THE REPUBLIC OF UGANDA

Ministry of Health

ADDENDUM TO THE NATIONAL ANTIRETROVIRAL TREATMENT GUIDELINES

DECEMBER 2013

ADDENDUM TO THE ANTIRETROVIRAL TREATMENT GUIDELINES FOR UGANDA

Foreword

Ministry of Health in collaboration with partners has rolled out comprehensive HIV prevention, care and treatment with a significant focus on Prevention of Mother to Child Transmission (PMTCT) and Infant and Young Child Feeding (IYCF). This is in addition to the rapid scale up of ART amongst adults and children. Ministry of Health promotes integration of HIV services into the existing health care system in order to ensure sustainability. Hence, since 2011 the MOH has developed integrated ART, eMTCT and IYCF guidelines. The current guidelines are meant to facilitate integration of these services and promote a family-centred approach to HIV prevention, care and treatment.

The 2011 guidelines have been revised to incorporate the 2013 recommendations from WHO and the current national program evidence. It is important to note that these guidelines address the critical areas of key populations and serodiscordance and also expand the eligibility criteria for ART by raising the cut-off CD4 point to 500 cells/mm^3. This is a programmatically significant milestone in achieving the country goal of attaining universal access to care and treatment and reaching the country targets and elimination commitments.

The other key areas that have been incorporated in the 2013 guidelines are the diagnosis and management of cryptococcal infections, family planning in the context of ART, which areas had previously not been well addressed. The country will continue to roll out the new eMTCT initiative of lifelong treatment of pregnant and lactating mothers aimed at elimination of new paediatric HIV infection through vertical transmission. The new guidelines also recommend treating all children below 15 years irrespective of CD4 count in order to improve enrolment of children into care and treatment. Furthermore, these guidelines address key aspects of adolescence HIV services.

These guidelines have been developed as an addendum to the 2011 Integrated Guidelines for use by health workers at all level health service delivery. The guidelines will go a long way to assist health workers to provide high quality and standardized HIV prevention, care and treatment services to people living with HIV (PLHIV). It is my sincere hope that this document will contribute tremendously to efforts geared towards the HIV-free generation.

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Addendum to National ART Integrated Guidelines

1- Serodiscordance

An HIV positive adult in a stable relationship with an HIV negative partner who is motivated to commence and adhere to early combination ART, and provided both partners in the couple have recently been tested for HIV and counseled as a couple, should be commenced on combination ART regardless of their CD4 count.

2- Contraceptives and ARVs

Contraception is an important component of comprehensive HIV care as unplanned pregnancy can cause social, financial and physical problems to women, especially those who are HIV positive. In addition, reduction in unplanned pregnancy in women who are HIV positive can also reduce potential for mother to child transmission of HIV. However, contraception in HIV positive couples is a complex issue, and couples should be adequately counseled to enable them to make the best contraceptive choice. Women and couples should be counseled that condoms provide coverage from STI and HIV transmission, whereas other forms of contraception do not.

Whilst recent evidence from some studies shows an increased risk of HIV infection in HIV negative women using injectable hormonal contraception, other studies show no increased risk. No increased risk of HIV acquisition has been found in women using oral hormonal contraception. The WHO advises that women taking hormonal contraceptives should be counseled to use condoms to reduce risk of HIV acquisition.

There is some observational evidence that women using injectable hormonal contraception may be more likely to transmit HIV to their partners. This has not been found in women using oral hormonal contraceptives. HIV positive women using hormonal contraception should be advised to use condoms to prevent against HIV transmission to their partners.

Women seeking contraception should be advised that there is no evidence that hormonal contraception causes a decrease in CD4 count, an increase in viral load, or progression to AIDS event or death.

Drug interactions are common with HIV drugs and contraceptives. The following table summarizes possible interactions between ART and hormonal contraception currently available from MOH, and advise on management of these interactions.

Type of Contraception	HIV drug				
	NRTI (AZT/3TC/ FTC/TDF/ABC)	Nevirapine	Efavirenz	LPR/r	ATZ/r
Combined oral *(microgynon, Lofeminal)*	Nil	Risk of contraceptive failure– must be used with a barrier method	Risk of contraceptive failure– must be used with a barrier method	Risk of contraceptive failure– must be used with a barrier method	Risk of contraceptive failure – must be used with a barrier method *(COCP with higher dose ethynl estradiol is advised)*
Emergency contraception *(Postinor-2)*	Nil	Levels of levonorgestrel reduced – increase dose of Postinor to 4 tablets	Levels of levonorgestrel reduced – increase dose of Postinor to 4 tablets	Levels of levonorgestrel reduced – increase dose of Postinor to 4 tablets*	Levels of levonorgestrel reduced – increase dose of Postinor to 4 tablets *
Injectable *(Depo-Provera)*	Nil	Nil	Limited information, additional barrier method advised	Nil	Limited information, alternative method advised
Implants (Implanon, Jadelle)	Nil	Levels of levonorgestrel reduced, additional barrier method advised	Levels of levonorgestrel reduced, additional barrier method advised	Levels of levonorgestrel reduced, additional barrier method advised	Limited information, alternative method advised
IUD *(TCu 380A)*	Nil	Nil	Nil	Nil	nil
Condoms	Nil	Nil	Nil	Nil	nil

*very little information – awaiting confirmation

There are no significant drug interactions of hormonal contraception on levels of these ART drugs.

There are a few things to consider when providing Family Planning counseling to HIV positive women. If an HIV positive woman comes for FP and is on ARVs. Find out what specific ARVs she is taking.

- If a client is on Nevirapine in whatever combination and wants to start or is using Depo-Provera, emphasize that it is important to return for her next injection on the date indicated on her appointment card. She can also come just before that date in case she cannot make it on the appointment date. The 2 week grace period (providing the injection up to 2 weeks late) is NOT advisable for these clients because Nevirapine may reduce the progestin in DMPA at the end of the three months
- If a client is taking Nevirapine in whatever combination and wants to start combined oral contraceptives (COCs) emphasize that it's important to take the pills (COCs) regularly everyday or she is more likely to get pregnant.
- Rifampicin that is used for treatment of tuberculosis interferes with combined oral contraceptive pills, progestin only pills and Norplant rendering them less effective. The most effective family planning method for such a client is Depo-Provera.
- When an HIV positive client is given Rifampicin, Efavirenz is usually given instead of Nevirapine.
- If a woman is taking Efavirenz and wants to start a family, help her to select a VERY EFFECTIVE family planning method. If client desires Depo-Provera, advise client to come to the clinic immediately every three months for the repeat injection.
- Dual protection family planning services should be promoted among women living with HIV and their husbands/partners to help them avoid unintended pregnancies, HIV transmission and/or re-infection. Female and male condoms are currently the only barrier devices against transmission or acquisition of HIV. All sexually-active people should be offered "dual protection" against unintended pregnancy and HIV or other sexually transmitted infections. Strategies using "proven" methods to meet this goal include being in a monogamous relationship in which both partners are free of STIs/HIV and at least one is using effective contraception.
- Dual method use where one method is used to protect against unintended pregnancy (often a hormonal method or other highly effective non-coitally dependent contraceptive) and a second is used to protect against STIs.

Initiate family planning services as an integral component of ART services as women attending ART clinics have sustained contact with health workers and this can be used as an opportunity to provide them with family planning services

There is conflicting data regarding the increased risk of acquisition and or the spread of HIV and injectable hormonal contraception among HIV sero-discordant couples. Hormonal contraception doesn't increase the risk of HIV disease progression and it should be offered as a family planning option in the HIV positive women.

3- Management of HIV-infected patients with active tuberculosis

Timely ART initiation in eligible patients is an important component of effective ART services. In the past, a delay in initiating ART in patients with TB and HIV often was favored because of the potential complications of high pill burden, additive toxicities, drug interactions, adherence, and the potential for development of IRIS. Recently, three randomized controlled trials showed that starting ART at 2 vs. 8-12 weeks reduced mortality in patients co-infected with TB and with CD4 levels < 50/µl. AIDS Clinical Trials Group (ACTG) 5164 demonstrated that in patients with OI's (excluding tuberculosis), starting ART within 2 weeks reduced mortality and AIDS progression by 50%. In each of these studies, immune reconstitution inflammatory syndrome (IRIS) was more common in patients initiating ART earlier than in patients starting ART later, but the syndrome was infrequently associated with mortality. Both ART and TB treatment should be continued while managing IRIS. Patients with mild or moderately severe IRIS can be managed symptomatically or treated with non-steroidal anti-inflammatory agents. Patients with more severe IRIS can be treated successfully with corticosteroids.

The new findings mean that the current paradigm that ART is not an "emergency" must be revised in a subset of patients.

The principles for treatment of active tuberculosis (TB) disease in HIV-infected patients remain the same as those for HIV uninfected patients. However,

- All HIV-infected patients with diagnosed active TB should be started on TB treatment immediately.
- All HIV-infected patients with diagnosed active TB should be treated with antiretroviral therapy (ART).

- All TB patients co-infected with HIV should be offered ART irrespective of CD4 cell count no later than 8 weeks and within 2 weeks of starting TB treatment among those with advanced immune suppression (CD4 <50).
- In HIV infected patients with TB meningitis, ART should be deferred until 2 months after initiation of TB treatment.
- In all HIV-infected pregnant women with active TB, ART should be started as early as feasible, both for maternal health and for prevention of mother-to-child transmission (PMTCT) of HIV

It is important to anticipate and to manage the immune reconstitution inflammatory syndrome that will likely occur with earlier initiation of ART in patients with TB or other OIs.

Particular attention should be paid to the interaction between anti-retroviral and anti-tuberculosis drugs

4. Cryptococcal Disease and HIV

The recommendations on diagnosis, prevention and management of cryptococcal disease (meningeal and non-meningeal) in adults, adolescents, and children are based on several guiding principles:

- Early ART initiation is the most important and cost-effective preventive strategy to reduce the incidence and high mortality associated with cryptococcal meningitis. Patients should ideally initiate ART at a CD4 count of 500 cells/mm^3, and definitely before a decline in the CD4 cell count to less than 200 cells/mm^3, or development of WHO stage 3 or 4 disease.
- Early diagnosis is key to improving mortality due to cryptococcal disease. Clinicians need to have a low threshold for suspecting cryptococcal meningitis.
- Reliable access to rapid diagnostic CrAg assays, either lateral flow assay (LFA) or latex agglutination (LA) for use with serum or plasma and/or cerebrospinal fluid (CSF) should be prioritized.
- Prompt referral for HIV testing and care should be undertaken as soon as appropriate following diagnosis of cryptococcal disease, to facilitate early HIV diagnosis, uptake of ART and retention in care.
- Optimal use of antifungal treatment regimens and approaches can improve survival, clinical and neurological outcomes, and rapid fungal clearance, while minimizing drug related toxicities.

The major recommendations include:

a. Screening and Prevention of cryptococcal disease

All ART naïve PLHIV with CD4 levels of less than 100cells/mm^{3}should be screened for presence of cryptococcal antigen (CrAg) either using serum or plasma irrespective of symptoms. It is recommended that CrAg screening is done using either CrAg LFA or CrAg LA, depending on availability of tests. The LFA can be used with either serum or plasma, including left over plasma after CD4 testing.

Routine screening is not necessary/indicated for patients with prior history of cryptococcal meningitis; however, evaluation for relapse disease and/or IRIS is recommended if with new symptoms of meningitis. CSF culture is the key diagnostic test for distinguishing IRIS from relapse. In the absence of culture, an elevated CSF WBC count >25 cells/mm^3 is more suggestive of IRIS in a person compliant with anti-fungal and antiretroviral medications.

The routine use of antifungal primary prophylaxis for cryptococcal disease in HIV-infected adults, adolescents and children with a CD4 count less than 100 cells/mm^3, and who are CrAg-negative or where CrAg status is unknown, is not recommended prior to ART initiation, unless a prolonged delay in ART initiation is likely.

In the event of a delay in initiating ART, the patient should be re-evaluated for symptoms and signs of meningitis and a serum CRAG test repeated 6 weeks after the first test. Routine serum or plasma CrAg screening in ART-naïve adults (but not adolescents or children), followed by pre-emptive anti-fungal therapy if CrAg positive may be considered prior to ART initiation in patients with a CD4 count less than 100 cells/mm^3, and where this population also has a high prevalence of cryptococcal antigenemia[1].

The prevalence of cryptococcal antigenemia in PLHIV in Uganda with CD4 <100 cells/mm^3 is between 5-10%. Treatment of asymptomatic CrAg positive persons is fluconazole 800mg/day for 2 weeks followed by fluconazole 400mg/day for 8 weeks (see algorithm in figure below).

b. Diagnosis of cryptococcal disease

Rapid CrAg assay (either LFA or LA) using serum or plasma is the preferred diagnostic approach for non-meningeal cryptococcal disease and where appropriate (for symptomatic patients) prompt lumbar puncture (LP) for diagnosis of meningeal disease[2].

c. Induction, consolidation and maintenance treatment regimens

For the two-week induction treatment phase, a regimen containing amphotericin B combined with Flucytosine or fluconazole is the recommended option. In settings where amphotericin B is not available, regimens containing fluconazole combined

with flucytosine, or high-dose fluconazole monotherapy (1200mg/day) are suboptimal alternative options. For the eight-week consolidation treatment phase, a regimen containing oral fluconazole is the recommended option. For the maintenance treatment phase, a regimen containing oral fluconazole is the recommended option. Maintenance is given to prevent recurrence of disease after treatment and is also termed "secondary prophylaxis".

Induction Phase	**Consolidation phase**	**Maintenance phase**
2 weeks a) Amphotericin B 0.7-1mg/kg /day with Flucytosine, or High doze fluconazole 800mg/day b) Adequate rehydration	8 weeks • Fluconazole 400-800mg/ day (or 0.6mg/kg/day in children) *Begin ART at 4-5 weeks after diagnosis*	Fluconazole 200mg/day until 1 year on ART and CD4≥ 200 if viral load monitoring is not available, or CD4 ≥ 100 for > 6months with suppressed viral load. In children, fluconazole can be stopped when they reach a CD4 >25%.
2 weeks (Alternative) • 1200mg of Fluconazole/ day (or 0.6mg/kg/day in children)		

[1]For patients whose CD4 count has dropped to <100 cells/μL whilst on treatment (ART failure, interruption of treatment), a CrAg test should performed and anti -fungal therapy can considered until CD4 count rises to >200.

[2] Performing other tests for the etiology of meningitis including cells, protein, glucose and culture should be done. India ink testing of CSF alone will miss 15% of cryptococcal meningitis cases.

d. Prevention, monitoring and management of amphotericin B toxicity

In HIV-infected patients receiving amphotericin B-containing induction treatment regimens, adequate pre-hydration and electrolyte replacement MUST be done, together with toxicity monitoring to minimize the serious amphotericin B-related toxicities of hypokalaemia and nephrotoxicity. Healthcare Providers should monitor serum Potassium and Creatinine levels at treatment initiation, then at least twice a week to detect changes in renal function. Routine administration of 40 mEq/day of potassium chloride can decrease the incidence of amphotericin-related hypokalemia. Drug administration should only follow confirmation of adequate rehydration. Consider alternate day Amphotericin if creatinine is >3mg/dl.

e. Adequate control of elevated CSF Pressure

Control of increased intracranial pressure improves survival by 25% in persons with cryptococcal meningitis. All patients with a CSF Pressure > 250 mm H_2O will need a therapeutic LP the following day to reduce the CSF pressure to < 200 mm. In the absence of a manometer, one may use an IV giving set to create an improvised manometer measuring the height with a meter stick. Typically by removing 20-30 mL of CSF (even in the absence of a manometer). Most patients will need 2-3 LPs.

f. Timing of ART initiation

In HIV-infected patients with a recent diagnosis of cryptococcal meningitis, ART initiation should be deferred until there is evidence of a sustained clinical response to anti-fungal therapy and after 4 weeks of induction and consolidation treatment with amphotericin B-containing regimens, or after 4-6 weeks of treatment with a high dose oral fluconazole induction and consolidation regimen. It is important to evaluate patients for other opportunistic infections at this time.

g. Discontinuation of treatment maintenance (secondary prophylaxis)

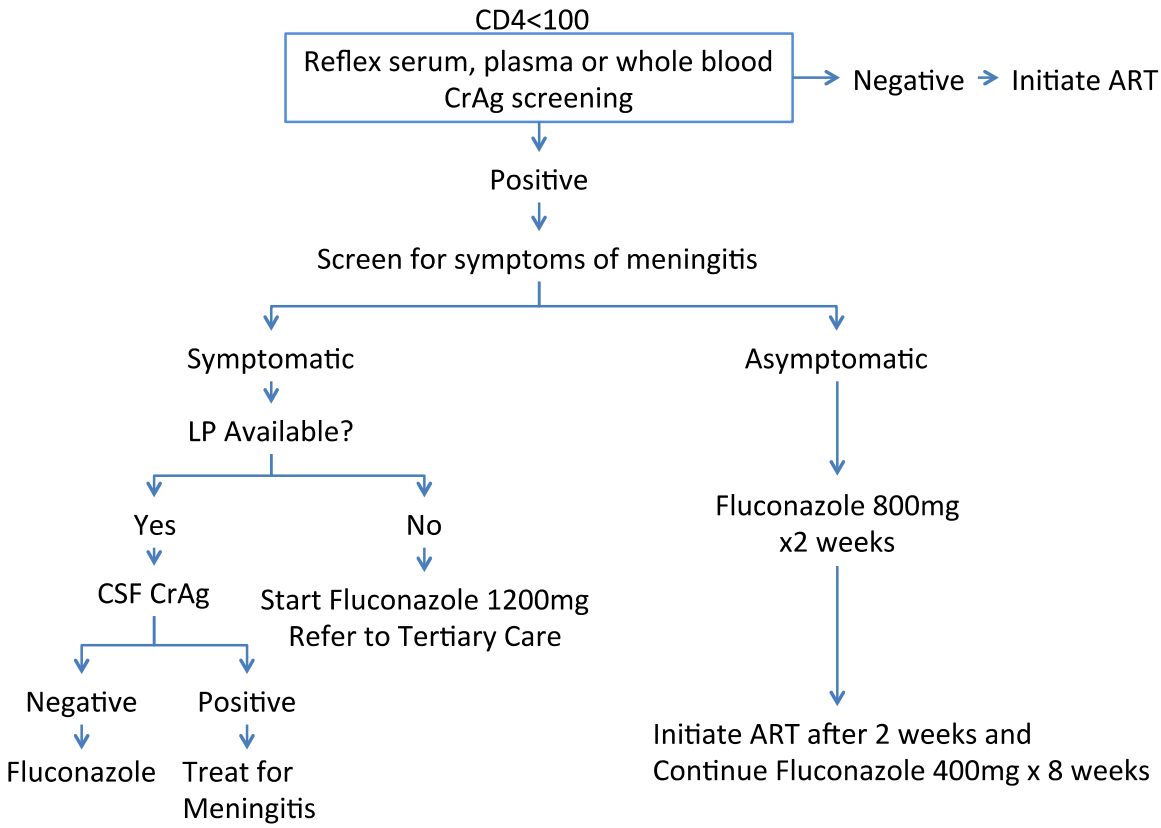
In HIV-infected adults, adolescents and children above two years of age with successfully treated cryptococcal disease, discontinuation of anti-fungal maintenance treatment is recommended when patients are stable and adherent to ART and anti-fungal maintenance therapy for at least one year and show evidence of immune reconstitution. In children aged less than two years with successfully treated cryptococcal disease, anti-fungal maintenance treatment should NOT be discontinued.

h. Special considerations during treatment:

- Antifungals and Aminoglycosides, e.g. Gentamicin: Increased risk of nephrotoxicity
- Antifungals and Cardiac Glycosides, e.g. Digoxin: Increased risk of cardiac toxicity, especially in clients with Hypokalemia
- Antifungals and Antiepileptic medicines: Antifungals may increase serum concentration of Carbamazepine, alprazolam and other benzodiazepines
- Amphotericin B and non-potassium sparing diuretics: Increased risk of hypokalemia
- Amphotericin B and Flucytosine: Amphotericin B can decrease renal clearance of 5-FC, and increase cellular uptake, which may increase the risk of 5-FC toxicity.
- Nevirapine use and Fluconazole: Fluconazole increases plasma concentration of Nevirapine and some Protease inhibitors

- TB medicines and Fluconazole: Rifampicin increases the metabolism of Fluconazole, thus increase dose of Fluconazole by 50%.
- Pregnant and breastfeeding women: Whereas there is no data against the use of Amphotericin B in pregnancy, it is not encouraged. There have been numerous reports of multiple congenital abnormalities associated with long term use of high dose Fluconazole in the first trimester of pregnant women. Flucytosine is teratogenic in animals and should only be used when no alternative is available
- Liver disease: Use with caution

Algorithm for Cryptococcal Antigen Screening in Health Facilities.



LP, lumbar puncture; CM, cryptococcal meningitis; CrAg, cryptococcal antigen; Flu, fluconazole

5- ART in Adults

- When to Start ART in Adults and Adolescents

  ART should be initiated in all individuals with HIV with CD4>350 cells/mm^3 and $\leq$ 500 cells/mm^3 regardless of clinical stage. However, priority should be given to individuals with advanced forms of disease (Clinical Stage 3 & 4) or CD4 < 350 cells/mm^3

✓ ART should be initiated in all individuals with HIV regardless of WHO Clinical Stage or CD4 in the following situations:

- HIV and active TB disease
- HIV and HBV co-infection with evidence of severe chronic liver disease
- HIV + partner in serodiscordant couples
- HIV + persons who are considered as MARPs in the hotspots (Commercial Sex Workers, Fisher folks and Truckers)

✓ ART in MARPs

HIV + fisher folks, commercial sex workers and truckers operating in hotspots should initiate ART irrespective of CD4 count since they are considered a major source of new infections. The rapid rate of transmission through this group builds up the community viral load which maintains transmission of HIV at a high level. Putting them on treatment will therefore lower the community viral load and minimize transmission rates of new infections.

✓ When to Start ART in Pregnant and Breastfeeding Women

For programmatic and operational reasons, all pregnant and breastfeeding women with HIV should initiate ART as lifelong treatment

✓ ARVs and Duration of Breastfeeding

Key principles and recommendations of 2010 remains. These include: Exclusive breastfeeding for six months and continue breastfeeding and complementary feeding for the first 12 months of life

- ✓ What ART Regimens to Start in Adults
    - First Line for Adults: 2 NRTI and 1 NNRTI
        - Preferred: TDF + 3TC + EFV
        - If the preferred choice is contraindicated or not available then consider the following:
            - AZT + 3TC + EFV
            - AZT + 3TC + NVP
            - TDF + 3TC + NVP
            - D4T use as 1st line be discontinued because of its well recognized metabolic toxicities
    - First Line for Pregnant and Breastfeeding Women and their Infants:
        - Once daily fixed dose combination of TDF+3TC+EFV recommended for pregnant including 1st trimester and breast feeding women for PMTCT
    - Infants of mothers receiving ART and are breastfeeding should receive 6 weeks of infant prophylaxis with daily NVP
    - If infants are receiving replacement feeding they should be given 6 weeks of daily NVP

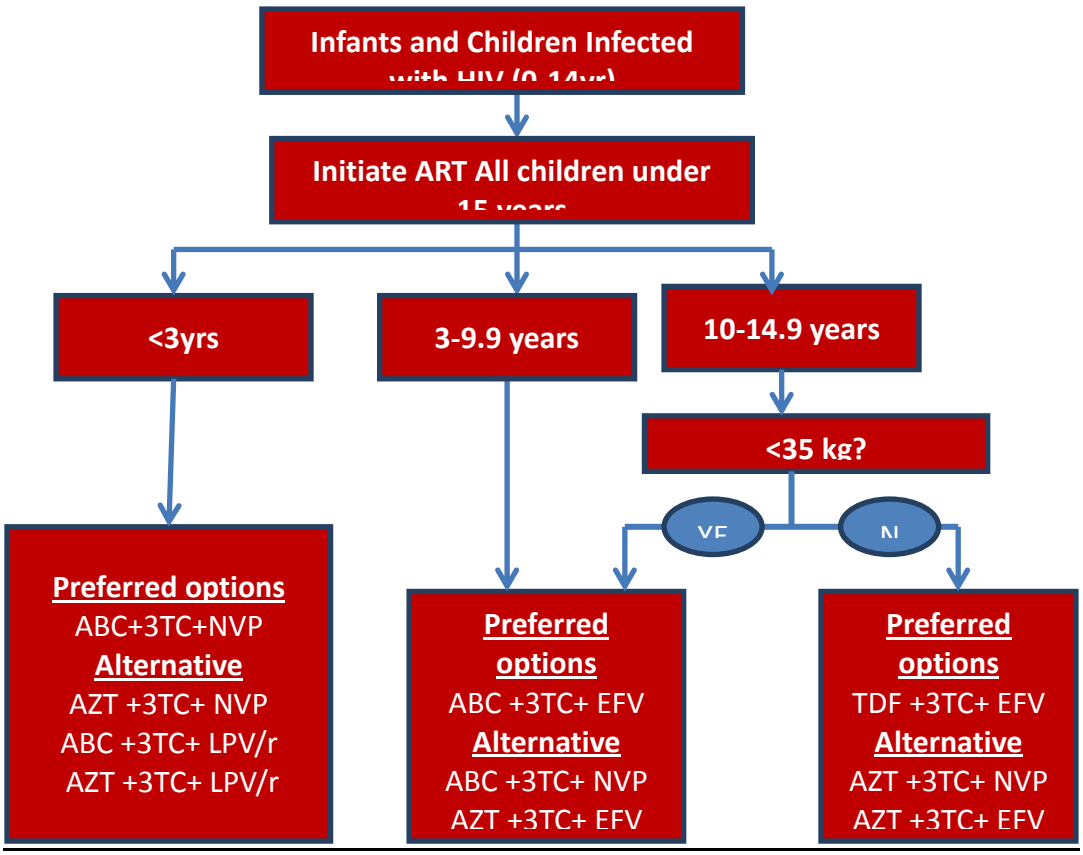
6-ART in Children

- When to Initiate ART in Children:
  TREAT ALL CHILDREN UNDER 15 YEARS IRRESPECTIVE OF CD4 COUNT OR WHO CLINICAL STAGING.
  All children less than 15 years of age should be initiated on ART irrespective of CD count and WHO clinical staging. HIV modeling data shows that 146,538 (83%) of the 176,948 children currently living with HIV in Uganda will be eligible for ART based on the revised WHO guidelines. However due to programmatic reasons which include; low CD4 access (41%) CD4 among children and challenges of staging children which would lead to eligible

children being missed, the paediatric HIV technical working group therefore recommended treatment of all children.

- To ensure adherence to treatment and retention in HIV care;
  - The program will ensure continuously supply of ARV's.
  - Programs for psychosocial support and adherence will be instituted.
  - Children older than 10 years will have their HIV status disclosed by care giver with support of counselors.

ARV REGIMENS- 1ST LINE



- **Phase out D4T use in Children**
  D4T use in children will be phased out and children on D4T will be transitioned to AZT based regimens.

2ND LINE ARV'S FOR CHILDREN

1st Line regimen	2nd line regimen
ABC+3TC+NVP ABC+3TC+EFV	AZT+3TC+LPV/r
ABC+3TC+LPV/r	AZT+3TC+(EFV or NVP)
AZT+3TC+LPV/r	ABC+3TC+(EFV or NVP)
AZT+3TC+NVP AZT+3TC+EFV	ABC+3TC+LPV/r
TDF+3TC+EFV TDF+3TC+NVP	AZT+3TC+ATV/R

7- ART in Adolescents

Introduction

With the help of antiretroviral therapy, increasing numbers of children with vertical transmission of HIV are growing to adolescence and adulthood. HIV-infected adolescents include long-term survivors of mother-to-child transmission, those infected through sexual abuse occurring in childhood and those who contracted the disease during adolescence through sexual relationships. This is a heterogeneous group including those who are in school, out of school, heads of household, orphans and adolescents under the care of adult guardians. Some know their HIV sero-status while others are not yet disclosed to. Some of them are in long term relationships.

This patient population is the only category with increasing HIV related deaths which areprimarily due to poor prioritization of adolescentsin national HIV plans, inadequate provision of accessible and acceptable HIV testingand counseling (HTC) and treatment services and lack of support for adolescents to remain in care andadhere to antiretroviral therapy (ART). Therefore inorder to protect this special group, health care providers need to commit time and effort to making adolescent services visible, flexible, affordable, confidential, culturally appropriate and universally available. The ART programmes in this era need to look beyond initiating patients on antiretroviral therapy, but they also need to look at issues regarding adherence to long-term therapy while preventing early treatment failure, and secondary transmission to uninfected partners.

Definitions

An adolescent is that person aged between 10-19years (WHO definition) while a young person is that aged between 10-24 years. There are three stages of adolescent development: Early adolescence 10-13 years; middle adolescence 14-16 years; and late adolescence 17-21 years. Adolescents are a unique group of people with special needs and it is a critical period which is characterized by rapid physical, emotional, cognitive and social changes.

Stages of Adolescent development:			
	Early Adolescence (10-13)	***Mid Adolescence (14-16)***	***Late Adolescence (17-21+)***
Physical	Sex drive begins. Rapid physical change	Maturation complete. Sex drive surges	Maturation complete
Social	Peer pressure. Separation from parents begins.	Peer group sets standards. Peak conflict with parents.	Close friendships. Intimacy. Beginning of rapprochement with parents
Psychological	Concrete thinking. Poor future orientation. Narcissism Body image	Focus on identity. Omnipotence Questioning mores. Introspection	Focus on role in society. Idealism. Future oriented. Refinement of values
Sexual	Interest usually exceeds activity	Increasing sexual behaviorexperimentation	Orientation consolidates

Special issues of HIV infected adolescents

These include; access to HIV counseling and testing (HTC) services , linkage to care, adherence, dealing with disclosure, discrimination and isolation; high risk behaviors such as early and unwanted pregnancy,involvement in commercial sex workers, men who have sex with men, transgender issuesand drug and alcohol abuse.

At the same time, there are two groups of adolescents living with HIV, those infected perinatally and those who acquire HIV during adolescence, often have different, if overlapping, needs and challenges. Some of these needs and challenges include transitioning of HIV care, and specific psychosocial needs.

Linkage to Care and Youth Friendly Services

The care of adolescents and young people with HIV needs to be driven by low cost and innovative approaches that contribute to attracting this group to access HTC services, enroll into care, and retaining them once they have made contact with the health services. It is therefore recommended that HTC with linkage to prevention, care and treatment be accessible to all adolescents with special focus on key populations (commercial sex workers, men who have sex with men, transgender issues and drug and alcohol abuse).

High quality of care must be assured, which includes:

- Non-judgmental attitudes by service providers regardless of their own beliefs and values
- Sensitization to issues of stigma, fear and discrimination
- There is need to redress the power imbalance that exists between health care providers and patients. While providing sexual and reproductive health and HIV services to the adolescents there is need to have the skills to respond to HIV related stigma and discrimination to encourage testing and disclosure, and to the desire of young people living with HIV to have children. Adolescents prefer to be seen by the same providers for reasons of trust and confidentiality, both of which are essential for the provision of comprehensive care.
- They also prefer health care settings that are oriented to their age group and providers who are attuned to their needs .The state of the ART for adolescent care is a 'one-stop shop', multidisciplinary model that integrates primary care with HIV, mental health, prevention, and case management services.

It is possible to create a provider team within the existing service delivery structures that understands adolescents, and wants to work with them. Availability of flexible appointments that do not conflict with school or work, attention to payment barriers, and walk-in opportunities for youth (who may not plan ahead) can facilitate adolescents' participation in health services.

Legal Issues

Health workers need to understand that young people have their right to health care, including testing for HIV. Health workers also need to understand the law of the land regarding age of consent, and age of consensual marriage, and be prepared to work with the social service to support the young people. For adolescents under 18 years, the testing and counseling services need to consider the best interest of the child as well as appropriate referrals to child protection

HIV care and treatmentadherence

Adolescents living with HIV are composed of 2 categories; the long term survivors of vertical transmission (on treatment or slow progressors) and those that are horizontally infected either through sexual activity or other means like injecting drugs. For the HIVmedication to be effective, it requires strict adherence to prevent the emergence of resistant HIV. When considering prescribing options for adolescents, health workers should provide the simplest and most efficacious regimens as well as provide psychosocial support.

It is therefore recommended that the health workers should be trained in basic HIV management and on how to work with adolescents in order to improve adherence to treatment as well as improve retention in care.

Psychosocial Issues

Understanding adolescent development is crucial for viewing the adolescent as a health care client and participant in treatment. In addition to the physical changes of puberty, adolescence consists of a series of cognitive, emotional and psychosocial developmental phases.

The five major psychosocial issues include:

Being informed of HIV status

Adolescents living with HIV are composed of 2 categories; the long term survivors of vertical transmission (on treatment or slow progressors) and those that are horizontally infected either through sexual activity or other means like injecting drugs. HTC is essential in achieving universal access to HIV prevention, care and treatment; therefore, it's important for adolescents to know their HIV status. Some adolescents (e.g. vertically infected) may not be aware of their HIV status even when they are on treatment.

Therefore it is important for all adolescents to know their HIV status and by helping them cope with their HIV infection, it is necessary to simultaneously instill hope and provide support for the challenging years ahead. They may have difficulty comprehending the concepts of disease latency and asymptomatic infection. Adolescents without apparent symptoms must learn to strike a balance between unhealthy denial of their condition and morbid preoccupation. Individual counseling should be offered to those adolescents with specific issues that are identified by the health caregivers. Age specific psychosocial support (peer support groups) networks should be formed to help in the reduction in stigma, coping with the infection, and having hope for the future.

However access to HTC by adolescents has generally been low; therefore in order to improve, the HIV-testing programs should address issues that increase uptake like creating demand for the service through the social media, sports activities, making services adolescent / youth friendly, address age of consent andalso focus on access by the key populations (commercial sex workers, men who have sex with men, transgender people and drug and alcohol abuse). In addition to primary care sites, venues that should consider offering routine HIV counseling and testing include; mobile units, school-based health clinics, drug treatment facilities, and family planning programs. Services need to be youth-friendly, flexible, free, or low cost, and help overcome barriers such as transportation. Young people need special help with the implications of partner disclosure.

Health providers should establish the momentum for youth-sensitive follow-up, including treatment and counseling:

- To provide basic HIV information,
- Assess risk and obtaining consent during the pre-test counseling visit,
- Promote preventive healthy behaviors, assess substance use and discuss family planning issues.

The counseling session is an invaluable opportunity to educate teenagers about condom use and safer sex, whether or not testing occurs. Effective HIV counseling for adolescents should be culturally sensitive and tailored to the developmental needs of adolescents. Youth considered potentially self-destructive or impulsive require careful assessment before testing. Counseling adolescents poses particular challenges, for example special sensitivity is required to address their level of sexual and emotional development. Effort should also be put on ensuring that adolescents return for a follow-up visit when they receive their test results, special effort such as telephone/SMS reminders or provision of transport reimbursement.

Beyond providing basic information, health facilities should use interventions that increase self-esteem, individual competencies and psycho-social skills. They should also incorporate a peer-Support model (involvement of peers), and take advantage of adolescents' inherent abilities to diffuse the information and skills they acquire into the community at-large. The HTC policy recommended age of assent for HIV testing as 12 years; however the authorities should bear in mind that children have a right to enjoy the highest standard of health and should not be deprived of their rights to access these services.

Disclosure and partner notification

As children with perinatally acquired infection grow into adolescents, it is of paramount importance that health providers begin the process of supporting the parents / caregivers to disclose their HIV status to them if they have not already been informed of their diagnosis. However for adolescents who know their status, they should be counseled about the potential health benefits and risks of disclosure of their HIV status to others and empowered and supported to determine when, how and whom to disclose. This is essential if the adolescent is to become a partner in the therapeutic alliance. It helps to bring the adolescent to terms with their disease condition, promote adherence, increase risk reduction for reinfection, and decrease treatment failure. Even for adolescents who have acquired HIV through sexual encounter and other means, many times they may not initially be informed of their status, and the disclosure process takes long. In both situations, it is preferable that someone who is emotionally close to the adolescent makes the first move to disclose, and this should be done with the assistance of a qualified counselor.

A major initial hurdle confronting HIV-positive adolescents is deciding when and to whom they should disclose their status. Although the involvement of a supportive adult (preferably a parent) is ideal, many youth fear losing the love of their parent or hurting them.

Disclosure becomes a particularly salient issue with advancing disease because it is difficult to conceal medications from the people with whom one lives. Disclosure to sexual partners is ethically compelling but complicated.

- The aim should be to ensure that HIV-positive adolescents inform any sexual partners and always engage in safe sex (i.e. consistent, correct condom use).
- Disclosure and partner notification should therefore be well planned.
- Health workers are encouraged to help the adolescent to 'play out the scenario' and offer to participate in the disclosure process.

A new compelling phenomenon among HIV-infected adolescents is the growing desire to have children of their own, in order to 'propagate and pass on their genes' and often they will not disclose to their partners for fear of rejection. When adolescents become pregnant they must be facilitated to join the PMTCT program as well as the family support groups.

Mental illness and substance abuse

Mental illness and substance abuse are frequently seen co-morbidities for HIV-positive adolescents, and need to be identified early because failure to identify and address these issues will hobble a patient's ability to cope with his or her disease. Furthermore, adherence to antiretroviral treatment is likely to be problematic. Mental health practitioners should ideally be part of the clinical team and should intervene as needed with such therapies as medication and individual and peer group support. In any case every effort should be made to identify and refer patients who need specialized care.

Age transitions

Health workers should support the transition of the HIV infected patient from pediatric to adolescent services, and finally to adult care programs. The adolescents require programs that address their specific needs, ranging from psychosocial to infrastructural needs were feasible. They face the concurrent challenges of health care maintenance, medication adherence, and illness within the context of maturing sexuality and establishing an independent life.

Prevention and community involvement

For HIV-infected adolescents and youth, the term 'prevention' must be looked at from the broad aspect of preventing early and unwanted pregnancies; preventing sexually transmitted infections; and preventing the development of a resistant viral strain while on treatment. In addition, 'positive prevention' should be encouraged to ensure that the adolescent does not become a driver of the HIV epidemic. Other basic preventive measures should also be part of the holistic care package, including provision of clean water and insecticide-treated mosquito nets. A comprehensive prevention strategy requires multiple levels that target young people's various psychosocial and health care needs. The range of prevention can be briefly summarized as "ABC": abstain, be faithful, and use condoms. Although each of these steps is important, none can stand alone or is perfect for all adolescents all of the time. We recommend the continued use of the abstinence and behavioral change for the youth strategy (ABY) for the adolescents and young people.

Community based approach is critical for programs focusing on HIV in young people. It is essential for raising awareness regarding HIV care, treatment and prevention services among at-risk youth, and their providers. Given that most adolescents living with HIV are unaware of their infection, linkages with agencies serving high-risk youth are crucial for the success of facility based services. These connections are not by themselves sufficient to identify HIV-positive youth and

bring them into care, however. Social marketing campaigns that span the continuum from HIV prevention through testing and care can make a major contribution .In addition, using adolescents and youth as peer educators and distributors for the condoms makes it more acceptable for their peers.

8-Second Line: What ARV Regimen to Switch to

Second Line ART in adults consists of 2 NRTI and a ritonavir boosted PI. The following sequence of NRTI options is recommended:

- After failure on TDF + 3TC , use AZT+3TC
- After failure on AZT+3TC, use TDF + 3TC
- Use of backbone NRTI as FDC recommended
- Heat stable FDC of ATV/r and LPV/r are the preferred boosted PI options for 2nd Line

9-Third Line ART

Failure to both the first line and secondline ART is relatively uncommon in new ART programmes but in mature ART programmes, some cases of failure to both these regimens have been documented. The treatment failure may arise from poor adherence to effective ART, adherence to ineffective regimens as in cases of infection with a primarily ART resistant HIV or in cases where resistance to treatment emerges on treatment based on unique characteristics of the infecting virus. Ideally, ART switch for secondline failure ought to be guided by results or ART-resistance testing, which should always be interpreted in combination with the knowledge of previous firstline ART resistance mutations which could be archived. In absence of ART-resistance testing, third Line regimens should include new drugs with minimal risk of cross resistance to previously used regimens, such as integrase inhibitors, PIs and second generation NNRTIs

Modifiable factors e.g. poor adherence or drug interaction should be addressed before effecting the switch to this salvage / thirdline ART.

The recommended regimen for 3rd line is Darunavir+Raltegravir+2NRTI

Patients on a failing second line regimen with no new ARV options should continue with a tolerated regimen

10-Definitions of clinical, immunological and virological failure for the decision to switch ART regimens

a) Clinical Failure

Adults and adolescents: New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4) in a patient who has been on effective treatment for at least 6 months.

Children: New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 with exception of TB) in a patient who has been on effective treatment for at least 6 months.

Note: i) In clinical failure, take caution that the condition is differentiated from Immune Reconstitution Inflammatory Syndrome (IRIS) occurring after initiating ART

ii) For adults, certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure.

b) Immunological Failure

Adults and adolescents: CD4 count falls to the baseline (or below) or Persistent CD4 levels below 100 cells/mm^3 after 6 months of initiation of treatment without concomitant or recent infection to cause a transient decline in the CD4 cell count.

Children: Younger than 5 years – Persistent CD4 levels below 200 cells/mm or <10% after 6 months of initiation of treatment; Older than 5 years – Persistent CD4 levels below 100 cells/mm^3after 6 months of initiation of treatment.

Note: Clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure. A better marker is viral load determination.

c) Virological Failure

Virological failure will be defined as two consecutive DBS viral loads above 5000 copies/ml at least 6 months apart. Subsequent repeat plasma viral load above 1000 copies/ml will be confirmatory of viological failure.

Note: i) An individual must have been taking ART for at least 6 months before it can be determined that a regimen has failed.

ii) An intervention to support adherence must have been conducted within the intervening period.

11-Monitoring ART Response and Diagnosis of Treatment Failure

Viral load is recommended as the preferred monitoring approach to diagnose and confirm ARV treatment failure. The first viral load should be done at 6 months of initiation of therapy and every 12 months thereafter in both adults and children.

CD4 count will be primarily for determining eligibility for initiation on ART for adult PLHIV, not for routine monitoring of ART response.

If viral load is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure.

12-Interventions to Optimize Adherence

Mobile phone text messaging is recommended as a reminder tool for promoting adherence to ART as part of a package of adherence interventions.

13-Service Integration and Linkage

In lifelong treatment for pregnant mothers, ART should be initiated and maintained in eligible pregnant and breastfeeding mothers and in infants at maternal and child health care settings with linkage and referral to ongoing HIV care and ART 18 months after delivery.

In HIV/TB co-management, TB treatment may be provided for individuals living with HIV in HIV care settings where TB diagnosis has also been made.

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