acidosis	Increased lactate with pH <7.3 without life threatening consequences	Increased lactate with pH <7.3 with life-threatening consequences

Sources: World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents. Recommendations for a public health approach, 2010 revision. Geneva: WHO; 2010. Available from: http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf;

4 ADULT AND ADOLESCENT OPPORTUNISTIC INFECTION PROPHYLAXIS

This section provides detailed guidance on the prevention of selected OIs commonly seen in PLHIV in the Caribbean region. Sources for these recommendations include the website HIV Web Study[4], CDC's OI guidelines[5] and the US National Institutes for Health[3] which have been adapted for the Eastern Caribbean region. Not all treatments listed may be available in the OECS but are included in case referral outside the region is an option. For management of OIs not listed below, please consult the CDC OI Guidelines.

Preferred and alternative treatment options are presented; each recommendation includes a rating of its strength as well as the quality of the evidence supporting it, coded as follows.

Strength of recommendation:

Both strong evidence for efficacy and substantial clinical benefit support recommendation for use. Should always be offered.

A. Both strong evidence for efficacy and substantial clinical benefit support recommendation for use. Should always be offered.

B. Moderate evidence for efficacy, or strong evidence for efficacy but only limited clinical benefit, supports recommendation for use. Should generally be offered.

C. Evidence for efficacy is insufficient to support a recommendation for or against use, or evidence for efficacy might not outweigh adverse consequences (e.g., drug toxicity, drug interactions) or cost of treatment or alternative approaches. Optional.

D. Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use. Should generally not be offered.

E. Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use. Should never be offered.

Quality of the evidence supporting the recommendation

I. Evidence from at least one properly-designed randomized, controlled trial.

II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), or from multiple time-series studies, or dramatic results from uncontrolled experiments.

III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

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[4] HIV Web Study. Seattle: University of Washington; c2004–13 [updated 7 Mar 2013]. Available from: www.hivwebstudy.org.

[5] Centers for Disease Control and Prevention. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Recommendations from the CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR. 2009 Apr 10; 58(4).
Available from: http://www.cdc.gov/mmwr/pdf/rr/rr5804.pdf

[3] Guidelines for the prevention and treatment of Opportunistic infections in HIV infected adults and adolescents. Available from https://aidsinfo.nih.gov/guidelines.

4.1 Primary Prophylaxis of OIs among Adults and Adolescents.

Table 13: Prophylaxis to prevent first episode of OIs9

Table 4.1 Primary Prophylaxis of HIV associated opportunistic Infections among adults and adolescents			
Pathogen	**Indication**	**Preferred**	**Alternative**
***Pneumocystis jirovecii* pneumonia (PCP)**	CD4 count <200 cells/μL **(AI) OR** oropharyngeal candidiasis **(AII)** , CD4 count <14% or history of AIDS-defining illness **(BII) ,** CD4 count >200 but <250 cells/μL if monitoring CD4 count every 1–3 months is not possible **(BII)** ***Note: Patients who are receiving pyrimethamine/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional PCP prophylaxis (AII).***	Co-trimoxazole 1 double strength (DS) PO (orally) QD (daily) **(AI)**; **OR** 1 single strength (SS) QD **(AI)**	Co-trimoxazole: 1 DS PO TIW **(BI)**; **OR** Dapsone: 100 mg PO QD **OR** 50 mg PO twice a day BID **(BI)**; **OR** Dapsone: 50 mg PO QD + pyrimethamine: 50 mg PO QW + leucovorin 25 mg POQW **(BI)**; (Dapsone 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly (BI); **OR** Aerosolized pentamidine: 300 mg via Respigard nebulizer QM **(BI)**; **OR** Atovaquone: 1,500 mg PO QD **(BI)**; **OR** Atovaquone 1,500 mg + pyrimethamine 25 mg + leucovorin 10 mg PO daily **(CIII)**
***Toxoplasma gondii* encephalitis**	Toxoplasma IgG positive patients with CD4 count <100 cells/μL **(AII),** Seronegative patients receiving PCP prophylaxis not active against toxoplasmosis should have toxoplasma serology retested if CD4 count decline to <100 cells/μL **(CIII)** Prophylaxis should be initiated if seroconversion occurred **(AII)** ***Note: All regimens recommended for primary prophylaxis against toxoplasmosis are also effective as PCP prophylaxis.***	Co-trimoxazole: 1 DS PO QD **(AII)**	Co-trimoxazole: 1 DS PO TIW **(BIII)**; **OR** Co-trimoxazole: 1 SS PO QD **(BIII)**; **OR** Dapsone: 50 mg PO QD + pyrimethamine: 50 mg PO weekly + leucovorin: 25 mg PO weekly **(BI)**; **OR** Dapsone: 200 mg PO weekly + pyrimethamine: 75 mg PO weekly + leucovorin: 25 mg PO weekly **(BI) OR** Atovaquone: 1,500 mg PO QD , with or without pyrimethamine: 25 mg PO QD + leucovorin: 10 mg PO QD **(CIII)**

Table 4.1 Primary Prophylaxis of HIV associated opportunistic Infections among adults and adolescents			
Pathogen	**Indication**	**Preferred**	**Alternative**
***Mycobacterium tuberculosis* infection (treatment of latent TB [LTBI])**	Positive diagnostic test for LTBI, no evidence of active TB, and no prior history of treatment for active or latent TB **(AI)** Negative diagnostic test for LTBI, but close contact with a person with infectious pulmonary TB and no evidence of active TB **(AII)** A history of untreated or inadequately treated healed TB (i.e., old fibrotic lesions) regardless of diagnostic tests for LTBI and no evidence of active TB **(AII)**	Isoniazid: 300 mg PO QD **(AII) OR** 900 mg PO twice weekly (BIW) **(BII)** for 9 months—both PLUS pyridoxine: 50 mg PO QD **(BIII)**;	Rifampicin: 600 mg PO QD x 4 months **(BIII)**; **OR** Rifabutin: (dose adjusted based on concomitant HAART) x 4 months **(BIII)** Rifapentine (see dose below) PO + INH 900 mg PO + pyridoxine 50 mg PO] once weekly x 12 weeks **Rifapentine dose:** 32.1 to 49.9 kg: 750 mg 50 kg: 900 mg ***Rifapentine only recommended for patients receiving raltegravir or efavirenz-based ART regimen.*** ***For persons exposed to drug resistant TB, select anti-TB drugs after consultation with experts or public health authorities (AII).***
Disseminated *Mycobacterium avium* complex (MAC)	CD4 count <50 cells/μL— after ruling out active MAC infection **(AI)**	Azithromycin: 1,200 mg PO once weekly **(AI) OR** Clarithromycin 500 mg PO BID **(AI), OR** Azithromycin 600 mg PO twice weekly (**BIII**)	Rifabutin: 300 mg PO QD **(BI)** (dosage adjustment based on drug-drug interactions with HAART). ***Rule out active TB before starting rifabutin***
Streptococcus pneumoniae	CD4 count >200 cells/μL and no receipt of pneumococcal vaccine in the past 5 years **(AII)** CD4 count <200 cells/μL— vaccination can be offered **(CIII)** In patients who received pneumococcal vaccination when CD4 count <200 cells/μL, but has increased to >200 cells/μL in response to HAART **(CIII)**	PCV13 0.5 mL IM x 1 **(AI).** PPV23 0.5 mL IM or SQ at least 8 weeks after the PCV13 vaccine (**AII).** PPV23 can be offered at least 8 weeks after receiving PCV13 **(CIII) OR** can wait until CD4 count increased to ≥200 cells/ μL (**BIII).**	PPV23 0.5 mL IM or SQ x 1 **(BII)**

Table 4.1 Primary Prophylaxis of HIV associated opportunistic Infections among adults and adolescents			
Pathogen	**Indication**	**Preferred**	**Alternative**
	For individuals who have previously received PPV23 Re-vaccination • If age 19–64 years and ≥5 years since the first PPV23 dose • If age ≥65 years, and if ≥5 years since the previous PPV23 dose	One dose of PCV13 should be given at least 1 year after the last receipt of PPV23 **(AII).** PPV23 0.5 mL IM or SQ x 1 **(BIII)** PPV23 0.5mL IM or SQ x 1 **(BIII)**	
Influenza A and B	All HIV-infected patients **(AIII)**	Inactivated influenza vaccine: 0.5 mL IM annually **(AIII)** Live-attenuated influenza vaccine is contraindicated in HIV-infected patients **(AIII).**	
Histoplasma capsulatum	CD4 count ≤150 cells/μL and at high risk because of occupational exposure or live in a community with a hyperendemic rate of histoplasmosis (>10 cases/100 patient-years) **(CI)**	Itraconazole: 200 mg PO QD **(CI)**	
Syphilis	Individuals exposed to a sex partner with a diagnosis of primary, secondary, or early latent syphilis within past 90 days**(AII), OR** Individuals exposed to a sex partner >90 days before syphilis diagnosis in the partner, if serologic test results are not available immediately and the opportunity for follow-up is uncertain **(AIII)**	Benzathine penicillin G 2.4 million units IM for 1 dose **(AII).**	**For penicillin-allergic patients:** Doxycycline 100 mg PO BID for 14 days **(BII), OR** Ceftriaxone 1 g IM or IV daily for 8–10 days **(BII), OR** Azithromycin 2 g PO for 1 dose **(BII)**
Coccidioidomycosis	Positive IgM or IgG serologic test in a patient from a disease-endemic area; and CD4 count <250 cells/μL **(CIII)**	Fluconazole: 400 mg PO QD **(CIII); OR** Itraconazole: 200 mg PO BID **(CIII)**	

Table 4.1 Primary Prophylaxis of HIV associated opportunistic Infections among adults and adolescents			
Pathogen	**Indication**	**Preferred**	**Alternative**
***Varicella zoster* virus (VZV)**	**Post-exposure**—close contact with a person who has active varicella or herpes zoster: For susceptible patients (those who have no history of vaccination or of either condition or are known to be VZV seronegative) **(AIII)** **Post-exposure prevention: (AIII)** Close contact with a person with chickenpox or herpes zoster; and is susceptible (i.e., no history vaccination or of either condition, or known to be VZV seronegative)	**Pre-exposure prevention:** Primary varicella vaccination (Varivax), 2 doses (0.5 mL SQ each) administered 3months apart **(CIII).** ***If vaccination results in disease because of vaccine virus, treatment with acyclovir is recommended (AIII).*** **Post-exposure prevention:** Varicella-zoster immunoglobulin (VariZIG) 125 international units per 10 kg (maximum 625 international units) IM, administered as soon as possible and within 10 days after exposure **(AIII)** **Individuals receiving monthly high-dose IVIG (>400 mg/kg) are likely to be protected if the last dose of IVIG was administered <3 weeks before exposure.**	**Pre-exposure prevention:** VZV-susceptible household contacts of susceptible HIV-infected persons should be vaccinated to prevent potential transmission of VZV to their HIV-infected contacts **(BIII).** **Alternative post-exposure prevention:** Acyclovir 800 mg PO 5 x/day for 5–7 days **(BIII), OR** Valacyclovir 1 g PO TID for 5–7 days **(BIII)** ***The alternatives are not well studied in the HIV population.*** ***If antiviral therapy is used, varicella vaccines should not be given until at least 72 hours after the last dose of the antiviral drug.***
Human papillomavirus (HPV)	Women aged 13–26 years **(BIII)**	HPV quadrivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 **(BIII),OR** HPV bivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 (**BIII), OR** HPV 9-valent vaccine 0.5 mL IM at months 0, 1–2, and 6 **(BIII)**	

Table 4.1 Primary Prophylaxis of HIV associated opportunistic Infections among adults and adolescents			
Pathogen	**Indication**	**Preferred**	**Alternative**
Human papillomavirus (HPV)	Males aged 13–26 years **(BIII)**	HPV quadrivalent vaccine 0.5 mL IM at months 0, 1–2, and 6 **(BIII), OR** HPV 9-valent vaccine 0.5mL IM at months 0, 1–2,and 6 **(BIII)**	
HAV	HAV-susceptible patients who have chronic liver disease, are injection drug users, or are men who have sex with men **(AII)**	Hepatitis A vaccine 1 mL IM x 2 doses at 0 and 6–12months **(AII).** ***IgG antibody response should be assessed 1 month after vaccination; non-responders should be revaccinated when CD4 count >200 cells/μL. (BIII).***	For patients susceptible to both HAV and hepatitis B virus (HBV) infection: Combined HAV and HBV vaccine (Twinrix®), 1 mL IM as a 3-dose (0,1, and 6 months) or 4-dose series (days 0, 7, 21 to 30, and 12 months)**(AII)**
HBV	Patients without chronic HBV or without immunity to HBV (i.e., anti-HBs <10 international units/mL) (**AII)** Patients with isolated anti-HBc and negative HBV DNA **(BII)** Early vaccination is recommended before CD4 count falls below 350 cells/μL **(AII).** - ***However, in patients with low CD4 cell counts, vaccination should not be deferred until CD4 count reaches >350 cells/μL, because some patients with CD4 counts <200 cells/μL do respond to vaccination (AII).***	HBV vaccine IM (Engerix-B 20 μg/mL **or** Recombivax HB 10 μg/mL), 0, 1, and 6 months (**AII), OR** HBV vaccine IM (Engerix-B 40 μg/mL **or** Recombivax HB 20 μg/mL) 0, 1, 2 and 6 months **(BI), OR** Combined HAV and HBV vaccine (Twinrix), 1 mL IM as a 3-dose (0, 1, and 6 months) **or** 4-dose series (days 0, 7, 21 to 30, and 12 months) **(AII)** ***Anti-HBs should be obtained 1 month after completion of the vaccine series.*** ***Patients with anti-HBs <10 international units/mL at 1***	Some experts recommend vaccinating with 40 *μg* doses of either vaccine **(CIII)**

Table 4.1 Primary Prophylaxis of HIV associated opportunistic Infections among adults and adolescents			
Pathogen	**Indication**	**Preferred**	**Alternative**
		month are considered nonresponders **(BIII).**	
HBV	**Vaccine Non-Responders:** Anti-HBs <10 international units/ mL 1 month after vaccination series Patients with low CD4 counts at time of first vaccine series, consider delay revaccination until after a sustained increase in CD4 count with ART (**CIII).**	Re-vaccinate with a second vaccine series **(BIII)**	HBV vaccine IM (Engerix-B 40 µg/mL or Recombivax HB 20 µg/mL), 0, 1, 2 and 6 months **(BI).**

4.4 Immunization among adults and adolescents

Immunizations for HIV-infected adults in the OECS are the same as those for HIV-uninfected adults, with the following exceptions:

- MMR and varicella should not be administered to severely immunosuppressed persons (e.g., CD4 less than 200, or recent Opportunistic Infection), as MMR and varicella are live attenuated vaccines
- Pneumococcal vaccination (polysaccharide PPSV 23-valent vaccine, and/or conjugate PCV 7valent vaccine) are recommended for HIV-infected adults, given the increased susceptibility of PLHIV to pneumococcal pneumonia.

The following immunization schedule[6] represents the ideal set of immunizations for adult PLHIV. Not all vaccines may be routinely available in the OECS but are included in case the patient is able to obtain vaccines overseas.

Table 14: Immunization schedule for Adults and Adolescents with HIV

Vaccine	Age group (years)		
	19–49	50–64	≥65
Influenza	1 dose annually		
Pneumococcal 13 –valent conjugate (PCV 13)	1 dose		
Pneumococcal (polysaccharide) (PPSV23)	Administer 8 weeks after PCV 13. Second dose 5 years after 1st dose of PPSV 23.		
Hepatitis B	3 doses (0, 1–2, 4–6 mos.)		
Tetanus, diphtheria, pertussis (Td/Tdap)	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 years		1 dose Td booster every 10 years
HPV (female)	3 doses through age 26		
HPV (male)	3 doses through age 26 years. Prioritise MSM- at higher risk.		
Zoster vaccine			Single dose >60 years- contraindicated in severely immunocompromised persons. (CD4<200). Recommended regardless of past

[6] Centers for Disease Control and Prevention. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Recommendations from the CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR. 2009 Apr 10; 58(4). Available from: http://www.cdc.gov/mmwr/pdf/rr/rr5804.pdf.

Vaccine	Age group (years)		
	19–49	50–64	≥65
			episode of zoster.
Measles, mumps, rubella (MMR)	***Do not administer to severely immunosuppressed persons(CD4 <200)***		
Varicella	***Do not administer to severely immunosuppressed persons (CD4<200)***		
Hepatitis A	2-3 doses depending on the vaccine		
Hepatitis B	3 doses		
Meningococcal 4 valent conjugate (MenACWY)	2 doses , two months apart		

	For all persons in this category who meet the age requirements and who lack evidence of immunity (e.g., lack of documentation of vaccination or have no evidence of prior infection)		Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

Adapted from recommended Adult Immunization Schedule US 2016. Morbidity and Mortality Weekly Report (MMWR) on February 4, 2016.https://www.cdc.gov/vaccines/schedules/downloads/past/2016-adult.pdf.

4.3 Treatment of opportunistic infections among adults and adolescents

This section provides detailed guidance on the management of selected OIs commonly seen in PLHIV in the Caribbean region. Sources for these recommendations include the website HIV Web Study[7] and the United States CDC's OI guidelines[8], which have been adapted for the Eastern Caribbean region. Not all treatments listed may be available in the OECS but are included in case referral outside the region is an option. For management of OIs not listed below, please consult the original CDC OI guidelines.

Preferred and alternative treatment options are presented; each recommendation includes a rating of its strength as well as the quality of the evidence supporting it, coded as follows. The strength of the recommendation is outlined in section 4.0 above. Treatment and secondary prophylaxis is detailed in table 15 below.

[7] HIV Web Study. Seattle: University of Washington; c2004–13 [updated 7 Mar 2013]. Available from: www.hivwebstudy.org.

[8] Centers for Disease Control and Prevention. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Recommendations from the CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR. 2009 Apr 10; 58(4). Available from: http://www.cdc.gov/mmwr/pdf/rr/rr5804.pdf

Table 15: Treatment and secondary prophylaxis therapy of HIV-associated opportunistic infections in adults and adolescents

OI	Preferred therapy	Alternative therapy
PCP	**Moderate-to-severe PCP:** Co-trimoxazole (15–20 mg TMP and 75–100 mg SMX/kg/day IV Q6H or Q8H) **(AI)**; (S witch to PO after clinical improvement) **(AI)** Duration of therapy: 21 days **(AII)** **Mild to -moderate PCP:** Co-trimoxazole : [TMP 15–20 mg and SMX 75–100 mg]/kg/day, PO in 3 divided doses **(AI)**; **OR** Co-trimoxazole (160 mg/800 mg or DS 2 tablets) TID **(AI)** Duration of therapy: 21 days **(AII)** **Secondary prophylaxis after treatment** Co-trimoxazole (160 mg/800 mg or DS tablet PO QD) **(AI)**; **OR** Co-trimoxazole (80 mg/400 mg or SS tablet PO QD) **(AI)**	**Moderate-to-severe PCP:** Pentamidine (4 mg/kg IV QD infused over ≥60 minutes) **(AI)**; certain specialists reduce dose to 3 mg/kg IV QD because of toxicities **(BI)**; **OR** Primaquine (30 mg [base] PO QD) + clindamycin (600 mg q6h IV or 900 mg IV q8h **OR** Clindamycin((450 mg PO q6h or 600 mg PO q8h) **(AI)** **Mild-to-moderate PCP:** Dapsone (100 mg PO QD) and TMP (15 mg/kg/day PO [3 divided dose]) **(BI)**; **OR** Primaquine30 mg [base] PO QD) + clindamycin **(BI)**; **OR** Atovaquone (750 mg PO BID with food) **(BI)** **Secondary prophylaxis:** Co-trimoxazole (160 mg/800 mg or DS PO 3 x week (TIW) **(BI)**;**OR** Dapsone (50 mg PO BID or 100 mg PO QD) **(BI)**; **OR** Dapsone (50 mg PO QD) + pyrimethamine (50 mg PO QW) + leucovorin (25 mg PO QW) **(BI)**; **OR** Dapsone (200 mg PO) + pyrimethamine (75 mg PO) + leucovorin (25 mg PO QW) **(BI)**; **OR** Atovaquone (1,500 mg PO QD) **(BI)**; **OR** Atovaquone (1,500 mg) + pyrimethamine (25 mg) + leucovorin (10 mg) PO QD **(CIII)**
Corticosteroids are indicated (AI): PaO_2 <70 mmHg at room air OR alveolar-arterial O_2 gradient >35 mmHg **Prednisone doses (beginning as early as possible and within 72 hours of PCP therapy) (AI):** **Days 1–5: 40 mg PO BID** **Days 6–10: 40 mg PO QD** **Days 11–21: 20 mg PO QD** ***IV methylprednisolone can be administered as 75% of prednisone dose*** **Clinicians use corticosteroid in patients with moderate-to-severe PCP. The benefits started after 72 hours of treatment is unknown (BIII)**		

OI	Preferred therapy	Alternative therapy
TE	**Preferred Treatment of Acute Infection: (AI)** Pyrimethamine 200 mg PO 1 time, followed by weight-based therapy: If <60 kg, pyrimethamine 50 mg PO once daily + sulfadiazine 1000 mg PO q6h + leucovorin 10–25 mg PO once daily. If ≥60 kg, pyrimethamine 75 mg PO once daily + sulfadiazine 1500 mg PO q6h + leucovorin 10–25 mg PO once daily • Leucovorin dose can be increased to 50 mg daily or BID. **Duration for Acute Therapy**: At least 6 weeks **(BII); (** longer duration if clinical or radiologic disease is extensive or response is incomplete at 6 weeks) **Chronic Maintenance Therapy:** Pyrimethamine 25–50 mg PO daily + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses) + leucovorin 10–25 mg PO daily **(AI)**	**Alternative treatment of acute infection** Pyrimethamine (leucovorin) + clindamycin 600 mg IV or PO q6h **(AI), OR** TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg) IV or PO BID (BI), **OR** Atovaquone 1500 mg PO BID with food + pyrimethamine (leucovorin) **(BII) OR** Atovaquone 1500 mg PO BID with food + sulfadiazine 1000–1500 mg PO q6h (weight-based dosing, as in preferred therapy) **(BII), OR** Atovaquone 1500 mg PO BID with food **(BII), OR** Pyrimethamine (leucovorin)* + azithromycin 900–1200 mg PO daily **(CII)** **Chronic Maintenance Therapy:** Clindamycin 600 mg PO q8h + (pyrimethamine 25–50 mg + leucovorin 10–25 mg) PO daily (**BI), OR** TMP-SMX DS 1 tablet BID (**BII), OR** TMP-SMX DS 1 tablet once daily (**BII); OR** Atovaquone 750–1500 mg PO BID + (pyrimethamine 25 mg + leucovorin 10 mg) PO daily **(BII),OR** Atovaquone 750–1500 mg PO BID + sulfadiazine 2000–4000 mg PO daily (in 2–4 divided doses **[BII]), OR** Atovaquone 750–1500 mg PO BID with food **(BII)** ***Pyrimethamine and leucovorin doses are the same as for preferred therapy.***
Sulfa desensitization should be attempted should be attempted for patients with allergy (BI) and is detailed in **Appendix 4A.** Atovaquone should be administered until therapeutic doses of TMP-SMX are achieved (CIII). Adjunctive corticosteroids (e.g., dexamethasone) should only be administered when clinically indicated to treat mass effect associated with focal lesions or associated edema (BIII); discontinue as soon as clinically feasible. Anticonvulsants should be administered to patients with a history of seizures (AIII) and continued through acute treatment, but should not be used as seizure prophylaxis (AIII).		

OI	Preferred therapy	Alternative therapy
Cryptosporidiosis	Initiate or optimize ART for immune restoration to CD4 count >100 cells/μL (**AII),** and Aggressive oral or IV rehydration and replacement of electrolyte loss **(AIII),** and Symptomatic treatment of diarrhea with anti-motility agents (AIII). ***Tincture of opium may be more effective than loperamide in management of diarrhea (CII)***	No therapy has been shown to be effective without ART. The following can be used in conjunction with ART Nitazoxanide 500–1000 mg PO BID for 14 days (**CIII), OR** Paromomycin 500 mg PO QID for 14–21 days (**CIII)**
Microsporidiosis	**For GI Infections Caused by Enterocytozoon bienuesi:** Initiate or optimize ART as immune restoration to CD4 count >100 cells/μL (**AII);PLUS** Manage severe dehydration, malnutrition, and wasting by fluid support (**AII)** and nutritional supplement **(AIII)** **For Intestinal and Disseminated (Not Ocular) Infections Caused by Microsporidia Other Than E. bienuesi and Vittaforma corneae:** Albendazole 400 mg PO BID (AII), continue until CD4 count >200 cells/μL for >6 months after initiation of ART **(BIII)** **For Ocular Infection:** Topical fumagillin bicylohexylammonium (Fumidil B) eye drops: 3 mg/mL in saline (fumagillin 70 μg/mL)—2 drops q2h for 4 days, then 2 drops QID **(BII)** + albendazole 400 mg PO BID, for management of systemic infection **(BIII)** Therapy should be continued until resolution of ocular symptoms and CD4 count increase to >200 cells/μL for >6 months in response to ART (**CIII).**	**For GI infections caused by Gbienuesi:** Fumagillin 60 mg/day (BII) and TNP-470 (a synthetic analog of fumagillin) (BIII) may be effective Nitazoxanide (1000 mg BID) may have some effect but response may be minimal in patients with low CD4 cell counts (CIII). **For Disseminated Disease Attributed to Trachipleistophora or Anncaliia:** Itraconazole 400 mg PO daily + albendazole 400 mg PO BID (CIII) ***Antimotility drugs can be used for diarrhea control if required (BIII).***
Mycobacterium tuberculosis (TB) Disease	**Initial Phase (2 Months, Given Daily, 5–7Times/Week by DOT) (AI):** INH + [RIF or RFB] + PZA + EMB (AI), **Continuation Phase** INH + (RIF or RFB) daily (5–7 times/week) (AIII) **Total Duration of Therapy (For Drug-Susceptible TB):** Pulmonary drug-susceptible TB: 6 months (**BII)** Pulmonary TB and culture- positive after 2 months of TB treatment: 9 months **(BII)**	**Treatment for Drug-Resistant TB Resistant to INH:** (RIF or RFB) + EMB + PZA + (moxifloxacin or levofloxacin) for 2 months (BII); followed by (RIF or RFB) + EMB + (moxifloxacin or levofloxacin) for 7 months **(BII)** **Resistant to Rifamycins +/- Other Drugs:** Regimen and duration of treatment should be individualized based on resistance pattern, clinical and microbiological responses, and in close consultation with experienced specialists **(AIII)**

OI	Preferred therapy	Alternative therapy
	Extra-pulmonary TB w/CNS infection: 9–12 months **(BII);** Extra-pulmonary TB w/bone or joint involvement: 6 to 9 months **(BII);** Extra-pulmonary TB in other sites: 6 months **(BII)** ***Total duration of therapy should be based on number of doses received, not on calendar time.***	
Adjunctive corticosteroid improves survival for TB meningitis and pericarditis (AI). Therapeutic drug monitoring should be considered in patients receiving rifamycin and interacting ART. Paradoxical IRIS that is not severe can be treated with NSAIDs without a change in TB or HIV therapy (BIII). For severe IRIS reaction, consider prednisone and taper over 4 weeks based on clinical symptoms (BIII).		
Disseminated Mycobacterium avium Complex (MAC) Disease	**Initial Therapy with 2 drugs :** Clarithromycin 500 mg PO BID (**AI)** + ethambutol 15 mg/kg PO daily (**AI),OR** Azithromycin 500–600 mg + ethambutol 15 mg/kg) PO daily (**AII)** if drug interaction or intolerance to clarithromycin **Duration of therapy** At least 12 months. Discontinue if no signs and symptoms of MAC disease and sustained (>6 months) CD4 count >100 cells/μL in response to ART	Consider a third or fourth drug for patients with advanced immunosuppression (CD4 counts <50 cells/μL), high mycobacterial loads (>2 log CFU/mL of blood), or in the absence of effective ART (**CIII).** **Third or Fourth Drug Options** RFB 300 mg PO daily (dosage adjustment may be necessary based on drug interactions) (**CI),** Amikacin 10–15 mg/kg IV daily (**CIII) OR** Streptomycin 1 g IV or IM daily (**CIII), OR** Moxifloxacin 400 mg PO daily (CIII) or Levofloxacin 500 mg PO daily **(CIII)**
Testing of susceptibility to clarithromycin and azithromycin is recommended (BIII). NSAIDs can be used for patients who experience moderate to severe symptoms attributed to IRIS (CIII). If cases of persistent IRIS symptoms, short-term (4–8 weeks) systemic corticosteroids (equivalent to 20–40 mg prednisone) can be used (CII).		
Bacterial Respiratory Diseases (with focus on pneumonia)	**Empiric Outpatient Therapy:** A PO beta-lactam (+ a PO macrolide (azithromycin or clarithromycin) (AII) Preferred beta-lactams: high dose amoxicillin or amoxicillin/ clavulanate Alternative beta-lactams: cefpodoxime **or** cefuroxime, **For penicillin-allergic patients:** Levofloxacin 750 mg PO once daily **(AII),** or moxifloxacin 400 mg PO once daily (**AII)** **Duration of therapy:** 7–10 days (a minimum of 5 days). *Patients should be afebrile for 48–72 hours and clinically stable before stopping antibiotics*	**Empiric Outpatient Therapy:** A PO beta-lactam + PO doxycycline (**CIII)** **Preferred beta-lactams**: highdose amoxicillin or amoxicillin/ clavulanate **Alternative beta-lactams:** cefpodoxime or cefuroxime **Empiric Therapy for Non-ICU Hospitalized Patients:** IV beta-lactam + doxycycline (**CIII)** **Empiric Therapy For ICU Patients:** **For penicillin-allergic patients:** Aztreonam IV + (levofloxacin

OI	Preferred therapy	Alternative therapy
	Empiric Therapy for Non-ICU Hospitalized Patients: An IV beta-lactam + a macrolide (azithromycin or clarithromycin) (**AII)** Preferred beta-lactams: ceftriaxone, cefotaxime, or ampicillin-sulbactam **For penicillin-allergic patients:** Levofloxacin, 750 mg IV once daily (**AII), OR** moxifloxacin, 400 mg IV once daily (AII). **Empiric therapy for ICU patients** IV beta-lactam + IV azithromycin (**AII), OR** IV beta-lactam + (levofloxacin 750 mg IV once daily **OR** moxifloxacin 400 mg IV once daily) (**AII)** **Preferred beta-lactams**: ceftriaxone, cefotaxime, or ampicillin-sulbactam **Empiric Therapy for Patients at Risk of Pseudomonas Pneumonia:** IV antipneumococcal, antipseudomonal beta-lactam + (ciprofloxacin 400 mg IV q8–12h or levofloxacin 750 mg IV once daily) (**BIII)** **Preferred beta-lactams:** piperacillin-tazobactam, cefepime, imipenem, or meropenem. **Empiric Therapy for Patients at Risk for Methicillin-Resistant Staphylococcus aureus Pneumonia:** Add vancomycin IV or linezolid (IV or PO) to the baseline regimen (**BIII).** ***Addition of clindamycin to vancomycin (but not to linezolid) can be considered for severe necrotizing pneumonia to minimize bacterial toxin production (CIII).***	750 mg IV once daily or moxifloxacin 400 mg IV once daily) **(BIII)** **Empiric Therapy for Patients at Risk of Pseudomonas Pneumonia:** IV antipneumococcal, antipseudomonal beta-lactam + an aminoglycoside + azithromycin (**BIII), OR** Above beta-lactam + an aminoglycoside + (levofloxacin 750 mg IV once daily or moxifloxacin 400 mg IV once daily) (**BIII), OR** **For penicillin-allergic patients:** Replace the beta-lactam with aztreonam (**BIII)**
Bacterial Enteric Infections: Empiric Therapy pending definitive diagnosis.	Empiric antibiotic therapy is indicated for patients with advanced HIV (CD4 count <200 cells/μL or concomitant AIDS-defining illnesses), with clinically severe diarrhea (≥6 stools per day or bloody stool) and/or accompanying fever or chills. **Empiric Therapy:** Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (**AIII)**	Ceftriaxone 1 g IV q24h (**BIII), OR** Cefotaxime 1 g IV q8h (**BIII)**

OI	Preferred therapy	Alternative therapy
Salmonellosis	Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h, if susceptible (**AIII)** **Duration of Therapy:** **For gastroenteritis without bacteremia:** CD4 count ≥200 cells/μL: 7–14 days (**BIII)** CD4 count <200 cells/μL: 2–6 weeks (**CIII)** **For gastroenteritis with bacteremia:** CD4 count ≥200/μL: 14 days (**AIII**); longer duration if bacteremia persists or if the infection is complicated (e.g., if metastatic foci of infection are present) (**BIII).** CD4 count <200 cells/μL: 2–6 weeks (**CIII)** **Secondary Prophylaxis** for: Patients with recurrent Salmonella gastroenteritis +/- bacteremia (**CIII), OR** Patients with CD4 <200 cells/μL with severe diarrhea **(CIII)**	Levofloxacin 750 mg (PO or IV) q24h **(BIII), OR** Moxifloxacin 400 mg (PO or IV) q24h (**BIII), OR** TMP, 160 mg-SMX 800 mg (PO or IV) q12h (**BIII), OR** Ceftriaxone 1 g IV q24h **(BIII), OR** Cefotaxime 1 g IV q8h (**BIII)**
Shigellosis	Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h **(AIII)** **Duration of Therapy**: Gastroenteritis: 7–10 days **(AIII)**	Levofloxacin 750 mg (PO or IV) q24h **(BIII), OR** Moxifloxacin 400 mg (PO or IV) q24h (**BIII), OR** TMP 160 mg-SMX 800 mg (PO or IV) q12h (**BIII**) **OR** Azithromycin 500 mg PO daily for 5 days **(BIII)**
Campylobacteriosis	**Mild Disease and If CD4 Count >200 cells/μL**: Withhold therapy unless symptoms persist for more than several days (**CIII)** **Mild-to-Moderate Disease (If Susceptible**): Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (**BIII), OR** Azithromycin 500 mg PO daily **(BIII)** **For Campylobacter Bacteremia**: Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (BIII) + an aminoglycoside (**BIII).** **Duration of Therapy:** Gastroenteritis: 7–10 days (**AIII)** (5 days with azithromycin) Bacteremia: ≥14 days **(BIII)** Recurrent bacteremia: 2–6 weeks (**BIII**)	**Mild-to-Moderate Disease (If Susceptible):** Levofloxacin 750 mg (PO or IV) q24h (**BIII), OR** Moxifloxacin 400 mg (PO or IV) q24h (**BIII)** **Bacteremic patients:** Add an aminoglycoside **(BIII).** ***Effective ART may reduce the frequency, severity, and recurrence of campylobacter infections*** ***Antimotility agents should be avoided (BIII).***
Bartonellosis	**Bacillary Angiomatosis, Peliosis Hepatis, Bacteremia, and Osteomyelitis:**	**Bacilliary Angiomatosis, Peliosis Hepatis, Bacteremia, And Osteomyelitis:**

OI	Preferred therapy	Alternative therapy
	Doxycycline 100 mg PO or IV q12h **(AII), OR** Erythromycin 500 mg PO or IV q6h **(AII)** **CNS Infections:** Doxycycline 100 mg +/- RIF 300 mg PO or IV q12h **(AIII)** **Confirmed Bartonella Endocarditis:** Doxycycline 100 mg IV q12h + gentamicin 1 mg/kg IV q8h for 2 weeks, then continue with doxycycline 100 mg IV or PO q12h (**BII)** **Other Severe Infections:** Doxycycline 100 mg PO or IV +/- RIF 300 mg PO or IV) q12h **(BIII), OR** Erythromycin 500 mg PO or IV q6h) +/- RIF 300 mg PO or IV q12h (**BIII)** **Duration of Therapy:** At least 3 months **(AII)**	Azithromycin 500 mg PO daily **(BIII)** Clarithromycin 500 mg PO BID (**BIII)** **Confirmed Bartonella Endocarditis but with Renal Insufficiency**: Doxycycline 100 mg IV + RIF 300 mg PO or IV q12h for 2 weeks, then continue with doxycycline 100 mg IV or PI q12h **(BII)**
Syphilis (Treponema pallidum Infection)	**Early Stage, primary and Early-Latent Syphilis):** Benzathine penicillin G 2.4 million units IM for 1 dose **(AII)** **Late-Latent Disease (>1 year or of Unknown Duration, and No Signs of Neurosyphilis):** Benzathine penicillin G 2.4 million units IM weekly for 3 doses (**AII)** **Late-Stage (Tertiary–Cardiovascular or Gummatous Disease):** Benzathine penicillin G 2.4 million units IM weekly for 3 doses (**AII**) **Neurosyphilis (Including Optic or Ocular Disease):** Aqueous crystalline penicillin G 18–24 million units per day (administered as 3–4 million units IV q4h or by continuous IV infusion) for 10–14 days (AII) +/- benzathine penicillin G 2.4 million units IM weekly for 3 doses after completion of IV therapy (**CIII)**	**Early Stage (Primary and Secondary and Early-Latent Syphilis**): **For penicillin-allergic patients** Doxycycline 100 mg PO BID for 14 days **(BII),OR** Ceftriaxone 1 g IM or IV daily for 10–14 days **(BII), OR** Azithromycin 2 g PO for 1 dose (**BII)** **Late-Latent Disease (>1 year or of Unknown Duration, and No Signs of Neurosyphilis):** **For penicillin-allergic patients** Doxycycline 100 mg PO BID for 28 days (BIII) **Neurosyphilis:** Procaine penicillin 2.4 million units IM daily **PLUS** probenecid 500 mg PO QID for 10–14 days (BII) +/- benzathine penicillin G 2.4 million units IM weekly for 3 doses after completion of above (**CIII),** **For penicillin-allergic patients:** Desensitization to penicillin is the preferred approach (**BIII);** if not feasible, ceftriaxone, 2 g IV daily for 10–14 days **(BII)**
Mucocutaneous candidiasis	**Oropharyngeal Candidiasis;** **Initial Episodes (For 7–14 Days):** Oral Therapy -Fluconazole 100 mg PO daily **(AI), OR** Topical Therapy-Clotrimazole troches, 10 mg PO 5 times daily **(BI), OR**	**Oropharangeal Candidiasis:** **Initial Episodes (For 7–14 Days):** Oral Therapy - Itraconazole oral solution 200 mg PO daily **(BI), OR**

OI	Preferred therapy	Alternative therapy
	Miconazole mucoadhesive buccal 50-mg tablet—apply to mucosal surface over the canine fossa once daily (do not swallow, chew, or crush) (**BI**) **Esophageal Candidiasis (For 14–21 Days):** Fluconazole 100 mg (up to 400 mg) PO or IV daily **(AI), OR** Itraconazole oral solution 200 mg PO daily **(AI**) **Uncomplicated Vulvo-Vaginal Candidiasis**: Oral fluconazole 150 mg for 1 dose (**AII**), **OR** Topical azoles (clotrimazole, butoconazole, miconazole, tioconazole, or terconazole) for 3–7 days (**AII)** **Severe or Recurrent VulvoVaginal Candidiasis**: Fluconazole 100–200 mg PO daily for ≥7 days **(AII), OR** Topical antifungal ≥7 days (**AII)**	Posaconazole oral suspension 400 mg PO BID for 1 day, then 400 mg daily **(BI)** Topical Therapy- Nystatin suspension 4–6 mL QID or 1–2 flavored pastilles 4–5 times daily **(BII)** **Esophageal Candidiasis (For 14–21 Days):** Voriconazole 200 mg PO or IV BID **(BI), OR** Anidulafungin 100 mg IV 1 time, then 50 mg IV daily **(BI), OR** Caspofungin 50 mg IV daily **(BI), OR** Micafungin 150 mg IV daily **(BI), OR** Amphotericin B deoxycholate 0.6 mg/kg IV daily **(BI), OR** Lipid formulation of amphotericin B 3–4 mg/kg IV daily (**BIII)** **Uncomplicated Vulvo-Vaginal Candidiasis:** Itraconazole oral solution 200 mg PO daily for 3–7 days (**BII**)
Suppressive therapy usually not recommended (BIII) unless patients have frequent or severe recurrences. **If Decision Is to Use Suppressive Therapy:** **Oropharyngeal candidiasis: Fluconazole 100 mg PO daily or three times weekly (BI), OR Itraconazole oral solution 200 mg PO daily (CI)** **Esophageal candidiasis: Fluconazole 100–200 mg PO daily (BI), OR Posaconazole 400 mg PO BID (BII)** **Vulvo-vaginal candidiasis: Fluconazole 150 mg PO once weekly (CII)**		
Cryptococcosis	**Cryptococcal Meningitis Induction Therapy (for at least 2 weeks, followed by consolidation therapy):** Liposomal amphotericin B 3–4 mg/kg IV daily + flucytosine 25 mg/kg PO QID (**AI)** **Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy):** Fluconazole 400 mg PO (or IV) daily **(AI)** **Maintenance Therapy:** Fluconazole 200 mg PO daily for at least 12 months (**AI)** **Non-CNS, Extrapulmonary Cryptococcosis and Diffuse Pulmonary Disease:** Treatment same as for cryptococcal meningitis (**BIII**) **Non-CNS Cryptococcosis with Mild to-Moderate Symptoms and Focal Pulmonary Infiltrates:** Fluconazole, 400 mg PO daily for 12 months (**BIII)**	**Cryptococcal meningitis Induction Therapy (for at least 2 weeks, followed by consolidation therapy):** Amphotericin B deoxycholate 0.7 mg/kg IV daily + flucytosine 25 mg/kg PO QID (**AI), OR** Amphotericin B lipid complex 5 mg/kg IV daily + flucytosine 25 mg/kg PO QID **(BII), OR** Liposomal amphotericin B 3-4 mg/kg IV daily + fluconazole 800 mg PO or IV daily (**BIII), OR** Amphotericin B deoxycholate 0.7 mg/kg IV daily + fluconazole 800 mg PO or IV daily (**BI), OR** Fluconazole 400–800 mg PO or IV daily + flucytosine 25 mg/kg PO QID (**BII), OR** Fluconazole 1200 mg PO or IV daily (**CII)** **Consolidation Therapy (for at least 8 weeks (AI), followed by maintenance therapy):** Itraconazole 200 mg PO BID for 8 weeks—less effective than fluconazole (CI)

OI	Preferred therapy	Alternative therapy
		Maintenance Therapy: No alternative therapy recommendation
Dose adjustments of flucytosine dose in patients with renal dysfunction. Addition of flucytosine to amphotericin B has been associated with more rapid sterilization of CSF and decreased risk for subsequent relapse. Patients receiving flucytosine should have either blood levels monitored (peak level 2 hours after dose should be 30–80 mcg/mL) or close monitoring of blood counts for development of cytopenia. Opening pressure should always be measured when an LP is performed (AII). Repeated LPs or CSF shunting are essential to effectively manage increased intracranial pressure (BIII). Corticosteroid should not be routinely used during induction therapy unless it is used for management of IRIS (AI).		
Histoplasmosis	**Moderately Severe to Severe Disseminated Disease** **Induction Therapy (for at least 2 weeks or until clinically improved):** Liposomal amphotericin B 3 mg/ kg IV daily (**AI)** **Maintenance Therapy** Itraconazole 200 mg PO TID for 3 days, then 200 mg PO BID **(AII)** **Less Severe Disseminated Disease Induction and Maintenance Therapy:** Itraconazole 200 mg PO TID for 3 days, then 200 mg PO BID **(AII)** **Duration of Therapy:** At least 12 months **Meningitis Induction Therapy (4–6 weeks):** Liposomal amphotericin B 5 mg/ kg/day **(AIII)** **Maintenance Therapy**:- Itraconazole 200 mg PO BID to TID for ≥1 year and until resolution of abnormal CSF findings **(AII)** **Long-Term Suppression Therapy:** **For patients with severe disseminated or CNS infection (AIII) after completion of at least 12 months of therapy; and those who relapse despite appropriate therapy (BIII):** Itraconazole 200 mg PO daily (**AIII)**	**Moderately severe to severely Disseminated Disease Induction Therapy (for at least 2 weeks or until clinically improved):** Amphotericin B lipid complex 3 mg/kg IV daily (**AIII), OR** Amphotericin B cholesteryl sulfate complete 3 mg/kg IV daily (**AIII)** **Maintenance Therapy or Treatment of Less Severe Disease**: Voriconazole 400 mg PO BID for 1 day, then 200 mg BID (**BIII), OR** Posaconazole 400 mg PO BID (**BIII)** Fluconazole 800 mg PO daily (**CII)** **Meningitis**: No alternative therapy recommendation Long-Term **Suppression Therapy:** Fluconazole 400 mg PO daily (**BIII)**

OI	Preferred therapy	Alternative therapy
Coccidioidomycosis	**Clinically Mild Infections (e.g., Focal Pneumonia**): Fluconazole 400 mg PO daily **(AII), OR** Itraconazole 200 mg PO BID **(BII)** **Bone or Joint Infections:** Itraconazole 200 mg PO BID (**AI**) **Severe, Non-Meningeal Infection (Diffuse Pulmonary Infection or Severely Ill Patients with Extrathoracic, Disseminated Disease):** Lipid formulation amphotericin B 3-5 mg/kg IV daily (**AIII), OR** Amphotericin B deoxycholate 0.7–1.0 mg/kg IV daily (**AII)** **Duration of therapy:** continue until clinical improvement, then switch to a triazole (**BIII)** **Meningeal Infections:** Fluconazole 400–800 mg IV or PO daily (**AII)**	**Mild Infections (Focal Pneumonia) For Patients Who Failed to Respond to Fluconazole or Itraconazole**: Posaconazole 300mg delayedrelease tablet PO BID x 1 day, then once daily (**BIII), OR•** Posaconazole 400 mg oral suspensio PO BID **(BII), OR** Voriconazole 200 mg PO BID (**BIII)** **Bone or Joint Infection:** Fluconazole 400 mg PO daily (**BI)** **Severe, Non-Meningeal Infection (Diffuse Pulmonary Infection or Severely Ill Patients with Extrathoracic, Disseminated Disease):** Add a triazole (fluconazole or itraconazole) 400 mg per day to amphotericin B therapy and continue triazole once amphotericin B is stopped (**BIII).** **Meningeal Infections:** Itraconazole 200 mg PO TID for 3 days, then 200 mg PO BID (**BII), OR** Voriconazole 200–400 mg* PO BID (**BIII), OR** Posaconazole 300 mg delayedrelease tablet PO BID x 1 day, then once daily (**CIII), OR** Posaconazole 400 mg oral suspensio PO BID (**CIII) OR** Intrathecal amphotericin B deoxycholate, when triazole antifungals are ineffective (**AIII)**
Therapy should be given for at least 12 months and usually much longer; discontinuation is dependent on clinical and serological response. Therapy should be lifelong in patients with meningeal infections because relapse occurs in 80% of HIV-infected patients after discontinuation of triazole therapy (AII).		
Cytomegalovirus (CMV) Disease	**CMV Retinitis Induction Therapy (followed by Chronic Maintenance Therapy):** **For Immediate Sight-Threatening Lesions (within 1500 microns of the fovea):** Intravitreal injections of ganciclovir (2 mg) or foscarnet (2.4 mg) for 1-4 doses over a period of 7-10 days to achieve high intraocular concentration faster (**AIII); PLUS** Valganciclovir 900 mg PO BID for 14– 21 days, then 900mg once daily (**AI):** **For Peripheral Lesions**: Valganciclovir 900 mg PO BID for 14– 21 days, then 900 mg once daily	**CMV retinitis** **For Immediate Sight-Threatening Lesions (within 1500 microns of the fovea):** Intravitreal therapy as listed in the Preferred section, plus one of the following: Alternative Systemic Induction Therapy (followed by Chronic Maintenance Therapy): Ganciclovir 5 mg/kg IV q12h for 14–21 days (**AI), OR** Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h for 14–21 days **(AI), OR** Cidofovir 5 mg/kg/week IV for 2 weeks; saline hydration before and after therapy and probenecid, 2 g PO 3 hours before dose,

OI	Preferred therapy	Alternative therapy
	(**AI)** **Chronic Maintenance**: Valganciclovir 900 mg PO daily (AI) for 3-6 months until ART induced immune recovery. **CMV Esophagitis or Colitis:** Ganciclovir 5 mg/kg IV q12h; may switch to valganciclovir 900 mg PO q12h once the patient can tolerate oral therapy (**BI**) **Duration of therapy:** 21–42 days or until symptoms have resolved (CII) **CMV Neurological Disease** Treatment should be initiated promptly Ganciclovir 5 mg/kg IV q12h + (foscarnet 90 mg/kg IV q12h or 60 mg/kg IV q8h) to stabilize disease and maximize response, continue until symptomatic improvement and resolution of neurologic symptoms (**CIII)** ***Optimize ART to achieve viral suppression and immune reconstitution (BIII).***	followed by 1 g PO 2 hours and 8 hours after the dose (total of 4 g) (**BI).** **Chronic Maintenance (for 3-6 months until ART induced immune recovery** Ganciclovir 5 mg/kg IV 5–7 times weekly **(AI), OR** Foscarnet 90–120 mg/kg IV once daily (**AI), OR** Cidofovir 5 mg/kg IV every other week with saline hydration and probenecid as above **(BI)** **CMV Esophagitis or Colitis:** Foscarnet 90 mg/kg IV q12h or 60 mg/kg q8h (BI) for patients with treatment-limiting toxicities to ganciclovir or with ganciclovir resistance, **OR** Valganciclovir 900 mg PO q12h in milder disease and if able to tolerate PO therapy **(BII),** **Duration of therapy:** 21–42 days or until symptoms have resolved (**CII)** **Mild disease**, if ART can be initiated without delay, consider withholding CMV therapy (CIII)
Herpes Simplex Virus (HSV) Disease	**Orolabial Lesions** (5–10 Days): Valacyclovir 1 g PO BID (**AIII),OR** Famciclovir 500 mg PO BID (**AIII), OR** Acyclovir 400 mg PO TID (**AIII)** **Initial or Recurrent Genital HSV (5–14 Days):** Valacyclovir 1 g PO BID (**AI), OR** Famciclovir 500 mg PO BID (**AI), OR** Acyclovir 400 mg PO TID (**AI**) **Severe Mucocutaneous HSV:** Initial therapy acyclovir 5 mg/kg IV q8h (AIII) After lesions begin to regress, change to PO therapy as above. Continue until lesions are completely healed. **Chronic Suppressive Therapy For patients with severe recurrences of genital herpes (AI) or patients who want to minimize frequency of recurrences (AI):** Valacyclovir 500 mg PO BID (AI) Famciclovir 500 mg PO BID (AI)	**Acyclovir-Resistant HSV Preferred Therapy:** Foscarnet 80–120 mg/kg/day IV in 2–3 divided doses until clinical response (**AI)** **Alternative Therapy (CIII):** IV cidofovir (dosage as in CMV retinitis),**OR** Topical trifluridine,**OR** Topical cidofovir,**OR** Topical imiquimod **Duration of Therapy:** 21–28 days or longer

OI	Preferred therapy	Alternative therapy
	Acyclovir 400 mg PO BID (AI) **Continue indefinitely regardless of CD4 cell count.**	
Varicella Zoster Virus (VZV) Disease	**Primary Varicella Infection (Chickenpox) Uncomplicated Cases (For 5–7 Days):** Valacyclovir 1 g PO TID (**AII), OR** Famciclovir 500 mg PO TID (**AII)** **Severe or Complicated Cases**: Acyclovir 10–15 mg/kg IV q8h for 7–10 days (**AIII)** May switch to oral valacyclovir, famciclovir, or acyclovir after defervescence if no evidence of visceral involvement (**BIII).** **Herpes Zoster (Shingles) Acute Localized Dermatomal:** 7–10 days; consider longer duration if lesions are slow to resolve Valacyclovir 1 g PO TID **(AII), OR** Famciclovir 500 mg TID **(AII)** **Extensive Cutaneous Lesion or Visceral Involvement:** Acyclovir 10–15 mg/kg IV q8h until clinical improvement is evident (**AII)** May switch to PO therapy (valacyclovir, famciclovir, or acyclovir) after clinical improvement (i.e., when no new vesicle formation or improvement of signs and symptoms of visceral VZV), to complete a 10–14 day course (BIII). **Progressive Outer Retinal Necrosis (PORN):** (Ganciclovir 5 mg/kg +/- foscarnet 90 mg/kg) IV q12h + (ganciclovir 2 mg/0.05mL +/- foscarnet 1.2 mg/0.05 ml) intravitreal injection BIW (**AIII)** **Initiate or optimize ART (AIII) Acute Retinal Necrosis (ARN):** (Acyclovir 10-15 mg/kg IV q8h) + (ganciclovir 2 mg/0.05mL intravitreal injection BIW X 1-2 doses) for 10-14 days, followed by valacyclovir 1g PO TID for 6 weeks (**AIII)**	**Primary Varicella Infection(Chickenpox) Uncomplicated Cases (For 5-7 Days):** Acyclovir 800 mg PO 5 times/ day (**BII)** **Herpes Zoster (Shingles) Acute Localized Dermatomal**: • 7–10 days; consider longer duration if lesions are slow to resolve Acyclovir 800 mg PO 5 times/ day (**BII)**

OI	Preferred therapy	Alternative therapy
HPV	**Patient-Applied Therapy for Uncomplicated External Warts** Podophyllotoxin (e.g., podofilox 0.5% solution or 0.5% gel): Apply to all lesions BID for 3 consecutive days, followed by 4 days of no therapy, repeat weekly for up to 4 cycles, until lesions are no longer visible (**BIII), OR** Imiquimod 5% cream: Apply to lesion at bedtime and remove in the morning on 3 nonconsecutive nights weekly for up to 16 weeks, until lesions are no longer visible. Each treatment should be washed with soap and water 6–10 hours after application **(BII**), **OR** Sinecatechins 15% ointment: Apply to affected areas TID for up to 16 weeks, until warts are completely cleared and not visible (**BIII).**	**Provider-Applied Therapy for Complex or Multicentric Lesions, or Lesions Inaccessible to Patient Applied Therapy**: Cryotherapy (liquid nitrogen or cryoprobe): Apply until each lesion is thoroughly frozen. Repeat every 1–2 weeks for up to 4 weeks, until lesions are no longer visible (**BIII),OR** Trichloroacetic acid or bichloroacetic acid cauterization: 80%–90% aqueous solution, apply to wart only, allow to dry until a white frost develops. Repeat weekly for up to 6 weeks, until lesions are no longer visible (**BIII), OR** Surgical excision (**BIII) OR** Laser surgery (**CIII)** to external or anal warts, **OR** Podophyllin resin 10%–25% in tincture of benzoin: Apply to all lesions (up to 10 cm2), then wash off a few hours later, repeat weekly for up to 6 weeks until lesions are no longer visible **(CIII).**
Hepatitis B Virus (HBV) Disease	**ART is recommended for all HIV/ HBV-co-infected patients regardless of CD4 cell count (AII).** ART regimen should include 2 drugs that are active against both HBV and HIV, such as [tenofovir 300 mg + emtricitabine 200 mg (or lamivudine 300 mg)] PO once daily (+ additional drug(s) for HIV) (**AIII).** Duration: Continue treatment lifelong ART (**CIII)**	**Patients who refuse or are Unable to Take ART or Who Are HIV Long-Term Non-Progressors**: **HBV treatment is indicated for patients with elevated ALT and HBV DNA >2,000 IU/ mL significant liver fibrosis, advanced liver disease or cirrhosis (AI).** Peginterferon alfa-2a 180 µg SQ once weekly for 48 weeks (**CIII), OR** Peginterferon alfa 2b 1.5 µg/kg SQ once weekly for 48 weeks (CIII). ***If Tenofovir Cannot Be Used as Part of HIV/HBV Therapy (Because of Current or High Risk of Renal Dysfunction):*** ***Use a fully suppressive ART regimen without tenofovir, and with the addition of entecavir (dose adjustment according to renal function) (BIII).***
Progressive Multifocal Leukoencephalopathy (PML) (JC Virus Infections	No specific antiviral therapy for JC virus infection. Treatment approach is to reverse the immunosuppression caused by HIV. Initiate ART immediately in ART naive patients **(AII).**	Corticosteroids may be used for PML-IRIS characterized by contrast enhancement, edema or mass effect, and with clinical deterioration (BIII)

OI	Preferred therapy	Alternative therapy
Isosporiasis	**Acute Infection:** TMP-SMX (160 mg/800 mg) PO (or IV) QID for 10 days **(AII), OR** TMP-SMX (160 mg/800 mg) PO (or IV) BID for 7–10 days (**BI)** Can start with BID dosing first and increase daily dose and/or duration (up to 3–4 weeks) if symptoms worsen or persist (**BIII)** IV therapy may be used for patients with potential or documented mal-absorption. **Chronic Maintenance Therapy (Secondary Prophylaxis):** In patients with CD4 count <200/ µL, TMP-SMX (160 mg/800 mg) PO TIW (**AI)**	**Acute infection:** Pyrimethamine 50–75 mg PO daily + leucovorin 10–25 mg PO daily (**BIII), OR** Ciprofloxacin 500 mg PO BID for 7 days (CI) as a second line alternative. **Chronic Maintenance Therapy (Secondary Prophylaxis):** TMP-SMX (160 mg/800 mg) PO daily or (320 mg/1600 mg) TIW **(BIII**) Pyrimethamine 25 mg PO daily + leucovorin 5–10 mg PO daily **(BIII)** Ciprofloxacin 500 mg TIW **(CI)** as a second-line alternative

Table 16: Criteria for discontinuing and restarting OI prophylaxis for adults and adolescents with HIV

OI	Criteria for discontinuing primary prophylaxis	Criteria for restarting primary prophylaxis	Criteria for discontinuing secondary prophylaxis/chronic maintenance therapy	Criteria for restarting secondary prophylaxis/chronic maintenance
PCP	CD4 count >200 cells/μL for >3 months in response to HAART **(AI)**	CD4 count <200 cells/μL **(AIII)**	• ≥CD4 count increased from <200 cells/μL to >200 cells/μL for 3 months in response to HAART **(BII)** • If PCP is diagnosed when CD4 count >200 cells/μL, prophylaxis should probably be continued for life regardless of CD4 count rise in response to HAART **(BIII)**	CD4 count <200 cells/μL **(AIII)**, **OR** PCP recurred at a CD4 count >200 cells/μL **(CIII)**
Toxoplasma gondii encephalitis	CD4 count increased to >200 cells/μL for >3 months in response to ART **(AI)**	CD4 count <100 to 200 cells/μL (**AIII)**	Successfully completed initial therapy, remain free of signs and symptoms of TE, **and** CD4 count >200 cells/μL for >6 months in response to ART **(BI).**	CD4 count <200 cells/μL (**AIII)**
Micro-sporidiosis	Not applicable	Not applicable	-No signs and symptoms on non-ocular microsporidiosis and CD4 count >200 cells/μL for >6 months in response to HAART **(BIII)** -Patients with ocular microsporidiosis should be on therapy indefinitely regardless of CD4 count **(BIII)**	No recommendation
Disseminated MAC	≥CD4 count >100 cells/μL for 3 months in response to HAART **(AI)**	CD4 count <50 cells/μL **(AIII)**	If the following criteria **(BII)** is fulfilled: • ≥Completed 12 months therapy; **and** • No signs and symptoms of MAC; and • ≥Have sustained (6 months) CD4 count>100 cells/μL in response to HAART	CD4 count <100 cells/μL **(AIII)**

OI	Criteria for discontinuing primary prophylaxis	Criteria for restarting primary prophylaxis	Criteria for discontinuing secondary prophylaxis/chronic maintenance therapy	Criteria for restarting secondary prophylaxis/chronic maintenance
Salmonellosis	Not applicable	Not applicable	Resolution of Salmonella infection and after response to ART with sustained viral suppression and CD4 counts >200 cells/μL (**CII)**	Not recommended
Bartonellosis	Not applicable	Not applicable	If the following criteria is fulfilled **(CIII)**: • Received 3–4 months of treatment • ≥CD4 count >200 cells/μL for 6 months	No recommendation
Mucosal candidiasis	Not applicable	Not applicable	If used, reasonable to discontinue when CD4 count >200 cells/μL **(CIII)**	No recommendation
Cryptococcal meningitis	Not applicable	Not applicable	If the following criteria is fulfilled **(BII)**: • Completed initial (induction and consolidation) therapy, **and** • Received at least 1 year of maintenance therapy, and • Remain asymptomatic of cryptococcal infection, **and** • CD4 count ≥100 cells/μL for >3 months	CD4 count <100 cells/μL **(AIII)**
Histoplasma capsulatum	If used, CD4 count >150 cells/μL for 6 months on HAART **(BIII)**	For patients at high risk for acquiring histoplasmosis, restart at CD4 count 150 cells/μL **(CIII)**	If the following criteria is fulfilled **(AI)**: ≥Receive itraconazole for > 1 year **and** negative blood cultures and ≥CD4 count >150 cells/μL for 6 months in response to HAART **and** Serum *Histoplasma* antigen <2	≤CD4 count 150 cells/μL **(BIII)**
Coccidioidomycosis	CD4 count ≥250 cells/μL and with viral suppression while on ART (**CIII)**	If used, restart at CD4 count <250 cells/μL **(BIII)**	**Patients with focal coccidioidal pneumonia (CIII):** - Clinically responded to 6 months of antifungal therapy - CD4 count ≥250 cells/μL with viral suppression while on HAART Receiving HAART Suppressive therapy	No recommendation

OI	Criteria for discontinuing primary prophylaxis	Criteria for restarting primary prophylaxis	Criteria for discontinuing secondary prophylaxis/chronic maintenance therapy	Criteria for restarting secondary prophylaxis/chronic maintenance
			should be continued indefinitely, even with increase in CD4 count on HAART for patients with diffuse pulmonary **(AIII)**, disseminated **(AIII)**, or meningeal diseases **(AII)** • Should continue monitoring for recurrence with serial chest radiographs and coccidioidal serology every 6-12 months.	
CMV retinitis	Not applicable	Not applicable	-CD4 count >100 cells/μL for at least 3–6 months in response to HAART **(BII)** -Discontinue after consultating with an ophthalmologist, taking into account magnitude and duration of CD4 count increase, anatomic location of the lesions, vision in the contralateral eye, and the feasibility of regular ophthalmologic monitoring **(BII)** -Routine (every 3 months) ophthalmologic follow-up for early detection of relapse or immune restoration uveitis (**AII)**	CD4 count <100 cells/μL (**AIII)**
Isospora belli	Not applicable	Not applicable	Sustained increase in CD4 count to >200 cells/μL for >6 months in response to HAART and without evidence of *I. belli* infection **(BIII)**	No recommendation

Appendix

Appendix 4A: CO-TRIMOXAZOLE DESENSITIZATION AND SULFONAMIDE ALLERGY

Co-trimoxazole is the preferred antibiotic for prophylaxis and treatment of several common OIs. Most patients who report a non-severe allergic reaction to this drug or other sulfonamide-based drugs can be successfully 'desensitised', allowing them to take co-trimoxazole without adverse effects. However***, desensitization should not be attempted if the prior reaction included hepatitis, aseptic meningitis, or a severe hypersensitivity reaction (marked by high fever, severe rash, or mucosal involvement suggestive of Stevens-Johnson syndrome)***. An example desensitization protocol is presented in the table below.

Sample Co-trimoxazole Desensitization Protocol[9]

Use commercially available paediatric suspension (containing TMP 8 mg and SMX 40 mg per mL [40 mg/200 mg per 5 mL]), followed by double-strength tablets, as follows:

Days	Co-trimoxazole dosage	Volume or tablet
1–3	8 mg/40 mg	1 mL
4–6	16 mg/80 mg	2 mL
7–9	40 mg/200 mg	5 mL (or 1/2 single strength tablet)
9–12	80 mg/400 mg	1/2 double strength tablet (or 1 singlestrength tablet)
13 and thereafter	160 mg/800 mg	1 double strength tablet
*Note**: These day ranges are approximate; patients can be advanced more quickly or more slowly depending on their reactions to the dosages.***		

In the event of mild reaction (e.g., mild morbilliform rash without fever, systemic symptoms, or mucosal involvement), the dose can be reduced to the last tolerated step or continued at the same dosage for an additional day, while simultaneously treating the rash or reaction. Antihistamines or antipyretics may be used to treat symptoms of mild reactions. If the reaction diminishes, the patient may advance to the next dosage (consider more gradual increase of dosages); if the reaction worsens or if systemic symptoms develop, co-trimoxazole should be discontinued.

In the event of severe reaction (e.g., hepatitis; aseptic meningitis; or a severe hypersensitivity reaction including high fever, severe rash, or mucosal involvement suggestive of StevensJohnson syndrome), the desensitization regimen should be discontinued and the patient should be treated appropriately for the reaction. The patient should never be re-challenged with cotrimoxazole.

[9] United States AIDS Education and Training Centers National Resource Center. Sulfa desensitization. In guide for HIV/AIDS clinical care. Washington, DC: Health Resources and Services Administration; 2012. Available from: http://www.aidsetc.org/aidsetc?page=cg-1002_sulfa_densisitization.

5 ELIMINATION OF MOTHER TO CHILD TRANSMISSION OF HIVAND CONGENITAL SYPHILIS

The OECS has committed to the elimination initiative aimed at reducing the vertical transmission of HIV and the incidence of congenital syphilis (including stillbirths). This section addresses HIV in pregnancy and prevention and treatment of congenital syphilis.

5.1 HIV in pregnancy- Prevention of mother to child transmission

Management of HIV in pregnancy is aimed at providing ARVs to the HIV positive mother for her own health and preventing infection in the exposed infant. Prevention of Mother to Child Transmission (PMTCT) refers to interventions aimed at preventing transmission from the HIV infected mother to her infant during pregnancy, labour, delivery or breastfeeding.

5.1.1 HIV Testing in pregnant women

Prevention of mother to child transmission commences with the establishment of HIV status of the pregnant mother. In this regard, the OECS recommends that pregnant women should be offered HIV test at the time of antenatal care enrolment. If the HIV test is negative, a repeat test should be repeated in the third trimester. Preferably, HIV testing and counselling should be offered to couples (Couples HTC). With this approach, HIV testing, provision of results and counselling takes place simultaneously with both partners, thereby creating the opportunity for mutual disclosure, support to couples and the development of a joint HIV risk management plan. HIV testing should be conducted according to national algorithm, accompanied by pre and post-test counselling and aligned to the 5 "Cs" of HIV testing.

Majority of the pregnant women will be tested in an antenatal setting. However, some women will present for care during labour with an unknown HIV status. These women should be tested immediately using a rapid HIV test. In case of a positive result from a rapid HIV test, it should be assumed that the woman is truly HIV-infected and therefore PMTCT strategies should be immediately undertaken. Time does not allow for repeat confirmatory testing at that point, though it should still be performed post-delivery.

5.1.2 Management of the HIV pregnant woman

All pregnant women should be offered ARV as soon as possible, regardless of CD4 count or disease stage and maintained on lifelong ART. This approach known as Option B Plus has significant advantages over options A and B previously implemented and will accelerate the achievement of elimination of mother to child transmission and new paediatric infections in the OECS.

ART should be initiated in all pregnant and breastfeeding women living with HIV, regardless of WHO clinical stage and at any CD4 cell count and continued lifelong

Several scenarios are described in managing the pregnant woman and exposed infant, depending primarily on the time the pregnant woman accesses treatment in pregnancy. Five scenarios are described and include:

A. Pregnant women already on HAART
B. Women accessing ART for the first time during pregnancy

C. ARV Naïve HIV positive pregnant women presenting in labour
D. Pregnant women who decline to take HAART
E. Pregnant women who received no ART for PMTCT, either pre-partum or during labour.

The details of management of each scenario is described in summary **table 17.**

Table 17: Summary of PMTCT recommendations by scenario

Scenario	Mother	Infant*
A: Woman already on HAART pre-pregnancy	Continue with ART regimen during pregnancy, labour and delivery, and post-partum.	Daily AZT or NVP until 6 weeks of age
B: Woman initiating HAART during pregnancy	**Initiate HAART immediately:** **-Preferred regimen:** TDF (300mgs) +FTC (200mgs) + EFV (600mgs)- *Available in the OECS as a fixed dose combination pill of Atripla.* TDF (300mgs) +3TC (300mgs) + EFV (600mgs) -**Alternative regimens**: AZT (300mgs)+ 3TC (300mgs) + NVP(200mgs) AZT (300mgs)+ 3TC (300 mgs) + EFV(600mgs) **Second Line – 2NRTIs + PI** TDF (300mgs)+3TC(300)+ LPV/r (600mgs/150mgs)* TDT (300mgs) +FTC (200mgs) +LPV/r) 600mgs/150mgs) **LPV/r – there is low placental transfer and therefore recommended at an increased dose of 600mgs/150mgs twice daily.* *-Can substitute AZT for TDF in the mother's HAART regimen if TDF is contra-indicated (e.g., pre-existing renal disease)* *-Use EFV instead of NVP where CD4 counts are >250/mm³ due to a significantly higher risk of liver toxicity* *-PI is indicated as a second line.*	Daily AZT or NVP until 6 weeks of age
C. HIV-infected woman without any prenatal ART who presents in labour	Single-dose NVP(200mg) immediately; **PLUS** AZT (300mgs)/3TC (300mgs) three hours after sdNVP In the case of prolong labour repeat sdNVP(200mgs) after 24 hours Follow up with Dimune (AZT 300mgs+3TC 300mgs) twice daily for one week's post-partum.	**Dual prophylaxis** – AZT- twice daily **PLUS** NVP once daily for 6 weeks.

	Initiate HAART as soon as possible.	
D. Woman of unknown HIV status who presents in labour	Test for HIV (ideally using rapid test): If positive, manage as scenario C outlined immediately above Do not wait for confirmatory testing before proceeding with PMTCT interventions; assume she is HIV infected based upon one positive test result from rapid testing (but confirm after delivery). Initiate HAART as soon as possible.	Dual prophylaxis – AZT- twice daily **PLUS** NVP once daily for 6 weeks.
E: HIV-infected woman who has received no ART for PMTCT, either pre-partum or during labour	N/A -Have mother assessed post-partum for HAART need and enrolment into HIV care. Initiate HAART as soon as possible.	**Dual prophylaxis** – AZT- twice daily **PLUS** NVP once daily for 6 weeks. - Give AZT and NVP within 3 days of birth, otherwise it is not effective

Failure of treatment regimen

In the event of confirmed or suspected failure to first line therapy, considerations should be given to initiating patient on a second line regimen and similarly on third line is suspected second line failure. The recommended regimen is outlined in table 18.

Table 18: Recommend second and third line regimen for treatment failure

Population	First line regimen	Second line regimen	Third line regimen
Pregnant or breastfeeding women	2 NRTIs + EFV	2NRTIs + ATV/r or LPV/r **OR** 2NRTIs + DRV/r	DRV/r+ DTG(RAL) ± 1–2 NRTIs

5.1.3 Management of Exposed Infants

AZT or NVP is recommended for six weeks for infants of mothers who have been stable on ART prior to pregnancy and who have initiated ART during the antenatal period. In cases where the infant is considered high risk, **dual therapy with AZT and NVP** is recommended. High-risk infants are defined as those born to women with:

- established HIV infection who have received less than four weeks of ART at the time of delivery; **or**
- established HIV infection with viral load >1000 copies/mL in the four weeks before delivery, if viral load measurement available**; or**
- with incident HIV infection during pregnancy or breastfeeding; **or**
- identified for the first time during the postpartum period, with or without a negative HIV test prenatally.

Management of the exposed infant is outlined in summary table 7.1. Daily dosing of AZT or NVP and in cases of dual therapy is recommended for the exposed infant. Dosing recommendations are presented in tables 19 and 20.

*Table 19: NVP dosing for infants, birth to six weeks of age**

Infant birth weight	NVP daily dosing
Birth weight <2,000 g**	2 mg/kg per day, once daily**
Birth weight 2,000–2,499 g	10 mg once daily
Birth weight ≥ 2,500 g	15 mg once daily
***Based on the dosing required to sustain exposure in the infant of >100 ng/ml with the least dose changes.**	
****** Low birth weight infants should receive mg/kg dosing; suggested starting dose is 2 mg/kg once daily. Therapeutic drug monitoring is recommended.**	

Table 20: AZT dosing for infants, birth to six weeks of age

Infant gestational age at birth	AZT dosing
< 30 weeks' gestation at birth	2 mg/kg/dose PO (or 1.5 mg/kg/dose IV) started as soon after birth as possible, preferably within 6–12 hours of delivery, then every 12 hours, advanced to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours after age 4 weeks
30 – 35 weeks' gestation at birth	2 mg/kg/dose PO (or 1.5 mg/kg/dose IV), started as soon after birth as possible, preferably within 6–12 hours of delivery, then every 12 hours, advanced to 3 mg/kg/dose PO (or 2.3 mg/kg/dose IV) every 12 hours at age 15 days
> 35 weeks' gestation at birth	4 mg/kg/dose PO twice daily, started as soon after birth as possible and preferably within 6–12 hours of delivery (or, if unable to tolerate oral agents, 3 mg/kg/dose IV, beginning within 6–12 hours of delivery, then every 12 hours)

5.1.4 Monitoring Antiretroviral Therapy during Antenatal Care

Women on antiretroviral therapy should return for weekly visits for at least the first 2 weeks, then move to one visit every 4 weeks until 38 weeks gestation when weekly visits should resume. Patients who are experiencing side effects, problems with adherence or other issues, such as hyper-emesis, should be in more frequent contact with their clinics. At each follow-up visit, providers should assess adherence to ARVs as well as associated adverse reactions and provide interventions or support as indicated. Laboratory investigations (such as liver function- and haemoglobin tests) for adverse effects should be performed 2 weeks after starting antiretroviral therapy; haemoglobin should be monitored monthly thereafter. Patients should be given CD4 count- and viral load monitoring tests as recommended for non-pregnant HIV-infected adults. See details in table 3.5 in the section of the guidelines on ARV management for adults and adolescents. At each follow-up visit, providers should determine patient adherence to safer sex practices and provide interventions or support as indicated.

5.1.5 Considerations on the Model of Infant Delivery

Elective caesarean section, when performed before the onset of labour or membrane rupture, has been associated with reduced MTCT among women not receiving HAART. If the pregnant woman is not on HAART prior to delivery, or is on HAART but is known to have a viral load >1,000 copies/mL at the time of delivery, elective caesarean section can be considered to reduce the risk of MTCT. However, clinicians must take into account the potential risks of elective caesarean section, as this procedure is generally associated with higher levels of morbidity and mortality, as compared with vaginal deliveries.

5.1.6 Other Management considerations of the HIV-infected Woman in Labor

Labor for pregnant women with HIV infection should be managed in the same way as uninfected women's labor. Adherence to universal precautions is important, such as the use of protective gear (e.g., gowns, gloves, boots, protective eyewear), safely use and dispose of sharps, sterilise equipment, and safely dispose of contaminated materials. Cervical examinations should only be performed when absolutely necessary and invasive procedures including episiotomy should be conducted only when indicated with minimise the use of forceps or vacuum extractors. At all times, avoid artificially rupturing the membranes unless obstetrically indicated. Similarly, avoid 'milking' the umbilical cord, prolong rupture of membranes (rupture of the membranes for more than 6 hours is associated with an increased risk of MTCT) and using straight suture needles if possible to reduce the risk of needlestick. Clamp and cut the umbilical cord immediately after delivery and, if possible, avoid using a scalpel to cut the umbilical cord and use special care in handling the placenta.

Other management considerations of the HIV-exposed Infant

Using a glove, the HEI should receive a bath as soon as possible after delivery with soap and water. Routine post-delivery care should be administered, including weighing and measuring the infant, vitamin K prophylaxis, and eye care. Cord blood samples for blood group and Hb electrophoresis screen should be collected as usual. Unnecessary invasive procedures should be avoided and required vaccination administered.

5.1.7 HIV and Breastfeeding

Breast feeding increases the risk of HIV transmission**.** Breastfeeding by HIV-infected mothers is formula, and the social acceptability of formula feeding. However, some mothers may want to, or feel compelled to breastfeed for a variety of reasons. In these cases the following is recommended to reduce the risk of MTCT via breastfeeding:

- Continue exclusive breastfeeding for the first 6 months of life, meaning that the infant receives only breastmilk without any supplemental or mixed feedings (i.e., no water, tea, porridge).
- Gradually introduce mixed feedings thereafter, concomitant with breastfeeding for the first 12 months of life or until a nutritionally adequate and safe diet without breastmilk can be provided. Because rapid weaning has also been associated with HIV transmission to the infant and maternal mastitis, encourage gradual weaning over 1 month.

- ❖ For infants and mothers on antiretroviral prophylaxis for PMTCT, continue their ARVs for 1 week following complete weaning.
- ❖ Unless the mother is on HAART, give the infant NVP daily throughout the entire period of breastfeeding, stopping 1 week after complete weaning.

5.1.8 HIV testing

Infants of HIV-infected mothers are termed 'HIV-exposed infants' (HEI) until their HIV status is definitively established. HEIs require early testing with NAAT using DNA PCR DBS for establishing HIV diagnosis. See figure 6.1in section on ARV therapy in children, for detailed algorithm on diagnosis of HIV in infants and children.

5.1.9 Co-Trimoxazole prophylaxis

Co-trimoxazole is an antimicrobial medication that can prevent bacterial infections as well as *Pneumocystis* pneumonia (PCP) and toxoplasmosis. *PCP is a leading cause of death in HIV-infected infants*. Long-term Co-trimoxazole prophylaxis has resulted in fewer opportunistic infections, improvements in quality of life and increased survival in patients with HIV. The benefits of providing Co-trimoxazole prophylaxis to *all* exposed infants far outweighs the risks associated with taking the medicine. Co-trimoxazole contains two medications: Trimethoprim and Sulphamethoxazole (sometimes referred to as TMP-SMX, Septrin or CTX). CTX suspension formulation is Trimethoprim 200mg and Sulphamethoxazole 40mg TMP/ 200mg SMX per 5ml.

> Co-trimoxazole prophylaxis is recommended to begin for all HIV-exposed infants starting at 4- 6 weeks of age (or as soon as possible thereafter) until breastfeeding has stopped and the infant has been diagnosed as HIV-negative.

The dose of Co-trimoxazole for infants is **5mg/kg (calculated on the TMP of co-trimoxazole)** and the required dose should be calculated at each monthly visit. Simplified once daily dosing is presented in Table 21.

Table 21: Simplified dosing of Co-trimoxazole

Drug	Drug Strength of tablet or oral liquid (mg or mg/5ml)	Number of tablets or millilitres by weight band once daily					Strength of adult tablet (mg)	Number of tablets by weight band
Weight		3-5.9kg	6-9.9kg	10-13.9kg	14-19.9kg	20-24.9kg		25-34.9kg
Co-trimozaxole	Suspension 200/40 per 5 ml	2.5ml	5ml	5ml	10ml	10ml	-	-
	Tablet 100/20mg	1	2	2	4	4	-	-
	Tablet 400/80mg	-	0.5	0.5	1	1	400/80mg	2
	Tablet 800/160mg	-	-	-	0.5	0.5	800/160mg	1

5.1.10 Immunizations for HIV-exposed Infants (HEIs)

Vaccination for the HIIV exposed infants should follow the OECS recommended vaccination for infants and children with the following exceptions:

- BCG is contra-indicated in the HIV positive infant. It should be given until the infants HIV status is known. Once HIV infection is rules out, BCG can be administered.
- MMR and Varicella vaccines should not be administered to children who are severely immunocompromised (CD4% less than 15%).
- Inactivated Polio Vaccine (IPV) should be administered instead of Oral Polio Vaccine (OPV)
- Pneumococcal vaccination (polysaccharide PPSV 23-valent, and/or conjugate PCV 7-valent) is recommended for HIV-infected infants and children given their vulnerability to pneumococcal pneumonia. See http://www.cdc.gov/mmwr/pdf/rr/rr5811.pdf for details regarding paediatric pneumococcal vaccination options.

5.1.11 Follow-up Care of the HIV-infected Woman Post-partum and exposed infant.

Mother and infant should return for follow-up care at 4–6 weeks post-partum and linkages made for mother and infant HIV care with referral to the HIV clinic. Special attention should be paid in ensuring that the mother- baby pair has adequate ARVs and attend HIV clinic for timely follow up. Mothers should be educated on breast care and feeding. Family planning counselling should be initiated and referrals for follow-up services should be made, if indicated. Patient education, including nutrition and management of HIV, should be offered to the mother and her family; where applicable, referrals to a nutrition specialist and a social worker should be made.

Growth failure is a prominent feature of HIV infection. Nutritional assessment is important both as a diagnostic marker (when HIV status is unknown) and should be done at every visit beginning at birth or thereafter. The main goal is to prevent malnutrition, failure to thrive and to maximise growth in infected children.

5.2 HIV Positive Women and Reproductive Health Choices

Fertility is not affected by HIV infection; lower conception rates may occur as a result of behavioral change, existing sub fertility, low body mass index, AIDS, and inter current illness particularly pulmonary tuberculosis. Dual protection, the simultaneous use of an effective contraception method with consistent condom use, has been advocated to reduce the risk of unplanned pregnancy, horizontal transmission of HIV to a non-infected partner, transmission of resistant virus to a partner with HIV infection, and the risk of acquisition of other STIs including human papillomavirus (HPV). An overview of the various family planning options is presented in table 22.

Table 22: Overview of family planning options

Method	Notes for the HIV-positive Woman
Condoms (male & female) Emergency Contraception	Dual protection, the simultaneous use of an effective contraception method with consistent condom use, is recommended for effective prevention of unplanned pregnancy and HIV sexual transmission. Condoms are recommended whenever the patient is not actively trying to conceive; it provides benefit of protection against other STIs. Patients require adequate training in the application, storage and removal of condoms. Women using condoms alone for contraception must be advised about emergency contraception. The OECS recommend 1.5 mg single dose of Levonorgestrel taken within the first 72 hours of unprotected sexual intercourse to be effective.
Intrauterine device (copper-bearing or hormonal IUDs)	Most women can safely use the IUD. For HIV positive women, screening should be done for STIs. IUDs are contraindicated in the presence of STIs, PID, and cancer of the female reproductive organs or pelvic tuberculosis. For further information see WHOs decision making tool for Family Planning Clients and Providers.
Female sterilization	Women who are infected with HIV, have AIDS, or are on antiretroviral therapy can safely undergo female sterilization with proper informed consent. Special arrangements are needed to perform female sterilization on a woman with AIDS to prevent sepsis. Delay the procedure if she is currently ill with AIDS-related illness.

5.2.1 ARV and Drug Interactions with Contraceptives

The primary concern in HIV-infected women should be focused on effects the antiretroviral agents may have on the clinical effectiveness of available contraceptive choices (Table 1.15). Therefore, any non-barrier contraceptive should be used in conjunction with a barrier (condom) device, not only for pregnancy prevention but also to prevent HIV transmission. In addition, contraceptive agents may alter the pharmacokinetics and efficacy of certain antiretrovirals. Virologic responses to antiretroviral therapy should be monitored closely when used in combination with nonbarrier contraceptives. Pharmacokinetic interaction should be considered when combined oral contraceptives and antiretrovirals are used together and certain agents should not be used concurrently and presented in table 23.

Table 23: ARV Drug Interactions with contraceptives

Antiretroviral Agent	Interaction with Contraceptives or Recommendations
NRTIs	No effect
NNRTs Efavirenz	Progestin levels markedly decreased Decreased exposure with implant Effectiveness of emergency contraception may be diminished Barrier method should be used
NNRTs- Nevirapine	Additional methods recommended; alternative methods can be considered. No dose adjustment needed
PIs- Lopinavir/ritonavir	Additional methods recommended; alternative methods can be considered
PIs Ritonavir	Use alternative contraceptive method

Source Ouellet 1998; Mildvan 2002; Chu 2005; Anderson 2011; El-Ibiary 2008; Crauwels 2009; DHHS Perinatal

5.3 Congenital Syphilis

Congenital Syphilis can be prevented with effective identification of syphilis in pregnant women. As per MCH guidelines in OECS there should be routine serologic screening of pregnant women during the first prenatal visit, in the third trimester and at delivery if at risk. There is no need for routine screening of newborn sera or umbilical cord blood.

5.3.1 Syphilis in Neonates <30 days of age

Clinical signs and symptoms, evaluation and treatment is described in table 24.

Table 24: Probable scenarios, Evaluation and Treatment of Neonates <30 days of age.

Congenital Syphilis	Clinical Signs and symptoms	Recommended Evaluation	Treatment	Follow up
Scenario 1: Proven or highly probable congenital syphilis	Neonate with: abnormal physical examination, consistent with congenital syphilis. A serum quantitative nontreponemal serologic titer that is fourfold higher than the mother's titer; A positive darkfield test or PCR of lesions or body fluid(s).	CSF analysis for VDRL. Cell count, and protein. CBC, differential and platelet count. Other tests as clinically indicated (e.g., long-bone radiographs, chest radiograph, liver-function tests, neuroimaging, ophthalmologic examination, and auditory brain stem response).	**Aqueous crystalline penicillin G** 100,000–150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days **OR** **Procaine penicillin G** 50,000 units/kg/dose IM in a single daily dose for 10 days	All neonates with reactive nontreponemal tests should receive: Examination and serologic testing (i.e., a nontreponemal test) every 2–3 months until the test becomes nonreactive. In the neonate who was not treated because congenital syphilis was considered less likely or unlikely, nontreponemal antibody titers should decline by age 3 months and be nonreactive by age 6 months, indicating that the reactive test result was caused by passive transfer of maternal IgG antibody. At 6 months, if the nontreponemal test is nonreactive, no further evaluation or treatment is needed; if the nontreponemal test is still reactive, the infant is likely to be infected and should be treated. Treated neonates that exhibit persistent nontreponemal test titers by 6–12 months should be re-evaluated through CSF examination and managed in consultation with an expert. Retreatment with a 10-day course of a penicillin G regimen may be indicated. Neonates with a negative nontreponemal test at birth and whose
Scenario 2: Possible Congenital Syphilis	Neonate with has a normal physical examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold the maternal titer and one of the following: Mother was not treated, inadequately treated, or has no documentation of having received treatment. or Mother was treated with erythromycin or a regimen other than those recommended in these guidelines (i.e., a nonpenicillin G regimen). or Mother received recommended treatment <4 weeks before delivery.	CSF analysis for VDRL, cell count, and protein. CBC, differential, and platelet count. Long-bone radiographs A complete evaluation is not necessary if 10 days of parenteral therapy is administered, although such evaluations might be useful. For instance, a lumbar puncture might document CSF abnormalities that would prompt close follow-up. Other tests (e.g., CBC, platelet count, and bone radiographs) can be performed to further support a diagnosis of	**Aqueous crystalline penicillin G** 100,000–150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days Or **Procaine penicillin G** 50,000 units/kg/dose IM in a single daily dose for 10 days or **Benzathine penicillin G** 50,000 units/kg/dose IM in a single dose	

Congenital Syphilis	Clinical Signs and symptoms	Recommended Evaluation	Treatment	Follow up
		congenital syphilis		mothers were seroreactive at delivery should be retested at 3 months to rule out serologically negative incubating congenital syphilis at the time of birth. Treponemal tests should not be used to evaluate treatment response because the results are qualitative and passive transfer of maternal IgG treponemal antibody might persist for at least 15 months. Neonates whose initial CSF evaluations are abnormal should undergo a repeat lumbar puncture approximately every 6 months until the results are normal. A reactive CSF Venereal Disease Research Laboratory (VDRL) test or abnormal CSF indices that persist and cannot be attributed to other ongoing illness requires retreatment for possible neurosyphilis and should be managed in consultation with an expert.
Scenario 3: Congenital Syphilis less likely	Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold the maternal titer and both of the following are true: Mother was treated during pregnancy, treatment was appropriate for the stage of infection, and treatment was administered > 4 weeks before delivery and Mother has no evidence of reinfection or relapse.	No evaluation is recommended	**Benzathine penicillin G** 50,000 units/kg/dose IM in a single dose*	
Scenario 4: Congenital Syphilis unlikely	Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold the maternal titer and both of the following are true: Mother's treatment was adequate before pregnancy and Mother's nontreponemal serologic titer remained low and stable (i.e., serofast) before and during pregnancy and at delivery (VDRL <1:2; RPR <1:4).	No evaluation is recommended	No treatment is required, but infants with reactive nontreponemal tests should be followed serologically to ensure the nontreponemal test returns to negative (see Follow-Up). Benzathine penicillin G 50,000 units/kg as a single IM injection might be considered, particularly if follow-up is uncertain and the neonate has a reactive nontreponemal test.	

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

5.3.2 Syphilis in Infants and Children (aged >1month) with Congenital Syphilis

Any child with suspected congenital syphilis should receive full evaluation which includes CSF analysis for VDRL, cell count, and protein, CBC, differential, and platelet count and other tests as clinically indicated (e.g., long-bone radiographs, chest radiograph, liver function tests, abdominal ultrasound, ophthalmologic examination, neuroimaging, and auditory brain-stem response). Treatment is detailed in table 25 below.

Table 25: Treatment of syphilis in infants and children >1 month and congenital syphilis

Recommended regimen

- Aqueous crystalline penicillin G 200,000–300,000 units/kg/day IV, administered as 50,000 units/kg every 4–6 hours for 10 days.
- After the 10 days course, consider a single dose of benzathine penicillin G 50,000 units/kg IM up to the adult dose of 2.4 million units in a single dose. *This provides more comparable duration of treatment in those who have no clinical manifestations and normal CSF.*
- *IF* **There are no clinical manifestations of congenital syphilis and the evaluation (including the CSF examination) is normal- Treat with benzathine penicillin G, 50,000 U/kg IM X 3 weekly doses.**

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf.

Other management considerations for congenital syphilis

There should be follow up examinations and serologic testing every 3 months until the test becomes nonreactive or the titer has decreased fourfold. In cases where titers increase for more than 2 weeks or there is no fourfold decrease after 12–18 months, re-evaluate the infant or child (e.g., through CSF examination). Abnormal initial CSF evaluations will require a repeat lumbar puncture approximately every 6 months until the results are normal. Treat for neurosyphilis in cases where after 2 years, abnormal CSF indicies persist. After 2 years of follow-up, a reactive CSF VDRL test or abnormal CSF indices that persists. Infants and children with penicillin allergy should be desensitised and treated.

6 ANTIRETROVIRAL THERAPY IN CHILDREN

HIV disease progresses faster in children infected with HIV through perinatal transmission underscoring the need for early diagnosis and treatment. The increased access to early infant diagnosis and the simplification of paediatric HAART regimens in the OECS has enhanced the management and prognosis for children infected with HIV. Children who are sexually active or victims of sexual assault can also acquire HIV infection. These guidelines emphasize the importance of using potent first line regimens, the impact of single dosing and use of fixed dose combinations on adherence and the use of an appropriate non- thymidine analogue as first line in preserving AZT as a potential second line. Additionally, harmonization of ARVs for older children with FDCs used for adults is recommended. Optimizing first-line ART in children is important to achieve effective and rapid control of viral replication in the context of high viral load and rapid infant growth.

6.1 History of Paediatric HIV transmission

Transmission from mother to infant is the main source of HIV infection in infants and children. The infant is at risk of becoming infected in utero, during labour, delivery, and during breastfeeding. In the absence of intervention, approximately 25-30% of infants born to HIV infected mothers will acquire HIV. Further the greatest risk of transmission occurs during labour and delivery because as the infant passes through the genital tract, the infant's skin and mucous membranes are exposed to the mother's blood and secretions. Breastfeeding also poses a risk of transmission between 10% and 20% and the longer the mother breastfeeds, the greater the risk. Comparatively, mixed breastfeeding increases mother-to-infant HIV transmission nearly four-fold after six months and is associated with a three-fold greater risk of death by age six months. Cummulative risk is outlined in table 26.

Table 26: Risk of HIV transmission

Timing	Cumulative Risk of Transmission
During Pregnancy (In Utero)	~ 1-5%
During Labor and Delivery (Intrapartum)	~ 15-20%
Overall without Breastfeeding	~ 25-30%
Overall with Breastfeeding to 6 months	~ 25-35%
Overall with Breastfeeding to 18-24 months	~ 30-45%

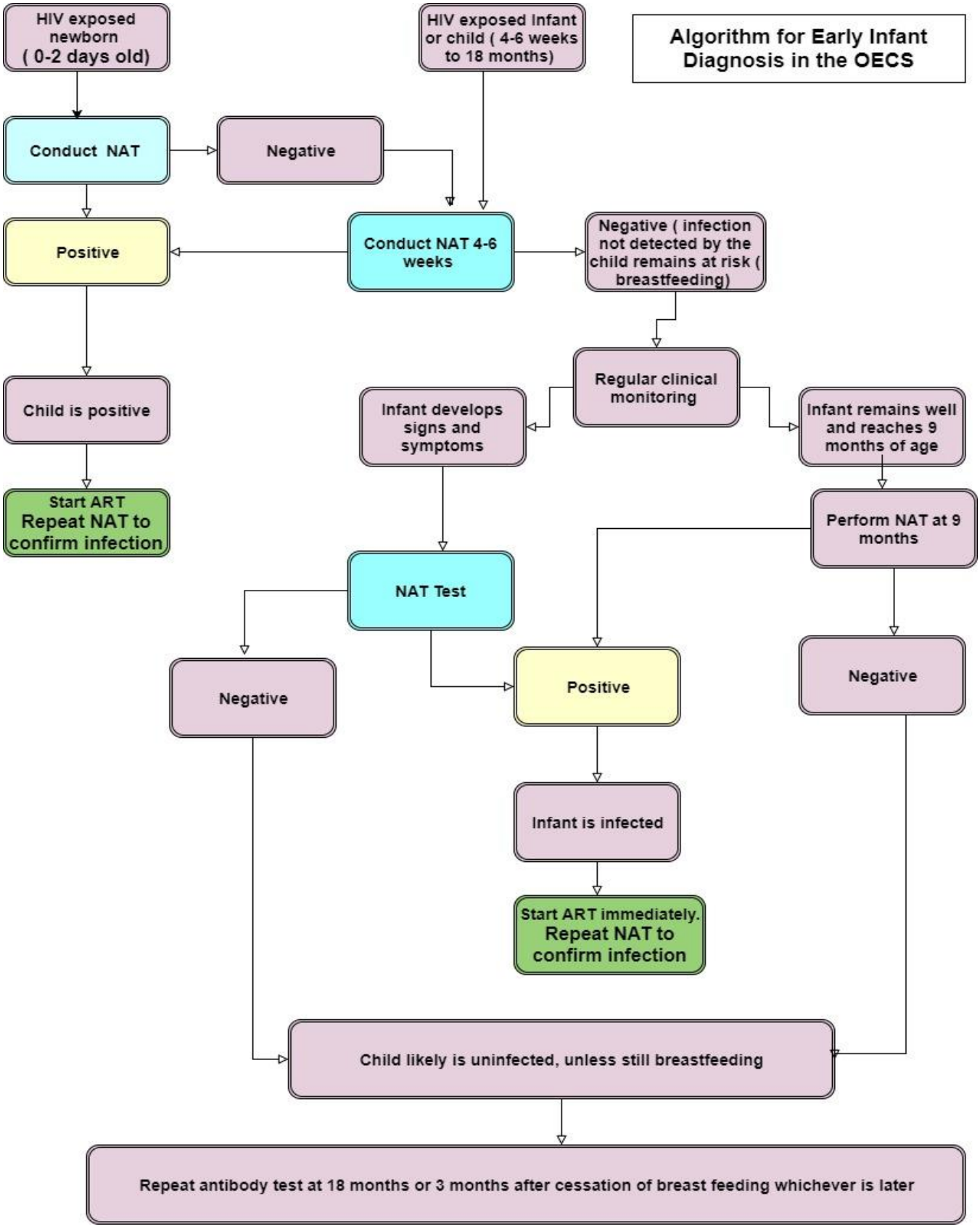
After infection, HIV rapidly populates the body using CD4+ T-lymphocytes to replicate. HIV destroys CD4 cells, weakening the entire immune system, and leaves the infant or child vulnerable to opportunistic infections. Children, particularly infants and younger children, having not yet had fully developed immune systems are at particularly high risk for morbidity and mortality due to HIV and opportunistic infections. Of children infected with HIV perinatally, approximately 10-25% rapidly develops profound immunosuppression and few of these children will survive past age two in the absence of HAART. Another 70-85% may progress slower; though still have a more rapid progression to clinical AIDS than adults. This more rapid clinical course emphasizes the importance of early identification, diagnosis and appropriate treatment for children potentially infected with HIV.

6.2 HIV Diagnosis in Children

Early infant diagnosis and initiation on ART is essential, as untreated HIV infections among infants is associated with high mortality in the first year of life. In the HIV exposed infant, infection is confirmed only with virologic testing using nucleic acid testing (NAT) technologies. In this regard, virologic testing such as HIV DNA on whole blood specimen or Dry Blood Spot (DBS) is recommended. HIV DNA with DBS is used in the OECS and recommended as early as possible with the first test done by 4-6 weeks of age. Serologic testing is not adequate as maternal HIV antibodies transplacentally transmitted can persist up to 18 months of age.

In children older than 18 months of age, serological testing is used in the same manner as in adults in alignment with national testing algorithm. Testing of infant and children less than 18 months is presented in detail in Figure 7.

Figure 7: Testing algorithm for exposed infants and children less than 18 months



6.3 Management of HIV infected children

Once the diagnosis is confirmed, preparation should commence to initiate ART as soon as possible. A baseline and ART pre initiation assessment are important steps in preparing for ART.

6.3.1 Baseline and Pre-Initiation assessment of HIV infected infant and children

Baseline pre initiation assessments will serve to provide counselling and support for children and/or caregivers in relation to the care and management of the child. HIV infected infants and children should undergo a thorough physical examination including establishing clinical disease stage, presented in table 27.

Table 27: WHO Clinical Staging of Paediatric HIV and AIDS

Clinical stage 1
Asymptomatic
Persistent generalised lymphadenopathy
Clinical stage 2
Unexplained persistent hepatosplenomegaly
Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)
Herpes zoster
Lineal gingival erythema
Recurrent oral ulceration
Papular pruritic eruption
Fungal nail infections
Extensive wart virus infection
Extensive molluscum contagiosum
Unexplained persistent parotid enlargement
Clinical stage 3
Unexplained moderate malnutrition not adequately responding to standard therapy
Unexplained persistent diarrhoea (14 days or more)
Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one month)
Persistent oral candidiasis (after first 6 weeks of life)
Oral hairy leukoplakia
Acute necrotising ulcerative gingivitis or periodontitis
Lymph node TB
Pulmonary TB
Severe recurrent bacterial pneumonia
Acute necrotizing ulcerative gingivitis or periodontitis
Symptomatic lymphoid interstitial pneumonitis
Chronic HIV-associated lung disease including brochiectasis
Unexplained anaemia (<8.0 g/dl), neutropaenia (<0.5 × 10^9/mL) and/or chronic thrombocytopaenia (<50 × 10^9 per mL)
Clinical stage 4

Unexplained severe wasting,* stunting or severe malnutrition not responding to standard therapy **Pneumocystis pneumonia (PCP)** Recurrent severe bacterial infections (e.g., empyema, pyomyositis, bone or joint infection, or meningitis but excluding pneumonia) Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site) Extrapulmonary TB Kaposi's sarcoma Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) CNS toxoplasmosis (after one month of life) HIV encephalopathy CMV infection: retinitis or CMV infection affecting another organ, with onset at age more than one month Extrapulmonary cryptococcosis (including meningitis) Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis) Chronic cryptosporidiosis (with diarrhoea) Chronic isosporiasis Disseminated non-tuberculous mycobacterial infection Cerebral or B-cell non-Hodgkin's lymphoma Progressive multifocal leukoencephalopathy (PML) HIV-associated cardiomyopathy or nephropathy
Persistent weight loss of >10% of baseline or <5th percentile on weight-for-height chart on 2 consecutive measurements >1 month apart in the absence of another aetiology or concurrent illness.

Monitoring of the HIV infected child comprises of routine monitoring of any child accessing Maternal and Child Health (MCH) services as well as specific monitoring required to adequately manage HIV infection. The monitoring schedule is detailed in table 28 below.

Table 28: Baseline and ongoing monitoring schedule for HIV infected infants and children

Test	Enrollment	Pre-Initiation	Ongoing Care
Clinical			
Complete Physical Exam	Yes	Yes	Continued focused physical exams based on regimens, risks, and patient concerns.
Weight	Yes	Yes	Every Visit
Height	Yes	Yes	Every Visit
Head Circumference	Yes	Yes	Every Visit until age 2.
Developmental Milestones Assessment	Yes	Yes	At a minimum every 3 months during clinical encounters.
Treatment Readiness and Adherence Counselling	As needed	Yes	At every clinical encounter and medication pickup.
Laboratory			
HIV Test (DBS confirmed by	Yes	-	-

another DBS and or rapid test after 18 months)			
CD4 Count and CD4%	Yes	Yes	Baseline and every 6 months. More frequent testing is determined by the physician on a case by case basis.
Viral Load	Yes	Yes	Baseline (pre initiation), repeated 6 months post initiation and yearly thereafter for virologically suppressed patient. More frequent testing is determined by the physician on a case by case basis.
CBC with Differential (Minimum of Hb and WBC)	Yes	Yes	Only as needed. AZT based regimen: Check 4-6 weeks after initiating AZT. Recheck at 3 and 6 months. If results are normal, check as needed based on patient's symptoms.
Electrolytes, blood urea nitrogen, creatinine levels Creatinine (serum)	Yes	Yes	Not necessary unless symptomatic or on a TDF-based regimen. Adolescents taking TDF should monitor creatinine every 6 months.
Liver Function Test (Minimum of ALT and AST)	Yes	Yes	2-4 weeks after initiation, thereafter every 6 months NVP-based regimen: Check at 2 weeks and 4 weeks after starting a NVP based regimen. Recheck at 3 and 6 months. If results are normal, can check every 12 months thereafter unless patient becomes symptomatic.
Urinalysis	Yes	No	As needed
PPD/Mantoux (not applicable once child has a history of latent or active TB disease)	Yes	If > 12mos since last PPD	Annually until positive. If Mantoux converts to positive, follow pathway for TB assessment
Serologic testing for toxoplasma gondii			Optional
Hepatitis B (HBsAg)	Yes	-	As needed.
RPR/VDRL	Yes	-	Annually if sexually active or high risk
Screening for other sexually transmitted infections	Yes*		*For sexual assault cases and children who are sexually active -Chlamydia, Trichomonas, Gonnorhoea is mandatory and HTLV I and 2 and HCV is recommended.

6.3.2 ARV Treatment of HIV infected children

ART treatment is recommended in the HIV exposed infant with an initial positive virologic test result (HIV DNA). Concurrently, a repeat sample should be taken for confirmation of the diagnosis, however this should not delay initiation of treatment.

6.3.2.1 When to Start Treatment

ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count. Priority should be given to the following groups.

- All Children ≤2 years of age or children < 5 years of age with WHO clinical stage 3 or 4 or CD4 count ≤750 cells/mm³ or CD4 percentage <25%,
- All children > 5 years of age with WHO HIV clinical stage 3 or 4 disease or CD4 count ≤350 cells/mm³
- ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of antituberculosis treatment, regardless of the CD4 cell count and clinical stage.

6.3.2.2 What to Start

The preferred first line regimen remains 2 NRTI and 1 NNRTI, however considerations must be given to selecting a potent preferred first line which preserves AZT as a second line. Table 29 presents the treatment regimen for infants and children less than 3 years and those between 3-10 years. For simplified paediatric dosing see appendices 6A, 6B, 6C and 6D.

Table 29: Recommended Treatment Regimen for infants and children

	Preferred First Line	**Alternate First Line**
Children 3 years to less than 10 years	ABC + 3TC + EFV	ABC+3TC+NVP AZT + 3TC + EFV AZT_3TC+NVP TDF+ 3TC (or FTC) + EFV TDF+3TC(or FTC) +NVP
Infants and Children less than 3 years	ABC + 3TC + LPV/r* AZT+3TC+LPV/r *2-3 months LPV/r syrup *3-36 months- PLV/r pellets	ABC + 3TC + NVP AZT+_3TC+ NVP Special Circumstances** ABC +AZT + 3TC + RAL AZT+3TC+RAL
Infants and children less than 3 years developing TB disease* **	ABC + 3TC + AZT is recommended for those who develop TB while on treatment with NVP or LPV/r (*Once TB therapy has been completed, this regimen should be stopped and the initial regimen should be restarted)*	

*LPV/r syrup requires cold chain, is unpalatable and has the potential for suboptimal adherence. Dose of LPV/r for children younger than 6 weeks of age should be calculated using body surface area. LPV/r pellets is heat stable, palatability is also suboptimal and can negatively impact adherence
** Special circumstances- situations where preferred or alternative regimens may not be available or suitable because of significant toxicities, anticipated drug–drug interactions, drug procurement and supply management issues or for other reasons. RAL is approved for use in infants and children from the age of 4 weeks, but there is very limited evidence on the use as a preferred first line. It should be considered in cases where LPV/r is not an option and there is a high risk for NNRTI resistance.
***Administering LPV/r with TB treatment reduced drug levels by rifampicin.

6.3.2.3 ART considerations when managing HIV infected infants and children

Several additional ART considerations are important in prescribing ART for HIV infected children.

- ABC and AZT were comparable in their clinical, immunological and virological response, as well as safety and tolerability. The choice between the two as the preferred first line has an impact on second line ART. Specifically failure of AZT will result in the accumulation of thymidine analogue mutations and will reduce susceptibility to ABC or TDF in a subsequent regimen. For these reasons, ABC + 3TC should remain the preferred option for the first-line NRTI backbone.
- For children less than 3 years of age, evidence demonstrates a reduced risk of discontinuing treatment and viral failure or death when started on LPV/r-based instead of an NVP-based regimen. The following is noted in relation to the preferred use of LPV/r. There is demonstrated superiority of LPV/r based over NVP-based regimens for treating young children, ***regardless of NNRTI exposure.***
- LPV/r has a better resistance profile and protects against the selection of NRTI resistance without compromising the use of other PIs in second-line regimens.
- Where viral load monitoring is available, LPV/r can be switched with EFV at 3 years of age after viral suppression is sustained. This PI sparing strategy aims to reduce exposure to LPV/r and preserves PI-based therapy for second-line ART.
- Evidence demonstrates detectable NNRTI resistance even among HIV-infected infants and young children without any history of exposure to ARV drugs for PMTCT or whose exposure status is unknown. This suggest that exposure to NNRTI for PMTCT may not be an accurate marker for identifying children at higher risk of HIV resistance to NNRTIs. If treatment with LPV/r is not available, consider a NVP based regimen. EFV is not recommended for children younger than 3 years and weighing less than 10 kg.
- ATV is approved for use for children 3 months and older. ATV single-strength capsules should be administered with RTV 100 mg for all weight bands. The ATV powder formulation enables administration of ATV to infants and children as young as 3 months. Infants and children weighing 5–10 kg should be administered 200 mg of ATV powder (4 packets, 50 mg per packet) with 80 mg of RTV oral solution (5 ml). For tablets- 200 mg should be used for weight 25.0–29.9 kg and 300-mg for 30.0–34.9 kg.
- TDF is only approved for use for children 2 years and older. Target dose: 8 mg/kg or 200 mg/m2 (maximum 300 mg).
- NVP dose escalation with half dose for 2 weeks when initiating ART is still recommended to avoid toxicity from high initial NVP levels.

❖ Where possible, fixed dose combinations, dispersible and scored tabs should be considered for ease of dosing and improved adherence.

6.3.3.3 First-line Regimen Treatment Failure—When to Switch Regimens

Clinical failure is defined as the appearance or reappearance of WHO clinical stage 3 or stage 4 events (with the exception of TB) after at least 24 weeks on HAART in a treatment-adherent child. Clinical failure should prompt HIV viral load testing to determine whether or not virologic failure has in fact occurred.

Immunological failure is defined as developing or returning to the following age-related immunological thresholds after at least 24 weeks on HAART in a treatment-adherent child:

- Persistent CD4 count <200 cells/mm^3 or CD4 percentage <10% for a child less than 5 years of age.
- Persistent CD4 count <100 cells/mm^3 for a child 5 years of age or older.

Immunologic failure should prompt HIV viral load testing to determine whether or not virologic failure has in fact occurred.

Virologic failure is defined as a persistent viral load above 1,000 RNA copies/ml, after at least 24 weeks on HAART in a treatment-adherent child. A single viral load measurement of greater than 1,000 copies/mL should prompt adherence counseling for the child and/or caregiver, followed by repeat virologic testing three months later. Once virologic failure is established, second line therapy is recommended. Patient, family members and care givers should be counselled on the importance of adherence and be provided with any necessary psychosocial or other forms of support that may impact positively on adherence.

6.3.3.3.1 First Line Treatment Failure- What to start.

If the viral load remains elevated, a genotypic resistance assay should be used to guide the selection of second-line therapy. In the absence of genotypic testing, second line regimen defined on empiric evidence is recommended as outlined in table 30.

Table 30: Recommended Second Line Therapy for HIV infected infants and children

	Failing first line regimen	Preferred second line regimen	Alternative second line regimen
Less than 3 years	ABC+3TC + LPV/r AZT+3TC+LPV/r	AZT+3TC + RAL ABC+3TC+RAL	Maintaining the failing LPV/r-based regimen and switch to 2 NRTIs + EFV at 3 years of age
	ABC +3TC + NVP AZT+3TC+ NVP	AZT+3TC+ LPV/r ABC+3TC+LPV/r	AZT+3TC + RAL ABC+3TC+RAL
3 years to less than 10 years	ABC+3TC+LPV/r AZT+3TC+LPV/r	AZT+3TC+EFV ABC+3TC+EFV	AZT+3TC+RAL ABC+3TC+RAL
	ABC+3TC + EFV (or NVP) AZT+3TC+EFV(or NVP)	AZT+3TC +LPV/r ABC +3TC+LPV/r	AZT+3TC +ATV/r ABC +3TC+ATV/r

6.3.3.4 Third line therapy

If second line-therapy fails, the recommended third line therapy is based on empiric evidence. Where possible, genotyping should be used to determine resistance profile and third line therapy. In the OECS, clinical teams should consult with the OECS HTEP TB/ HIV clinical forum when switching patients to third line. Recommended third line therapy is outlined in table 31below.

Table 31 ***Recommended third line regimen in children***

Population	First line	Second Line	Third Line
Children 0-10 years of age	2 NRTI + LPV/r	If less than 3 years of age: 2 NRTIs + RAL	RAL (or DTG)f + 2 NRTIs **OR** DRV/rg + 2 NRTIs **OR** DRV/rg + RAL (or DTG)f ± 1–2 NRTIs
		If older than 3 years: 2 NRTIs + EFV or RAL	
	2NRTI+EFV	2 NRTIs + ATV/re or LPV/r	

LIST OF APPENDICES

Appendix 6 A: Twice daily dosing of liquid formulation for infants younger than 4 weeks of age

Drug	Strength	2-3kg	3-4kg	4-5kg
AZT	10mg/ml	1ml	1.5ml	2ml
NVP	10mg/ml	1.5ml	2ml	3ml
3TC	10mg/ml	0.5ml	0.8ml	1ml
LPV/r	80/20mg/ml	0.6ml	0.8ml	1ml

Appendix 6 B. Simplified twice daily dosing of child-friendly solid formulations

Drug	Strength of paediatric	Children 4weeks of age and above										Strength of adult tab (mg)	Number of tablets by weight-band	
		Number of tablets by weight-band morning and evening												
		3–5.9 kg		6–9.9 kg		10–13.9 kg		14–19.9 kg		20–24.9 kg			25–34.9 kg	
		am	pm	am	pm	am	pm	am	pm	am	pm		am	pm
Single drugs														
AZT	60 mg tab	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg	1	1
ABC	60mg tab	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg	1	1
NVP	50 mg tab	1	1	1.5	1.5	2	2	2.5	2.5	3	3	200 mg	1	1
LPV/r	100mg/25 mg(tab)	-	-	-	-	2	1	2	2	2	2	100mg/25 mg	3	3
	40mg/10mg (pellets)	2	2	3	3	4	4	5	5	6	6	100mg/25 mg	3	3
DRV	75mg tab	-	-	-	-	3	3	5	5	5	5	-	-	-
RTV	25mg chewable tabs	-	-	-	-	3	3	4	4	6	6	400mg	1	1
	100mg chewable tab	-	-	-	-	-	-	1	1	1.5	1.5	400mg	1	1
	100mg/sachet (granules)	0.25	0.25	0.5	0.5	-	-	-	-	-	-	-	-	-
Combinations														
AZT/3TC	60mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150	1	1
AZT/3TC/NVP	60mg/30mg/50mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150/200	1	1
ABC/AZT/3TC	60mg/60mg/30mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/300/150	1	1
ABC/3TC	60mg/30mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600/300	0.5	0.5
ABC/3TC	120mg/60mg	0.5	0.5	0.5	1	1	1	1	1.5	1.5	1.5	600/300	0.5	0.5

Appendix 6C: Simplified twice daily dosing of liquid formulation and number of tablets or capsules of adult solid formulation

Drug	Strength of paediatric liquid (mg/ml) and adult tab/cap (mg)	Children 4 weeks of age and above									
		Number of tablets/capsules or ml by weight-band morning and evening									
		3–5.9 kg		6–9.9 kg		10–13.9 kg		14–19.9 kg		20–24.9 kg	
		am	**pm**	**am**	**pm**	**am**	**pm**	**am**	**pm**	**am**	**pm**
AZT	10 mg/ml; 300 mg	6 ml	6 ml	9 ml	9 ml	12 ml	12 ml	0.5	0.5	1	0.5
ABC	20 mg/ml; 300 mg	3 ml	3 ml	4 ml	4 ml	6 ml	6 ml	0.5	0.5	1	0.5
3TC	10 mg/ml; 150 mg	3 ml	3 ml	4 ml	4 ml	6 ml	6 ml	0.5	0.5	1	0.5
NVP	10 mg/ml; 200 mg	5 ml	5 ml	8 ml	8 ml	10 ml	10 ml	1	0.5	1	0.5
LPV/r	80/20 mg/ml	1 ml	1 ml	1.5 ml	1.5 ml	2 ml	2 ml	2.5 ml	2.5 ml	3 ml	3 ml
DRV	100mg/ml	-	-	-	-	2.5	2.5	3.5	3.5	-	-

Appendix 6D. Simplified once daily dosing of child-friendly solid formulations

Drug	**Strength of tab/cap (mg)**	**Infants and Children 4 weeks of age and older** **Number of tablets or capsules by weight-band once daily**					**Strength of adult tab (mg)**	**Number of tablets or capsules by weight-band once daily**
		3–5.9 kg	**6–9.9 kg**	**10–13.9 kg**	**14–19.9 kg**	**20–24.9 kg**		**25–34.9 kg**
		Once daily	**Once daily**	**Once daily**	**Once daily**	**Once daily**		**Once daily**
Single drugs								
EFV*	200 mg	-NR	NR	1	1.5	1.5	200 mg	2
ATV	100mg (capsules)	-	-	1	2	2	300mg	**2 (100mg) or 1 (300mg)
ddI***	125 mg or 200 mg EC	NR	NR	1 (125 mg)	1 (200 mg)	2 (125 mg)	125 mg EC	2
TDF	Oral powder scoops 40 mg/scoop	-	-	3	-	-	300mg	***2 (100 mg) or 1 (300 mg)
	Tablets 150 mg or 200 mg				1 (150mg)	1 (200mg)		

Combination								
ABC/3TC	60mg/30mg	2	3	4	5	6	600mg/300mg	1
ABC/3TC	120mg/60mg	1	1.5	2	2.5	3	600mg/300mg	1

[*] ***EFV is not recommended for children below 3 years and weighing less than 10 kg.***

****ATV and TDF- 200 mg should be used for weight 25.0–29.9 kg and 300-mg tablets for 30.0–34.9 kg.**

[***] ***ddI EC is not recommended for children weighing less than 10 kg; this dose is recommended only for those 10 kg and above.***

NR = not recommended ***EC = enteric coated***

7. PROPHYLAXIS AND TREATMENT OF OPPORTUNISTIC INFECTION IN INFANTS AND CHILDREN

This section provides detailed guidance on the management of selected OIs commonly seen in HIV-infected children in the Caribbean region. These recommendations have been adapted for the Eastern Caribbean region from paediatric OI guidelines written by the CDC et al[10]. Not all treatments listed may be available in the OECS but are included in case referral outside the region is an option. For management of OIs not listed below, please consult the CDC OI Guidelines.[26]

Preferred and alternative treatment options are presented; each recommendation includes a rating of its strength as well as the quality of the evidence supporting it, coded as follows.

Strength of recommendation:

A. Both strong evidence for efficacy and substantial clinical benefit support recommendation for use. Should always be offered.
B. Moderate evidence for efficacy, or strong evidence for efficacy but only limited clinical benefit, supports recommendation for use. Should generally be offered.
C. Evidence for efficacy is insufficient to support a recommendation for or against use, or evidence for efficacy might not outweigh adverse consequences (e.g., drug toxicity, drug interactions) or cost of treatment or alternative approaches. Optional.
D. Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use. Should generally not be offered.
E. Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use. Should never be offered.

Quality of the evidence supporting the recommendation

I. Evidence from at least one properly-designed randomized, controlled trial.

II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one centre), or from multiple time-series studies, or dramatic results from uncontrolled experiments.

III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

7.1 Prophylaxis and treatment of OIs in children.

Primary prophylaxis is treatment given to an HIV positive patient to prevent the first episode of an opportunistic infection. Table 7.1 outlines the preferred and alternative choice for primary prevention as well as the indication of discontinuing and restarting primary prophylaxis. Secondary Prophylaxis Primary is treatment given to an HIV positive patient to prevent the reoccurrence of an opportunistic infection. Tables 32 and 33 outline the recommendations for the secondary prophylaxis and treatment of OIs respectively.

[10] Centers for Disease Control and Prevention. Guidelines for prevention and treatment of opportunistic infections in HIV-exposed and HIV-infected children: Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR. 2009 Sep 4; 58(11).
Available from: http://www.cdc.gov/mmwr/pdf/rr/rr5811.pdf.

*Table 32: **Prophylaxis to prevent first episode (Primary Prophylaxis) of OI in HIV-exposed- and HIV-infected infants***

Preventive regimen				
Pathogen	Indication	First choice	Alternative	Discontinuing and restarting primary prophylaxis and other comments
PCP[a]	HIV-infected or HIV-indeterminate infants aged 1–12 months regardless of CD4 count or % HIV infected children aged 1– 5 years with CD4 count <500 cells/mm^3 or CD4 percentage <15%; HI infected children aged 6– 12 years with CD4 count <200 cells/mm^3 or CD4 percentage <15%	• TMP-SMX (Cotrimoxazole): TMP 2.5–5 mg/kg body weight/dose with SMX 12.5–25 mg/kg body weight/dose twice per day. Dosing based on TMP component. • ***The total daily dose should not exceed 320 mg TMP and 1600 mg SMX.*** **Several dosing schemes have been used successfully—** • Given 3 days per week on consecutive days or on alternate days • Given 2 days per week on consecutive days or on alternate days • Given every day (total daily dose of TMP 5–10 mg/kg body weight given as a single dose each day)	**Dapsone:** Children aged >1 month: 2 mg/kg body weight (max. 100 mg) PO QD; **OR** 4 mg/kg body weight (max. 200 mg) PO QW (**BI**) **Atovaquone:** Children aged 1–3 months and >24 months-12 years: 30 -40mg/kg body weight PO QD with food **OR** Children aged 4–24 months: 45 mg/kg body weight PO QD with food. (**BI**) Children Aged ≥13 Years: 1500 mg (10 cc oral yellow suspension)per dose by mouth once daily **Aerosolized pentamidine:** Children aged >5 years: 300 mg every month by nebulizer (**BI**)	**Criteria for Discontinuing Primary Prophylaxis:** ***Note: Do not discontinue in HIV infected children aged <1 year*** After ≥6 Months of ART: • Aged 1 to <6 years; CD4 percentage ≥15% or CD4 count is ≥500 cells/mm3 for >3 consecutive months, **OR** • Aged ≥6 years, CD4 percentage ≥15% or CD4 count is ≥200 cells/ mm3 for >3 consecutive months **Criteria for Restarting Primary Prophylaxis:** • Aged 1 to < 6 years with CD4 percentage <15 or CD4 count <500 cells/mm3 • Aged ≥6 years with CD4 percentage <15% or CD4 count <200 cells/mm3

Preventive regimen				
Pathogen	Indication	First choice	Alternative	Discontinuing and restarting primary prophylaxis and other comments
MTB ***Isoniazid sensitive***	**Indication:** • Positive TST (TST ≥5 mm) or IGRA without previous TB treatment • Close contact with any infectious TB case (repeated exposures warrant repeated post-exposure prophylaxis) • TB disease must be excluded before starting treatment. • No indication for pre-exposure and post-treatment prophylaxis.	Isoniazid: 10– 15 mg/kg body weight (max. 300 mg) PO QD for 9 months (**AII**); **OR** 20–30 mg/kg body weight (max. 900 mg) PO 2 x QW for 9 months (**BII**)	Rifampicin: 10–20 mg/kg body weight (max. 600 mg) PO QD for 4–6 months (**BIII**)	**Criteria for Discontinuing Prophylaxis**: Only with documented severe adverse event, which is exceedingly rare. **Adjunctive Treatment:** Pyridoxine 1–2 mg/kg body weight once daily (maximum 25–50 mg/day) with isoniazid; pyridoxine supplementation is recommended for exclusively breastfed infants and for children and adolescents on meat- and milk-deficient diets; children with nutritional deficiencies, including all symptomatic HIV infected children; and pregnant adolescents and women.
MTB Isoniazid resistant	Same as previous pathogen; increased probability of exposure to isoniazid-resistant TB	Rifampicin: 10–20 mg/kg body weight (max. 600 mg) PO QD for 4–6 months (**BIII**)		
MDR (isoniazid and rifampicin)	Same as previous pathogen; increased probability of exposure to MDR TB	Consult with a specialist on the choices of drugs		

Preventive regimen				
Pathogen	Indication	First choice	Alternative	Discontinuing and restarting primary prophylaxis and other comments
MAC[b]	**For children** -aged >6 years with CD4 count <50 cells/mm^3; -aged 2to <6years with CD4 count <75 cells/mm^3; -aged 1–2 years with CD4 count <500 cells/mm^3; -aged <1 year with CD4 count <750 cells/mm^3	Clarithromycin: 7.5 mg/kg body weight (max. 500 mg) orally 2 x QD (**AII**); **OR** Azithromycin: 20 mg/kg body weight (max. 1,200 mg) PO once weekly (QW) (**AII**)	Azithromycin: 5 mg/kg body weight (max. 250 mg) PO QD (**AII**); Children aged >6 years: Rifabutin (300 mg PO QD) (**BI**)	**Criteria for Discontinuing Primary Prophylaxis:** Do not discontinue in children age <2 years. **After ≥6 months of ART and:** • Aged 2 to 6 years with CD4 >200 cells/mm3 for >3 consecutive months •1Aged ≥6 years with CD4 count >100 cells/mm3 for >3 consecutive months **Criteria for Restarting Primary Prophylaxis**: • Aged 2 to <6 years with CD4 count <200 cells/mm3 • Aged ≥6 years with CD4 count <100 cells/mm3
Varicella Zoster Virus	Substantial exposure to varicella or shingles with no history of varicella or zoster **OR** Seronegative status for VZV by a sensitive, specific antibody assay **OR** Lack of evidence for age appropriate vaccination	Varicella-zoster immune globulin (VariZIG): 125 IU per 10 kg (max. 625 IU) IM, administered within 96 hrs after exposure[d](**AIII**)	If VariZIG is not available or >96 hrs have passed since exposure, some experts recommend prophylaxis with acyclovir—20 mg/kg body weight (max. 800 mg) per dose orally 4 times a day for 5–7 days Another alternative to VariZIG is IV immunoglobulin (IVIG)—400 mg/kg, administered once within 96 hrs after exposure (**CIII**)	
Vaccine preventable pathogens	Standard recommendations for HIV-exposed and HIV infected children	Routine vaccinations as per the OECS schedule with exceptions for the HIV exposed infant and positive children.		

Preventive regimen				
Pathogen	Indication	First choice	Alternative	Discontinuing and restarting primary prophylaxis and other comments
Toxoplasma gondii	Immunoglobulin G (IgG) antibody to *Toxoplasma* and severe immunosuppression: - -HIV-infected children aged <6 years with CD4 percentage <15%; -HI infected children aged >6 years with CD4 count <100 cells/mm^3 (**BIII**)	**Co-trimoxazole:** 150/750 mg/m^2 body surface area PO QD by mouth (**BIII**) **Acceptable alternative dosage schedules for same dosage (AI):** -Single dose PO 3 x QW on consecutive days; -2 divided doses PO QD; **OR** - 2 divided doses PO 3 x QW on alternate days	**Children aged >1 month:** -Dapsone: 2 mg/kg body weight **OR** 15 mg/m^2 body surface area (max. 25 mg) PO QD; **PLUS** Pyrimethamine: 1 mg/kg body weight (max. 25 mg) PO QD; **PLUS** Leucovorin: 5 mg PO every 3 days (**BI**) **Atovaquone:** -Children aged 1–3 months and >24 months: 30 mg/kg body weight PO QD; -Children aged 4–24 months, 45 mg/kg body weight PO QD. with or without pyrimethamine: 1 mg/kg body weight or 15 mg/m^2 body surface area (max. 25 mg) PO QD; **PLUS** Leucovorin (5 mg PO every 3 days) (**CIII**) **Acceptable Alternative Dosage Schedules for TMP-SMX**: • TMP-SMX 150/750 mg/m2 body surface area per dose once daily by mouth 3 times weekly on 3 consecutive days per week • TMP-SMX 75/375 mg/m2 body surface area per dose twice daily by mouth every day • TMP-SMX 75/375 mg/m2 body surface area per dose twice daily by	**Criteria for Discontinuing Primary Prophylaxis:** ***Note: Do not discontinue in children aged <1 year*** • After ≥6 months of ART, **and** • Aged 1 to <6 years; CD4 percentage is ≥15% for >3 consecutive months • Aged ≥6 years; CD4 count >200 cells/mm3 for >3 consecutive months **Criteria for Restarting Primary Prophylaxis:** • Aged 1 to <6 years with CD4 percentage <15% • Aged ≥6 years with CD4 count <100 to 200 cells/mm3

Preventive regimen				
Pathogen	Indication	First choice	Alternative	Discontinuing and restarting primary prophylaxis and other comments
			mouth 3 times weekly on alternate days.	
S. Pnuemonia and Invasive bacterial infections	Pneumococcal, meningococcal, and Hib vaccines Hypogammaglobulinemia (i.e., IgG <400 mg/dL)			**Criteria for discontinuing primary prophylaxis:** • Resolution of hypogammaglobulinemia Criteria for restarting primary prophylaxis: • Relapse of hypogammaglobulinemia
CMV	CMV antibody positivity and severe immunosuppression (i.e., CD4 cell count 100 cells/mm3 for children ≥6 years; CD4 percentage >10% in children	**For older children** who can receive adult dose (based on their BSA)- valganciclovir tablets 900 mg orally once daily with food (CIII) **For children aged 4 months–16 years,**- valganciclovir oral solution 50 mg/mL (at dose in milligrams = 7 x BSA x CrCl up to maximum CrCl of 150 mL/min/1.73 m2) orally once daily with food (maximum dose 900 mg/day)		**Criteria for Discontinuing Primary Prophylaxis:** CD4 cell count >100 cells/mm3 for children ≥6 years; CD4 percentage >10% in children <6 years **Criteria for Considering Restarting Primary Prophylaxis:** CD4 cell count,50 cell/mm3 in children ≥6 years; CD4 percentage <5% in children <6 years

[a] Daily co-trimoxazole reduces the frequency of certain bacterial infections. Co-trimoxazole, dapsone-pyrimethamine, and possibly atovaquone (with or without pyrimethamine) protect against toxoplasmosis; however, data have not been prospectively collected. Compared with weekly dapsone, daily dapsone is associated with lower incidence of PCP but higher hematologic toxicity and mortality. Patients receiving therapy for toxoplasmosis with sulfadiazine-pyrimethamine are protected against PCP and do not need co-trimoxazole. [b] Substantial drug interactions can occur between rifamycins (i.e., rifampicin and rifabutin) and PIs and NNRTIs; a specialist should be consulted. [c] Children routinely being administered IVIG should receive VariZIG if the last dose of IVIG was administered >21 days before exposure. [d] As of 2007, VariZIG can be obtained only under a treatment Investigational New Drug protocol (1-800-843-7477, FFF Enterprises, Temecula, CA, US.) [e] Protection against toxoplasmosis is provided by the preferred anti-Pneumocystis regimens and possibly by atovaquone.

Table 7.2 Prophylaxis to prevent OI recurrence (secondary prophylaxis) in HIV-exposed and HIV-infected infants and children				
Preventative regimen				
Pathogen	**Indication**	**First choice**	**Alternative**	**Discontinuing and restarting secondary prophylaxis and other comments**
PCP[a]	Prior PCP	• TMP-SMX (Cotrimoxazole): TMP2.5–5 mg/kg body weight/dose with SMX 12.5–25 mg/kg body weight/dose twice per day. ***Dosing based on TMP component.*** •The total daily dose should not exceed 320mg TMP and 1600 mg SMX. **Several dosing schemes have been used successfully—** • Given 3 days per week on consecutive days or on alternate days • Given 2 days per week on consecutive days or on alternate days • Given every day (total daily dose of TMP 5–10 mg/kg body weight given as a single dose each day)	**Dapsone:** -Children aged >1 month: 2 mg/kg body weight (max. 100 mg) PO QD or 4 mg/kg body weight (max. 200 mg) orally weekly (**BI**) **Atovaquone:** Children Aged 1–3 Months and>24 Months–12 Years: • 30-40 mg/kg body weight/dose by mouth once daily with food Children Aged 4–24 Months: • 45 mg/kg body weight/dose by mouth once daily with food Children Aged ≥13 Years: • 1500 mg (10 cc oral yellow suspension) per dose by mouth once daily **Aerosolized pentamidine:** -Children aged >5 years: 300 mg every month by nebulizer (**BI**)	**Criteria for Discontinuing Secondary Prophylaxis:** Note: Do not discontinue in HIV infected children aged <1 year After ≥6 Months of ART: • Aged 1 to <6 years; CD4 percentage ≥15% or CD4 count is ≥500 cells/mm3 for >3 consecutive months, **OR** • Aged ≥6 years, CD4 percentage ≥15% or CD4 count is ≥200 cells/ mm3 for >3 consecutive months **Criteria for Restarting Primary Secondary Prophylaxis:** • Aged 1 to < 6 years with CD4 percentage <15 or CD4 count <500 cells/mm3 • Aged ≥6 years with CD4 percentage <15% or CD4 count <200 cells/mm3

***Toxoplasma gondii*[a]**	Prior *Toxoplasma* encephalitis	Sulfadiazine 42.5–60mg/ kg body weight per dose twice daily* (maximum 2–4 g per day) by mouth; **PLUS** Pyrimethamine: 1 mg/kg body weight or 15 mg/m^2 body surface area (max. 25 mg) PO QD; **PLUS** Leucovorin: 5 mg orally every 3 days (**AI**)	Clindamycin 7–10 mg/kg body weight per dose by mouth 3 times daily; **PLUS** Pyrimethamine: 1 mg/kg body weight or 15 mg/m^2 body surface area (max. 25 mg) PO QD; **PLUS** Leucovorin: 5 mg orally every 3 days (**BI**) **Children Aged 1–3 Months and >24Months:** • Atovaquone 30 mg/kg body weight by mouth once daily • Leucovorin, 5 mg by mouth every 3 days • TMP-SMX, 150/750 mg/m2 Body surface area once daily by mouth **Children Aged 4–24 Months:** • Atovaquone 45 mg/kg body weight by mouth once daily, with or without Pyrimethamine 1 mg/kg body weight or 15 mg/m2 body surface area (maximum 25 mg) by mouth once daily, **PLUS** • Leucovorin, 5 mg by mouth every 3 days • TMP-SMX, 150/750 mg/m2 Body surface area once daily by mouth	**Criteria for Discontinuing Secondary Prophylaxis if All of the Following Criteria are fulfilled:** • Completed ≥6 months of ART, completed initial therapy for TE, asymptomatic for TE, and • Aged 1 to < 6 years; CD4 percentage ≥15% for >6 consecutive months • Aged ≥6 years; CD4 cell count >200 cells/mm3 for >6 consecutive months. **Criteria For Restarting Secondary Prophylaxis:** • Aged 1 to <6 years with CD4 percentage <15%. • Aged ≥6 years with CD4 cell count <200 cells/mm3.
MAC[b]	Prior disease	Clarithromycin: 7.5 mg/kg body weight (max. 500 mg) orally 2 x QD (**AII**); **PLUS** Ethambutol: 15–25 mg/kg body weight (max. 2.5 g) PO QD with or without food (**AII**);	Azithromycin: 5 mg/kg body weight (max. 250 mg) PO QD (**AII**); **PLUS** Ethambutol: 15–25 mg/kg body weight (max. 2.5 g) PO QD with or without food (**AII**); **Children aged >5 years**	**Criteria for Discontinuing Secondary Prophylaxis fulfillment of All of the following Criteria:** • Completed ≥6 months of ART • Completed ≥12 months MAC therapy • Asymptomatic for signs and symptoms of MAC

			who received rifabutin as part of initial treatment: Rifabutin 5 mg/kg body weight (maximum 300 mg) orally once daily with food	• Aged 2 to <6 years with CD4 count >200 cells/ mm3 for ≥6 consecutive months • Aged ≥6 years with CD4 count >100 cells/mm3 for ≥6 consecutive months **Criteria for Restarting Secondary Prophylaxis:** • Aged 2 to <6 years with CD4 count <200 cells /mm3 • Aged ≥6 years with CD4 count <100 cells/mm3
Coccidioidomycosis	Documented disease	Fluconazole: 6 mg/kg body weight (max. 400 mg) PO QD (**AII**)	Itraconazole: 2–5 mg/kg body weight (max. 200 mg) orally per dose 2 x QD (**AII**)	Lifelong secondary prophylaxis with fluconazole for patients with meningitis or disseminated disease in the immunocompromised patient is recommended. Secondary prophylaxis should be considered after treatment of milder disease if CD4 count remains <250 cells/mm3 or CD4 percentage <15%.
Cryptococcus neoformans	Documented disease	Fluconazole: 6 mg/kg body weight (max. 200 mg) PO QD (**AI**)	Itraconazole oral solution: 5 mg/kg body weight (max. 200 mg) PO QD (**BI**)	**Criteria For Discontinuing Secondary prophylaxis if All of the following Criteria are fulfilled:** • Age ≥6 years • Asymptomatic on ≥12 months of secondary prophylaxis • CD4 count ≥100 cells/mm3 with undetectable HIV viral load on ART for >3 months **Criteria for Restarting Secondary Prophylaxis:** • CD4 count <100/mm3
Histoplasma capsulatum	Documented disease	Itraconazole oral solution: 5 mg/kg body weight (max. 200 mg) PO per dose 2 x QD (**AII**)	Fluconazole: 3–6 mg/kg body weight (max. 200 mg) PO QD (**CII**)	

Microsporidiosis	Disseminated, nonocular infection caused by microsporidia other than *Enterocytozoon bieneusi* or V. Cornea	Albendazole: 7.5 mg/kg body weight (max. 400 mg/dose) per dose orally 2 x QD (**AII**) until immune reconstitution after initiation of HAART		**Criteria For Discontinuing Secondary Prophylaxis:** • After initiation of ART, resolution of signs and symptoms and sustained immune reconstitution (more than 6 month
	Ocular infection	Topical fumagillin bicylohexylammonium(Fumidil B): 3 mg/mL in saline (fumagillin 70 μg/mL) eye drops—2 drops every 2 hrs for 4 days, then 2 drops 4 x QD (investigational use only in the US) (**BII**); **PLUS** Albendazole: 7.5 mg/kg body weight (max. 400 mg/dose) PO 2 x QD to manage systemic infection (**BIII**)		**Criteria For Discontinuing Secondary Prophylaxis:** • After initiation of ART, resolution of signs and symptoms and sustained immune reconstitution (more than 6 month
CMV	Prior retinitis, neurologic disease, or gastrointestinal disease with relapse	Ganciclovir: 5 mg/kg body weight IV QD (**AI**); **OR** **• For older children who can receive adult dose (based on their BSA),** valganciclovir tablets 900 mg orally once daily with food, **OR** • For children age 4 months 16 years,- valganciclovir oral solution 50 mg/mL (at dose in milligrams = 7 x BSA x CrCl up to maximum CrCl of 150 mL/min/1.73 m2) orally once daily with food, **OR** Foscarnet: 90–120 mg/kg body weight IV QD (**AI**); **OR** Valganciclovir: 900 mg PO 1 time QD with food for older children who can receive adult dosing (**AI**)	Cidofovir 5 mg/ kg body weight per dose IV every other week. Must be given with probenecid and IV hydration. **For retinitis:** Ganciclovir sustained release implant: Every 6–9 months; **PLUS** Ganciclovir: 30 mg/kg body weight orally 3 x QD (**BIII)**	**Criteria for Discontinuing Secondary Prophylaxis if All of the following Criteria Are fulfilled:** Completed ≥6 months of ART Consultation with ophthalmologist (if retinitis) Age <6 years with CD4 percentage ≥15% for >6 consecutive months Age ≥6 years with CD4 cell count >100 cells/mm3 for >6 consecutive months For retinitis, routine (i.e., every 3–6 months) ophthalmological follow-up is recommended for early detection of relapse or immune restoration uveitis. **Criteria for Restarting Secondary**

				Prophylaxis: Age <6 years with CD4 percentage <15% Age ≥6 years with CD4 cell count <100 cells/mm3
S. pneumoniae and other Invasive bacterial Infections[c]	>2 infections in a 1year period in children who are unable to take ART	Co-trimoxazole: 75/375mg/m^2 body surface area PO QD divided into in 2 doses (**BI**)	IVIG: 400 mg/kg body weight every 2–4 weeks (**BI**) Antibiotic chemoprophylaxis with another active agent (**BIII**)	**Criteria for Discontinuing Secondary Prophylaxis**: Sustained (≥ 3 months) immune reconstitution (CD4 percentage ≥25% if ≤6 years old; CD4 percentage ≥20% or CD4 count >350 cells/mm3 if >6 years old). **Criteria For Restarting Secondary Prophylaxis**: >2 serious bacterial infections in a 1-year period despite ART.
Bartonellosis	Frequent or severe recurrences	Doxycycline: 2–4 mg/kg body weight (max. 100–200 mg/day) per day PO 1 x QD **or** divided into 2 doses (**AIII**) ***Note: Tetracyclines contraindicated in children <8 years of age***	One of the macrolide antibiotics (**AIII**)—e.g., azithromycin, 5–12 mg/kg body weight (max. 600m/day) PO 1 x QD; **OR** Clarithromycin: 15 mg/kg body weight (max.1g/day) PO QD divided into 2 doses; **OR** Erythromycin: 30–50 mg/kg body weight (max. 2 g/day) PO QD divided into 2 doses (**AIII**)	
***Candida* (oesophageal)**	Not routinely recommended, but can be considered for frequent severe recurrences.	Fluconazole: 3–6 mg/kg body weight (max. 200 mg) PO QD **OR** Itraconazole oral solution, 2.5 mg/kg body weight/ dose twice daily (**BI**)		**Criteria for Discontinuing Secondary Prophylaxis:** When CD4 count or percentage has risen to CDC immunologic Category 2 or 1. **Criteria for Restarting Secondary Prophylaxis:** quent severe recurrences

HSV	Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease	**Mucocutaneous Disease:** • Acyclovir 20 mg/kg body weight/dose (maximum 800 mg/dose) by mouth BID. **Suppressive Therapy After Neonatal Skin, Eye, Mouth, or CNS Disease:** • Acyclovir 300 mg/m2 Body surface area/dose by mouth TID for 6 months.	Mucocutaneous Disease, For Adolescents old enough to receive adult dosing: • Valacyclovir 500 mg by mouth BID, **OR** • Famciclovir 500 mg by mouth BID .	**Criteria for Discontinuing Secondary Prophylaxis:** After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established

[a] Pyrimethamine plus sulfadiazine, and possibly atovaquone, confers protection against PCP as well as against toxoplasmosis. Although the clindamycin-plus-pyrimethamine or atovaquone-with/without-pyrimethamine regimens are recommended for adults, they have not been tested in children. However, these drugs are safe and are used for other infections in children. [b] Substantial drug interactions might occur between rifabutin and PIs and NNRTIs; a specialist should be consulted. [c] Antimicrobial prophylaxis should be chosen on the basis of microorganism identification and antibiotic susceptibility testing. Cotrimoxazole, if used, should be administered daily. Health-care providers should be cautious about using antibiotics solely for this purpose because of the potential for development of drug-resistant microorganisms. IVIG might not provide additional benefit to children receiving daily co-trimoxazole but might be considered for children who have recurrent bacterial infections despite cotrimoxazole prophylaxis. Choice of antibiotic prophylaxis versus IVIG also should involve consideration of adherence, ease of IV access, and cost. If IVIG is used, respiratory syncytial virus (RSV) IVIG (750 mg/kg body weight), not monoclonal RSV antibody, can be substituted for IVIG during the RSV season to provide broad anti-infective protection, if this product is available.

7.2 Immunizations for HIV-infected Infants and Children

Immunization recommendations for HIV-infected children in the OECS are the same as immunization recommendations for non-HIV infected children, with the following exceptions:

- BCG is contra-indicated;
- MMR and Varicella vaccines should not be administered to children who are severely immunocompromised (CD4% less than 15%).
- Inactivated Polio Vaccine (IPV) is preferred over Oral Polio Vaccine (OPV). Pneumococcal vaccination (polysaccharide PPSV 23-valent, and/or conjugate PCV 7-valent) is recommended for HIV-infected infants and children given their vulnerability to pneumococcal pneumonia. See http://www.cdc.gov/mmwr/pdf/rr/rr5811.pdf for details regarding paediatric pneumococcal vaccination options.

These recommendations also correspond to perinatally HIV-exposed infants (HEIs) who are awaiting laboratory confirmation that they are HIV-uninfected. Once HIV infection has been ruled out in an HEI, the normal vaccination schedule can be followed.

7.3 Paediatric Opportunistic Infections Treatment Guidelines

This section provides detailed guidance on the management of selected OIs commonly seen in HIV-infected children in the Caribbean region. These recommendations have been adapted for the Eastern Caribbean region from paediatric CDC 2009 guidelines and 2013 updates of US National Institutes of Health[11]. Not all treatments listed may be available in the OECS but are included in case referral outside the region is an option. For management of OIs not listed below, please consult the original guidance of CDC and NIH.

Preferred and alternative treatment options are presented in table 33. Recommendations of the strength and quality of the evidence is the same as that used for primary prophylaxis.

[11] Centers for Disease Control and Prevention. Guidelines for prevention and treatment of opportunistic infections in HIV-exposed and HIV-infected children: Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR. 2009 Sep 4; 58(11).
Available from: http://www.cdc.gov/mmwr/pdf/rr/rr5811.pdf.

Table 33: Treatment of opportunistic Infection in the HIV infected children

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
Bacterial infections			
Bacterial pneumonia (*Streptococcus pneumoniae;* occasionally *Staphylococcus aureus, Hib, Pseudomonas aeruginosa*)	**Ceftriaxone:** 50–100 mg/kg body weight per day or 25–50 mg/kg body weight per dose twice daily IV or IM (max 4 g/day), in 1 or 2 divided doses (**AIII**); **OR** **Cefotaxime:** 40-50 mg/kg body weight per dose 4 times daily, or 50–65 mg/kg body weight 3 times daily (max 8– 10 g/day) IV. (**AIII**)	Cefuroxime, 35–50 mg/kg body weight per dose 3 times daily (max 4–6 g/day) IV (**AIII**)	For children who are receiving effective ART, have mild or no immunosuppression, and have mild to moderate community-acquired pneumonia, oral therapy option would be **amoxicillin 45 mg/kg body weight** per dose twice daily (maximum dose: 4 g per day). Add **azithromycin** for hospitalized patients to treat other common community-acquired pneumonia pathogens (M. pneumoniae, C. pneumoniae). Add **clindamycin or vancomycin** if methicillin resistant S. aureus is suspected (base the choice on local susceptibility patterns). For patients with neutropenia, chronic lung disease other than asthma (e.g., LIP, bronchiectasis) or ndwelling venous catheter, consider regimen that includes activity against P. aeruginosa (such as **ceftazidime or cefepime instead of ceftriaxone**). Consider PCP in patients with severe pneumonia or more advanced HIV disease. Evaluate for tuberculosis, cryptococcosis, and endemic fungi.

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
Bartonellosis	**Cutaneous bacillary angiomatosis infections:** -Erythromycin: 30–50 mg/kg body weight (max. 2 g/day) per day orally divided into 2–4 doses, **or** if unable to take oral medication, 15–50 mg/kg body weight (max. 2 g/day) per day IV in divided doses 4 times a day (**AII**) -Doxycycline:2–4 mg/kg body weight (max.100–200 mg/day) PO QD **or** IV 1 x QD or divided into 2 doses(**AII**); Tetracyclines contraindicated in children <8 years of age ***Treatment duration: 3 months***	Azithromycin: 5–12 mg/kg body weight (max. 600 mg/day) PO 1 x QD (**BIII**) Clarithromycin: 15 mg/kg body weight (max. 1 g/day) PO QD divided into 2 doses (**BIII**)	Severe Jarisch-Herxheimer–like reaction can occur in the first 48 hours after treatment Long-term suppression with erythromycin or doxycycline may be considered in patients with relapse or reinfection (**CIII**)
Bartonellosis	**CNS infections, bacillary peliosis, osteomyelitis, severe infections:** Doxycycline:2–4 mg/kg body weight (max. 100–200 mg/day) per day orally or IV 1 x QD or divided into 2 doses(**AIII**); Tetracyclines contraindicated in children <8 years of age ***Treatment duration: 4 months***	Rifampicin: 20 mg/kg body weight (max. 600 mg/day) per day orally or IV 1 x QD **or** divided into 2 doses; can be used in combination with erythromycin or doxycycline in patients with more severe infections (**BIII**)	
Syphilis	**Congenital** **Proven or Highly Probable Disease:** • Aqueous crystalline penicillin G 100,000–150,000 units/kg body weight per day, administered as 50,00 units/kg body weight per dose IV every 12 hours for the first 7 days of life, and then every 8 hours for 10 days • **If diagnosed after 1 month of age,** aqueous penicillin G 200,000– 300,000 unit/kg body weight per day, administered as 50,000 units/kg body weight per dose IV every 4–6 hours (maximum 18–24 million units per day) for 10 days **Possible Disease:**	**Congenital Proven or Highly Probable Disease (Less Desirable if CNS Involvement):** • Procaine penicillin G 50,000 units/kg body weight IM once daily for 10 days Possible Disease: • Treatment options are influenced by several factors, including maternal treatment, titer, and response to therapy; and infant physical exam, titer, and test results.	For treatment of congenital syphilis, repeat the entire course of treatment if >1 day of treatment is missed. Examinations and serologic testing for children with congenital syphilis should occur every 2–3 months until the test becomes non-reactive or there is a fourfold decrease in titer. Children with increasing titers or persistently positive titers (even if low levels) at ages 6–12 months should be evaluated and considered for re-treatment. In the setting of maternal and possible infant HIV

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	• Treatment options are influenced by several factors, including maternal treatment, titer, and response to therapy; and infantphysical exam, titer, and test results. Scenarios that include variations of these factors are described and treatment recommendations **Early Stage (Primary, Secondary, Early Latent):** • Benzathine penicillin 50,000 units/kg body weight (maximum 2.4 million units) IM for 1 dose Late Latent: • Benzathine penicillin 50,000 units/kg body weight (maximum 2.4 million units) IM once weekly for 3 doses **Neurosyphilis (Including Ocular):** • Aqueous penicillin G 200,000–300,000 units/kg body weight per day administered as 50,000 units/kg body weight per dose IV every 4–6 hours (maximum 18–24 million units per day) for 10–14 days		infection, the more conservative choices among scenario specific treatment options may be preferable. Children and adolescents with acquired syphilis should have clinical and serologic response monitored at 3, 6, 9, 12, and 24 months after therapy.
Mycobacterial infections			
MTB	**Pulmonary TB/ Intrathoracic disease** **Intensive phase (8 wks) (AI):** -Isoniazid: 10–15 mg/kg body weight (max. 300 mg/day) PO 1 x QD; **PLUS** -Rifampicin: 10–20 mg/kg body weight (max. 600 mg/day) PO 1 x QD; **PLUS** -Pyrazinamide: 20–40 mg/kg (max. 2 g/day)	Alternative drug for rifampicin is rifabutin: 10–20 mg/kg body weight (max. 300 mg/day) PO 1 x QD (same dose is for intermittent 2 or 3 x QW regimen) (BIII) Alternative drug for ethambutol is	Directly observed therapy should be standard of care for children with TB (**AII**) Potential drug interactions should be carefully reviewed In HAART-naive child, initiate therapy for TB 2–8 weeks before starting antiretroviral drugs (**BII**);

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	body weight PO 1 x QD; **PLUS** -Ethambutol: 15–25 mg/kg body weight (max. 2.5 g/day) PO 1 x QD (AI) **Continuation phase- 7 months (for drug- susceptible TB) (AI):** Daily: Isoniazid: 10–15 mg/kg body weight (max. 300 mg/day) PO 1x QD; **PLUS** Rifampicin: 10–20 mg/kg body weight (max. 600 mg/day) PO 1 x QD (AI) ***Treatment duration (drug sensitive TB)* (AIII):** Pulmonary TB: 9 months for HIV infected child (6 months if not HIV infected) **Extrapulmonary TB/ Extra Thoracic** : 12 months Lymph node TB—treat as minimal intrathoracic disease. Bone or joint disease–consider extending continuation phase to 10 months (for total duration of therapy of 12 months). **TB Meningitis:** • As alternative to ethambutol or streptomycin, 20–40 mg/kg body weight (maximum 1 g/day) IM once daily—during intensive phase, consider ethionamide, 15–20 mg/kg body weight by mouth (maximum 1 g/day), initially divided into 2 doses until well tolerated) • Consider extending continuation phase to	streptomycin: 20–40 mg/kg body weight (max. 1 g/day) IM PO 1 x QD (or 20 mg/kg as intermittent 2 or 3 times weekly regimen) (BIII) Ethionamide: 15–20 mg/kg body weight orally (max. 1 g/day) divided into 2 or 3 doses per day should be used for TB meningitis (AIII). **Drug-resistant TB: *Resistance to isoniazid alone:*** -Discontinue isoniazid Rifampicin **PLUS** Pyrazinamide **PLUS** Ethambutol (ethionamide or streptomycin can be substituted for ethambutol if *M. tuberculosis* isolate is susceptible to these agents) (BII) ***Resistance to rifampicin alone:*** -Discontinue rifampicin Isoniazid **PLUS** Pyrazinamide **PLUS** Ethambutol **PLUS** Streptomycin for first 2 mos. followed by a continuation phase of Isoniazid **PLUS** Pyrazinamide **PLUS** Ethambutol to complete 12- to 18-month course (BIII) **For older adolescents:** Isoniazid **PLUS** Pyrazinamide **PLUS** Ethambutol **PLUS**	For children already receiving HAART in whom TB is diagnosed, the child's ARV regimen should be reviewed and altered, if needed, to ensure optimal treatment for both TB and HIV and to minimize potential toxicities and drug-drug interactions (**AIII**) For children with severe immunosuppression (CD4 percentages <15% for children >6 yrs old, <100 cell/μL), continuation phase for drug-susceptible TB should include either daily or thrice weekly treatment; twice-weekly regimens should *not* be used because they may lead to rifamycin resistance in immunosuppressed patients (**AII**) Pyridoxine should be administered if isoniazid or cycloserine is administered (**AII**) Adjunctive treatment with corticosteroids is indicated for children with CNS disease (**AII**) and can be considered for children with pleural or pericardial effusions, severe miliary disease, and significant endobronchial disease (**BIII**) Children receiving ethambutol who are old enough to undergo routine eye testing should have monthly monitoring of visual acuity and colour discrimination (**AIII**) Thiacetazone can cause severe or fatal reactions in HIV-infected children, including rash and aplastic anaemia, and should not be used (**EIII**) For drug-resistant strains, ≥2 drugs to which the isolate is susceptible should be administered (minimum of 3 drugs should be administered

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	10 months (for total duration of therapy of 12 months). • Discuss with an expert. Drug-Resistant TB **MDR-TB:** • Therapy should be based on resistance pattern of child (of source case where child's isolate is not available); consult an expert. **Treatment Duration:** • 18–24 months after nonbacteriological diagnosis or after culture conversion; ≥12 months if minimal disease	a fluoroquinolone for 2 months, followed by Isoniazid **PLUS** Ethambutol **PLUS** a fluoroquinolone to complete 12- to 18-month course (BIII) **Multidrug resistance:** Therapy should be based on resistance pattern (of child or of source case when child's isolate is not available), and children should be managed in consultation with an expert (AIII) **Treatment duration (drug-resistant TB) (AIII):** *Single drug—isoniazid-resistant TB: 9–12 months* (BII) *Single drug—rifampicin-resistant TB: 12–18 months* (BIII) ***MDR-TB: 18–24 months after culture conversion in children with bacteriologic confirmation; ≥12 months in children who were culture negative at treatment initiation***	through the continuation phase of therapy) **Second-line drugs for MDR-TB:** -Amikacin: 15–30 mg/kg body weight (max. 1 g/day) IM 1 x QD -Capreomycin: 15–30 mg/kg body weight (max. 1 g/day) IM 1 x QD -Ciprofloxacin: 10–15 mg/kg body weight PO 2 x QD (max. 1.5 g/day); -Levofloxicin: (500– 1,000 mg PO 1 x QD); **OR** -Moxifloxacin: 400 mg PO 1 x QD (fluoroquinolones are not labeled for use in children <18 years old because of concerns about potential effects on cartilage; use in younger persons requires assessment of potential risks and benefits) (**CIII**) -Cycloserine: 10–20 mg/kg body weight (max. 1 g/day) PO 1 x QD -Ethionamide/prothionamide: 15–20 mg/kg body weight (max. 1 g/day) PO in 2–3 divided doses -Kanamycin: 15–30 mg/kg body weight (max. 1 g/day) IM 1 x QD –Para-aminosalicylic acid: 200– 300 mg/kg body weight PO divided into 3–4 doses per day max. 10 g/day) -Streptomycin: 20–40 mg/kg body weight (max. 1 g/day) IM PO 1 x QD
MAC	Initial treatment (≥2 drugs) (**AI**): Clarithromycin: 7.5– 15 mg/kg body weight (max. 500 mg/dose) PO 2 x QD (**AI**); **PLUS** Ethambutol: 15–25 mg/kg body weight (max. 2.5 g/day) PO 1 x QD (**AI**), followed by chronic suppressive therapy. For severe disease, add rifabutin: 10–20 mg/kg	Azithromycin (10–12 mg/kg body weight [max. 500 mg/day] PO 1 x QD if intolerant to clarithromycin) (**AII**) If rifabutin cannot be administered (or if a fourth drug is needed for patients with more severe	Combination therapy with a minimum of 2 drugs is recommended (**AI**) Clofazamine is associated with increased mortality in HIV-infected adults and should not be used (**EII**). Children receiving ethambutol who are old enough to undergo routine eye testing should have monthly monitoring of visual acuity and colour discrimination (**AIII**). Fluoroquinolones (e.g., ciprofloxacin,

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	body weight (max. 300 mg/day) PO 1 x QD (**CI**)	symptoms or disseminated disease): Ciprofloxacin (10–15 mg/kg body weight PO 2 x QD [max. 1.5 g/day]); **OR** Levofloxicin (500 mg orally PO 1 x QD); **OR** Amikacin (15–30 mg/kg body weight IV in 1 or 2 divided doses [max. 1.5 g/day]) (**CIII**)	levofloxacin) are not labeled for use in children <18 years because of concerns about potential effects on cartilage; use in younger persons requires an assessment of potential risks and benefits (**CIII**). Chronic suppressive therapy (secondary prophylaxis) is recommended in children and adults after initial therapy
		Fungal Infections	
Aspergillosis	Voriconazole: 6–8 mg/kg body weight per dose IV or 8 mg/kg body weight (max. 400 mg) per dose PO 2 x QD on day 1, followed by 7 mg/kg body weight (max. 200 mg) per dose IV or PO 2 x QD **(AI)** *Treatment duration >12 weeks, but duration should be individualized according to the patient's clinical response* **Invasive disease:** Amphotericin B: 0.5– 1.5 mg/kg body weight IV 1 x QD (**AI**) *Treatment duration: Based on presence of deep tissue foci and clinical response; in patients with candidemia, treat until 2–3 weeks after last by positive blood culture* (**AIII)**	Amphotericin B deoxycholate: 1.0–1.5 mg/kg body weight IV 1 x QD (**AIII**) Lipid formulations of amphotericin B: 5 mg/kg body weight IV 1 x QD (**AIII**) Caspofungin: 70 mg/m^2 body surface area (max. 70 mg) IV as loading dose, then 50 mg/m^2 body surface area (max. 50 mg) IV 1 x QD (**CIII**)	Potential for significant pharmacokinetic interactions between PIs or NNRTIs with voriconazole and should be used cautiously in these situations. Consider therapeutic drug monitoring and dosage adjustment if necessary
Candidiasis	**Oropharyngeal disease:** Fluconazole 6–12 mg/kg body weight (max 400 mg/dose) by mouth once daily (**AI**) Clotrimazole trouches: 10 mg troche PO 4 x QD (**BII**) Nystatin suspension: 4–6 mL PO 4 x QD; **OR** one to two 200,000 U flavored pastilles orally 4–5 x QD (**BII**) ***Treatment duration: 7–14 days*** **Oesophageal disease**:	Oropharyngeal disease (Aged 2–17 years, loading dose of 3 mg/kg body weight/ daily and then maintenance at 1.5 mg/kg body weight/dose daily IV **Caspofungin** **Infants aged <3 months**, 25 mg/m2 body surface area/dose daily IV **Aged 3 months–17 years**, 70 mg/m2/day IV loading dose followed	Itraconazole oral solution should not be used interchangeably with itraconazole capsules. Itraconazole capsules are generally ineffective for treatment of esophageal disease. Central venous catheters should be removed, when feasible, in HIV-infected children with fungemia. In uncomplicated catheter-associated C. albicans candidemia, an initial course of

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	Fluconazole: 6 -12 mg/kg body weight orally once on day 1, then 3–6 mg/kg body weight (max. 600 mg/dose) PO 1 x QD (**AI**) Itraconazole oral solution, 2.5 mg/kg body weight/dose by mouth twice daily (**AI**) ***Treatment duration: Minimum of 3 weeks and for at least 2 weeks following the resolution of symptoms*** **Invasive Disease: Critically Ill** Echinocandin Recommended: **Anidulafungin** **Aged 2–17 years**, Load with 3 mg/kg body weight/daily dose and then maintenance at 1.5 mg/kg body weight once daily **Aged ≥18 years,** 200 mg loading dose, then 100 mg once daily **Caspofungin** Infants aged <3 months, 25 mg/m2 body surface area/dose once daily IV Aged 3 months–17 years 70 mg/m2 body surface area/day loading dose followed by 50 mg/m2 once daily (maximum, 70 mg) (note: dosing based on surface area is recommended for children for caspofungin); Aged ≥18 years, 70-mg loading dose, then 50 mg once daily; **Micafungin** Neonates, up to 10–12 mg/kg bodyweight/dose daily IV may be required to achieve therapeutic concentrations. Infants <15 kg body weight, 5–7 mg/kg/day Children ≤40 kg body weight and aged 2–8 years, 3–4 mg/kg body weight/ dose daily IV	by 50 mg/m2 /day IV (maximum 70 mg). **Aged ≥18 years**, 70-mgoading dose IV, then 50 mg/dose daily IV **Micafungin** **Neonates,** up to 10–12 mg/kg bodyweight/dose daily IV may be required to achieve therapeutic concentrations. **Infants, <15 kg body weight,** 5–7 mg/kg body weight/dose daily IV **Children ≤40 kg body weight** and aged 2–8 years, 3–4 mg/kg body weight/dose daily IV **Children ≤40 kg body weight** and aged 9–17 years, 2–3 mg/kg body weight/dose daily IV **Children >40 kg body weight,100 mg/dose daily IV fluconazole** Children, 6–12 mg/kg body weight/dose daily for infants and children of all ages (maximum dose: 600 mg daily). **Invasive Disease:** Fluconazole 12 mg/kg body weight IV once daily (maximum 600 mg/day) for minimum 2 weeks after last positive blood culture (if uncomplicated candidemia) Lipid formulations of	amphotericin B followed by fluconazole to complete treatment can be used (use invasive disease dosing). Voriconazole has been used to treat esophageal candidiasis in a small number of HIV-uninfected immunocompromised children. **Voriconazole Dosing in Pediatric Patients:** • 9 mg/kg body weight/dose every 12 hours IV loading for day 1, followed by 8 mg/kg body weight/dose IV every 12 hours. • Conversion to oral voriconazole should be at 9 mg/kg body weight/dose orally every 12 hours. • Children aged ≥12 years and weighing at least 40 kg can use adult dosing (load 6 mg/ kg body weight/dose every 12 hours IV on day 1, followed by 4 mg/kg bodyweight/dose every 12 hours IV. Conversion to oral therapy at 200 mg every 12 hours by mouth.) **Anidulafungin in Children Aged 2–17 Years** • Loading dose of 3 mg/kg body weight/once daily followed by 1.5 mg/kg body weight/once daily (100 mg/day maximum). If a neonate's creatinine level is >1.2 mg/dL for >3 consecutive doses, the dosing interval for fluconazole 12 mg/kg body weight may be prolonged to one dose every 48 hours until the serum creatinine level is <1.2 mg/dL **Treatment Duration:** • Patients with esophageal candidiasis should be

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	Children ≤40 kg body weight and aged 9–17 years, 2–3 mg/kg body weight/dose daily Children >40 kg body weight, 100 mg/dose daily IV **Not Critically Ill** Fluconazole Recommended: 12 mg/kg body weight/dose daily (max dose: 600 mg) for infants and children of all ages Avoid fluconazole for C. krusei and C. glabrata, avoid echinocandin for C. parapsilosis. ***Treatment duration: Based on presence of deep tissue foci and clinical response; in patients with candidemia, treat until 2–3 weeks after last by positive blood culture*** **(AIII**)	amphotericin B, 5 mg/kg body weight IV once daily	treated for a minimum of 3 weeks and for at least 2 weeks following resolution of symptoms.
Coccidioidomycosis	**Severe Illness with Respiratory Compromise due to Diffuse Pulmonary or Disseminated Non Meningitic Disease:** -Amphotericin B deoxycholate 0.5–1.0 mg/kg body weight IV once daily, until clinical improvement. - A lipid amphotericin B preparation can be substituted at a dose of 5 mg/kg body weight IV once daily (dosage of the lipid preparation can be increased to as much as 10 mg/kg body weight IV once daily for life threatening infection). -After the patient is stabilized, therapy with an azole (fluconazole or itraconazole) can be substituted and continued to complete a 1-year course of antifungal therapy.	**Severe Illness with Respiratory Compromise Due to Diffuse Pulmonary or Disseminated Non Meningitic Disease (If Unable to Use Amphotericin**): -Fluconazole 12mg/kg body weight (maximum 800 mg) per dose IV or by mouth once daily. Treatment duration - total of 1 year, followed by secondary prophylaxis.	Surgical debridement of bone and lung lesions may be helpful. Itraconazole is the preferred azole for treatment of bone infections. Triazole can be added to amphotericin B therapy and continue triazole once amphotericin B is stopped (**BIII**) Chronic suppressive therapy (secondary prophylaxis) with fluconazole or itraconazole is recommended for children after initial induction therapy for disseminated disease and is continued lifelong for meningeal disease. Therapy with amphotericin results In a more rapid clinical response in severe, non-meningeal disease.

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
Cryptococcus neoformans	**CNS disease:** Acute therapy (minimum 2-week induction followed by consolidation therapy) -Amphotericin B: 1.0 mg/kg body weight (or liposomal amphotericin B, mg/kg body weight) IV QD; **PLUS** Flucytosine: 25 mg/kg body weight PO QD divided 4 x QD (**AI**); **OR** Liposomal amphotericin B: 4–6 mg/kg body weight IV 1 x QD (especially in children with renal insufficiency or infusion-related toxicity to amphotericin B); **PLUS** Flucytosine: 100 mg/kg body weight PO QD divided 4 x QD (**AII**) **Consolidation therapy** (followed by chronic suppressive therapy): Fluconazole: 12 mg/kg body weight on day 1 and then 10–12 mg/kg body weight (max. 800 mg) QD IV or PO for a minimum of 8 weeks (**AI**) **Localized disease including isolated pulmonary disease (CNS not involved):** Fluconazole: 12 mg/kg body weight on day 1 and then 6– 12 mg/kg body weight (max. 600 mg) IV or PO QD (**AIII**) **Treatment Duration:** ***Length of initial therapy for non-CNS disease depends on site and severity of infection and clinical response*** **Disseminated disease (CNS not involved) or severe pulmonary disease:** Amphotericin B: 0.7– 1.0 mg/kg body weight; **OR** Amphotericin liposomal: 3–5 mg/kg body	**CNS Disease Acute Therapy (Minimum 2-Week Induction Followed by Consolidation Therapy)** **If Flucytosine Not Tolerated or Unavailable**: **-A** Liposomal amphotericin B, 6 mg/kg body weight IV once daily **OR** Amphotericin B Lipid Complex, 5 mg/kg body weight IV once daily, **OR** Amphotericin B deoxycholate, 1.0–1.5 mg/kg body weight IV once daily alone **OR** **B**. in combination with high dose fluconazole (12 mg/kg body weight on day 1 and then 10–12 mg/kg body weight [max 800 mg] IV). **If Amphotericin B-Based Therapy Not Tolerated:** -Fluconazole, 12 mg/kg body weight on day 1 and then 10–12 mg/kg body weight (maximum 800 mg) IV **OR** by mouth once daily **PLUS** Flucytosine, 25 mg/kg body weight per dose by mouth given 4 times daily **Consolidation Therapy (followed by secondary prophylaxis):** Itraconazole 5–10 mg/kg body weight by mouth given once daily, **OR**	In patients with meningitis, CSF culture should be negative before initiation of consolidation therapy. Liquid preparation of itraconazole (if tolerated) is preferable (but more expensive) over tablet formulation because of better bioavailability (**BIII**). Serum concentrations of itraconazole should be monitored to optimize drug dosing. Amphotericin B may increase toxicity of flucytosine by increasing cellular uptake or impairing its renal excretion or both. Flucytosine dose should be adjusted to keep drug levels at 40–60 μg/mL. Oral acetazolamide should not be used to reduce intracranial pressure in cryptococcal meningitis (**DIII**). Chronic suppressive therapy (secondary prophylaxis) with fluconazole is recommended for children after initial therapy.

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	weight; **OR** Amphotericin lipid complex: 5 mg/kg body weight IV 1 x QD (with or without flucytosine) (**AIII**) ***Treatment duration: Length of initial therapy for non-CNS disease depends on site and severity of infection and clinical response***	2.5–5 mg/kg body weight given twice daily (maximum 200 mg/dose) for a minimum of 8 weeks. A loading dose (2.5–5 mg/kg body weight per dose 3 times daily) is given for the first 3 days (maximum200 mg/ dose; 600 mg/day). **Localized Disease Including Isolated Pulmonary Disease (CNS Not Involved)** Amphotericin B, 0.7–1.0 mg/kg body weight, **OR** Amphotericin liposomal 3–5 mg/kg body weight, **OR** Amphotericin lipid complex, 5 mg/kg body weight IV once daily **Disseminated Disease (CNS Not Involved) or Severe, Pulmonary Disease:** Fluconazole, 12 mg/kg body weight on day 1 and then 6– 12 mg/kg body weight (maximum 600 mg) IV or by mouth once daily	
Histoplasma capsulatum	Mild disseminated disease: Itraconazole oral solution: Initial loading dose of 2–5 mg/kg body weight per dose (max. 200 mg) PO 3 x QD for first 3 days of therapy, followed by 2–5 mg/kg body weight (max. 200 mg) per dose 2 x QD for 12 months (AII) **Moderately severe to severe**	**Moderately severe to severe disseminated disease or CNS infection:** ute therapy (minimum 1- to 2week induction, longer if clinical improvement is delayed or at least 4– 6 weeks if CNS involved, followed by consolidation therapy): Amphotericin B	Urine antigen should be monitored to identify relapse Serum concentrations of itraconazole should be monitored and reach 1 μg/mL at steady-state; levels exceeding 10μg/mL should be followed by dose reduction. Urine antigen should be monitored to identify

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	disseminated disease: Acute therapy (minimum 1- to 2-wk induction, longer if clinical improvement is delayed, followed by consolidation therapy) Liposomal amphotericin B, 3 mg/kg body weight IV 1 x QD (AI) **Consolidation therapy (followed by chronic suppressive therapy):** Itraconazole oral solution: initial loading dose of 2–5 mg/kg body weight per dose (max. 200 mg) orally 3 x QD for first 3 days of therapy, followed by 2–5 mg/kg body weight (max. 200 mg) per dose 2 x QD for 12 months (AII) **CNS infection** Acute therapy (4–6 weeks, followed by consolidation therapy): Liposomal amphotericin B, 5 mg/kg body weight IV 1 x QD (AII) Consolidation therapy (followed by chronic suppressive therapy): Itraconazole oral solution: initial loading dose of 2–5 mg/kg body weight per dose (max. 200 mg) orally 3 x QD for first 3 days of therapy, followed by 2–5 mg/kg body weight (max. 200 mg) per dose2 x QD for ≥12 months and until histoplasmal antigen is no longer detected (AII).	deoxycholate: 1 mg/kg body weight IV 1 x QD (**AIII**)	relapse. A high relapse rate with CNS infection occurs in adults, thereby requiring longer therapy; treatment in children is anecdotal and expert consultation should be considered. Chronic suppressive therapy (secondary prophylaxis) with itraconazole is recommended for children after initial therapy.
PCP	TMP-SMX 3.75–5 mg/kg body weight/dose TMP(based on TMP component) every 6 hours IV or orally given for 21 days (followed by secondary prophylaxis dosing) ***Treatment duration (followed by chronic***	**If TMP-SMX-Intolerant or Clinical Treatment Failure After 5–7 Days of TMP-SMX Therapy** Pentamidine 4 mg/kg body weight/dose IV/IM once daily is the	Dapsone: 2 mg/kg body weight PO 1 x QD (max. 100 mg/day) PLUS TMP: 15 mg/kg body weight orally per day divided into 3 doses has been used in adults (**BI**), but data in children are limited (**CIII**) Primaquine base: 0.3 mg/kg body weight PO 1 x QD (max. 30 mg/day), **PLUS** clindamycin: 10 mg/kg body weight IV or orally (max. 600 mg IV and 300–

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	***suppressive therapy): 21 days* (AII)**	first choice. **Alternative regimen**. Note: Pentamidine can be changed to atovaquone after 7–10 days IV therapy. **Atovaquone** **Daily Dosing:** • Children aged 1–3 months and >24 months–12 years: 30-40 mg/kg body weight/dose by mouth once daily with food • Children aged 4–24 months: 45mg/kg body weight/dose by mouth once daily with food **Twice-Daily Dosing*:** • Children aged ≥13 years: 750 mg/dose by mouth twice daily *Some experts use twice-daily dosing of atovaquone as alternative treatment for PCP in children aged <12 years: • Children aged 1–3 months and >24 months to 12 years: 15–20 mg/kg body weight /dose by mouth twice daily with food • Children aged 4–24 months: 22.5mg/kg body weight/dose by mouth twice daily with food.	450 mg orally) every 6 hours has been used in adults (**BI**), but data in children are not available (**CIII**). Indications for corticosteroids (**AI**): PaO2 <70 mmHg at room air or alveolar-arterial oxygen gradient >35 mm Hg Prednisone dose: 1 mg/kg body weight PO 2 x QD for 5 days, then 0.5–1.0 mg/kg body weight PO 2 x QD for 5 days, then 0.5 mg/kg body weight PO 1 x QD for days 11–21 Chronic suppressive therapy (secondary prophylaxis) with cotrimoxazole is recommended for children and adults after initial therapy (table 29) (**AI**).
Parasitic Infections			
Cryptosporidiosis	Effective HAART—immune reconstitution may lead to microbiologic and clinical response (**AII**)	No consistently effective therapy exists for cryptosporidiosis in HIV infected persons; optimized HAART and a trial of nitazoxanide can be considered: Nitazoxanide (data from	Supportive care: Hydration, correct electrolyte abnormalities, nutritional support (**AIII**). Antimotility agents (e.g., loperamide) should be used with caution in young children (**CIII**).

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
		immunocompetent children) (**BI**), HI uninfected; (**CIII**), HIV-infected) in combination with effective HAART: 1–3years: 100 mg PO 2 x QD 4–11 years: 200 mg PO 2 x QD ≥12 years: 500 mg PO 2 x QD ***Treatment duration: 3-14 days<14 days***	
Microsporidiosis	Effective HAART— immune reconstitution may lead to microbiologic and clinical response(**AII**) **For disseminated (not ocular)** and intestinal infection attributed to microsporidia other than *Enterocytozoon bienuesi*: Albendazole: 7.5 mg/kg body weight (max. 400 mg/dose) per dose PO 2 x QD (**AII**). *Treatment duration: continue until immune reconstitution after initiation of HAART* (**AIII**) **For ocular infection:** Topical fumagillin bicylohexylamm onium (Fumidil B): 3 mg/mL in saline (fumagillin 70 μg/mL) eye drops—2 drops every 2 hours for 4 days, then 2 drops 4 x QD (investigational use only in US) (**BII**); **PLUS** Albendazole: 7.5 mg/kg body weight (max. 400 mg/dose) PO 2 x QD for management of systemic infection (**BIII**) ***Treatment duration: continue indefinitely to prevent recurrence or relapse* (BIII)**		Supportive care: Hydration, correct electrolyte abnormalities, nutritional support (**AIII**) Antimotility agents (e.g., loperamide) should be used with caution in young children (**CIII**)
Isosporiasis (Cystoisospori	TMP-SMX 5 mg/kg body weight of TMP component given twice daily by mouth	Pyrimethamine 1 mg/kg body weight plus folinic acid 10-25 mg by	If symptoms worsen or persist, the TMP-SMX dose may be increased to 5 mg/kg/day given 3–4 times

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
asis)	for 10 days	mouth once daily for 14 days **Second-Line Alternatives:** •Ciprofloxacin 10–20 mg/kg body weight/day twice daily by mouth for 7 days • Nitazoxanide (see doses below) for 3 consecutive days • Children 1–3 years: 100 mg by mouth every 12 hours • Children 4–11 years: 200 mg by mouth every 12 hours • Adolescents ≥12 years and adults: 500 mg by mouth every 12 hours	daily by mouth for 10 days or the duration of treatment may be lengthened. Duration of treatment with pyrimethamine has not been well established. Ciprofloxacin is generally not a drug of first choice in children due to increased incidence of adverse events, including events related to joints and/or surrounding tissues.
Giardiasis	Tinidazole, 50 mg/kg by mouth, administered as 1 dose given with food (maximum 2 g). **Nitazoxanide**: • 1–3 years: 100 mg by mouth every 12 hours with food for 3 days • 4–11 years: 200 mg by mouth every 12 hours with food for 3 days • ≥12 years: 500 mg by mouth every 12 hours with food for 3 days	Metronidazole 5 mg/kg by mouth every 8 hours for 5-7 days.	Supportive Care: Hydration • Correction of electrolyte abnormalities • Nutritional support Antimotility agents (e.g., loperamide) should be used with caution in young children.
Toxoplasma gondii	**Congenital Toxoplasmosis:** Pyrimethamine loading dose—2 mg/kg body weight by mouth once daily for 2 days, then 1 mg/kg body weight by mouth once daily for 2–6 months, then 1 mg/kg body weight by mouth 3 times weekly, **PLUS** Leucovorin (folinic acid) 10 mg by mouth or IM with each dose of pyrimethamine, **PLUS** Sulfadiazine 50 mg/kg body weight by mouth twice daily **Treatment Duration: 12 months** **Acquired Toxoplasmosis** **Acute Induction Therapy (Followed by**	**For Sulfonamide-Intolerant Patients**: Clindamycin 5–7.5 mg/kg body weight (maximum600 mg/dose) by mouth or IV per dose given 4 times a day combined with pyrimethamine and Leucovorin.	**Congenital Toxoplasmosis:** For infants born to mothers with symptomatic Toxoplasma infection during pregnancy, empiric therapy of the newborn should be strongly considered irrespective of the mother's treatment during pregnancy. **Acquired Toxoplasmosis:** • Pyrimethamine use requires CBC monitoring at least weekly while on daily dosing and at least monthly while on less than daily dosing. • TMP-SMX—TMP 5 mg/kg bodyweight **PLUS** SMX 25 mg/kg body weight per dose IV or by mouth given twice daily has been used as an alternative to pyrimethamine sulfadiazine in adults, but has not been studied in children.

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	Chronic Suppressive Therapy): Pyrimethamine: loading dose—2 mg/kg body weight (maximum 50 mg) by mouth once daily for 3 days, then 1 mg/kg body weight(maximum 25 mg) by mouth once daily **PLUS** Sulfadiazine 25–50 mg/kg body weight (maximum 1–1.5 g/dose)by mouth per dose 4 times daily, **PLUS** Leucovorin 10–25 mg by mouth once daily, followed by chronic suppressive therapy. **Treatment Duration (Followed by Chronic Suppressive Therapy):** ≥6 weeks (longer duration if clinical or radiologic disease is extensive or response incomplete at 6 weeks)		• Corticosteroids (e.g., prednisone, dexamethasone) have been used in children with CNS disease when CSF protein is very elevated (>1,000mg/dL) or there are focal lesions with significant mass effects, with discontinuation as soon as clinically feasible. • Anticonvulsants should be administered to patients with a history of seizures and continued through the acute treatment; but should not be used prophylactically.
Viral Infections			
CMV	**Symptomatic congenital infection with neurologic involvement:** Ganciclovir: 6 mg/kg body weight IV every 12 hours for 6 weeks (**BI**) **Disseminated disease and retinitis (induction therapy (followed by chronic suppressive therapy):** Ganciclovir: 5 mg/kg body weight IV every 12 hours for 14–21 days (may be increased to 7.5 mg/kg body weight IV 2 x QD), then 5 mg/kg per day for 5– 7 days per week for chronic suppression (**AI**) **CNS disease (followed by chronic suppressive therapy):** Ganciclovir: 5 mg/kg body weight IV every 12	**Disseminated disease and retinitis (induction therapy followed by chronic suppressive therapy):** Foscarnet: 60 mg/kg body weight IV every 8 hours or 90mg/kg body weight per dose IV every 12 hours for 14– 21 days, then 90–120 mg/kg once a day for chronic suppression (**AI**) **Alternatives for Retinitis (Followed by Chronic Suppressive Therapy):** -Valganciclovir tablets 900 mg per dose orally twice daily for 14–21 days, followed by chronic	Valganciclovir is used in adults. Data on valganciclovir dosing in young children for treatment of retinitis are unavailable, but consideration can be given to transitioning from IV ganciclovir to oral valganciclovir after improvement of retinitis is noted. • Intravitreal injections of ganciclovir, foscarnet, or cidofovir are used in adults for retinitis but are not practical for most children. • Combination ganciclovir and foscarnet is associated with substantial rates of adverse effects, and optimal treatment for neurologic disease in children is unknown, particularly if receiving optimized ART. • Chronic suppressive therapy (secondary prophylaxis) is recommended in adults and children

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	hours; **PLUS** Foscarnet: 60 mg/kg body weight IV every 8 hours (or 90mg/kg body weight per dose IV every 12 hours), continued until symptoms improve (**BII**), followed by chronic suppression.	suppressive therapy. *Note: This is an option in older children who can receive the adult dose (based on their BSA).* - IV ganciclovir plus IV foscarnet (at above induction doses) may be considered as initial induction therapy in children with sight threatening disease or for treatment following failure/relapse on monotherapy. - Cidofovir is also used to treat CMV retinitis in adults intolerant to other therapies. Induction dosing in adults is 5 mg/kg body weight IV once weekly for 2 weeks, followed by chronic suppressive therapy however, data on dosing in children are unavailable. Must be given with probenecid and IV hydration.	following initial therapy of disseminated disease, retinitis, neurologic disease, or GI disease with relapse.
HBV	**Treatment for both HIV and HBV:** 3TC: 4 mg/kg body weight orally (max. 150 mg/dose) 2 x QD as part of a fully suppressive HAART regimen (**BII**) Include TDF (300 mg PO 1 x QD) as part of HAART regimen with 3TC for older children who can receive adult dosing (**BII**) If child is on HAART containing 3TC or FTC and has detectable HBV DNA **(assume 3TC/FTC resistance)**: If child is old enough to receive adult dosing,	Interferon-alfa: 10 million units/m^2 body surface area subcutaneously 3 x weekly for 6 months (sometime used for retreatment of failed lower-dose interferon therapy) (**CII**) Alternative for 3TC: FTC 6 mg/kg body weight (max. 200 mg) 1 x QD (**BIII**)	Indications for treatment include (**BII**): Detectable serum HBV DNA, with or without positive HBeAg, for >6 months; **and** Persistent (>6 months) elevation of serum transaminases (twice or more the upper limit of normal); **OR** Evidence of chronic hepatitis on liver biopsy Interferon-alfa is contra-indicated in children with decompensated liver disease; significant cytopenias; severe renal, neuropsychiatric, or cardiac disorders; and autoimmune disease (**EII**). Choice of HBV treatment options for HBV/HCV co-infected children depends on whether concurrent

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	continue 3TC (or FTC) (**CIII**); If child is old enough to receive adult dosing and is not on TDF, add TDF (300 mg orally once daily) to HAART regimen (**BII**); **OR** add adefovir (10 mg orally once daily) to HAART regimen (**BII**) If child is not old enough to receive adult dosing, administer 6month course of interferon-alfa as above in addition to HAART regimen (**BII**); continue 3TC (or FTC) (**CIII**).		HIV treatment is warranted 3TC and FTC have similar activity (and have cross-resistance) and should not be administered together . Adefovir is not approved for use in children but is under study in HIV uninfected children for treatment of chronic HBV; it can be considered for older HIV-infected children who can receive adult dosage IRIS may be manifested by dramatic increase in transaminases as CD4 counts rise within the first 6–12 weeks of HAART; distinguishing between drug-induced hepatotoxicity or other causes of hepatitis and IRIS may be difficult In children receiving 3TC, FTC, and/or TDF, clinical and laboratory exacerbations of hepatitis (flare) may occur if the drug is discontinued; thus, once antiHBV/HIV therapy has begun, it should be continued unless contraindicated or until the child has been treated for >6 months after HBeAg seroconversion and can be closely monitored on discontinuation (**BIII**). If anti-HBV therapy is discontinued and a flare occurs, reinstitution of therapy is recommended because a flare can be life threatening (**BIII**). Entecavir and telbivudine have been approved for use in adults with HBV; no data exist on safety or efficacy of these medications in children.
HCV	Interferon-alfa PLUS ribavirin combination therapy (**BIII**): Pegylated IFN-α: Peg-IFN 2a 180 /1.73 m2 body surface area subcutaneously once per week (maximum dose 180 µg)**OR** 181 Peg-IFN 2b 60 µg/m2 body surface area once per week **PLUS** Ribavirin (oral): **7.5 mg/kg** body weight QD	For children in whom ribavirin is contraindicated (e.g., unstable cardiopulmonary disease, preexisting anaemia or haemoglobinopathy): Interferon-alfa–2a or –2b: 3–5 million units/m^2 body surface area (max. 3	Length of treatment for HIV/HCV co-infected children is unknown and based on recommendations for HIV/ HCV-coinfected adults (**BIII**). Treatment of HCV in children <3 years generally is not recommended (**DIII**). Indications for treatment are based on recommendations in HIV/HCV co-infected adults;

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	in 2 divided doses (fixed dose by weight recommended): **25–36 kg:** 200 mg am and pm **>36–49 kg:** 200 mg in am and 400 mg in pm **>49–61 kg**: 400 mg in am and pm **>61–75 kg:** 400 mg in am and 600 mg in pm **>75 kg**: 600 mg in am and pm ***Treatment duration: 48 weeks, regardless of HCV genotype*** **(BIII)**	million units/dose) subcutaneously or IM 3 x weekly (**BII**)	because HCV therapy is more likely to be effective in younger patients and in patients without advanced disease or immunodeficiency, treatment should be considered for all HIV/HCV infected children >3 years who have no contra-indications for treatment (**BIII**). IRIS may be manifested by dramatic increase in transaminases as CD4 counts rise within the first 6–12 weeks of HAART; distinguishing between drug-induced hepatotoxicity or other causes of hepatitis and IRIS may be difficult. Interferon-alfa is contra-indicated in children with decompensated liver disease, significant cytopenias, severe renal or cardiac disorders, and autoimmune disease (**EII**). Ribavirin is contra-indicated in children with unstable cardiopulmonary disease, severe preexisting anaemia, or haemoglobinopathy (EII). Didanosine combined with ribavirin may lead to increased mitochondrial toxicities; concomitant use is contraindicated (EIII). Ribavirin and AZT both are associated with anaemia and when possible should not be administered together (DII). Pegylated interferon-alfa is not approved for use in children although it is under study; in adults with chronic HCV warranting treatment, pegylated interferon-alfa– 2a (180 µg) or –2b (1.5 µg/kg) subcutaneously once weekly PLUS ribavirin is the treatment of choice (AI).

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
HSVs	**Neonatal CNS or disseminated disease:** Acyclovir: 20 mg/kg body weight IV per dose 3 x daily for 21 days (**AI**) **Neonatal skin, eye, or mouth disease:** Acyclovir: 20 mg/kg body weight IV per dose 3 x daily for 14 days (**AI**) **CNS or disseminated disease in children outside the neonatal period**: Acyclovir: 10 mg/kg ((up to 20 mg/kg bodyweight/dose in children <12years) body weight IV 3 x daily for 21 days (**AII**) **Moderate-to-severe symptomatic gingivostomatitis:** Acyclovir: 5–10 mg/kg body weight per dose IV 3 x daily (**AI**) After lesions began to regress, change to oral acyclovir (**AI**); continue therapy until lesions completely heal. **Recurrent Herpes Labialis:** Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth QID for 5 days. **Recurrent Genital Herpes** Acyclovir 20 mg/kg body weight (maximum 400 mg/dose) dose by mouth TID for 5 days **Children with HSV Keratoconjunctivitis:** Often treated with topical trifluridine (1%) or acyclovir (3%) applied as 1–2 drops 5 times daily. Add oral acyclovir to the topical therapy.		**For neonatal CNS disease:** Repeat CSF HSV DNA polymerase chain reaction (PCR) should be performed at days 19–21 of therapy; do not stop acyclovir until repeat CSF HSV DNA PCR is negative (**BIII**) Suppressive secondary prophylaxis can be considered for children with severe and recurrent gingivostomatitis (**AI**)

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	Children with ARN: For children old enough to receive adult dose, acyclovir 10–15 mg/kg body weight/dose IV every 8 hours for 10–14 days, followed by oral valacyclovir 1 g/dose TID for 4–6 weeks As an alternative, oral acyclovir 20mg/kg body weight/dose QID for 4–6 weeks after IV acyclovir for 10–14 days		
HPV	**Podofilox** solution/gel (0.5%) applied topically twice daily for 3 consecutive days weekly for <4 weeks (patient applied) (**BIII**) **Imiquimod cream (5%)** applied topically at night for 3 nonconsecutive nights per week for up to 16 weeks and washed off 6–10 hours after each application (patient applied) (**BII**) **Trichloroacetic acid or BCA(80 90%)** applied topically weekly for up to 3–6 weeks (health care provider applied) (**BIII**) **Podophyllin resin**, 10%–25% suspension in tincture of benzoin, applied topically and washed off several hours after; later repeated weekly for 3–6 weeks (**CIII**) **Cryotherapy** with liquid nitrogen or cryoprobe applied every 1–2 weeks (BIII) **Surgical** removal either by tangential excision, tangential shave excision, curettage, or electrosurgery.	Individual external genital wart lesions can be removed by cryotherapy or electro-dessication; may be repeated every 1–2 weeks (**BIII**). Veragen, patient self-applied 3 x daily for up to 16 weeks (**CIII**). Laser ablation or surgical excision for recalcitrant cases.	Prevention of HPV complications best achieved by HPV vaccination, ideally in childhood/adolescence prior to sexual debut. Abnormal Pap test cytology should be referred to colposcopy for diagnosis and management
Varicella Zoster Virus (VZV)	**Chickenpox** **Children with No or Moderate Immune Suppression (CDC Immunologic Categories 1 and 2) and Mild Varicella Disease:** Acyclovir 20 mg/kg body weight/dose by	**Patients Unresponsive to Acyclovir:** Foscarnet (40–60 mg/kg body weight/dose IV every 8 hours) for 7-10 days or until no new lesions have appeared for 48 hours (AI)	IV acyclovir dosing in children aged ≥1 year can be based on body surface area (500 mg/m^2/dose IV every 8 hours) instead of on body weight. Consult with an ophthalmologist experienced in

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	mouth (max 800 mg/dose) QID for 7–10 days and until no new lesions for 48 hours **Children with Severe Immune Suppression** Acyclovir 10 mg/kg body weight 500 mg/m2/dose IV every 8 hours for 7–10 days and until no new lesions for 48 hours **Zoster Children with Uncomplicated Zoster:** Acyclovir 20 mg/kg body weight/dose (max 800 mg/dose) by mouth QID for 7–10 days. **Children with Severe Immunosuppression** **Trigeminal or Sacral Nerve Involvement, Extensive Multidermatomal, or Disseminated Zoster**: Acyclovir 10 mg/kg body weight/dose IV every 8 hours until cutaneous lesions and visceral disease are clearly resolving, then can switch to acyclovir by mouth to complete a 10- to 14-day course **Children with Progressive Outer Retinal Necrosis:** Ganciclovir 5 mg/kg body weight/dose IV every 12 hours, **PLUS** Foscarnet 90 mg/kg body weight/dose IV) every 12 hours, **PLUS** Ganciclovir 2 mg/0.05 mL intravitreal twice weekly and/or foscarnet 1.2 mg/0.05 mL intravitreal twice weekly **Children with ARN:** Acyclovir 10–15 mg/kg body weight/dose IV every 8 hours daily for 10–14 days, followed by Oral valacyclovir 1 g/dose TID for 4–6		managing children with VZV retinitis (**AIII**).

Treatment Regimens			
Infection	**Preferred therapies and duration**	**Alternative therapies**	**Other options or issues**
	weeks (for children old enough to receive adult dose). **Alternative oral acyclovir dose: 20 mg/kg body** weight/dose QID for 4–6 weeks intravitreal twice weekly (**AIII**) **ute retinal necrosis:** Acyclovir: 10 mg/kg body weight IV 3 x daily for 10–14 days, followed by oral valacyclovir, 1 g per dose 3 x daily for 4–6 weeks (for children old enough to receive adult dose); alternative oral acyclovir: 20 mg/kg body weight for 4–6 weeks (**AIII**)		

8 HIV IN SPECIAL CIRCUMASTANCES

8.1 TB-HIV coinfection in adults and adolescents

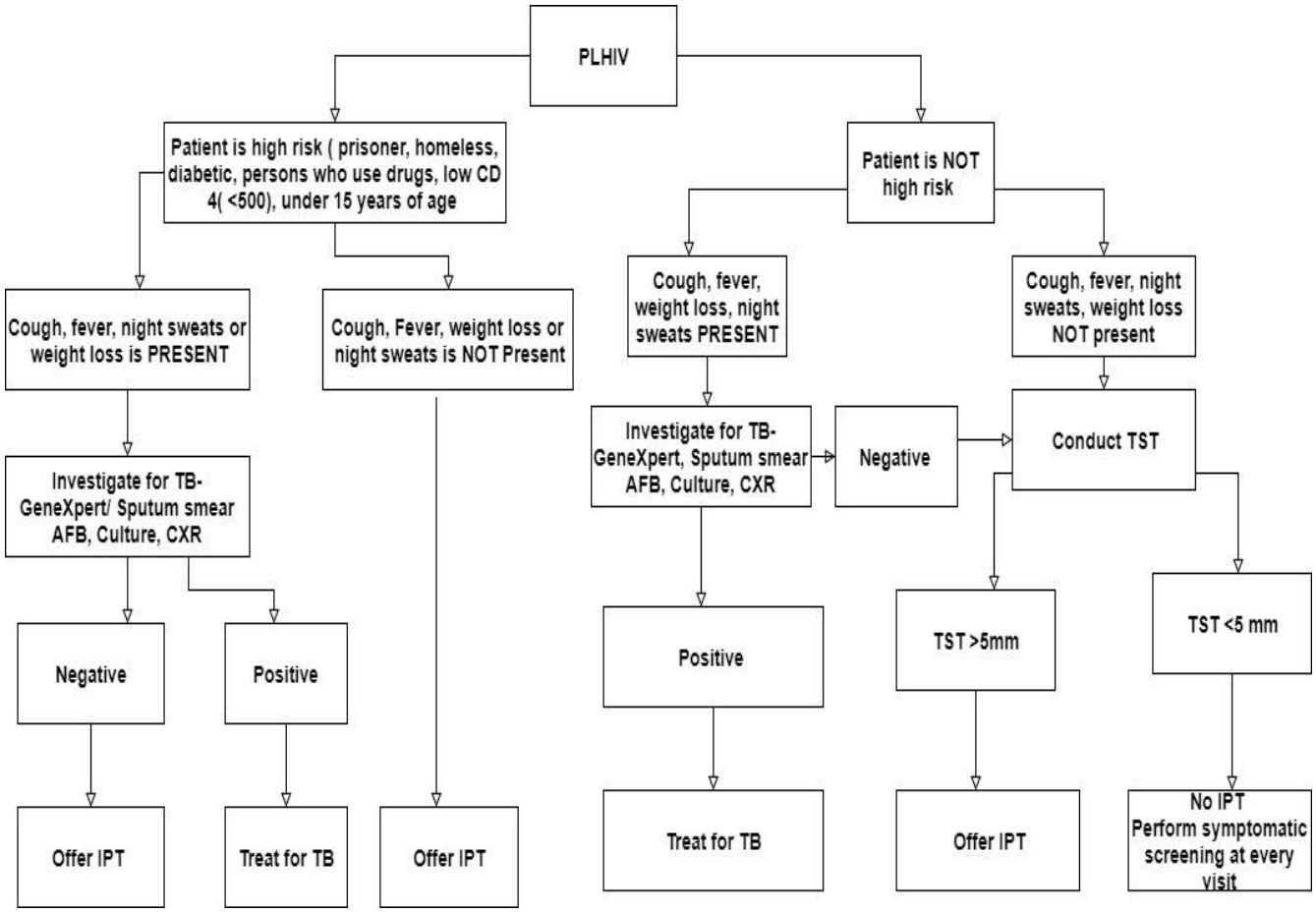
TB is one of the most common opportunistic infections globally and in the OECS and continues to be a major cause of mortality among the HIV population. All persons with or suspected of having TB should be tested for HIV, as very often TB can also be the first clinical indication that the patient may be HIV positive.

Routinely, at every visit, PLHIV should be screened for TB symptoms which includes fever, cough of any duration, weight loss and night sweats. This helps to identify suspected TB patients for further investigation. Additionally, PLHIV on ART developing TB should be investigated for ART treatment failure.

8.1.1 Screening, Diagnosis, and Isoniazid Preventative Therapy (IPT)

All PLHIV should be screened for TB disease using a clinical algorithm at every visit. Clinical symptomology screening is the first level of screening and comprises of four symptoms as defined by WHO. These are current ***cough, fever, weight loss, or night sweats***. Persons with no clinical symptoms should be offered a Tuberculin skin test (TST). Those with a reaction of greater than 5 mm should be placed on IPT. Persons a higher risk (***prisoners, diabetics, the homeless, persons who use drugs, children 15 years and younger and persons with CD4 count of less than 500 cell/mm3)*** and persons who are symptomatic should undergo additional investigations (Gene Xpert, AFB, Culture or CXR) to rule out TB disease. Persons testing positive should be treated for TB disease and persons testing negative should be placed on IPT. Patient should be evaluated at every clinic visit using WHO recommended screening of cough, fever, weight loss and night sweats. See detailed algorithm below in figure 8.

Figure 8: Algorithm for TB screening among People living with HIV



Source; Guidelines for intensified tuberculosis case finding and isoniazid preventative therapy for people living with HIV in resource constrained settings- WHO, 2011

Isoniazid is the drug of choice for TB prophylaxis and is compatible with ARV drugs. However LFTs should be monitored closely and considerations should be given to avoiding AZT because of the shared toxicity of peripheral neuropathy. In this regard, Vitamin B 6 should be given concurrently. The duration of ITP for patient with HIV is for at least **6 months.** Dosing for INH and B6 is outline in table 8.1.

Table 8.1 Recommended dosages for Isoniazid Preventative Therapy (IPT)

	Adult Dose	Pediatric Dose
Isoniazid	300mg once daily	10-15 mg/kg once daily
Vitamin B6	50mg once daily	25-50mg/kg once daily

Source; Guidelines for intensified tuberculosis case finding and isoniazid preventative therapy for people living with HIV in resource constrained settings- WHO, 2011

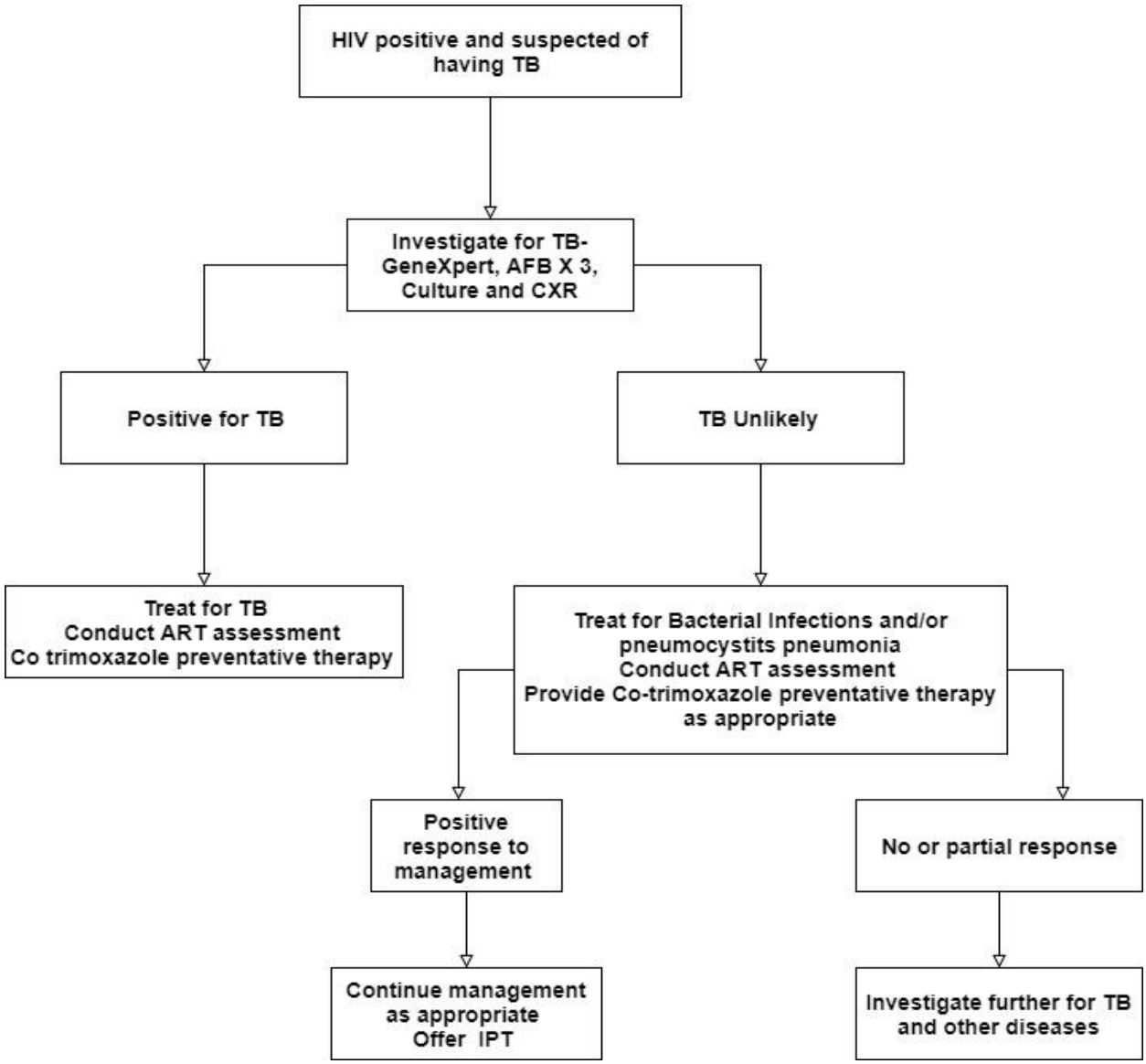
8.1.2 Management of Active Tuberculosis in HIV patients.

Tuberculosis could occur at high CD4 counts but is associated with rapid HIV disease progression and high mortality rates. As such, ***ART should be started in all TB patients living with HIV, regardless of CD4 cell count. For HIV patients not on ART, TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment. Patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment.***

In starting ART in TB patients, careful attention should be paid to the drug- drug in selecting the appropriate regimen and all patients should be monitored closely for IRIS. PLHIV on ART developing TB warrants an investigation for ART treatment failure and the need for adherence support and counselling.

Patients suspected of having TB is based on WHO symptomology and includes any adult with a **history of cough for more than 2 weeks, fever, weight loss and night sweats**. These patients should be investigated and offered TB treatment once TB is confirmed. Others should be offered treatment for bacterial infections, pneumoncystitis pneumona. See detailed algorithm as figure 9.

Figure 9: Algorithm for managing PLHIV suspected of having TB



Medication used for treatment of TB in HIV positive patients remains the same as for those who are HIV negative and comprises of bactericidal and bacteriostatic agents as detailed in table 34 below.

Table 34: Essential anti-TB Treatment Medications

Drugs	Mode of action	Recommended Dose mg/kg (Daily)
Isoniazid (H)	Bactericidal	5 (4-6)
Rifampicin (R)	Bactericidal	10 (8-12)
Pyrazinamide (Z)	Bactericidal	25 (20-30)
Ethambutol (E)	Bacteriostatic	15 (15-20)
Streptomycin (S)	Bactericidal	15 (12-18)

Treatment of TB comprises of two phases: an intensive and continuation phase. Depending on the category of TB, treatment duration and regimen may vary. Categories of TB include:

1. Based on the anatomical site of TB disease:
    - ❖ Pulmonary TB (PTB) refers to TB involving the lung parenchyma. Miliary tuberculosis is classified as pulmonary TB because there are lesions in the lungs. Tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extrapulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of pulmonary TB.
    - ❖ Extrapulmonary TB (EPTB) refers to TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges. Diagnosis of EPTB is made only with a positive TB culture
2. Based on the bacteriological results for PTB cases
    - ❖ Smear positive- one or more sputum smear specimens at the start of treatment are positive for AFB
    - ❖ Smear negative- sputum is smear-negative but culture-positive for M. tuberculosis
      OR smear negative with radiographic abnormalities consistent with active pulmonary TB and clinician to treat with a full course of anti-TB
3. Based on the history of previous treatment
    - ❖ New patients - never had treatment for TB, or have taken anti-TB drugs for less than 1 month.
    - ❖ Previously treated patients- have received 1 month or more of anti-TB drugs in the past.
4. Based on the effectiveness of TB treatment
    - ❖ Drug susceptible TB
    - ❖ Drug Resistant TB

Based on the category of TB the following is treatment is recommended. Daily treatment, Direct Observe Therapy (DOT) and the use of Fixed Dose combination therapy is recommended. The standard regimen for TB treatment is 2 month intensive therapy of HRZE, followed by 4 months of HR. This treatment is recommended for PTB as well as for EPTB with the exception TB of the nervous system, bones or joints where longer duration is recommended. For previously treated TB cases, specimen for culture and drug susceptibility testing (DST) should be obtained at or before the start of treatment. DST should be performed for at least isoniazid and rifampicin. Results of DST should guide the choice of regimen. In the event DST is unavailable, empiric treatment is recommended as outlined in table 35 below.

Table 35: Treatment regimen by TB category

TB Treatment category	Clinical Case Presentation	Treatment Regimen	
		Initial phase	Continuation phase
New patients	New smear^{+} PTB; New smear^{-} with extensive lung involvement, severe EPTB	2 HRZE	4 HR
Previously Treated or Retreatment	Smear^{+} PTB: relapse, Rx failure, Rx after default	2HRZES+1HRZE	5HRE
Confirmed or suspected MDR	Smear^{+} after supervised Rx as a re-treatment case; proven or suspected MDR TB	Individualized regimen containing second line drugs and based on DST testing.	

Key: ***E*** *= ethambutol;* ***H*** *= isoniazid;* ***R*** *= rifampicin;* ***S*** *= streptomycin;* ***Z*** *= pyrazinamide;*

8.1.3 Choice of HAART for TB-HIV coinfection

Rifampicin, a cornerstone of TB treatment, induces cytochrome P450 in the liver, altering levels of many medications, including several antiretrovirals. This results in rapid clearance of antiretrovirals leading to sub-therapeutic drug levels and ultimately HIV drug resistance. *Rifampicin reduces NVP levels to as low as 58% and these drugs should generally not recommended for co administration*. While small reductions of serum levels of EFV also occur, EFV should preferably be used with a rifampicin-based TB regimen with careful monitoring. *Rifampicin also reduces serum levels of LPV/r by 75% and should not be co administered.*

All patients with drug-susceptible pulmonary TB who are living with HIV and receiving antiretroviral therapy during TB treatment, a 6-month standard treatment regimen is recommended over an extended treatment for 8 months or more. ARV regimen first line and second line for TB patients are detailed in tables 36 and 37. Additional details on HAART regimen and required dose adjustment for TB medications are presented in appendix 8A.

Table 36: First Line HAART in TB patients

	Drug regimen
Preferred Regimen	Tenofovir(300mgs)/Emtricitabine (200mgs)(TDF/FTC)+ Efavirenz(600mgs)
Alternate Regimen	AZT(300mgs)+3TC (150 mgs)+ Efavirenz (600mgs)

Table 37: Second Line HAART in TB patients

	Drug Regimen
Preferred Regimen	Tenofovir(300mgs)/Emtricitabine (200mgs)(TDF/FTC)+ AZT (300mgs) + Lopinavir/ Ritonavir (400/100mgs)
TB regimen	Substitute Rifampicin with Rifabutin 150mgs orally three times weekly. (Rifampicin reduces the levels of LPV/r by 75%)

For patients using HAART regimen that includes NVP or LPV/r, substitute in the TB regimen Rifampicin with Rifabutin.
In cases where none of the regimen in above table applies, a triple nucleoside regimen of Tenofovir/Emtricitabine (TDF/FTC) (300mgs/200mgs) one tablet daily with AZT (Zidovudine) 300mg twice daily is recommended.

8.2 Treatment of TB and HIV in children

Children with TB/HIV coinfection should be treated for both diseases as early as possible.

8.2.1 Tuberculosis Treatment in children with TB HIV coinfection

Most children with TB have uncomplicated (smear-negative) pulmonary/intrathoracic TB. Cases are managed based on whether it's a new, retreatment or drug resistant case. Treatment is also dependent on the type of TB. Severe forms of extrapulmonary TB including TB meningitis may require longer and more potent treatment. Regimen and dosing are outlined in tables 38 and 39 below.

Table 38: Recommended regimen for Treatment of TB in children

TB Diagnostic Category	**Clinical Presentation**	**Regimen**	
		Initial Phase	**Continuation Phase**
New Case	New Smear positive PTB	2HRZE	4HR or 6HE
	New smear negative PTB with extensive parenchymal involvement		
	Severe forms of EPTB (other than Tb meningitis)		
	Severe concomitant HIV disease		
	Miliary TB, Bone TB, TB Meningitis	2HRZE	10HR
Retreatment case	Previously treated smear positive PTB. -Relapse -Treatment after default -Treatment failure	HRZE/1HRZE	5HRE
Suspected MDR Cases	Chronic and MDR TB	Refer to the specialist at the Chest Clinic/ National TB programme	
H- Isoniazid/INH; R- Rifampicin; Z-Pryazinamide; E-Ethambutol			

Table 39: Dosing for Anti-tuberculosis drugs

DRUG	DOSAGE
Isoniazid (INH), H)	10 (10-15) Maximum dose 300mg/day
Rifampicin (RIF, R)	15mg/kg (10-20mg) maximum dose 600 mg/day
Pyrazinamide (PZA,Z)	35mg/kg (30-40mg) maximum dose 2000mg/day
Ethambutol (EMB,E)	20mg/kg (15-25 mg) maximum dose 1000 mg/day
Streptomycin (SM,S)	15 mg/kg (12-18mg) maximum dose 1000mg/ day IM

8.2.2 ARV Treatment in children with TB HIV coinfection

Children infected with HIV and diagnosed with TB should be started on ART should be started as soon as possible within 8 weeks of TB treatment initiation. Drug-drug interactions should be taken into consideration when selecting treatment regimen example LPV/r reduces rifampicin levels and can result in suboptimal TB treatment. In this regard, WHO recommends the use of triple-nucleoside therapy as a suitable option, with substitution of a standard first-line regimen once TB treatment is completed. Additionally, "super-boosting" LPV/r with additional ritonavir (RTV) (1:1 instead of 4:1 LPV/r ratio, i.e. equal doses of LPV and RTV) to manage rifampicin-based TB co-treatment in children on an LPV/r-based regimen is also recommended. Treatment outlined in table 40 based on what treatment is being initiated.

Table 40: Management of children with TB/HIV co infection

Age group	Recommended Regimen	Comments
Children and adolescents initiating ART while on TB treatment		
<3 years of age	Triple NRTI (AZT + 3TC + ABC)	-This is the preferred regimen for children <3 years of age. EFV is approved for children >3years. - Triple NRTI is only recommended for the duration of TB treatment particularly in children <3 years of age as the rifampicin levels are reduced with LPV/r. - PI- or NNRTI-based regimen should be restarted when rifampicin-based therapy ends.
3 years and older	Two NRTIs + EFV or Triple NRTI (AZT + 3TC + ABC)	
Children and infants initiating TB treatment while receiving ART- recommended standard 2 NRTIs and NRTI		
<3 years of age and receiving standard NNRTI based regimen (two NRTIs + EFV or NVP)	Continue with NVP ensuring that the dose 200mg/m2 **OR** Triple NRTI (AZT + 3TC + ABC)	-Triple NRTI is should be considered as the preferred option for children younger than 3 years who are receiving an LPV/r-based regimen when starting TB treatment. - EFV-based regimen in children under 3 years is not recommended because pharmacokinetic data are needed to ensure that the co-administration of rifampicin does not decrease drug levels below the therapeutic level.

>3 years and receiving standard NNRTI based regimen (two NRTIs + EFV or NVP)	If the child is receiving EFV, continue the same regimen. If the child is receiving NVP, substitute with EFV or Triple NRTI (AZT + 3TC + ABC)	Triple NRTI can be considered as the preferred regimen for children older than 3 years in cases of failure on an NNRTI-based regimen.
Children and infants initiating TB treatment while receiving ART- recommended standard 2 NRTIs and PI		
<3 years of age and on standard PI based regimen (two NRTIs + LPV/r)	Triple NRTI (AZT + 3TC + ABC) **OR** Continue LPV/r, adding RTV to achieve the full therapeutic dosed	Super boosting of ritonavir- increase RTV until it reaches the same dose as LPV in mg, in a ratio of 1:1
>3 years and on standard PI based regimen (two NRTIs + LPV/r)	***If the child has NO history of failure of an NNRTI based regimen:*** Substitute with EFV **OR** Triple NRTI (AZT + 3TC + ABC) **OR** Continue LPV/r, adding RTV to achieve the full therapeutic dosed. ***If the child has a history of failure of an NNRTI based regimen:*** Triple NRTI (AZT + 3TC + ABC) **OR** Continue LPV/r, adding RTV to achieve the full therapeutic dose.	Preferred option- Substitution with EFV EFV could be maintained after TB treatment ends to enable simplification and harmonization with the ARV drug regimens used for older children.

8.2.3 Considerations for Infants and Children with TB and HIV

TB is the most common cause of death in hospitalized a children living with HIV. Routine screening using TB symptomology of fever, cough of any duration, weight loss and night sweats, helps to expedite TB diagnosis or initiate preventative treatment. The combined use of isoniazid preventive therapy (IPT) and ART prevents TB infection and reduces mortality.

8.2.4 Prevention TB in Children- Isoniazid preventive therapy

Preventative therapy should be considered in the following circumstances:

- HIV infected children who have poor weight gain, fever or current cough or contact history with a TB case may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, offer IPT regardless of their age.
- HIV infected children who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case should receive Isoniazid Preventative Therapy (IPT) -10 mg/kg/day for six months.
- HIV-infected infants and children exposed to TB through household contacts, but with no evidence of active disease, should receive isoniazid preventive therapy (IPT)—10 mg/kg/daily (maximum dose 300 mg daily) for 6 months. See ***Appendix 8B*** for simplified dosing CTX of IPT.

- ❖ HIV infected children who are less than 12 months of age, have contact with a TB case and are evaluated for TB (using investigations) should receive six months of IPT if the evaluation shows no TB disease.
- ❖ HIV infected children, after successful completion of treatment for TB, should receive IPT for an additional six months.

8.3 HIV Prevention

8.3.1 Preexposure prophylaxis.

Oral Pre Exposure Prophylaxis (PrEP) is the use of antiretroviral (ARV) drugs before HIV exposure by people who are not infected, in order to block the acquisition of HIV. Clinical trials have demonstrated its efficacy in prevention HIV infection and PreP is now adapted as a key component of effective combination prevention. High-quality clinical data from multiple countries of variable socioeconomic profiles demonstrate effectiveness of daily anti-retroviral therapy for prevention of HIV acquisition among serodiscordant heterosexuals (Baeten et al., 2012), Men and transgender women who have sex with men (MSM-TG) (Grant et al., 2010), and high-risk heterosexuals (Thigpen et al., 2012), and injection drug users (Choopanya et al., 2013).

PreP for prevention of HIV infection is becomingly increasingly relevant in a changing HIV environment where high risk behavior is juxtaposed with the search for education on prevention. This leaves many HIV programs obligated to finding adequate prevention and treatment options for both the HIV negative and positive patients. More so among vulnerable groups, including, Men who have sex with Men, sex workers and heterosexuals with substantial risk of HIV infection. Substantial risk of HIV infection is defined as someone who is sexually active in a high HIV prevalence population or geographical location who has had any of the following risk factors in the past 6 months:

1. Vaginal or anal intercourse without a condom with more than one partner, OR
2. A recent history (in the last 6 months) of a sexually transmitted infection (STI) by lab testing or self-report or syndromic STI treatment, OR
3. Has used post-exposure prophylaxis (PEP) for sexual exposure in the past 6 months.

The consideration and use of PreP in the OECS is therefore an active discussion that merits early planning and use of Prep. The OECS is planning a pilot experience to introduce PrEP for high risk individuals - not only serodiscordant couples - as part of HIV combination prevention strategies that is currently being implemented as part of the Global Fund Grant QRB-C-OECS. Interestingly, some clinicians and their patients have already started using Prep. For those who have done so, the benefits often outweigh the risks.

PreP can be quite beneficial to serodiscordant couples. Consistent daily use serves as treatment as prevention. The use of a two-drug combination of TDF and FTC reduces the chance of HIV transmission. In many randomized control trails, it reduces the incidence of Herpes infection in both heterosexual and transgender women and genital ulcer infection in Men who have sex with Men. Prep reduces the chances of secondary transmission from partners. It has low mainly GI side effects such as nausea, diarrhea and abdominal cramping and slight elevation in creatine that resolves shortly after treatment. For many on hormonal contraception, opioid or amphetamines, there is little drug interaction and it is also recommended in pregnancy and breast feeding. These tremendous benefits make PreP a powerful tool in the prevention of HIV.

Table 41 Exposure risk for HIV Transmission

However, the use of Prep does involve strict adherence. The user need to be cognizant of the need for continuous laboratory HIV testing and monitoring of creatine and must be used in caution for patient with preexisting renal disease and risk factors for renal disease including diabetes, hypertension and those over 45 years of age. It also important that clinician support patients in stigma and discrimination emanating from the use of Prep. Although more research needs to be carried out to ascertain the effect of drug resistance, when to stop and use of special formulation in pregnancy the use of PreP has been recommended by the FDA and WHO because the benefits outweigh the risk.

Programmatic Approach

From a programmatic perspective the use of PreP does harmonize with the efforts of treatment as Prevention in the OECS. ***The single tab formulation of TDF/FTC is consistent with the one pill a day regimen (TDF/FTC/EFV) for staring ART in Adolescent and Adults, prevention of mother to child transmission, treatment of Hepatitis co-infection and patients with TB/HIV co-infection***. It is easily available and cost effective with equitable access within the OECS as managed by the OECS Pharmaceutical procurement service (PPS). Hence Prep is a responsible choice from both the individual and programmatic perspective and redounds to the benefit of the patient, the community and health care system.

General considerations in administering PreP are as following;

- There are no major **safety issues or side effects** associated with Prep.
- The **risk of drug resistance** to FTC is extremely low is would mainly occur among people who were acutely infected with HIV when initiating PrEP.
- PrEP does not appear to affect the effectiveness of hormonal contraception.
- No evidence indicates that PrEP leads to **risk compensation in sexual practices**, such as decreased condom use or more sexual partners. However patients should be counselled on safe sex practices including partner reduction and consistent and correct condom use.
- **HIV testing is required before PrEP is offered** and regularly (every three months) while PrEP is taken. The frequent HIV testing during PrEP use presents an ideal opportunity for STI screening and management. PreP should NOT be offered if the person is tested HIV positive.
- **Monitoring of renal function** through creatinine testing is preferred before starting PrEP and quarterly during PrEP use for the first 12 months, then annually thereafter. PreP should not be offered if Creatinine Clearance of less than 60mL/min.
- Test for **Hepatitis B virus (HBV)** as withdrawal of ARV used for PreP, also effective in HBV treatment, can result in virological and clinical relapse. People with detectable HBsAg and alanine transaminase (ALT) elevated more than twice the upper limit of normal or clinical signs of cirrhosis could benefit from long-term therapy for HBV.
- **Adherence is critica**l to the effectiveness of Prep. All persons starting on Prep should be counselled on the importance of adherence, possible side effects which are generally mild and do not require discontinuing PreP.
- More information is needed to better understand the interactions between **PrEP and hormone therapy** used by transgender people.

PrEP may be discontinued 28 days after the last potential exposure to HIV if people do not have continuing substantial risk for acquiring HIV.

For further update on PreP please refer to the latest WHO and CDC guidelines. Prep continues to be a useful armament in the prevention and treatment of HIV infection in the OECS.

8.3.2 Post exposure prophylaxis

Exposure	Average per-episode risk
Occupational	
Percutaneous (blood)	0.3%
Mucocutaneous (blood)	0.09%
Non-occupational	
Receptive anal intercourse	1–2%
Insertive anal intercourse	0.06%
Receptive vaginal intercourse	0.1–0.2%
Insertive vaginal intercourse	0.03–0.14%
Receptive oral (male)	0.06%
Needle-sharing	0.6%

HIV post-exposure prophylaxis (PEP) refers to the set of services that are provided to an individual who has been exposed to HIV in order to mitigate that exposure. These services comprise first aid; counselling that includes an assessment of risk for HIV; HIV testing; and, depending on the outcome of the exposure assessment, a possible prescription of a **28-day course of ARVs**, with appropriate support and follow-up.

There are two main types of exposure to HIV:

1. Non occupational - through sexual contact (consensual sex or sexual assault) and needle sharing among injecting drug users and
2. Occupational exposure- through exposure associated with one's occupation such as clinicians, laboratory personnel, emergency rescue staff, waste-disposal workers, law enforcement personnel, and fire-fighters, all of whom may be exposed to blood and other potentially infectious body fluids while performing their duties.

In some consensual sex may require post exposure prophylaxis. This/ should be managed as in a similar way as non-occupational sexual assault cases. Law enforcement and forensic evidence may not be required.

The levels of risk for contracting HIV infection related to a particular exposure experienced are summarized in table 41. Anyone who has sustained an exposure to HIV should be counselled on the level of risk and informed that PEP, with a timely course of antiretroviral therapy (ART), can reduce, although not eliminate, the risk of HIV transmission.

8.3.2.1 Sexual Assault and Non Occupational Exposures

For people who have been sexually assaulted, at the initial post assault visit, crisis intervention including emotional support, should be provided and the law enforcement contacted and incident reported. Evidence should be collected correctly and as soon as possible for forensic purposes and could include oral, anal and vaginal swab depending on the site of exposure.

A general examination and risk assessment for HIV transmission should be conducted and patients HIV status with pre and post-test counselling established as soon as possible. As appropriate the first dose of ART for PEP should be offered. Patient should also be examined and tested for other sexually transmitted infections and offered empiric treatment for gonorrhoea, chlamydia, and trichomonas. Pregnancy testing and emergency contraception should be to women of childbearing age. For all patients, laboratory testing related to the prescribed ART used for PEP should be done at baseline and could include CBC, liver function, creatinine, and estimated glomerular filtration rate.

Risk Assessment for Sexual Assault: The risk of becoming infected with HIV from sexual assault may be higher than from consensual sex. This is because the presence of physical trauma increases transmission risk. Risk also varies by sexual act; for example, receptive anal- and vaginal intercourse are riskier than insertive and oral intercourse (see table 7.9). Additionally, STIs elevate transmission risk, as does being an adolescent girl—the immaturity of the vaginal and cervical cells increase susceptibility to HIV infection—and being a female who uses Depo-Provera (medroxyprogesterone acetate).

Occupational Exposure

Occupational exposure occurs mainly among workers during the execution of their duties. Similar to sexual assault cases, persons with occupational exposure should be offered emergency intervention in decontaminating the exposure site. See Box 8.1. Exposed persons should also have a risk assessment conducted, HIV status determined and eligibility for PEP established. Initial ART should be offered as soon as possible and follow up laboratory monitoring conducted.

An incident report should be made to the employees' supervisor.

In conducting a risk assessment to establish the need for PEP the paramaters described in table 42 can be used as guide.

Eligibility for PEP is defined by the risk assessment as well as additional factors. Eligibility is outlined in box 8.2.

Box 8.1 Occupational Exposure

Decontaminate the Exposure Site and Administer First Aid

First aid as well as decontamination of the exposure site should be performed immediately. This will reduce contact time with the source person's blood, body fluids, or tissues. Management will vary according to the specific scenarios;

- <u>If skin is broken during an injury with a used needle or sharp instrument:</u>
  - Do not squeeze or rub the injury site.
  - Wash site immediately using soap or a mild disinfectant solution that will not irritate the skin- use chlorhexidine gluconate solution.
  - Do not use strong solutions, such as bleach or iodine, to clean the site because these may irritate the wound and make the injury worse.
- <u>If splash contact occurs on unbroken skin:</u>
  - Wash the area immediately.
  - Do not use strong disinfectants.
  - Unbroken skin is an excellent barrier to HIV in blood and other potentially infectious bodily fluids. PEP ART is not recommended in this setting.
- <u>If the eye sustains splash contact:</u>
  - Irrigate the exposed eye immediately with water or normal saline.
  - Sit in a chair, tilt the head back, and have a colleague gently pour water or normal saline over the eye, pulling the eyelids up and down to make sure the eye is cleaned thoroughly.
  - If contact lenses are worn, leave them in place while irrigating the eye, as they form a protective barrier. Once the eye has been cleaned, remove the contact lenses and clean them as normal; this will make them safe to wear again.
  - Do not use soap or disinfectant on the eye.
- <u>If splash contact occurs to the mouth:</u>
  - Spit the fluid out immediately.
  - Rinse the mouth thoroughly, using water or saline, and spit again. Repeat this process several times.
  - Do not use soap or disinfectant in the mouth.

Table 42: Exposures versus non-exposures to HIV

Exposures
Transfusion of blood or blood components
IV, intramuscular or subcutaneous injury with a needle contaminated with a potentially infectious body fluid,[12] whether or not the injury results in visible bleeding
Any mucous membrane or break in the skin (e.g., non-healed wound or dermatologic condition that compromises the integrity of the skin) exposed to a potentially infectious body fluid
Human bites: Exposure to the individual doing the biting if the skin was broken resulting in visible bleeding; Exposure to the bitten individual if the skin was broken and visibly bleeding AND the individual who was doing the biting was bleeding in the mouth at the time of the bite.
Non-exposures
Intact skin or healed wound/skin lesion contaminated with potentially infectious body fluid. IV, intramuscular or subcutaneous injury with a needle contaminated with a fluid that is not potentially infectious.
Mucous membrane or break in the skin exposed to a fluid that is not potentially infectious and not visibly bloody.

[12] For exposures to HIV, potentially infectious body fluids include blood, amniotic fluid, spinal fluid, pleural fluid, pus, or any fluid that is visibly bloody. Saliva, urine, and feces are not considered to be potentially infectious for HIV unless visibly bloody.

Box 8.2 Eligibility criteria for PEP

1. <72 hours has elapsed since exposure.
2. The exposed individual is HIV negative.
3. The source of exposure is HIV-infected or is of unknown HIV status.
4. There is a defined risk of exposure for **sexual assault cases:**
   - ❖ The exposed individual received oral sex with ejaculation or vaginal or anal intercourse without a condom or with a condom that broke or slipped.
   - ❖ There was contact between the perpetrator's blood or ejaculate and the exposed person's mucous membrane or some non-intact skin.
   - ❖ The exposed individual was drugged or otherwise unconscious at time of assault and is uncertain about the nature of the potential exposure.
   - ❖ The person was gang raped.
5. There is a defined risk of exposure for **occupational assault cases:**
   - ❖ Exposure was to blood, body tissues, visibly bloodstained fluid, concentrated virus, CSF, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, or amniotic fluid.
   - ❖ The skin was penetrated with spontaneous bleeding or deep puncture, or a significant amount of fluid was splashed on a mucous membrane, or non-intact skin sustained prolonged contact with an at-risk substance.
   - ❖ The skin was penetrated by a recently used hollow bore needle or other sharp object that was visibly contaminated with blood.

7.3.2.2 Management of PEP

The following principles should be used to guide PEP management.

1. PEP is most effective if given as soon as possible (and no later than 72 hours) after the exposure. In the case of ongoing sexual assault that occurs over a number of hours or days, the 72-hour time limit should be applied to the most recent potential exposure.
2. Triple therapy is the recommended approach for the OECS and the standard regimen should comprise of 2 NRTIs and 1 PI. See table 8.11 below for the detailed regimen.
3. If the source person is of unknown HIV status, and based on risk assessment and eligibility, PEP is recommended. Whenever feasible (and following informed consent), HIV testing of source people is strongly recommended.
4. Rapid testing should be done to establish the HIV status of the exposed person. Persons testing HIV negative should be offered PEP. Persons testing HIV positive should NOT be offered PEP and referred for HIV clinical management.
5. The recommended duration for PEP is **28 days.** Patients starting on PEP should be counselled on the importance, efficacy and need for adherence to ART and follow up.
6. Appropriate laboratory monitoring should be conducted and would depend on the type of exposure.
7. Empiric treatment for other sexually transmitted infections should be offered.
8. Emergency contraception- All women of childbearing age who are raped should be offered a pregnancy test as part of sexual assault care services. If the initial pregnancy test is negative, offer emergency contraception with levonorgestrel in a single dose (1.5 mg) or as a split dose (0.75 mg each taken 12 hours apart). In the OECS levonorgestrel 1.5 mg tab generally used and can be given up to 120 hours (5 days) after a sexual assault.

See figure10 depicting the algorithm for determining the need for PEP

Figure 10: Algorithm for PEP

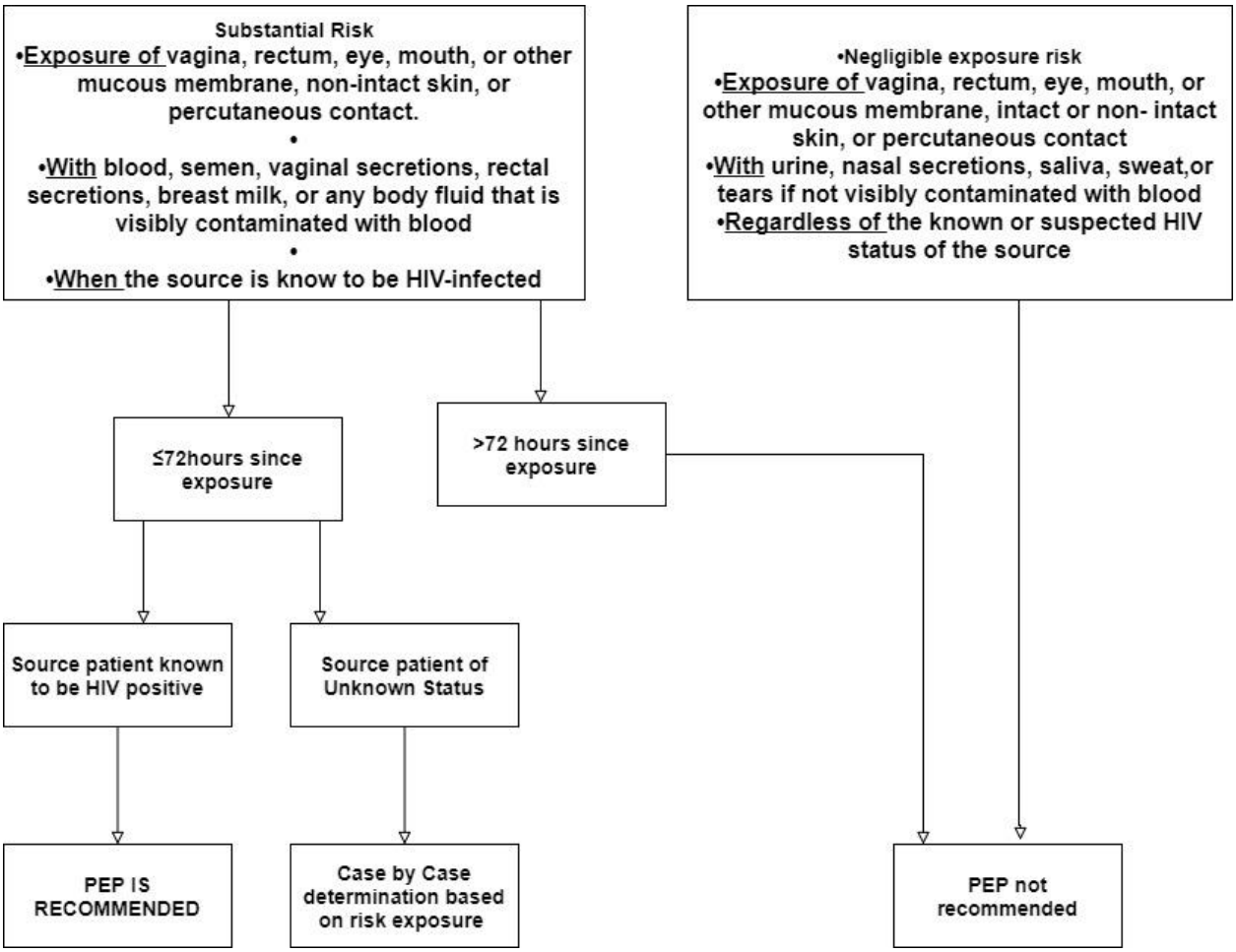


Table 8.11 Standard PEP ART regimen for adults and children

Preferred regimen – Adults and adolescent	Preferred regimen for children <10 years of age.
TDF + 3TC or FTC +LPV/r or ATV/r Adult dose: TDF 300mg once daily + 3TC 300 mg once daily+ LPV/r 400mgs/100mgs twice daily (or LPV/r 800mgs/200mgs once daily) for 28 days	AZT + 3TC +LPV/r Paediatric dose is weight-based

Follow-up

A series of follow-up visits should be scheduled to discuss side effects from and adherence to PEP ART; mental health needs; referrals for other support services; and further investigation, prophylaxis, and treatment for STIs and HBV, if warranted. Additionally, HIV tests should be repeated at 4–6 weeks and then again at 3 and 6 months. Table 43 presents a summary of PEP.

Table 43: Summary of PEP

Item	Recommended action and notes
Eligibility	Exposure within 72 hours
	Exposed individual is HIV negative
	Significant exposure
	Source of exposure is HIV-infected or of unknown HIV status
Informed consent for PEP	Information about risks and benefits Consent may be given verbally
Medicine	Triple therapy is recommended using 2 NRTIs+1 PI
Duration of therapy	28 days
Additional Management	Emergency contraception in sexual assault cases Treatment for Other STIs in sexual assault cases.
HIV testing with informed consent and pre- and post-test counselling according to protocols	Baseline HIV test in exposed person Follow-up HIV testing 3–6 months after exposure Rapid HIV test the source person if feasible; use informed consent and standard operating procedures
Additional laboratory evaluations	Pregnancy testing Haemoglobin (for AZT-containing PEP regimens)
	HBV and HCV screening if available and based on the prevalence of the diseases
Counselling	For adherence; side effects; risk reduction; trauma or mental health problems; and social support and safety
Referral	Referrals as appropriate
Record-keeping	Maintain accurate, confidential records
Clinical follow-up	Assess and manage side effects
	Assess and support adherence

8.4 HIV and Hepatitis B

8.4.1 HIV and Hepatitis B (HBV)

Hepatitis B, which is caused by infection with Hepatitis B Virus (HBV), has an incubation period ranging from 6 weeks to 6 months. It can be self-limiting or chronic. In adults, approximately half of newly acquired infections are symptomatic and around 1% result in acute liver failure and death. Symptoms range from mild (e.g., flu like symptoms) to severe (e.g., fever, jaundice, encephalopathy, abdominal pain, dark urine, pale stool).

The main route of transmission is through percutaneous, or mucous membrane exposure to blood or body fluids that contain blood infected with HBV. The risk of HBV transmission is close to 3% per contact exposure and so universal safety precautions must be followed in all health care institutions. Persons who have sex with an infected partner, multiple partners, MSM, history of STDs and injection drug use are vulnerable.

Unlike HAV, HBV has serious sequelae, including cirrhosis of the liver and hepatocellular carcinoma, which can lead to premature death. Many persons control the infection to become chronic carriers.

8.4.1.1 Diagnosis of HBV

Hepatitis B, acute or chronic, must be diagnosed via serologic testing. A complete HBV antibody profile that includes the following analyses is ideal for diagnosis and management:

- IgM antibody to Hepatitis B core antigen (IgM anti-HBc) is diagnostic of acute or recently acquired HBV infection.
- Antibody to HBsAg (anti-HBs) is produced after a resolved infection and is the only HBV antibody marker present after vaccination.
- HBsAg with a negative test for IgM anti-HBc indicates chronic HBV infection.

8.4.1.2 Treatment of HBV

In the case of HIV-HBV co-infection, two NRTIs, TDF and FTC or 3TC, are used in combination with an NNRTI (preferably EFV) to manage both diseases.

Antiretroviral therapy should be initiated to treat HIV infection in all patients who are co-infected with HIV and HBV, regardless of CD4 count. Priority should be given to patients with evidence of hepatic inflammation – as evidenced by elevated ALT/SGPT levels.

Two agents active against HBV should be used in antiviral therapy for maximal HBV virologic suppression and to prevent emergence of resistance. Therefore, TDF and 3TC or FTC should be used in antiretroviral regimen. Once ARVs are initiated, every effort should be made to continue TDF and 3TC/FTC to prevent a flare of hepatitis with discontinuation and prevent emergence of resistance with monotherapy. This may require dose adjustments of TDF in the case of renal insufficiency.

8.4.1.3 Monitoring

Suppression of HIV viral load should be monitored as per guidelines and can be used as a surrogate measure for HBV virologic suppression. Regular monitoring of liver function should be done as per guidelines. Screening is recommended for hepatocellular carcinoma and should be done with liver ultrasound performed every six months. Patients with well controlled HIV infection could be screened every 12 months. All patients with evidence of cirrhosis should continue screening every 6 months.

8.4.1.4 Prevention

Two products have been approved for preventing Hepatitis B: the Hepatitis B vaccine and Hepatitis B immune globulin (HBIG).

HBIG provides temporary (3–6 months) protection from HBV infection and is typically used as a Pre exposure prophylaxis measure, either adjunct to vaccination in previously unvaccinated persons, or alone in persons who have not responded to the vaccine series administered both pre- and post-exposure.

The Hepatitis B Vaccines are Recombivax HB and Energix. A combination vaccine for HAV and HBV is also available it is called Twinrix. The goal of vaccination is to prevent infection. The approved vaccination schedule options for adolescents and adults for Energix and Recombivax HB are presented in table 44.

Table 44: HBV vaccination dosing and schedule

Option	Type of Vaccine	Timeline
Two Dose Schedule	Recombivax	With a 4 months interval between doses.
Three dose Schedule		
Dose 1	Recombivax, Engerix and Twinrix	0, 1 month then 6 months
Dose 2	Recombivax and Engerix	0, 1 month then 4 months
Dose 3	Recombivax and Engerix	0, 2 months then 4 months

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Infants born to mothers infected with HBV must be given HBIG after birth, followed by the complete routine childhood HBV immunization series. According to the WHO, it is safe for mothers to breastfeed their babies, though women with cracked nipples must proceed with caution.

8.4.1.4 Pre exposure vaccination/prophylaxis

Hepatitis B vaccination is recommended for all unvaccinated children and adolescents, all unvaccinated adults at risk for HBV infection (especially IDU, MSM, and adults with multiple sex partners), and all adults seeking protection from HBV infection. Hepatitis B vaccine should be routinely offered to all unvaccinated persons attending STD clinics and to all unvaccinated persons seeking evaluation or treatment for STDs in other settings, especially correctional facilities, facilities providing drug-abuse treatment and primary care services.

8.4.1.5 Post exposure prophylaxis

Both passive-active PEP (the simultaneous administration of HBIG [i.e., 0.06 mL/kg] and hepatitis B vaccine at separate sites) and active PEP (the administration of hepatitis B vaccination alone) have been demonstrated to be highly effective in preventing transmission after exposure to HBV.

For unvaccinated persons exposed to a source patient who is HBsAg positive, administer Hepatits B vaccine series and HBIG. For vaccinated persons exposed to a source patient who is HBsAg positive, administer Hepatitis B vaccine boosters.

For unvaccinated persons exposed to a source patient of unknown HBsAg, administer Hepatitis B vaccine series. For vaccinated persons exposed to a source patient of unknown HBsAg, no treatment is required.

Pregnant women at risk for HBV should be test at first prenatal visit and at delivery. Pregnant women at risk for HBV should receive hepatitis B vaccination.

8.4.2 Hepatitis C

Hepatitis C, which is caused by Hepatitis C Virus (HCV), can be highly contagious, with as much as 30% risk of exposure per contact event. The average time from exposure to antibody to HCV seroconversion is 8–9 weeks. Individuals with typical infections have mild symptoms or are

asymptomatic. Chronic infection develops in 70–80% of HCV-infected persons, of which 60–70% develop evidence of active liver disease. HCV can lead to hepatocellular carcinoma.

The primary mode of transmission of Hepatitis C is injection drug use, though it can also be transmitted through blood transfusion, so blood donors should be carefully screened as a matter of course. Although HCV is not efficiently transmitted sexually, high-risk behaviours like unprotected sexual contact and injection drug use increase the likelihood of transmission, particularly within vulnerable groups. For this reason, it is important to consider offering HCV testing to injection drug users who may be accessing care at STI treatment clinics, HIV testing and counselling facilities, or other public health settings where such services are available. Correctional facilities should also perform HCV testing.

8.4.2.1 Diagnosis

For HIV positive patients screening should be performed at baseline and annually for persons sexually active or use intravenous drugs. Anti-HCV testing, which detects the presence of HCV antibodies, is recommended for routine screening of symptomatic persons based on their risk of exposure (e.g., injection drug use, percutaneous needlestick injury). Testing should include HCV antibody testing using EIA or enhanced chemiluminescence immunoassay, and, if recommended, supplemental antibody tests. Followed by NAAT to detect HCV RNA for those with a positive antibody result.

8.4.2.2 Treatment

Therapeutic agents can help to achieve sustained virological suppression of HCV and remission of liver disease. Treatment options has significantly advanced over the recent 5-10 years. Previously and still practiced, combination therapy with pegylated interferon and ribavirin was the choice for patients with chronic HCV infection.

Recent advances in the development of oral agents resulted in the FDA approval of several drugs from the protease inhibitor class, direct acting antivirals such as boceprevir and telaprevir**.** Subsequently, a polymerase inhibitor, sofosbuvir, a once daily pill. This was later combined with ledipasvir as Harvoni. In clinical trials, Harvoni cured Hepatitis C after 12 weeks of treatment in 94% of patients.

Antiretroviral treatment should be administered according to guidelines.

8.4.2.3 Monitoring

Liver function test should be monitored every six months or more frequently as determined by the physician. Patients with evidence of cirrhosis (splenomegaly, stigmata of end-stage liver disease, or imaging suggestive of cirrhosis) should be screened for hepatocellular carcinoma with ultrasound every 6 months.

8.4.2.4 Prevention

No vaccine is available to prevent hepatitis C and prophylaxis with immunoglobin is not an effective PEP measure.

Persons with HCV infection should be provided information regarding how to protect their liver from further harm (i.e., hepatotoxic agents) and should seek treatment, particularly with newer direct acting

antivirals that has the potential to cure the disease. Counselling of persons with HCV should include advise on not to donate blood, body organs, other tissue, or semen, not to share any personal items that might have blood on them (e.g., toothbrushes and razors) and to cover cuts and sores on the skin to keep the virus from spreading by blood or secretions. Women with HCV infection do not need to avoid pregnancy or breastfeeding. Persons who use or inject drugs should be counseled about the importance of stopping drug-use behaviors and provided with assistance to enter and complete substance- abuse treatment (including relapse prevention).Persons who continue to inject drugs despite counseling should be encouraged to never reuse or share syringes, water, or drug preparation equipment and to clean the injection site before injection with a new alcohol swab. Importantly, they should safely dispose of syringes after use, practice consistent and correct condom use. Partners of index patients should be investigated and managed appropriately.

8.5 HIV-Dengue Fever Co-infection

Dengue fever is endemic in some areas of the Caribbean with reported outbreaks of virus types 1, 2 and 3. Particularly with dengue hemorrhagic fever, patients who are co-infected with HIV and dengue fever, and who are taking ARV drugs that may cause anaemia or hemorrhagic reactions should be monitored carefully.

8.6 HIV and Mental Health Illnesses.

Mental illness comprises collectively all diagnosable mental disorders being characterized by alterations in thinking, mood, or behavior associated with distress and/or impaired functioning.
Mental illness is more common among HIV positive persons than the general population. The more common disorders among PLHIVs are depression, anxiety, post-traumatic stress disorder (PTSD), panic disorder, risk for suicide or violence, and obsessive compulsive disorder (OCD).

8.6.1 Depression

Depression is the most frequent mental health disorder characterized by depressed or sad mood, diminished interest in activities which used to be pleasurable, weight gain or loss, psychomotor agitation or retardation, fatigue, inappropriate guilt, difficulties concentrating, as well as recurrent thoughts of death. In general, antidepressants are used to treat the symptoms of depression. A simple tool can be applied to screen for depression. A Patient Health Questionnaire 2 (PHQ2) can be applied as the initial screening tool and should be administered at every visit. If positive the PHQ 2 should be followed through with the 9 item questionnaire. Both are outlined below in tables 45 and 46.

Table 45: PHQ – 2 Question depression screening

PHQ 2		
In the last 2 weeks have you be bother by any of the following		
	Yes	No
1. Little interest or pleasure in doing things		
2. Feeling down, depressed, or hopeless		

Source: www.phqscreeners.com accessed on July 9, 2017

Table 46: PHQ -9 Question depression screening

PHQ 2 Nine questions				
	Not at all	Several days	More than half the days	Every day
1. Little interest or pleasure in doing things				
2. Feeling down, depressed, or hopeless				
3. Trouble falling or staying asleep, or sleeping too much				
4. Feeling tired or having little energy				
5. Poor appetite or overeating				
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down				
7. Trouble concentrating on things, such as reading the newspaper or watching television				
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual				
9. Thoughts that you would be better off dead or of hurting yourself in some way				

Source: www.phqscreeners.com accessed on July 9, 2017

HIV patients should be screened prior to initiation of ARVs and should be monitored closely, particularly with the use of EFV.

8.6.2 Anxiety

Anxiety characterized by excessive and unrealistic worry about everyday tasks or events, or may be specific to certain objects or rituals are the most common, treatable psychiatric conditions in PLHIV. The major types of anxiety disorders are adjustment disorder, panic disorder and agoraphobia, social phobia, OCD, PTSD, and generalized anxiety disorder (GAD).

Symptoms may include shortness of breath, chest pains, palpitations, dizziness, numbness or tingling, nausea or the sensation of choking, uneasiness, nightmares, uncontrollable, and obsessive thoughts. Anxiety can be induced by ARVs (EFV) and other medications such as acyclovir, corticosteroids, isoniazid, and interferon.

Screening for anxiety can be done using the PHQ anxiety questions outlined in table 47 below.

Table 47: PHQ Anxiety screening

Questions about anxiety	Yes	No
1. In the last 4 weeks, have you had an anxiety attack — suddenly feeling fear or panic?		
2. Has this ever happened before?		
3. Do some of these attacks come suddenly out of the blue — that is, in situations where you don't expect to be nervous or uncomfortable?		
4. Do these attacks bother you a lot or are you worried about having another attack?		

Source: www.phqscreeners.com accessed on July 9, 2017

An anxiety attack can be further understood using the detailed questionnaire as outline in table 48 below.

Table 48: PHQ detailed questions on anxiety attack.

Questions about anxiety attack	Yes	No
1. Were you short of breath?		
2. Did your heart race, pound, or skip?		
3. Did you have chest pain or pressure?		
4. Did you sweat?		
5. Did you feel as if you were choking?		
6. Did you have hot flashes or chills?		
7. Did you have nausea or an upset stomach, or the feeling that you were going to have diarrhea?		
8. Did you feel dizzy, unsteady, or faint?		
9. Did you have tingling or numbness in parts of your body?.		
10. Did you tremble or shake?		
11. Were you afraid you were dying?		

Source: www.phqscreeners.com accessed on July 9, 2017

Medications used to treat anxiety disorders include selective antidepressants such as selective serotonin reuptake inhibitors(SSRIs), benzodiazepines, antihistamines, tricyclic antidepressants. Non-pharmacological treatments of HIV-related anxiety include muscle relaxation, behavioral therapies, acupuncture, meditation techniques, self-hypnosis and individual imagery psychotherapy, cognitive-behavioral therapy, psycho-education, aerobic exercise, and supportive group therapy.

8.6.3 Management of Mental Illness Disorders in Patients Using ART

HIV positive patients should be screened at baseline and regularly for mental health issues. Importantly, a good patient history to establish previous or current mental health issue is critical. It is important to be aware of trigger factors such as patient learning of their HIV status, disclosure to sex partners,

family, and friends, physical illness, AIDS diagnosis and hospitalisation. In addition to pharmacotherapy, psychosocial support and counselling is important.
ART management should be according to guidelines, however close monitoring should be conducted with the use of ARV that triggers or exacerbates psychotic episodes such as EFV.
For patients diagnosed with mental health issues and responding poorly to treatment, refer for specialist psychiatrist treatment.

8.7 HIV in Older Adults

Effective antiretroviral therapy (ART) has prolonged the lifespan of people living with HIV. Non HIV/AIDS-related conditions now account for most morbidity and mortality among older people with HIV infection. Aging HIV-infected population (between 50-65 years of age) are now living with high rates of co-morbid conditions compared with their non HIV-infected counterparts. /The goals of caring for older people with HIV infection are to minimize illness and frailty, optimize health and well-being, and prolong life.
People with HIV may develop chronic diseases associated with aging earlier in life resulting in the development of multiple co-morbid conditions. Aging also compounds the immunological impact of HIV and accelerate HIV disease progression and places the elderly at particular risk for polypharmacy with increased drug-drug interaction and adverse events. It also can negatively affect cognitive function and quality of life. It is therefore critical that an older adult be thoroughly assessed new signs and symptoms at every visit and disease progression. Monitor for changes in sight and hearing, basic and instrumental activities of daily living and the need for home care, assisted or skilled nursing services.
ARVs and the Older patients: In the context of initiating ARVS as soon as possible for all HIV infected persons, patients >50 of age are considered a priority group. Older untreated HIV-infected persons have more rapid disease progression than younger persons and immunologic response is less robust. Earlier initiation will achieve better immunologic response.

Appendix 8A: HAART REGIMEN OPTIONS AND ADJUSTMENTS FOR TB INFECTED PATIENTS RECEIVING A RIFAMYCIN

HAART regimen	Potentially interacting ARV	ARV/rifamycin dosing recommendations			
		Rifabutin		Rifampicin	
		ARV dose	Rifabutin dose	ARV dose	Rifampicin dose
2 NRTI + EFV (preferred if possible)	EFV	600 mg QD	450 mg QD *OR* 600 mg 3 x a week	600 mg QD	600 mg QD
Triple NRTI	none	No change	300 mg QD	No change	600 mg QD
2 NRTI + NVP [a b c]	NVP	200 mg BID	300 mg QD	200 mg BID	600 mg QD
2 NRTI + LPV/r [b c]	LPV/r	400 mg/100 mg BID	150 mg every other day (QOD) *or* 3 x a week	Do not co administer	Do not co administer
2 NRTI + SQV/r [b c]	SQV/r	400 mg/400 mg BID	150 mg QOD *OR* 3 x a week	400 mg/400 mgBID *OR* 1,000 mg/100 mg BID	600 mg QD
2 NRTI + ATV [b]	ATV	400 mg QD	150 mg QOD	Contra-indicated	Contra-indicated
2 NRTI + f-APV [b]	f-APV	1,400 mg BID	150 mg QD *OR* 300 mg 3 x a week	Contra-indicated	Contra-indicated
2 NRTI + IDV [b]	IDV	1,000–1,200 mg Q8H	150 mg QD	Contra-indicated	Contra-indicated
2 NRTI + NFV	NFV	1,250 mg BID	150 mg QD	Contra-indicated	Contra-indicated
2 NRTI + IDV/r [b c]	IDV/r	800 mg/100 mg BID *or* 800 mg/200 mg BID	150 mg QOD *OR* 3 x a week	Contra-indicated	Contra-indicated
2 NRTI + ATV/r [b c]	ATV/r	300 mg/100 mg QD	150 mg QOD *OR* 3 x a week	Contra-indicated	Contra-indicated
2 NRTI + f-APV/r [b c]	f-APV/r	700 mg/100 mg BID *or* 1,400 mg/200 mg QD	150 mg QOD *OR* 3 x a week	No data	No data

[a] *Switching to an EFV-based or triple NRTI regimen is preferred in this scenario due to the high potential for liver toxicity when NVP is administered with a rifamycin, as well as uncertainty over appropriate dose adjustments of NVP and the rifamycins.*

[b] *Substituting back to the original regimens once rifampicin containing regimen is completed can be considered. Note that when switching back from EFV to NVP no lead-in dose is required.* [c] *Careful clinical and laboratory monitoring (e.g. ALT) is advised when NVP or boosted PIs are administered concurrently with rifampicin.*

Appendix 8B: Simplified dosing of isoniazid and co-trimoxazole prophylaxis for infants and children who are at least 4 weeks of age

Drug	**Drug Strength of tablet or oral liquid (mg or mg/5ml)**	**Number of tablets or millilitres by weight band once daily**					**Strength of adult tablet (mg)**	**Number of tablets by weight band**
		3-5.9 kg	6-9.9kg	10-13.9kg	14-19.9kg	20-24.9kg		25-34.9kg
Isoniazid	100mg	0.5	1	1.5	2	2.5	200mg	1
Co-trimoxazole	Suspension 200/40 per 5 ml	2.5ml	5ml	5ml	10ml	10ml	-	-
	Tablet 100/20mg	1	2	2	4	4	-	-
	Tablet 400/80mg	-	0.5	0.5	1	1	400/80mg	2
	Tablet 800/160mg	-	-	-	0.5	0.5	800/160mg	1
Isoniazid + co-trimoxazole + B6	Tablets (scored) 300 mg/960 mg/25 mg	-	-	-	0.5	0.5	960mg/300 mg/ 25 mg	1

9 PREVENTION, TREATMENT AND CONTROL OF SEXUALLY TRANSMITTED INFECTIONS

9.1 Introduction

These guidelines are designed for clinical practitioners in the OECS involved in the prevention, treatment, care, and support of patients with STIs. This section on STIs are included in this guidelines because many clinical practitioners who manage the care and treatment of HIV-infected patients are also involved in STIs care and treatment. Moreover, from a technical standpoint, there are myriad parallel issues between HIV and other STIs, particularly related to vertical transmission and prevention. Patients with HIV infection are not infrequently infected with a concomitant STI, which can produce a synergistic relationship as they potentiate each other's progression. This argument forms the basis for integrating STI prevention and management with HIV treatment, care, and support, and producing a common platform for delivering standardized care throughout the OECS.

The guidelines focus on prevention and syndromic management, complemented by aetiological diagnosis and are applicable in patient care settings that serves persons at risk for STIs such as primary health care, STI and HIV clinics, reproductive and family planning clinics, maternal and child health clinics and correctional health care facilities.

New recommendations presented in the Centers for Disease Control and Prevention, Sexually Transmitted Diseases Treatment Guidelines, 2015 are incorporated. The recommendations contained herein should be regarded as a source of clinical guidance.

9.2 Theoretical Approach

The management of STIs in adults, adolescents, and children is generally similar, albeit with some differences. In adults, sexual partners are the main vector of transmission. In infants, this is primarily through mother to child transmission, whether viral, as in the case of perinatal HIV infection or bacterial, as in the case of gonococcal conjunctivitis. Thus, when STI is found in an infant, active examination and treatment must be done for the infant, the mother, and her partner(s), and prevention counselling must be offered. These steps reduce morbidity and mortality and interrupt the potential for disease transmission, thereby safeguarding both the individual family and public health.

The symptoms of STIs in children and adolescents are very similar to those in adults. Many young adolescents may be asymptomatic and have advanced ascending cervical infections because of the biological immaturity of the genital tract. Physical examination should be done on a case-by-case basis; speculum examination is generally not required for children. The diagnostic methods and offending organisms are standard for all age groups. In terms of treatment, drug dosing must be carefully calculated, taking into account the weight of the child. Proper dosage and treatment optimization is associated with adherence and successful treatment.

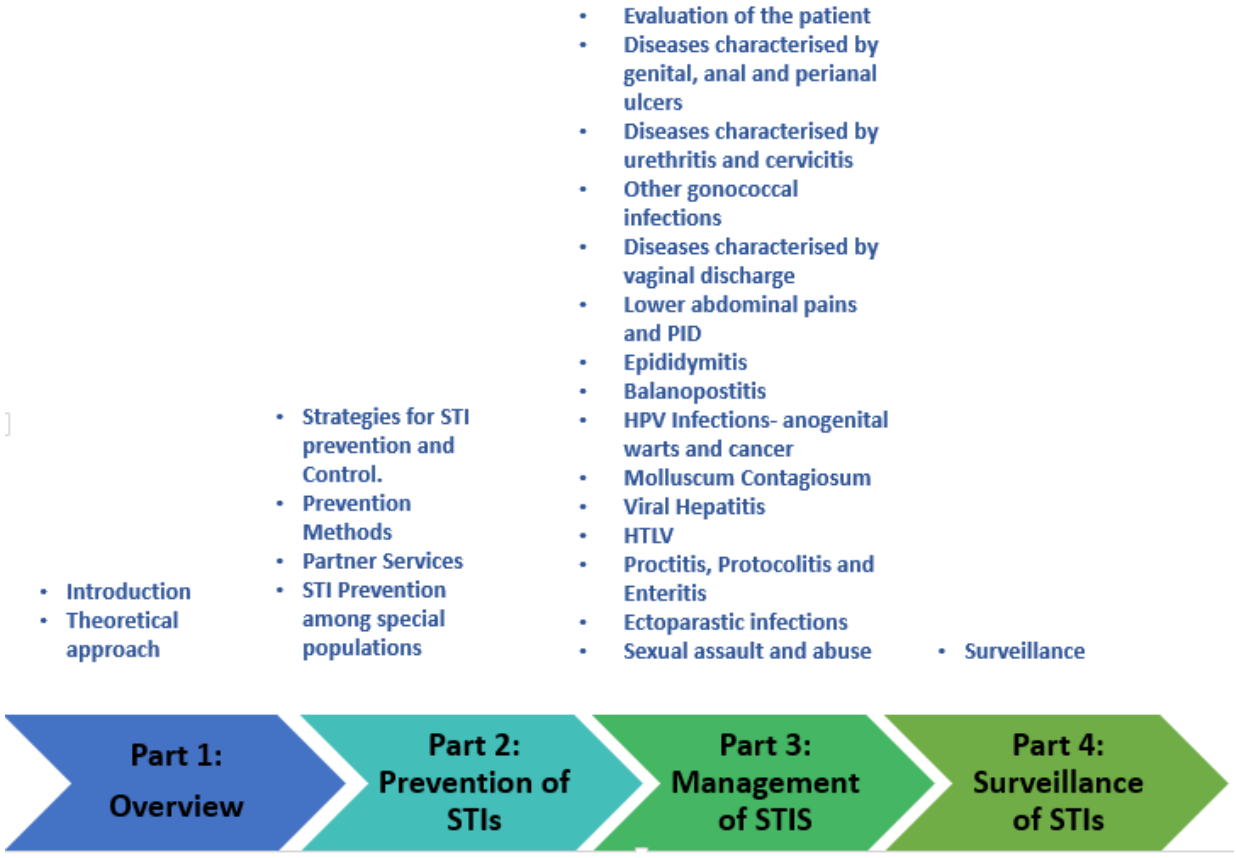
A comprehensive, patient-sensitive approach is needed in the management of STIs in children and adolescents. During the treatment process, a detailed history must be taken, including investigation of interactions between the child and household members and/or friends, to explore the possibility of incest or child sexual assault. When the only evidence is the isolation of an offending organism and/or the identification of antibodies to a sexually transmissible agent, the findings should be carefully confirmed. It is the clinician's duty to report sexual assault and rape cases to the appropriate authorities as required by OECS territory specific regulations. Case management should be done in

consultation with key persons, including parents, paediatrician, and social workers. Parents have legal authority over their children and should be informed of all aspects of their children's treatment and care and provide parental consent.

These guidelines focus on prevention and control as cost-effective strategies in reducing STI-related morbidity and mortality in the individual and in the community. To effectively achieve this, the multidisciplinary clinical team comprising of physicians, nurses, pharmacists, social workers, laboratory technicians and adjunct health care workers must be cognizant of their roles in conducting patient education, assessing risk and recommending appropriate testing and treatment for STIs. Clinical teams should also discuss STI prevention including abstinence, condom use, pre-exposure vaccination as appropriate and partner testing and treatment. Where necessary, appropriate referrals for additional services and follow up should be issued. As a public health responsibility, practititioners should report to the appropriate public health agencies on notifiable STI and/or HIV/AIDS cases in accordance with OECS territory specific regulations. Overarching to the delivery of services, privacy and confidentiality remains paramount.

The guidelines are organized in four main parts with subsections addressing specific syndromes and etiological agents as seen in figure 11.

Figure 11: Organisation of the STI guidelines



9.2 Prevention and Control of STIs

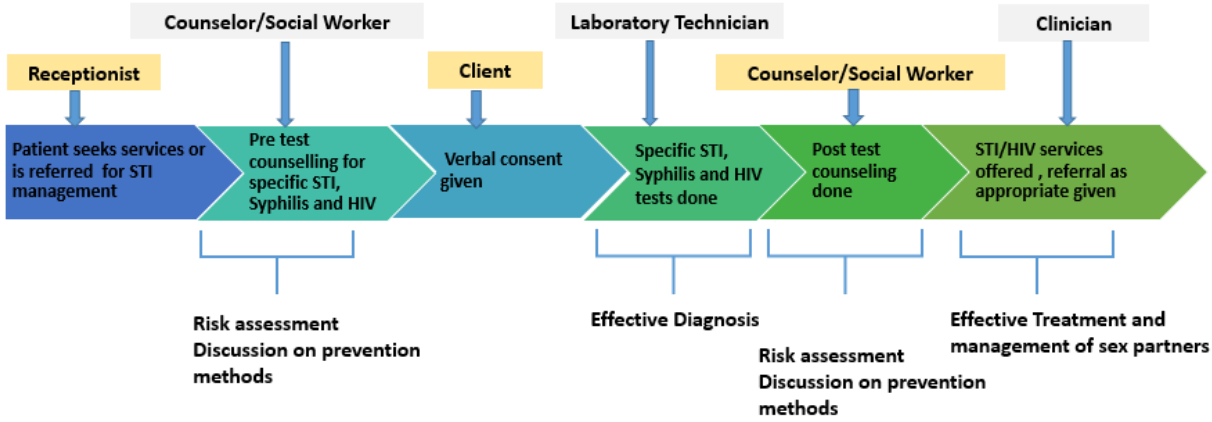
This section of the guidelines recognizes the importance of prevention of STIs and focuses on key strategies of achieving this, describes in detail proven prevention methods and discusses the

importance of partner services including contact tracing and managing partners of patients with STIs. The recognition is made of the increased risk for acquiring and transmitting STIs among several populations and outlines key prevention intervention for these populations. Five key strategies are recommended for the OECS as follows;

1. Accurate risk assessment
2. Prevention methods
3. Identification of asymptomatically infected persons and persons with symptoms associated with STDs;
4. Effective diagnosis, treatment, counseling, and follow up of infected persons;
5. Evaluation, treatment, and counseling of sex partners of persons who are infected with an STD.

The figure 12 below delineates the process for incorporating STI prevention and control strategies for patients seeking STI services or those referred to the health facility.

Figure 12: Process for STI Prevention and Control



Accurate risk assessment and discussion on prevention methods are key components of pre and post- test counselling, but should be discussed at every level of interaction with the patient. It is recommended that pre and post-test counselling be conducted by a social worker/counsellor with relevant the skills, experience and expertise. This is particularly important in ***pre-test counselling*** when establishing patient's trust and building upon it by actively listening and showing empathy and understanding. Open ended questions should be used for probing and establishing rapport, for example ***"Tell me about any new sex partners you've had since your last visit," and "What has your experience with using condoms been like?"*** . Use clear, understandable and non-judgmental language such as ***"Are your sex partner's men, women, or both?" Have you ever had a sore or scab on your penis?'.*** Use normalizing language such as ***"Some of my patients have difficulty using a condom with every sex act. How is it for you?"*** This will allow the health care worker to gather a good sexual history and conduct detailed risk assessment.

The 5P approach defined by the US Centers of Disease Control and comprising of history taking on **P**artners, **P**ractices, **P**revention of Pregnancy, **P**rotection from STIs and **P**ast History of STIs is recommended in the OECS. See details in Box 9.1.

Box 9.1 The Five Ps- Partners, Practice, Prevention of Pregnancy, Protection from STDs, and Past History of STDs

1. Partners "Do you have sex with men, women, or both?", "In the past 2 months, how many partners have you had sex with?" "In the past 12 months, how many partners have you had sex with?", "Is it possible that any of your sex partners in the past 12 months had sex with someone else while they were still in a sexual relationship with you?"

2. Practices "To understand your risks for STDs, I need to understand the kind of sex you have had recently.", "Have you had vaginal sex, meaning 'penis in vagina sex'?" If yes, "Do you use condoms: never, sometimes, or always?"
"Have you had anal sex, meaning 'penis in rectum/ anus sex'?" If yes, "Do you use condoms: never, sometimes, or always?" "Have you had oral sex, meaning 'mouth on penis/ vagina'?" For condom answers: If "never": "Why don't you use condoms?" If "sometimes": "In what situations (or with whom) do you use condoms?"

3. Prevention of pregnancy "What are you doing to prevent pregnancy?"

4. Protection from STDs "What do you do to protect yourself from STDs and HIV?"

5. Past history of STDs "Have you ever had an STD?", "Have any of your partners had an STD?"
Additional questions to identify HIV and viral hepatitis risk include: "Have you or any of your partners ever injected drugs?" "Have your or any of your partners exchanged money or drugs for sex?" "Is there anything else about your sexual practices that I need to know about?"

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

The STI/ HIV result should be issued with ***post test counselling***. Persons testing positive for HIV or other STI, focus should be placed on linkage to HIV services and treatment of the STIs. Persons testing negative should receive counselling on risk reduction and encouraged to repeat test depending on the risk factor such as being in the window period or a member of the key population. High-intensity behavioral counseling such as **client- centered STD/HIV prevention counselling** directed at a person's risk, the situations in which risk occurs, and the use of personalized goal-setting strategies is recommended. Risk reduction and prevention interventions should be prioritised to include for some STIs, abstinence until treatment is completed, partner treatment, partner reduction and condom use among others. Patients should be educated on the signs and symptoms, complications and treatment of STIs. Counselling should be focused on patients understanding and dealing with incurable STIs (e.g., HIV, HSV), which may be transmitted to the partner(s) or spouse, eliciting contact information and discussing approaches to notify sexual partners. Related social issues such as risk of violence, stigma and discrimination and disclosure should be discussed. Patients should be empowered to take control of their lives and be responsible for disease prevention. Confidentiality remains overarching to the post test counselling process.

9.3 Prevention Methods

Discussing risk reduction requires an understanding of the preventions methods, their efficacy and availability in the OECS. Recommended prevention methods include:

- **Pre exposure vaccination** is effective and available for human papillomavirus (HPV), Hepatitis A and B viruses (HAV, HBV).
- ***HPV vaccination*** is recommended for boys and girls aged 11 or 12 years. This should be administered beginning at 9 years of age and is recommended through age 26 years for all females and through age 21 years for all males that have not received any or all of the vaccine doses. For persons with **HIV infection and for MSM**, vaccination is recommended through age 26 years.
- ***Hepatitis B vaccination*** is recommended for all unvaccinated, uninfected persons being evaluated or treated for an STD.
- ***Hepatitis A and B vaccination*** are recommended for MSM, injection-drug users (IDUs), persons with chronic liver disease (CLD), and persons with HIV infection who have not yet been infected with one or both types of hepatitis virus.
- **Abstinence-** patients should be counselled on abstinence to avoid transmission of STIs. Further, persons undergoing treatment for a STI should be counselled on abstinence from sexual intercourse until completion of the entire course of medication, partner reduction and being in mutually monogamous relationship.
- **Condoms**-correct and consistent use of male condoms for preventing transmission. Althoigh less used, female condoms provided the advantage of being a female controlled method of STI prevention. The most common brand in the OECS is the FC2 condom.
- **Cervical diaphrams** are not widely used in the OECS. They, however they confer some protect against cervical gonorrhea, chlamydia, and trichomoniasis but should not be relied on as the sole source of protection against HIV or other STDs.
- **Non specific topical microbicides and spermicides** are ineffective for preventing HIV, Some spermicides might disrupt genital or rectal epithelium and have been associated with an increased risk for HIV infection. No proven topical antiretroviral agents exist for the prevention of HIV. Like cervical diaphrams, spermicides are not commonly used in the OECS.
- **Male circumcision** reduces the risk for HIV and some STDs in heterosexual men.
- **Emergency Contraception** - Unprotected intercourse exposes women to risks for STDs and unplanned pregnancy. Women should be counselled in the option of emergency contraception (EC) if pregnancy is not desired. ECPs are available in the following formulations: ulipristal acetate in a single dose (30 mg), levonorgestrel in a single dose (1.5 mg) or as a split dose (0.75 mg each taken 12 hours apart), or combined estrogen and progestin. In the OECS levonorgestrel 1.5 mg tab generally used. ECPs are most efficacious when initiated as soon as possible after unprotected sex but have some efficacy up to 5 days later. ECPs are ineffective (but not harmful) if the woman is already pregnant
- **Postexposure Prophylaxis for HIV and STD** - Guidelines for the use of postexposure prophylaxis (PEP) aimed at preventing HIV infection and other STDs as a result of sexual exposure are discussed in under special circumstances in the guidelines. Genital hygiene methods (e.g., vaginal washing and douching) after sexual exposure are ineffective in protecting against HIV and STDs and might increase the risk for bacterial vaginosis (BV), some STDs, and HIV infection.
- **Antiretroviral treatment** of persons with HIV Infection decreases the risk for transmission to the uninfected partner by 96%. HIV positive persons in serodiscordant relationship should be offered ARVS as a prevention method for the HIV negative partners and should receive counselling to that effect.
- **Preexposure Prophylaxis for HIV (PreP)** with daily administration of oral antiretrovirals among the key population of men who have sex with men has also been effective in reducing the rate of HIV acquisition among this populations. The fixed dose combination of Truvada (tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC)) is the drug of choise. Currently, PreP is not

prescribed in the OECS

- **HIV seroadaptation strategies** is commonly practiced among serodiscordant couples in the MSM community and include ***serosorting and seropositioning***. Serosorting includes limiting anal sex to a partner with similar HIV status and seropositioning refers to the HIV positive partner being the receptive partner for anal sex. Patients should be counselled that serosorting confers greater risk of HIV infection than consistent condom use, but is lower risk compared with anal intercourse without a condom and without serosorting. While serosorting and seropositioning reduces the risk for HIV, there increased risk of STDs including chlamydia and gonorrhea. While it is a practice in the community, serosorting and seropositioning is not recommended since there are MSM who are HIV positive are unaware of their status, MSMs make incorrect assumptions about the HIV status of their partners and some MSM with HIV infection might not disclose their HIV status.
- **Retesting after treatment** to detect repeat infections of chlamydia, gonorrhea, or trichomoniasis can detect repeat infection and potentially can be used to enhance population-based prevention. Persons testing positive for chlamydia or gonorrhea should be recommended for retesting 3 months after treatment. Similarly, persons with a syphilis diagnosis should undergo follow-up serologic syphilis testing (See specifics in the section on management of STIs). Repeat testing for HIV negative persons are is also recommended among the key populations, persons suspected to be in the window period and pregnant women in the third trimester.

9.4 Partner Services

Partner services refers to a continuum of clinical evaluation, counseling, diagnostic testing, and treatment designed to increase the number of infected persons brought to treatment and to disrupt transmission networks.

Treatment of sex partners reduces the risk of reinfection and therefore constitute an integral component of a comprehensive STI programme. Accordingly, all persons with STIs should be encouraged to notify their sex partners and urge them to seek medical evaluation and treatment. They should be advised to bring their primary sex partner when returning for treatment so that both persons could be concurrently managed. Alternatively, patients can authorize the clinical team to contact and notify partners.

A specific component of partner services is **Expedited Partner Therapy (EPT)**. This is the clinical practice of treating the sex partners of persons with chlamydia or gonorrhea infections by providing medications or prescriptions to the patient. Providing medication is the preferred approach over prescription. Patients provide partners with these therapies without the health-care provider having examined the partner. All partners in the last 60 days should be treated. If the patient has not had sex in the 60 days before diagnosis, providers should attempt to treat a patient's most recent sex partner. Medication or prescriptions provided for EPT should be accompanied by treatment instructions, appropriate warnings about taking medications (if the partner is pregnant or has an allergy to the medication), general health counseling, and a statement advising that partners visit the clinic as early as possible for medical evaluation.

9.5 Reporting and Confidentiality

The accurate and timely reporting of STDs is integral to public health efforts to assess morbidity trends, allocate limited resources and assist in partner notification and treatment. STD/HIV and acquired immunodeficiency syndrome (AIDS) cases should be reported in accordance with OECS territory specific statutory regulations.

9.6 STI Prevention among special populations

In the OECS, priority is place on several high risk populations in acquiring and reducing STI transmission.

9.6.1 Prevention among pregnant women

Intrauterine or perinatally transmitted STDs can have severe complications on pregnant women, their partners, and their fetuses. All pregnant women in the OECS should therefore be screened as follows:

- HIV and syphilis serologic test at the first prenatal visit. Women testing negative should be retested in the third trimester.
- Hepatitis B surface antigen (HBsAg) at the first prenatal visit even if the pregnant woman has been previously vaccinated or tested. Pregnant women with high risk for Hepatitis B (multiple sex partners, recent treatment for STI and Hep B positive partner) and with clinical hepatitis should be retested at the time of admission for delivery. Vaccinate pregnant women at risk, once Hepatitis B is ruled out and there is no prior vaccination.
- Hepatitis C, HTLV I and HTLV I test at the first prenatal visit.
- Pregnant women at increased risk for Chlamydia and gonorrhea infection should be routinely screened for *Chlamydia trachomatis and Gonococcal infection* at the first prenatal visit. Women tested positive should be treated. Retest in the third trimester to prevent maternal postnatal complications and chlamydial and gonococcal infection in the neonate.
- All pregnant women should be screened for cervical cancer with a Papanicolau (Pap) test.
- All symptomatic women should be valuated and treated for STIs.

9.6.2 Prevention among adolescents

Adolescences who initiate sex early, have a history of sexually transmitted infections and are from the community of young men who have sex with men (YMSM) are at an increased risk for STIs. At risk also, are adolescents who reside in detention facilities and inject drugs. The following are primary prevention recommendations for adolescents.

- HPV vaccination for females:
  - Bivalent, quadrivalent, or 9-valent, is recommended routinely at aged 11 and 12 years, administered beginning at 9 years of age.
  - Bivalent, quadrivalent or 9- valent at aged 13–26 years who have not yet received all doses or completed the vaccine series.
- HPV vaccines for males:
  - Quadrivalent or 9-valent is recommended routinely at aged 11 and 12 years, administered beginning at 9 years of age.
  - Vaccination with quadrivalent or the 9-valent HPV vaccine at aged 13–21 years who have not yet received all doses or completed the vaccine series, although males aged 22–26 years also can be vaccinated .
  - For persons with HIV infection and for MSM, HPV vaccination is recommended through age 26.
- The Hepatitis B vaccination (HBV) series is recommended for all adolescents and young adults who have not previously received the HBV vaccine. (See section on Hepatitis under management of STIs).
- The Hepatitis A vaccination (HAV) series should be offered to adolescents and young adults who have not previously vaccinated.

9.6.3 Prevention among children

Management of children who have STDs requires close cooperation between clinicians, laboratorians,

and child- protection authorities. Official investigations, when indicated, should be initiated promptly. Certain diseases (e.g., gonorrhea, syphilis, genital and anal warts, HPV and chlamydia), if acquired after the neonatal period, strongly suggest sexual contact.

9.6.4 Prevention among persons in correctional facilities

Persons entering correctional facilities have high rates of STIs (including HIV) and viral hepatitis. This is especially so for those younger persons. The following is recommended in relation to screening:

- Women ≤35 and men <30 years should be screened for chlamydia and gonorrhea at intake into correctional facilities.
- HIV, Syphilis, Hepatitis A and C and HTLV 1 and 2 testing at intake into the correctional facility.

9.6.5 Prevention among Men Who Have Sex with Men (MSM)

The following is recommended:

- HIV and syphilis serology every six months, if HIV status is unknown or negative.
- *N. gonorrhoeae* and *C. trachomatis* test in men who have had insertive intercourse during the preceding year
- *N. gonorrhoeae* and *C. trachomatis* test for rectal infection in men who have had receptive anal intercourse during the preceding year and for pharyngeal infection among those who have had receptive oral intercourse during the preceding year.
- HPV quadrivalent vaccine through age 26 years.
- Anal cytology to screen for anal cancer, followed by high resolution anoscopy for persons with abnormal cytologic results.
- HBsAg testing for chronic Hepatitis B infection. Vaccination for HAV and HBV is recommended for all MSM in whom there is no previous infection or vaccination.
- Annual Serologic screening for HCV is recommended at initial evaluation of persons with newly diagnosed HIV infection.

9.6.6 Prevention among Female Commercial Sex Workers (FCSW)

FCSW are at high risk for HIV infection and STIs. The following is recommended:

- HIV and syphilis serology every six months, if status is unknown or negative.
- A test *N. gonorrhoeae* and *C. trachomatis*
- HPV quadrivalent vaccine through age 26 years.
- HBsAg testing for chronic Hepatitis B infection. Vaccination for HAV and HBV is recommended for all FCSW in whom there is no previous infection or vaccination.
- Annual Serologic screening for HCV is recommended at initial evaluation of persons with newly diagnosed HIV infection.

9.6.7 Prevention among Women Who Have Sex with Women (WSW)

Skin-to-skin transmission of HPV is common among WSW. WSW are therefore at risk for acquiring HPV from both their female partners and from current or prior male partners, and thus are at risk for cervical cancer. Routine cervical cancer screening should be offered to all women, regardless of sexual orientation or sexual practices, and women should be offered HPV vaccine as per guidelines.

9.6.8 Prevention among Transgender Population

Transgender persons who identify with a sex that differs from that they were assigned at birth. Transgender women ("trans-women" or "transgender male to female") identify as women but were born with male anatomy and Transgender men (also referred to as "trans-men" or "transgender female to male") identify as men but were born with female anatomy. This population generally has the highest HIV prevalence among all key populations in the Caribbean. There is limited data in relation to

STIs. Providers caring for transgender women and men should have knowledge of their patients' current anatomy and patterns of sexual behavior before counseling them about STD and HIV prevention. The majority of transgender women and men in the OECS have not undergone genital affirmation surgery and may retain a functional penis in the case of transgender women and vagina and cervix in the case of transgender men. Transgender women therefore might engage in insertive oral, vaginal, or anal sex with men and women and transgender men can be at risk for bacterial STIS, cervical HPV and cervical cancer. It is therefore important for clinicians to access transgender women and men for STIs and HIV based on current anatomy and sexual behaviors.

9.7 Management of Sexually Transmitted Infections

The management of sexually transmitted infections comprises of a thorough evaluation of the patient which includes a comprehensive history taking, physical examination (including examination of the reproductive system), laboratory diagnostic testing, treatment, patient education and follow up. Each of these is addressed in detail in this section.

9.7.1 Evaluation and management of the STI patient

A comprehensive, in-dept evaluation of the STI patient is the bedrock for management of the patient. It commences with a thorough history and physical examination, clinical investigation and resulting in a differential diagnosis. Key elements of the steps are outlined below and constitute the standard of care provided by the OECS.

- History taking, including behavioural, demographic and medical risk assessment. This includes a detailed sexual, substance use/recreational drug use and prior STIs history and treatment.
- Physical examination, particularly of the genital area and the reproductive organs.
- Initial investigations, as indicated by the history and physical examination.
- Diagnosis, established either through syndromic or laboratory-based methodologies
- Treatment that is prompt, optimal, and based on the presumed or established diagnosis
- Patient education and counselling detailed in sections in sections 8.2,8.3 and 8.4.
- Clinical follow up.

9.7.2 History Taking

A comprehensive history taking is important in patient's evaluation. This should be done in a non-discriminatory and non judgemental way and with sensitivities around gender identifty for key populations discussed earlier. Additionally, history taking should occur in an environment that provides privacy for the patient. The key components of a comprehensive history taking include:

- Background- this includes basic demographic information. For women, gynaecological information such as last menstrual period, gravida, history of PaP smear. Past medical history should examine any allergies to medications, co-morbid diseases, previous hospitalization, immunizations, blood transfusions and surgeries. A social history of alcohol and drug use, incarceration, transactional sex and domestic violence is also important.
- Presenting complaints- important to establishing diagnosis, the details of presenting complaints should be explored in addition to establishing the chief complaint. Details of signs and symptoms should include duration, colour of discharge, presence of rash and itching among others.
- Specific assessment in establishment risk using the "Five P risk assessment" framework.

9.7.3 Physical Examination

Physical examination must be patient-focused and specific. The antecedent history should serve as a guide for building the differential diagnosis and to verify the patient's primary complaints. There are common elements in the examination of men and women. Focused examinations based on the anatomy, sexual practices and risk behaviours may also be required. Elements of physical examinations are presented in table 49.

Table 49: Elements of physical examination

Common elements for men and women	Women specific	Men Specific
Mouth: Oral manifestations, including ulcers, plaques, masses, redness Skin: Ulcers, rashes, plaques, raised lesions, nodules, distribution Nodes: Distribution—inguinal, femoral, cervical, nature (tenderness, suppurated) Abdominal examination: Tenderness, masses, discolouration Anal and perianal area Genitalia	Observation and inspection: Vulva, vagina, introitus, perineum, mons pubis, anus (look for discharges, ulcers, plaques, erythema, pigmentation) Speculum examination: Vaginal vault—posterior fornix, lateral walls, cervix (look for discharges, erythema, oedema, ulcers) Digital examination: Cervix, uterus, adnexa (look for tenderness, masses, position, mobility)	Foreskin, glans penis, mons pubis, urethra (look for ulcers, discharges) Testes, scrotum (assess size, shape, symmetry, tenderness) Anus (look for discharges, tenderness, ulcers, masses) Prostate (assess size, median sulcus, tenderness)

9.7.4 Initial Investigations

The method of investigation used will depend on the symptoms, sexual risk behaviour, and site exposed during sexual intercourse. There may be the need to examine multiple sites.

Although the gold standard of diagnosis is laboratory confirmation, this may not always be possible. Where syndromic management is used, efforts should be made at intervals to supplement the diagnosis with laboratory testing to confirm the utility of the syndromic approach and to identify resistant organisms. The main investigations used for STI diagnosis are described in table 50 below.

Table 50: Menu of investigations for STIs

Swabs	Urinalysis	Special consideration for women
Men: Urethral Gram stain, culture and sensitivity(gonorrhea,chlamydia) Women: High vaginal: Wet mount examination (trichomoniasis, bacterial vaginosis, candida) Endocervical: Gram stain, culture and sensitivity (gonorhoea, chlamydia) Consider anal swabs in both sexes based on symptoms and risk factors	Microscopy culture and sensitivity Point of care nucleic acid amplification testing (NAAT), if available	Pap test with or without visual inspection with ascetic acid (VIA) Pregnancy test Pelvic ultrasound for pelvic inflammatory disease (PID), where clinical findings are non-diagnostic CBC

9.7.5 Diagnosis, Treatment, Patient Education, and Follow-up

Patient history, physical examination and laboratory results taken together should guide diagnosis and treatment. Diagnoses and treatment plans will vary by syndrome and specific infectious aetiology, as detailed in the diseases specific sections below. In cases where laboratory diagnosis is possible, etiological management would be the prioritised. In other cases, syndromic management will be instituted.

9.8 Diseases categorised by Genital, Anal and Perianal Ulcers

Genital ulcer disease (GUD) is a syndrome of ulcerative, erosive, pustular, or vesicular genital lesion(s), with or without regional lymphadenopathy. The more common STIs associated with genital ulcer are Genital Herpes and Syphilis. Less common is Chancroid, Granuloma Inguinale (Donovanosis) and Lymphogranuloma venerum (LGV).

Diagnosis

Clinical diagnosis of GUD is often inaccurate, particularly in settings where several aetiologies are common. Moreover, clinical manifestations and patterns of GUDs may be further altered in the presence of HIV infection. Diagnosis is often inadequate when based solely on history and physical examination. Table 51provides a differential diagnosis of the most prevalent causes of GUD in the OECS region.

Table 51: Differential diagnosis of genital ulcers

Condition	Causative Organism	Painful lesions	Lymphadenopathy	No of ulcers
Herpes	HSV-1 or -2	Yes (vesicular)	Yes	More likely multiple than one
Syphilis	*Treponema pallidum*	No	Yes	More likely one than multiple
Chancroid	*H. ducreyi*	Yes	Yes (suppurative)	One or more
Granuloma inguinale (donavanosis)	*Klebsiella granulaomatis*	No	No	One
Lymphogranuloma venerum (LGV)	*C. trachomatis*— serovars L1, L2, or L3	Yes	Yes ('groove sign' may suppurate)	Often transient and unnoticed

Treatment

A comprehensive treatment regimen is necessary to cover most of the causative organisms of GUD and therefore a syndromic approach is recommended. Persons with GUD have an increased risk of acquiring and transmitting HIV and therefore early is essential to reducing HIV transmission in the infected individual and their partner(s) based on syndromic management or eitiological agent where possible. Details of etiological management and syndromic management is described in the sections below.

9.8.1 Genital Herpes

Genital herpes is a chronic, life-long viral infection, often with a prodrome of fever and malaise and with early presentation of painful vesicular lesions that appear in crops and resolve within 9–14 days. Two types of HSV can cause genital herpes: HSV-1 and HSV-2. Recurrent genital herpes are caused by predominantly by HSV-2. Persons with undiagnosed HSV-2 may shed virus intermittently in the anogenital area and can result in person-to-person transmission. The majority of genital herpes infections are inadvertently transmitted by individuals in such circumstances—those who are unaware that they have the infection or are asymptomatic when transmission occurs.

The break in the epidermis caused by HSV creates a portal of entry for the HIV virus, thus facilitating the transmission and acquisition of HIV. Symptoms of recurrent genital herpes infections are often more severe and occur with greater frequency in persons co-infected with HIV and HSV. Treatment with HAART and prophylactic antiviral medication can help to reduce the severity of symptoms.

Diagnosis

The diagnosis of genital herpes is often made on clinical findings. Virological- and type-specific serological testing, cell culture and PCR can be used of diagnosis. Screening for HSV-1 and HSV-2 in the general population is not indicated.

Treatment

Antiviral chemotherapy is the mainstay of treatment. The strength and frequency of the treatment regimen is determined by the severity and stage of infection, and should be optimised to achieve viral suppression. Pregnant women who have an outbreak of genital herpes in the period immediately prior to delivery are advised to have a caesarean section to avoid transmitting the virus to the infant. Treatment is summarized in table 52.

Table 52: Summary treatment regimens for the treatment of genital herpes

Disease	Recommended regimen(s)
First clinical episode of genital herpes	• Acyclovir: 400 mg PO TID x 7–10 days; **OR** • Acyclovir: 200 mg PO 5/day x 7–10 days; **OR** • Valacyclovir: 1 g PO BID x 7–10 days **OR** **Treatment can be extended if healing is incomplete after 10 days of therapy.*
Established HSV 2 infections Recurrent episode of genital lesions among persons with symptomatic first-episode genital HSV-2 infection. With established HSV 2 infection, there can be intermittent asymptomatic shedding. Antiviral therapy is administered as: suppressive therapy to reduce the frequency of recurrences or episodically to ameliorate or shorten the duration of lesions. Suppressive therapy has the additional advantage of decreasing the risk for genital HSV-2 transmission to sexual partners.	
Established HSV infection in the HIV-uninfected person: *Suppressive* therapy	• Acyclovir: 400 mg PO BID; **OR** • Valacyclovir: 500 mg PO QD **OR** • Valacyclovir: 1 g PO QD **Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in persons who have very frequent recurrences (i.e., ≥10 episodes per year).*
Episodic therapy for recurrent episodes (Effective episodic treatment of recurrent herpes requires initiation of therapy within 1 day of lesion onset or during the prodrome that precedes some outbreaks)	• Acyclovir: 400 mg PO TID x 5 days; **OR** • Acyclovir: 800 mg PO BID x 5 days; **OR** • Acyclovir: 800 mg PO TID x 2 days; **OR** • Valacyclovir: 500 mg PO BID x 3 days; **OR** • Valacyclovir: 1 g PO QD x 5 days

Established HSV infection in the HIV-coinfected person - *Suppressive therapy*	• Acyclovir: 400–800 mg PO BID or TID; **OR** • Valacyclovir: 500 mg PO BID
Severe HSV Disease (patients who have severe HSV disease or complications that necessitate hospitalization (e.g., disseminated infection, pneumonitis, or hepatitis) or CNS complications (e.g., meningoencephalitis)	• Acyclovir 5–10 mg/kg IV every 8 hours for 2–7 days or until clinical improvement is observed followed by oral antivirals for 10 day • ***HSV encephalitis requires 21 days of intravenous therapy***
Genital Herpes in Pregnancy	**Suppressive therapy of pregnant women with recurrent genital herpes** • Acyclovir 400 mg orally three times a day OR • Valacyclovir 500 mg orally twice a day *Treatment recommended starting at 36 weeks of gestation should be administered IV to pregnant.* ***For severe infection- IV antivirals.*** *Suppressive acyclovir treatment late in pregnancy reduces the frequency of recurrences and frequency for cesarean delivery.*
Neonatal Herpes	**Herpes limiting to the skin and mucus membranes** • Acyclovir 20 mg/kg IV every 8 hours for 14 days **Disseminated herpes and herpes of the CNS** • Acyclovir 20 mg/kg IV every 8 hours for 21 days
Antiviral Resistant HSV- All acyclovir-resistant strains are also resistant to valacyclovir, and most are resistant to famciclovir.	**Consider management with a specialist: Options include** • Foscarnet (40–80 mg/kg IV every 8 hours until clinical resolution is attained) • Intravenous cidofovir 5 mg/kg once weekly might also be effective. • Imiquimod and cidofovir gel 1%; are topical alternatives. – apply daily for 5 consecutive days.

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Genital Herpes

- ❖ Counsel patients on the natural history of the disease, emphasizing the potential for recurrent episodes, asymptomatic viral shedding and the potential for transmission. Emphasize the value and effectiveness of therapy and the importance of the management of sex partners. General prevention messages should include abstaining from sexual activity with uninfected partners when lesions or prodromal symptoms are present, consistent and correct condom use. The risk for HIV transmission and neonatal HSV infection should be discussed.
- ❖ Management of sex partners- Patients should inform current sex partners about genital herpes and future partners before initiating a sexual relationship. Symptomatic sex partners should be evaluated and treated as per guidelines. Asymptomatic sex partners should be offered type-specific serologic testing for HSV infection.
- ❖ **HIV co infection-** episodes of genital, perianal, or oral herpes are generally more prolonged and severe. Lesions are more severe, painful, and atypical. HSV shedding is increased in persons with HIV infection. Antiretroviral therapy reduces the severity and frequency of symptomatic

genital herpes, however frequent subclinical shedding still occurs. Initiation of ART can result in immune reconstitution syndrome, worsening the clinical manifestations of genital herpes.

- **HSV and Pregnancy**- All pregnant women should be asked whether they have a history of genital herpes. Risk of mother to child transmission is high (30%-50%) among women who acquire genital herpes near the time of delivery. Risk of mother to child transmission is lower (<1%) among women with prenatal histories of recurrent herpes or who acquire genital HSV during the first half of pregnancy. Prevention of neonatal herpes depends both on preventing acquisition during late pregnancy and avoiding exposure of the neonate to herpetic lesions and viral shedding during delivery. Women without known genital or orolabial herpes should be counseled to abstain from vaginal and oral sex during the third trimester with partners known or suspected of having genital or orolabial herpes. Women with recurrent genital herpetic lesions at the onset of labor should deliver by cesarean delivery to reduce the risk of neonatal HSV infection.

9.8.2 Granuloma Inguinale (Donovanosis)

Donovanosis is caused by the intracellular Gram-negative bacterium *Klebsiella granulomatis*, (previously known as *Calymmatobacterium granulomatis*). The disease presents clinically as painless, slowly progressive, ulcerative lesions without regional lymphadenopathy. The lesions are highly vascular; easily bleed on contact and characterized by their beefy red appearance.

Diagnosis

The causative organism is difficult to culture. Diagnosis requires visualization of dark-staining Donovan bodies on tissue crush preparation or biopsy.

Treatment

Table 53 describes the recommended and alternative treatment regimens for Donavanosis.

Table 53: Treatment of Donavanosis

Recommended regimen	Alternative regimen
Azithromycin 1 g orally once per week **OR** 500 mg daily for at least 3 weeks and until all lesions have completely healed *If improvement is not evident in the first few days of therapy, then add*: Gentamicin 1 mg/kg IV every 8 hours.	• Doxycycline 100 mg orally twice a day for at least 3 weeks and until all lesions have completely healed **OR** • Ciprofloxacin 750 mg orally twice a day for at least 3 weeks and until all lesions have completely healed **OR** • Erythromycin base 500 mg orally four times a day for at least 3 weeks and until all lesions have completely healed **OR** • Trimethoprim-sulfamethoxazole one double-strength (160 mg/800 mg) tablet orally twice a day for at least 3 weeks and until all lesions have completely healed

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Granuloma Inguinale

All patients should be followed through until all signs and symptoms resolve and should be tested for HIV. All sex partners should be treated, if they had sexual contact with the patient during the 10 days preceding the patient's onset of symptoms. Avoid doxycycline in the second and third trimester because of the risk for discoloration of teeth and bones. Persons who are HIV positive should receive the same treatment as an HIV negative person.

9.8.3 Inguinal Buboes

Inguinal buboes are often caused by Chancroid and Lymphogranuloma Venerum (LGV). These organisms may produce painful enlargement of the lymph glands in the groin area, which are often fluctuant. It should be noted, however, that other non-STI organisms, such as TB, may also produce similar symptoms. Syndromic treatment is therefore recommended for clinical manifestations of inguinal buboes.

Treatment

The recommended syndromic treatment for inguinal buboes can be seen in the table 54 below.

Table 54: Treatment of inguinal buboes

	Recommended regimen
	• Ciprofloxacin: 500 mg orally 2 x a day for 3 days; PLUS • Doxycycline: 100 mg orally 2 x a day for 14 days; **OR** Erythromycin: 500 mg orally 2 x a day for 14 days

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. MMWR. 2010 Dec 17; 59(12). Available from: http://www.cdc.gov/std/treatment/2010/STD-Treatment-2010-RR5912.pdf.

Other management considerations for Inguinal Buboes

Some cases may require treatment longer than the recommended 14 days. Fluctuant lymph nodes should be aspirated through healthy skin. Incision and drainage or excision of nodes may delay healing and should not be attempted.

9.8.4 Chancroid

Chancroid is caused by the organism *Haemophilus ducreyi*, which is still prevalent in the region. Clinically, it presents as a painful genital ulcer with tender suppurative inguinal adenopathy. Chancroid is a risk factor in the transmission and acquisition of HIV infection. A probable diagnosis of chancroid for both clinical and surveillance purposes can be made if all of the following criteria are met:

1. The patient has one or more painful genital ulcers.
2. The patient has no evidence of *T. pallidum* infection by dark field examination of the ulcer exudate or by a serologic testing for syphilis performed at least 7 days after the onset of ulcers.
3. The clinical presentation, appearance of genital ulcers, and, if present, regional lympadenopathy are typical for chancroid.
4. A test for HSV performed on the ulcer exudate is negative.

Diagnosis

A definitive diagnosis of chancroid requires the identification of *H. ducreyi* on special culture media. Confirmatory diagnosis of chancroid is often challenging and so it is usually based on clinical grounds.

Treatment

Table 55 describes the recommend etiological treatment based on a confirmed diagnosis

Table 55: Treatment of Chancroid

Recommended regimen
• Azithromycin: 1 g orally in a single dose; **OR** • Ceftriaxone: 250 mg intramuscularly (IM) in a single dose; **OR** • Ciprofloxacin: 500 mg orally 2 x a day for 3 days; **OR** • Erythromycin base: 500 mg orally 3 x a day for 7 days

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Chancroid

1. Test for HIV infection at the time chancroid is diagnosed. If negative, repeat serologic test syphilis and HIV infection in 3 months after the diagnosis of chancroid.
2. Follow up
   - Patients should be re-examined 3–7 days after initiation of therapy.
   - If no clinical improvement in 3-7 days consider whether 1) the diagnosis is correct, 2) the patient is coinfected with another STI, 3) the patient is infected with HIV, 4) the treatment was not used as instructed, or 5) there is antimicrobial resistance.
   - Healing time for the ulcer is dependent on the size of the ulcer; large ulcers might require >2 weeks. In addition, healing is slower for some uncircumcised men who have ulcers under the foreskin.
   - Clinical resolution of fluctuant lymphadenopathy is slower than that of ulcers and might require needle aspiration or incision and drainage, despite otherwise successful therapy.
3. Management of sex partners- Treat sex partners if they had sexual contact with the patient during the 10 days preceding the patient's onset of symptoms.

9.8.5 Lymphogranuloma Venerum

LGV is caused by *Chlamydia trachomatis* serovars L1, L2, or L3. The most common clinical manifestation of LGV among heterosexuals is tender inguinal and/or femoral lymphadenopathy that is typically ***unilateral.*** An ephemeral genital ulcer papule or pustule sometimes appears at the site of inoculation. By the time the patient seeks medical care, the lesion has often disappeared. In terms of sexual practices, rectal exposure for either men or women can result in proctocolitis, including mucoid and/or haemorrhagic rectal discharge, anal pain, constipation, fever and/or tenesmus. Complications include colorectal fistulae and strictures.

Diagnosis

Diagnosis is based on clinical suspicion, epidemiologic information, and the exclusion of other aetiologies for proctocolitis, inguinal lymphadenopathy, and genital or rectal ulcers. A lymph node specimen can be tested for chlamydia by culture, direct immunofluorescence, or nucleic acid detection. Chlamydia serology (compliment fixation titres >1:64) can support the diagnosis of LGV in the appropriate clinical context.

Treatment

Once confirmed etiological treatment is recommended as described in Table 56.

Table 56: Treatment of LGV

Recommended regimen	Alternative regimen
Doxycycline: 100 mg orally twice a day for 21 days	• Erythromycin base: 500 mg orally 4 x a day for 21 days • Treat pregnancy and lactating women with erythromycin.

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Lymphogranuloma Venerum

Follow up patients until signs and symptoms have resolved Treatment cures infection and prevents ongoing tissue damage/ scarring. Buboes might require aspiration through intact skin or incision and drainage to prevent the formation of inguinal/ femoral ulcerations. Conduct testing for other STIs such as HIV, syphilis, gonorrhoea. Treat sex partners if they had sexual contact with the patient within the 60 days preceding the patient's onset of symptoms. HIV positive patients should receive the same treatment as HIV negative patients.

9.9 Syphilis

Syphilis is a systemic disease caused by the spirochaete *Treponema pallidum*. The disease is divided into stages based on clinical findings which guide treatment and follow-up.

Stages of Infection are:

1) **Primary syphilis** infection (i.e., ulcers or chancre at the infection site).
2) **Secondary syphilis**- more disseminated signs and symptoms, including the classic palmar/plantar rash or a desquamating rash of the palms and soles; a papular squamous eruption that may be generalized on the body; alopecia; iritis; condyloma lata; and generalized lymphadenopathy. Rash may resemble pityriasis rosea, guttate psoriasis, and drug- or viral eruptions. Can also be presented as neurologic deficit—hearing loss, vision loss, or neuropathy. Liver irritation with a raised ALT/AST may also occur.
3) **Tertiary syphilis** (i.e., cardiac, gummatous lesions, tabes dorsalis, and general paresis), but not neurosyphilis (normal Cerebro-spinal fluid- CSF)
4) **Latent Syphilis** is characterized by sero-reactivity without other evidence of primary, secondary, or tertiary disease (i.e., those lacking clinical manifestations).
   - **Early latent syphilis** – that is syphilis acquired within the preceding year. May present without any obvious clinical signs but serological findings may be elevated. Diagnosis of early latent syphilis is made if, during the year preceding the diagnosis, the patient had 1) a documented

seroconversion or a sustained (>2 week) fourfold or greater increase in nontreponemal test titers; 2) unequivocal symptoms of primary or secondary syphilis; or 3) a sex partner documented to have primary, secondary, or early latent syphilis.

- **Late latent syphilis** – is having syphilis for more than a year or syphilis of unknown duration.

5) **Neurosyphilis** occurs at any stage when *T. pallidum* infects the central nervous system. Syphilitic uveitis or other ocular manifestations (e.g., neuroretinitis and optic neuritis) can be associated with neurosyphilis. A CSF examination should be performed in all instances of ocular syphilis. Manifestations of neurosyphilis are catergorised as early or late neurological manifestations. Early neurologic manifestations (i.e., cranial nerve dysfunction, meningitis, stroke, acute altered mental status, and auditory or ophthalmic abnormalities) are usually present within the first few months or years of infection. Late neurologic manifestations (i.e., tabes dorsalis and general paresis) occur 10–30 years after infection. Infection can also be classified as acquired through sex or blood transfusions and congentital through mother to child transmission.

Diagnosis

Types of laboratory tests

1) Diagnosis of early syphilis- Dark field examination for *T. pallidum* in lesion exudate or tissue. The test is however less reliable in examining rectal and non-penile genital lesions and not suitable for examining oral lesions due to commensal treponemes.
2) Serological Tests - A presumptive diagnosis of syphilis is possible with the use of two types of serological tests:
   - Non-treponemal antibody testing that includes Venereal Disease Reference Laboratory (VDRL) and Rapid Plasma Reagin (RPR).
   - Treponemal tests that include Fluorescent treponemal antibody abosorbed (FTA-ABS) test,*T. pallidum* passive particle agglutination (TP-PA) assay, Treponema Pallidum Hemaglutination Assay(TPHA),Various Enzymes Immunoassays EIAs, Chemiluminescence immunoassays, Immunoblots and Rapid Treponemal Assays.

To correctly diagnose syphilis, more than one type of serological test must be used because each test has its own limitations. For example, false positive non-treponemal test results can also occurs with various medical conditions, this includes other infections (e.g. HIV), autoimmune conditions, immunizations, pregnancy, injection drug use and older age. Therefore, persons with a reactive non-treponemal test should always receive a treponemal test to confirm the diagnosis of syphilis.

Laboratory monitoring of patients is critical in understanding response to treatment. This is best done using a combination of treponemal- (TPHA) and non-treponemal tests (VDRL and RPR). Non-treponemal antibody titres usually correlate with disease activity and are used to help determine the stage of the infection, monitor treatment response, and assess reinfection. A fourfold titre decrease in non-treponemal test (e.g., from 1:16–1:4 or from 1:32–1:8) is indicative of a positive treatment response. The non-treponemal tests, VDRL and RPR are equally valid assays, but quantitative results from the two tests cannot be compared directly because RPR titres are often slightly higher than VDRL titres. Because of this, it is important to compare the same non-treponemal test when determining treatment response for a patient.

VDRL or RPR tests are often negative in late syphilis but this does not exclude the need for treatment. Other treponemal infections, such as yaws or pinta, may give positive serogical test results for syphilis although the RPR or VDRL result is usually of low titre (1:8). Because it is not possible to exclude latent syphilis in this situation, it is recommended that these patients be managed as though they have syphilis.

Treponemal tests, once reactive, usually remain reactive for life regardless of treatment, although some cases will sero-revert if the patient is treated during the primary stage.

Serofast refers to situation where patients, despite undergoing effective treatment for syphilis, continue to have a reactive non-treponemal test, usually with a VDRL or RPR titre of <1:4. They are then considered to be in a serofast state, can remain so for the rest of their lives and do not require any further treatment. Regardless of the stage of syphilis, in serofast patients, annual serological monitoring for a period of 5 years is required. High-risk patients should undergo periodic serological monitoring every 3–6 months to monitor possible reinfections.
In suspected neurosyphilis cases, CSF-VDRL test is the standard serologic test for diagnosis.

Treatment

Penicillin G administered parenterally is the preferred drug for treating persons in all stages of syphilis. Treatment of syphilis is detailed in table 57 below.

Table 57: Treatment of Syphilis

Stage of Syphilis	Recommended Treatment (Adults)	Alternative (penicillin allergy)	Treatment in Children	Retreatment
Primary and Secondary Syphilis	**Benzathine penicillin G** 2.4 million units IM in a single dose	Doxycycline 100mg bid 14 days **OR** Tetracycline 500mg qid 14 days **OR** Ceftriaxone 1-2g IM or IV for 10 to 14 days **OR** Azithromycin 2g single dose. (must not be used in MSM, HIV or pregnancy).	**Benzathine penicillin G** 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose	Treatment failure or reinfection- Persistence or reoccurrence of signs and symptoms, plus at least a fourfold increase in nontreponemal test titer persisting for >2 weeks **Benzathine penicillin G 2.4 million units IM for 3 weeks**
Early Latent Syphilis	**Benzathine penicillin G** 2.4 million units IM in a single dose	Doxycycline 100mg bid 28 days **OR** Tetracycline 500mg qid 28 days	**Benzathine penicillin G** 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose	A CSF examination should be performed if 1) a sustained (>2 weeks) fourfold increase or greater in titer is observed, 2) an initially high titer (≥1:32) fails to decline at least fourfold within 12–24 months of therapy, or 3) signs or symptoms attributable to syphilis develop **Benzathine penicillin G** 2.4 million units IM in a single dose
Late Latent Syphilis	**Benzathine penicillin G** 7.2 million units total, administered as 3 doses of 2.4 million		**Benzathine penicillin G** 50,000 units/kg IM, up to the adult	

	units IM each at 1-week intervals		dose of 2.4 million units, administered as 3 doses at 1-week intervals (total 150,000 units/kg up to the adult total dose of 7.2 million units)	
Tertiary Syphilis (gummas and cardiovascular syphilis) with normal CSF	**Benzathine penicillin G** 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals			
*Tertiary Syphilis- a CSF evaluation should be performed to rule out neurosyphilis prior to starting therapy.				
Neurosyphilis and Ocular Syphilis	**Aqueous crystalline penicillin G** 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 day **OR** **Procaine Penicillin G** 2.4 million units IM once dailyfor 10-14 days **PLUS** **Probenecid** 500mgs orally four times a day for 10-14 days	Ceftriaxone 2g daily either IM or IV for 10-14 days.		Consider retreatment if the cell count has not decreased after 6 months, or if the CSF cell count or protein is not normal after 2 years.
General Notes: Patients with more than 14 days interval between doses- consider repeating the full course. Alternative regimens recommended in cases of penicillin allergy of the non-pregnant adult should have close serological and clinical monitoring, especially for HIV positive persons There is no alternative regimen to penicillin is available for the treatment of neurosyphilis, congenital syphilis and syphilis in pregnant women. Pregnancy: Parenteral penicillin G is the only therapy with documented efficacy for syphilis during pregnancy. Pregnant women allergic to penicillin should be desensitised and treated Pregnant women missing any dose of treatment should repeat the full course of therapy. For women who have primary, secondary, or early latent syphilis, a second dose of benzathine penicillin 2.4 million units IM can be administered 1 week after the initial dose Treatment for HIV positive patients with syphilis is the same as HIV negative persons in all stages.				

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Syphilis

1. The **Jarisch-Herxheimer reaction** is an acute febrile reaction frequently accompanied by headache, myalgia, fever, and other symptoms that can occur within the first 24 hours after the initiation of any

therapy for syphilis. Patients should be informed about this possible adverse reaction. This Jarisch-Herxheimer reaction might induce early labor or cause distress in pregnant women.

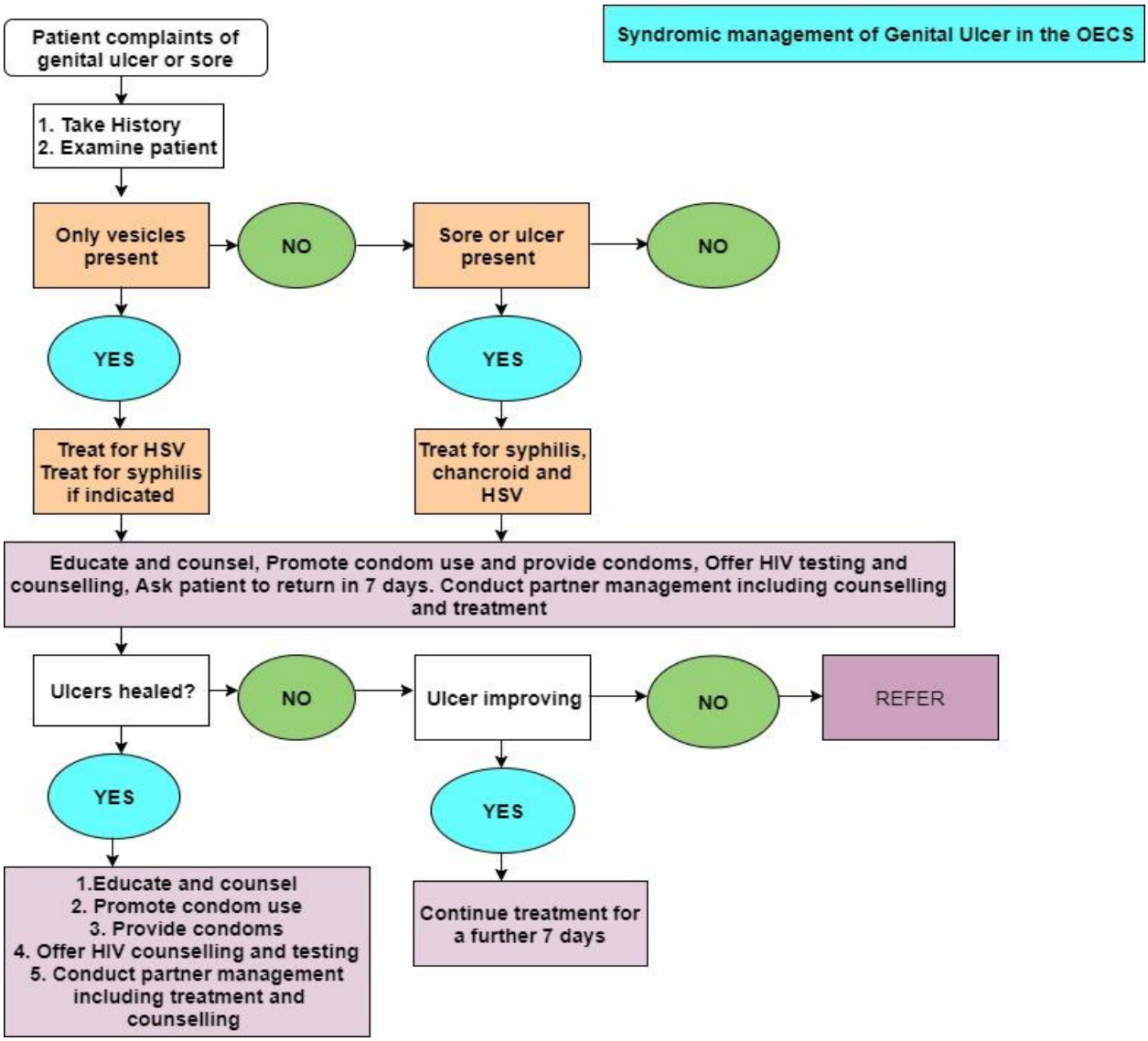
2. **Follow-up and monitoring** of treatment response should be conducted as follows:
   - **Patients with primary and secondary syphilis**
     - Follow up testing at 3 months, 6 months, and 1 year after treatment.
     - Treatment Failure or Reinfection- Persistence or reoccurrence of signs and symptoms, plus at least a fourfold increase in nontreponemal test titer persisting for >2 weeks is a likely indication of treatment failure or re-infection. Failure of nontreponemal test titers to decline fourfold within 6–12 months after therapy for primary or secondary syphilis may also be indicative of treatment failure. This can also be attributed to the person's stage of syphilis (earlier stages are more likely to decline fourfold and become negative) and initial nontreponemal antibody titers (lower titers are less likely to decline fourfold than higher titers). In these cases retreat and reevaluate for HIV infection.
   - **Patients with latent syphilis**
     - Follow up nontreponemal serologic tests should be repeated at 6, 12, and 24 months.
     - A CSF examination should be performed if 1) a sustained (>2 weeks) fourfold increase or greater in titer is observed, 2) an initially high titer (≥1:32) fails to decline at least fourfold within 12–24 months of therapy, or 3) signs or symptoms attributable to syphilis develop.
     - Patients with CSF abnormalities should be treated for neurosyphilis.
     - Patients with no negative CSF findings, retreat for latent syphilis.
   - **Patients with tertiary syphilis**:
     - Follow up test at 6 months and 1 year after treatment, then yearly for 5 years if they remain serofast above non-reactive post treatment.
   - **Patients with Neurosyphilis**
     - In cases where CSF pleocytosis was present initially, repeat CSF examination every 6 months until the cell count is normal.
     - Consider retreatment if the cell count has not decreased after 6 months, or if the CSF cell count or protein is not normal after 2 years.
3. **Infants and children** aged ≥1 month who receive a diagnosis of syphilis should be reviewed and evaluated to establish congenital or acquired syphilis. These children should also be evaluated of sexual abuse.
4. All persons with syphilis infection should be tested for **HIV infection**.
5. **Syphilis in HIV positive patients- the following should be considered;**
   - Diagnostic considerations is the same as for HIV negative persons.
   - Considered neurosyphilis in the differential diagnosis of neurologic signs and symptoms in persons with HIV infection.
   - Likelihood of an increased neurologic complications among HIV positive patients with early syphilis and higher rates of serologic treatment failure with recommended regimen.
   - Antiretroviral therapy as per current guidelines might improve clinical outcomes in persons with HIV infection and syphilis.

- ❖ CSF abnormalities (e.g., mononuclear pleocytosis and elevated protein levels) are common in persons with HIV infection. The clinical and prognostic significance is unknown.
- ❖ All patients with HIV infection and primary or secondary syphilis should be evaluated clinically and serologically for treatment failure at 3, 6, 9, 12, and 24 months after therapy.
- ❖ Consider CSF examination and retreatment for patients whose nontreponemal test titers do not decrease fourfold within 12–24 months of therapy.

6. **Syphilis in Pregnancy-** the following is noted
   - ❖ All pregnant women should receive serological screen for syphilis at the first antenatal visit using a non-treponemal antibody testing (VDRL or RPR) and repeated in the third trimester. In cases where a treponemal test (e.g., EIA or CIA) is used, all positive tests should be accompanied by a quantitative nontreponemal test (RPR or VDRL) as titers for these are important benchamarks for monitoring treatment response. Serologic titers should be repeated at 28–32 weeks' gestation and delivery.
   - ❖ There is no alternative to penicillin for pregnant women; all women should be desensitised and treated. Tetracycline and doxycycline are contraindicated in the second and third trimester of pregnancy and erythromycin and azithromycin do not reliably cure maternal infection or treat an infected fetus. Management in the second half of pregnancy, should include sonographic fetal evaluation for congenital syphilis. Sonographic signs of fetal or placental syphilis (i.e., hepatomegaly, ascites, hydrops, fetal anemia, or a thickened placenta) indicate a greater risk for fetal treatment failure.
   - ❖ Any woman with foetal death after 20 weeks of gestation should be tested for syphilis.
   - ❖ Possible marker for early infection and bacteremia is quantitative maternal nontreponemal titer, especially if >1:8 and poses a significant risk for antepartum fetal infection or congenital syphilis. Pregnant women with latent syphilis and serofast low antibody titers still present significant risk for fetal infection. Women with rising or persistently high antibody titers might indicate reinfection or treatment failure, and treatment should be considered.
   - ❖ There is an increased risk for premature labor and/or fetal distress if syphilis treatment precipitates the Jarisch-Herxheimer reaction among women treated in second half of pregnancy.
   - ❖ All pregnant women with syphilis should be counselled on adherence to treatment. Women who miss any dose of therapy must repeat the full course of therapy.
   - ❖ All pregnant women with Syphilis should be tested for HIV and vice versa.

7. **Treatment and Management of Sexual Partners** – Sex partners should be offered presumptive treatment for early syphilis if they have had sexual contact with the patient within **90 days** preceding the diagnosis. This should be done even if serologic test results are negative.

Figure 13: *Syndromic management of Genito Ulcer disease*



Source : World Health Organization. Guidelines for the management of sexually transmitted infections. Geneva: WHO; 2003. Available from: http://www.who.int/hiv/pub/sti/en/STIGuidelines2003.pdf.

9.9.1 Congenital Syphilis

See section 5 on elimination of mother to child transmission.

9.9.2 Management of persons with Penicillin Allergy

Penicillin is the drug of choice in treating syphilis. In some cases, alternative non penicillin antibiotic regimen is recommended for patients with allergy to penicillin. *For neurosyohilis, congenital syphilis and syphilis in pregnant women, there is no alternative recommendation and therefore penicillin remains the drug of choice.* Penicillin allergy in these populations will require induction of drug tolerance also known as desenitisation.

Penicillin allergy triggers an immunoglobulin E (IgE)-mediated allergic response and manifests as urticaria, angioedema, or anaphylaxis (i.e., upper airway obstruction, bronchospasm, or hypotension). Re-administration of penicillin to patients with a history of IgE-mediated hypersensitivity reactions can

be life threatening. Skin testing can identify person with penicillin allergy. Testing must be performed in a monitored setting in which treatment for an anaphylactic reaction is available. The following categories should undergo a skin test:

1. Persons with a history of penicillin-related anaphylaxis or other IgE-mediated reactions, asthma, or other diseases that would make anaphylaxis more dangerous and
2. Persons being treated with beta-adrenergic blocking agents should be tested with 100-fold dilutions of the full-strength skin-test reagents before being tested with full-strength reagents.

The test is usually performed using prepared antigens such as Pre-Pen (Major Determinant) and Penicillin G (Minor Determinant). An epicutaneous (prick) tests on the volar surface of the forearm is done. The test is positive if the average wheal diameter after 15 minutes is ≥4 mm larger than that of negative controls; otherwise, the test is negative. Histamine controls should be positive to ensure that results are not falsely negative because of the effect of antihistaminic drugs.
If epicutaneous tests are negative, then perform **intradermal injections** using negative control and antigen solutions on volar surface of the forearm. An intradermal test is positive if the average wheal diameter 15 minutes after injection is >2 mm larger than the initial wheal size and also is >2 mm larger than the histamine controls. Otherwise, the tests are negative. If the duplicates are discordant, a second set of duplicate tests can be used to resolve the ambiguity.

Desensitisation

Persons with a positive skin test can be desensitised. Desenitisation can be oral or intravenous. Oral desensitisation is usually the preferred option; it is safer and easier to perform. The procedure usually takes 4–12 hours, and should be performed in hospital setting with capacities to manage anaphylactic shock. After desensitization, penicillin can be administered. The desensitisation schedule is detailed in table 58 below.

Table 58: Desensitisation schedule

Penicillin V suspension dose[b]	Amount[c] (units/mL)	mL	Units	Cumulative dose (units)
1	1,000	0.1	100	100
2	1,000	0.2	200	300
3	1,000	0.4	400	700
4	1,000	0.8	800	1,500
5	1,000	1.6	1,600	3,100
6	1,000	3.2	3,200	6,300
7	1,000	6.4	6,400	12,700
8	10,000	1.2	12,000	24,700
9	10,000	2.4	24,000	48,700
10	10,000	4.8	48,000	96,700
11	80,000	1.0	80,000	176,000
12	80,000	2.0	160,000	336,000
13	80,000	4.0	320,000	656,700
14	80,000	8.0	640,000	1,296,700

Note: Observation period was 30 minutes before parental administration of penicillin. [a] *Wendele GD (1985); see works cited. Reprinted with permission from the New England Journal of Medicine.*

[b] *Interval between doses = 15–30 minutes; elapsed time = 4–8 hours; cumulative dose = 1.3 million units.* [c] *The specific amount of drug was diluted in approximately 30 ml of water and then administered orally.*

9.10 Diseases characterized by urethritis and cervicitis

9.10.1 Urethritis

Urethritis or urethral inflammation can be caused by infectious or noninfectious conditions. Urethral discharge can be mucoid, mucopurulent, or purulent. Other symptoms include dysuria and urethral pruritis. The most frequent causes of infectious urethritis are *N. gonorrhoeae* and *C. trachomatis,* and to a lesser extent *Mycoplasma genitalium,* HSV, Epstein Barr Virus, adenovirus and *T.vaginalis.* Infectious urethritis can be broadly classified as Gonococcal urethritis and Non- Gonococcal.

Diagnosis

Urethritis can be diagnosed as follows:

1. For gonococcal urethritis- Gram or Methylene Blue (MG)/Gentian Violet (GV) stain of urethral secretions demonstrating ≥2 WBC per oil immersion field. Gonococcal infection is detected by the presence of WBC containing Gram Negative Intracellular Diplococci (GNID) in Gram stain or intracellular purple diplococci in MB/GV smears.
2. Positive leukocyte esterase test on first-void urine or microscopic examination of sediment from a spun first- void urine demonstrating ≥10 WBC per high power field.
3. NAAT testing for *C. trachomatis* and *N. gonorrhoeae* is recommended when Gram or MB/GV is unavailable or if used and there is no intracellular gram negative or purple diplococcic.
4. For Non gonococcal urethritis (NGU) is suspected if Gram or MB/GV stain is negative for *N. gonorrhoea*. NAATs can be used to confirm the pathogen.

Treatment

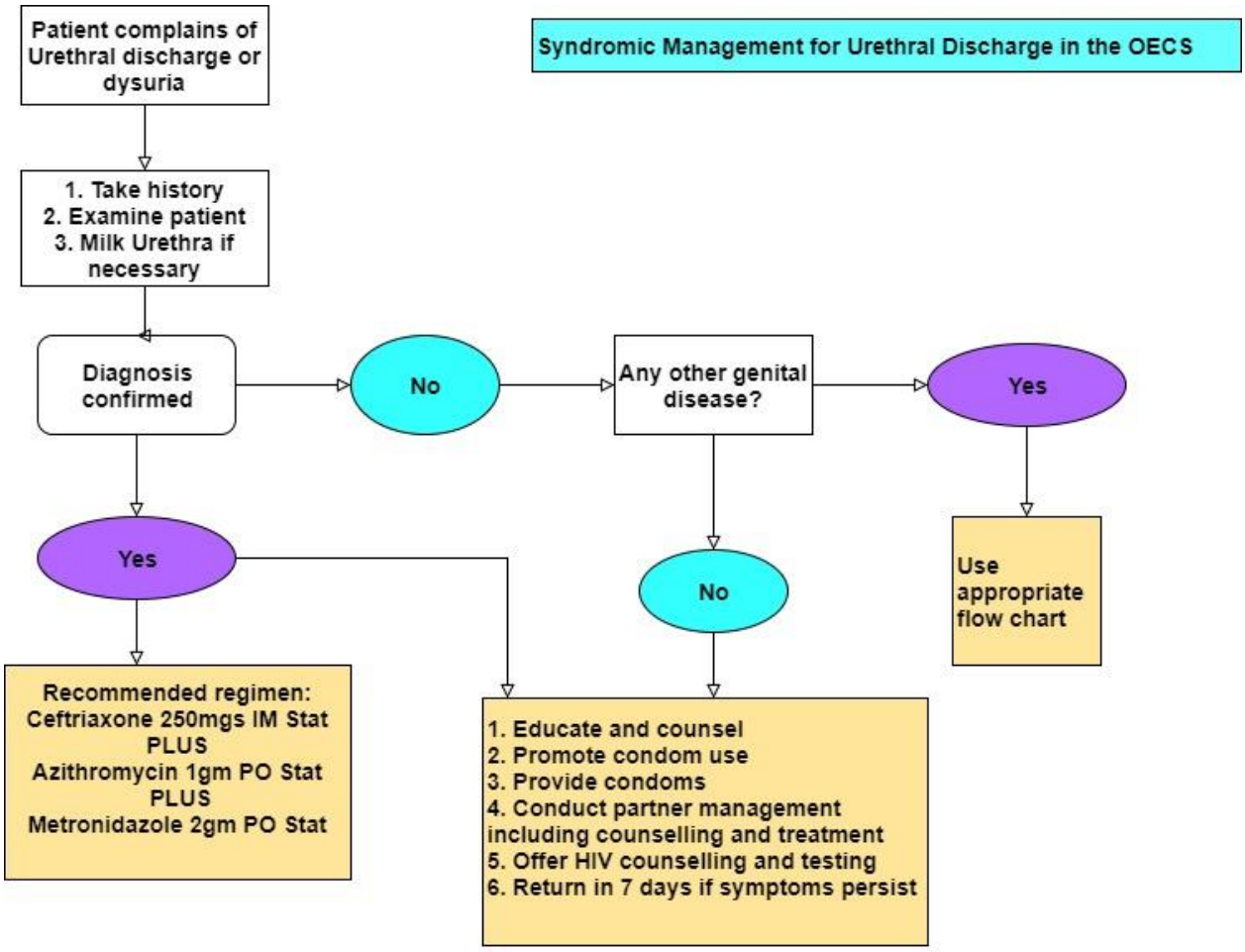
Table 59 and figure 14 delineate a management plan for urethritis.

Table 59 Management plan for urethritis

<table>
<tr><th colspan="2">Treatment steps</th></tr>
<tr><td colspan="2">• Perform urethral swab for Gram stain culture and sensitivity
• Offer prevention counselling—condoms, condom demonstration
• Conduct serology for HIV, HTLV-1 or -2 , VDRL, HAV, HBV, HCV
• Use recommended treatment regime
• Consider partner-expedited therapy for consorts who are not likely to come in for treatment and have no treatment contra-indications
• Recommend no sexual activity until treatment is completed and until partner has been treated</td></tr>
<tr><th colspan="2">Treatment for Gonococcal Urethritis</th></tr>
<tr><th>Recommended regimen</th><th>Alternative regimen</th></tr>
<tr><td>Ceftriaxone: 250 mg IM stat; PLUS
Azithromycin: 1g PO stat; PLUS
Metronidazole: 2g PO stat</td><td>If ceftriaxone is not available:
Cefixime 400 mg orally in a single dose PLUS
Azithromycin 1 g orally in a single dose</td></tr>
<tr><th colspan="2">Treatment for Non Gonococcal Urethritis</th></tr>
<tr><th>Recommended regimen</th><th>Alternative regimen</th></tr>
<tr><td>Azithromycin 1 g orally in a single dose
OR
Doxycycline 100 mg orally twice a day for 7 days</td><td>Erythromycin base 500 mg orally four times a day for 7 days OR
Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days OR
Levofloxacin 500 mg orally once daily for 7 days OR
Ofloxacin 300 mg orally twice a day for 7 days.</td></tr>
<tr><th colspan="2">Treatment of persistent /recurrent NGU</th></tr>
<tr><td colspan="2">M. genitalium, especially following doxycycline therapy- in these cases, the following is recommended
• Men with poor compliance, retreat with original regimen
• For men initially treated with doxycycline- Azithromycin 1 g orally in a single dose should be administered
• For men who fail azithromycin- moxifloxacin 400 mg orally once daily for 7 days</td></tr>
<tr><td colspan="2">T. vaginalis may also cause persistent NGU. In these cases the following is recommended.
Metronidazole 2 g orally in a single dose OR
Tinidazole 2 g orally in a single dose.</td></tr>
<tr><td colspan="2">[a]Partner-expedited therapy: Providing appropriate therapy for the index case's contact(s); this is done especially when the partner cannot be relied upon to come in for examination and treatment.</td></tr>
</table>

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Figure 14: *Algorithm for the clinical management of urethral discharge*



Source : World Health Organization. Guidelines for the management of sexually transmitted infections. Geneva: WHO; 2003. Available from: http://www.who.int/hiv/pub/sti/en/STIGuidelines2003.pdf.

Other management considerations for Urethral Discharge

Counsel to abstain from sexual intercourse until patient and partner(s) have been adequately treated (i.e., for 7 days after single-dose therapy or until completion of a 7-day regimen and symptoms resolved). Advise patients to return for reevaluation should symptoms persist and repeat testing after 3 months. Evaluate, test and presumptively treat persons who have had sexual contact with the patient during the 60 days preceding the onset of symptoms. If the last sexual intercourse was >60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated. Test for other STIs including HIV and syphilis.

9.10.2 Cervical infections- Cervicitis

Vaginal discharge also occurs as a result of cervical infection (cervicitis) primarily caused by Neisseria gonorrhoeae and Chlamydia trachomatis. For symptomatic women two major diagnostic signs include 1) a purulent or mucopurulent endocervical exudate visible in the endocervical canal or on an endocervical swab specimen (commonly referred to as mucopurulent cervicitis) and 2) sustained endocervical bleeding easily induced by gentle passage of a cotton swab through the cervical os. There may also be intermenstrual bleeding for e.g. after sexual intercourse. A large proportion of

women with cervical infection are generally asymptomatic, but there is an increased risk for PID and other complications.
Table 60 below presents a summary of risk factors, symptoms and diagnosis of the various pathogens associated with cervical infections

Table 60: Etiology, risk factors, symptoms and laboratory diagnosis of cervicitis

Etiology	Risk factors	Symptoms	Laboratory Diagnosis
Cervicitis			
Nisseria Gonnohrea- bacterial infection	Younger age New sex partner Sex partner with concurrent partners Multiple sex partners Unprotected sex Diagnosis of previous STs	In many cases the N. Gonorrohrea and C. tachomatis are asymptomatic. Increased vaginal discharge Painful urination Vaginal bleeding between periods, such as after vaginal intercourse Painful intercourse Abdominal or pelvic pain	N. Gonnorhoea- Vaginal and cervical swab- NAAT is the most sensitive and therefore recommended for detecting N. Gonnorhoea. >10 WBC per high power field in vaginal fluid is indicative of endocervical inflammation caused by N. gonnorhoea. Gram Stain- polymorphonuclear leukocytes with intracellular Gramnegative diplococci is diagnostic for infection. Gram stain has high specificity (>99%) and therefore a positive test confirms disgnosis. With a lower sensitivity (>95%), a negative Gram stain should not be considered sufficient for ruling out infection in asymptomatic persons.
Chlamydia Trachomatis- bacterial infection			C. Trachomatis- Testing of first-catch urine or collecting swab specimens from the endocervix or vagina NAATs are the most sensitive tests for these specimens and therefore are recommended for detecting C. trachomatis infection >10 WBC per high power field in vaginal fluid is indicative of endocervical inflammation caused by C. trachomatis

Treatment of Cervicitis

Treatment of Cervicitis is summarized in table 61.

Table 61: Treatment of Cervicitis

	Recommended Regimens	Alternative Regimens	Treatment in pregnancy
Nisseria Gonorrhoea	**Dual therapy** Ceftriaxone 250 mgs IM – single dose **PLUS** Azithromycin 1 gm orally as a single dose		
	The dual combination therapy improves treatment efficacy and potentially slows the emergence and spread of resistance to cephalosporins. *Recommended that both therapy should be administered together, preferably at the clinics under direct observation by a health care worker*		
C. Trachomatis	Azithromycin 1 gm orally as a single dose **OR** Doxycycline 100mgs orally twice daily for 7 days	Erythromycin base 500 mg orally four times a day for 7 days **OR** Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days **OR** Levofloxacin 500 mg orally once daily for 7 days **OR** Ofloxacin 300 mg orally twice a day for 7 days	**Recommended Regimen** Azithromycin 1 gm orally as a single dose **Alternative Regimens** Amoxicillin 500 mg orally three times a day for 7 days **OR** Erythromycin base 500 mg orally four times a day for 7 days **OR** Erythromycin base 250 mg orally four times a day for 14 days **OR** Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days **OR** Erythromycin ethylsuccinate 400 mg orally four times a day for 14 days ***Doxycycline is contraindicated in the second and third trimesters of pregnancy***

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Cervicitis

Where possible, treatment should be provided on site and directly observed. Patients should be counselled on abstaining from sexual activity for 7 days after treatment and until all sex partners are adequately treated. All sex partners in the last 60 days preceding onset of symptoms or gonorrhea diagnosis) should be referred for evaluation, testing, and presumptive dual treatment. In cases where

the last sexual intercourse was >60 days, the most recent partner should be managed. Patients should be tested for Syphilis, and HIV. Patients with HIV positive should be treated in the same was as those who are not HIV positive. Patients should be retested after three months

9.10.3 Chlamydial Infections among Neonates

C. trachomatis infection of neonates results from perinatal exposure to the mother's infected cervix. C. trachomatis infection is most frequently manifested by conjunctivitis that develops 5–12 days after birth. Less frequently, it can involve the mucous membranes of the eye, oropharynx, urogenital tract, and rectum. C. trachomatis infection can also cause a subacute, afebrile pneumonia with onset at ages 1–3 months and has been the most frequent identifiable cause ophthalmia neonatorium and pneumonia.

9.10.3.1Ophthalmia Neonatorum Caused by C. trachomatis

Ophthalmia neonatorun should be considered for all infants aged ≤30 days that have conjunctivitis, especially if the mother has a history of chlamydia infection. Specimen from the everted eyeball is for tissue culture and non-culture testing such as direct fluorescence antibody (DFA) and NAAT for diagnosis.

9.10.3.2 Infant Pneumonia caused by C. trachomatis

Chlamydia pneumonia typically occurs at 1–3 months of age and is a subacute pneumonia. Characteristic signs include 1) a repetitive staccato cough with tachypnea and 2) hyperinflation and bilateral diffuse infiltrates on a chest radiograph. Peripheral eosinophilia (≥400 cells/mm3) is frequently present. All infants aged 1-3 months suspected of having pneumonia should be tested for C. trachomatis. This is particularly important for mothers with a history of chlamydial infection. Testing can be done using tissue culture test and non-culture tests (e.g., DFA and NAAT) utilizing nasopharyngeal specimens

9.10.3.3 Chlamydial Infections among Infants and Children

Although perinatally transmitted, C. trachomatis infection of the nasopharynx, urogenital tract, and rectum might persist for 2–3 years. Sexual abuse must be considered.

NAAT is recommended for establishing diagnosis and can be used for vaginal and urine specimens from girls. There is insufficient to recommend the use of NAAT in boys. Culture is still the preferred method for detection of urogenital C. trachomatis in boys and at extragenital sites in boys and girls. Treatment is outlined in table 62 below.

Table 62: Treatment of Chlamydial Infections among Infants and Children

	Recommended Regimen	Alternative Regimen
Opthalmia Neonatorum **Infant pneumonia cause by C. Trachomatis**	Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days	Azithromycin suspension, 20 mg/kg/day orally, 1 dose daily for 3 days
	Efficacy of erythromycin treatment is about 80%, re-evaltion with a second course of therapy in both cases is recommended. An association between oral erythromycin and azithromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for signs and symptoms of IHPS. Topical antibiotic therapy alone is inadequate and is unnecessary when systemic treatment is administered	
Chlamydial Infections Among Infants and Children Who Weigh <45 kg	Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days	Limited data on the use of azithromycin as an alternative regimen
Chlamydial Infections Among Infants and Children Who Weigh ≥45 kg but Who Are Aged <8 Years	Azithromycin 1 g orally in a single dose	
Recommended Regimens for Children Aged ≥8 years	Azithromycin 1 g orally in a single dose **OR** Doxycycline 100 mg orally twice a day for 7 days	

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Chlamydial infections in infants and children

Prenatal screening and treatment of pregnant women is the best method for preventing chlamydial infection among neonates. Patients should be reevaluate patient to determine the effectiveness of treatment/cure. A second course of therapy may be required. Evaluate and management mothers and their sex partners with presumptive treatment of chlamydia.

Although the efficacy of neonatal ocular prophylaxis with erythromycin ophthalmic ointments to prevent chlamydia ophthalmia is not clear, ocular prophylaxis with these agents prevents **gonococcal ophthalmia** and therefore should be administered

9.10.4 Other Gonococcal infections

9.10.4.1 Other Gonococcal Infections in adults and adolescents

Gonococcal infection is a common cause of urethral infections in men and pelvic inflammatory disease in women. These are discussed in the relevant sections. Gonococcal infections in adults and adolescents can manifest in other areas and include:

- Infections of the cervix, urethra and rectum
- Infection of the pharynx
- Gonococcal conjunctivitis
- Disseminated gonococcal infection- manifests as disseminated diseases with petechial or pustular acral skin lesions, asymmetric polyarthralgia, tenosynovitis, or oligoarticular septic arthritis. The infection is complicated occasionally by perihepatitis and rarely by endocarditis or meningitis.

Diagnosis

Specific microbiological diagnosis include culture and NAAT. Culture is generally performed on endo-cervical and urethral swabs, is available for detection of rectal, oropharyngeal, and conjunctival gonococcal infection. NAAT is used for endo-cervical swabs, vaginal swabs, urethral swabs (men), and urine (from both men and women). Gram stain has high specificity (>99%) and sensitivity (>95%). A Gram stain of urethral secretions that demonstrates polymorphonuclear leukocytes with intracellular Gram negative diplococci can be considered diagnostic for infection with N. gonorrhoeae in symptomatic men.

Because of lower sensitivity, a negative Gram stain should not be considered sufficient for ruling out infection in asymptomatic men.

9.10.4.1.1 Antimicrobial-Resistant N. gonorrhoeae

Gonorrhea treatment is complicated by the ability of N. gonorrhoeae to develop resistance to antimicrobials. Over the recent past, the epidemiology of antimicrobial resistance has guided decisions such as the discontinuation of fluroquinolones and retention of cephalosporins for treatment. With concern for the emerging gonococcal resistance, CDC's 2010 STD treatment guidelines recommended dual therapy for gonorrhea with a cephalosporin plus either azithromycin or doxycycline. Aligned to this, dual therapy is the recommended approach for the OECS as outlined below.

9.10.4.1.2 Dual Therapy for Gonococcal Infections

Dual therapy improves treatment efficacy and slows the emergence and spread of resistance to cephalosporins. Azithromycin as the second antimicrobial is preferred to doxycycline because of convenience and compliance advantages of single-dose therapy. Additionally, there is higher prevalence of gonococcal resistance to tetracycline than to azithromycin. Also, there is greater efficacy of azithromycin 1 g for the treatment of uncomplicated urogenital GC and pharyngeal infection. Further, dual therapy which includes azithromycin is effective in cases of coinfection with N. gonnorhoea and C. trachomatis.

Treatment

Dual therapy for other gonococcal infections is described in table 63.

Table 63: Summary of treatment recommendation for other gonococcal infections

	Recommended regimen	**Alternative regimen**
1.Uncomplicated Gonococcal infection of the cervix, urethra and rectum 2. Uncomplicated gonococcal infections of the pharynx 3. Gonococcal Conjunctivitis**	Ceftriaxone 250 mg IM in a single dose **PLUS** Azithromycin 1g orally in a single dose	Cefixime 400 mg orally in a single dose **PLUS** Azithromycin 1 g orally in a single dose *Use cefixime when ceftriaxone is unavailable ** *Gonococcal conjunctivitis consider one time lavage of the infected eye with saline*
Disseminated gonococcal infection (DGI) – Arthritis and Arthritis-dermatitis syndrome	Ceftriaxone 1 g IM or IV every 24 hours **PLUS** Azithromycin 1 g orally in a single dose	Cefotaxime 1 g IV every 8 hours or Ceftizoxime 1 g IV every 8 hours **PLUS** Azithromycin 1 g orally in a single dose
For arthritis-dermatitis syndrome, the provider can switch to an oral agent guided by antimicrobial susceptibility testing 24–48 hours after substantial clinical improvement, for a total treatment course of at least 7 days		
Disseminated gonococcal infection (DGI) – Gonococcal Meningitis and Endocarditis	Ceftriaxone 1–2 g IV every 12–24 hours PLUS Azithromycin 1 g orally in a single dose	
Therapy for meningitis should be continued with recommended parenteral therapy for 10–14 days. Parenteral antimicrobial therapy for endocarditis should be administered for at least 4 weeks.		
Patients with allergy to cephalosporins	Potential therapeutic options Gemifloxacin 320 mg PO single dose PLUS azithromycin 2 g PO single dose OR Gentamicin 240 mg IM single dose PLUS azithromycin 2 g PO single dose	
EPT	Cefixime 400 mg orally in a single dose PLUS Azithromycin 1 g orally in a single dose	
For appropriate cases, administer the same day, preferably under direct observation. Patients with HIV infection should receive the same treatment.		

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for gonococcal infections in adults and adolescents

Counsel on abstaining from sexual activity for 7 days after treatment and until all sex partners are adequately treated (7 days after receiving treatment and resolution of symptoms, if present). Administer medications on site, same day and preferably under direct observation.

Recent sex partners (i.e., persons having sexual contact with the infected patient within the 60 days preceding onset of symptoms or gonorrhea diagnosis) should be referred for evaluation, testing, and presumptive dual treatment. If the patient's last potential sexual exposure was >60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated.
EPT can be delivered to the partner by the patient. Test for other STDs, including chlamydia, syphilis, and HIV.

9.10.4.2 Gonococcal infections among Neonates

Gonococcal infection among neonates results from perinatal exposure to the mother's infected cervix. It is usually an acute illness that manifests 2–5 days after birth. Severe manifestations which can include sepsis, arthritis and meningitis and less severe include rhinitis, vaginitis, urethritis, and infection at sites of fetal monitoring. Prenatal screening and treatment of pregnant women is the best method for preventing GC infection among neonates. Gonococcal infection in the neonates is manifested in several ways.
Gonococcal opthalmia neonatorum is prevented through the administration of Erythromycin (prophylactic agent) instilled into both eyes of all newborn infants.
Risk factors for gonococcal opthalmia in infants include those who did not receive ophthalmia prophylaxis and whose mothers had no prenatal care or have a history of STDs or substance abuse. Diagnosis is made with culture, however presumptive treatment can be made when intracellular gram-negative diplococci are identified on Gram stain of conjunctival exudate.
Disseminated Gonococcal Infection (DGI) is a rare complication of neonatal gonococcal infection and may present as sepsis, arthritis, Gonococcal scalp abscesses in neonates can result from fetal monitoring through scalp electrodes. Treatment of gonoccal infections in neonates is outlined in table 64.

Table 64: Treatment of gonococcal infections in neonates

	Recommended regimen
Ophthalmia Neonatorun Prophylaxis	Erythromycin (0.5%) ophthalmic ointment in each eye in a single application at birth *Instill in both eyes as soon as possible after delivery.
Gonococcal Ophthalmia	Ceftriaxone 25–50 mg/kg IV or IM in a single dose, not to exceed 125 mg
DGI and Gonococcal Scalp Abscesses in Neonates	Ceftriaxone 25–50 mg/kg/day IV or IM in a single daily dose for 7 days, with a duration of 10–14 days if meningitis is documented
Neonates born to mothers who have gonococcal infections	Ceftriaxone 25–50 mg/kg IV or IM in a single dose, not to exceed 125 mg
Test neonate simultaneously for Chlamydia-use specimen from inverted eyelid and evaluate neonate for disseminated infection. No data is exist on the benefits of dual theraphy for the treatment of GC infection in neonates	

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

9.10.4.3 Gonococcal Infections Among Infants and Children

Sexual abuse is the most frequent cause of gonococcal infection in infants and children. For preadolescent girls, vaginitis is the most common manifestation of this infection; gonococcal associated PID after vaginal infection can be less common in preadolescents than adults. Among sexually abused children, anorectal and pharyngeal infections with N. gonorrhoeae are frequently asymptomatic. Culture is the preferred method of diagnosis. Treatment is outlined in table 65.

Table 65: Treatment of other gonococcal infections among infants and children

Scenarios	Recommended Regimen
Infants and Children Who Weigh ≤45 kg and Who Have Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis	Ceftriaxone 25–50 mg/kg IV or IM in a single dose, not to exceed 125 mg IM
Children Who Weigh >45 kg and Who Have Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis	Ceftriaxone 250 mg IM in a single dose PLUS Azithromycin 1g orally in a single dose
Children Who Weigh ≤45 kg and Who Have Bacteremia or Arthritis	Ceftriaxone 50 mg/kg (maximum dose: 1 g) IM or IV in a single dose daily for 7 days
Children Who Weigh >45 kg and Who Have Bacteremia or Arthritis	Ceftriaxone 1 g IM or IV in a single dose daily every 24 hours for 7 days
No data is exist on the benefits of dual therapy for the treatment of GC infection in infants and children	

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

9.11 Diseases characterized by Vaginal Discharge

Vaginal Discharge Syndrome is caused primarily as result of infection to the vagina (vaginitis) and cervix (cervicitis). Cervicitis is detailed above under the section on urethral discharge. Vaginal infections (vaginitis) is discussed in this section and a syndrome approach to management is recommended in-order to adequately address causative agents of vaginitis and cervicitis

9.11.1 Vaginal Infections (Vaginitis)

Abnormal vaginal discharges are one of the most common presenting symptoms in women. The vaginal discharge is usually present with a change in the amount, colour, or smell, as well as presence of irritation, itching, or burning. Vaginal cleansing practices, such as vaginal douches can also change the vaginal pH balance, thereby increasing the risks of: vaginal discharges, worsening cervicitis, and creating higher levels of infection.

An accurate diagnosis will entail obtaining an accurate medical history, examination, and laboratory testing to determine the etiology of vaginal symptoms.
The three diseases most frequently associated with vaginal infection are:

1. Bacterial Vaginosis BV (40-45%) - replacement of the vaginal flora by an overgrowth of anaerobic bacteria including Prevotella sp., Mobiluncus sp., G. vaginalis, Ureaplasma, Mycoplasma, and numerous fastidious or uncultivated anaerobes.
2. Trichomoniasis (15-20%) T. vaginalis.
3. Vulvovaginal Candidiasis (20-25%) - *C. albicans, C. tropicalis, and C. glabrata* - this is often not an STI, but is included in this section because it is frequently diagnosed in women who have vaginal symptoms associated with STIs.

While table 66 presents a brief comparison of the three vaginal dischages, each of the causes of vaginal discharge will be addressed separately in the sections below utilizing an eitiological approach.

Table 66: Symptoms and Diagnosis of Vaginal Discharges

Condition	Symptoms	Discharge	Vulvar/ vaginal inflammation	PH	Amine	Microscopy
Normal exam	None	Variable clear or white	None	≥ 4.5	None	Lactobacilli
Vulvo-vaginal candidiasis	Vulvar irritation	White clumpy 'cottage cheese'	Vaginal epithelium, introitus, vulva	≤ 4.5	None	White blood cells (WBC), fungal elements (branched hyphae and pseudo hyphae)
Trichomonal vaginitis	Profuse discharge	Profuse frothy, green, or yellow diffuse, malodorous, or yellow-green with or without vulvar irritation	Vaginal and vulvar	>4.5 (often >5.0)	Maybe	WBC, trichomonads
Bacterial vaginosis	Malodour	Moderate, thin, homogenous grey	None	>4.5	Yes	Clue cells, few lactobacilli

9.11.1.1 Bacterial vaginosis

Bacterial vaginosis is the most prevalent cause of vaginal discharges or malodor in women. It results from a relative loss of lactobacillus in the vagina and an overgrowth of other bacteria. The typical presentation is in the form of a thin, homogenous, malodourous discharge, which can be greyish white or yellowish in colour. The discharge is often uncomfortable due to its amount and odour. Related vaginal pain or vulvar irritation is uncommon. Tables 67 and 68 outlines the risk factors, symptoms and diagnosis and treatment of BV.

Table 67: Risk factors, symptoms and diagnosis of BV

Etiology	Risk factors	Symptoms	Increased risk for	Diagnosis	
				Clinical Criteria	Laboratory Diagnosis
Bacterial Vaginosis (BV) - most prevalent cause of vaginal discharge					
BV is a polymicrobial clinical syndrome resulting from replacement of the normal hydrogen peroxide producing Lactobacillus sp. in the vagina with high concentrations of anaerobic bacteria (e.g., Prevotella sp. and Mobiluncus sp.), G. vaginalis, Ureaplasma, Mycoplasma, and numerous fastidious or uncultivated anaerobes.	1. Multiple male or female partners, 2. New sex partner, 3. Douching, 4. Lack of condom use, 5. Lack of vaginal lactobacilli	Thin, homogenous discharge which can be greyish white or yellowish in colour.	Other STDS (HIV, N. gonorrhoeae, C. trachomatis, and HSV-2) Increases the risk for HIV transmission to male sex partners.	Three of the following symptoms: Homogeneous, thin, white discharge that smoothly coats the vaginal walls; Clue cells (e.g., vaginal epithelial cells studded with adherent coccoobacilli) on microscopic examination; A pH of vaginal fluid >4.5; A fishy odor of vaginal discharge before or after addition of 10% KOH (i.e., the whiff test).	Gold Standard- Gram Stain (concentration of lactobacilli (i.e., long Gram-positive rods), Gram Negative and Gram-variable rods and cocci (i.e., G. vaginalis, Prevotella, Porphyromonas, and peptostreptococci), and curved Gramnegative rods (i.e., Mobiluncus) characteristic of BV

Treatment of Bacterial Vaginosis (BV)

Table 68: Treatment of BV

Recommended regimen	Alternative regimens	Treatment for recurrent/persistent infection	Treatment of pregnant women
Metronidazole: 500 mg orally twice a day for 7 days; OR Metronidazole gel: 0.75% 1 full applicator (5 g) intravaginally once a day for 5 days; OR Clindamycin cream: 2% 1 full applicator (5 g) intravaginally at bedtime for 7 days * *Treatment remains the same for HIV positive persons*	Tinidazole: 2 g orally once daily for 2 days; OR Tinidazole: 1 g orally once daily for 5 days; OR Clindamycin: 300 mg orally twice a day for 7 days; OR Clindamycin ovules: 100 mg intravaginally once at bed time for 3 days	-For the first recurrence, repeat treatment. -With multiple reccurrences treat with: 0.75% metronidazole gel twice weekly for 4–6 months oral nitroimidazole (metronidazole or tinidazole 500 mg twice daily for 7 days) followed by intravaginal boric acid 600 mg daily for 21 days and then suppressive 0.75% metronidazole gel twice weekly for 4–6 months as suppressive therapy Monthly oral metronidazole 2 g administered with fluconazole 150 mg as suppressive therapy	Metronidazole: 500 mg orally twice a day for 7 days; **OR** Metronidazole: 250 mg orally 3 times a day for 7 days; **OR** Clindamycin: 300 mg orally twice a day for 7 days
Notes: Consuming alcohol should be avoided during treatment and for 24 hours thereafter. **Metronidazole and clindamycin should be avoided during the first trimester.** **Clindamycin cream is oil-based and might weaken latex condoms and diaphragms for 5 days after use (refer to clindamycin product labeling for additional information).**		Notes: For recurring cases consider that antimicrobial resistance might be predictive of risk for treatment failure leading to persistent and recurrent BV.	Notes: Treatment for bacterial vaginosis should be avoided during the first trimester of pregnancy unless the benefits outweigh the risks for adverse events Pregnant women should have a follow-up visit 1 month after completing treatment.

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.

Other Management Considerations for Bacterial Vaginosis

Patients should be counselled to return for evaluation if symptoms reoccur. For recurring cases consider that antimicrobial resistance might be predictive of risk for treatment failure leading to persistent and recurrent BV. BV appears to recur with higher frequency in women who have HIV infection. All women with BV should be tested for HIV and other STIs.

9.11.1.2 Trichomoniasis

Trichomoniasis is caused by the protozoan parasite Trichomonas Vaginalis (T. Vaginalis) and is the most prevalent non-viral sexually transmitted infection.

Table 69: Risk factors, Symptoms and Diagnosis of Trichomoniasis

Etiology	Risk factors	Symptoms	Increased risk for	Laboratory Diagnosis
Trichomoniasis - most prevalent non-viral sexually transmitted infection.				
Trichmonas Vaginalis- Protozoan parasite	1.Multiple partners 2. Lack of condom use 3. History of other STIs 4. Previous episodes of Trichomoniasis.	Vaginal discharge that is diffuse, malodorous, or yellow-green with or without vulvar irritation. **Asymptomatic-** 70%–85% of persons have minimal or no symptoms. Asymptomatic infections might last for months to years and is readily passed between sex partners.	Two-three fold increased risk for HIV Premature rupture of membranes, low birth weight infant, pre term birth and other adverse pregnancy outcomes PID for HIV positive women.	1. Most common method of diagnosis- Wet Mount Microscopy (poor sensitivity 51-66%) 2. Culture-sensitivity of 75%–96% and a specificity of up to 100%. Specimen -vaginal secretions (Women) and urethral swab (Men) 3. NAAT Test - Nucleic Acid Aplification Test (highly sensitive) - Gold Standard 4. APTIMA T. vaginalis assay (Hologic Gen-Probe (high sensitivity and high specificity) ***Wet mount prep should be evaluated as early as possible - sensitivity decreases by 20% after 1 hour***

Table 70: Treatment of Trichomoniasis

Recommended Regimens	**Alternative Regimen**	**Treatment for recurrent /persistent infection**	**Treatment of pregnant women**
Metronidazole 2 g orally in a single dose OR Tinidazole 2 g orally in a single dose	Metronidazole 500 mg orally twice daily for 7 days.	Treatment failure (reinfection excluded), treat patient and partner with metronidazole or tinidazole at 2 g orally for 7 days.	Metronidazole 2 gms orally
Notes: Alcohol consumption should be avoided during treatment with nitroimidazoles. To reduce the possibility of a disulfiram- like reaction, abstinence from alcohol use should continue for 24 hours after completion of metronidazole or 72 hours after completion of tinidazole. Tinidazole is generally more expensive, reaches higher levels in serum and the genitourinary tract, has a longer half-life than metronidazole (12.5 hours versus 7.3 hours), and has fewer gastrointestinal side effects. Metronidazole regimens have cure rates of approximately 84%–98% and tinidazole regimen approximately 92%–-100% Avoid tinidazole in pregnant women. Defer breastfeeding deferred for 72 hours following a single 2-g dose of tinidazole ***M****ost recurrent result from reinfection, some infections might be attributed to antimicrobial resistance*			

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other Management Considerations for Trichomoniasis

Patients should be counselled to abstain from sex until they and their sex partners are treated. Concurrently all sex partners should be treated and patient retested within three months following initial treatment. Patient should be tested for HIV

9.11.1.3 Vulvovaginal Candidiasis

Candidiasis is a fungal infection common in women of childbearing age. Pruritus (itching) is the predominant symptom, accompanied by a thick, odourless, white vaginal discharge, sometimes 'cottage cheese-like' in appearance, which can extend from inside the vagina to the vulva and inguinal region. Vulvar involvement can cause burning during urination, pain during sex, and noticeable discomfort. Unlike bacterial vaginosis, there is no prominent odour in vaginal candidiasis.

Table 71: Risk factors, Symptoms and Diagnosis of Vulvovaginal Candidiasis

Etiology	Risk factors	Symptoms	Laboratory Diagnosis
Vulvovaginal Candidiasis (VVC)			
Caused by Candida Albicans, Candida Sp. Or yeasts	1. Inappropriate antibiotic use 2. Increased estrogen levels 3. Uncontrolled diabetes 4. Impaired immune system 5 unprotected sex.	Symptoms- pruritus, vaginal soreness, dyspareunia, external dysuria, pains, swelling and redness. Signs include vulvar edema, fissures, excoriations and abnormal thick curdy vaginal discharge.	Signs and symptoms of vaginitis and either 1) Wet preparation (saline, 10% KOH) or Gram stain of vaginal discharge demonstrates budding yeasts, hyphae, or pseudohyphae OR 2) Culture or other test yields a positive result for a yeast species. For complicated VVC-Vaginal cultures to confirm clinical diagnosis and identify unusual species, including nonalbicans species. *Existing signs or symptoms and negative wet mount- vaginal cultures for Candida should be considered. If Candida cultures cannot be performed for these women, empiric treatment can be considered.

Treatment of Vulvovaginal Candidiasis

Treatment varies for uncomplicated and complicated cases.

Table 72: Treatment recommendations for vaginal candidiasis

Uncomplicated Vaginal Candidiasis	Complicated Vaginal Candidiasis
Clotrimazole 1% cream 5 g intravaginally daily for 7–14 days **OR** Clotrimazole 2% cream 5 g intravaginally daily for 3 days **OR** Miconazole 2% cream 5 g intravaginally daily for 7 days **OR** Miconazole 4% cream 5 g intravaginally daily for 3 days **OR** Miconazole 100 mg vaginal suppository, one suppository daily for 7 days **OR** Miconazole 200 mg vaginal suppository, one suppository for 3 days **OR** Miconazole 1,200 mg vaginal suppository, one suppository for 1 day **OR** Tioconazole 6.5% ointment 5 g intravaginally in a single application **OR** Butoconazole 2% cream (single dose bioadhesive product), 5 g intravaginally in a single application **OR** Terconazole 0.4% cream 5 g intravaginally daily for 7 days **OR** Terconazole 0.8% cream 5 g intravaginally daily for 3 days **OR** Terconazole 80 mg vaginal suppository, one suppository daily for 3 days Oral Agent: Fluconazole 150 mg orally in a single dose	Recurrent (≥4 symptomatic episodes in 1 year): 7–10 days of topical therapy **OR** Initiation- 100 mg, 150 mg or 200mgs of oral dose of fluconazole every third day for a total of 3 doses (days 1, 4, and 7); Maintenance-100mg, 150 mg or 200mgs oral dose of fluconazole weekly for 6 months Severe: 7–14 days of topical azole therapy or 150 mg of oral fluconazole repeated in 72 hours; adjunctive use of nystatin cream or low-potency steroid cream may be beneficial Non-albicans: 7–14 days of nonfluconazole therapy; 600 mg of boric acid in a gelatin capsule vaginally once daily for 14 days Immunocompromised: 7–14 days of topical therapy Pregnant: 7 days of topical agents; fluconazole is contra-indicated
Patients should be informed that oil-based creams and suppositories might weaken latex condoms.	

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

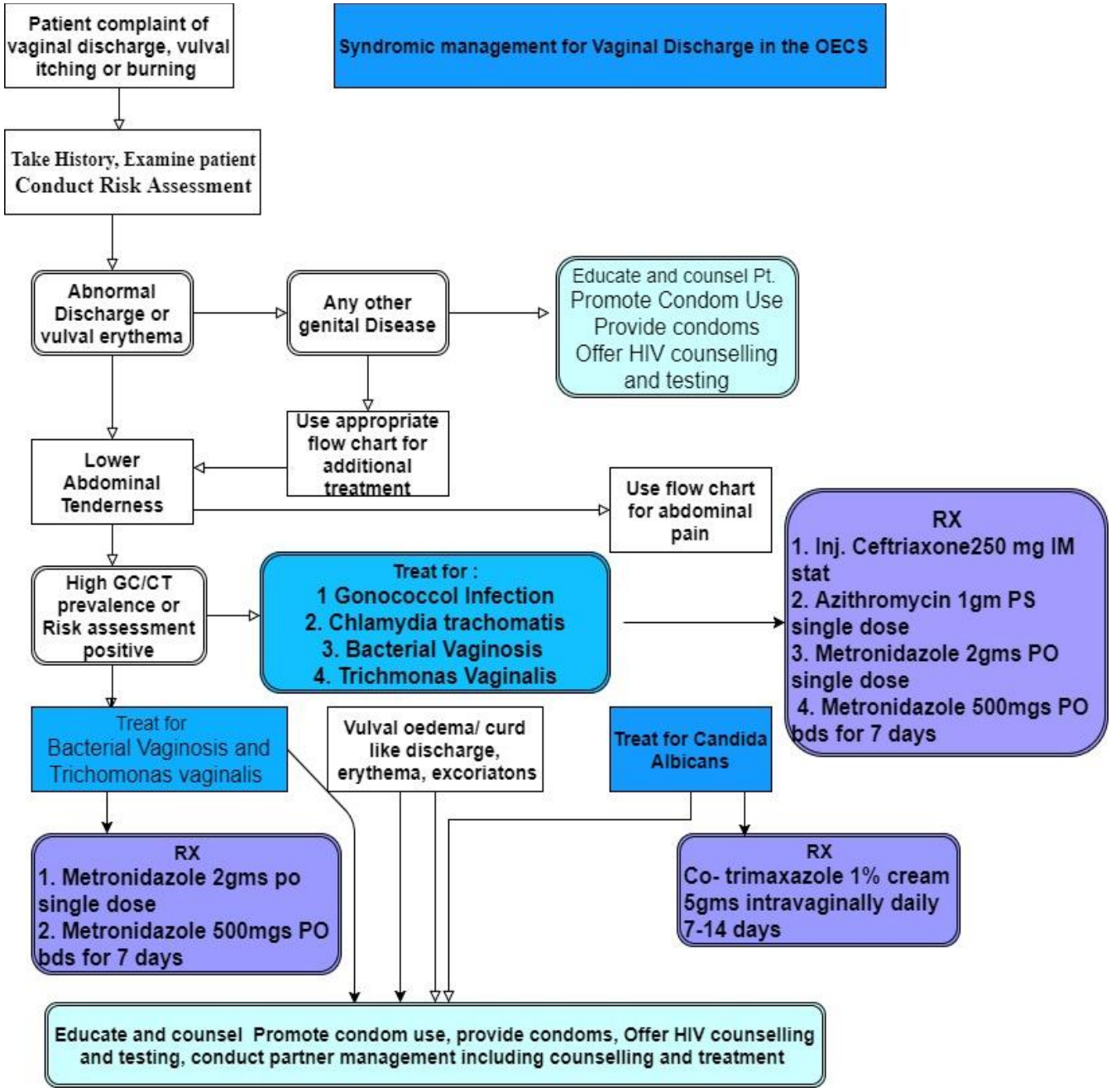
Other management considerations for Vulvovaginal Candidiasis

Patients are instructed to return only if symptoms persist or recur within 2 months. Routine treatment of sex partners is not indicated. Women with HIV infection have greater vaginal candida colonization rates compared to seronegative women. The rates correlate with increasing severity of immunosuppression. Treatment for uncomplicated and complicated VVC in women with HIV infection should not differ from that for seronegative women. The use of prolonged conventional therapy is recommended for immunocompromised women. Oral fluconazole is contra-indicated in pregnancy. Use only topical azole in pregnancy.

9.11.1.4 Syndromic management of vaginal discharge

In many cases, large proportions of women with cervical infection are asymptomatic making vaginal discharge highly indicative of vaginal infection, but poorly predictive for cervical infection. Thus in applying a syndromic approach to management all women presenting with vaginal discharge should receive treatment for vaginal infection as well as cervical infection. See figure 15 for algorithm.

Figure 15: *Algorithm on syndromic management for vaginal discharge*



Source : World Health Organization. Guidelines for the management of sexually transmitted infections. Geneva: WHO; 2003. Available from: http://www.who.int/hiv/pub/sti/en/STIGuidelines2003.pdf.

9.12 Lower Abdominal Pain and Pelvic Inflammatory Disease

All sexually active women presenting with lower abdominal pain must be evaluated for the presence of PID. PID is a spectrum of inflammatory disorders that often ascend from the lower- to the upper-genital tract; it can include any combination of cervicitis, endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. Symptoms suggestive of PID include abdominal pain, dyspareunia, bleeding between periods, dysuria, fever, and sometimes nausea and vomiting. *N. gonorrhoeae* and *C. trachomatis*, are implicated in many cases, however, microorganisms that comprise the vaginal flora (e.g., anaerobes, *G. vaginalis, Hib, Mobilincus,* enteric Gram-negative rods) have also been associated with PID.

The sequelae of PID can be damaging and lead to ectopic pregnancy, chronic lower abdominal pain, and infertility.

Diagnosis

PID may be difficult to diagnose because of the wide variation in clinical manifestations; many women with PID have subtle or mild symptoms. Delays in diagnosis and treatment probably contribute to inflammatory sequelae in the upper reproductive tract.

PID becomes highly probable as a diagnosis when one or more of the following symptoms and signs are seen in a woman in whom pregnancy has been excluded:
Symptoms may include lower abdominal pain, which is typically bilateral,deep dyspareunia, abnormal vaginal bleeding, including post coital, intermenstrual and menorrhagia and abnormal vaginal or cervical discharge which is often purulent. On examination, specific signs include lower abdominal tenderness, which is typically bilateral, adnexal tenderness on bimanual vaginal examination, cervical motion tenderness on bimanual vaginal examination and fever (>38°C). Diagnosis is enhanced with the presence of abnormal cervical or mucopurulent discharge, abundant WBCs on saline or wet mount, elevated erythrocyte sedimentation rate (ESR) or C - reactive protein (CRP) and laboratory documentation of cervical infection with *C. trachomatis* or *N. gonorrhoeae.*

Differential Diagnosis

The differential diagnosis for lower abdominal pain is broad and takes into account adjacent organ systems. Particular attention must be given to surgical emergencies such as ectopic pregnancies and appendicitis which can be life threatening. Therefore, careful evaluation of the patient is imperative for diagnosis. The differential diagnosis should be conducted for ectopic pregnancy, appendicitis, urinary tract infection, endometriosis, vaginitis and Irritable Bowel Syndrome (IBS).

Treatment

If an acute emergency has been ruled out, patients suspected of PID can be treated on an outpatient basis. In general, clinicians should err on the side of over diagnosis and treat suspected cases. If the patient is sexually active and has pelvic or lower abdominal pain without another cause, then empiric treatment is recommended
Many cases of PID go undiagnosed and untreated, leading to tubal scaring and infertility. To avoid such long term sequelae—combined with the fact that there are many asymptomatic infections—clinicians should have a high index of suspicion to treat for PID. Physicians should consider hospitalisation of the patient in cases where diagnosis is uncertain, surgical emergencies, such as appendicitis and ectopic pregnancy, cannot be excluded or a tubo- ovarian, pelvic abscess is suspected. Consideration for hospitalisations should also be given to pregnant women, any person whose severe illness precludes management on an outpatient basis (nausea, vomiting, high fever) and persons who failed to respond to outpatient therapy.

Table 73: Treatment of lower abdominal pain

First step

Ascertain the cause of lower abdominal pain; if in doubt, refer to hospital (see above on issues to consider for hospital diagnosis of PID)

Outpatient management for PID

Perform pregnancy test

- Conduct serology testing for HIV, VDRL, HAV, HBV, HCV
- Perfom high vaginal- and endocervical swabs for culture and sensitivity
- Perfom urinalysis and urine culture
- Conduct ultrasound; if not available, refer
- Perform CBC with differential and ESR/CRP
- Perform a vaginal saline wet mount with pH
- Perform KOH wet mount and whiff test
- Examine and treat any male sex partners from the last 60 days, also treating for gonorrhoea and chlamydia, regardless of aetiology of PID
- Consider partner-expedited therapy[a] for consorts who are not likely to come in for treatment and have no treatment contra-indications
- Recommend no sexual activity until treatment is completed and until partner has been treated
- Notify as per National Guidelines

TREATMENT

OUTPATIENT TREATMENT

- Ceftriaxone: 250 mg IM in a single dose PLUS
- Doxycycline 100 mg orally twice a day for 14 days PLUS
- Metronidazole 500 mg orally twice a day for 14 days* OR
- Cefoxitin: 2 g IM in a single dose; PLUS
- Probenicid: 1 g orally administered concurrently in a single dose; PLUS
- Doxycycline 100 mg orally twice a day for 14 days PLUS
- Metronidazole 500 mg orally twice a day for 14 days* OR
- Cefotaxime: 500 mg in a single dose; PLUS
- Doxycycline: 100 mg orally 2 x a day for 14 days; PLUS
- Metronidazole: 500 mg orally 2 x a day for 14 days
- ***with or without Metronidazole***

Recommended inpatient Treatment Regimen	Alternative Regimen
• Cefotetan 2 g IV every 12 hours PLUS • Doxycycline: 100 mg orally or IV every 12 hours; OR • Cefoxitin: 2 g IV every 6 hours; PLUS • Doxycycline: 100 mg orally or IV every 12 hours; OR • Clindamycin: 900 mg IV every 8 hours; PLUS • Gentamicin: Loading dose IV or IM (2 mg/kg of body weight), followed by a maintenance dose (1.5 mg/kg) every 8 hours; single daily dosing (3–5mg/kg) can be substituted	• Ampicillin/sulbactam: 3 g IV every 6 hours; PLUS • Doxycycline: 100 mg orally or IV every 12 hours

[a] Partner-expedited therapy: Providing appropriate therapy for the index case's contact(s); this is done especially when the partner cannot be relied upon to come in for examination and treatment.; [b] Patients taking metronidazole should be cautioned about taking alcohol. [c] Therapy should be continued for at least three days after the patient has improved and should then be followed by doxycycline 100 mg PO BD for 14 days

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Lower Abdominal Pain and PID

1. Counsel on to abstain from sexual intercourse until therapy is completed, symptoms have resolved, and sex partners have been adequately treated.
2. If there is no clinical improvement after 72 hours of treatment, patient should be reevaluated.
3. Retesting for gonorrhea and chlamydia at 3 months.
4. Sexual contacts during the 60 days preceding the onset of symptoms should be evaluated, tested, and presumptively treated for chlamydia and gonorrhea. If the last sexual intercourse was >60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated. Strategies for partner management should be used including partner expedited therapy.
5. Due to the high risk of maternal morbidity and pre term delivery, pregnant women should be managed in an inpatient setting
6. Intrauterine device- The risk for PID associated with IUD use is primarily confined to the first 3 weeks after insertion. These cases do not warrant the removal of the IUD, but rather the patient should be treated as per protocol described above. If after 48-72 hours there is no clinical improvement, consider removing the IUD.

9.13 Epididymitis

Epididymitis is a clinical condition that is subdivided into acute and chronic syndromes. Acute epididymitis is defined as pain, swelling, and inflammation of the epididymis lasts for <6 weeks. Most acute episodes of epididymitis involve the testis, and lead to a condition often referred to as epididymo-orchitis. Chronic epididymitis is characterized by a history of discomfort and/or pain in the scrotum, testis, or epididymis that has lasted >6 weeks.. Chronic epididymitis is also subcategorized—inflammatory or obstructive chronic epididymitis and/or chronic epididymalgia.

In men <35 years old, epididymitis is often caused by STIs—mainly gonorrhoea and chlamydia—but can be caused by other enteric organisms (e.g., *E. coli*, *Klebsiella*, and *Pseudomonas*). It is typically seen in male partners who perform insertive anal sex. Sexually transmitted acute epididymitis is accompanied by a urethritis, which is typically asymptomatic.

For men >35 years old, sexually transmitted epididymitis is uncommon. Generally in this age group, non-sexually transmitted epididymitis is associated with urinary tract instrumentation or surgery, systemic diseases, and immunosuppresion. A broader differential is therefore required in men >35 presenting with epididymitis.

Unlike acute epididymitis, chronic infectious epididymitis is most frequently seen in granulomatous reactions, like TB. TB lesions are usually secondary to lesions found elsewhere in the body, such as the lungs. The diagnosis should be suspected if the patient has a history of TB, has been exposed to someone with TB, or is not improving despite antibiotic treatment.

In pre-pubertal children with epididymitis, potential aetiological agents may be coliforms, pseudomonas infection, or mumps virus. Clinically, mumps epididymo-orchitisis usually follows a week of parotid enlargement. Testicular torsion should be considered as a part of the differential

diagnosis, as this condition requires immediate surgical referral. Other conditions such as tumors and trauma must also be considered.

Diagnosis

The diagnosis of epididymitis is made on clinical grounds. Patients who have acute epididymitis typically have unilateral testicular pain and tenderness; palpable swelling of the epididymis is usually present. This swelling can spread to the testis, with associated swelling and tenderness in the spermatic cord.

If, on physical examination, the testes are found to be elevated or rotated, then there must be a high index of suspicion for torsion of the testes. This is even more conclusive when there is a history of trauma. Testicular torsion is a surgical emergency and must be considered in all cases. Notably, it occurs more frequently in adolescents and in men who have no evidence of inflammation.

A urethral swab for gonorrhoea and chlamydia should be done and urinalysis conducted on first-void urine sample for leukocyte esterase or microscopy for >10 WBC per high power field. In addition to the specific treatment detailed in table 9.25 below, advise should be given for bed rest, scrotal elevation, and analgesia prescribed

Treatment

Table 74: Management of epididymitis and scrotal swelling

Recommended Regimens
For acute epididymitis most likely caused by sexually transmitted chlamydia and gonorrhea
Ceftriaxone: 250 mg IM in a single dose; PLUS Doxycycline: 100 mg PO 2 x day for 10 days
For acute epididymitis most likely caused by sexually-transmitted chlamydia and gonorrhea and enteric organisms (men who practice insertive anal sex)
Ceftriaxone: 250 mg IM in a single dose; PLUS Levofloxacin: 500 mg PO once daily for 10 days; OR Ofloxacin: 300 mg PO twice a day for 10 days.
For acute epididymitis most likely caused by enteric organisms
Levofloxacin: 500 mg PO once daily for 10 days; OR Ofloxacin: 300 mg PO twice a day for 10 days.

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Epididymitis

1. Advise patient to return within 72 hours if symptoms have not resolve.
2. A high index of suspicion for spermatic cord (testicular) torsion must be maintained in men who present with a sudden onset of symptoms associated with epididymitis. This is considered a surgical emergency and should be corrected in a timely manner as testicular viability could be compromised.
3. All sex partners within the last 60days preceding the onset of symptoms, should be referred to for evaluation, testing, and presumptive treatment. If the last sexual intercourse was >60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated

4. Recommend abstinence from sexual intercourse until both patients and partners have been adequately treated and symptoms have resolved
5. Conduct serology for other STIs including HIV

8.14 Balanoposthitis

Balanoposthitis refers to inflammation of the glans penis (balanitis) and the foreskin (posthitis).
This condition is most commonly caused by Candidal infection. Other pathogens include *Bacteroides*, *Gardnerella*, and *Streptococcus.* In rare cases pathogens like *Streptococcus pyogenes, Prevotella melaninogenica, Cordylobia anthropophaga, Providencia stuartii,* and *Pseudomonas aeruginosa have been documented.* Presenting symptoms include scaly or ulcerated rash, soreness, dyspareunia, itching, inability to retract the foreskin, discharge from the glans, and odour. Complications are mild, but in immunosuppressed patients—such as diabetics and PLHIV—it can lead to recalcitrant infections, despite therapy. In PLHIV, balanoposthitis can progress to fungal septicemia if left untreated.

Diagnosis

The diagnosis of balanoposthitis can be made on clinical grounds but requires laboratory confirmation:

1. Wet prep of swab taken from the underside of the foreskin using KOH to identify pseudohyphae.
2. Sub-preputial swab for bacterial culture.
3. The presence of aceto-white changes with application of 5% aceto-acidic acid suggest HPV infection, which can be seen in association with balanoposthitis.

Treatment

Empiric treatment with antifungal is recommended (antibiotic cream is optional). Proper hygiene daily washing with foreskin retraction and thorough drying of the penis and foreskin is advised.

Table 75: Recommended treatment for balanoposthitis

Recommended Regimens
Clotrimazole: 1% cream applied to the penis or foreskin daily for 7–14 days OR
Miconazole: 2% cream applied to the penis or foreskin daily 7–14 days; **PLUS**
Antibacterial ointment (fucidic acid [Fucidin] or mupirocin [Bactroban])

9.15 Human Papilloma Virus Infections

HPV is a small, slow growing DNA virus belonging to the papovavirus group. There are more than 50 types of HPVs, causing conditions ranging from benign to oncogenic. About 90% of genital warts are caused by HPV types 6 and 11—both of which are benign. HPV types 6 and 9 have been associated with conjunctival, nasal, oral and laryngeal warts. Clinically, genital warts are often asymptomatic, though depending on the size and anatomic location, they may produce symptoms such as pain or puritis. The morphology often varies, but they are usually flat, papular, or pedunculated growths on the genital mucosa. Most genital warts are painless and do not lead to serious complications, unless they cause vaginal obstruction in pregnant women or laryngeal papillomatosis in infants. Laryngeal papillomatosis, though uncommon, is an important clinical situation that must be considered in babies that have progressive hoarseness and stridor. In HIV infected patients, genital warts may grow rapidly and are often difficult to control.

Unlike the benign type HPVs, the oncogenic ones cause dysplasia in the epithelial cell lining of the site of inoculation (e.g., cervix, anus, vulva, throat) leading to the development of abnormal cells lines and eventually cancer. HPV types 16 and 18causes most cervical, penile, vulvar, vaginal, anal, and oropharyngeal cancers and precancers. This section describes specific prevention methods with vaccination and diagnosis and treatment of anogenital warts and HPV associate cancers and precancers.

9.15.1 Prevention

The following are the recommendations in relation to vaccination

1. HPV vaccines are administered as a 3-dose series of IM injections over a 6-month period. The second and third doses are given 1–2 and 6 months after the first dose. The same vaccine product should be used for the entire 3-dose series.
2. The bivalent vaccine (Cervarix) prevents infection with HPV types 16 and 18, a quadrivalent vaccine (Gardasil) prevents infection with HPV types 6, 11, 16, and 18, and a 9-valent vaccine that prevents infection with HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58.
3. For girls, bivalent or quadrivalent vaccine is recommended routinely at ages 11–12 years and can be administered beginning at 9 years of age ; girls and women aged 13–26 years who have not started or completed the vaccine series should receive the vaccine.
4. For boys, quadrivalent or 9-valent HPV vaccine is recommended routinely at ages 11–12 years and can be vaccinated beginning at 9 years of age. Boys and men aged 13–21 years who have not started or completed the vaccine series should receive the vaccine.
5. For unvaccinated, immunocompromised persons (including persons with HIV infection) and MSM, vaccination is recommended through age 26 years.
6. HPV vaccines can be administered regardless of history of anogenital warts, abnormal Pap/HPV tests, or anogenital precancer.
7. Women who have received HPV vaccine should continue routine cervical cancer screening if they are aged ≥21 years
8. Risk reduction including consistent and correct use of condoms, partner reduction and abstinence from sexual activity.

9.15.2 Anogenital Warts

The majority (90%) of anogenital warts are caused by non-oncogenic HPV types 6 or 11. In addition to anogenital warts, HPV types 6 and 11 have been associated with conjunctival, nasal, oral, and laryngeal warts. Anogenital warts are flat, papular, or pedunculated growths on the genital mucosa and usually asymptomatic. Depending on the size and anatomic location, they can become symptomatic with patients complaining of pain and itching. Common areas for anogenital warts include around the vaginal introitus, under the foreskin of the uncircumcised penis, and on the shaft of the circumcised penis. Intra-anal warts are observed predominantly in persons who have had receptive anal intercourse.

Diagnosis

This is generally made by visual inspection and can be confirmed by biopsy in case of atypical lesions. Indications for biopsy include uncertainty of diagnosis, non-responsive lesions to standard therapy or worsening of the disease during treatment. These situations are likely particularly in the immunocompromised patients such as HIV. Persons with external anal warts also have intra-anal warts and therefore might benefit from an inspection of the anal canal by digital examination, standard endoscopy, or high-resolution anoscopy.

Treatment

Treatment is aimed at wart removal and improvement in symptoms. HPV can resolve spontaneously, anogenital warts can resolve spontaneously within a year and therefore it would be acceptable to forgo treatment for 1 year. Treatment might reduce the warts, but probably do not eradicate HPV infectivity.

Table 76: Treatment of anogenital warts

Disease	**Recommended regimens**	
	Patient-applied	**Provider-administered**
External genital warts (penis, groin, scrotum, vulva, perineum, external anus, and perianus)	Imiquimod 3.75% (applied once at bedtime, every night for up to 16 weeks) or 5% cream(applied once at bedtime, three times a week for up to 16 weeks);**OR** Podofilox 0.5% solution or gel-Apply 2 x daily for 3 days followed by 4 days of no treatment, repeating cycle up to 4 x (total volume of podofilox should not exceed 0.5 ml per day; **OR**	Cryotherapy with liquid nitrogen or cryoprobe; repeat applications every 1–2 weeks; **OR** Surgical removal either by tangential scissor excision, tangential shave excision, curettage or electrosurgery; **OR** Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80–90% followed by powdering of the treated areas with talc or sodium bicarbonate to remove unreacted acid.
Notes- Immiquimod- The treatment area should be washed with soap and water 6–10 hours after the application. Podopyllin (10%-25%) is no longer a recommended regimen because of the number of safer regimens available, and severe systemic toxicity has been reported when podophyllin resin was applied to large areas of friable tissue and was not washed off within 4 hours. Should be provider administered Should be applied to each wart and then allowed to air-dry before the treated area comes into contact with clothing. (Over-application or failure to air-dry can result in local irritation caused by spread of the compound to adjacent areas and possible systemic toxicity). If necessary can be repeated weekly. Podophyllin (10%-25%) To avoid the possibility of complications associated with systemic absorption and toxicity, 1) application should be limited to <0.5 mL of podophyllin or an area of <10 cm2 of warts per session; 2) the area to which treatment is administered should not contain any open lesions, wounds, or friable tissue; and 3) the preparation should be thoroughly washed off 1–4 hours after application.		
Cervical warts	Cryotherapy with liquid nitrogen; **OR** Surgical removal; **OR** TCA or BCA 80%–90% solution,	
Vaginal warts	Cryotherapy with liquid nitrogen; (The use of a cryoprobe in the vagina is not recommended because of the risk for vaginal perforation and fistula formation); **OR** Surgical removal; **OR** TCA or BCA 80% to 90% applied to warts. Repeat weekly is necessary.	
Urethral meatus warts	Cryotherapy with liquid nitrogen; **OR** Surgical removal.	
Intra- Anal warts	Cryotherapy with liquid nitrogen; **OR** Surgical removal; **OR** TCA or BCA 80–90% to warts.	

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Note: The removal of a lesion does not mean that the HPV infection has been cured.

Other management considerations for Anogenital Warts.

1. Most anogenital warts respond within 3 months of therapy. Factors that might affect response to therapy include immunosuppression and treatment compliance.
2. A new treatment modality should be selected when no substantial improvement is observed after a complete course of treatment or in the event of severe side effects; treatment response and therapy-associated side effects should be evaluated throughout the course of therapy.
3. Podofilox (podophyllotoxin), podophyllin, and sinecatechins should not be used during pregnancy. Imiquimod appears to pose low risk but should be avoided.
4. Anogenital warts can proliferate and become friable during pregnancy. Although removal of warts during pregnancy can be considered, resolution might be incomplete or poor until pregnancy is complete.
5. Although rare, HPV types 6 and 11 can cause respiratory papillomatosis in infants and children. The route of transmission (i.e. transplacental, perinatal, or postnatal) and whether cesarean section prevents respiratory papillomatosis in infants and children also is not fully understood. Cesarean delivery is indicated if there is obstructed to the pelvic outlet or if vaginal delivery would result in excessive bleeding. It is not indicated to prevent transmission of HPV infection to the newborn.
6. Immunocompromised persons are more likely to develop anogenital warts than those who do not have HIV infection. The lesions are generally larger in number and size, less responsive to therapy and with more frequent reoccurrences. Treatment however is no different from that of an immunocompetent person.
7. Immunocompromised persons also have greater likelihood of squamous cell carcinomas and therefore biopsy for confirmation of diagnosis for suspicious cases is recommended.

9.15.3 HPV associated with Cancers and Precancers

Persistent infection with oncogenic types of HPV has a causal role in nearly all cervical cancers and in many vulvar, vaginal, penile, anal, and oropharyngeal cancers. However, the only HPV-associated cancer for which routine screening is recommended is cervical cancer.

9.15.3.1 Cervical cancer screening

A. Screening with Pap test and HPV test

1. Routine cervical screening should be performed starting at age 21 years and continue through age 65 years.
2. All screening tests must be processed by certified labs that have either conventional or liquid based cytologic tests (e.g., Pap tests). The results reporting system should be based on the following **Bethesda terminology:**
   - Atypical squamous cells (ASC)
   - ASC of undetermined significance (ASC-US)
   - ASC—cannot exclude high-grade squamous intraepithelial lesion (HSIL)
   - Low-grade squamous intraepithelial lesion (LSIL)
   - High grade squamous intraepithelial lesion (HSIL)

The **CIN (cervical intraepithelial neoplasia)** identifies how much of the lining of the cervix is invaded by abnormal cells. CIN Classifications are as follows:

- CIN I: Mild dysplasia; abnormal cells can be found in 1/3 of the lining of the cervix
- CIN II: Moderate dysplasia; abnormal cells can be found in 2/3 of the lining of the cervix
- CIN III: Severe dysplasia; abnormal cells can be found in more than 2/3 of the lining of the cervix and up to the full thickness of the lining

3. Annual cervical cancer screening is no longer recommended for all women. Screening is recommended as follows:
   - Ages 21-29- every 3 years with Pap test.
   - Ages 30–65 years, Pap test every 3 years or a Pap test PLUS HPV test (co-testing) every **5 years**. (An HPV test checks for the virus and a Pap Test checks for abnormal cervical cells)
4. Women who have received HPV vaccines, should be screened the same way as the unvaccinated.
5. Pregnant women should be screened at the same intervals as non-pregnant women. A swab, Ayre's spatula, or cytobrush can be used for obtaining Pap tests in pregnant women.
6. There is an increased risk for cervical precancers and cancers in women with HIV infection. These women should be screened within 1 year of sexual activity or initial HIV diagnosis using conventional or liquid-based cytology (Pap test); testing should be repeated 6 months later.
7. Prevalence of oncogenic HPV types are high among adolescents (<21 years), and oncogenic HPV and squamous intraepithelial lesions caused by HPV in adolescent girls are more likely to regress than those in older women. Therefore, cervical cancer screening and HPV testing are not recommended in this population.
8. There is a high rate of progression of abnormal cytology among adolescents with HIV. They should be should screened 1 year after onset of sexual activity, regardless of age or mode of HIV infection (e.g., perinatally acquired or sexually acquired).

B. Screening with VIA

VIA is another viable method for cervical cancer screening. It is a low cost technique applicable for resource limited settings, with the advantage of having immediate results. It is best used for women in their 30s and 40s who may have precancerous and cancerous lesions and who have certain risk factors, including high parity, oral contraceptive use, smoking, and HIV infection. Screening women once every 3 years still gives a 90% detection rate and therefore is quite effective given the 10– 15 year latency period of cervical cancer.

VIA is very simple and involves applying a cotton swab dipped in 5% trichloroacetic acid (the same strength found in typical vinegar) to the cervix, coating it. The clinician should look for aceto-white changes on the cervix, focusing on the squamocolumnar junction. Whether the patient needs referral depends on the following criteria:

A negative VIA is considered when there is normal squamocolumnar junction. In these cases, advise patient to return for another VIA within 1–3 years, unless high risk (uses hormonal contraceptives, is a smoker, has high parity, is HIVinfected), in which case the patinet should return in 1 year.

A positive VIA is considered when

- Lesion extends beyond squamocolumnar junction to transformation zone but <70% of cervix and within limits of probe. In these cases treat with cryotherapy.
- Lesion is >70% and 2mm beyond limits of probe. In these cases, refer for colposcopy and biopsy.
- If lesion is cancerous (ulcerative, bleeds easily, fungating mass). In these cases, refer immediately to gynaecologist for surgery (total abdominal hysterectomy plus chemotherapy/radiation, based on clinical staging.

Follow up recommendations

- Women with abnormal Pap test, follow-up care should be provided including linkages for appropriate management. With of potential harms of overtreatment and low risk for cancer, more conservative management for women aged 21–24 years and cytology should be repeated in 12 months

- Women testing HPV negative, a repeat HPV and Pap test in 3 years is recommended.
- Women with unsatisfactory cytology, regardless of negative HPV result, a repeat cytology is required in 2–4 months.
- Women with discordant results (normal Pap test and positive HPV test) , then HPV 16/18 testing is recommended. If positive, women should immediately receive colposcopy. If negative, repeat the HPV co-test in 1 year.
- Women with LSIL or HSIL, management should be provided by a specialist.

9.15.4 Anal Cancer

There is insufficient data to recommend cytology for HIV infected persons, MSM and the general population. However an annual digital anorectal examination may be useful to detect masses that could be anal cancer in persons with HIV infection and possibly HIV-negative MSM with a history of receptive anal intercourse. Oncogenic HPV tests are not clinically useful for anal cancer screening among MSM because of a high prevalence of anal HPV infection.

9.16 Molluscum Contagiosum

Molluscum contagiosum are lesions on the skin caused the DNA poxvirus, which is an unclassified member of the *Poxviridae* family. There are four types of molluscum contagiosum virus, these are type I, type II, type III and type IV. Most of the infections are caused by type I (96%) and Type II (3%).

These skin lesions characteristically consist of a single or more often, multiple, rounded, dome-shaped, pink, waxy papules that are 2–5 mm (rarely up to 1.5 cm, in the case of a giant molluscus) in diameter. The papules are umbilicated and contain a caseous plug, which gives a central white core appearance. Lesions may be located anywhere on the body. Distribution is influenced by the mode of transmission, type of clothing worn, and climate.

In children, they are usually found on the face, trunk, and extremities and in adults, on the groin and genitalia. In sexually active individuals, the lesions may be confined to the penis, pubis and inner thighs

In children, the virus is most often transmitted through regular contact, whereas in adults, it is mostly sexually transmitted. Its appearance outside of the genital area in adults is unusual and may be a presenting sign of yet-to-be-diagnosed HIV infection.

Complications of molluscum contagiosum include skin irritation, inflammation, and secondary infections, such as *Staphylococcal* abscesses and a necrotizing cellulitis due to *Pseudomonas*. In HIV-infected patients, the lesions can be quite extensive and may produce some level of disfigurement. Lesions may also take a prolonged period of time to resolve, even with therapy.

Diagnosis

Molluscum contagiosum can be diagnosed on clinical grounds based on the distinct papular lesion with central umbilication. If diagnosis is uncertain, lesions may be biopsied. Characteristic intracytoplasmic inclusion bodies (molluscum bodies or Henderson-Paterson bodies) are seen on histologic examination. PCR can be used to detect the poxvirus in skin lesions.

Treatment

Therapeutic options for molluscum contagiosum can be divided into the following broad categories: benign neglect, direct lesional trauma, antiviral therapy and immune response stimulation

- **Benign neglect:** Lesions often resolve spontaneously in healthy patients and therefore ignoring the lesions is a good option particularly in treating children, to minimize their discomfort.
- **Direct lesional trauma:** minor trauma to molluscum lesions frequently produces an inflammatory response by the Henderson-Paterson bodies and resolution of the lesion. To provoke this response

physical trauma and caustic topical agents can be inflicted upon the lesions. These caustic agents include Tretinoin, salicylic acid, and potassium hydroxide. Cantharidin, silver nitrate, trichloroacetic acid, and phenol. Physical trauma to individual molluscum contagiosum lesions can be performed with cryotherapy, lasers, curettage, expression of the central core with tweezers, rupture of the central core with a needle or a toothpick, electrodessication, shave removal, or duct tape occlusion

- **Antiviral therapy:** In immunocompromised patients, improvement of lesions has been observed in individual patients treated with ritonavir, cidofovir (intravenous and topical) and zidovudine.
- **Immune Response Stimulator:** Imiquimod cream, intra-lesional interferon alfa and topical injections of streptococcal antigen are effective in treating patients with resistant molluscum contagiosum Imiquimod 1% cream applied 3 times weekly or 5% cream applied at every bedtime for 4 weeks appears to be effective treatment in children and in some patients with AIDS-associated molluscum contagiosum. A newer compound, Veregen, is a sinecatechin, the 15% ointment is applied topically 3 times a day.

Patients treated for molluscum contagiosum should receive follow-up and repeat treatment may be necessary, depending on the resolution of the lesions. Combination therapy may be required in complicated cases (e.g., dual therapy with HAART, curettage in HIV-infected patients).

Other management considerations for Molluscum Contagiosum

For adults and adolescents, prevention advice would include abstaining from sexual contact during symptomatic period, avoiding autoinoculation of the lesion by manipulation (e.g., shaving) and practicing good hygiene.

9.17 Viral Hepatitis

Viral Hepatitis is an inflammatory state caused by a viral agent. Sexually transmitted viral hepatitis are discussed in this guideline and include Hepatitis A, B and C.

9.17.1 Hepatitis A

Hepatitis A, which is caused by infection with Hepatitis A Virus (HAV), has an incubation period of 28 days (range 15 to 50 days). The infection produces a self-limiting disease that does not result in chronic infection or chronic liver disease. Symptoms are typical of an acute viral illness—fever, malaise, myalgia, lymphadenopathy, and jaundice. Ten to 15% of individuals with HAV experience a relapse of acute symptoms within 6 months.

The main mode of transmission is faecal-oral but it can also be transmitted through oral sexual practices. High-risk groups include MSM, injection drug users, and persons with chronic liver disease.

Diagnosis

Hepatitis A can be diagnosed on clinical and a positive serologic antibody test indicating the presence of IgM antibody to HAV.

Treatment

Treatment – there is no special treatment for acute hepatitis A. Generally patients are given supportive care. Patients who are acutely ill and have serious signs and complications of acute liver failure (e.g., jaundice, pale stools, dark urine) or those who are dehydrated should be hospitalized. Medications that are metabolized by the liver must be used with caution in persons with hepatitis A as they may cause liver damage.

Prevention
Vaccination is the most effective means of preventing HAV infections among persons at risk. Currently there are two vaccines available, HAVRIX and VAQTA and is recommended for found to be antibody negative by HAV testing.

Table 77: Hepatitis A vaccination dosing and schedule

Vaccine	Age (yrs)	Dose	Volume (mL)	Two dose schedule (months)
HAVRIX	1 -18	720 (EL.U)	0.5	0 (6-12)
	>18	1,440 (EL.U)	1.0	0(6 -12)
VAQTA	1-18	25 (U)	0.5	0(6-18)
	>18	50 (U)	1.0	0(6-18)

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Pre-exposure Vaccination
Hepatitis A vaccine should be offered to the following at risk groups: 1) all MSM; 2) drug users (injection and non-injection illicit drugs); and 3) persons with Chronic Liver Disease (CLD), including persons with chronic HBV and HCV infection who have evidence of CLD. If persons are at risk for both Hepatitis A and Hepatitis B, the combined vaccine can be considered.

Post exposure prophylaxis
Persons who recently have been exposed to HAV and who previously have not received hepatitis A vaccine should be administered a single dose of monovalent hepatitis A vaccine or IG (0.02 mL/kg) as soon as possible, ideally within 2 weeks of exposure.

9.17.2 Hepatitis B

Hepatitis B, which is caused by infection with Hepatitis B Virus (HBV), has an incubation period ranging from 6 weeks to 6 months. It can be self-limiting or chronic. In adults, approximately half of newly acquired infections are symptomatic and around 1% result in acute liver failure and death. Symptoms range from mild (e.g., flu like symptoms) to severe (e.g., fever, jaundice, encephalopathy, abdominal pain, dark urine, pale stool).

The main route of transmission is through percutaneous, or mucous membrane exposure to blood or body fluids that contain blood infected with HBV. The risk of HBV transmission is close to 3% per contact exposure and so universal safety precautions must be followed in all health care institutions. Persons who have sex with an infected partner, multiple partners, MSM, history of STDs and injection drug use are vulnerable.

Unlike HAV, HBV has serious sequelae, including cirrhosis of the liver and hepatocellular carcinoma, which can lead to premature death. Many persons control the infection to become chronic carriers.

Diagnosis
Hepatitis B, acute or chronic, must be diagnosed via serologic testing. A complete HBV antibody profile that includes the following analyses is ideal for diagnosis and management:

- IgM antibody to Hepatitis B core antigen (IgM anti-HBc) is diagnostic of acute or recently acquired HBV infection.
- Antibody to HBsAg (anti-HBs) is produced after a resolved infection and is the only HBV antibody marker present after vaccination.
- HBsAg with a negative test for IgM anti-HBc indicates chronic HBV infection.

Treatment

No specific therapy is available for persons with acute HBV infection. Treatment is usually supportive care. Persons with chronic infection should be referred to a physician experienced in the management of chronic liver disease. Therapeutic agents can help to achieve sustained suppression of HBV replication and remission of liver disease. Treatment is mainly based on interferons (pegylated interferon alfa-2a) and antivirals, such as NRTIs.

In the case of HIV-HBV co-infection, two NRTIs, TDF and FTC or 3TC, are used in combination with an NNRTI (preferably EFV) to manage both diseases.

Prevention

Two products have been approved for preventing Hepatitis B: the Hepatitis B vaccine and Hepatitis B immune globulin (HBIG).

HBIG provides temporary (3–6 months) protection from HBV infection and is typically used as a Pre exposure prophylaxis measure, either adjunct to vaccination in previously unvaccinated persons, or alone in persons who have not responded to the vaccine series administered both pre- and post-exposure.

The Hepatitis B Vaccines are Recombivax HB and Energix. A combination vaccine for HAV and HBV is also available it is called Twinrix. The goal of vaccination is to prevent infection. The approved vaccination schedule options for adolescents and adults for Energix and Recombivax HB are as follows:

Table 78: HBV vaccination dosing and schedule

Option	Type of Vaccine	Timeline
Two Dose Schedule	Recombivax	With a 4 months interval between doses.
Three dose Schedule		
Dose 1	Recombivax, Engerix and Twinrix	0, 1 month then 6 months
Dose 2	Recombivax and Engerix	0, 1 month then 4 months
Dose 3	Recombivax and Engerix	0, 2 months then 4 months

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Infants born to mothers infected with HBV must be given HBIG after birth, followed by the complete routine childhood HBV immunization series. According to the WHO, it is safe for mothers to breastfeed their babies, though women with cracked nipples must proceed with caution.

Pre exposure vaccination/prophylaxis

Hepatitis B vaccination is recommended for all unvaccinated children and adolescents, all unvaccinated adults at risk for HBV infection (especially IDU, MSM, and adults with multiple sex partners), and all adults seeking protection from HBV infection. Hepatitis B vaccine should be routinely offered to all unvaccinated persons attending STD clinics and to all unvaccinated persons seeking evaluation or treatment for STDs in other settings, especially correctional facilities, facilities providing drug-abuse treatment and primary care services.

Post exposure prophylaxis

Both passive-active PEP (the simultaneous administration of HBIG [i.e., 0.06 mL/kg] and hepatitis B vaccine at separate sites) and active PEP (the administration of hepatitis B vaccination alone) have been demonstrated to be highly effective in preventing transmission after exposure to HBV.

For unvaccinated persons exposed to a source patient who is HBsAg positive, administer Hepatits B vaccine series and HBIG. For vaccinated persons exposed to a source patient who is HBsAg positive, administer Hepatitis B vaccine boosters.

For unvaccinated persons exposed to a source patient of unknown HBsAg, administer Hepatitis B vaccine series. For vaccinated persons exposed to a source patient of unknown HBsAg, no treatment is required.

Pregnant women at risk for HBV should be test at first prenatal visit and at delivery. Pregnant women at risk for HBV should receive hepatitis B vaccination.

9.17.3 Hepatitis C

Hepatitis C, which is caused by Hepatitis C Virus (HCV), can be highly contagious, with as much as 30% risk of exposure per contact event. The average time from exposure to antibody to HCV seroconversion is 8–9 weeks. Individuals with typical infections have mild symptoms or are asymptomatic. Chronic infection develops in 70–80% of HCV-infected persons, of which 60–70% develop evidence of active liver disease. HCV can lead to hepatocellular carcinoma.

The primary mode of transmission of Hepatitis C is injection drug use, though it can also be transmitted through blood transfusion, so blood donors should be carefully screened as a matter of course. Although HCV is not efficiently transmitted sexually, high-risk behaviours like unprotected sexual contact and injection drug use increase the likelihood of transmission, particularly within vulnerable groups. For this reason, it is important to consider offering HCV testing to injection drug users who may be accessing care at STI treatment clinics, HIV testing and counselling facilities, or other public health settings where such services are available. Correctional facilities should also perform HCV testing.

Diagnosis

Anti-HCV testing, which detects the presence of HCV antibodies, is recommended for routine screening of symptomatic persons based on their risk of exposure (e.g., injection drug use, percutaneous needlestick injury). Testing should include HCV antibody testing using EIA or enhanced chemiluminescence immunoassay, and, if recommended, supplemental antibody tests. Followed by NAAT to detect HCV RNA for those with a positive antibody result.

Treatment

Therapeutic agents can help to achieve sustained virological suppression of HCV and remission of liver disease. Treatment options have significantly advanced over the recent 5-10 years. Previously and still practiced, combination therapy with pegylated interferon and ribavirin was the choice for patients with chronic HCV infection.

Recent advances in the development of oral agents resulted in the FDA approval of several drugs from the protease inhibitor class, direct acting antivirals such as boceprevir and telaprevir**.** Subsequently, a polymerase inhibitor, sofosbuvir, a once daily pill. This was later combined with ledipasvir as Harvoni. In clinical trials, Harvoni cured Hepatitis C after 12 weeks of treatment in 94% of patients. In the OECS, Hepatitis C medications are unavailable.

Prevention

No vaccine is available to prevent hepatitis C and prophylaxis with immunoglobin is not an effective PEP measure.

Persons with HCV infection should be provided information regarding how to protect their liver from further harm (i.e., hepatotoxic agents) and should seek treatment, particularly with newer direct acting antivirals that has the potential to cure the disease. Counselling of persons with HCV should include advise on not to donate blood, body organs, other tissue, or semen, not to share any personal items that might have blood on them (e.g., toothbrushes and razors) and to cover cuts and sores on the skin to keep the virus from spreading by blood or secretions. Women with HCV infection do not need to avoid pregnancy or breastfeeding. Persons who use or inject drugs should be counseled about the importance of stopping drug-use behaviors and provided with assistance to enter and complete substance- abuse treatment (including relapse prevention).Persons who continue to inject drugs despite counseling should be encouraged to never reuse or share syringes, water, or drug preparation equipment and to clean the injection site before injection with a new alcohol swab. Importantly, they should safely dispose of syringes after use, practice consistent and correct condom use. Partners of index patients should be investigated and managed appropriately.

9.18 Human T-lymphotrophic Virus Infection (HTLV)

HTLV was the first retrovirus discovered. It belongs to the *Retroviridae* family in the genus *Deltaretrovirus* and is comprised of four strains (types 1, 2, 3 and 4); types 1 and 2 are dominant in the OECS. HTLV-1 and -2 are endemic to Japan as well as the Caribbean region, and affect 15–20 million people worldwide. The prevalence of HTLV in some Caribbean countries, such as Jamaica and Trinidad, has reached as high as 6% in the last decade.

HTLV-1 and -2 can be transmitted via sexual contact, breastmilk, childbirth, injection drug use, blood transfusions, and mucous membrane exposure.

HTLV-1 is the more clinically significant strain. Acute HTLV-1 infection is rare—most infections are latent and asymptomatic. Symptoms mimic a typical viral syndrome, with fever, headache, myalgia, and lymphadenopathy. Some individuals infected with HTLV-1 develop a rapidly fatal adult T-cell leukemia. Others experience neurological changes, including a debilitative myelopathy (known as HTLV-1–associated myelopathy [HAM] or 'tropical spastic paraparesis' [Note: Subsequently refered to as 'HAM'], which may lead to urinary or faecal incontinence, lower motor weakness, and erectile dysfunction. Still others develop uveitis, infective dermatitis, or other inflammatory disorders. HTLV-2 is associated with milder neurologic disorders and chronic pulmonary infections.

Many HIV-infected patients are co-infected with HTLV-1. Their inflammatory response is more severe, leading to exacerbation in chronic co-morbid diseases, such as peripheral neuropathy, arthritis, and asthma. Patients with an HIV-HTLV co-infection may experience greater morbidity, leading to a reduced quality of life.

Diagnosis

HTLV-1 and -2 infections are detected using ELISA, which then must be confirmed with Western blot, immunofluorescence assay, or PCR. PCR or EIA with virus-specific synthetic peptides is necessary to distinguish between HTLV-1 and HTLV-2. PCR is also necessary in infants who may have false-positive results because of circulating maternal anti-HTLV antibodies. It is also used to determine the HTLV viral load, which is helpful in determining disease progression in patients with HAM.

Due to the distinct possibility of co-infection, patients diagnosed with HTLV-1 or HTLV-2 should:

- Consider being tested for HIV.
- Have routine blood work performed, including: CBC with differential and peripheral blood smear, complete chemistry with calcium level, liver function tests, and LDH.
- Have the following laboratory testing: Viral hepatitis serology (A, B, C), RPR, purified protein derivative, *Strongyloides stercoralis* serology, and stool examination for ova and parasites.

The florid immunosuppression and inflammatory response induced by HTLV may predispose individuals to OIs. Therefore, screening for TB and *Strongyloides stercoralisi* is recommended. Clinicians should also consider the likelihood of other OIs, such as molluscum contagiousum and complications of *Staphylococcus* and *Streptococcal* infections like skin abscess and renal failure.

Treatment

No treatment intervention exists for acute or chronic HTLV infection. Patients should be managed within a chronic disease framework, with regular visits to their health care providers based on prevailing signs and symptoms. Visits should include a full physical examination, including thorough ophthalmological- and neurological examinations, as well as additional blood work, such as CBC with peripheral blood smear.

Treatment for complications like adult T-cell leukemia should be the same as in any other case.
Treatment for HAM is currently limited to symptomatic therapy. Consultations with an infectious disease specialist, a neurologist and an oncologist are advised depending on the HTLV-induced complications.

In patients co-infected with HIV and HTLV-1, a hyperimmune proliferative response and an abnormally high CD4 count may occur. This may lead to a false interpretation of the actual immune status of the individual, which has implications for starting HAART. In cases of this coinfection, it is better to use the CD4 percentage as a determination, as it gives a truer picture of the patient's immune status.

Prevention

Preventing HTLV-1 and -2 infections is the cornerstone of controlling their spread.
Considerations should be given to both horizontal and vertical transmission. Prevention should focus on consistent and correct condom use, avoidance of breastfeeding screening of blood donors, avoidance of blood donors. Partners of index patients should be referred for investigation and management.

9.19 Proctitits, Proctocolitis and Enteritis

Sexually transmitted gastrointestinal syndromes include proctitis, proctocolitis, and enteritis. Evaluation for these syndromes should include appropriate diagnostic procedures (e.g., anoscopy or sigmoidoscopy, stool examination, and culture).

Proctitis, an inflammation of the rectum (i.e., the distal 10–12 cm), occurs predominantly among persons who participate in receptive anal intercourse and associated with anorectal pain, tenesmus, or rectal discharge. The common pathogens involved include N. gonorrhoeae, C. trachomatis, T. pallidum, and HSV.

Proctocolitis is acquired primarily through receptive anal intercourse (can also be acquired though oral- anal contact) and is associated with symptoms of proctitis, diarrhea or abdominal cramps, and inflammation of the colonic mucosa extending to 12 cm above the anus. The common pathogens involved include Campylobacter sp., Shigella sp., Entamoeba histolytica, and LGV serovars of C. trachomatis. CMV or other opportunistic agents can be involved in immunosuppressed HIV-infected patients.

Enteritis occurs through oral-anal contact and usually results in diarrhea and abdominal cramping without signs of proctitis or proctocolitis. Sexual transmission as the modeof spread, should be considered in outbreaks of gastrointestinal illness occur among social or sexual networks of MSM. Among persons with HIV infection, enteritis can be caused by pathogens that may not be sexually transmitted, including CMV, Mycobacterium avium–intracellulare, Salmonella sp., Campylobacter sp., Shigella sp., Cryptosporidium, Microsporidium, and Isospora.

Diagnosis

Diagnosis include examination by anoscopy, a gram-stained smear of any anorectal exudate from anoscopic or anal examination should be examined for polymorphonuclear leukocytes.

Table 79: Treatment of Acute Proctitis

Recommended Regimen	Special circumstance
Ceftriaxone 250 mg IM in a single dose PLUS Doxycycline 100 mg orally twice a day for 7 days	MSM with bloody discharge, perianal ulcers or mucosal ulcers Ceftriaxone 250 mg IM in a single dose **PLUS** Doxycycline 100 mg orally twice a day for **3 weeks** *If painful ulcers – treat for genital herpes (see section on HSV)*

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other Management Considerations for HTLV

1. Counsel to abstain from sexual intercourse until they and their partner(s) have been adequately treated (i.e., until completion of a 7-day regimen and symptoms resolved).
2. Conduct additional testing for STIs- HIV, Syphilis.
3. Retest after 3 months- N. Gonorrhoes and C. Trachomatis.
4. Sexual contacts during the 60 days preceding the onset of symptoms should be evaluated, tested, and presumptively treated for chlamydia and gonorrhea. If the last sexual intercourse was >60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated. Strategies for partner management should be used including partner expedited therapy.

9.20 Exoparasitic Infections

STI-related ectoparasitic infections are usually found in adults rather than children. The clinical presentation depends on the causative organism.

9.20.1 Scabies

Scabies is caused by the mite *Sarcoptes scabiei*, which burrows into the skin of the infected individual. Protease enzymes in the faecal matter induce a hypersensitivity reaction that causes puritis. Puritis occurs about 2–6 weeks after infestation, though subsequent infestation may produce sensitization and lead to puritis within 24 hours of infection. The mites produce burrows, papules, pustules, nodules, occasionally urticarial papules, and plaques, usually located between web space of fingers, flexor aspects of the wrists, axilla, antecubital area, abdomen, umbilicus, genitals, gluteal areas, and feet. In women, the nipples and areolae of the breasts often are affected. In men, red papules or nodules are typically found on the penile glans, shaft, and scrotum. Compared with adults, scabies in infants and young children tends to be more disseminated and, while the head and face usually are spared in adults, they may be affected in the very young. Complications from scabies include secondary bacterial infections such as impetigo, furunculosis and cellulitis.

Crusted scabies (e.g., Norwegian scabies) is an aggressive form of scabies that usually occurs in the debilitated, malnourished, in PLHIV, including persons receiving systemic or potent topical glucocorticoids, organ transplant recipients, persons with HIV infection or human T-lymphotrophic virus-1-infection, and persons with hematologic malignancies.

Diagnosis

Diagnosing the presence of *Sarcoptes scabiei* relies on the identification of mites, eggs, eggshell fragments, or mite pellets (scybala). This is best tested by placing a drop of mineral oil directly over the burrow on the skin and then superficially scraping it longitudinally and laterally with a scalpel blade. Failure to find mites under the microscope does not rule out the diagnosis. Final diagnosis is based on history, physical examination of/for burrows, and microscopic examination of mites, eggs, and scybala on mineral oil preparation.

Treatment

Treatment for scabies requires careful monitoring and a combination of therapies, with consideration to the index patient, their partners, and household contacts. Treatment of the index patients involves whole body treatment application at night followed by bathing with soap for optimal results.

Table 80: Recommended treatment for Scabies

Recommended Regimen	Alternative Regimen
Permethrin 5% cream applied to all areas of the body from the neck down and washed off after 8–14 hours. Repeat 1 week later if necessary. Infants and young children should be treated with permethrin.	Lindane (1%) 1 oz of lotion or 30 g of cream applied in a thin layer to all areas of the body from the neck down and thoroughly washed off after 8 hours ***Lindane is recommended as an alternative regimen because of toxicity and should only be used if the patient cannot tolerate the recommended therapies or if these therapies have failed.*** ***Lindane should not be used immediately after a bath or shower.*** ***Lindane should not be used by persons who have extensive dermatitis or children aged <10 years.*** ***Seizures have occurred when lindane was applied after a bath or used by patients who had extensive dermatitis. Aplastic anemia after lindane use also has been reported.***
Ivermectin 200ug/kg orally, repeated in 2 weeks	
Notes: Infants and young children aged <10 years should not be treated with lindane.	

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for Scabies

1. Bedding and clothing should be decontaminated (i.e., either machine-washed, machine-dried using the hot cycle, or dry cleaned) or removed from body contact for at least 72 hours.
2. Persons with scabies should be advised to keep fingernails closely trimmed to reduce injury from excessive scratching.
3. Persons who have had sexual, close personal, or household contact with the patient within the month preceding scabies infestation should be examined. Those found to be infested should be provided treatment accordingly.
4. Scabies epidemics frequently occur in nursing homes, hospitals, residential homes, children homes (orphanages) and drop in centers. All persons including staff and the family members irrespective of whether they are itching should be treated. The entire population should be treated Ivermectin especially if treatment with topical scabicides fails.

9.20.2 Pediculosis Pubis

Pediculosis pubis (lice) is caused by the louse *Phthirus pubis*. There are three different types of lice: *Pediculosis capitis* (head lice), *Pediculosis corporis* (body lice), and *Pediculosis pubis* or *Pthirus pubis* (pubic lice, sometimes called 'crabs'). Lice spreads from person to person via close physical contact or through fomites (e.g., combs, clothes, hats, linens). Overcrowding encourages the spread of lice. The body louse is the vector of typhus, trench fever, and relapsing fever.

Pthirus pubis (pubic lice) is an STI. Pubic lice are white to gray and oval in shape, and have a smaller abdomen than both *Pediculosis capitis* and *Pediculosis corporis*. Their average life span is about 24 hours. Humans are the only reservoir for them and transmission occurs through intimate sexual and non-sexual contact. Infestation is usually found around the coarse hairs on the groin and perianal areas but it can also extend to the eyelashes, eyebrows, facial hair, axillary hair, and occasionally the periphery of the scalp.

The bite of the pubic louse produces an inflammatory reaction; symptoms include itching, scratching, erythema, and skin irritation that can be very disconcerting to the infected individual.
After being bitten, small blue spots can appear on the skin resulting in hyperpigmentation. Extensive infestation can lead to systemic symptoms of fever, malaise, and secondary bacterial skin infection involving *Staphylococcal* and *Streptococcal* bacteria.

Diagnosis

Diagnosis is based on a thorough history and physical examination, including a careful search for adult lice and eggs. It may be helpful to look in the hair for an area of scabs with nits. Nits attach to hair and are not loose and flaky. It might be necessary to examine nits or scabs with a microscope; placing cellulose tape over an infested area then putting the lice-stuck tape on a microscopic slide is an easy way to prepare them for examination. A Woods lamp examination of the area considered to be

infested is another way to determine the presence of pubic lice—they will show up yellow-green under fluorescence.

Treatment

Table 81: Recommended treatment for pubic lice

Recommended Regimens	Alternative Regimens	Treatment in Pregnant and lactating women
Permetherin 1% cream rinse daily for 3 days applied to affected areas and washed off after 10 minutes; may be repeated in 1 week **OR** Pyrethirins with piperonyl butoxide applied to the affected area and washed off after 10 minutes.	Malathion 0.5% lotion applied for 8–12 hours then washed off **OR** Ivermectin 250ug/kg orally, repeated in 2 weeks	Permetherin 1% cream rinse daily for 3 days applied to affected areas and washed off after 10 minutes; may be repeated in 1 week **OR** Pyrethirins with piperonyl butoxide applied to the affected area and washed off after 10 minutes.
Notes: Malathion can be used when treatment failure is believed to have occurred as a result of resistance. Ivermectin might not prevent recurrences from eggs at the time of treatment, and therefore treatment should be repeated in 14 days. Ivermectin should be taken with food because bioavailability is increased, in turn increasing penetration of the drug into the epidermis. Lindane use during pregnancy has been associated with neural tube defects and mental retardation. It can also accumulate in the placenta and in breast milk.		

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Other management considerations for pediculosis pubis

1. In patients with damaged or excoriated skin, consider dose modification to compensate for increased absorption of topical agents.
2. Testing for other STIs—especially HIV—should be considered for persons presenting with lice infection.
3. Pediculosis of the eyelashes should be treated with occlusive ophthalmic ointment or petroleum jelly to the eyelid margins twice a day for 10 days.
4. Bedding and clothing should be decontaminated or removed from body contact for at least 72 hours.
5. Sex partners within the previous months should be treated.
6. Avoid sexual contact until both partners are treated.

9.21 Sexual Assault, Abuse and STIs

9.21.1 Sexual Assault and Abuse and STDs Adolescents and Adults

This section of the guidelines addresses the identification, prophylaxis, and treatment of STDs and conditions among adolescent and primarily adult female sexual assault survivors.

Examinations of survivors of sexual assault should be conducted by an experienced clinician in a way that minimizes further trauma to the survivor. The decision to obtain genital or other specimens for STD diagnosis should be made on an individual basis with consideration for any legal requirements. Collection of sample should not delay empiric prophylactic antimicrobial treatment.

The more common diagnosed infections associated with sexual assault include Trichomoniasis, BV, gonorrhea, and chlamydia. Sexual assault is also associated with HBV and can be prevented through post exposure vaccination (see section on Hepatitis B). Similary, female survivors are at a risk for acquiring HPV, however because of the efficacy of the HPV vaccine is high, HPV vaccination is also recommended for females through age 26 years.
All reproductive-aged female survivors should be evaluated for pregnancy including a point of care pregnancy test.

Evaluating Adolescents and Adults for STDs Initial Examination

The following can be considered:

- NAATs for C. trachomatis and N. gonorrhoeae at the sites of penetration or attempted penetration.
- NAATs from a urine or vaginal specimen or point-of-care testing (i.e., DNA probes) from a vaginal specimen for T. vaginalis.
- Point-of-care testing and/or wet mount with measurement of vaginal pH and KOH application for the whiff test from vaginal secretions should be done for evidence of BV and candidiasis, especially if vaginal discharge, malodor, or itching is present.
- Rapid testing for HIV to consider post exposure prophylaxis
- A serum sample for evaluation of hepatitis B, and syphilis infections.

Treatment

Presumptive treatment is recommended:
An empiric antimicrobial regimen for chlamydia, gonorrhea, and trichomonas.

Table 82: Treatment for sexual assault cases

Recommended regimen
Ceftriaxone 250 mg IM in a single dose PLUS Azithromycin 1 g orally in a single dose PLUS Metronidazole 2 g orally in a single dose OR Tinidazole 2 g orally in a single dose

Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

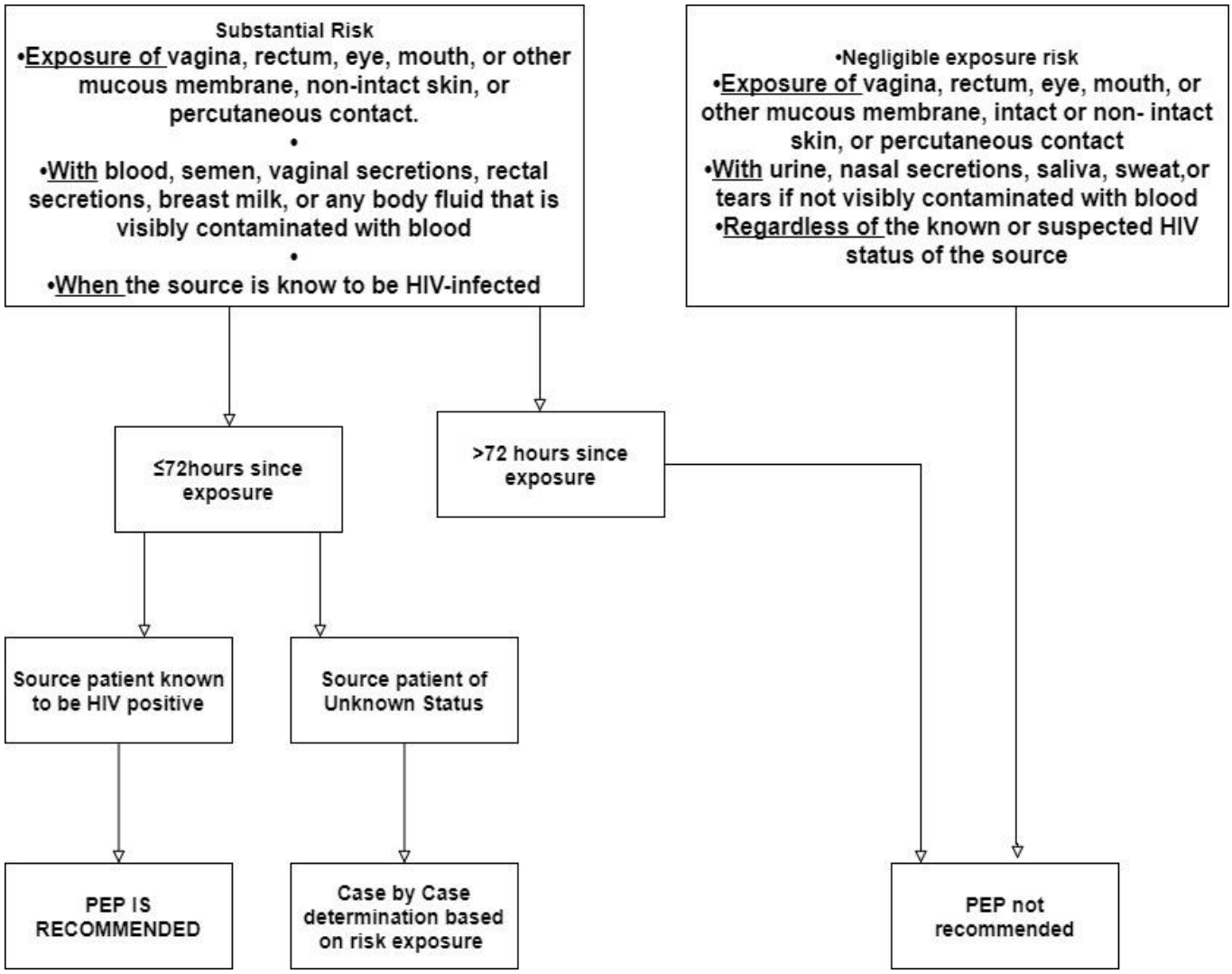
Other management considerations for sexual assault cases

- Emergency contraception for women of reproductive age.
- Hepatitis B post exposure prophylaxis as follows:
  - Postexposure hepatitis B vaccination without HBIG in cases where the hepatitis status of the assailant is unknown and the survivor is unvaccinated. Administer vaccine at the time of initial examination with repeat doses at 1-2 and 4-6 months
  - Postexposure hepatitis B vaccination with HBIG in cases where the assailant is HBsAg-positive and the survivor is unvaccinated. Administer vaccine at the time of initial examination with repeat doses of the vaccine at 1-2 and 4-6 months
  - Survivors who were previously vaccinated but did not receive postvaccination testing should receive a single vaccine booster dose (see section on hepatitis B).
- HPV vaccination:
  - Female survivors aged 9–26 years and male survivors aged 9–21 years.

- MSM with who have not received HPV vaccine or who have been incompletely vaccinated, vaccine can be administered through age 26 years.
- Administer vaccination at the time of the initial examination, and follow-up dose administered at 1–2 months and 6 months after the first dose.

- Post exposure prophylaxis (PEP) for HIV. Assessment of the risk and recommendation for PEP is done on a case by case basis. In the event that a decision is made to start PEP, this should be done as early as possible and no later than 72 hours post assault. The framework, figure 8.5 recommended by CDC is also applicable to the OECS and is used to evaluate the need for PEP for sexual assault cases. In the event that PEP is recommended, patient should have a negative HIV test an initial assessment and followed up based on the PEP algorithm defined in figure 16.

Figure 16: *HIV post exposure algorithm*



Source: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR. 2015; 64(3) (12). Available from: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

9.21.2 Sexual Assault or Abuse of Children

Sexually transmitted infections in children beyond the neonatal period strongly suggests sexual abuse. Postnatally acquired gonorrhea and syphilis; chlamydia infection; and nontransfusion, nonperinatally acquired HIV are indicative of sexual abuse. Sexual abuse should be suspected when genital herpes, T.

vaginalis, or anogenital warts are diagnosed. Most HBV infections in children result from household exposure to persons who have chronic HBV infection rather than sexual abuse.
Sexual abuse among children should be investigated clinicians who have experience and training in all elements of the evaluation of child abuse, neglect, and assault. Report to social services and legal authorities should be done in compliance with Member State specific regulations.

Evaluating Children for STDs

Evaluations of children for sexual assault or abuse should be conducted in a manner designed to minimize pain and trauma to the child and performed by an experienced clinician to avoid psychological and physical trauma to the child.

The decision to obtain genital or other specimens from a child to evaluate for STDs must be made on an individual basis; however, children who received a diagnosis of one STD should be screened for all STDs.

If a child has symptoms, signs, or evidence of an infection that might be sexually transmitted, the child should be tested for common STDs before the initiation of any treatment that could interfere with the diagnosis of those other STDs. Because of the legal and psychosocial consequences of a false-positive diagnosis, only tests with high specificities should be used. The potential benefit to the child of a reliable STD diagnosis justifies deferring presumptive treatment until specimens for highly specific tests are obtained by providers with experience in the evaluation of sexually abused and assaulted children. Evaluations should be scheduled on a case-by-case basis according to history of assault or abuse and in a manner that minimizes the possibility for psychological trauma and social stigma. If the initial exposure was recent, the infectious organisms acquired through the exposure might not have produced sufficient concentrations of organisms to result in positive test results or examination findings. Alternatively, positive test results following a recent exposure might represent the assailant's secretions (but would nonetheless be an indication for treatment of the child). A second visit approximately 2 weeks after the most recent sexual exposure should be scheduled to include a repeat physical examination and collection of additional specimens to identify any infection that might not have been detected at the time of initial evaluation. A single evaluation might be sufficient if the child was abused for an extended period of time and if a substantial amount of time elapsed between the last suspected episode of abuse and the medical evaluation. Compliance with follow-up appointments might be improved when law enforcement personnel or child protective services are involved.

9.2 Factors that should lead the physician to consider screening for STD include:

1. Child has experienced penetration or has evidence of recent or healed penetrative injury to the genitals, anus, or oropharynx.
2. Child has been abused by a stranger.
3. Child has been abused by a perpetrator known to be infected with an STD or at high risk for STDs (e.g., intravenous drug abusers, MSM, persons with multiple sexual partners, and those with a history of STDs).
4. Child has a sibling, other relative, or another person in the household with an STD.
5. Child lives in an area with a high rate of STD in the community.
6. Child has signs or symptoms of STDs (e.g., vaginal discharge or pain, genital itching or odor, urinary symptoms, and genital lesions or ulcers).
7. Child or parent requests STD testing.

Examination of Children with STIs- the following is recommended

1. Visual inspection of the genital, perianal, and oral areas for genital discharge, odor, bleeding, irritation, warts, and ulcerative lesions. Obtain specimen from all vesicular or ulcerative genital or perianal lesions for viral culture or PCR.

2. Collect specimens from the pharynx and anus in boys and girls, the vagina in girls, and the urethra in boys for N. Gonorrhoea culture.
3. For boys with a urethral discharge, a meatal specimen discharge is an adequate substitute for an intraurethral swab specimen.
4. Culture for C. trachomatis from specimens collected from the anus in both boys and girls and from the vagina in girls.
5. Culture for T. vaginalis infection and wet mount of a vaginal swab specimen for T. vaginalis infection.
6. Wet mount of a vaginal swab specimen for BV.
7. Collection of serum samples to be evaluated, preserved for subsequent analysis, and used as a baseline for comparison with follow-up serologic tests.
8. Conduct HIV rapid test -Children might be at higher risk for HIV acquisition than adolescent and adult sexual assault or sexual abuse survivors because the sexual abuse of children is frequently associated with multiple episodes of assault and mucosal trauma might be more likely.

(Serologic testing for HIV infection should be considered for sexually abused children. The decision to test for HIV infection should involve the family, if possible, and be made on a case by-case basis depending on the likelihood of infection among assailant(s).

Sera can be tested for antibodies to T. pallidum, HIV, and HBV. Decisions regarding the infectious agents for which to perform serologic tests should be made on a case-by-case basis.

Treatment

Presumptive treatment for children who have been sexually assaulted or abused is not recommended because 1) the incidence of most STDs in children is low after abuse/assault, 2) prepubertal girls appear to be at lower risk for ascending infection than adolescent or adult women, and 3) regular follow-up of children usually can be ensured.

Other Management Considerations for sexual assault of children

Child sexual assault survivors are generally at risk of future sexual assault and an increased risk of future unsafe sexual practices. This puts them at higher risk for HPV infection and therefore vaccination is recommended for children who are victims of sexual abuse or assault at age ≥9 years who have not initiated or completed immunization.

9.22 Surveillance

Surveillance—the process by which behaviour is monitored for the purpose of influencing, managing, directing, or protecting the health of the individual and the public—is an important part of STI management. Surveillance is done at all levels of the health care system. Examining the various STI trends in the community enables clinicians to identify high-risk groups and also to employ programmatic interventions that aim to improve quality of life for patients and the public. Surveillance reports should be shared with all stakeholders so that they know what is going on in various regions of the country. Ideally, an annual surveillance report detailing the incidence and prevalence of various diseases around the country would be written by the epidemiology department of the ministry of health.

Data collection and reporting on observed trends are needed for clinical monitoring and programme performance evaluation. It is important that registers are established to keep records of key clinical and programme indicators, such as attendance and STIs diagnosed, and to capture demographic information, such as age and sex of patients. This information, when cross-tabulated, serves to answers questions like who is accessing care and which STIs are most affecting certain groups. Based on this data, targeted interventions can then be planned, organized, and implemented to more effectively control the spread of STIs. Further, data can be used to measure the success of programmes as well as to improve programme activities to better deliver services to the community.

Apart from programmatic monitoring, it is essential that clinical information be collected and reported for the purpose of treatment decision-making. Registers of drug sensitivities related to antimicrobial and antiviral medications used in care should be established, supplemented by research surveys and studies to ascertain drug resistance patterns, especially in the case of gonorrhoea, which can be difficult to treat due to emerging resistance. The information gleaned from such clinical evidence would strengthen microbiological surveillance and early warning systems for drug resistance, which, in turn, provide the basis for updating STI/HIV treatment and care guidelines.

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